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DRUGS AND DRIVING: A SELECTED BIBLIOGRAPHY. SUPPLEMENT THREE

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16. Abstract

This report presents a bibliography of literature dealing primarily with the relationship of drug use (other than alcohol alone) and highway safety. This volume is the fourth of a series of annotated bibliographies designed to provide ready access to archival, technical, and popular publications. This supplement updates previous bibliographic reports and continues coverage of research areas that support the development and application of methods to study the drug and driving problem. This report provides a detailed description of the scope and method of the literature search and review effort that resulted in this compilation.

The bibliography consists of four appendices, including a Topical Index, an Author Index, a Title Index, and an Abstract Index, which contains approximately six hundred abstracts of the selected publications. A revised topical index provides access to abstracts according to type of publication, area of drug and driving research, methods applied in research on drugs and highway safety, drugs and classes of drugs. Within the topical index, drugs are cross-indexed by generic and trade names. A drug classification scheme is provided.

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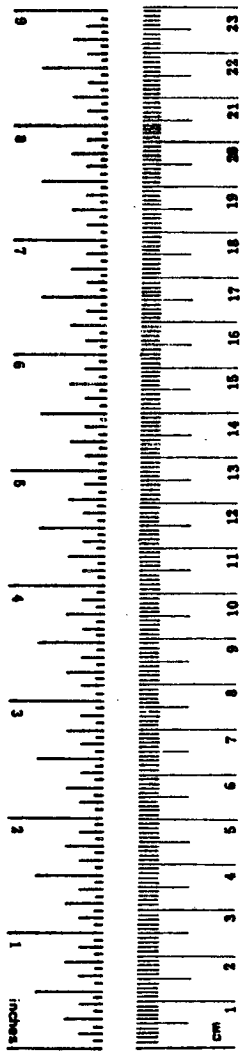
METRIC CONVERSION FACTORS

Approximate Conversions to Metric Measures

Symbol	When You Know	Multiply by	To Find	Symbol
		LENGTH		
in	inches	*2.5	centimeters	cm
ft	feet	30	centimeters	cm
yd	yards	0.9	meters	m
mi	miles	1.6	kilometers	km
		AREA		
in^2	square inches	6.5	square centimeters	cm^2
ft^2	square feet	0.09	square meters	m^2
yd^2	square yards	0.8	square meters	m^2
mi^2	square miles	2.6	square kilometers	km^2
	acres	0.4	hectares	ha
		MASS (weight)		
oz	ounces	28	grams	g
lb	pounds	0.45	kilograms	kg
	short tons (2000 lb)	0.9	tonnes	t
		VOLUME		
tsp	teaspoons	5	milliliters	ml
Tbsp	tablespoons	15	milliliters	ml
fl oz	fluid ounces	30	milliliters	ml
c	cups	0.24	liters	l
pt	pints	0.47	liters	l
qt	quarts	0.96	liters	l
gal	gallons	3.8	liters	l
ft^3	cubic feet	0.03	cubic meters	m^3
yd^3	cubic yards	0.76	cubic meters	m^3
		TEMPERATURE (exact)		
°F	Fahrenheit temperature	5/9 (after subtracting 32)	Celsius temperature	°C

*1 in = 2.54 (exactly). For other exact conversions and more detailed tables, see NBS Misc. Publ. 286, Units of Weights and Measures, Price $2.25, SD Catalog No. C13.10:286.



Approximate Conversions from Metric Measures

Symbol	When You Know	Multiply by	To Find	Symbol
		LENGTH		
mm	millimeters	0.04	inches	in
cm	centimeters	0.4	inches	in
m	meters	3.3	feet	ft
m	meters	1.1	yards	yd
km	kilometers	0.6	miles	mi
		AREA		
cm^2	square centimeters	0.16	square inches	in^2
m^2	square meters	1.2	square yards	yd^2
km^2	square kilometers	0.4	square miles	mi^2
ha	hectares (10,000 m^2)	2.5	acres	
		MASS (weight)		
g	grams	0.035	ounces	oz
kg	kilograms	2.2	pounds	lb
t	tonnes (1000 kg)	1.1	short tons	
		VOLUME		
ml	milliliters	0.03	fluid ounces	fl oz
l	liters	2.1	pints	pt
l	liters	1.06	quarts	qt
l	liters	0.26	gallons	gal
m^3	cubic meters	35	cubic feet	ft^3
m^3	cubic meters	1.3	cubic yards	yd^3
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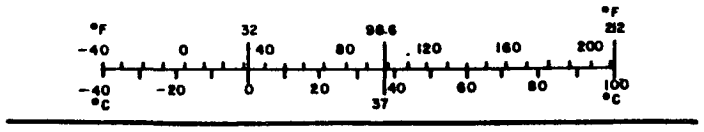

ACKNOWLEDGEMENT

This report results from efforts by many persons. It continues a series of bibliographic reports devoted to literature pertaining to drugs and highway safety.

The basic design of these reports was developed by Kent B. Joscelyn, J.D., and Roger P. Maickel, Ph.D. Volumes supplementing the parent bibliography both update the collection of literature abstracts and expand the scope of specific topics covered. Mr. Joscelyn guided the present study effort and the production of this report.

The introductory report contained in this bibliographic supplement was prepared by Alan C. Donelson, Ph.D., who also supervised the literature search, document collection, review, abstracting, and indexing described in this report. Dr. Donelson also extensively revised the topical index contained in this volume, in particular, the indexing and classifying of drugs.

Other staff members of the Policy Analysis Division were instrumental in preparing and producing this volume.

Mary B. Veldkamp, B.A., A.M.L.S., a medical librarian specialist, conducted manual and computer-assisted searches of the literature and collected documents for review. She also prepared, edited, and indexed the abstracts contained in this bibliography. Without her dedicated efforts and her ability to sift through and collate literature relevant to drugs and highway safety, this report would never have been.

Lawrence D. Segel, B.A., developed the programs that created the computer-based bibliographic files that allowed production of this report. Without his contribution, the processing and presenting of the vast amounts of collected material would have been impossible. He used proprietary programs available through the Michigan Terminal System at The University of Michigan, including TEXTEDIT, developed by Daniel J. Fox, Manager of Systems and Programming and Assistant Director of the Statistical Research Laboratory. These programs, when fully applied, offer an opportunity to access bibliographic files and to conduct searches for topics of special interest. The literature base now includes the material contained in all volumes of this series.

Jerry S. Vidis, B.S. (Pharmacy), M.S., greatly assisted in several areas of effort. He participated in the design and development of drug indices, identifying alternative drug names and classifying substances mentioned in the literature. Mr. Vidis also made a key contribution in the final production of the report. He coordinated the application of the TEXTEDIT program and the computerized typesetting capability of the Wayne State University Computer Center. The format of the camera-ready copy was produced by computer and then printed on a Xerox 9700 page printer.

Other HSRI personnel also made important contributions. Anne L. VanDerworp served as Word Processing Supervisor/Editor. Doris L. Dunger of the Word Processing staff entered drafts of report text into computer files. The clerical staff of the Policy Analysis Division under the supervision of Janet C. Peters also assisted in the production of this report.

We thank all who contributed.

Kent B. Joscelyn
Principal Investigator

Alan C. Donelson
Principal Investigator

PREFACE

This report presents an annotated bibliography of literature dealing primarily with the relationship between drug use (other than alcohol alone) and highway safety. This report was prepared by the Policy Analysis Division of The University of Michigan Highway Safety Research Institute (HSRI) for the National Highway Traffic Safety Administration as part of a larger research program on drugs and driving. A reader interested in the subject area will find other reports produced under the research program of value.

This report was prepared under contract number DOT-HS-7-01530, entitled "Drug Research Methodology." Under this same contract, a series of workshops on methodological issues in research on drugs and highways safety was conducted. The workshops addressed discrete--but interrelated--topics. The workshop reports are:

- Drug Research Methodology. Volume One. The Alcohol-Highway Safety Experience and Its Applicability to Other Drugs.
- Drug Research Methodology. Volume Two. The Identification of Drugs of Interest in Highway Safety.
- Drug Research Methodology. Volume Three. The Detection and Quantitation of Drugs of Interest in Body Fluids from Drivers.
- Drug Research Methodology. Volume Four. Epidemiology in Drugs and Highway Safety: The Study of Drug Use Among Drivers and Its Role in Traffic Crashes.
- Drug Research Methodology. Volume Five. Experimentation in Drugs and Highway Safety: The Study of Drug Effects on Skills Related to Driving.

Other reports prepared under the HSRI project include the previous volumes in this series of bibliographic volumes:

- Joscelyn, K.B., and Donelson, A.C. 1979. Drugs and Driving: A Selected Bibliography. Supplement One. National Highway Traffic Safety Administration technical report DOT-HS-803-879;
- Veldkamp, M.B.; Donelson, A.C.; and Joscelyn, K.B. 1980. Drugs and Driving: A Selected Bibliography. Supplement Two. National Highway Traffic Safety Administration contract no. DOT-HS-7-01530.

as well as a comprehensive review of past, ongoing, and planned efforts related to the study of and the response to the drug and driving problem:

- Joscelyn, K.B.; Donelson, A.C.; Jones, R.K.; McNair, J.W.; and Ruschmann, P.A. 1980. Drugs and Highway Safety 1980. National Highway Traffic Safety Administration contract no. DOT-HS-7-01530.

The latter report supported the preparation of a report to Congress by the U.S. Department of Transportation as requested in Section 212 of Title II of the Surface Transportation Act of 1978 (the Highway Safety Act of 1978). This section required the Secretary of Transportation to report to Congress concerning efforts to detect and prevent marijuana and other drug use by motor vehicle operators:

- U.S. Department of Transportation. 1980. Marijuana, Other Drugs and Their Relation to Highway Safety. A Report to Congress. National Highway Traffic Safety Administration report no. DOT-HS-805-229.

The reports cited above developed from and extended similar work done under earlier contracts from NHTSA:

- Joscelyn, K.B., and Maickel, R.P. 1977. Drugs and Driving: A Research Review. National Highway Traffic Safety Administration technical report DOT-HS-802-189.
- Joscelyn, K.B., and Maickel, R.P. 1977. Drugs and Driving: A Selected Bibliography. National Highway Traffic Safety Administration technical report DOT-HS-802-188.
- Joscelyn, K.B., and Maickel, R.P. eds. 1977. Report On An International Symposium on Drugs and Driving. National Highway Traffic Safety Administration technical report DOT-HS-802-187.
- Joscelyn, K.B.; Jones, R.K.; Maickel, R.P.; and Donelson, A.C. 1979. Drugs and Driving: Information Needs and Research Requirements. National Highway Traffic Safety Administration technical report DOT-HS-804-774.
- Jones, R.K., and Joscelyn, K.B. 1979. Alcohol and Highway Safety 1978: A Review of the State of Knowledge. National Highway Traffic Safety Administration technical report DOT-HS-803-714.
- Jones, R.K., and Joscelyn, K.B. 1979. Alcohol and Highway Safety 1978: A Review of the State of Knowledge. Summary Volume. National Highway Traffic Safety Administration technical report DOT-HS-803-764.
- Jones, R.K.; Joscelyn, K.B.; and McNair, J.W. 1979. Designing A Health/Legal System: A Manual. The University of Michigan Highway Safety Research Institute report no. UM-HSRI-79-55.

These reports provide entry points to the literature on alcohol, other drugs, and highway safety for readers desiring general reviews as well as information on specific topic areas. In addition, the reports can serve as sources for identifying both U.S. and foreign literature pertinent to each reader's needs.

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1.0 INTRODUCTION

This report presents an annotated bibliography of literature pertaining to drugs and highway safety. This volume is the fourth of a series of bibliographic reports, prepared for the U.S. Department of Transportation National Highway Traffic Safety Administration (NHTSA) and produced under contract DOT-HS-7-01530, entitled "Drug Research Methodology."

The report is intended as a resource document. Its purpose is to aid current efforts in determining the relationship of drugs and highway safety. The primary objective is the presentation of literature, not the analysis of research. The contents of the report are representative, but not inclusive, of the available literature. No claim of scientific validity of all the materials included is made.

1.1 Background

The extent to which the use of drugs by drivers contributes to highway safety problems is unknown (Joscelyn and Maickel 1977a; Willette 1977; Organisation for Economic Co-operation and Development 1978; Seppala, Linnoila, and Mattila 1979; Joscelyn, Jones, Maickel and Donelson 1979). Research has not established that any drug besides alcohol increases the probability of a traffic crash and associated losses. (The term "alcohol" is used here and throughout this report to mean ethyl alcohol, or ethanol.) Although present knowledge about drugs and driving is limited, available evidence indicates that drugs alone or in combination with alcohol or other drugs can impair driving skills and may increase the likelihood of traffic crashes. Further inquiry in this area is warranted. Among the factors that limit the state of knowledge are problems and issues in major areas of drug and driving research.

In November 1976, The University of Michigan Highway Safety Research Institute (HSRI) received a contract entitled "Drug Research Methodology" from the National Highway Traffic Safety Administration (NHTSA). Its general objectives were:

- to develop a greater understanding of the nature of the drug and driving problem on the basis of existing literature; and
- to define directions for future research with greater precision than has been done in the past NHTSA-sponsored efforts.

The project emphasized the generation of possible solutions to research issues in drugs and highway safety. The overall task is to identify and develop methods of research in the area of drugs and driving. Specific objectives of this study were:

- to identify problem areas that should be addressed in drug methodology;
- to identify alternative approaches to research that could be implemented with current technology; and

- to provide a listing of priority items of research that NHTSA could address in the foreseeable future.

To accomplish these objectives, an approach based on workshops was used to examine issues in four distinct but interrelated areas:

- The Identification of Drugs of Interest in Highway Safety;
- The Detection and Quantitation of Drugs of Interest in Body Fluids from Drivers;
- Epidemiology in Drugs and Highway Safety: The Study of Drug Use Among Drivers and Its Role in Traffic Crashes; and
- Experimentation in Drugs and Highway Safety: The Study of Drug Effects on Skills Related to Driving.

The division of topics had advantages as well as a possible disadvantage. For example, on one hand, a tighter focus on specific issues could be achieved. On the other hand, for some topics the wisdom and expertise of participants in other workshops might be lost. To offset this disadvantage, summaries of earlier workshops were mailed to invitees, and participants were later asked to comment on findings as well as issues in those areas.

These workshops, conducted in the spring and summer of 1978, were highly productive and brought to focus other issues in related areas of drugs and driving. In 1978, a contract modification called for additional workshops within the scope of the statement of work. In January 1978, a fifth workshop dealt with the alcohol and highway safety experience and its relation to the study and control of the drug and driving problem.

Under this contract also, a literature search and review task was carried out. Its purpose was twofold:

- to update the literature review performed for NHTSA under contract DOT-HS-4-00994 (Joscelyn and Maickel 1977a,b,c); and
- to satisfy informational needs in the design and conduct of workshops on methodological issues related to drugs and highway safety.

An earlier report produced under this contract (Joscelyn and Donelson 1979) was the first supplement to the parent bibliography. This report is the third supplement. A detailed account of the history of this bibliographic series follows.

1.2 History of the Bibliographic Series

This bibliography is the product of a continuing literature search conducted under the sponsorship of the U.S. Department of Transportation National Highway Traffic Safety Administration (NHTSA) as part of efforts under contracts DOT-HS-4-00994, DOT-HS-5-01217, and DOT-HS-7-01530.

Contract DOT-HS-4-00994, received by Indiana University (IU) from NHTSA in June 1974 and entitled "Drug/Driving Research Review and Symposium," reviewed the relationship between the use and abuse of drugs (other than alcohol alone) and highway safety. The principal investigators for this project, Kent B. Joscelyn and Roger P. Maickel, developed the basis from which later contracts efforts were derived.

The central objectives of the IU study may be summarized as follows:

- to ascertain and document on the basis of existing research literature the relationship between drug use (other than alcohol alone) and highway safety;
- to ascertain the "state of the art" of research in the field of drugs and highway safety; and
- to define areas in drugs and highway safety that require further research and suggest, insofar as present knowledge permits, possible drug/driving countermeasures that can be implemented in the immediate future.

The research plan to achieve these objectives contained several elements. A literature search identified published literature to be included in the study. An international symposium provided a forum to determine the state of the art in current knowledge and to develop directions for future research. Finally, a research review collated and synthesized the information obtained in the literature search and symposium. The project produced a series of reports (Joscelyn and Maickel 1977a,b,c), one of which is the parent volume of this bibliographic series, entitled "Drugs and Driving: A Selected Bibliography" (DOT-HS-802-188) and produced from the file of reports compiled under that contract.

Under Contract DOT-HS-5-01217, entitled "The State of Knowledge and Information Needs in Alcohol/Drugs and Highway Safety," the examination of drugs and highway safety was part of a larger project involving alcohol-related objectives. For example, two reports on the state of knowledge about alcohol and highway safety were prepared (Jones and Joscelyn 1979a,b). The general objectives of this project related to drugs (other than alcohol alone) were:

- to critically review, evaluate, and summarize existing knowledge concerning the drug/crash problem; and
- to recommend further research on the drug/crash problem that is a priority need and is likely to produce the most significant results.

In pursuing these objectives, the role of drugs in highway crashes was examined from the following topical standpoints:

- problem definition,
- measurement of agent effects,
- measurement of agent presence,
- relationship between agent presence and driver impairment, and
- countermeasures.

The critical review of existing information in these areas led to a summary of current knowledge and recommendations for future directions in research (Joscelyn et al. 1979). As part of the literature examination and review process, a literature search was performed. The document identification and collection activity was broad-based to (1) supplement the existing information base and (2) satisfy literature requirements in hitherto unsearched areas. This effort enlarged the hard copy file of documents developed under DOT-HS-4-00994.

The present contract, DOT-HS-7-01530 (described above in Section 1.1), extended literature search activities. A first supplement to the parent bibliography was produced, including literature identified under DOT-HS-5-01217 and DOT-HS-7-01530. The literature search and review task continued and led to the preparation of three additional supplements. This report is the third supplement to the parent volume.

1.3 Report Organization

This report consists of a series of introductory sections and a set of appendixes that index and reference publications relevant to drugs and highway safety.

Section 2.0 describes the technical approach to compiling the bibliography. The scope of topics and the criteria for selection of literature are defined.

Section 3.0 describes the format of the bibliography and the use of its indexes.

Appendix A is a detailed topical index that includes comprehensive subindexes for drugs discussed in the selected literature.

Appendixes B and C index the literature alphabetically by title and author(s), respectively.

Appendix D is the collection of abstracts of literature related to drugs and highway safety.

2.0 TECHNICAL APPROACH

The general approach to compiling this bibliographic supplement continues that used under contract DOT-HS-4-00994 to produce the parent volume (Joscelyn and Maickel 1977b). The literature search included both manual and computer-assisted techniques. The scope of recent search under the present contract broadened somewhat compared to the previous effort, so that additional sources were used.

The technical approach was designed to meet three main objectives:

- to maintain comprehensive files of literature specifically dealing with issues related to drugs and driving;
- to broaden the topical scope of the bibliography, including literature pertaining to specific research requirements and information needs in drugs and highway safety; and
- to provide access to the main bodies of relevant literature and especially to major area reviews.

Our primary concern has been to include all documents directly related to the general topic area of drugs and driving. The expanded scope of bibliographic coverage, however, proportionately increased the representation of support areas indirectly related to drugs and highway safety. The collected material is not all-inclusive of the available literature in these areas. However, an attempt was made to identify and collect major reviews of subtopical areas, and to provide ready access to peripheral research relevant to the central objectives of drugs and highway safety efforts. The identification and collection of other bibliographies and research compilations supported this objective.

Literature search activity encompassed technical and nontechnical sources as well as scientific literature bases. Consequently, the bibliography contains entries from the general literature and from the archival literature. As pointed out in the parent volume, caution must be exercised in using the bibliographic references. We remind the reader here to consult each original article of interest to determine its degree of relevance for special concerns, and to assess independently its scientific validity.

In the attempt to include research areas indirectly related to drugs and highway safety, several massively documented areas were touched upon. The sheer volume of available material required exclusionary criteria. The following sections present a detailed description of the literature search and selection process that led to the production of this bibliography.

2.1 Literature Search Scope and Document Selection

This section discusses the major topic areas in which literature was identified for inclusion in the bibliography. It defines the scope of the literature search in terms of specific research areas and describes criteria used to exclude documents of lesser importance.

The expansion in bibliographic topics is intended to better represent the multidisciplinary nature of the field. Epidemiology and experimentation are two general approaches used to define the drug and driving problem. Within these distinct research branches are specific research requirements, information needs, and methodological issues. There are also areas of related needs, due to the complementary nature of these research approaches. In the following subsection, a brief background discussion of drug and driving research is presented to develop the rationale of the literature search.

2.1.1 Research in the Field of Drugs and Highway Safety. As stated from the outset, the existence of a "drug-and-driving problem" remains a presumption. The role of drugs in traffic crash causation is still hypothetical and unconfirmed. Broadly speaking, determining the relationship between the use of drugs (other than alcohol) alone by drivers and highway safety requires systematic research. This research constitutes a many-faceted study of drug interactions with individual, vehicular, and environmental factors related to driving. A multidisciplinary approach must be engaged to define a problem so complex as this one. As an applied research field, drugs and highway safety involves the conjunction of pharmacology and pharmaco-behavioral sciences with highway safety research and its allied concerns.

The central objectives of research on drugs and highway safety concern problem definition and countermeasure development. The "state of the knowledge" is such that much basic and applied research is required to determine adequately the nature and extent of any drug-and-driving problem. If a problem is identified, additional research will be necessary to develop and to evaluate alternative approaches to deal with it. Ancillary research areas also contribute significantly in the overall endeavor. For example, research in these areas provides:

- information on which to base decisions regarding experimental design or countermeasure development;
- methodological support in exploratory research or in project evaluation; and
- technological support in the execution of experiments or surveys or in the implementation of countermeasures.

Because the capability of these areas for meeting requirements of drug and driving research warrants periodic assessment, we consider that access to this special literature is desirable and should be included.

Bodies of literature relevant to the information needs of drug and highway safety research can be outlined in terms of major research areas and supporting fields. In the following subsection, the scope of the literature search is defined.

2.1.2 Scope of Literature Search. To describe the literature search, literature in relevant areas of research is described below. Criteria for exclusion of documents are specified within each area.

2.1.2.1 Epidemiological Literature. The epidemiological approach to the study of drugs and driving includes both direct and indirect lines of research. The direct assessment of actual highway safety risk attributable to drug use by drivers involves field surveys. Methodological issues involve study design and methods for the analysis of drugs in body fluids from drivers. All literature directly related to the epidemiological study of drugs and driving was collected upon identification.

The indirect assessment of drug use by the general or special populations aids in the estimation of drug risk potential. Thus, literature pertaining to drug usage patterns was identified and collected. Toxicological studies that indicated drugs likely to be misused or used to excess were also deemed relevant. Reports describing drug user characteristics were considered important in the identification of target groups for countermeasure activity. Reports of this nature were excluded if the drugs or specific topic areas were deemed inappropriate to the indirect assessment of potential crash risk due to drug use by drivers.

Literature dealing with basic issues in epidemiologic research was also included in the bibliography if the documents were related to the study of drug-related problems in society. Reports describing general drug screening were collected as described below.

2.1.2.2 Experimental Literature. In the experimental approach to the study of drugs and driving, the nature and magnitude of drug effects on driving skills is measured under controlled conditions. Types of experiments range from those related to the actual driving task (for example, closed course driving tests) to simple tests of human performance (for example, choice reaction time). All identified studies involving the perceptual, sensory, and psychophysical evaluation of drug effects in man were included in the bibliography. While some reports did not mention driving per se, these were included on the basis of their similarity to experimental drug and driving research. Experimental investigations that attempt to characterize the nature of drug effects in man were also included if, in the judgment of the compiler, they might support the analysis of driver impairment by drugs. Reports dealing with drug effects in animals were generally excluded; exceptions included studies that contributed to the

understanding of the nature of drug effects in man, and reports that simultaneously dealt with drug effects in man, with the chemical analysis for drugs and metabolites of drugs in body fluids, or both.

Papers dealing with methodological issues in behavioral research were included on the basis of their relevance to measuring drug effects on human performance related to driving. Reviews of behavioral research methods were also collected.

2.1.2.3 Literature Concerning Drug Analysis. In the epidemiology of drugs and highway safety, analytical capability appears required for the detection, identification, and quantitation of drugs in body fluids from drivers. Depending on specific study objectives, a general drug screening system may be employed for the purpose of drug detection and preliminary identification. Confirmatory drug analysis methods usually permit quantitation. Specific screening techniques, also useful in the systematic approach to drug screening in body fluids, have an important place in drug and driving research.

All identified reports describing general drug screening methods were included in the bibliography. Documents dealing with specific screening methodology and confirmatory/quantitative methods were included (1) if the drugs were determined in biological specimens and (2) if the drugs were of possible interest in highway safety (see Joscelyn and Donelson 1980a; Joscelyn et al. 1980). Since the body of literature pertaining to drug analysis is massive and ever expanding, particular emphasis has been placed on the identification and collection of methodology reports in which drug concentrations were determined in human subjects.

Technical reviews of the "state of the art" in drug analysis are important to the area of countermeasure development. Evaluations of drug analytical methodology and intercomparisons of specific methods are useful in the design of research involving drug analysis. Therefore, reviews of analytical techniques and their application to drug analysis were included in the bibliography.

The epidemiological study of drug use among drivers may also require the use of independent laboratories for the purpose of drug analysis. Laboratory evaluation may become important in this regard. Papers dealing with quality control and proficiency testing were included as distinct topic areas.

2.1.2.4 Drug Concentration-Effect Literature. Meaningful interpretation of epidemiologic data on drug concentrations in accident- and nonaccident-involved drivers requires a substantial information base relating drug concentrations in body fluids to drug effects. Greatest interest in the significance of blood concentrations of drugs has been evident in the area of clinical pharmacology. Relatively few reports could be identified that correlated drug levels with performance of driving-related skills.

Most identified reports dealing with correlations between drug concentrations in body fluids and drug effects were included in the bibliography. Although some investigations used measures of drug effect unrelated to the driving task per se, other considerations contributed to their relevancy. These reports cited drug analysis methods adequate for the determination of therapeutic drug levels and reported drug blood concentrations resulting from common dosage levels. They also described the effects of therapeutic drugs that might increase a driver's risk of accident. Reports that inadequately described these aspects of clinical investigation were excluded from the bibliography.

2.1.2.5 Drug Concentration Literature. Data pertaining to the therapeutic or toxic blood concentrations of drugs in body fluids are important for the following reasons:

- approximate drug concentrations representing threshold ranges for therapeutic, impairing, and toxic effects are indicated;
- the sensitivity required of analytical methodology for the detection, identification, and quantitation of drugs in body fluids is specified prior to selection of drug analysis methods;
- the time course of pharmacokinetic phases of absorption, distribution, metabolism, and excretion is described as reflected in blood concentrations of parent drug and (some) metabolites; and
- the intersubject (interpatient) variability in drug blood concentrations after single- and/or multiple-dose administration is indicated.

The relevance of these data is found in the interpretation of drug concentration data from epidemiologic research; in designing and developing countermeasures; in the designing of drug screening methodology and the selection of adequate confirmatory and quantitative methods; and in assessing the use of drug concentration as a valid measure of drug effect.

Literature reports containing drug concentration data are diverse in nature and type. Compilations presenting comprehensive tabulations of drug concentration ranges were identified and collected. Less inclusive reports of a toxicological nature were also included in the bibliography. Reports of epidemiological findings including drug concentrations determined in nondriver groups were included only if the drugs themselves were of interest in highway safety.

Specific reports of human drug concentration data were also considered within the scope of this topic area. Often in the clinical or experimental context, drug concentrations in the blood would be determined following acute and chronic drug administration. In fact, many of these documents were included as a result of relevance to other areas. However, purely pharmacokinetic or drug metabolism studies involving drugs of interest were also identified and collected. Reports of specific analytical methods for these drugs would often involve determination of drug concentrations in body

fluids as a demonstration of method applicability. Many of this latter type of document were identified and collected in the search of literature pertaining to drug analysis. While these studies typically involved small groups of subjects, the preliminary indication of drug concentration variability among subjects was considered useful.

2.1.2.6 Miscellaneous Topic Areas. Several other topic areas were included within the scope of the literature search.

Socio-legal studies dealing with drug-related problems in society were included if a relation to the drugs and driving problem was evident. Literature pertaining to the development, evaluation, and implementation of drug countermeasures was identified and collected. Reports dealing with alcohol only were generally excluded. Exceptions included documents dealing with general countermeasure issues applicable also to other drugs.

General pharmacological effects of drugs whose use by drivers may increase traffic crash risk were also of interest. Abstracts in this bibliography include literature on drug interactions, studies of the sites and mechanisms of drug action, and reports dealing with the time-dependency of drug effects. As an information base for the interpretation of drug concentration data, reviews and individual reports that discuss factors influencing drug concentration-effect relationships were compiled. Articles and papers dealing with the basic pharmacology of drugs or drug classes were generally excluded.

The following section briefly outlines the literature search methods used in the compilation of this bibliography.

2.2 Literature Search Methods

The literature search procedure involved the following steps:

- identification;
- collection; and
- review.

Following these steps, documents were abstracted (if not already abstracted) and included in the bibliography according to selection criteria.

2.2.1 Manual Literature Search. On the basis of previous efforts in preparing previous volumes (Joscelyn and Maickel 1977b; Joscelyn and Donelson 1979; Veldkamp, Donelson, and Joscelyn 1980) a list of journals in which relevant documents had been frequently identified was compiled. Journal issues were searched for related material as they appeared. Journals pertaining to research areas newly included within the scope of the bibliography were searched according to the specific topic area.

Author indexes were used to identify recent reports by active researchers in the field of drugs and highway safety. Other bibliographic services (such as Highway Safety Literature) and selected abstract series (for example, CA Selects: Forensic Chemistry) proved useful in identifying relevant papers. Bibliographies from major reviews of topic areas within the scope of our literature source were also searched.

2.2.2 Computer-assisted Searching. Computer-based information retrieval services played an important role in identifying literature pertaining to drugs and driving. Two data bases were used in compiling this bibliography: Exerpta Medica and Medline. Exerpta Medica identifies articles from over 3,500 biomedical journals published throughout the world since 1974. It covers the entire field of human medicine and related disciplines, including forensic science, health economics, and public health. Medline, a data base maintained by the National Library of Medicine, contains references to over 500,000 citations from 3,000 biomedical journals published throughout the world since 1966.

Each data base was searched for papers concerned with three separate but related concepts of the general area of drugs and traffic safety. The primary area of interest was that of drug effects on psychomotor performance related to driving. Included under this concept were various aspects of drug effects on sensory, psychological, cognitive, and physiological parameters.

A second area of interest was that of the nature and extent of drug use and abuse, especially as it relates to driving, that is, the epidemiology of drug use and its consequences. Computer searching of this concept yielded papers on drug use in the general population as well as subpopulations such as automobile drivers, accident victims, psychiatric patients, and specific ethnic groups.

The third major area of interest was that of the presence and amount of drugs in body fluids, their behavior, and their analysis. This area included such topics as pharmacokinetics, drug interactions, drug monitoring, and analytical methods.

These computer searches were done by the staff of the Highway Safety Research Institute Information Center and the University of Michigan Medical Library. Periodic updates were done in order to provide continuing surveillance of recently published material.

2.2.3 Other Search Methods and Efforts. The topic area drugs and driving is one of the search topics of the HSRI Information Center. The Information Center staff broadly searches highway safety and other literature sources, continually adding selected publications to the extensive HSRI document collection. Upon identifying publications dealing with drugs and highway safety, the staff collects them or brings them to our attention for inclusion in the drug and driving bibliography.

In addition to the formal search methods described above, the staff is in personal communication with leading researchers in the field. Previously unidentified material and conference papers were frequently received during the course of the literature search by research staff and the HSRI Information Center.

No matter how thorough and extensive a literature search and review task becomes, cost, time, and other constraints influence the final work product. In the following section, limitations on the literature search are described and the effectiveness of criteria for document selection is briefly discussed.

2.3 Limitations of Literature Search and Document Selection Procedures

Joscelyn and Maickel (1977b) discussed general and specific limitations applying to the parent bibliography. Some limitations in the original work apply equally to succeeding volumes. The expanded search relative to the first bibliography has engendered other problems. This section describes factors that influenced the comprehensiveness and the quality of material included in this report. The discussion incorporates points made previously in Joscelyn and Maickel (1977c).

The omission of relevant material is inevitable. A number of factors war against the ideal of all-inclusiveness, and may lie well beyond the control of compilers. For example, the literature search task has occupied a subsidiary position relative to other contract objectives. Available resources--both staff time and funding level--limited the search and collection of literature. This nearly universal restriction was ameliorated by efficient planning and by the previous effort devoted to the parent bibliography. In many areas, including the general topic of drugs and driving, the literature search was a simple update of that comprehensive collection.

A fundamental limitation arises from the nature of the literature base pertaining to the field of drugs and highway safety. Drugs and highway safety is an applied field of loosely knit research areas. The determination of drug influence on traffic crash causation requires a systematic, multidisciplinary approach. "Drugs and driving," however, remains an isolated, special topic in journals serving the respective disciplines. Thus, the relevant documents to be identified are scattered throughout many journals and other literature sources. Multidisciplinary fields provide other pitfalls for broad-based literature searches. Although many research areas as such are reasonably well-defined, their relation to drugs and highway safety often is not. Many reports occupy a gray area of semi-relevance in which the personal biases of reviewers hold sway. Time and cost limits forced cursory searches of some relatively large research areas, for example, methodology in drug analysis and behavioral research.

The weaknesses and limitations of literature search methods exacerbate problems in dealing with the literature of drugs and highway safety. To search every likely publication for relevant material is impossible. The manual search is made manageable by selection of lists of journals and authors, abstract services, and other bibliographies. These tools aid in examining source material. The weaknesses and strengths of each index and list, however, are carried forth into the search. Titles and indexes included by document sources themselves may be incorrect; compilations of abstracts or bibliographies reflect the (unknown) biases of their compilers. The use of computer-assisted techniques is a valuable supplement to the literature search by manual means. The ability to elicit relevant output from information storage, search, and retrieval systems depends on the selection of key works or topic indicators as well as on the way a document was identified originally in the system. Some broad topics and specific issues appeared refractory to automated searches.

The fact that one can't find what isn't there also limits the apparent inclusivity of both bibliographies. The coverage of material published or issued within two years of the literature search is most likely incomplete. The publication process is itself lengthy; there is a significant "lag time" between the completion and reporting of research findings. The indexing and dissemination of abstracts as well as the entry of material into computer systems takes even longer since it follows initial publication. Foreign language publications share these--and exhibit other--problems. Mistranslations of titles and inaccurate or uninformative abstracts of article content combine with cost and availability factors in hindering the inclusion of foreign documents.

In addition to the directing influence of contract objectives, the personal biases of individual searchers and reviewers also affect the selection of documents. For example, a judgmental selection was necessary in peripheral research with massive documentation. Exclusionary criteria, described in section 2.1.2, aided in this process. Nevertheless, the distribution of reports within and among research areas reflects the impact of human value judgments.

The quality of selected documents is another matter requiring a cautionary note. A wide range of sources contributed the full spectrum of articles and reports: technical and nontechnical, general and archival, scientific and popular documents are included in this collection. Limitations of the literature base itself become important to the user, who must also evaluate the material.

In general, the published archival literature is viewed as factually accurate and reliable. This is due in part to a significant level of peer review during the editorial process. The rigor with which submissions are reviewed, however, varies. Data presentation, experimental design, and methodological accuracy may still be of

questionable validity. Statements made or conclusions drawn in discussion sections are usually those of the authors and are subject to bias and error. The technical literature includes reports published by government agencies, commercial organizations, private research foundations, and universities. Selections of this nature must be examined carefully since, for the most part, they represent literature that has not been subjected to any peer review process. For example, an independent assessment of methodology should always be made. The popular literature requires still more caution, since simplifications for the lay audience may blur critical distinctions, either intentionally or unwittingly. Articles written to persuade often downplay facts contrary to chosen sides of emotional issues. Controversial topics are present in drugs and driving, and their treatment in the popular literature deserves close inspection.

In summary, a general caveat included in the parent volume is repeated in this supplement. The reader should be careful to recognize that this selection does not represent an inclusive list of available literature, nor does it define the "state of the art" in drugs-and-driving research. It is believed, however, that the citations and accompanying abstracts present a useful and usable information base and form a valuable research collection.

2.4 Summary of Bibliographic Contents

This section has thus far detailed the technical approach used to compile material for this report. The scope and methods of literature search have been discussed with specific reference to topic areas in drugs and highway safety. This subsection focuses on what was found. A brief overview of the abstract collection presents information about the contents of this bibliography.

More than 600 abstracts comprise nine categories in Appendix D, Abstract Index. The single largest category is the D series (see section 3.1). This collection deals with the general topic of "drugs and driving" and with closely related subtopics. Although a detailed analysis of the available literature is not possible here, suggestive characteristics of the abstract collection are noted below.

The Topical Index in Appendix A indicates the relative representation of topical areas in the abstract collection. More experimental than epidemiological research is included. Reports of drug effects on human performance are most often included, but few involve actual vehicle-based driving tests. The sheer volume of experimental research is deceptive, however, since the number of drugs and variety of methods are great. Papers that concern drug detection and quantitation constitute another significant group of abstracts. Here, a bias toward gas chromatographic procedures is quite noticeable. The large number of citations that concern drug concentrations in body fluids derives

mainly from experimental and analytical reports. Relatively few abstracts are found in sections dealing with socio-legal and countermeasure topic areas, due more to the available literature than to efforts to collect it.

The primary purpose of this report is to identify and to present literature related to drugs and highway safety. Readers desiring a review and analysis of literature and a discussion of research in drugs and highway safety are here referred to other reports produced under Contracts DOT-HS-5-01217 and DOT-HS-7-01530 (Joscelyn et al. 1979; Joscelyn et al. 1980; Donelson et al. 1980; Joscelyn and Donelson 1980a,b,c,d). The use of this bibliography, its appendixes, and its collection of abstracts is covered in Section 3.0 and in Appendix A.

3.0 USE OF THE BIBLIOGRAPHY

This section presents in detail the format of the bibliography and the use of its indexes.

This bibliography is intended for use as a resource document for research in the field of drugs and highway safety. Its primary aims are as follows:

- to describe the literature base available to persons interested in drugs and highway safety;
- to provide a convenient means of access to the relevant literature in specific topic areas; and
- to give an accurate, informative indication of document contents to aid the user in selecting material for specific needs.

To facilitate use of this bibliography, the arrangement of bibliographic material is summarized in the next section. Subsequent sections deal separately with each appendix and describe the various indices.

3.1 Summary of Bibliography Contents

The bibliography consists of several indexes in addition to the primary content material. Four sections that comprise the bibliography are presented in the following appendixes:

- Appendix A: Topical Index
- Appendix B: Title Index
- Appendix C: Author Index
- Appendix D: Abstract Index

Each document entered into the bibliography is identified by a unique accession number. The accession number consists of letter-number combinations that sequence documents presented in Appendix D. In addition, an accession number allows preliminary identification of the general type of subject area of a document as well as the year of its publication. A sample number appears below.

UM-75-D0606

The first two letters (UM) signify that the selection was placed in the file by University of Michigan researchers. A previous designator used in the parent volume IU indicated researchers at Indiana University. All selections in this bibliographic supplement are from the University of Michigan effort and are prefaced by UM.

Immediately following the research designator, a pair of numbers (75) indicates the year of publication (1975). If the selection was presented at a conference, the year of presentation is given. If a document was both presented at a meeting and subsequently published, the publication date is used in the accession number and the selection is cited as published. Occasionally, both papers are included.

The letter preceding the last number set classifies the selection by category. Categories used for this supplement are as follows:

- A (bibliographies)
- B (books, collections of papers)
- C (countermeasures)
- D (selections dealing with drugs and driving or closely related topics)
- E (documents pertaining to epidemiology, the study of drug use in populations, and methodology)
- F (behavioral research methodology and studies of factors other than drugs that can impair driving skills)
- L (social and legal topics related to drug use and highway safety)
- M (methods and techniques for the analysis of body fluids for drugs)
- P (pharmacokinetics)

The last four digits simply represent the sequential assignment of documents to a given category. Appendix D lists the document abstracts alphabetically by category and sequentially by number within a category. Other appendixes list the accession number in whole or part to allow cross reference to Appendix D.

The following sections describe each index in more detail and provide suggestions for their use.

3.2 Topical Index (Appendix A)

A revised and expanded topical index has been developed to improve user access to document abstracts. To some extent, the changes reflect the reorganization of some topic areas under more general headings. However, the primary intent of the revision was to permit the inclusive citation of all selections in one or more topic areas or categories.

As in previous volumes, the index headings are not mutually exclusive. This has permitted multiple referencing for papers relevant to several topic areas. General categories have been included within the topical index. Used in combination with more specific headings (e.g., a drug name), selections more closely related to user needs may be quickly located. Detailed subheadings have been provided in those topical areas where a large number of selections have been included or where differentiation among closely related subtopics may be of value to the user.

Within the topical index are subindexes that list drug by name and by class. Section 8.0 is the Drug Name Subindex, which indexes drugs cited in the literature alphabetically by common, nonproprietary nomenclature, generic or chemical. Chemical names were used to identify a compound only when necessary. Also included in the Drug Name Subindex are common trade names of prescription and other therapeutic drugs, cross-referenced to generic names under which accession numbers are cited.

Section 9.0 is the Drug Class Subindex. Section 9.1 indexes literature pertaining generally to drug classes; section 9.2 lists members of drug classes indexed in Section 8.0. Finally, in section 9.3, a drug classification scheme is presented, incorporating chemical, pharmacological, and therapeutic classes in outline form. Members of each class are listed alphabetically under each heading.

The drug classification scheme was developed so that readers interested in literature pertaining to all members of a drug class could identify both which drugs of a class were indexed and which documents pertain to one or more members of a class. In general, only documents dealing substantively with a drug indexed in Section 8.0 are listed by accession number. Every effort was made to identify the most appropriate name for each drug or substance (hereafter referred to as the "preferred drug name") as well as placing each drug into the proper drug class or classes. Toward this end, many references were investigated and those found to be most useful are listed below.

Griffith, M.C., ed. 1979. USAN and the USP Dictionary of Drug Names. Rockville, Md.: United States Pharmacopeial Convention, Inc.

Kastrup, E.K., ed. 1980. Facts and Comparisons. St. Louis: Facts and Comparison, Inc.

Windholz, M., ed. 1976. The Merck Index. 9th ed. Rahway, N.J.: Merck and Co., Inc.

Goodman, L.S., and Gilman, A., eds. 1975.. The Pharmacological Basis of Therapeutics. 5th ed. New York: Macmillan Publishing Co., Inc.

Lowry, W.T., and Garriott, J.C. 1979. Forensic Toxicology: Controlled Substances and Dangerous Drugs. New York: Plenum Press.

Vinson, J.A., ed. 1979. Cannabinoid Analysis in Physiological Fluids. Washington, D.C.: American Chemical Society.

Reilly, M.J., ed. 1979. Hospital Formulary Service. Washington, D.C.: American Society of Hospital Pharmacists.

Remington's, Pharmaceutical Sciences. 1975. 5th ed. Easton, Pa.: Mack Publishing.

Wade, A., ed. 1977. Martindale's: The Extra Pharmacopeia. 27th ed. London: Pharmaceutical Press.

Modell, W., ed. 1979. Drugs in Current Use and New Drugs. New York: Springer Publishing

Lewis, A.J., ed. 1973. Modern Drug Encyclopedia and Therapeutic Index. 12th ed. New York: Dun-Donnelly Publishing.

Claus, E.P.; Tyler, V.E.; and Brady, L.R. 1979. Pharmacognosy. 6th ed. Philadelphia: Lea Febiger

When multiple names for a drug or substance were found, the preferred drug name was chosen based on information from the above references as to its accepted or official name. The preferred drug name was thus defined as:

a) the U.S. Adopted Name for a chemical or substance, if such a name had been assigned;
b) for substances that did not appear in the USAN dictionary, the other references were searched and the most frequently used name and spelling of that name was adopted; and
c) if no entry for a chemical was found in the reference, the spelling used by the author was adopted.

If a discrepancy existed between the author's spelling and the spelling for the preferred drug name found in the references, an additional entry was added to the Drug Name Subindex that shows the author's spelling and directs the reader to the preferred spelling.

An exception was made in the use of U.S. Adopted Names for drug products containing more than one active ingredient. These products are listed in the Drug Name Subindex by brand name and followed by the list of active ingredients, in parentheses.

Finally, to aid users that may have a brand name but not the preferred drug name (for drugs marketed in the U.S., this is the generic name), representative brand names for the more common drug products and for drug products referenced in the abstracted document by brand name have been included in the Drug Name Subindex. Note that brand names included in the subindex are not all-inclusive but are a sample of all possible brand names for the drug products cited in abstracted documents.

To aid in the identification of recent publications, all documents cited by accession number in the Topical Index include the last two digits of the year of publication.

The organization of the Topical Index is presented in outline form in the first pages of Appendix A. An explanation of each topical heading is provided. The type of documents indexed under each heading is described in a general and inclusive manner. Use of the drug and chemical indexes is further detailed.

3.3 Title Index (Appendix B)

All selections are listed alphabetically by title in Appendix B. Titles as originally published have been used. Foreign language titles are followed by an English translation in brackets. The abstract itself may be consulted to identify the original language. Associated with each title is the full accession number. The abstract of the document may be found by referring to Appendix D. (See below).

3.4 Author Index (Appendix C)

All names that appear as editors, authors, or compilers have been included in the Author Index. Editors and compilers have been identified by the abbreviations ed. and comp., respectively. The publications associated with each name are identified by accession number. All authors are listed regardless of their order of appearance on the original publication. The year of publication is also indicated.

3.5 Abstract Index (Appendix D)

Literature abstracts are presented in Appendix D. The general approach followed for abstract preparation is that outlined in "NHTSA Document Analysis Manual," Rev. Ed. (HS-820-085). Within space limitations and other constraints, the bibliographic effort has been responsive to requests for increased information content. The following paragraphs describe the format and abbreviations used in preparing the abstracts.

Each document is identified by an accession number located immediately above and to the right of the abstract. (Government documents are further identified by report numbers cited below each abstract.) Accession numbers are continued serially from previous volumes. Headnotes identifying the number of the first abstract on each page are provided to facilitate use of Appendix D.

The importance of full, accurate referencing is reflected in document citation. Full titles of articles and other documents have been provided, along with the initials and last names of each author. The journal name has been given in full. Volume and issue numbers, full paging, and date of publication have been included.

In accordance with the aims of the bibliography as a resource document, each abstract is intended to provide an accurate indication of document contents. The primary purpose of the abstract collection is to allow the user to make a preliminary selection of literature relevant to specific needs, eliminating from consideration selections whose main focus is not appropriate. As noted above, the informative capacity of this abstract collection has been maximized within space and time constraints. Inherent limitations in the bibliographic effort have prevented the preparation of informative abstracts consistent with the length and quality of some abstract services, such as the Highway Safety Literature System.

Also in previous volumes, author-prepared abstracts were used when consistent with the standards described above. Often a journal abstract was modified by HSRI staff to include more information. Abstracts were prepared only for those selections without an appropriate synopsis. Abstracts prepared by indexing or bibliographic services were used when author abstracts were not available, or when their use allowed the efficient presentation of more complete information.

In order to inform the reader as to the source of abstracts included in Appendix D, letter combinations signifying the various sources utilized in this bibliography are included in parentheses at the end of each abstract. The following designations are used:

- JA, JAM (journal abstract, journal abstract modified);
- AA, AAM (author abstract, author abstract modified);
- HSL, HSLM (abstract from Highway Safety Literature [HSL], modified abstract from HSL);
- EM, EMM (abstract from Exerpta Medica [EM], modified abstract from EM);
- CA, CAM (abstract from other computer data base [for example, Medline], modified abstract from computer data base); and
- HSRI (abstract prepared by HSRI staff).

Such designations as JA, AA, HSL, etc., identify abstracts used verbatim; the designations JAM, AAM, and HSLM indicate that some modification of the original abstract was made. Most often, additional material was included to increase the information content without altering the main structure of the abstract. If the preparation of an abstract resulted in a substantial revision of an abstract, the designation HSRI was used. Newly prepared abstracts were also given this latter designation.

Additional information regarding each selection is presented along with the abstract, including:

- the number of references cited in the publication;
- the number of pages, if not included in the citation;
- the language of the publication, if not English;
- the report number, if a technical or government publication; and
- a set of keywords that indicate where in the Topical Index the document was indexed.

3.6 Computerization of Drug and Driving Literature Base

The preparation, indexing, and compilation of abstracts for hundreds of documents collected over several years comprise a gargantuan task. The editing, correction, and (ultimately) the production of this bibliography were particularly suited for computerization. The University of Michigan Michigan Terminal System (MTS) and the availability of data base storage and text processing programs facilitated this process and allowed the efficient, reliable production of this bibliography.

Several programs from different sources at The University of Michigan were applied. Two data base management programs were used: TAXIR (developed by the university Computing Center staff) and DRUGIN (developed at HSRI for an unrelated project funded by the Motor Vehicle Manufacturers Association). These programs allow efficient storage and simple access to each bibliographic entry. Output from these programs is fed into

INDEX (developed by The University of Michigan Computing Center) and TEXTEDIT (a text processing program developed by The University of Michigan Statistical Research Laboratory).

When fully developed, the computerized drug and driving literature base will be accessible to persons interested in conducting their own computer searches on topics related to drugs and highway safety.

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DRUGS AND DRIVING:

A SELECTED BIBLIOGRAPHY

SUPPLEMENT THREE

APPENDIX A

TOPICAL INDEX

TOPICAL INDEX USAGE GUIDE

The organization of the topical index is presented below in outline form. Explanatory paragraphs are associated with each topical and subtopical heading. The purpose of this presentation is to define the scope of each heading in the topical index, and to facilitate the location of relevant documents.

1.0 REVIEWS AND COMPILATIONS

This section contains topic headings pertaining both to general and to specific research areas in drugs/highway safety. In addition, headings indicating certain types of documents are included. The selections for the most part do not report original research. Cited documents not strictly of a review nature do treat subject matter in a general and nonexperimental fashion. Collections of research reports and other compilations are cited under the appropriate category. These documents may also be cited under specific research areas elsewhere in the topical index.

1.1 Reviews of Drugs and Highway Safety

These selections deal directly with aspects of the drugs and driving problem. While not all treat the problem in a comprehensive fashion, most documents utilize findings from several research areas in discussing specific topics.

1.2 Research on the Use of Drugs

This section includes reviews of research done attempting to determine the prevalence of drug use and abuse in both the general population and the driving population as well as various subpopulations. Reviews of geographic and temporal patterns of drug use are also cited here.

1.3 Research on the Effects of Drugs

The study and characterization of drug effects are topic areas included under this heading. Two subtopical divisions differentiate between selections:

1.3.1 Reviews of Drugs or Classes of Drugs. Reviews of the biochemical, pharmacological, behavioral, and other effects of specific drugs or drug classes are included.

1.3.2 Reviews of the Relationships Between Drug Effects and Their Concentration in Body Fluids. The interpretation of drug levels in body fluids and the characterization of drug concentration-effect relationships are subjects of referenced documents. Selections of a general nature as well as reviews of specific drugs or drug classes are included.

1.4 Methodology in Drugs and Highway Safety

Selections reviewing the methodology of epidemiologic and experimental studies of drug use are included here. Issues and problems in methodology are discussed and specific methodologies evaluated, referenced according to the type of data collection used.

1.4.1 Methodology in Survey Research. Reviews of studies describing and evaluating the use of questionnaires, interviews, and examination of driving records to determine drug use and abuse are referenced.

1.4.2 Methodology in Behavioral Research. Documents under this heading pertain to the study of behavior related to driving or to the methodology used in the assessment of drug effects on human performance.

1.4.3 Methodology in Drug Analysis. This section includes reviews of studies using the most direct approach to assessing drug involvement in traffic crashes--determining the identity and amounts of drugs in driver body fluids--and the methodological issues involved. Technical reviews of specific analytical methods are referenced here.

1.5 Selected Reviews

Reviews not specifically related to the above subheadings are cited here. The primary subject matter of each selection is indicated in parentheses.

1.6 Compilations

Collections of research reports, monographs, and other unitary aggregations of material related to one or more research areas in drugs/highway safety are referenced. Conference proceedings are included under this heading.

2.0 EPIDEMIOLOGIC RESEARCH

Under this general heading, studies related to the incidence and distribution of drug use are cited, based on observation of the real world. Documents are cited under three subheadings according to the population or subgroup studied.

2.1 Studies of Drug Use Among Drivers and Its Consequences

Research studies directly pertaining to drug use in the driving population are cited. Documents are referenced under the three types of data collection used.

2.1.1 Analysis of Drivers' Body Fluids for Drugs. Cited here are studies directly determining the identity and amounts of drugs in driver body fluids. Studies involving drinking drivers, "driving under the influence" cases, accident-involved drivers, and fatally injured drivers are included.

2.1.2 Self-Reported Drug Use by Drivers. Investigations of self-reported drug use based on questionnaires and interviews are referenced. Studies of type or specific drug used and frequency of use are included.

2.1.3 Record-Based Surveys. Studies indirectly assessing the effects of certain types of drug use on driving performance by analysis of driving and arrest records of drug user groups are included.

2.2 Studies of Drug Use in Nondriving-Specific Populations

Referenced are studies of medical, nonmedical, and quasi-medical drug usage patterns among the general population.

2.2.1 National Surveys. Cited here are surveys of drug use on the national level in both the United States and in foreign countries, based on data gathered from such sources as household interviews, prescription sales, and arrest statistics.

2.2.2 Regional or Local Surveys. Surveys of drug use among subpopulations from specific geographical areas or with specific demographic characteristics are cited. Studies of street drug analysis programs and studies of drug use among university students and emergency room admissions are of the type of papers cited here.

2.3 Crash Investigation

Included here are studies of traffic accidents that investigate the causes or factors associated with crashes such as environment, behavioral patterns, vision, and vigilance.

3.0 EXPERIMENTAL RESEARCH

Under this general heading, all studies are included which involve the "laboratory approach" in investigating the effects of drug use. Two complementary subclassification schemes have been developed. First, drug studies are differentiated according to the number of drugs administered to experimental subjects. Second, the documents are cited under subheadings which specify the type of methodology or experimental test used to study drug effects. The drugs used in these studies are cited individually in Section 8.0, Drug Name Subindex.

The combined use of general and specific topic headings allows the user to locate directly those documents closely related to subjects of special concern. For example, psychological studies involving marijuana may be quickly identified by comparing accession numbers under the respective headings. Selections pertaining to this research area are indicated by matching accession numbers. Combined use of more general headings will locate certain types of experimental study, irrespective of the drugs employed.

Specific types of experimental study related to drug concentration-effect relationships as well as investigations involving animal research are also included in this section. Subheadings are described in greater detail below.

3.1 Studies of Drugs Administered Alone

Cited documents include those experiments involving the study of one drug, in addition to placebo. Reports which describe the effects of several drugs, but whose experimental design allowed the separate study of each are differentiated as follows:

3.1.1 Studies Comparing Different Drugs. Studies that examine the effects of drugs which have similar chemical structures and are in the same therapeutic class are cited.

3.1.2 Studies of Acute Doses. Investigations of the effects of a drug administered once to experimental subjects are cited. Studies involving both acute and chronic dose regimens are cited under each appropriate subheading. Dose-response studies, where single doses of increasing amounts of drugs are administered, are cross-referenced below.

3.1.3 Studies of Chronic Doses. Investigations in which the subjects are administered two or more serial doses of a drug are included. Chronic dosage studies involving the examination of drug effects following the first dose in a series are cited also as acute dosage studies.

3.1.4 Studies Relating Dose and Effects. Investigations which examine subject responses to two or more dosage levels of a drug (excluding placebo) are referenced.

3.1.5 Other Studies. In this category studies investigating the effects of undetermined dosages of single drugs are cited such as those to which some individuals are habitually or occupationally exposed. Examples include studies of the effects of carbon monoxide in professional drivers, effects of halothane and nitrous oxide in operating room personnel, and effects of smoking on auditory vigilance.

3.2 Studies of Two or More Drugs Administered Together ("Drug Interaction" Studies)

Investigations which examine the combined effects of two or more drugs are classified as the following:

3.2.1 Studies of Combined Effects of Drugs. Investigations are cited which deal specifically with the interactions of drugs administered in such a way as their separate effects overlap. Studies include those which attempt to describe the additive effects of drug combinations.

3.2.2 Other Studies. Miscellaneous reports dealing with drug combinations are included in this section. The interaction of conditions resulting from use (e.g., tolerance, enzyme induction) and the effects of specific compounds are topic cited under this heading.

3.3 Research on the Effects of Drugs or on Driving Performance Skills

Experimental studies involving drug effects in man are cited according to the methodology used or the general test methods employed. Special subheadings are described.

Also referenced under this heading are studies of various components of driving performance, categorized by the general test methods used to assess them.

3.3.1 Studies with Behavioral Methods Related to the Driving Task. The evaluation of drug effects on driving performance may be made utilizing the actual driving task or laboratory simulation. Three main subheadings have been used to classify relevant studies:

3.3.1.1 Tests on the Open Road. Studies in which subjects administered drugs were observed in actual driving situations are included.

3.3.1.2 Tests on Closed Driving Courses. Cited are studies in which experimental subjects drive a motor vehicle in a closed course or in an area devoid of actual traffic situations.

3.3.1.3 Tests on Driving Simulators. All studies are referenced which include a laboratory test, simple or complex, which is designed to replicate, at least in part, the actual driving task. Other tests related to driving skills are cited below.

3.3.2 Studies with Psychophysical Tests. Nearly all laboratory tests of human performance related to driving involve the participation of psychological (or mental) and physical (or somatic) functions. The relative significance of these various functions in a given test is often unclear. Therefore, a series of approximate classifications are used as described. Under this general heading, tests which involve perceptual elements in the measurement of motor or sensory performance specify the inclusion of a document. Those studies involving several different tests are cited under each appropriate subheading.

3.3.2.1 Tests of Psychomotor Skills. Investigations which employ tests of psychomotor behavior are cited. Simple and complex tests of reaction time, tests of balance and steadiness, tracking tasks other than driving simulation, and eye-hand coordination tasks are examples of experimental methods considered to be psychomotor tests.

3.3.2.2 Tests of Sensory Functions. Studies which use methods which measure sensory functions are included. The critical flicker fusion frequency test and tests of visual and audio acuity are examples of such methods.

3.3.3 Studies with Psychological Tests. Investigations are cited which employ tests which measure the effects of drugs on psychological functions. Tests of memory, learning, perception, mood, and mental performance are among those which qualify a document for this classification.

3.3.4 Studies with Physiological Tests. Investigations which include the measurement of physiological parameters are cited under this subheading. Galvanic skin response, heart rate, and electroencephalographic effects are specific examples.

3.3.5 Clinical Studies. Investigations are cited which study the effects of drugs in patient groups or which attempt to determine the clinical efficacy of drugs in patients. Those studies employing similar tests to those described above are cross-referenced accordingly.

3.3.6 Studies Including Self-Evaluation of Drug Effects by Test Subjects. Investigations which include self-evaluation of drug effects by experimental subjects are included. Subject ratings of the intensity or nature of a drug's effect, or the degree of performance impairment, are examples of the self-evaluation approach which classify documents under this subheading.

3.3.7 Factors Influencing the Effects of Drugs on Human Behavior. Cited here are studies on nondrug factors possibly influencing the effects of drugs on human behavior. Studies of variables possibly accounting for the wide range of response to drugs among individuals are referenced under the following categories.

3.3.7.1 Age. Studies of the influence of physiological, psychological, and pharmacokinetic correlates of age on drug effects are cited. Investigation of protein binding in the elderly is an example of the studies included.

3.3.7.2 Gender. Comparisons of drug effects in male and female subjects are cited. The possible influence on drug effects of differences in role perception, perceived social expectations, and physiology are discussed in studies cited here.

3.3.7.3 Personality. Cited here are studies attempting to determine how such personality traits as introversion and extroversion, anxiety, willingness to take risks, and artistic tendencies influence effects of drugs in individuals.

3.3.7.4 Other. Referenced are studies investigating the influence on drug effects of such variables as socioeconomic background of the subject, prior drug experience, social and physical setting of the drug experience, and physical characteristics of the drug.

3.4 Research on the Relationship Between Drug Effects and Their Concentration in Body Fluids

The need to quantify drug effects by means of objective, chemical measures, and the importance of data interpretation in field survey of drugs in drivers led to the inclusion of this section dealing with the topic of drug concentration-effect relationships. Documents are differentiated according to their relevance to drug effects on driving performance:

3.4.1 Studies of Skills Related to Driving. Cited are studies which attempt to correlate behavioral measures related to the driving task and drug levels in body fluids.

3.4.2 Clinical Studies. Studies are included which describe the efficacy of therapeutic drugs in terms of drug concentration in the blood or other body fluids.

3.5 Research Involving Animals

Generally, studies of drug effects in animals were excluded from this bibliography. Documents relevant to the nature of drug effects in man, or which report relevant research involving the incidental use of animals, are included under this subheading.

4.0 DETECTION, IDENTIFICATION, AND QUANTITATION OF DRUGS IN BIOLOGICAL SPECIMENS

This general heading includes those topic areas directly or indirectly related to the detection, isolation, identification, or quantitative determination of drugs (and metabolites) in biological liquids. Studies involving the development, evaluation, and application of drug analysis methods are specifically cited.

Main divisions within this general research area reflect whether the methodology has been applied to the screening of one or more drugs in unknown samples, or to the determination of specific drugs known to be present in solution. Within each major subheading, reports are distinguished by the type of techniques used to determine drug presence. Investigations pertaining to the evaluation of analytical methods and to the evaluation of laboratories engaged in drug analysis are cited under separate subheadings as described below.

4.1 General Methods of Screening for Drugs

Reports concerning the development or application of methodology designed to detect a wide range of drugs with diverse chemical structures are classified according to the following types of techniques:

4.1.1 Thin-Layer and Paper Chromatography. Methods which involve the separation of drugs by paper or thin-layer chromatographic techniques are referenced. Techniques used to confirm or quantitate results of the separation step may be other than paper or thin-layer chromatography.

4.1.2 Optical Techniques. Documents pertaining to methods primarily involving absorption spectrophotometry or spectrophotofluorometry are cited. Common techniques include ultraviolet, visible, and infrared absorption spectrometry, as well as fluorometric procedures.

4.1.3 Gas Chromatography. Methods involving vapor phase column chromatography are included under this heading. With the exception of gas chromatography, almost all of the referenced methods utilize columns containing a high-boiling, inert liquid (stationary phase) coated on a solid support--a technique called gas-liquid chromatography. A variety of detectors which can be used to increase sensitivity are also indexed here, including flame ionization, nitrogen-phosphorous, electron capture, and mass spectrometer detectors. The special instances in which a mass spectrometer is used as a gas chromatographic detector are cited in the following section.

4.1.4 Other Techniques. Methods which involve the application of an analytical technique to general drug screening, and which are not included in the above sections, are cited under this heading. Reports dealing with general drug screening by gas chromatograph-mass spectrometric and high-pressure-liquid-chromatographic techniques are included.

4.1.5 Screening Systems. Screening methods which employ two or more primary analytical techniques in general drug screening are referenced.

4.2 Specific Methods of Screening for Drugs

Articles describing methods developed for the specific analysis of individual drugs, small groups of drugs, therapeutic drug classes (e.g., anticonvulsive agents), or chemically-related drugs (e.g., barbiturates) are cited under this heading. The primary purpose of these methods is the detection and identification of specific drugs which may be present in body fluid samples. The differentiation of reports is similar to that used above for general screening methodology:

4.2.1 Thin-Layer and Paper Chromatography. See Section 4.1.1 for an explanation of the topic heading.

4.2.2 Optical Techniques. See Section 4.1.2 for an explanation of the topic heading.

4.2.3 Gas Chromatography. See Section 4.1.3 for an explanation of the topic heading.

4.2.4 Immunoassay. The immunochemical methods are characterized by their use of antibodies obtained from the antisera of animals injected with drug-attached antigens. Papers on the basic theory and techniques of the four most common techniques are referenced: free radical assay technique, enzyme multiplied immunoassay technique, hemagglutination inhibition, and flame ionization.

4.2.5 Other Techniques. Techniques not specifically included in the above section are included under this heading. Examples are mass fragmentography, differential pulse polarography, and "hybrid" methods using a combination of techniques such as high pressure liquid chromatography-mass spectrometry.

4.3 Methods for Confirmatory/Quantitative Drug Analysis

Included are articles describing analytical methods which are used to confirm the identity of drugs detected by other methods and/or which are used to quantitate specific drugs present in biological liquids. Documents are cited according to specific techniques, as follows:

4.3.1 Optical Techniques. See Section 4.1.2 for an explanation of the topic heading.

4.3.2 Gas Chromatography. See Section 4.1.3 for an explanation of the topic heading.

4.3.3 Gas Chromatography-Mass Spectrometry. Quantitative or confirmatory methods which utilize a gas chromatography-mass spectrometer (GC-MS) are referenced. Several GC-MS ionization modes, including electron-impact and chemical ionization techniques, may be represented.

4.3.4 Immunoassay. See 4.2.4 for an explanation of the topic heading.

4.3.5 Other Techniques. Confirmatory/quantitative methods not specifically included in the above sections are included under this heading.

4.4 Evaluation of Analytical Methods

Articles which deal with the evaluation of drug analytical methodology are cited in one of the two following categories:

4.4.1 Evaluation of Methods. Included are reports which detail the development and evaluation of drug analysis methods, or which evaluate a method or technique currently available for use.

4.4.2 Intermethod Comparison. Included are reports which describe the evaluation of newly developed methods by comparison with established methods, or which evaluate existing methods (in terms of cost, availability, analytical characteristics, etc.) for specific purposes, for example, the analysis of morphine.

4.5 Evaluation of Analytical Performance

Documents dealing with the evaluation of laboratory analytical performance are included under this heading. Articles are cited under two separate headings:

4.5.1 Quality Control. Intra-laboratory aspects of analytic capability are topics included under this heading. The accuracy and precision of an analytical procedure, as well as consistency of method application are examples of factors involved in quality control.

4.5.2 Testing Laboratory Proficiency. Documents included under this heading pertain to the external evaluation of laboratories for proficiency in drug analysis. Studies include the multi-laboratory assessment of analytic capability as well as discussions of methodology appropriate for use in proficiency testing.

5.0 CONCENTRATIONS OF DRUGS IN THE HUMAN BODY

The importance of drug concentration data, for data interpretation as well as in the design of drug screening systems, is reflected in this general topic area. Reports which contain drug concentration data or which deal specifically with the determination of drug levels in body fluids are cited under three categories:

- Data compilations (5.1),
- Incidental reports of drug concentrations following drug administration (5.2), and
- Factors which influence the concentration of drugs in body fluids (5.3).

These categories are further broken down as described below:

5.1 Compilations.

Reports which contain collections of drug concentration data are cited under two main subheadings as follows:

5.1.1 Tabulated Data. Documents which report general data pertaining to therapeutic, toxic, or fatal levels of drugs in body fluids are included.

5.1.2 Epidemiologic Research. Collections of drug concentration data which result from original research are cited according to the following populations:

5.1.2.1 Studies of Drugs in Drivers. Investigations of actual drug levels in the body fluids of drivers are cited.

5.1.2.2 Studies of Drugs in Patients. Drug concentration data obtained from patients, including drug-overdose victims, are contained in referenced documents.

5.1.2.3 Studies of Drugs in Other Groups. Drug concentration data collections not specifically included above are cited. Reports primarily deal with the determination of drug blood levels in drug-involved deaths.

5.2 Specific Reports of Drug Concentrations in Man

Articles in which the determination of drug body fluid levels followed the administration of one or more dosage levels are here cross-referenced according to the mode of drug administration and according to the type of study in which these determinations were made:

5.2.1 Studies with Acute Doses. Investigations in which drug concentration determinations were made following a single drug dose administration are cited. Studies which involve the one-time administration of a drug to experimental subjects described as "chronic users" are included under this heading.

5.2.2 Studies with Chronic Doses. Investigations in which drug concentration determinations were made following two or more dose administrations are cited.

5.2.3 Studies of Pharmacokinetics. More extensive investigations into the level of drugs in body fluids as a function of time after drug administration are included under this heading. Relevant reports are classified according to the mode of drug administration:

5.2.3.1 Acute Doses. See Section 5.2.1 for an explanation of the topic heading.

5.2.3.2 Chronic Doses. See Section 5.2.2 for an explanation of the topic heading.

5.2.4 Studies Correlating the Concentrations of Drugs in Different Body Fluids. Investigations which attempt to correlate human drug levels in two or more body fluids are referenced. Experiments usually involve the simultaneous collection of different body fluid samples following the administration of a single drug.

5.3 Studies of Factors Influencing Drug Concentrations in Body Fluids

Articles dealing with background variables which influence drug levels are included under this heading. Both experimental reports and review documents are cited according to the following subheadings:

5.3.1 Absorption and Distribution of Drugs. Reviews and studies of variables which operate during the pharmacokinetic phases of drug absorption and distribution are cited. The relationship of bioavailability in drug formulation and variability of patient response, and the influence of simultaneous food intake on resulting drug levels are examples of specific topics.

5.3.2 Metabolism of Drugs. Factors such as metabolic enzyme induction and inhibition and the first-pass metabolism of administered drugs are included under this heading.

5.3.3 Analytical Variables. Documents which discuss the influence of analytical methods on the objective determination of drug levels in body fluids are cited.

5.3.4 Other Factors. Articles which deal in a general way with this topic area, or which deal with factors not specified above, are included under this heading.

6.0 SOCIOLEGAL STUDIES

Documents concerned with the social and legal factors involved in the drug-driving problem are classified according to specific issues in the topic area.

6.1 Research with Human Subjects

In this section are cited papers concerned with the ethical considerations of using humans in scientific research, particularly laboratory experimentation. Cited are papers dealing with studies of driving performance, behavior, and drug effects.

6.2 Informed Consent

Papers in this section discuss the historical, theoretical, ethical, legal, and practical aspects and implications of informed consent in medical procedures and experimental research. Studies discussing the implications of informed consent for both researcher and subject are included.

6.3 Researcher Privilege

At present, most state laws require that researchers disclose relevant data obtained in laboratory experimentation or scientific research in a court of law even though disclosure of that data might subject the individual to criminal prosecution or civil liability. Papers cited here discuss the issue of exempting the researcher from being forced to testify against a subject.

6.4 Right of Privacy/Confidentiality

Due to the personal and potentially incriminating nature of the data collected for drug and driving research, it is unlikely that a representative sample of the general driving population or accident population will cooperate with researchers unless they have assurance that this information will not be made public. Cited in this category are papers dealing with the subject's right of privacy, particularly the legal complexities involved.

6.5 Other Sociolegal Topics

Cited are papers on a broad variety of sociolegal subjects not related to those above. This category includes publications discussing scheduling of drugs, federal regulations for drugs, prosecution and adjudication of drug-impaired driving, decriminalization of marijuana, state medico-legal death investigative systems, and government drug control programs.

7.0 COUNTERMEASURES IN DRUGS AND HIGHWAY SAFETY

Referenced here are papers on efforts to reduce the drug-driving problem. Underlying theories of these countermeasure programs, their development activities, and implementation are described and evaluated. Studies are cited under the following subheadings indicating chronological stage of development.

7.1 Concepts

Social, legal, political, psychological, and economic theories, considerations, and implications of countermeasures for drug abuse and unsafe driving are discussed in papers referenced in this category. Specifically included are papers discussing conceptual frameworks and themes for drug abuse treatment programs, public information and education campaigns, and legislation related to the drug-driving problem.

7.2 Development, Testing, and Evaluation

Referenced are studies reporting specific programs or types of programs directed at reducing use of drugs while driving, drug abuse, and unsafe driving. These programs are described and evaluated in terms of their history, objectives, activities, and results.

7.3 Demonstration and Implementation

Papers referenced here provide practical recommendations for carrying out countermeasure programs for the drug-driving problem. Also referenced are representative pamphlets of some recent public information and education campaigns.

8.0 DRUG NAME SUBINDEX

This section provides an index of papers by drug. In general, papers are not listed under a given drug if the study only mentions the drug in an incidental or anecdotal manner. Rather, an attempt was made to list only those papers containing significant information about a drug.

Papers pertaining to each drug are listed under its preferred name by accession number in alphanumeric order. An asterisk beside an accession number indicates that the cited document (1) contains information concerning drug concentrations in body fluids or (2) reports the measurement of body fluid concentrations following the drug's administration to human subjects.

Three types of drug names are used in this drug index. The majority of drugs are identified by a preferred drug name, that is, the chemical or generic name. Under this preferred drug name all relevant papers are cited. For preparations having no chemical or generic name or containing more than one drug, trade names are used. Accession numbers are listed under a trade name only when there is no other chemical or generic name. For all other trade names the reader is referred to the preferred drug name for the relevant accession numbers.

A third type of drug identification that appears occasionally in this index is the drug class name. Papers will be cited under a drug class name only when no specific drug is mentioned in the paper. In all other cases relevant papers will be cited under the preferred drug name or trade name.

9.0 DRUG CLASS SUBINDEX

The purpose of this section is to aid the user in identifying common therapeutic uses of a drug and to provide a succinct listing of identified drugs by type. The classification scheme developed for Supplement One was revised for this bibliographic supplement.

Three separate lists of drug classes comprise this subindex: Section 9.1 identifies documents that refer to drug classes, rather than specific drugs or substances. Section 9.2 shows each drug class followed by preferred drug names from the Drug Name Subindex (Section 8.0). The final listing, Section 9.3, presents the drug classification scheme. The outline is structured by prefix numbers for the different drug classes. The number is divided into three parts, separated by dashes. The first part identifies the general group of drug classes; the second, two-digit part identifies the major drug classes, and the last digit identifies minor drug classes. In this way, drugs that are chemically, pharmacologically, or therapeutically similar can be identified by using Sections 9.2 or 9.3, and the documents discussing them can be located by referring to Section 8.0. Also, articles that only discuss a class of drugs, rather than individual agents, are easily found in Section 9.1.

TOPICAL INDEX

1.0 REVIEWS AND COMPILATIONS

1.1 Reviews of Drugs and Highway Safety

78-B0019 71-D1014 72-D1015 75-D1017 66-D1021 76-D1044 78-D1046
77-D1051 78-D1052 79-D1053 77-D1057 76-D1064 78-D1065 79-D1066
78-D1074 78-D1079 77-D1081 77-D1150 76-D1176 68-D1188 75-D1189
75-D1190 75-D1191 78-D1192 78-D1193 73-D1197 78-D1201 79-D1204
78-D1205 79-D1212 79-D1213 79-D1214 79-D1234 78-D1235 79-D1236
77-D1245 79-D1246 79-D1251 79-D1252 80-D1262 79-D1270 79-D1282
79-D1283 79-D1284 79-D1285 79-D1292 74-E0091 63-L0124

1.2 Research on the Use of Drugs

74-A0022 74-A0023 74-A0024 74-A0025 74-A0026 74-A0027 79-A0029
78-A0030 78-B0019 73-C0022 75-D1034 79-D1056 78-D1068 78-D1201
78-D1205 77-D1223 79-D1234 70-D1237 79-D1242 80-D1262 76-E0075
77-E0076 78-E0077 78-E0078 75-E0079 76-E0082 74-E0086 79-E0088
74-E0091 79-E0095 78-E0103 79-E0110 74-E0116 75-E0117 78-E0122
77-E0148 77-L0139 77-L0140

1.3 Research on the Effects of Drugs

1.3.1 Reviews of Drugs or Classes of Drugs

74-A0025 74-A0026 74-A0027 78-B0019 54-D1008 76-D1013 70-D1026
77-D1069 78-D1084 77-D1085 76-D1103 77-D1107 78-D1108 75-D1112
75-D1115 77-D1160 78-D1161 78-D1169 78-D1174 78-D1175 78-D1184
78-D1201 78-D1205 79-D1207 79-D1211 79-D1212 78-D1219 79-D1221
78-D1225 79-D1234 78-D1235 79-D1236 70-D1237 79-D1238 79-D1250
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78-E0078 79-E0097 78-E0103 74-E0116 75-E0117 77-L0139 77-L0140

1.3.2 Reviews of the Relationships Between Drug Effects and Their Concentration in Body Fluids

78-D1174 78-D1175 78-D1219 79-D1234 79-D1238 78-E0078 78-P0054
77-P0065 78-P0067

1.4 Methodology in Drugs and Highway Safety

1.4.1 Methodology in Survey Research

75-D1047 78-D1201 80-D1262 79-D1289 77-E0076 75-E0079 76-E0080
76-E0081 78-E0099 77-E0108 78-E0121 79-E0123 79-E0135

1.4.2 Methodology in Behavioral Research

78-D1187 78-D1201 80-D1262 79-D1276 76-E0075 78-E0077 76-E0080
76-E0081 79-F0042 79-F0045 77-F0049 79-F0052 79-F0053 78-F0056
78-F0057 79-F0063 80-F0066 80-F0073

1.4.3 Methodology in Drug Analysis

78-D1201 78-D1205 79-D1238 80-D1262 79-D1290 76-M0296 77-M0303
77-M0309 77-M0323 79-M0331 77-M0334 77-M0336 78-M0337 77-M0340
78-M0344 79-M0355 78-M0367 77-M0368 77-M0369

1.5 Selected Reviews

78-B0019 (drugs, society, and human behavior)
76-D1013 (drug induced depression)
77-D1016 (epilepsy and driving)
75-D1018 (psychosis and driving)
78-D1068 (phencyclidine intoxication)
75-D1115 (drug use in sports)
79-D1116 (solvent abuse)
79-D1118 (dangers and benefits of cocaine use)
77-D1119 (adverse behavioral effects of benzodiazepines)
77-D1144 (relationship between clinical effects of clozapine and EEG)
78-D1146 (behavioral toxicology of metals)
76-D1180 (ethical responsibility of the pharmaceutical industry)
78-D1181 (therapeutic uses of the benzodiazepines in clinical pharmacology)
79-D1207 (disulfiram treatment of alcoholism)
79-D1238 (biochemistry of marijuana)
79-D1265 (drug-alcohol interactions and effects of other polydrug abuse)
79-D1268 (behavioral effects of carbon monoxide)
78-D1272 (polydrug abuse)
78-D1279 (therapeutic use of coca)
79-D1286 (the role of mental and psychiatric disease in traffic safety)
77-E0085 (investigation and reporting of drug deaths)
78-E0090 (relationship between drug addiction and criminality)
79-E0095 (drug use by the elderly)
79-E0098 (state of the art of epidemiological science)
76-E0146 (physician prescribing habits)
55-F0037 (medical aspects of placebo use)
71-F0038 (therapeutic uses of placebos)
77-M0294 (proficiency assessment programs in toxicology)
76-M0297 (quality control of drug estimations)
73-M0299 (laboratory standardization)

1.6 Compilations

74-A0022 (nonmedical use of drugs and sexual behavior)
74-A0023 (user and nonuser attitudes toward nonmedical drug use)
74-A0024 (influence of family and peers on drug use)
74-A0025 (effects of nonmedical use of drugs on pregnancy and neonates)
74-A0026 (relationship between nonmedical use of drugs and all modes of death)
74-A0027 (lifestyles of heroin addicts)
74-A0028 (cocaine)
78-A0031 (driving by the medically impaired)
76-B0008 (drug assays for biological fluids)
74-B0017 (drug use by the elderly)
72-B0018 (human factors in traffic safety)
78-B0020 (relationship between blood levels of psychoactive drugs and clinical response)
70-B0021 (physical, mental, and psychological impairment and traffic safety)
79-B0022 (extent and treatment of drug abuse)
77-B0023 (forensic pathology techniques)
78-B0024 (drug abuse around the world)
78-D1178 (behavioral effects of heavy metals)
77-D1185 (research problems in behavioral pharmacology)
78-D1203 (psychosocial issues of drug use)
79-D1288 (alcohol, drugs, and traffic safety)
59-D1297 (alcohol, drugs, and traffic safety)
77-E0076 (epidemiologic aspects of heroin and other narcotics)
78-E0077 (self-administration of abused substances)
78-E0078 (effects and use of phencyclidine)
75-E0079 (predicting adolescent drug abuse)
76-E0081 (data analysis methodology)
76-E0082 (personality and drug use)
77-E0083 (drugs and psychopathology)
77-E0084 (drug use and minorities)
78-E0107 (history of psychoactive substance use)
79-E0109 (international drug use)
74-E0116 (effects, use, and decriminalization of marijuana and hashish)
75-E0117 (effects, use, and decriminalization of marijuana and hashish)
75-F0039 (aminergic hypotheses of behavior)

77-F0040 (psychodynamics of drug dependence)
78-F0041 (research and treatment implications of behavioral tolerance)
79-F0043 (behavioral analysis and treatment of substance abuse)
77-F0051 (state of the art of psychopharmacology)
77-L0139 (effects, use, and decriminalization of marijuana)

2.0 EPIDEMIOLOGIC RESEARCH

2.1 Studies of Drug Use Among Drivers and Its Consequences

2.1.1 Analysis of Drivers' Body Fluids for Drugs

79-D1035 76-D1045 78-D1089 78-D1149 79-D1167 78-D1202 74-D1216
74-D1228 78-D1231 79-D1233 74-D1239 79-D1255 78-D1258 79-D1261
80-D1299 63-D1302 79-F0059 74-M0315

2.1.2 Self-Reported Drug Use by Drivers

79-D1035 77-D1166 79-D1208 78-D1222 74-D1228 79-D1233 74-D1239
79-D1240 79-D1241 78-D1248 79-D1271 78-D1280 79-E0105

2.1.3 Record-Based Surveys

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78-D1258 79-D1281 69-F0044 78-L0116 77-L0123 78-L0141 78-L0142

2.2 Studies of Drug Use in Nondriving-Specific Populations

2.2.1 National Surveys

78-D1005 79-D1041 78-D1186 79-D1271 79-D1281 77-E0087 79-E0094
76-E0104 79-E0113 74-E0116 78-E0122 79-E0124 79-E0136 79-E0138
79-E0139 73-E0141 74-E0142 75-E0143 76-E0144 79-E0145 76-E0147
78-L0137

2.2.2 Regional or Local Surveys

73-C0022 71-D1020 76-D1045 75-D1047 79-D1117 78-D1206 79-D1208
77-E0087 74-E0089 78-E0092 77-E0096 78-E0099 79-E0100 79-E0101
79-E0105 76-E0106 76-E0111 75-E0112 79-E0113 77-E0114 79-E0115
75-E0117 78-E0118 78-E0119 78-E0120 79-E0126 79-E0127 78-E0128
78-E0129 77-E0130 78-E0131 78-E0132 79-E0133 80-E0134 79-E0137
78-E0140 79-L0138

2.3 Crash Investigation

79-D1167 77-D1227 74-D1228 79-D1229 76-D1230 79-D1240 78-E0093
77-E0096 71-F0046 79-F0060

3.0 EXPERIMENTAL RESEARCH

3.1 Studies of Drugs Administered Alone

3.1.1 Studies Comparing Different Drugs

75-D1002 78-D1003 73-D1007 78-D1011 75-D1040 79-D1043 74-D1048
63-D1054 78-D1059 79-D1060 74-D1062 64-D1071 72-D1072 78-D1082
77-D1086 77-D1088 78-D1090 77-D1091 77-D1092 76-D1095 78-D1096
77-D1098 76-D1099 78-D1102 77-D1109 78-D1110 78-D1120 78-D1121
78-D1122 78-D1123 79-D1125 76-D1129 77-D1137 77-D1141 78-D1153
77-D1154 77-D1155 77-D1156 78-D1159 77-D1163 73-D1164 77-D1165
76-D1168 77-D1194 69-D1196 78-D1209 79-D1210 70-D1220 72-D1226
77-D1247 75-D1253 79-D1254 76-D1256 79-D1257 79-D1259 79-D1269
79-D1293 79-D1294 79-D1295 79-D1296 63-D1300 63-D1301 78-P0090

3.1.2 Studies of Acute Doses

77-D1006 62-D1009 73-D1024 76-D1027 51-D1028 53-D1029 69-D1032
71-D1033 75-D1040 74-D1048 75-D1049 78-D1055 74-D1062 73-D1063
64-D1071 72-D1072 79-D1073 76-D1077 77-D1078 78-D1080 78-D1082
78-D1090 77-D1091 77-D1092 76-D1095 78-D1097 76-D1099 78-D1100

77-D1111 78-D1113 78-D1123 76-D1128 78-D1130 78-D1133 78-D1134
78-D1136 77-D1137 76-D1139 78-D1145 77-D1147 78-D1148 78-D1153
77-D1156 78-D1159 77-D1165 76-D1168 79-D1173 77-D1177 78-D1179
77-D1182 77-D1194 77-D1200 78-D1209 70-D1220 78-D1243 77-D1247
79-D1254 79-D1259 79-D1260 80-D1266 79-D1269 79-D1275 79-D1283
79-D1287 79-D1293 79-D1295 79-D1296 70-D1298 63-D1300 63-D1301
77-P0058 77-P0091

3.1.3 Studies of Chronic Doses

75-D1002 78-D1003 74-D1010 74-D1048 78-D1050 76-D1058 78-D1059
79-D1060 74-D1061 70-D1070 77-D1088 77-D1093 77-D1094 78-D1096
77-D1098 78-D1102 77-D1109 78-D1110 78-D1120 78-D1121 78-D1124
79-D1125 78-D1127 76-D1129 78-D1132 77-D1137 78-D1138 78-D1140
77-D1141 78-D1142 77-D1143 74-D1151 77-D1154 77-D1162 78-D1171
78-D1172 78-D1187 64-D1195 69-D1196 79-D1210 77-D1215 72-D1226
79-D1244 79-D1249 75-D1253 79-D1254 76-D1256 79-D1257 78-D1263
78-D1264 78-D1267 80-D1278 79-D1294 63-D1300 63-D1301

3.1.4 Studies Relating Dose and Effects

75-D1002 77-D1004 73-D1007 71-D1020 73-D1025 73-D1030 78-D1038
79-D1043 74-D1048 63-D1054 72-D1072 79-D1073 75-D1076 79-D1083
77-D1088 76-D1095 78-D1097 75-D1105 78-D1113 78-D1124 77-D1126
76-D1128 78-D1132 78-D1133 74-D1135 78-D1152 78-D1159 78-D1170
78-D1183 77-D1194 76-D1224 77-D1247 75-D1253 76-D1256 79-D1257
80-D1266 79-D1269 79-D1293 79-D1295 63-D1301 77-P0091

3.1.5 Other Studies

62-D1012

3.2 Studies of Two or More Drugs Administered Together ("Drug Interaction" Studies)

3.2.1 Studies of the Combined Effects of Drugs

73-D1007 70-D1023 73-D1025 78-D1038 77-D1039 79-D1043 78-D1059
77-D1086 79-D1087 78-D1106 77-D1109 78-D1121 78-D1136 77-D1137
77-D1147 77-D1155 78-D1159 77-D1162 77-D1165 78-D1209 70-D1220
77-D1247 79-D1259 78-D1263 79-D1287 79-D1296 63-D1300 63-D1301
69-F0055 77-P0058

3.2.2 Other Studies

80-D1278 70-D1298

3.3 Research on the Effects of Drugs or on Driving Performance Skills

3.3.1 Studies with Behavioral Methods Related to the Driving Task

3.3.1.1 Tests on the Open Road

79-D1060 69-F0044 79-F0064 80-F0067 78-F0068 79-F0071
79-F0072 80-F0073

3.3.1.2 Tests on Closed Driving Courses

75-D1037 75-D1040 78-D1243 77-D1247 79-D1275 79-D1294
79-D1296 80-F0067

3.3.1.3 Tests on Driving Simulators

71-D1020 76-D1058 78-D1132 77-D1163 64-D1195 79-D1210
72-D1226 75-D1253 79-D1283 79-D1287 63-D1300 69-F0044
79-F0048 79-F0050 78-F0058 79-F0064 78-F0068

3.3.2 Studies with Psychophysical Tests

3.3.2.1 Tests of Psychomotor Skills

77-D1006 78-D1011 76-D1019 73-D1025 76-D1027 51-D1028
78-D1038 77-D1039 75-D1040 72-D1042 74-D1048 75-D1049
63-D1054 78-D1059 74-D1061 74-D1062 70-D1070 64-D1071

79-D1073 75-D1076 76-D1077 78-D1080 78-D1082 79-D1083
77-D1086 78-D1090 77-D1092 77-D1093 77-D1094 76-D1095
78-D1096 76-D1099 78-D1100 78-D1102 77-D1104 78-D1106
77-D1109 78-D1110 78-D1113 78-D1121 78-D1122 78-D1123
78-D1127 76-D1128 78-D1130 78-D1132 78-D1136 77-D1137
78-D1140 78-D1145 77-D1147 78-D1148 78-D1153 77-D1154
77-D1155 73-D1164 78-D1170 78-D1172 77-D1194 69-D1196
77-D1200 78-D1209 79-D1210 70-D1220 72-D1226 79-D1244
79-D1249 79-D1254 76-D1256 79-D1257 79-D1259 79-D1269
78-D1274 79-D1293 69-F0055 79-F0062 79-F0065 77-P0058

3.3.2.2 Tests of Sensory Functions

78-D1011 76-D1027 73-D1030 69-D1032 71-D1033 78-D1038
79-D1043 63-D1054 74-D1061 74-D1062 77-D1086 78-D1096
76-D1099 77-D1137 77-D1141 78-D1159 73-D1164 78-D1170
77-D1177 77-D1182 69-D1196 79-D1254 79-D1269 79-D1293
79-D1295 63-D1301 79-F0048 78-F0058 79-F0065 78-F0069
80-F0070

3.3.3 Studies with Psychological Tests

62-D1009 78-D1011 71-D1020 73-D1024 76-D1027 51-D1028 53-D1029
78-D1038 75-D1040 76-D1058 79-D1060 74-D1061 73-D1063 64-D1071
72-D1072 75-D1076 77-D1078 77-D1086 77-D1091 77-D1094 76-D1095
78-D1097 77-D1098 76-D1099 78-D1101 78-D1102 77-D1104 75-D1105
77-D1109 78-D1110 77-D1111 78-D1120 78-D1121 78-D1124 79-D1125
76-D1128 76-D1129 78-D1130 78-D1131 78-D1133 78-D1134 74-D1135
78-D1136 78-D1138 76-D1139 78-D1140 78-D1142 77-D1143 78-D1145
77-D1147 78-D1152 77-D1155 77-D1156 73-D1164 77-D1165 78-D1170
78-D1171 78-D1172 77-D1177 78-D1179 77-D1182 78-D1187 69-D1196
75-D1199 77-D1200 79-D1210 79-D1244 79-D1249 75-D1253 79-D1254
76-D1256 79-D1257 80-D1266 78-D1267 79-D1269 79-D1293 79-F0048
79-F0052 79-F0053 79-F0054 79-F0062 80-F0067 77-P0091

3.3.4 Studies with Physiological Tests

75-D1002 75-D1049 74-D1062 72-D1072 76-D1077 77-D1078 78-D1082
79-D1087 78-D1090 77-D1092 77-D1093 78-D1101 78-D1131 78-D1133
74-D1135 76-D1139 77-D1141 78-D1158 77-D1162 77-D1163 77-D1165
76-D1168 78-D1172 79-D1173 78-D1183 64-D1195 75-D1199 77-D1200
79-D1210 78-D1243 75-D1253 78-D1263 78-D1274 70-D1298 78-P0090

3.3.5 Clinical Studies

74-D1010 76-D1019 76-D1058 74-D1061 73-D1063 77-D1094 78-D1102
79-D1125 76-D1129 78-D1132 77-D1143 78-D1183 78-D1187 70-D1220
75-D1253 79-D1260 78-D1264 78-D1267 78-D1273 78-D1274 80-D1278
78-E0128

3.3.6 Studies Including Self-Evaluation of Drug Effects by Test Subjects

77-D1004 70-D1023 75-D1049 79-D1060 72-D1072 78-D1082 79-D1083
77-D1086 78-D1090 77-D1091 76-D1095 78-D1096 78-D1097 76-D1099
75-D1105 78-D1106 77-D1109 78-D1113 78-D1122 77-D1126 76-D1128
78-D1134 77-D1141 78-D1145 78-D1152 77-D1154 77-D1155 77-D1156
78-D1159 78-D1183 75-D1199 78-D1209 79-D1210 75-D1253 79-D1254
76-D1256 79-D1260 79-D1269 80-D1299 63-D1301 77-P0091

3.3.7 Factors Influencing the Effects of Drugs on Human Behavior

3.3.7.1 Age

3.3.7.2 Gender

78-D1113

3.3.7.3 Personality

77-D1109

3.3.7.4 Other

73-D1083 (schizophrenia)
78-D1100 (user expectation of drug effect)
79-D1117 (frequency of marijuana use)
76-D1128 (individual sleep patterns)
76-D1224 (previous chronic hashish use)
80-D1278 (other drug use)
79-F0061 (color of drug)

3.4 Research on the Relationship Between the Effects of Drugs and Their Concentration in Body Fluids

3.4.1 Studies of Skills Related to Driving

71-D1020 77-D1104 77-D1194 80-D1299 77-P0058

3.4.2 Clinical Studies

78-D1075 77-D1162 78-D1274 77-P0068 78-P0072 78-P0074

3.5 Research Involving Animals

78-D1003 62-D1012 61-D1036 78-D1067 75-D1114 77-D1157 75-D1198
77-D1215 78-P0049 78-P0090

4.0 DETECTION, IDENTIFICATION, AND QUANTITATION OF DRUGS IN BIOLOGICAL SPECIMENS

4.1 General Methods of Screening for Drugs

4.1.1 Thin-Layer and Paper Chromatography

78-M0342 77-M0369

4.1.2 Optical Techniques

77-M0369

4.1.3 Gas Chromatography

76-M0298 78-M0349 77-M0369

4.1.4 Other Techniques

78-M0292 78-M0300 77-M0308 78-M0318 78-M0320 78-M0324 78-M0327
78-M0328 77-M0343 78-M0365 77-M0369

4.1.5 Screening Systems

76-M0298 77-M0307 78-M0317 78-M0341 79-M0378

4.2 Specific Methods of Screening for Drugs

4.2.1 Thin-Layer and Paper Chromatography

77-M0325 79-M0362 78-M0363 78-M0372 77-P0056 79-P0062

4.2.2 Optical Techniques

77-E0102 79-M0362 80-M0375

4.2.3 Gas Chromatography

77-E0102 77-M0304 77-M0319 77-M0347 78-M0348 79-M0362

4.2.4 Immunoassay

78-M0295 77-M0322 77-M0345 78-M0353 77-M0360 73-M0361 79-M0362

4.2.5 Other Techniques

78-M0302 78-M0306 77-M0310 78-M0311 79-M0314 74-M0315 78-M0321
78-M0326 77-M0346 78-M0350 78-M0351 77-M0356 77-M0359 79-M0362
79-M0366 78-M0373 77-P0056 79-P0062

4.3 Methods for Confirmatory/Quantitative Analysis

4.3.1 Optical Techniques

79-M0379

4.3.2 Gas Chromatography

78-M0301 78-M0312 78-M0313

4.3.3 Gas Chromatography-Mass Spectrometry

77-M0335 77-M0338 79-M0376 79-M0379

4.3.4 Immunoassay

77-M0371

4.3.5 Other Techniques

77-M0291 77-M0305 78-M0311 79-M0314 78-M0316 77-M0339 76-M0370
78-P0047 78-P0048

4.4 Evaluation of Analytical Methods

4.4.1 Evaluation of Methods

78-M0330

4.4.2 Intermethod Comparison

78-M0321 74-M0329 78-M0332 77-M0335 79-M0379

4.5 Evaluation of Analytical Performance

4.5.1 Quality Control

78-M0333 78-M0352 78-M0364

4.5.2 Testing Laboratory Proficiency

77-M0293 78-M0352 77-M0358 77-M0369 79-M0374 79-M0377

5.0 CONCENTRATIONS OF DRUGS IN THE HUMAN BODY

5.1 Compilations

5.1.1 Tabulated Data

73-D1031 77-D1218 76-P0090

5.1.2 Epidemiologic Research

5.1.2.1 Studies of Drugs in Drivers

78-D1149

5.1.2.2 Studies of Drugs in Patients

78-D1102 78-P0066 79-P0083

5.1.2.3 Studies of Drugs in Other Groups

78-D1005 79-D1041 79-E0125 79-M0376

5.2 Specific Reports of Drug Concentrations in Man

5.2.1 Studies with Acute Doses

78-D1055 78-D1075 77-E0102 79-M0366 77-P0068 78-P0074

5.2.2 Studies with Chronic Doses

77-D1004 78-D1050 78-D1131 78-D1152 74-D1216 79-P0083

5.2.3 Studies of Pharmacokinetics

5.2.3.1 Acute Doses

78-D1101 77-D1126 79-D1238 78-M0354 77-M0371 78-P0047
78-P0048 77-P0058 77-P0060 77-P0069 78-P0072 77-P0079
77-P0080

5.2.3.2 Chronic Doses

78-D1050 77-D1104 79-D1238 78-M0354 77-P0050 77-P0051
77-P0056 77-P0076 77-P0080 79-P0083

5.2.4 Studies Correlating the Concentrations of Drugs in Different Body Fluids

77-D1162 79-P0064

5.3 Studies of Factors Influencing Drug Concentrations in Body Fluids

5.3.1 Absorption and Distribution of Drugs

78-P0053 79-P0062 77-P0063 79-P0064 77-P0070 77-P0071 78-P0073
77-P0077 77-P0079 77-P0081 79-P0082 79-P0085

5.3.2 Metabolism of Drugs

77-P0056 77-P0075 77-P0079 70-P0089

5.3.3 Analytical Variables

79-P0086 79-P0087 79-P0088 72-P0091

5.3.4 Other Factors

77-P0050 77-P0051 77-P0052 79-P0055 78-P0057 78-P0059 77-P0061
78-P0073 77-P0078 79-P0084 70-P0089

6.0 SOCIOLEGAL STUDIES

6.1 Research with Human Subjects

78-L0134

6.2 Informed Consent

78-L0117 79-L0118 78-L0134

6.3 Researcher Privilege

75-L0127

6.4 Right of Privacy/Confidentiality

75-L0127

6.5 Other Sociolegal Topics

74-A0023 76-C0020 73-C0034 78-D1205 78-D1235 70-D1237 80-D1262
79-D1291 74-E0116 75-E0117 77-F0047 78-L0119 78-L0121 71-L0122
72-L0125 78-L0126 74-L0128 79-L0129 79-L0130 78-L0131 78-L0132
78-L0134 79-L0135 78-L0136 78-L0137 79-L0138 77-L0139 77-L0140
78-L0141 78-L0142 79-L0143 71-L0144 77-M0343

7.0 COUNTERMEASURES IN DRUGS AND HIGHWAY SAFETY

7.1 Concepts

77-C0018 76-C0020 72-C0023 71-C0024 79-C0027 78-C0032 78-D1186
78-D1201 79-D1246 79-D1292 78-E0131 79-L0129 78-L0133 79-L0135
79-L0138

7.2 Development, Testing, and Evaluation

72-C0019 76-C0021 73-C0026 79-C0029 74-C0030 76-C0031 79-C0033
77-D1051 79-D1066 78-D1186 79-D1204 80-D1262 79-D1291 79-E0113
79-E0115 79-E0127 79-E0137 78-L0116 77-L0120 77-M0357

7.3 Demonstration and Implementation

73-C0025 79-C0028

8.0 DRUG NAME SUBINDEX

9.0 DRUG CLASS SUBINDEX

9.1 Drug Class and Accession Number List

Analgesics and Antipyretics
79-D1211 79-D1212 78-D1258 79-D1281 79-E0109 79-E0115 76-E0147
78-M0349

Androgens
75-D1115

Anesthetics
72-D1042 78-D1201 79-D1212 79-D1282

Anorectic (Appetite Control) Agents
76-E0147

Antacids and Adsorbants
79-D1281

Anti-Anginal Agents
79-D1211 79-D1212

Anti-Coagulants
79-D1211

Anti-Parkinsonism Agents
78-D1127

Antibiotics
79-D1211 79-D1212 76-E0147 71-L0144 78-M0337

Anticonvulsants (Anti-Epileptics)
75-D1076 79-D1211 79-D1212 78-M0337 77-P0075

Antidepressants
74-D1061 77-D1069 78-D1124 78-D1201 79-D1211 79-D1212 79-D1265
79-D1292 78-E0122 76-E0147 79-E0155 78-M0317 78-M0337 77-M0345
78-M0349 78-M0353

Antihistamine Agents
54-D1008 79-D1211 79-D1212 78-D1235 79-D1265 79-D1281 76-E0147
78-M0349 78-P0072

Autonomic Nervous System (ANS) Agents
79-D1292

Barbiturates
79-D1035 79-D1211 78-D1235 78-D1280 79-D1292 74-E0089 79-E0097
79-E0105 79-E0113 79-E0115 75-E0117 78-E0129 78-E0132 79-L0138
71-L0144 74-M0315 78-M0320 78-M0324 77-M0340 78-M0352

Cannabis Sativa L. and Related Agents
78-L0131 78-M0302 78-M0316 77-M0322* 79-M0362* 79-M0366

Cardiovascular Agents
76-E0147

Central Nervous System (CNS) Agents
78-B0020 75-D1047 76-E0104 78-P0067

Diuretics
79-D1281 76-E0147

Hallucinogens and Related Agents
78-B0019 78-D1201 79-D1212 74-E0086 74-E0089 79-E0105 79-E0115
79-E0136 79-E0139 79-L0135 78-L0141 78-L0142

Heavy Metals and Heavy Metal Antagonists
78-D1146

Herbicides
76-E0106

Hormones, Synthetic Substitutes, and Antagonists
76-E0147

Hypotensive (Antihypertensive) Agents
79-D1211 79-D1212

Insulins and Anti-Diabetic Agents
79-D1211 79-D1212 76-E0147

Major Tranquilizers (Antipsychotics and Neuroleptics)
79-D1212

Minor Tranquilizers (Anti-Anxiety and Ataractics)
74-D1061 77-D1119 79-D1265 79-D1281 79-D1285 79-D1292 78-E0122

Muscle Relaxants (Central)
79-D1212

Neurochemicals, Neurotransmitters, and Neurohormones
75-F0039

Opiates and Related Agents
74-A0026 78-B0019 76-D1013 78-D1131 78-D1201 78-D1202 79-D1211
79-D1241 79-D1265 77-E0076 74-E0089 78-E0090 78-E0107 79-E0109
79-E0113 79-E0115 78-E0118 78-E0119 78-E0132 79-E0136 79-E0139
78-F0041 78-L0134 79-L0135 78-M0365

Oral Contraceptives
78-B0019 79-D1281

Other Toxicants
78-D1169 79-E0115 79-E0136 79-E0139 79-L0135

Parasympatholytic (Cholinergic Blocking) Agents
79-D1212

Penicillins
79-D1281

Pesticides
76-E0106

Sedatives and Hypnotic Agents
78-B0019 74-C0030 76-D1013 76-D1128 78-D1201 79-D1212 78-D1258
79-D1265 79-D1281 79-D1292 78-E0077 79-E0115 78-E0122 79-E0126
79-E0136 79-E0139 76-E0147 79-L0135 79-L0138 78-L0141 78-L0142
74-M0315

Stimulants
78-B0019 76-D1013 78-D1108 75-D1115 78-D1179 78-D1201 79-D1211
79-D1212 78-D1258 79-D1265 78-D1280 74-E0089 79-E0105 79-E0109
78-E0132 79-E0136 79-E0139 79-L0135 78-L0141 78-L0142 78-M0320
77-M0340 78-M0365

Sulfonamides
77-M0368

Sympathomimetic (Adrenergic) Agents
75-F0039 78-M0365

Tetracyclines
79-D1281

Tranquilizers
78-B0019 78-D1201 79-D1211 79-D1232 78-D1235 79-D1270 59-D1297
74-E0089 79-E0115 78-E0122 79-E0136 79-E0139 76-E0147 79-L0135

Volatile Solvents
79-A0029 79-D1116 78-D1169 78-D1171 74-E0089 79-E0115 79-E0136
79-E0139 79-L0135

9.2 Drug Class and Drug Name List

Adrenals
- corticosterone
- dexamethasone
- fludrocortisone
- methylprednisolone sodium succinate
- triamcinolone

Analgesics and Antipyretics
- acetaminophen
- alclofenac
- aminopyrine
- antipyrine
- carbamazepine
- cyclazocine
- Distalgesic(R) (dextropropoxyphene + acetaminophen)
- hydroxychloroquine
- indomethacin
- methotrimeprazine
- phenacetin
- phenazopyridine
- phenylbutazone
- propoxyphene
- propyphenazone
- salicylate
- tramadol

Androgens
- testosterone

Anorectic (Appetite Control) Agents
- chlorphentermine
- clortermine
- dextroamphetamine
- diethylpropion
- fenfluramine
- levamphetamine
- phenmetrazine
- phentermine

Anti-Anginal Agents
- amyl nitrite
- bupranolol
- isosorbide dinitrate
- propranolol

Anti-Arrhythmia Agents
- chinidine
- disopyramide
- lidocaine
- mexiletine
- practolol
- procainamide
- propranolol
- quinidine sulfate

Anti-Asthmatics
- aminophylline
- ephedrine
- etofylline
- proxyphylline
- theophylline

Anti-Coagulants
- dicumarol
- heparin
- warfarin

Anti-Emetics

buclizine
chlorpromazine
cyclizine
metoclopramide
prochlorperazine
promethazine
propiomazine
tiapride
trimethobenzamide hydrochloride

Anti-Inflammatory Agents (Steroidal)
fludrocortisone

Anti-Parkinsonism Agents
levodopa
procyclidine

Anticonvulsants (Anti-Epileptics)
bromine
carbamazepine
clonazepam
ethosuximide
mephenytoin
methsuximide
nitrazepam
phenobarbital
phenytoin
primidone
sulthiame
valproate sodium

Antidepressants
amitriptyline
clomipramine
desipramine
doxepin
imipramine
isocarboxazid
lithium
mianserin
nomifensine
nortriptyline
oxypertine
phenelzine
protriptyline
tandamine
tranylcypromine
trazodone
viloxazine

Antidiarrhea Agents
difenoxin

Antiflatulents (Carminatives)
myristica

Antifungal Antibiotics
flucytosine

Antihistamine Agents
Actifed(R) (pseudoephedrine HCl + triprolidine HCl)
azatadine
chlorpheniramine
clemastine
cyclizine
dexchlorpheniramine
diphenhydramine
diphenylpyraline
Dristan(R) (phenylephrine HCl + chlorpheniramine maleate + aspirin)
hydroxyzine
ketotifen
mebhydrolin
methapyrilene

phenindamine
terfenadine
tripelennamine
triprolidine hydrochloride

Antineoplastic Agents
fluorouracil
methotrexate
procarbazine
testolactone
vinblastine sulfate
vincristine sulfate

Antituberculars
cycloserine
rifampin

Barbiturates
amobarbital
barbital
butabarbital
butalbital
heptabarbital
methohexital
pentobarbital
phenobarbital
secobarbital
Tuinal(R) (amobarbital sodium + secobarbital sodium)

Blood Derivatives
albumin
bilirubin
purine
pyrimidine

Cannabis Sativa L. and Related Agents
cannabichromene
cannabichromenic acid
cannabicyclol
cannabidiol
cannabidiolic acid
cannabielsoic acid
cannabigerol
cannabigerolic acid
cannabinol
cannabinolic acid
hashish
marijuana
delta-1-tetrahydrocannabinolic acid

Cannabis Sativa L. and Related Agents
delta-8-tetrahydrocannabinol
delta-9-tetrahydrocannabinol
delta-9-trans-tetrahydrocannabinol

Cardiac Glycosides
digitalis
digitoxin
digoxin

Cephalosporins
cefazolin
cephalexin
cephalothin
cephradine

Decongestant and Cold Preparations
phenylephrine
phenylpropanolamine
pseudoephedrine

Diagnostic Agents
diatrizoic acid

iodipamide

Diuretics
- bendroflumethiazide
- cyclothiazide
- methyclothiazide
- spironolactone

Emetics
- apomorphine

Enzyme Inhibitors
- allopurinol
- oxypurinol

Estrogens
- estradiol
- estrogen
- piperazine estrone sulfate

Expectorant and Cough Preparations (Antitusive Agents)
- codeine

Ganglionic Blocking and Stimulating Agents
- 2,5-dimethoxy-4-methylamphetamine (DOM) (STP)
- nicotine

Gases
- carbon monoxide
- nitrous oxide
- oxygen

General Anesthetics
- enflurane
- halothane
- hexobarbital
- nitrous oxide
- propanidid
- thiopental

Hallucinogens and Related Agents
- bufotenine
- cyclohexamine (PCE)
- N,N-diethyltryptamine (DET)
- N,N-dimethyltryptamine (DMT)
- 2,5-dimethoxy-4-bromoamphetamine (DOB)
- 2,5-dimethoxy-4-methylamphetamine (DOM) (STP)
- lysergic acid diethylamide (LSD)
- mescaline
- 5-methoxy-3,4-methylenedioxyamphetamine (MMDA)
- 4-methoxyamphetamine (PMA)
- methylenedioxyamphetamine (MDA)
- myristica
- nitrous oxide
- phencyclidine
- phenethylamine (PEA)
- 1(1-phenylcyclohexyl) pyrrolidine
- psilocin
- psilocybin
- 3,4,5-trimethoxyamphetamine
- yohimbine

Heavy Metals and Heavy Metal Antagonists
- copper
- lead
- mercury
- zinc

Hypotensive (Antihypertensive) Agents
- bendroflumethiazide
- clonidine
- cyclothiazide
- methyclothiazide

methyldopa
propranolol
reserpine
trimethaphan camsylate

Insulins
insulin

Laxatives
dioctyl sodium sulfosuccinate

Local Anesthetics
coca
cocaine
lidocaine
mepivacaine
prilocaine
procaine

Major Tranquilizers (Antipsychotics and Neuroleptics)
butaperazine maleate
chlorpromazine
chlorprothixene
clazepam
clozapine
droperidol
flupentixol
fluphenazine
halazepam
haloperidol
loxapine
mesoridazine
perazine
perphenazine
prochlorperazine
promethazine
reserpine
sulforidazine
sulpiride
thioridazine
tiapride
trifluoperazine
triflupromazine hydrochloride

Metabolites of Drugs and Other Agents
7-acetamido clonazepam
6-O-acetylmorphine
N-acetylprocainamide
7-amino clonazepam
benzoylecgonine
carbamazepine-10,11-epoxide
demethylchloroimipramine
N-1-desalkylflurazepam
N-1-desalkyl-3-hydroxyflurazepam
desmethylchlordiazepoxide
N-desmethyldiazepam
desmethyldoxepin
didesethylflurazepam
10,11-dihydroxycarbamazepine
2-ethylidene-1,5,-dimethyl-3,3-diphenylpyrrolidine
flurazepam-N-1-acetic acid
N-1-hydroxyethylflurazepam
4-hydroxy-2-ethyl-2-phenylglutarimide
10-hydroxynortriptyline
3-hydroxypinazepam
monodesethylflurazepam
morphine 3-ethereal sulfate
morphine 3-glucuronide
morphine 3,6-diglucuronide
morphine 6-glucuronide
normeperidine
normorphine
normorphine 6-glucuronide

norpropoxyphene
oxazepam
psilocybin
ritalinic acid
temazepam
delta-1-tetrahydrocannabinolic acid
11-nor-delta-9-THC-9-carboxylic acid

Minor Tranquilizers (Anti-Anxiety and Ataractics)
bromazepam
buclizine
chlordesmethyldiazepam
chlordiazepoxide
clobazam
clorazepate
N-desmethyldiazepam
diazepam
etifoxine
hydroxyzine
lorazepam
medazepam
meprobamate
methyloxazepam
oxanamide
oxazepam
phenaglycodol
pinazepam
temazepam
tofizopam
trazodone
triflubazam (ORF 8063)
tybamate

Miotics
echothiophate iodide

Muscle Relaxants (Central)
benzoctamine
carisoprodol
diazepam

Mydriatics
atropine sulfate
scopolamine
tropicamide

Neurochemicals, Neurotransmitters, and Neurohormones
gamma-hydroxybutyric acid (GABA)
levarterenol
serotonin

Neuromuscular Blocking (Antimuscarinic) Agents
clidinium bromide
isopropamide
propantheline

Nonbarbiturates
benzoctamine
bromine
carbromal
chloral hydrate
chlormethiazole
diphenhydramine
ethanol (ethyl alcohol)
ethchlorvynol
flunitrazepam
flurazepam
fosazepam
glutethimide
hydroxyzine
methaqualone
methotrimeprazine
methyprylon

nitrazepam
propiomazine
triazolam

Opiates and Related Agents
1-alpha-acetylmethadol
apomorphine
codeine
difenoxin
fentanyl
heroin
hydromorphone
ketobemidone
levallorphan
methadone
morphine
nalorphine
naloxone
naltrexone
norcodeine
normorphine
opium
pentazocine
pethidine

Oral Contraceptives
ethynodiol diacetate

Oral Hypoglycemics
acetohexamide
chlorpropamide
phenformin
tolbutamide

Other Anti-Infective Agents
nitrofurantoin
trimethoprim

Other Antibiotics
amikacin
chloramphenicol
erythromycin
gentamicin

Other Cardiovascular Agents
ephedrine

Other CNS Agents
3-(2-benzylmethylaminoethyl) benzoic acid methyl ester hydrochloride (PRL-8-53)
fenmetozole
lithium

Other Electrolytic, Caloric, and Water Balance Agents
cyclamate

Other Toxicants
butyl nitrite
glue (model builder's)
paint, spray

Parasympatholytic (Cholinergic Blocking) Agents
atropine sulfate
clidinium bromide
Donnatal(R) (phenobarbital + atropine sulfate + hyoscine HBr + hyoscyamine sulfate)
isopropamide
methscopolamine
myristica
physostigmine
procyclidine
propantheline
scopolamine

Penicillins

ampicillin
cloxacillin
methicillin
penicillin V potassium

Pituitary
$ACTH_{4-10}$ (Org OI-63)
luteinizing hormone (LH)

Plasmodicides
amodiaquine
chloroquine
hydroxychloroquine
quinine

Progestogens
hydroxyprogesterone
norethindrone
norgestrel

Sedatives and Hypnotic Agents
apronalide
Mandrax(R) (methaqualone + diphenhydramine)

Skin and Mucous Membrane Preparations
salicylic acid
triclobisonium chloride

Stimulants
amphetamine
1-benzylpiperazine
caffeine
clortermine
coca
cocaine
cotinine
dextroamphetamine
ephedrine
ethamivan
fenethylline
kola
levamphetamine
methamphetamine
methylphenidate
nicotine
theophylline

Sulfonamides
sulfadiazine
sulfameter
sulfamethoxazole
sulfasalazine
sulfisoxazole

Sulfones
dapsone

Sympatholytic (Adrenergic Blocking) Agents
atenolol

Sympathomimetic (Adrenergic) Agents
chlorphentermine
dextroamphetamine
diethylpropion
dopamine
ephedrine
fenfluramine
isoproterenol
levarterenol
phentermine
phenylephrine
phenylpropanolamine
pseudoephedrine

Thyroid and Anti-Thyroid
- levothyroxine

Trichomonacides
- metronidazole

Unclassified Agents
- calcium carbimide
- disulfiram
- ginseng
- 3-methylamino-1,1 diphenylprop-1-ene (BW247)
- Mobiletten(R)
- oxyphencycline
- 1-phenylcyclohexalamine
- 1-piperidinocyclohexane-carbonitrile
- tobacco
- trithiozine
- tryptamine
- UK-14,304

Uricosurics and Other Antigout Agents
- allopurinol

Vasodilating Agents
- amyl nitrite
- hexobendine
- Instenon(R) (hexobendine + etamivan + etofylline)
- oxprenolol
- papaverine
- pindolol

Vitamins
- copper
- alpha-tocopheryl acetate
- l-tryptophan
- vitamin B complex
- zinc

Volatile Solvents
- chloroform
- ethylbenzene
- gasoline
- xylene

9.3 Drug Classification Scheme

1-00-0 Central Nervous System (CNS) Agents

1-01-0 Anesthetics

1-01-1 Local Anesthetics
- coca
- cocaine
- lidocaine
- mepivacaine
- prilocaine
- procaine

1-01-2 General Anesthetics
- enflurane
- halothane
- hexobarbital
- nitrous oxide
- propanidid
- thiopental

1-02-0 Anticonvulsants (Anti-Epileptics)
- bromine
- carbamazepine
- clonazepam
- ethosuximide
- mephenytoin
- methsuximide
- nitrazepam
- phenobarbital
- phenytoin
- primidone
- sulthiame
- valproate sodium

1-03-0 Antidepressants
- amitriptyline
- clomipramine
- desipramine
- doxepin
- imipramine
- isocarboxazid
- lithium
- mianserin
- nomifensine
- nortriptyline
- oxypertine
- phenelzine
- protriptyline
- tandamine
- tranylcypromine
- trazodone
- viloxazine

1-04-0 Cannabis Sativa L. and Related Agents
- cannabichromene
- cannabichromenic acid
- cannabicyclol
- cannabidiol
- cannabidiolic acid
- cannabielsoic acid
- cannabigerol
- cannabigerolic acid
- cannabinol
- cannabinolic acid
- hashish
- marijuana
- delta-1-tetrahydrocannabinolic acid

delta-8-tetrahydrocannabinol
delta-9-tetrahydrocannabinol
delta-9-trans-tetrahydrocannabinol

1-05-0 Hallucinogens and Related Agents
bufotenine
cyclohexamine (PCE)
N,N-diethyltryptamine (DET)
N,N-dimethyltryptamine (DMT)
2,5-dimethoxy-4-bromoamphetamine (DOB)
2,5-dimethoxy-4-methylamphetamine (DOM) (STP)
lysergic acid diethylamide (LSD)
mescaline
5-methoxy-3,4-methylenedioxyamphetamine (MMDA)
4-methoxyamphetamine (PMA)
methylenedioxyamphetamine (MDA)
myristica
nitrous oxide
phencyclidine
phenethylamine (PEA)
1(1-phenylcyclohexyl) pyrrolidine
psilocin
psilocybin
3,4,5-trimethoxyamphetamine
yohimbine

1-06-0 Opiates and Related Agents
1-alpha-acetylmethadol
apomorphine
codeine
difenoxin
fentanyl
heroin
hydromorphone
ketobemidone
levallorphan
methadone
morphine
nalorphine
naloxone
naltrexone
norcodeine
normorphine
opium
pentazocine
pethidine

1-07-0 Stimulants
amphetamine
1-benzylpiperazine
caffeine
clortermine
coca
cocaine
cotinine
dextroamphetamine
ephedrine
ethamivan
fenethylline
kola
levamphetamine
methamphetamine
methylphenidate
nicotine
theophylline

1-08-0 Sedatives and Hypnotic Agents
apronalide
Mandrax(R) (methaqualone + diphenhydramine)

1-08-1 Barbiturates
- amobarbital
- barbital
- butabarbital
- butalbital
- heptabarbital
- methohexital
- pentobarbital
- phenobarbital
- secobarbital
- Tuinal(R) (amobarbital sodium + secobarbital sodium)

1-08-2 Nonbarbiturates
- benzoctamine
- bromine
- carbromal
- chloral hydrate
- chlormethiazole
- diphenhydramine
- ethanol (ethyl alcohol)
- ethchlorvynol
- flunitrazepam
- flurazepam
- fosazepam
- glutethimide
- hydroxyzine
- methaqualone
- methotrimeprazine
- methyprylon
- nitrazepam
- propiomazine
- triazolam

1-09-0 Tranquilizers

1-09-1 Major Tranquilizers (Antipsychotics and Neuroleptics)
- butaperazine maleate
- chlorpromazine
- chlorprothixene
- clazepam
- clozapine
- droperidol
- flupentixol
- fluphenazine
- halazepam
- haloperidol
- loxapine
- mesoridazine
- perazine
- perphenazine
- prochlorperazine
- promethazine
- reserpine
- sulforidazine
- sulpiride
- thioridazine
- tiapride
- trifluoperazine
- triflupromazine hydrochloride

1-09-2 Minor Tranquilizers (Anti-Anxiety and Ataractics)
- bromazepam
- buclizine
- chlordesmethyldiazepam
- chlordiazepoxide
- clobazam
- clorazepate
- N-desmethyldiazepam
- diazepam
- etifoxine
- hydroxyzine
- lorazepam
- medazepam

meprobamate
methyloxazepam
oxanamide
oxazepam
phenaglycodol
pinazepam
temazepam
tofizopam
trazodone
triflubazam (ORF 8063)
tybamate

1-10-0 Other CNS Agents
3-(2-benzylmethylaminoethyl) benzoic acid methyl ester hydrochloride (PRL-8-53)
fenmetozole
lithium

2-00-0 Autonomic Nervous System (ANS) Agents

2-01-0 Parasympathomimetic (Cholinergic) Agents

2-02-0 Parasympatholytic (Cholinergic Blocking) Agents
atropine sulfate
clidinium bromide
Donnatal(R) (phenobarbital + atropine sulfate + hyoscine HBr + hyoscyamine sulfate)
isopropamide
methscopolamine
myristica
physostigmine
procyclidine
propantheline
scopolamine

2-03-0 Sympathomimetic (Adrenergic) Agents
chlorphentermine
dextroamphetamine
diethylpropion
dopamine
ephedrine
fenfluramine
isoproterenol
levarterenol
phentermine
phenylephrine
phenylpropanolamine
pseudoephedrine

2-04-0 Sympatholytic (Adrenergic Blocking) Agents
atenolol

2-05-0 Ganglionic Blocking and Stimulating Agents
2,5-dimethoxy-4-methylamphetamine (DOM) (STP)
nicotine

2-06-0 Muscle Relaxants and Spasmolitic Agents

2-06-1 Muscle Relaxants (Central)
benzoctamine
carisoprodol
diazepam

2-06-2 Neuromuscular Blocking (Antimuscarinic) Agents
clidinium bromide
isopropamide
propantheline

2-06-3 Neuromuscular Blocking (Depolarizing) Agents

2-07-0 Other ANS Agents

3-00-0 Cardiovascular Agents

3-01-0 Anti-Arrhythmia Agents
chinidine
disopyramide
lidocaine
mexiletine
practolol
procainamide
propranolol
quinidine sulfate

3-02-0 Hypotensive (Antihypertensive) Agents
bendroflumethiazide
clonidine
cyclothiazide
methyclothiazide
methyldopa
propranolol
reserpine
trimethaphan camsylate

3-03-0 Cardiac Glycosides
digitalis
digitoxin
digoxin

3-04-0 Vasoconstricting Agents

3-05-0 Vasodilating Agents
amyl nitrite
hexobendine
Instenon(R) (hexobendine + etamivan + etofylline)
oxprenolol
papaverine
pindolol

3-06-0 Antilipemic (Anticholesteremic) Agents

3-07-0 Anti-Anginal Agents
amyl nitrite
bupranolol
isosorbide dinitrate
propranolol

3-99-0 Other Cardiovascular Agents
ephedrine

4-00-0 Gastrointestinal (GI) Agents

4-01-0 Antacids and Adsorbants

4-02-0 Antidiarrhea Agents
difenoxin

4-03-0 Antiflatulents (Carminatives)
myristica

4-04-0 Cathartics and Laxatives

4-04-1 Cathartics

4-04-2 Laxatives
dioctyl sodium sulfosuccinate

4-05-0 Digestants

4-06-0 Emetics and Anti-Emetics

4-06-1 Emetics
apomorphine

4-06-2 Anti-Emetics
buclizine
chlorpromazine
cyclizine
metoclopramide
prochlorperazine
promethazine
propiomazine
tiapride
trimethobenzamide hydrochloride

4-99-0 Other GI Agents

5-00-0 Anti-Infective and Antineoplastic Agents

5-01-0 Amebicides

5-02-0 Anthelmintics

5-03-0 Antibiotics

5-03-1 Antifungal Antibiotics
flucytosine

5-03-2 Cephalosporins
cefazolin
cephalexin
cephalothin
cephradine

5-03-3 Penicillins
ampicillin
cloxacillin
methicillin
penicillin V potassium

5-03-4 Tetracyclines

5-03-5 Other Antibiotics
amikacin
chloramphenicol
erythromycin
gentamicin

5-04-0 Antituberculars
cycloserine
rifampin

5-05-0 Antivirals

5-06-0 Plasmodicides
amodiaquine
chloroquine
hydroxychloroquine
quinine

5-07-0 Sulfonamides
sulfadiazine
sulfameter
sulfamethoxazole
sulfasalazine
sulfisoxazole

5-08-0 Sulfones
dapsone

5-09-0 Treponemicides

5-10-0 Trichomonacides
metronidazole

5-11-0 Other Anti-Infective Agents
nitrofurantoin
trimethoprim

5-12-0 Antineoplastic Agents
fluorouracil
methotrexate
procarbazine
testolactone
vinblastine sulfate
vincristine sulfate

6-00-0 Other Therapeutic Agents

6-01-0 Antihistamine Agents
Actifed(R) (pseudoephedrine HCl + triprolidine HCl)
azatadine
chlorpheniramine
clemastine
cyclizine
dexchlorpheniramine
diphenhydramine
diphenylpyraline
Dristan(R) (phenylephrine HCl + chlorpheniramine maleate + aspirin)
hydroxyzine
ketotifen
mebhydrolin
methapyrilene
phenindamine
terfenadine
tripelennamine
triprolidine hydrochloride

6-02-0 Blood Derivatives, Formulation and Coagulation

6-02-1 Blood Derivatives
albumin
bilirubin
purine
pyrimidine

6-02-2 Anti-Anemia Agents

6-02-3 Coagulants

6-02-4 Anti-Coagulants
dicumarol
heparin
warfarin

6-02-5 Hemostatics

6-02-6 Thrombolitic Agents

6-03-0 Electrolytic, Caloric, and Water Balance Agents

6-03-1 Diuretics
bendroflumethiazide
cyclothiazide
methyclothiazide
spironolactone

6-03-2 Uricosurics and Other Antigout Agents
allopurinol

6-03-3 Caloric Agents

6-03-4 Other Electrolytic, Caloric, and Water Balance Agents
cyclamate

6-04-0 Antinauseants, Antivertigo, and Antimigraine Agents

6-05-0 Expectorant and Cough Preparations (Antitusive Agents)
codeine

6-06-0 Eye, Ear, Nose, and Throat (EENT) Preparations

6-06-1 Miotics
echothiophate iodide

6-06-2 Mydriatics
atropine sulfate
scopolamine
tropicamide

6-06-3 Vasoconstrictors (EENT)

6-06-4 Decongestant and Cold Preparations
phenylephrine
phenylpropanolamine
pseudoephedrine

6-06-5 Other EENT Preparations

6-07-0 Anti-Parkinsonism Agents
levodopa
procyclidine

6-08-0 Anorectic (Appetite Control) Agents
chlorphentermine
clortermine
dextroamphetamine
diethylpropion
fenfluramine
levamphetamine
phenmetrazine
phentermine

6-09-0 Analgesics and Antipyretics
acetaminophen
alclofenac
aminopyrine
antipyrine
carbamazepine
cyclazocine
Distalgesic(R) (dextropropoxyphene + acetaminophen)
hydroxychloroquine
indomethacin
methotrimeprazine
phenacetin
phenazopyridine
phenylbutazone
propoxyphene
propyphenazone
salicylate
tramadol

6-10-0 Anti-Inflammatory Agents (Steroidal)
fludrocortisone

6-11-0 Skin and Mucous Membrane Preparations
salicylic acid
triclobisonium chloride

6-12-0 Anti-Asthmatics
- aminophylline
- ephedrine
- etofylline
- proxyphylline
- theophylline

7-00-0 Hormones, Synthetic Substitutes, and Antagonists

7-01-0 Adrenals
- corticosterone
- dexamethasone
- fludrocortisone
- methylprednisolone sodium succinate
- triamcinolone

7-02-0 Androgens
- testosterone

7-03-0 Estrogens
- estradiol
- estrogen
- piperazine estrone sulfate

7-04-0 Progestogens
- hydroxyprogesterone
- norethindrone
- norgestrel

7-05-0 Oral Contraceptives
- ethynodiol diacetate

7-06-0 Gonadotropins

7-07-0 Other Corpus Luteum Hormones

7-08-0 Oxytocics

7-09-0 Insulins and Anti-Diabetic Agents

7-09-1 Insulins
- insulin

7-09-2 Oral Hypoglycemics
- acetohexamide
- chlorpropamide
- phenformin
- tolbutamide

7-10-0 Thyroid and Anti-Thyroid
- levothyroxine

7-11-0 Parathyroid

7-12-0 Pituitary
- $ACTH_{4-10}$ (Org OI-63)
- luteinizing hormone (LH)

7-13-0 Prostaglandins

7-14-0 Neurochemicals, Neurotransmitters, and Neurohormones
- gamma-hydroxybutyric acid (GABA)
- levarterenol
- serotonin

7-15-0 Hypothalamus

7-99-0 Miscellaneous Hormonal and Related Agents

8-00-0 Other Chemical Agents and Substances

8-01-0 Enzymes and Enzyme Inhibitors

8-01-1 Enzymes

8-01-2 Enzyme Inhibitors
allopurinol
oxypurinol

8-02-0 Vitamins
copper
alpha-tocopheryl acetate
l-tryptophan
vitamin B complex
zinc

8-03-0 Serum, Toxoids, and Vaccines

8-04-0 Heavy Metals and Heavy Metal Antagonists
copper
lead
mercury
zinc

8-05-0 Radioactive Agents

8-06-0 Diagnostic Agents
diatrizoic acid
iodipamide

8-07-0 Food Additives

8-08-0 Metabolites of Drugs and Other Agents
7-acetamido clonazepam
6-O-acetylmorphine
N-acetylprocainamide
7-amino clonazepam
benzoylecgonine
carbamazepine-10,11-epoxide
demethylchloroimipramine
N-1-desalkylflurazepam
N-1-desalkyl-3-hydroxyflurazepam
desmethylchlordiazepoxide
N-desmethyldiazepam
desmethyldoxepin
didesethylflurazepam
10,11-dihydroxycarbamazepine
2-ethylidene-1,5,-dimethyl-3,3-diphenylpyrrolidine
flurazepam-N-1-acetic acid
N-1-hydroxyethylflurazepam
4-hydroxy-2-ethyl-2-phenylglutarimide
10-hydroxynortriptyline
3-hydroxypinazepam
monodesethylflurazepam
morphine 3-ethereal sulfate
morphine 3-glucuronide
morphine 3,6-diglucuronide
morphine 6-glucuronide
normeperidine
normorphine
normorphine 6-glucuronide
norpropoxyphene
oxazepam
psilocybin
ritalinic acid
temazepam
delta-1-tetrahydrocannabinolic acid

11-nor-delta-9-THC-9-carboxylic acid

8-99-0 Unclassified Agents
- calcium carbimide
- disulfiram
- ginseng
- 3-methylamino-1,1 diphenylprop-1-ene (BW247)
- Mobiletten(R)
- oxyphencycline
- 1-phenylcyclohexalamine
- 1-piperidinocyclohexane-carbonitrile
- tobacco
- trithiozine
- tryptamine
- UK-14,304

9-00-0 Environmental Gases, Toxicants, and Pollutants

9-01-0 Gases
- carbon monoxide
- nitrous oxide
- oxygen

9-02-0 Air Pollutants

9-03-0 Pesticides

9-04-0 Herbicides

9-05-0 Insecticides

9-06-0 Volatile Solvents
- chloroform
- ethylbenzene
- gasoline
- xylene

9-07-0 Other Toxicants
- butyl nitrite
- glue (model builder's)
- paint, spray

DRUGS AND DRIVING:

A SELECTED BIBLIOGRAPHY

SUPPLEMENT THREE

APPENDIX B

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DRUGS AND DRIVING:

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APPENDIX D

ABSTRACT INDEX

UM-74-A0022

DRUGS AND SEX: THE NONMEDICAL USE OF DRUGS AND SEXUAL BEHAVIOR, P. Ferguson; T. Lennox; D.J. Lettieri, eds., NIDA Research Issues 2 (Nov 1974)

Presented here are summaries of the major research findings dealing with the nonmedical use of drugs and sexual behavior. This volume is intended especially for the researcher who lacks the time to scan all current information published in his area of interest. The predominant focus is on empirical research findings and major theoretical approaches published between January 1958 and January 1974 in the English language.

The summaries in this volume are classified into five sections. The first section includes studies dealing with multidrug effects on sexual experience. Comparisons were made of the effects of alcohol, marijuana, barbiturates, amphetamines, cocaine, amylnitrate, and heroin in heterosexual, homosexual, and bisexual users. The following sections include studies investigating the effects of marijuana, amphetamine, LSD, heroin, and methadone on sexual activity. Data concerning the sexual lives of the subjects vary widely from study to study and results often appear contradictory at this time.

Each summary is formulated and detailed to provide the reader with the purpose, methodology, findings, and conclusions of the original study. (HSRI)

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-184

KEYWORDS: Compilation. Review: Drug Use.

UM-74-A0023

DRUGS AND ATTITUDE CHANGE, P. Ferguson; T. Lennox; D.J. Lettieri, eds., NIDA Research Issues 3 (Nov 1974)

Presented here are summaries of the major research findings dealing with attitude and attitude change toward nonmedical drug use. This volume is intended especially for the researcher who lacks the time to scan all current information published in his area of interest The predominant focus is on empirical research findings and major theoretical approaches published between January 1958 and January 1974.

The summaries in this volume are classified into three sections. The first section concerns information about drugs and contains studies pertaining to such topics as the tendency of drug users to selectively expose themselves to information about drugs; the effect of school, family, news media, and personal experience; and drug education.

The second section of papers deals with user and nonuser attitudes toward drugs, and factors in attitude change in illicit drug use. The third section deals with such topics as communication processes in terms of verbal communication and social influence, public education, communication between drug therapists and patients, and the influence of setting on communication processes. (HSRI)

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-185

KEYWORDS: Compilation. Other Sociolegal Study. Review: Drug Use.

UM-74-A0024

DRUGS AND FAMILY/PEER INFLUENCE, P. Ferguson; T. Lennox; D.J. Lettieri, eds., NIDA Research Issues 4 (Nov 1974)

Presented here are summaries of the major research findings dealing with family and peer influences on adolescent drug use. This volume is intended especially for the researcher who lacks the time to scan all current information published in his area of

interest. The predominant focus is on empirical research findings and major theoretical approaches published between January 1958 and January 1974 in the English language.

The summaries in this volume are organized in five sections: (1) groups and gangs in the world of youthful drug use; (2) prediction factors for marijuana use; (3) the influence and interaction of the family of the addict; (4) parents as models; and (5) developmental factors related to childhood experience.

Each summary is formulated and detailed to provide the reader with the purpose, methodology, findings, and conclusions of the original study. (HSRI)

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-186

KEYWORDS: Compilation. Review: Drug Use.

UM-74-A0025

DRUGS AND PREGNANCY: THE EFFECTS OF NONMEDICAL USE OF DRUGS ON PREGNANCY, CHILDBIRTH, AND NEONATES, P. Ferguson; T. Lennox; D.J. Lettieri, eds., NIDA Research Issues 5 (Nov 1974)

Presented here are summaries of the major research findings dealing with drugs and pregnancy, particularly with the effects of nonmedical use of drugs on pregnancy, childbirth, and neonates. This volume is intended especially to aid researchers who find it difficult to scan all current information published in their area of interest. The predominant focus is on empirical research findings and major theoretical approaches published between January 1958 and January 1974 in the English language.

The summaries are organized into six sections: (1) overviews of genetics, epidemiology, and the effects of drugs on neonates; (2) literature reviews, chromosome studies, and teratogenesis studies relating to LSD; (3) the effects of heroin on mother and child, characteristics of neonates born to heroin users, and neonatal withdrawal management; (4) methadone; (5) comparative studies of the effects of methadone and heroin; and (6) selected briefly annotated studies.

Each summary is formulated and detailed to provide the reader with the purpose, methodology, findings, and conclusions of the original study. (HSRI)

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-187

KEYWORDS: Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Opiates and Related Agents: heroin. methadone. Compilation. Review: Drug Effects. Review: Drug Use.

UM-74-A0026

DRUGS AND DEATH: THE NONMEDICAL USE OF DRUGS RELATED TO ALL MODES OF DEATH, P. Ferguson; T. Lennox; D.J. Lettieri, eds., NIDA Research Issues 6 (Nov 1974)

Presented here are summaries of the major reseach findings dealing with the nonmedical use of drugs and their relationship to all modes of death. This volume is intended to aid researchers who find it difficult to find the time to scan all the information published in their area of interest. The predominant focus is on empirical research findings and major theoretical approaches published between January 1958 and January 1974 in the English language.

The summaries of the research findings are organized into six categories: (1) classification and reporting systems; (2) suicide and homicide; (3) opiate related death (incidence and cause); (4) opiate related death caused by infectious disease; and (5) death caused by abuse of inhalants, stimulants, analgesics, methadone, LSD, cannabis, and multidrugs; and (6) pathological findings of opiate-related deaths. For each paper a statement of purpose, a summary of the findings, methodology, theory, and practical conclusions are provided. (HSRI)

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-188

KEYWORDS: Opiates and Related Agents. Compilation. Review: Drug Effects. Review: Drug Use.

UM-74-A0027

DRUGS AND ADDICT LIFESTYLES: LIFESTYLE HISTORIES OF HEROIN USERS, P. Ferguson; T. Lennox; D.J. Lettieri, eds., NIDA Research Issues 7 (Nov 1974)

Presented here are summaries of the major research findings of the last fifteen years dealing with drugs and addict lifestyles. This volume is intended to aid researchers who find it difficult to find the time to scan all the information published in their area of interest. The predominant focus is on empirical research findings and major theoretical approaches.

Research findings are presented in five major categories: (1) life styles of heroin addicts, including typologies and careers; (2) the natural history of addiction beginning with the occasional user through the mature addict; (3) characteristics of heroin addicts, including psychosocial patterns and sexual and racial trends; (4) drug use patterns; and (5) theories of addiction.

For each research paper is provided a summary of purpose, methodology or theory used, major findings, and practical conclusions. (HSRI)

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-189

KEYWORDS: Opiates and Related Agents: heroin. Compilation. Review: Drug Effects. Review: Drug Use.

UM-74-A0028

A COCAINE BIBLIOGRAPHY-NONANNOTATED, J.L. Phillips; R.D. Wynne, eds., NIDA Research Issues 8 (Nov 1974)

This bibliography includes over eighteen hundred references from the scientific and popular literature on the socio-psychological, biomedical, political, and economic aspects of cocaine and to a lesser extent, coca, from 1585 to the present. This bibliography is a listing of the body of literature to be examined in development of a future monograph which will incorporate annotations of the major references in the field, statistical information concerning the use and abuse of cocaine, and the results of field studies of current street myths and rituals involving cocaine.

The bibliography is subdivided into four major sections: (1) newspaper stories and articles from the popular literature; (2) books on cocaine and coca; (3) documents, pamphlets, and government publications; and (4) scientific and technical journal articles. (AAM)

U.S. Department of Health, Education, and Welfare publication no. (ADM) 75-203

KEYWORDS: Local Anesthetics: cocaine. Stimulants: cocaine. Compilation.

UM-79-A0029

BIBLIOGRAPHY OF THE SOLVENT ABUSE LITERATURE, G.E. Barnes; B.A. Vulcano, International Journal of the Addictions, v14 n3 p401-21 (1979)

Presented here is a nonannotated bibliography of experimental and epidemiological literature dealing with solvent abuse. It is arranged alphabetically by author and emphasizes recently published journal articles in the English language. The bibliography includes references from previous bibliographies prepared in this area and recent references from Index Medicus and Psychological Abstracts. It includes approximately five hundred references. (HSRI)

KEYWORDS: Volatile Solvents. Review: Drug Use.

UM-78-A0030

PHENCYCLIDINE: A BIBLIOGRAPHY OF BIOMEDICAL AND BEHAVIORAL RESEARCH, R.L. Balster; R.S. Pross, Journal of Psychedelic Drugs, v10 n1 p1-15 (Jan-Mar 1978)

This bibliography covers the chemical, biomedical, and behavioral research literature dealing with phencyclidine published in the English language professional literature through early 1978. The major purpose of this bibliography is to facilitate phencyclidine research. It attempts to be exhaustive; however, it does not include

articles in the popular press, predominantly social-cultural studies, or the political-legal literature on PCP, nor does it include papers dealing with the use of the drug in veterinary practice, with PCP analogues, or with ketamine. Approximately two hundred nonannotated entries are listed alphabetically by author. (HSRI)

KEYWORDS: Hallucinogens and Related Agents: phencyclidine. Review: Drug Use.

UM-78-A0031

BIBLIOGRAPHIC CITATIONS ON DRIVING BY SPECIAL POPULATIONS AND THE MEDICALLY IMPAIRED, T.J. Naughton; J. Waller (1978)

This bibliography lists journal articles, books, government reports, and professional association publications concerning driving by the medically impaired and by special populations such as the elderly, youth, the physically and mentally handicapped, criminal offenders, and racial minorities. The publications listed are nearly all in the English language and are current through 1977. The bibliography is comprised of over four hundred nonannotated entries arranged alphabetically by author. (HSRI)

Dunlap and Associates, University of Vermont;

KEYWORDS: Compilation.

UM-78-A0031

BIBLIOGRAPHIC CITATIONS ON DRIVING BY SPECIAL POPULATIONS AND THE MEDICALLY IMPAIRED, T.J. Naughton; J. Waller (1978)

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Dunlap and Associates, University of Vermont;

KEYWORDS: Compilation.

UM-74-B0017

DRUG ISSUES IN GEROPSYCHIATRY, W.E. Fann; G.L. Maddox, eds., Baltimore: Williams and Wilkins (1974)

This volume represents the proceedings of the Conference on Psychopharmacology and the Management of the Elderly Patient held at Duke University in June 1973. The purpose of this conference was to bring together basic and clinical scientists, practicing clinicians, nurses, and other mental health professionals for a mutual exchange of ideas and data on the issue of the crucial role of pharmacological agents in psychiatric treatment of the aged. The scientists, clinicians, nurses, and medical sociologists whose work is presented here define and attempt to provide solutions to many of the problems encountered when psychotropic drugs are required in the care of the geriatric patient. In the first half of the volume the choice of agents, expected benefits, and possible detriments, as well as the biochemical systems affected by psychotropics, are considered. In the following section, the various interactions between patients and professionals, between professional colleagues, and between patients and the clinical environment as they converge around the central issues of drug management, efficacy, and safety are considered. (AAM)

122 pages 185 refs

KEYWORDS: Compilation.

UM-72-B0018

HUMAN FACTORS IN HIGHWAY TRAFFIC SAFETY RESEARCH, T.W. Forbes, ed., New York: John Wiley and Sons (1972)

Human capabilities are an essential consideration in the design of man-machine environmental systems for highway safety. Important research on human factors has been conducted during the past forty years, but reports of this research have previously been limited to scattered journals and specialized reviews. This book brings together investigations from many diverse areas of engineering, psychology, and highway safety in order that they might be studied in a unified way.

The book consists of seventeen chapters, each written by a specialist in a particular area of human factors studies. The introduction surveys the social importance of highway safety. Subsequent chapters treat such topics as characteristics of drivers, highway signs, skills and judgment, vehicle design, effects of driver fatigue, and the pedestrian. A chapter on the effects of alcohol and drugs on driving behaviors discusses the actions of sedatives, hypnotics, barbiturates, analgesics, pain reducers, psychotherapeutic drugs, antidepressants, central nervous system stimulants, antihistamines, hallucinogens, and other drugs. (AAM)

419 pages

KEYWORDS: Compilation.

UM-78-B0019

DRUGS, SOCIETY AND HUMAN BEHAVIOR. SECOND EDITION, O. Ray, St. Louis: The C.V. Mosby Co. (1978)

This book deals with drugs, drug use, and drug users. Its purpose is to enable the reader, particularly the college student, to reach a rational point of view on drug-taking behavior by separating fact from fantasy and rhetoric from reason. In addition to presenting the historical perspective on the psychosocial issues raised by advances in pharmacology and changes in society, the book reviews the many new scientific and technical advances affecting drug use.

The book deals with four main drug groups: (1) the "nondrug" drugs such as alcohol, nicotine, caffeine, oral contraceptives, and over-the-counter drugs; (2) psychotherapeutic drugs such as tranquilizers, stimulants, and depressants; (3) narcotics; and (4) hallucinogens, marijuana, and hashish. In addition, a discussion of basic pharmacological principles is presented.

Of particular interest is a discussion of the effects of drugs, including alcohol, on driving. Data from several epidemiological surveys are presented.

The author concludes that while there is some evidence that many drugs, particularly sedatives and drugs for psychiatric disorders, can interfere with a patient's ability to safely drive a car, it can not be determined whether the patient might not be more impaired from uncontrolled anxiety than from the drug used to treat it. (HSRI)

457 pages

KEYWORDS: Cannabis Sativa L. and Related Agents: hashish, marijuana. Ganglionic Blocking and Stimulating Agents: nicotine. Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: caffeine, nicotine. Hallucinogens and Related Agents. Opiates and Related Agents. Oral Contraceptives. Sedatives and Hypnotic Agents. Stimulants. Tranquilizers. Review. Review: Drug Effects. Review: Drug Use. Review: Drugs and Highway Safety.

UM-78-B0020

PHARMACOKINETICS OF PSYCHOACTIVE DRUGS: BLOOD LEVELS AND CLINICAL RESPONSE, L.A. Gottschalk; S. Merlis, eds., New York: Spectrum Publications (1976)

This book consists of papers dealing with pharmacokinetics and clinical response presented at the annual meeting of the American College of Neuropsychopharmacology in December 1974. The papers are organized into two categories: (1) methodological problems and approaches; and (2) the relationship between pharmacokinetics and clinical response. The first category discusses some of the problems encountered by different laboratories and in some instances provides useful and innovative solutions to these problems.

The section on the relationship between pharmacokinetics and clinical response adds more weight to the growing evidence that clinical psychiatric improvement is related to the proper concentration of psychoactive drugs in the blood. Other issues discussed include

the relationship of blood drug levels to clinical response with drug-responders and drug-nonresponders; the differential effects of drug blood levels among psychiatric patients; the relationship of the pharmacokinetics of a single dose of a psychoactive drug to the drug levels ensuing with continuous drug dosage; the prediction of clinical effect with continuous drug dosage based on the clinical effect after a single drug dose; the effect of the ingestion of other chemical substances such as alcohol; and the possible usefulness of electroencephalograms in monitoring the relationship of different drugs to clinical response. (HSRI)

255 pages 274 refs

KEYWORDS: Central Nervous System (CNS) Agents. Compilation.

UM-70-B0021

SEMINAR ON THE MEDICAL ASPECTS OF SAFE DRIVING, TORONTO, MAY 1-2, 1970, Toronto, Canada: Ontario Department of Transport (1970)

Recorded here are dialogues between and papers presented by panel members participating in the Ontario Department of Transport Seminar on the Medical Aspects of Safe Driving in May 1970. The goal of the seminar was to develop better understanding of the complex relationships between driving ability and the physical and mental factors affecting the driver. Top authorities from the medical, psychiatric, psychological, judicial, legal, and administrative fields from many jurisdictions participated in the seminar.

Some of the topics discussed were the relationships between driving ability and defective vision; driving ability and physical impairment; driving ability and psychological factors; and alcohol and driving behavior. Also discussed are recommendations aimed at identifying drivers with physical and mental deficiencies and at establishing standards of medical fitness related to driving competence of drivers of certain types of vehicles. Proposals are developed for solving problems involved in detecting and evaluating physical and mental deficiencies and reporting them to licensing authorities. The role, utilization, and functioning of medical advisory boards relating to driver licensing authorities are reviewed. (HSRI)

67 pages 0 refs

KEYWORDS: Compilation.

UM-79-B0022

HANDBOOK ON DRUG ABUSE, R.I. Dupont; A. Goldstein; J. O'Donnell; B. Brown, Washington, D.C.: U.S. Government Printing Office (Jan 1979)

This handbook is a compilation of recent research findings of forty authors in critical aspects of drug abuse. It has nine major sections: an overview of drug treatment; modalities for narcotic addicts; treatment methods for specific needs; drugs of recent public concern; drug problems in specific populations; psychological studies of drug users; epidemiological studies; and drug treatment in the future.

Special attention has been given to the issue of treatment. Various aspects of treatment are discussed, such as established modalities of treatment for narcotics addicts and their effectiveness; ancillary treatment programs; and treatment of specific populations such as youth, women, the elderly, and minority communities.

A separate section of the book is devoted to specific drugs or doses of drugs, such as PCP and amphetamines. One section looks at drug use from a psychosocial perspective, while another assumes an epidemiological viewpoint. Management, training, and prevention are discussed as special issues. The final section discusses research prospects and concludes with an assessment of the future direction of the drug abuse field.

This handbook is intended to be useful among professionals in the field of drug abuse prevention and treatment. (JAM)

452 pages

KEYWORDS: Compilation.

UM-77-B0023

FORENSIC PATHOLOGY. A HANDBOOK FOR PATHOLOGISTS, R.S. Fisher; C.S. Petty, eds., Washington, D.C.: U.S. Government Printing Office (Jul 1977)

The purpose of this handbook is provide for the pathologist a concise, portable source of information to assist him in the proper performance of the medical legal autopsy and in the objective presentation of the autopsy findings. The book has thirty-three chapters, each covering a specific aspect of the autopsy procedure or a type of death or injury. Each chapter is written by an expert in that area.

Some of the topics discussed are the following: autopsy protocol; preservation of medicolegal evidence; sudden infant death syndrome; the battered child; rape; drowning; drug deaths by injection; alcohol; therapeutic misadventure; and medicolegal investigation of the motor vehicle crash. In the last mentioned topic area, the authors stress the importance of examining the victim for alcohol, carbon monoxide, or a combination of either with barbiturates, tranquilizers, or other drugs as factors possibly contributing to the accident. (HSRI)

201 pages 0 refs

KEYWORDS: Compilation.

UM-78-B0024

THE INTERNATIONAL CHALLENGE OF DRUG ABUSE, R.C. Petersen, ed., NIDA Research Monograph 19 (1978)

This monograph is comprised of papers presented at the Sixth World Congress of Psychiatry in Honolulu, August 28 to September 3, 1977, concerning drug use and abuse. Special emphasis was given to the following areas: drug abuse and possible countermeasures which would be coordinated by the United Nations and the World Health Organization; psychobiology of drug abuse and affective disorders and mechanisms common to both; research on the biological bases of drug abuse; and treatment of drug abuse, including detailed reviews on narcotic antagonist therapy and long-acting methadone. (HSRI)

349 pages

U.S. Department of Health, Education and Welfare publication no. (ADM)78-654

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Local Anesthetics: coca. cocaine. Opiates and Related Agents: heroin. l-alpha-acetylmethadol. methadone. naltrexone. Stimulants: coca. cocaine. Compilation.

UM-77-C0018

COMBINED TREATMENT OF ALCOHOL AND DRUG-DEPENDENT PERSONS: A LITERATURE REVIEW AND EVALUATION, J.F.X. Carroll; T.E. Malloy, American Journal of Drug and Alcohol Abuse, v4 n3 p343-64 (1977)

This article reviews the literature in the mental health and substance abuse fields relating to the efficacy, practicality, and advantages of using combined treatment in treating alcoholism and drug dependence. A review of the substance abuse field literature concerning combined treatment of alcoholic and drug-dependent persons indicates a moderately favorable, albeit cautious degree of support for using combined treatment. Unfortunately, none of the articles arguing for or against combined treatment are buttressed by data derived from rigorous experimental data. With only one exception, all of the published reports of clinical experience with combined treatment have been positive.

Social forces contributing to the creation of an atmosphere conducive to experimenting with combined treatment are discussed. Various social, political, and economic forces of the 1960s such as the black, gay, and women's social reform movements created an atmosphere which approved of experimentation, deemphasized the disease model, and advocated discontinued use of "alcoholic" and "drug dependent" labels. A view was advanced that stressed the importance of the similarities rather than the differences between drug and alcohol abusers.

Finally, a series of questions is raised, the answers to which will likely determine the speed by which the substance abuse field as a whole will move toward adopting a combined treatment approach. (HSRI)

59 refs

KEYWORDS: Countermeasure Concepts.

UM-72-C0019

REVIEW AND EVALUATION OF LEGISLATIVE AND ENFORCEMENT PROGRAMS RELATED TO THE USE OF ALCOHOL AND OTHER DRUGS, P.J. Farmer, Proceedings of the Conference on Medical, Human, and Related Factors Causing Traffic Accidents, Including Alcohol and Other Drugs, Montreal, Canada, 30-31 May 1972, p55-69 (1972)

Presented here is a review of various legislative and enforcement programs in Canada designed to curb impaired driving, and an evaluation of their relative strengths and weaknesses. There are many variations in laws intended to control driving while impaired by alcohol or drugs which this author classifies into major categories. Type I makes it an offense to be in control of a motor vehicle while impaired by alcohol or drugs. Impairment is judged solely by observation or clinical examination. Clinical tests are not required and there is no reference to blood alcohol content. These laws are virtually impossible to enforce, and are therefore ineffective in controlling the D.W.I. problem.

Type II makes it an offense to drive a motor vehicle while impaired by alcohol, impairment being defined by blood alcohol content or by chemical test of blood, breath, or urine. A weakness of this type of law is that it defines presumptive impairment, which can lead to arguments as to whether a particular individual is impaired at a specific blood alcohol level.

Type III, legal limit legislation, makes it an offense to drive when a driver's blood alcohol content is greater than a specified limit as determined by chemical tests of blood, breath, or urine. These laws are usually much more effective since they avoid any argument about driver impairment.

Existing legislation in Canada has one major weakness. Present laws are no guarantee that persons with an alcohol problem will not drive again after being convicted of D.W.I. What is needed is compulsory treatment of alcoholics, ordered by the courts when they recognize a serious drinking problem in an offender.

Also discussed and evaluated are the various types of penalties and the effectiveness of the Canadian .08% law. The author concludes that immediate steps must be taken to change the law concerning chemical and breath tests. This can be done by making roadside screening tests mandatory on suspicion of drinking, after a moving violation, after an accident, and at roadblocks. Anything less than compulsory treatment of problem drinkers and D.W.I. repeaters, as well as chemical tests of efforts to control impaired regulations, will doom to failure all of Canada's efforts to control impaired driving. (HSRI)

20 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation.

UM-76-C0020

PANEL WORKSHOP: COURT MANDATED TREATMENT--OBSTACLE OR OPPORTUNITY? R.D. Atkins; L. Aumack; W.H. Booth, et al., Contemporary Drug Problems, v5 n3 p321-77 (1976)

Presented here is the dialogue of a panel workshop discussing the effects and implications of court ordered treatments. The panel attempted to determine: (1) whether treatment should be different for court mandated admissions and "voluntary" admissions; (2) the effect of court mandated referrals on the treatment program; and (3) whether there is enough compatible purpose and common understanding to support effective working relationships between the criminal justice system and the treatment system.

The panel opened with a description of several alternatives to prison and discussed these alternatives as compared to treatment within the prison setting. Two opposing views were voiced. Drug therapists criticized the dehumanizing atmosphere of the prison and urged that treatment be provided in the community. Representatives of the criminal justice system, however, believed that the public wants to keep criminals isolated and

is demanding more and longer prison sentences, making necessary treatment of drug addicts while they are in prison if they are to be treated at all.

Safe driving programs, both pre- and postconviction, were seen by panel members as being effective alternatives to prison fines, and more important, as providing society with a tool for reducing the slaughter caused by drunken driving.

Also discussed was the practice of court mandated treatment as an alternative to prison for drug and alcohol abusers convicted of criminal offenses. Some panel members felt that treatment programs have been overrated, and that courts and the criminal justice system are disillusioned with what they consider the failure of treatment. Others felt it was unrealistic to expect addiction treatment programs to "cure" criminal behavior. Treatment centers do not have the resources, the funding, or the mandate to cure the underlying causes of criminal behavior which include unemployment, poverty, lack of opportunities, and sociopathology. (HSRI)

0 refs

KEYWORDS: Countermeasure Concepts. Other Sociolegal Study.

UM-76-C0021

ANALYTISCHE-CHEMISCHE ASPECTEN VAN DE WIJZIGING VAN DE WEGENVERKEERSWET (I), W. Froentjes; J.B. Schute; T. Strengers; A.M.A. Verwey, v111 n14 p289-300 (1976)

The establishment in the law of a limit of 0.5 mg alcohol per ml blood as an objective norm for the criminal liability of vehicle drivers has placed a major part of the burden of proof in the hands of the analytical chemist. The interest of justice requires certain minimum norms for the quality of the blood sample, the performance of the analysis, and the computation of the analytical results. Moreover, in cases where a blood sample cannot be taken, standards for a substitute test are necessary as well as for a simple system for the performance of the required breath test. Rules are also necessary for independent expertise analysis on request of the accused. Since the law also prohibits the use in traffic of medicine and drugs that have a detrimental effect on driving ability, detection, quantitation, and other aspects of proof for drugs must also be studied.

This article consists of the reports of four authors who were assigned to an analytical committee, the purpose of which was to study formulation and testing of the regulations and requirements and to suggest recommendations for the execution of the new law. (JAM)

0 refs German

KEYWORDS: Countermeasure Development, Testing, and Evaluation.

UM-73-C0022

COMMUNICATING DRUG-ABUSE INFORMATION AMONG COLLEGE STUDENTS, G.J. Hanneman, The Public Opinion Quarterly, v37 p171-91 (Summer 1973)

This article compares the roles of traditional media and nonmedia sources in disseminating information on drug abuse and treatment among college students. First the specialized information needs of the public are described; then a study of 407 college students who replied to a questionnaire concerning drug-abuse information is presented. The correlation between information seeking and the convenience and credibility of drug-abuse information available to young people was hypothesized and tested in the subsequent study of college students.

The data indicate that users and nonusers exhibit different communication behavior about initial drug awareness, drug-abuse information seeking, conflict resolution, and other drug-related communication activity. Users, for example, do not usually rely on media for information, while most nonusers do. The data also supports the importance of interpersonal (friendship) networks. Friendship was found to play an important role in molding dealer behavior and in influencing drug use and information seeking.

The data suggests implications for the dissemination of drug-abuse communications. For instance, an over-all finding was that doctors, health centers, and hospitals were consistently cited as the preferred source for resolving information conflicts. These findings provide the basis for further investigations of the impact of drug-abuse communication on society, particularly the mediating role of mass communications. (HSRI)

42 refs

KEYWORDS: Epidemiology: Regional or Local Survey of Drug Use Patterns. Review: Drug Use.

UM-72-C0023

DRUG EDUCATION: TOWARD A RATIONAL APPROACH, M. Segal, The International Journal of the Addictions, v7 n2 p257-84 (1972)

This article deals with the development of drug education programs. Two important points are given consideration in doing this: first, establishing the program's goals; secondly, the manner of evaluating the established goals.

The author believes that a rational drug program should not be designed to convince an audience of one point of view, namely, that all drug use is bad. Rather the program should present scientifically sound data and allow for a free discussion of attitudes. Since the drug issue ranges over a multitude of disciplines, medical, psychological, sociological, legal, ethical, moral, and religious views should be taken into consideration. It is impossible, if a drug education program is to be rational, to be dogmatic about the potential dangers of marijuana and other psychochemical agents, particularly in view of the fact that scientific evidence has failed to prove that these drugs have necessarily harmful effects. (HSRI)

105 refs

KEYWORDS: Countermeasure Concepts.

UM-71-C0024

HAS DRUG AND ALCOHOL EDUCATION QUARANTINED STUDENT ATTITUDES? A NEW LOOK AT AN OLD PROBLEM, C.T. Abramo, Journal of Alcohol Education, v17 n1 p29-36 (Fall 1971)

This paper discusses the importance of verbal and nonverbal communications in preventive drug education in the schools. Today's schools have quarantined students from the adult community. Having nowhere else to turn, the young are forced upon their peers, accounting for the popularity of peer groups.

In a quarantined environment, objective and educational messages usually contain too much information that is irrelevant. The receiver cannot relate it to his situation, nor can he integrate it into his experiences. Success in drug or alcohol education thus is only accidental because the communicator can never be sure as to the relevance of the messages he is sending, nor can he be sure of their cumulative effect. The person who sends the communication has limited influence over his message, and the cognition of the communication is proportional to the interactional sequence in the self-image, presented image, and aspired-to image of the recipient.

Audio visual equipment, instructional tools, and formal lesson plans for drug and alcohol education are merely channels by which to transfer attitudes and values from the educator to the student. However, these channels are subject to interference based on the various perspectives of the educator and the differing views of the student. The innovating educator within an existing structured educational context must formulate a new role for himself that allows a systematized interaction with his students and that avoids dogmatism. (HSRI)

9 refs

KEYWORDS: Countermeasure Concepts.

UM-73-C0025

DRUG EDUCATION THROUGH THE NEWS MEDIA: SUGGESTIONS FOR REPORTERS AND DRUG PROGRAM DIRECTORS, Journal of Alcohol and Drug Education, v18 n3 p30-35 (Spring 1973)

Presented here is a compilation of suggestions for more effective drug education drawn from three separate meetings on the role of mass communication in alcohol and drug education. These suggestions reflect many of the ideas expressed by media representatives and drug program directors who attended the meetings.

Several aspects of mass communication's role in drug information are discussed: how to deal with drug program directors; types of communication that are most and least effective; reporting techniques; and technical pointers for drug program directors for preparing news release. (HSRI)

0 refs

KEYWORDS: Countermeasure Demonstration and Implementation.

UM-73-C0026

TELEVISED DRUG ABUSE APPEALS: A CONTENT ANALYSIS, G.J. Hanneman; W.J. McEwen, Journalism Quarterly, v50 n2 p329-33 (Summer 1973)

The purpose of this paper is to inform the reader of an exploratory study that was conducted to ascertain the quantitative and qualitative aspects of televised drug abuse advertising. These data provide information for future hypothesis-testing investigations into public service communications. The data also provide knowledge regarding the availability of drug abuse information through television.

In general, drug abuse appeals were found to be telecast primarily during times of lower audience attendance. Such messages included little specific informational content, were not directed at identifiable audience segments, customarily involved the use of actors or sports celebrities as sources, and used some type of fear appeal as a message strategy. The authors emphasize the need for a more specifically oriented informational strategy and underscore the potential danger in failing to systematically examine the characteristics of the intended audience before planning a persuasive antiabuse campaign. (JAM)

18 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation.

UM-79-C0027

SYSTEM ANALYSIS OF THE GENERAL DETERRENCE OF DRIVING WHILE INTOXICATED, L.G. Summers; D.H. Harris, Human Factors, v21 n2 p205-13 (1979)

A system analysis of the general deterrence of driving while intoxicated (DWI) is described. The analysis identified system elements relevant to the DWI decision and assessed potential countermeasures that might be employed in general deterrence programs. A framework for DWI general deterrence is defined. The analytical methods employed are described and the conclusions and recommendations derived from study results are presented.

Central to the study was a system model developed for interrelating factors that influence DWI deterrence, and an associated computer-based simulation program employed for examining DWI deterrence alternatives.

Some of the conclusions drawn are the following: 1) Any significant reduction of DWI trips and related accidents must necessarily be effected through general rather than specific deterrence. 2) DWI general deterrence depends critically upon drivers' perceived risk of DWI trips and on the risk aversion characteristics of potential drinking drivers. 3) Relatively small changes in perceived risk of DWI are capable of producing large changes in number of DWI trips and related accidents. 4) Increased enforcement actions reduce DWI trips and related accidents significantly only when combined with increased information feedback of the consequences of these actions. 5) The greatest potential for reduced DWI trips and related accidents is through widespread dissemination of information emanating from effective and consistent DWI enforcement and adjudication action. (JAM)

17 refs

KEYWORDS: Countermeasure Concepts.

UM-79-C0028

DRUGGED DRIVERS: WHAT CAN A PILL DO TO YOUR DRIVING REACTIONS? [Pamphlet] (1979)

This pamphlet cautions drivers about the dangers of using antihistamines, tranquilizers, and other commonly prescribed medicines while driving. It urges them to ask their physician or pharmacist about any side effects of a drug. Special emphasis is placed on the danger of mixing drugs with alcohol. (HSRI)

Pennsylvania Bureau of Traffic Safety

0 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Countermeasure Demonstration and Implementation.

UM-79-C0029

NATIONAL DRUG ABUSE TREATMENT UTILIZATION SURVEY (NDATUS). NATIONAL DRUG ABUSE TREATMENT: INSIGHTS AND PERSPECTIVES, Rockville, Md.: National Institute on Drug Abuse (1979)

This report reflects on analyses of data generated through the National Drug Abuse Treatment Utilization Survey (NDATUS), a federally mandated system conducted by the National Institute on Drug Abuse that measures the scope and use of drug abuse treatment in the United States. This ongoing survey collects national, regional, state, and clinical data from all treatment units whether or not they are federally funded. The data provide a basis for comparative analyses of treatment utilization across the country and for forecasts of resource requirements for drug abuse treatment services. NDATUS produces information which permits conclusions to be drawn about certain management and policy issues.

The report discusses several of these conclusions regarding the structure, operation, and delivery of drug abuse treatment services in the United States. These include the following: (1) In order to develop an effective network of local treatment units meeting national quality criteria, a federal, state, and local partnership is necessary. (2) Commitment of substantial federal funds over an extended period will be required if the national drug abuse treatment capacity is to be maintained. (3) As of 1977, drug treatment capacity was saturated; nevertheless, the system was providing most of the services required. (4) There has been a downward trend in the use of inpatient hospital care since 1975. Drug abuse treatment programs are moving toward more cost-effective use of treatment facilities. (5) With the realization that total abstinence cures are difficult to obtain and relapse is frequent, associated services such as education, prevention, and vocational rehabilitation have become recognized as necessary. However, the present system is not set up to provide the full depth of services necessary for treatment of drug abuses at a single location or in a coordinated way. (7) Integration of drug abuse programs into the health care system is favored. (HSRI)

24 pages 0 refs

National Institute on Drug Abuse DHEW publication no. (ADM) 79-778

KEYWORDS: Countermeasure Development, Testing, and Evaluation.

UM-74-C0030

EFFECTIVENESS OF DRUG EDUCATION CLASSES, F.S. Tennant; P.J. Mohler; D.H. Drachler; H.D. Silsby, American Journal of Public Health, v64 n5 p422-6 (May 1974)

The only technique of presenting drug education to a large population that has demonstrated any effectiveness has been a physician-administered drug classroom presentation to an organized audience. This paper describes the utilization of this technique and evaluates its effectiveness in decreasing drug abuse.

A drug education class was given by a physician to six U.S. Army units consisting of 947 soldiers. Of this group, 477 (50%) admitted on an anonymous questionnaire to illegal drug use at the time the class was given. Fifty-six percent of all personnel surveyed preferred a physician as their primary source of drug information, followed by a former drug addict.

The drug education class was conducted by a knowledgeable military physician. Colorful slides were used to explicitly illustrate and outline the medical and psychiatric complications and causes of hospitalization from drugs commonly abused by military personnel. Moral and legal issues were completely avoided.

Three months later the 947 participants were again administered a questionnaire in which drug users were specifically asked whether they decreased or stopped any illegal drug consumption as a result of the drug information class. Twenty-four percent of occasional hashish users and 9% of regular hashish users reported a decrease or discontinuation of drug use after the drug education class. Seventy-three percent of occasional users and 84% of regular users indicated that their usage remained unchanged. A small percentage stated that they had actually started smoking hashish as a result of the drug education class.

A more positive effect of the class was evident on drugs harder than hashish. A total of 39% of 151 LSD users, 24% of 170 amphetamine users, 25% of 189 barbiturate users, and 45% of 37 opiate users revealed a decrease or discontinuation in consumption as a result of the drug education class. The total number of active users of illegal drugs decreased from 447 (50.5%) to 372 (39.4%). During the twelve months after the class, drug-related hospitalizations were reduced by 50%--from twenty-two to eleven.

The authors conclude that although drug education classes by knowledgeable physicians have limited success, they may be the most effective way to educate large numbers of people about the effects of drug use and abuse. It is not known at this time how permanent the benefits of this type of drug education are. (HSRI)

13 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: hashish. Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Opiates and Related Agents: opium. Stimulants: amphetamine. Sedatives and Hypnotic Agents. Countermeasure Development, Testing, and Evaluation.

UM-76-C0031

PHARMACISTS TO PARTICIPATE IN PUBLIC EDUCATION PROGRAM, Palmetto Pharmacist, V15 n6 p9 (June 1976)

This brief article reports on a public information campaign designed to alert the driving public to the dangers of driving while under the influence of drugs other than alcohol. The South Carolina Pharmaceutical Association, in cooperation with the South Carolina Commission on Alcohol and Drug Abuse, attempted in the summer of 1976 to inform the public about the hazards of driving after using over-the-counter, illicit, and prescription drugs. Campaign methods included billboards, radio and TV spots, posters, bumper stickers, and newspaper advertisements. In addition, 100,000 leaflets were distributed to pharmacies warning customers of the dangers of driving after taking drugs. Pharmacists were asked to attach these leaflets to the prescription when purchased. (HSRI)

0 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation.

UM-78-C0032

DRUG EDUCATION: FOR WHOM? M. Hochhauser, Journal of Alcohol and Drug Education, v23 n3 p24-33 (Spring 1978)

Reviewed here are common problems and weaknesses found in many existing drug education programs. Traditional preventive drug education programs, which have usually been directed towards elementary and secondary school students, often suffer from serious methodological limitations: (1) They fail to reach individuals who develop drug abuse problems later in life such as the middle-aged and the elderly; (2) People in charge of drug education are often not specifically trained to deal with drug abuse; (3) Virtually no empirical research has been directed toward the less visible aspects of drug abuse such as drug use by women and the rapid increase in the number of drugs available; (4) Evaluation of existing drug education programs has been almost entirely lacking.

The author suggests several ways in which drug education programs might be improved: (1) Drug abuse education must reflect more of a life-span developmental approach to take into account the fact that problems with substance abuse can occur at virtually any time during an individual's lifetime. (2) Those involved in drug education must receive training specifically preparing them for drug education. This training must be multidisciplinary, encompassing behavioral, medical, social, legal, educational, economical, and political perspectives. (3) An effort should be made to reach

nonstudent adult target populations. (4) Methods not traditionally used in drug education should be used such as newspaper, radio, and television.

In summary, the author states that drug education must not end with a high school diploma. (HSRI)

32 refs

KEYWORDS: Countermeasure Concepts.

UM-79-C0033

DRUGS AND DRIVING [pamphlet] (1979)

This pamphlet, published by the National Institute on Drug Abuse, warns the reader about the dangers of combining drug use and driving. Special attention is given to the hazards caused by use of alcohol with drugs. The effects of several drug groups--both alone and in combination with alcohol--are discussed as they relate to driving performance. Marijuana, tranquilizers and other sedative hypnotics, stimulants, hallucinogens, PCP, and over-the-counter drugs are shown to impair driving performance.

The pamphlet concludes with an appeal to readers not to drive after taking any drug or combination of drugs and to ask their physician about side effects of any drug they may be taking.

0 refs

National Institute on Drug Abuse DHEW Publication no.(ADM)79-890

KEYWORDS: Countermeasure Development, Testing, and Evaluation.

UM-73-C0034

PUBLIC SERVICE ADVERTISING ON TELEVISION, G.J. Hanneman; W.J. McEwen; S.A. Coyne, Journal of Broadcasting, v17 n4 p387-404 (Fall 1973)

This study examines time and topic distribution of televised public service advertisements (PSAs). Its specific purpose was to analyze how "social problem" PSAs (those concerned with such topics as VD, alcoholism, drug abuse, and discrimination) are treated relative to other PSAs. The discussion also explores the role of public service advertising during periods when social crises (such as rampant drug abuse or an epidemic of VD) are apparent in American society.

In a content analysis of over 500 hours of on-the-air time data from both television broadcasters' logs and from actual observation, it was found that PSA time accounted for only 2% of total air time while commercial messages accounted for an estimated 20% of air time. Also more PSA time is broadcast on weekdays than on weekend days. Children's shows (30%), news and specials (18%), and talk shows (17%) account for the majority of PSA time broadcast.

In terms of PSA topic themes, the categories accounting for the greatest proportion of PSA time were social problems (18%), medical problems (15%), solicitations (13%), jobs and education (11%), and parks and forests (11%); yet overall, solicitation-type messages accounted for 25% of total PSA time.

The authors reach the conclusion that many significant decisions are yet to be made regarding the specific and implied obligations of broadcasters with regard to public service messages.

Additional research inquiry bearing on present and optimal impact of these messages must form the basis for such decisions. (HSRI)

6 refs

KEYWORDS: Other Sociolegal Study.

UM-75-D1002

SPECIFICITY OF BENZODIAZEPINE ACTION ON HUMAN SLEEP CONFIRMED. ANOTHER CONTRIBUTION OF AUTOMATIC ANALYSIS OF POLYGRAPH RECORDINGS, J.-M. Gaillard; C. Aubert, Biological Psychiatry, v10 n2 p185-97 (Apr 1975)

The present investigation was undertaken in order to test the hypothesis that benzodiazepine-induced modifications of sleep in human subjects is not a common effect of all psychotic drugs, but rather a specific one. Full-night polygraph recordings in three normal males and two normal females aged 20 to 27 years were automatically analyzed by means of a hybrid system.

Each of the three drugs tested in equimolar doses--thioridazine, pentobarbital, and oxazepam--induced characteristic effects on sleep. Thioridazine did not affect the quantity of slow-wave sleep or of REM sleep. REM sleep latency was significantly shortened, and the number of cycles during the night was increased. Pentobarbital influenced slow-wave sleep very slightly and decreased REM sleep, but did not modify the number of rapid eye movements with respect to REM sleep duration. Oxazepam decreased slow-wave sleep, REM sleep, and the density of REM sleep, the absolute number of REM being proportionally much more reduced than REM sleep itself. These findings are consistent with the idea that in some cases at least, drugs belonging to different chemical classes induce modifications of sleep specific for their class. (JAM)

33 refs

KEYWORDS: Barbiturates: pentobarbital. Major Tranquilizers (Antipsychotics and Neuroleptics): thioridazine. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): oxazepam. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Physiological Testing.

UM-78-D1003

RELATIONSHIP BETWEEN ANORECTIC AND REINFORCING PROPERTIES OF APPETITE SUPPRESSANT DRUGS: IMPLICATIONS FOR ASSESSMENT OF ABUSE LIABILITY, R.R. Griffiths; J.V. Brady; J.D. Snell, Biological Psychiatry, v13 n2 p283-90 (1978)

This study proposes an "anorectic-reinforcement ratio" for comparing the relative potency of a drug as an anorectic with its relative potency as a reinforcer. Such a measure provides for a potentially useful preclinical assessment of the extent to which anorectic applications of a compound involve exposure to the drug's reinforcing effects, and may indicate the degree to which use of the drug could be continued independently of its anorectic effects.

The reinforcing properties of cocaine and eight phenylethylamine anorectics (diethylpropion, d-amphetamine, phenmetrazine, chlorphentermine, phentermine, clortermine, fenfluramine, and phenylpropanolamine) were evaluated with a series of eleven chair-restrained baboons to determine the lowest dose of each compound which maintained intravenous self-infusion above saline control levels. To provide more information about anorectic potency of the drugs, an alternative set of values was derived by utilizing the lowest recommended daily human anorectic doses. These doses provided the numerator for computing a comparative set of ratio values. This ratio, based upon the relationship between determinations of reinforcing potency and therapeutic efficacy, may add a useful and important quantitative dimension to the preclinical assessment of relative abuse potential with appetite suppressant drugs. (HSRI)

21 refs

KEYWORDS: Anorectic (Appetite Control) Agents: chlorphentermine. clortermine. dextroamphetamine. diethylpropion. fenfluramine. phenmetrazine. phentermine. Decongestant and Cold Preparations: phenylpropanolamine. Local Anesthetics: cocaine. Stimulants: clortermine. cocaine. dextroamphetamine. Sympathomimetic (Adrenergic) Agents: chlorphentermine. dextroamphetamine. diethylpropion. fenfluramine. phentermine. phenylpropanolamine. Animal Research. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs.

UM-77-D1004

SUBJECTIVE RESPONSES AND EXCRETION PATTERNS OF DEXTROAMPHETAMINE AFTER THE ADMINISTRATION OF THERAPEUTIC DOSES, M.A. Evans; G. Wimbish; L. Griffis; R. Martz; D.J. Brown; B.E. Rodda; L. Lemberger; R.B. Forney, Journal of Forensic Sciences, v22 n1 p197-201 (Jan 1977)

Very little information is available concerning urinary excretion patterns after doses of dextroamphetamine in the therapeutic range. For this reason, the symptoms and excretion of dextroamphetamine in twelve healthy males between the ages of 21 and 30 under controlled laboratory conditions were examined. The study was conducted in a double-blind manner, and oral doses of 0,5,10, or 15 mg/70 kg body weight of dextroamphetamine sulfate were assigned according to randomized, complete block design. After administration, total urine output was collected for twelve hours; no attempt was made to control urinary pH to more realistically approach the general clinical usage of amphetamines. The urine was pooled into two six-hour segments and analyzed for amphetamine concentration. Subjective impressions of the treatments were also evaluated by means of the Cornell Medical Index Questionnaire which inquired about appetite, anxiety, weakness, and trembling.

Results showed that approximately 30% of the total dose was excreted within twelve hours after administration. The amount excreted agreed very closely with the doses given and paralleled the scores for subjective impressions by the subjects. This study indicates that under ordinary conditions (in which pH is not artificially controlled), therapeutic doses of dextroamphetamine can be detected in urine for up to twelve hours after oral administration. None of the subjects felt that their driving would be impaired by any of the doses administered. (JAM)

18 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine*. Stimulants: dextroamphetamine*. Sympathomimetic (Adrenergic) Agents: dextroamphetamine*. Drug Concentrations in Body Fluids: Chronic Dose Study. Experimentation: Dose-Effect Study. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1005

THE FORENSIC TOXICOLOGY OF COCAINE (1971-1976), B.S. Finkle; K.L. McCloskey, Journal of Forensic Sciences, v23 n1 p173-89 (Jan 1978)

This study assesses the role of cocaine in postmortem medicolegal investigation. Its primary objective was to determine whether cocaine is significant as a causative agent in a growing number of sudden, unexplained deaths. The report consists of a retrospective, collaborative survey and data evaluation carried out in 1976 and 1977. Two questionnaires were used to gather data, one of which provided information concerning analytical toxicology and laboratory resources, the other recorded individual case data.

The geographic area surveyed included 62.9 million people, or 29.8% of the U.S. population, and provided a total of 111 sudden, unexplained deaths in which cocaine was involved.

Several prominent conclusions were drawn from the study: (1) The national picture of cocaine deaths is not uniform or predictable since many jurisdictions do not report fatal cocaine cases. (2) The deceased population were predominantly young white males with a record of drug abuse. (3) They were a medically healthy group without significant psychiatric problems. (4) A notable number of heroin users was found among the victims. (5) Fatal toxicity from cocaine is rapid, with extremely fast onset of symptoms. Two-thirds of the victims died within five hours after administration of the drug. (6) In 70% of the 86 drug-caused deaths, the blood concentrations of cocaine were under 4.0 ug/ml and in more than one-third were 1.0 ug/ml or less. (7) For eight of the cases it was established that cocaine was ingested intranasally, clearly refuting opinions that nasal insufflation of cocaine is completely safe. (HSRI)

25 refs

KEYWORDS: Local Anesthetics: cocaine*. Stimulants: cocaine*. Epidemiologic Research: Drug Concentrations in Body Fluids. Epidemiology: National Survey of Drug Use Patterns.

UM-77-D1006

MARIJUANA: DIFFERENTIAL EFFECTS ON RIGHT AND LEFT HEMISPHERE FUNCTIONS IN MAN, R.C. Stillman; O. Wolkowitz; H. Weingartner; I. Waldman; E.V. DeRenzo; R.J. Wyatt, Life Sciences, v21 n12 p1793-1800 (15 Dec 1977)

Despite the abundance of research on human hemispheric differentiation and the development of sensitive reaction time methods for the quantitative measurement of hemispheric differences in function in the intact brains of noncommissurotomized

subjects, no systematic investigation utilizing these techniques has been made concerning the effects of experimentally administered psychoactive substances in man. This paper reports the first results from a series of experiments investigating the possibility of differential effects on the right and left hemispheres by marijuana.

Twenty-four normal, right-handed marijuana users aged 21 to 34 were tested for their reaction time to pictorial stimuli presented to the left and right cerebral hemispheres after smoking either placebo or 15 mg delta-9-THC cigarettes. The results showed that marijuana smoked at moderate doses produced a differential impairment of the reaction times. After smoking marijuana, responses to pictorial stimuli presented to the right hemisphere were slowed significantly less than to the left hemisphere. Responses to verbal stimuli (trigrams) were slowed equally in both hemispheres, preserving an initial left hemisphere superiority for this material. This suggests that marijuana may differentially change the processing speed or relative dominance of man's two cerebral hemispheres, depending on the nature of the material being processed.

This experiment provides evidence of a pharmacologically modifiable hemispheric differentiation in the human brain, in which the speed of information processing can depend on an interaction of the three conditions of (1) type of stimulus; (2) hemisphere initially stimulated; and (3) drug state. (HSRI)

13 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Experimentation: Acute Dosage Study. Psychomotor Tests.

UM-73-D1007

THE INFLUENCE OF ALCOHOL AND MARIJUANA ON A MANUAL TRACKING TASK, L.D. Reid; M.K.F. Ibrahim; R.D. Miller; R.W. Hansteen, International Automotive Engineering Congress, Detroit, Mich., Jan. 8-12, 1973 New York: Society of Automotive Engineers, Inc. (1973)

Two studies were done investigating the influence of alcohol and marijuana on the dynamic characteristics of human operators performing a manual tracking task. One study involved both alcohol and marijuana, the other alcohol alone. The approach taken involves the use of linear mathematical models to describe the human operator. Of primary interest was the assessment of the technique as a tool for the investigation of drug effects on human performance in situations resembling the car driving task.

The subjects used in both experiments were volunteer male university students over the age of twenty-one years who were alcohol and marijuana users. In the experiment testing both drugs, 40% pure ethyl alcohol was administered to achieve a peak BAL of either 0, 0.03, or 0.07%. Marijuana cigarettes were prepared to produce a dose of either 0, 21, or 88 mg of delta-9-THC/kg of subject body weight. In the experiment testing alcohol alone, the amount of alcohol was selected to produce a peak BAL of 0, 0.04, 0.07, or 0.10%. Subjects then participated in a compensatory tracking task.

The following conclusions were made concerning the two experiments: (1) At the 5% level only tracking scores for cases involving alcohol are significantly altered for the present task. (2) The linear modeling technique is capable of detecting the influence of drugs on the dynamic characteristics of the human operator. (3) For highly skilled human operators exhibiting a strong neuromuscular resonance, the influence of a high BAL percentage is to shift it to a lower frequency. For less skilled operators exhibiting no strong resonance, their describing function exhibited a noticeable increase in time delay in the presence of alcohol. (4) The presence of alcohol tends to reduce the bandwith of the man/machine system with only a slight effect on the phase margin. (5) The only marijuana influence detected in the describing function data was a slight resonance at high frequency. (JAM)

4 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Experimentation: Study of Combined Effects of Drugs.

UM-54-D1008

COMMENTS ON EFFECTS OF CERTAIN ANTIHISTAMINES, C. Landis, Health, Medical, and Drug Factors in Highway Safety. Proceedings of the Second Highway Safety Research Correlation Conference, 5-6 April 1954, p2.32-2.33, Washington, D.C.: National Academy of Sciences, (1954)

One probable source of human failure leading to highway accidents may be found in the side effects of medications. It is possible and critically important to obtain better measures of the side effects of chemical agents than are now available. Many chemical agents which are readily available to the general public have not been systematically investigated with respect to their side effects in humans. The investigation of these side effects is, at present, almost completely a problem of development of research methods and measures. Another obstacle to developing methods of studying and controlling side effects grows out of the vast individual differences in susceptibility to chemical agents among the normal, healthy human population. It is never safe to generalize as to the side effects of chemical agents. Finally, the possibility of prolonged effects is a complicating factor when determining test performance for as long as twenty-four hours after drug ingestion. (HSRI)

0 refs

KEYWORDS: Antihistamine Agents. Review: Drug Effects.

UM-62-D1009

THE EFFECTS OF D-AMPHETAMINE ON RISK TAKING, P.M. Hurst, Psychopharmacologia, v3 p283-90 (1962)

While there is much subjective evidence that amphetamines exert strong effects on mood, there is little objective behavioral evidence supporting it. This experiment attempted to test the hypothesis that d-amphetamine, through its effect upon optimism, increases risk-taking behavior. Risk-taking behavior of twenty-nine male penitentiary inmates was investigated utilizing a gambling situation involving cigarettes. The experimental situation consisted of choices between alternative gambles involving different amounts of risk. The subjects served as their own controls, with the number of high-risk choices made by each subject when under drug (10 mg d-amphetamine sulfate taken orally) being compared with the number of such choices made during his placebo session.

Results showed that the difference was significant in the direction of increased risk-taking under the drug. Nineteen of the twenty-nine subjects made more high-risk choices than they did during the control condition. The data showed a tendency for most subjects to prefer the low-risk alternative in the placebo condition. The results are interpreted as offering tentative support to the hypothesis that d-amphetamine increases risk-taking, although alternative interpretations are provided. (AAM)

15 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Stimulants: dextroamphetamine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Acute Dosage Study. Psychological Testing.

UM-74-D1010

HALOPERIDOL IN PSYCHOSOMATIC SYNDROMES, A. Shargil, Harefuah, v87 n8 p360-4 (1974)

The effect of a three-month course of treatment with 1.0 to 15 mg haloperidol (Halidol(R)) per day was studied in seventy outpatients, thirty-two of whom had stress erythrocytosis, twenty of whom exhibited psychosomatic symptoms, and twenty-six of whom experienced extreme anxiety and tension. Eight had more than one of these conditions. All seventy had been treated with various tranquillizers in addition to target medication without showing improvement. Treatment with haloperidol, however, resulted in marked improvement in the organic manifestations of the patients with stress erythrocytosis and in those with psychosomatic complaints. The preparation was more effective in cases with anxiety tensions than in cases with depressive manifestations. Adverse reactions were minimal and disappeared on reducing the dosage. There were no adverse effects on blood count, liver function, or blood chemistry. In one patient with reactive depression medication had to be stopped early in the study due to deterioration of the depressive state. Medication was discontinued in five other patients with depressive reactions after three months since there was no therapeutic effect.

Over half of the patients tested drive cars, and some work near highspeed machines. In no case was there reduced driving capacity or reaction capability. Some professional drivers actually reported improved driving ability under haloperidol because of improvement in mental state. (EMM)

11 refs Hebrew

KEYWORDS: Major Tranquilizers (Antipsychotics and Neuroleptics): haloperidol. Clinical Study. Experimentation: Chronic Dosage Study.

UM-78-D1011

DROWSINESS, IMPAIRED PERFORMANCE AND TRICYCLIC ANTIDEPRESSANT DRUGS, C. Bye; M. Clubley; A.W. Peck, British Journal of Clinical Pharmacology, v6 n2 p155-61 (Aug 1978)

Reports from clinical practice indicate that many tricyclic antidepressants cause drowsiness. In order to investigate this, the effects of various doses of amitriptyline, nortriptyline, protriptyline, and a chemically related potential antidepressant, BW247, on performance tests and subjective ratings were studied. Two separate trials were performed. In the first, twelve male volunteers aged 22 to 35 years participated. A further twelve, eight men and four women aged 21 to 48 years, participated in the second test. Both groups received drugs and lactose dummy in identical capsules at weekly intervals according to a balanced design, under double-blind conditions, and with standardized tests and environment. Tests assessed auditory vigilance, short-term memory, reaction time, arithmetic skills, digit symbol substitution, tapping, and visual analogue. Salivation rate, pupil size, heart rate, and systolic and diastolic blood pressure in the erect and supine positions were also measured.

Amitriptyline produced the most marked effects, with significant impairment in auditory vigilance after 6.25 mg. Auditory reaction time, tapping rate, arithmetic, and digit symbol substitutions were impaired by amitriptyline (12.5 and 25 mg), and all doses produced increased ratings of mental sedation. The effects began 1.5 hours after drug ingestion and lasted approximately five hours. Nortriptyline produced fewer effects which were later in onset. Tapping at 1.8 hours and auditory vigilance at 3.5 to 4.5 hours were impaired by nortriptyline (25 mg) whereas reaction time was prolonged by both doses at 5 hours. No change in rating of mental sedation occurred. No significant change in performance or subjective ratings followed protriptyline (10 mg) or BW247 (12.5 and 25 mg).

These findings are discussed in relation to the presence of secondary and tertiary amines on the side chain of the compounds and their relative abilities to block neuronal uptake of noradrenaline and 5-hydroxytryptamine. (JAM)

20 refs

KEYWORDS: Antidepressants: amitriptyline. nortriptyline. Unclassified Agents: 3-methylamino-1,1 diphenylprop-1-ene (BW247). Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests. Tests of Sensory Function.

UM-62-D1012

DISULFIRAMLIKE ACTIONS PRODUCED BY HYPOGLYCEMIC SULFONYLUREA COMPOUNDS, E.B. Truitt; G. Duritz; A. M. Morgan, R.W. Prouty, Quarterly Journal of Studies on Alcohol, v23 n2 p197-207 (Jun 1962)

In clinical tests the hypoglycemic sulfonylurea drugs carbutamide, tolbutamide, and chlorpropamide have been reported to produce intolerance to alcohol. The purpose of this investigation was to study the mechanism of this action and especially to determine whether it results from the hypoglycemic action of the drugs. The possibility of an adrenergic blocking action was also explored.

Two tests of disulfiramlike activity were used. In rats, doses of tolbutamide in the range of 65 to 250 mg per kg produced increased acetaldehyde (AcH) from 7.0 to 13.5 gamma per ml higher than in controls given only ethanol. The vasodepressor phase of blood pressure responses in five cats injected with 30 mg per kg of AcH was deeper by an average of 16.4 mm Hg whereas this phase of response to epinephrine was unchanged in five cats by 200 mg per kg of tolbutamide. Insulin (5 units per kg) did not change the vasodepressor response to either AcH or epinephrine (six cats). However, a dose of glucose (0.5 to 1.0g) sufficient to correct the hypoglycemia reversed the tolbutamide-induced potentiation of the hypotensive phase. A bradycardia of vagal origin occurred during the depressor phase of AcH after 200 mg of tolbutamide per kg but experiments with atropine indicated that this was not the cause of the greater fall. Chlorpropramide also was active in potentiating AcH vasodepression.

These actions of tolbutamide and chlorpropamide required large doses in the range of 150 to 250 mg per kg. The cardiovascular changes seem to be caused by interference with some glucose-dependent function which is affected by tolbutamide but not by insulin.

They do not seem to be related to an adrenergic blocking mechanism. The possibility of altering the response to alcohol by a drug affecting carbohydrate metabolism should be of interest in studying the relationship between these two factors. The hypoglycemic sulfonylurea drugs should be considered as less toxic drugs than disulfiram and calcium carbimide in the treatment of alcoholism. (JA)

19 refs

KEYWORDS: Oral Hypoglycemics: chlorpropamide, tolbutamide. Unclassified Agents: disulfiram. Animal Research. Experimentation: Other Single-Drug Study.

UM-76-D1013

DEPRESSIVE STATES INDUCED BY DRUGS OF ABUSE: CLINICAL EVIDENCE, THEORETICAL MECHANISMS AND PROPOSED TREATMENT. PART II, K. Blum, Journal of Psychedelic Drugs, v8 n3 p235-62 (Jul-Sep 1976)

This review focuses on three types of commonly abused drugs: narcotics (heroin and methadone), CNS stimulants (amphetamines and cocaine), and CNS depressants (barbiturates, minor tranquilizers, and alcohol). Possible mechanisms by which these drugs induce depression during use or abstinence are discussed, and possible modes of treatment are suggested for each type of drug.

Proper treatment of postamphetamine depression might include administration of an imipramine-type tricylic agent to raise catecholamine norepinephrine (NE) levels, or chlorimipramine and L-trytophan to raise catecholamine 5-hydronytryptamine (5HT) levels. Depression that manifests itself from amphetamine or cocaine abuse may take the form of frustration or anxiety and agitation. Thus, effective treatment might consist of a drug combining antianxiety and antidepressant action such as doxepin.

There is little evidence linking clinical depression with prolonged use of barbiturates. Until more research is done in this area, it would not be advisable to treat this type of depression with antidepressive agents or MAO inhibitors. One could propose drugs which raise the function activity of 5HT such as chlorimipramine or L-trytophan to counteract the 5HT deficit.

Patients undergoing alcohol detoxification also become depressed and require therapy. Studies dealing with treatment are inconsistent and controversial. At this point, however it appears that the best method of treatment would treat the depression with tricylic compounds, monoamine oxidase inhibitors, L-tryptophan, or drugs which raise both NE and 5HT. (HSRI)

165 refs

KEYWORDS: Opiates and Related Agents. Sedatives and Hypnotic Agents. Stimulants. Review. Review: Drug Effects.

UM-71-D1014

THE EFFECTS OF DRUGS ON DRIVING PERFORMANCE: A LITERATURE SURVEY, W.L. Howard; H.H. Davis, Charlottesville, Va.: Virginia Highway Research Council (Mar 1971)

Presented here is a survey of available research concerning the role of drugs in traffic crashes. Areas reviewed are the effects of marijuana in both simulated driving tests and on driving performance; the effects of narcotics, LSD, stimulants, and depressants on driving performance; the effects of drugs and alcohol combined; and drug-and-alcohol related accidents.

From the evidence reviewed, the authors conclude that (1) The number of drug abusers in the United States is rapidly increasing, and a significant proportion of drug abusers is driving while under the influence of drugs. (2) The four most commonly used drugs in order of their probable contribution to traffic accidents are central nervous system stimulants and depressants, hallucinogens, narcotics, and marijuana. (3) The major problem in defining the role drugs play in highway accidents is the lack of effective methods of drug detection. (4) Formidable medical evidence indicates that all drugs impair, to varying degrees, a person's ability to perform basic driving skills safely. (5) In addition to simulated driving tests, driving records of drug users and studies of fatal accidents show drug users to have more traffic accidents than nonusers. (6) The combined use of alcohol and drugs causes more impairment than the sum of their separate effects.

The authors recommend that publicity campaigns be launched to warn the public about the dangers involved in driving while using any drug, particularly in combination with alcohol. Furthermore, they advocate the development of an effective method of drug detection which would be an integral part of routine accident investigation. Finally, they recommend that pharmaceutical companies be forced to place tighter controls on their drug shipments. (HSRI)

1-18 pages 43 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-72-D1015

THE EFFECT OF MARIJUANA ON DRIVING PERFORMANCE, F.B. Benjamin, Current Research in Marijuana, M.F. Lewis, ed., p205-14, New YOrk: Academic Press (1972)

Presented here is a summary of the available data relating marijuana use to automobile driving. Two tables are presented: (1) acute marijuana effects; and (2) variables which could be responsible for marijuana accidents. The literature concerning the two areas is reviewed as it relates to driving skills. From this literature review the author concludes that preliminary evidence indicates that marijuana impairs the ability to drive. However, marijuana apparently is not a significant factor in the statistical incidence of fatal and nonfatal accidents. These two observations, if combined, indicate that either the marijuana smoker is conscious of the impairment and avoids driving, or that he manages to compensate for the deficiency, at least to some extent. (AAM)

18 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Review: Drugs and Highway Safety.

UM-77-D1016

REHABILITATION IN EPILEPSY, A.J. Arieff, Comprehensive Therapy, v3 n4 p13-18 (1977)

Provided here is an overview of the history, causes, and treatment of epilepsy. Drug intoxication is no longer necessary for a remission of seizures. In 80% of all patients, use of the proper drug or drugs can obtain a complete remission of all seizures. The spell-free patient may engage in any type of nonhazardous occupation. The epileptic patient should not operate machinery that might injure him or others were he to have a seizure.

The driving of a motor vehicle, however, remains a problem for the person suffering seizures. Not all states allow epileptics to drive a car. There is an increasing trend, however, for states to allow patients who have epileptic disorders to drive a car providing they have had no seizures for at least a year and are under competent and regular medical care. Only a small percentage of automobile accidents occur as a result of epileptic seizures.

Also described in this paper are obstacles to rehabilitation. Some of these are denial of illness, psychological reactions to the seizure, social and family reactions to patient, under- and overuse of drugs, and unpleasant publicity about epilepsy. (HSRI)

0 refs

KEYWORDS: Review.

UM-75-D1017

LANGZEITTHERAPIE UND VERKEHRSTUCHTIGKEIT [LONG-TERM MEDICATION AND TRAFFIC SAFETY], F. Schardt, Internistische Praxis, v15 n2 p429-38 (1975)

Presented in this paper is a review of the potential dangers caused by drugs and untreated medical conditions in traffic. Traffic safety can be endangered by illness, injury, long-term medication, attempts to demonstrate special achievements, lack of interest for traffic problems on the part of the physician, lack of advice to patients, and insufficient enlightenment of physicians and chronic patients. Traffic safety is assumed to be possible when no crisis or acute illness exacerbation is present, reaction capacity is not reduced by illness or medicants, stress threshold of patients is known,

and no additional alcohol or sedatives are taken. Traffic safety is reduced by sudden syncope, intoxication, hemorrhage, nervous irritability, tiredness, arteriosclerosis, and cardiac arrhythmia. Patients should not drive for at least six months after myocardial infarcation, Adam Stoke's syncope, carotid sinus syndrome heart failure (degree IV), mitral and aortic stenosis, hypertension under treatment, and preapoplectic signs and symptoms. Cirrhosis of the liver, ulcers caused by long-term medication, and postoperative long-term complications must also be considered for traffic safety. pDrivers take analgesics, sedatives, hypnotics, cardiocirculatory, and gastrointestinal medicants in decreasing order of frequency. Most drugs are metabolized by hydroxylases. These enzymes are inhibited by alcohol, thus additional alcohol intake can lead to undesired and dangerous effects. (EMM)

22 refs German

KEYWORDS: Review: Drugs and Highway Safety.

UM-75-D1018

ZUR BEURTEILUNG DER FAHREIGNUNG NACH ABGELAUFENER ENDOGENER PSYCHOSE [ASSESSMENT OF CAR DRIVING APTITUDE AFTER PAST ENDOGENOUS PSYCHOSIS], G. Heinz; R. Tolle, Nervenarzt, v46 n7 p355-60 (1975)

The controversy concerning the question of driving ability after previous endogenous psychosis is not yet over. The scientific literature of the last twenty years supports alongside two mutually contradictory points of view the possibility of a third standpoint which takes an intermediate position. This position advocates the obtaining of an expert medical opinion and a shortening of the waiting period required after psychoses before driving is permitted.

A review of current scientific literature indicates that the majority of scientific studies, especially the empirical investigations, agree that following previous endogenous psychoses, in general the aptitude for driving is regarded unimpaired so far as previous skill, measurements, and probability of behavior can be determined. Some factors, however, can be assessed neither overall nor by general principles. These include residual psychopathological symptoms which lead to permanent disability, effects of psychotropic drugs, and accident proness. Regarding the concept of waiting periods, it is unknown what this waiting period should be since psychoses in the general pattern of schizophrenia or manic depressive disease make such varied progress that no scientifically based assessments of risk can be made. In view of this, each case should be individually investigated and assessed. (EMM)

30 refs German

KEYWORDS: Review.

UM-76-D1019

THERAPEUTISCHE ASPEKTE BEI AKUTER LUMBAGO [THERAPEUTIC ASPECTS IN ACUTE LUMBAGO], C. Bremer; K.H. Leickert, Medizinische Welt, v27 n27 p1351-2 (1976)

Reported here are the results of a study that used diazepam to treat acute lumbago. The authors noted that acute lumbago in many cases could be improved by monotherapy with diazepam. This was confirmed by patient reports and by the results of psychomotor testing. In most cases where the pains were stopped by diazepam there were definite improvements in the parameters of the Schober distance and finger floor distance. Emotional tension was favorably influenced by diazepam in forty patients.

The effects of high initial doses of diazepam on driving and traffic safety are also examined. (CA)

0 refs German

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Clinical Study. Psychomotor Tests.

UM-71-D1020

AN EXPERIMENTAL APPROACH TO DRIVER EVALUATION USING ALCOHOL DRINKERS AND MARIHUANA SMOKERS, A. Binder, Accident Analysis and Prevention, v3 n4 p237-56 (Dec 1971)

Many difficulties present themselves in experimental studies of the effect of drugs on driving. Among these are artificiality, choosing appropriate and representative subjects, and safeguarding the welfare of those subjects. The purpose of this study was to combine the control of the experimental laboratory with the natural occurrence of drinking in subjects studied epidemiologically. For comparison purposes subjects smoking marijuana under both the drinking and the nondrinking conditions were also studied.

Three groups of subjects were studied: subjects who had been drinking alcoholic beverages, subjects who had been smoking marijuana, and controls. Forty drinkers and ten controls (aged 21 to 60) were recruited from bars in the Santa Monica area while twenty marijuana smokers (aged 19 to 25) were recruited from "grass parties" on a college campus. The recruits were driven to the laboratory, where they were tested for driving ability, and then driven back to the bar or party. They were asked to return to the laboratory for a nondrug testing session two weeks later. Upon arrival at the laboratory each subject completed a questionnaire and had his BAL and intelligence measured in both sessions. Subjects were then tested on a device which measured the types of skills used in driving.

The results of the testing led the experimenters to the following conclusions: (1) As average BAL increases, people respond more slowly in a central tracking task and more often respond erroneously to incidental cues. (2) The evaluation of intelligence by experimental personnel proved to be a valid indicator of adequacy of performance. This variable seemed to be as important as BAL in terms of predicting performance. (3) Not only is alcohol consumption associated with diminished overall performance, but increasing BAL seems to produce greater variability in response, possibly indicating overly strong reactive tendencies with elevated BAL. (4) Marijuana smoking does clearly produce a decrement in some components of driving performance.

The article concludes with a review of literature dealing with the effect of BAL on driving performance. (HSRI)

34 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol)*. Driving Simulator. Drug Concentration-Effect Study: Driving Skill Impairment. Epidemiology: Regional or Local Survey of Drug Use Patterns. Experimentation: Dose-Effect Study. Psychological Testing.

UM-66-D1021

THE DRUG IMPAIRED DRIVER, C.J. Rehling, Police, v11 n1 p15-17 (1966)

Presented here is a brief review of five classes of drugs and a discussion of their potential ability to impair driving. Narcotics, barbiturates, tranquilizers, antihistamines, and amphetamines are discussed. The author emphasizes that because so many drugs in common use have a sedative effect, danger lies in the use of almost any drug by the driver in modern traffic. The use of drugs holds much the same concern as the use of alcohol, since driver impairment is the common consequence.

The traffic problem requires laws designed to cope with the drugged driver as well as the drinking driver. Laws dealing merely with the habitual user of drugs and his driving are not meeting the major problem. It is the nonaddicted user who is the greater menance in traffic. Medical examination of any impaired driver in whom an alcohol test fails to account for his condition and laboratory identification of drugs in his immediate possession should be adopted as routine procedures by enforcement agencies. (AAM)

0 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-69-D1022

HIGHWAY CRASH AND CITATION PATTERNS AND CHRONIC MEDICAL CONDITIONS, J.A. Waller; J.T. Goo, Journal of Safety Research, v1 n1 p13-27 (Mar 1969)

Types of crashes and citations of 1701 drivers with chronic medical conditions known to the California Department of Motor Vehicles were compared to those of 921 drivers not known to have medical conditions. The purpose of the study was to determine whether drivers with chronic medical conditions not only have a higher rate of accidents on the

highway but also whether they tend to have crashes and citations with different characteristics from those drivers without medical conditions.

Drivers without medical conditions committed no errors in about half of their crashes, whereas those with alcoholism committed no errors in only 13%, and drivers with other medical conditions committed no errors in a third of their crashes. Greater proportions of crashes of drivers with medical conditions involved weaving or running off the road, momentary inattention, collision of single vehicles only, or collision with parked or stopped cars. Drivers with greater severity of illness or who were obviously impaired at the time of the crash had more crashes attributed to weaving, running off the road, or collisions with stopped or parked cars, and involved single vehicles, whereas those with least severe illness had a greater proportion attributed to inattention and similar poorly defined causes. Drivers under age thirty had greater proportions of crashes and citations related to risk taking activity, such as excessive speed for conditions and following too closely, whereas drivers age sixty or older had greater proportions of driving incidents suggestive of inability to perceive, properly judge, or adequately respond to traffic flow, for example, incidents involving failure to observe traffic signals or right of way.

Several recommendations to reduce the toll of highway crashes are briefly discussed. (JAM)

9 refs

KEYWORDS: Epidemiology: Record-Based Survey.

UM-70-D1023

METRONIDAZOLE EFFECT ON SOCIAL DRINKERS, H.D. Strassman; B. Adams; A.W. Pearson, Quarterly Journal of Studies on Alcohol, v31 n2 p394-8 (Jun 1970)

The value of the trichomonacidal agent metronidazole (Flagyl(R)) in treating alcoholism or reducing the craving for alcohol is at present uncertain. In this double-blind study, an attempt was made to determine whether metronidazole affects the drinking pattern of nonalcoholics. Twenty-five men and twenty women ranging in age from 20 to 55 were given 1 1/2 ounces of 80 proof alcohol to be consumed every half hour for three hours at a controlled cocktail party. Half of the group were then given 250 mg tablets of metronidazole, the rest were given placebo. Subjects were instructed to take four tablets each day (1g per day).

The second party was similar to the first except that on entering each subject was questioned about any effects experienced during the intervening week. Results showed no significant difference in the amount of alcohol consumed at the two parties by either group, as determined by blood alcohol content. There was no significant difference in the drinking pattern of the two groups during the time span of the experiment, and thus no significant effect of the treatment could be established. There was, however, a significant difference in the subjective reactions to the two treatments. A significantly greater number of subjects in the experimental group reported physical reactions, while fewer reported psychological reactions. Five experimental subjects reported a sour or bitter taste and no desire to drink, indicating a possible effect of metronidazole on the central nervous system which could affect the desire to drink. (HSRI)

4 refs

KEYWORDS: Trichomonacides: metronidazole. Experimentation: Study of Combined Effects of Drugs. Self-Evaluation of Drug Effects by Subjects.

UM-73-D1024

MARIJUANA INDUCED STATE-DEPENDENT VERBAL LEARNING, W.H. Rickles; M.J. Cohen; C.A. Whitaker; K.E. McIntyre, Psychopharmacologia, v30 n4 p349-54 (1973)

Thirty-two male subjects (18-27 years) who had smoked marijuana not more than three times per week and not less than once per month during the preceding year were given paired associate learning under either placebo or marijuana intoxication. A 2 x 2 experimental design was used to test for dissociation effects. Each subject was observed on two occasions, ten days apart, and was randomly assigned to one of four groups: placebo-placebo, placebo-marijuana, marijuana-placebo, or marijuana-marijuana.

Marijuana intoxicated subjects needed significantly more trials to reach criterion learning than subjects under placebo. Testing of recall, ten days later, demonstrated a significant state-dependent effect. These results suggest that in a group of social marijuana users, a moderately high dose of marijuana interferes with learning new material. Once information is learned, recall of items stored in long-term memory is superior when performed in the same drug state in which learning took place.

The authors conclude that though the number of experimental subjects in this study was small, the state-dependent marijuana effect is reliable. They discuss the results in terms of state-dependent theory and the effects of central nervous system drugs on learning models. (JAM)

18 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Experimentation: Acute Dosage Study. Psychological Testing.

UM-73-D1025

THE EFFECT OF BENZOCTAMINE AND ALCOHOL ON MOTOR-SKILLS USED IN CAR DRIVING, A.A. Landauer; W. Laurie; G. Milner, Forensic Science, v2 n2 p275-83 (May 1973)

Three groups, each of eleven healthy male subjects ranging in age from 21 to 38 years, were given either 40, 20, or 0 mg of benzoctamine (Tacitin(R)). They were tested with a battery of motor-skill tests and questionnaires both before and after alcohol intoxication (induced average blood alcohol level: 0.083%). The test battery included three reaction tests as measured by the Uniwest Driving Simulator, a modified tapping test, and a dot tracking test.

In three out of five measures performance decreased significantly after alcohol consumption. However, there was no significant difference in performance between the three groups of subjects in relation to the effects of benzoctamine. Subjects who had received 40 mg of benzoctamine felt less energetic than the subjects in the other two groups, as assessed by self-rating scales. A single dose of 40 mg of benzoctamine or two doses of 10 mg did not affect motor-skill performance and no potentiation of alcohol effects occurred in these subjects. However, the possibility of adverse idiosyncratic reactions must be remembered, therefore no drug should be prescribed for trivial or casual indications.

Attention is drawn to the importance of testing all drugs given to outpatients for any possible adverse effects if alcohol is also taken. The medical practitioner should pay attention to such factors as patient's suicide risk, drinking habits, driving behavior, and past history of specific drug sensitivities. The final choice of medication should take these variables into account. (JAM)

29 refs

KEYWORDS: Muscle Relaxants (Central): benzoctamine. Nonbarbiturates: benzoctamine. ethanol (ethyl alcohol)*. Experimentation: Dose-Effect Study. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests.

UM-70-D1026

DRUG-INDUCED DISTURBANCES OF VISION THAT MAY AFFECT DRIVING, W.M. Grant, Proceedings of the 11th Annual Meeting of the American Association for Automotive Medicine, A.H. Keeney, ed., p192-200, Springfield, Ill.: Charles C. Thomas Publishing (1970)

This paper reviews the literature concerning the effects of drugs and toxic substances on the eye which might have practical significance in driving. The paper is organized according to anatomic organs in view of the fact that vision may be affected by disturbances of the cornea, the pupil, the lens, the retina, the optic nerve, the brain, and the external eye muscles. For each anatomical structure, drugs which have an adverse effect are discussed.

The evidence indicates that the small disturbances of function of external eye muscles attributable to alcohol, barbiturates, carbon monoxide, and the amphetamines are almost neglibible in comparison with the effects of these substances on mental functions. It seems that visual disturbances are relatively trivial and therefore constitute only a small part of the drugs and driving problem.

When the cornea and lens are disturbed seriously from very toxic substances and central visual acuity is seriously impaired, the risk of driving dangerously tends to be reduced by the fact that such patients generally are aware of their problem and likely to seek help.

The most dangerous toxic disturbance of vision would involve blind areas eccentrically located in the horizontal field of vision, with no noticeable alteration of central visual acuity and with the patient not aware of anything wrong. This type of disturbance can be caused by chloroquine and related drugs. Particular attention should be given to patients taking these drugs, being especially alert to possible driving problems. (HSRI)

22 refs

KEYWORDS: Review: Drug Effects.

UM-76-D1027

DIE PERSONLICHKEITSSPEZIFISCHE WIRKUNG EINES TRANQUILIZERS [PERSONALITY-SPECIFIC ACTION OF A TRANQUILIZER], R. Richter; V. Hobi, Arzneimittelforschung, v26 n6 p1136-8 (1976)

Twenty-three emotionally unstable and 22 emotionally stable subjects were selected from a total sample of 147 students by three personality inventories (FPI, GT, MPI). In a 2^3 factor design the following effects of a single dose of 1.5 mg bromazepam against placebo were found: Fine-motor activity (tapping, line tracing) was stabilized independently of personality traits. However, performance in attention tests such as choice-reaction time tests was decreased in the emotionally stable group. In the emotionally unstable group, i.e., in those subjects for whom bromazepam could therapeutically be indicated, an advantageous drug effect on performance in these tests was evident. The following variables were not affected by personality or medication: afterimage of spiral rotor, critical flicker fusion, and the tracking task. (JA)

12 refs German

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): bromazepam. Experimentation: Acute Dosage Study. Psychological Testing. Psychomotor Tests. Tests of Sensory Function.

UM-51-D1028

PHYSIOLOGICAL PERFORMANCE FOLLOWING A HYPNOTIC DOSE OF A BARBITURATE, R.E. Goodnow; H.K. Beecher; M.A.B. Brazier; F. Mosteller; R. Tagiuri, Journal of Pharmacology and Experimental Therapeutics, v102 n1 p55-61 (May 1951)

This study attempts to investigate the nature and duration of the neuromuscular effects of the usual hypnotic dose (0.1g) of pentobarbital sodium.

Subjects were thirty male college students between the ages of 18 and 26. Half of them received orally 0.1 g pentobarbital sodium, the rest received a placebo in two sessions. A battery of tests assessing tapping speed, auditory reaction time, naming of opposites, memory for digits, and body temperature was administered six times within twenty-four hours.

Four tests, tapping speed, auditory reaction time, naming of opposites, and memory for digits, showed a significant deterioration in performance four hours after the barbiturate had been taken. This deterioration was found to continue in a highly suggestive (qualitative trend), but not statistically significant, degree until after fourteen hours postmedication. Loss in critical judgment was also evident. (HSRI)

14 refs

KEYWORDS: Barbiturates: pentobarbital. Experimentation: Acute Dosage Study. Psychological Testing. Psychomotor Tests.

UM-53-D1029

THE PERSISTENCE OF MENTAL IMPAIRMENT FOLLOWING A HYPNOTIC DOSE OF A BARBITURATE, J.M. von Felsinger; L. Lasagna; H.K. Beecher, Journal of Pharmacology and Experimental Therapeutics, v109 n3 p284-91 (Nov 1953)

This paper investigates the problem of measurement of the persistence of mental impairment following the ingestion of a hypnotic dose (0.1 gm) of pentobarbital sodium. The effects of pentobarbital sodium on a battery of tests designed to measure complex psychological functions were studied in twenty healthy male college students in two separate sessions. Subjects were given either 0.1 g pentobarbital sodium or placebo. Five hours after ingestion of the drug, a battery of tests was given which tested visual perception, serial learning, recall, association, attention, computation, auditory distraction, and ability to solve analogies.

As long as five and one-half to eight hours after ingestion of the drug, significant impairment of visual perception, attention, arithmetical performance, and recall was demonstrated. Associations were increased in number after drug administration, but these showed less relation to external stimuli than after the placebo. In a confusing and disturbing test situation, the drug effect was to facilitate resistance to distraction. Serial learning on the analysis test failed to show any drug effect.

These observations, therefore, corroborate the frequent complaint of "hang-over" after use of pentobarbital sodium for hypnotic purposes. It is suggested that the prolonged effects detected here must be considered as factors which limit the usefulness of this and similar agents when such persistence of effect might be undesirable; that is, where it is important that the individual's full mental facilities be available. (HSRI)

6 refs

KEYWORDS: Barbiturates: pentobarbital. Experimentation: Acute Dosage Study. Psychological Testing.

UM-73-D1030

CANNABIS INDUCED IMPAIRMENT OF PERFORMANCE OF A DIVIDED ATTENTION TASK, S. Casswell; D. Marks, Nature, v241 p60-1 (5 Jan 1973)

Driving can be described as a divided attention task in which the driver is forced to perform a compensatory tracking task while searching for and recognizing environmental signals. Ten naive subjects and ten experienced marijuana users, all male, were required to monitor and respond to two types of visual signals from different sources in order to determine the effects of cannabis on performance of a divided attention task. Using a double-blind design, placebo, 250 mg THC, or 500 mg THC were administered in counterbalanced order on three separate occasions approximately one week apart. A divided attention task in which subjects had to respond to central and peripheral light signals was begun thirty minutes after the subjects had finished smoking the cigarette.

Significantly more of both central and peripheral light signals were missed by subjects after smoking cigarettes containing delta-9-THC than after smoking placebo. There was no significant difference between experienced and naive subjects in the amount of impairment obtained. This decrement in performance on a divided attention task is similar to that found following alcohol intoxication and is believed to be associated with the frequent occurrence of alcohol-related accidents. (HSRI)

8 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Experimentation: Dose-Effect Study. Tests of Sensory Function.

UM-73-D1031

BIOLOGICAL THRESHOLD OF IMPAIRMENT DRUGS IN INDUSTRIAL PERFORMANCE, C.H. Hine, Activitas nervosa superior, v15 n4 p266-8 (1973)

The exact number of injury cases in industry which occur from drugs taken either for therapeutic reasons or for mood alteration is not known. While there is a large body of information about ethyl alcohol, relatively little is known regarding the amounts of other drugs required to produce specific changes in awareness, performance, mental alertness, and motor skills. Furthermore, the rate of metabolism and elimination is unknown for most drugs.

In this paper such data are presented for fifty compounds. These data are derived entirely from the author's experience with clinical observations and coroners' cases. For each drug, both chemical and proprietary names are listed. Blood level indicating impairment in pmm and detectability in urine are also provided.

The author believes that much more work has to be done in controlled testing of these drugs in order to obtain adequate information about them. (HSRI)

0 refs

KEYWORDS: Drug Concentrations in Body Fluids: Tabulated Data.

UM-69-D1032

AUDITORY AND VISUAL THRESHOLD EFFECTS OF MARIJUANA IN MAN, D.F. Caldwell; S.A. Myers; E.F. Domino; P.E. Merriam, Perceptual and Motor Skills, v29 p755-9 (1969)

This study attempted to measure auditory and visual acuity in a group of experienced marijuana smokers using standardized psychophysical techniques. Twenty experienced marijuana users with a mean age of 23.3 years smoked either cigarettes containing 3.93 mg delta-9-THC (experimental) or cigarettes containing alfalfa (control). In the experimental group, subjects were allowed to smoke as many marijuana cigarettes as they wished until they reached a high. Subjects were tested with a battery which included a visual brightness test, auditory threshold test, auditory intensity differential threshold test, and an auditory frequency differential threshold test.

The results indicate that marijuana minimally affects those measures of sensory acuity tested in this study. Comments of subjects indicated (1) the importance of suggestion in subjective effects of marijuana; (2) the importance of setting; and (3) the ability of subjects to "turn off" the high voluntarily. Therefore future studies should concern not only the pure pharmacologic effects of marijuana but also the psychologic factors involved. (HSRI)

7 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Experimentation: Acute Dosage Study. Tests of Sensory Function.

UM-71-D1033

PSYCHOTROPIC DRUG-INDUCED TRANSFORMATIONS OF VISUAL SPACE, R. Fischer; R.M. Hill, International Pharmacopsychiatry, v6 p28-37 (1971)

This paper explores and defines certain variables which appear to control drug induced inhibition or enhancement of the adaptation phenomenon. Fifteen students with a median age of 23 years and a functional visual acuity of at least 20/20 were studied prior to, 60 minutes after, 110 minutes after (at drug peak), and 280 minutes after oral ingestion of 16 mg/kg psilocybin.

It was found that ergotropic arousal-inducing drugs such as psilocybin, Ditran-type glycolates, and d-amphetamine significantly lower human spatial distortion thresholds, i.e., these drugs interfere with counter-adaptation to optical distortion, or the intention to see the world undistorted. The trophotropic arousal-inducing chlorpromazine, on the other hand, promotes such counter-adaptation, that is, the optimization of visual information. The interference with optimization is independent of the rate at which the distorting stimulus is presented.

Optimization is regarded here as a cortical (perceptual-behavioral) interpretive process while interference with and promotion of the optimization are subcortical influences. (JAM)

23 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Hallucinogens and Related Agents: psilocybin. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Metabolites of Drugs and Other Agents: psilocybin. Experimentation: Acute Dosage Study. Tests of Sensory Function.

UM-75-D1034

DRUG ABUSE AS EXCESSIVE BEHAVIOR, R.M. Gilbert, Addictions, v22 n4 p52-72 (Winter 1975)

Proposed and discussed here is the theory that drug abuse is excessive behavior. Using drugs does not become a problem until it is done to excess and disrupts the effective functioning of an organism. Up until then, it is a mere occurrence. It is possible

that drug abuse may in some fundamental way be similar to excessive eating and other compulsive behavior. Indeed, the pharmacological effects of drugs may not have very much to do with drug abuse. Because it is the excessive nature of the drug-taking behavior that is the problem, just as much as the fact that drugs are involved, it is as necessary to search for the causes of drug abuse among the causes of all kinds of excessive behavior as it is to focus upon the peculiarly pharmacological aspects of the drug-taking situation. For example, alcoholism may have as much in common with overeating as it has with social drinking.

The author proposes that a recently discovered experimental procedure known as schedule induction, which is capable of generating vast amounts of apparently unadaptive behavior, may provide a useful model for excessive human behavior in general and drug abuse in particular. If this model is valid, an attempt must be made to identify the conditions of everyday life that can induce excessive behavior. One approach might be to explore the possibly relevant common features of environment-behavior interactions of people who engage in conspicuous excessive behavior and compare them with the interactions of people who do not appear to behave excessively. (JAM)

0 refs

KEYWORDS: Ganglionic Blocking and Stimulating Agents: nicotine. Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: nicotine. Review: Drug Use.

UM-79-D1035

DRUGS (OTHER THAN OR IN ADDITION TO ETHYL ALCOHOL) AND DRIVING BEHAVIOR: A COLLABORATIVE STUDY OF THE CALIFORNIA ASSOCIATION OF TOXICOLOGISTS, G.D. Lundberg; J.M. White; K.I. Hoffman, Journal of Forensic Sciences, v24 n1 p207-15 (Jan 1979)

This study attempted to compare the specific observed driving behavior in real-life situations of individuals who were subsequently determined to have used drugs prior to driving to the behavior of those who had not used drugs. The test group consisted of 765 subjects in whose blood or urine one or more psychoactive drugs other than or in addition to ethyl alcohol had been found and in whom a driving behavior problem had been documented. The control group consisted of 71 individuals with a driving behavior problem who had been apprehended in the same areas and manner as the drug group, but in whom no drugs had been found. For each case a comprehensive data collection form gathered 375 data elements about demographic characteristics, drug use, health, and driving habits.

Several conclusions were made from the study: (1) The presence of psychoactive drugs other than or in addition to ethyl alcohol in persons with driving behavior problems was found frequently. These drivers usually had such major objective alterations in sensory-motor capabilities as impaired balance and coordination, slurred speech, and staggering. (2) Those psychoactive drugs other than ethyl alcohol that were most likely to be identified with driving problems were a variety of barbiturates, diazepam, methaqualone, chlordiazepoxide, meprobamate, and ethchlorvynol. (3) More than one-half of the time when one drug was found at least one other drug (including ethyl alcohol) was also present. (4) The presence of a detectable psychoactive drug was statistically associated with accidents at a highly significant range in comparison with the control group. (5) The correlation of blood levels of the various drugs and driving behavior problems, including accident and fatality, is not yet possible, due to lack of statistics. (HSRI)

4 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital. phenytoin. Barbiturates: amobarbital. butabarbital. butalbital. pentobarbital. phenobarbital. secobarbital. Hallucinogens and Related Agents: phencyclidine. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. meprobamate. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). ethchlorvynol. methaqualone. Barbiturates. Epidemiology: Analysis of Driver Body Fluids for Drugs. Epidemiology: Self-Reported Drug Use by Drivers.

UM-61-D1036

THE EFFECT OF CAFFEINE AND SECONAL ON A VISUAL DISCRIMINATION TASK, W. Pare, Journal of Comparative and Physiological Psychology, v54 n5 p506-9 (1961)

This study attempted to test three hypotheses concerning the effects of drugs on the learning process: (a) a depressant drug (seconal) inhibits retention of a previously

learned task; (b) a stimulant (caffeine) facilitates retention of a learned task; and (c) that neither facilitation nor inhibition of retention occurs if the drugs are administered after an hour interval following task acquisition.

Seventy-two male albino rats of the Wister strain were used, divided into four groups. All received mass training to criterion on a horizontal-vertical discrimination problem. Upon reaching criterion, three groups were injected with seconal, caffeine, and saline solution, respectively. The fourth group received no injections. Three subgroups within the injection groups received their appropriate drug or saline injections five seconds, two minutes, and one hour, respectively, after reaching criterion.

All subjects were tested for retention two days after time of injection. Retention data produced the following results: (1) Seconal-injected subjects manifested more errors on retention trials than other subjects. (2) The magnitude of errors on retention trials for the seconal subjects was inversely related to the criterion-injection interval. (3) Caffeine-injected rats manifested fewer errors on retention trials than other subjects. (4) The magnitude of errors on retention trials for caffeine subjects was positively related to the criterion-injection interval.

These results were discussed in terms of Hebb's dual-phase learning theory, which they appear to support. This theory suggests that learning involves a consolidation process based on a dual physiological process, that is, reverberation of neutral circuits comprising the memory-trace followed by organic change between the nerve cells. (AAM)

11 refs

KEYWORDS: Barbiturates: secobarbital. Stimulants: caffeine. Animal Research.

UM-75-D1037

THE COMBINED EFFECTS OF ALCOHOL AND COMMON PSYCHOACTIVE DRUGS. FIELD STUDIES WITH AN INSTRUMENTED AUTOMOBILE, A. Smiley; E. LeBlanc; I.W. French; R. Burford, Canadian Society of Forensic Science Journal, .v8 n2 p57-64 (1975)

This study describes a study on the effects of alcohol (at .06% BAC) alone and in combination with 50 mg diphenhydramine, 5 mg diazepam, 3-0.5 g marijuana cigarettes, or placebo on both high and low speed driving in an instrumented car. The purpose of this study was to describe the changes in driver behavior under various drug conditions.

Six male and two female subjects, aged 19 to 27 years, were tested once each day under one of the drug conditions. Thirty to ninety minutes after drug ingestion, subjects drove an instrumented car on an 8.5 mile section of unopened highway which contained three traffic lights, a half-mile slalom course, and opposing traffic. A peripheral vision secondary task was used for the purpose of increasing the visual task load on the subject to the level of the normal search and recognition task performed while driving. The following measures of driver performance were made: steering amplitude and frequency while driving 60 mph; steering amplitude while driving 25 mph; speed and speed variation at both 25 and 60 mph; number of pylons knocked down; and stopping accuracy.

For the speed measurements, the drug conditions in order of decreasing mean speed were: placebo; alcohol; alcohol with diphenhydramine; alcohol with diazepam; and alcohol with marijuana. For steering movement, the drug conditions in order of decreasing excess movement were: alcohol and marijuana; alcohol and diphenhydramine; alcohol; placebo; and alcohol and diazepam. For the slalom course, the best performance occurred for the placebo condition and the worst for the alcohol and marijuana condition. The conditions in order of decreasing mean stopping accuracy were: placebo; alcohol and diphenhydramine; alcohol and diazepam; alcohol; and alcohol and marijuana.

The results of this experiment show that alcohol alone and in combination with other drugs affects driving performance in different ways. Measures which most clearly differentiated between drug conditions were steering movement and average velocity. The authors conclude that further research in this area is needed before the manner in which driving behavior is affected by a drug can be related to physiological action of the drug. (HSRI)

12 refs

KEYWORDS: Antihistamine Agents: diphenhydramine. Cannabis Sativa L. and Related Agents: marijuana. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: diphenhydramine. ethanol (ethyl alcohol). Closed Course Driving.

UM-78-D1038

ACTIONS AND INTERACTIONS WITH ALCOHOL OF DRUGS ON PSYCHOMOTOR SKILLS: COMPARISON OF DIAZEPAM AND GAMMA-HYDROXYBUTYRIC ACID. M.J. Mattila; E. Palva; T. Seppala; R.U. Ostrovskaya, Archives internationales de pharmacodynamie et de therapie, v234 n2 p236-246 (Aug 1978)

Effects of gamma-hydrobutyric acid (GOBA) on psychomotor skills related to driving were studied in healthy student volunteers. The effects of oral GOBA (1.0 and 2.0 g), alone or in combination with 0.5 g/kg of ethyl alcohol, were compared in double-blind cross-over trials against oral diazepam (10 mg), alcohol (0.5 g/kg), and lactose placebo. Reactive and coordinative skills, attention, flicker fusion, proprioception nystagmus, Maddox wing, and subjective estimations were included.

The first single-dose trial with twelve volunteers revealed that neither GOBA (1.0 g) nor diazepam modified attention. Diazepam impaired reactive skills while coordinative skills remained largely uninfluenced by diazepam or GOBA. Both diazepam and GOBA impaired leg proprioception. Only diazepam acted as a sedative drug.

In the second trial with twelve volunteers, GOBA (1.0 g) slightly increased reaction mistakes whereas GOBA (2.0 g) did not. Both doses of GOBA were ineffective on coordinative skills, critical flicker fusion frequency, and proprioception. Alcohol alone (0.41 $\pm$ 0.047 mg/ml) improved rather than impaired skills. GOBA (1.0 g) and alcohol (0.36 $\pm$ 0.027 mg/ml) impaired reactive skills more than GOBA (2.0 g) did but no potentiation was seen. Diazepam impaired reactive and coordinative skills and flicker fusion. When diazepam was given on two consecutive days, some tachyphylaxis to the diazepam response was seen on coordinative skills but not on reactive skills or flicker fusion.

It is concluded that in recommended therapeutic doses GOBA neither impairs driving skills nor importantly increases the effects of low doses of alcohol. (JA)

26 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Neurochemicals, Neurotransmitters, and Neurohormones: gamma-hydroxybutyric acid (GABA). Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Dose-Effect Study. Experimentation: Study of Combined Effects of Drugs. Psychological Testing. Psychomotor Tests. Tests of Sensory Function.

UM-77-D1039

PSICOFARMACI ED IDONEITA ALLA GUIDA. EFFETTI DEL LEXIL SUI TEMPI DI REAZIONE [PSYCHOTROPIC DRUGS AND FITNESS TO DRIVE. EFFECTS OF LEXIL ON REACTION TIMES], M. Marigo; P. Lion, Gazetta Medica Italiana, Aggiornamenti Clinicoterapeutici, v136 n1 p1-10 (Jan 1977)

After a short outline of general problems regarding relationships between intake of psychotropic drugs and fitness to drive, the results of experimental research involving the examination of reaction times of twenty volunteers who had taken a combination of bromazepam and propantheline bromide are reported. Statistical processing of data obtained in the double-blind test suggests that performance at psychotechnical performance is not impaired by intake of this combination. (JA)

30 refs Italian

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): bromazepam. Neuromuscular Blocking (Antimuscarinic) Agents: propantheline. Parasympatholytic (Cholinergic Blocking) Agents: propantheline. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests.

UM-75-D1040

CLOBAZAM, FONCTIONS DE VIGILANCE ET CONDUITE AUTOMOBILE [CLOBAZAM: EFFECT ON VIGILANCE AND AUTOMOBILE DRIVING], J. Rigal; A. Savelli, Gazette Medicale de France, v82 n33 p3908-14 (10 Oct 1975)

Presented in this article is a review of clobazam and a report of two investigations of its effects on vigilance, attention, and coordination. The first study compared the effects of clobazam to those of diazepam on vigilance. Subjects were tested in word

association, avoiding obstacles, the digit finger test, the draught board, and recognition of complex figures.

In the second test the subjects were required to drive a car 100 km/hr after a ten-hour sleep. Thirty minutes before driving, each subject was administered 20 mg/kg clobazam or placebo. In neither test did clobazam appear to impair vigilance or driving ability. The authors conclude, on the basis of these experiments, that clobazam is compatible with safe driving. (HSRI)

0 refs French

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): clobazam. diazepam. Muscle Relaxants (Central): diazepam. Closed Course Driving. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests.

UM-79-D1041

CURRENT ROLE OF ALCOHOL AS A FACTOR IN CIVIL AIRCRAFT ACCIDENTS, L.C. Ryan; S. R. Mohler, Aviation, Space, and Environmental Medicine, v50 n3 p275-9 (Mar 1979)

This paper presents an analysis of alcohol-associated fatal accidents occurring in general aviation through 1976. It provides the reader with tables and statistical information on percent of total positive alcohol cases at various milligram percent levels, time of day that these accidents took place, and percent of accidents with alcohol as the causal factor at various phases of flight.

It is concluded that alcohol-associated general aviation fatal accidents have plateaued since 1969 at the 16% level, according to FAA records (15 mg % or higher blood level). According to a recent survey, about one-third of general aviation pilots considered flying after drinking within a time period which would result in a 15 mg % blood alcohol level or higher to be safe behavior.

The author concludes that an intensified pilot education program concerning the adverse effects of even small amounts of alcohol on safe flight is necessary. (HSRI)

11 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Epidemiologic Research: Drug Concentrations in Body Fluids. Epidemiology: National Survey of Drug Use Patterns.

UM-72-D1042

REAKTIONSZEITMESSUNGEN BEI OPERATIVEN EINGRIFFEN IN ORTLICHER SCHMERZAUSSCHALTUNG, P. Tetsch; E. Machtens; M. Voss, Schweizerische Monatsschrift Fuer Zahnheilkunde, v82 n3 p299-306 (1972)

This article concerns the investigation of acoustic, optical, and psychomotor reactions of 100 patients and 20 additional subjects before and after dental surgery under local anesthesia. It was found that reaction times are significantly prolonged and concludes that a reduction in traffic aptitude is possible. (JAM)

22 refs

KEYWORDS: Anesthetics. Psychomotor Tests.

UM-79-D1043

EFFECT OF ALCOHOL AND MARIJUANA ON EYE MOVEMENTS, R.W. Baloh; S. Sharma; H. Moskowitz; R. Griffith, Aviation, Space, and Environmental Medicine, v50 n1 p18-23 (Jan 1979)

This paper is concerned with the investigation of the isolated and combined effects of alcohol and marijuana on eye movements. The changes in saccade maximum velocity and the slow-component velocity of optokinetic nystagmus in twenty-four normal subjects, given alcohol alone, THC alone, and different combinations of the two, were measured.

Each subject was given an initial trial run and then tested three times (at weekly intervals) with either 0.0 mg THC or 100 mg THC/kg body weight at three different blood alcohol concentrations (0.0, 0.05 and 0.1%). A 2x3 factorial design was used. Saccades and smooth pursuit were induced by a dot of light moving in steps and ramps on a

modified television set. Optokinetic nystagmus was induced by a cloth drum completely surrounding the subject and moving at a constant velocity of 30 degrees per second. Alcohol (0.05 and 0.1%) alone produced significant ($p<0.05$) impairment of saccade maximum velocity and reaction time, smooth pursuit velocity, and optokinetic slow-component velocity. The addition of THC caused performance to further deteriorate at each blood alcohol level, but in all but one instance, the added effect was not statistically significant ($p>0.05$). At the THC and alcohol concentrations used in this study, the eye movement effects of alcohol overshadowed those of marijuana. (JAM)

30 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Experimentation: Study of Combined Effects of Drugs. Tests of Sensory Function.

UM-76-D1044

INTERACTION MEDICAMENTS, ALCOOL ET CONDUITE AUTOMOBILE [INTERACTION BETWEEN DRUGS, ALCOHOL, AND AUTO DRIVING], L. Manzo; M. DeBernardi; N. Lery, Bulletin de Medecine Legale Urgence Medicale Center Anti-Poison, v19 n1 p53-61 (1976)

The purpose of this paper is to inform the public about the hazards caused by mixing alcohol and drugs. A small quantity of alcohol can be dangerous, especially when mixed with a pharmaceutical preparation. This knowledge should be extended to traffic safety associations so that drivers will be aware that certain drugs may be dangerous when taken in combination with alcohol. It is proposed that study of the interaction of drugs and alcohol should be included in the program of preclinical research of all new drugs. It has even been advocated that as long as no precise information concerning the metabolism of a preparation is available, no alcohol should be used during the entire course of medical treatment. The concept of interaction gives rise to questions reaching even farther, viz., the possible interacting of alcohol with a motor vehicle driver's chemical, toxicological, and alimentary environment and the possibility of the consequences affecting not only traffic safety but occupational safety as well, especially in the case of machine operators. (JAM)

14 refs French

KEYWORDS: Review: Drugs and Highway Safety.

UM-76-D1045

ACCIDENTS CORPORELS GRAVES ET AGENTS PSYCHOTROPES [SERIOUS ACCIDENTAL PHYSICAL INJURIES AND PSYCHOTROPIC AGENTS], P. Hanote; J. Metrot; M.-J. Perez; P. Parent, Annales de Medicine des Accidents et du Traffic, n10 p18-20 (1976)

The relationship that exists between the taking of psychotropic substances and the number and gravity of all kinds of accidents is studied here. This research project covered 135 cases recorded systematically over a two-month period. Of these cases, 116 were able to be analyzed; they included 25 women and 91 men. Work injuries happened mostly to men between the ages of 30 and 50: 6 of these cases indicated excessive alcohol level in the blood; 4 cases indicated excessive medication alone; and 1 indicated a combination of alcohol with medication.

Out of eighty automobile accident-victims, ten cases of medication associated with a high level of alcohol in the blood were found. Among accident victims, women were found to take more medication than men. Medication affects men's driving less than women's driving. However, almost 50% of the men between the ages of 20 and 30 involved in accidents had a level of alcohol in their blood greater than 0.08%. (JA)

0 refs French

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Epidemiology: Analysis of Driver Body Fluids for Drugs. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-D1046

DRINKS, DRUGS AND DRIVING: A LOSING COMBINATION, THE EFFECTS OF MIXING ALCOHOL AND DRUGS ON DRIVING ABILITY, Smashed, Drinking and Driving, P19-20 (1978)

Presented here is a quiz to test one's knowledge of the dangers of driving while under the influence of an alcohol-drug mixture. It includes such topics as the influence of marijuana on perceptual functions, the effects of sedatives on mood changes when combined with alcohol, and the impairment caused by stimulants. (HSRI)

Transport Canada

0 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-75-D1047

PSYCHOTROPIC DRUGS AND IMPAIRMENT OF PSYCHOMOTOR FUNCTIONS, A. Penttila; H. Lehti; J. Lonnqvist, Psychopharmacologia, v43 n1 p75-80 (28 Jan 1975)

This article deals with the effects of psychotropic drug therapy on the operations of psychomotor functions as tested in a clinical examination of suspected drunken drivers. Some psychiatric and mental but otherwise healthy patients were examined; the type of medication and the number of drugs varied greatly. In seventy-one cases the mean degree of error in the clinical examination was higher, and in several of these, markedly higher than the reference values obtained earlier on suspected drunken drivers when the blood contained very small amounts of alcohol or none at all. Coarsely-divided nystagmus was registered in eighteen patients on psychotropes. This is an obvious sign of marked side-effect of medication, however, it was present less infrequently than in subjects who had ingested alcohol.

The present results indicate that application of the clinical examination method, which was originally developed for and related to the examination of alcohol cases, can be of value in assessing subjects on psychotropes, making it possible with clinical examination to obtain valuable medico-legal information on the impairment of physiological functions. (JAM)

26 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Central Nervous System (CNS) Agents. Epidemiology: Regional or Local Survey of Drug Use Patterns. Review: Survey Methodology.

UM-74-D1048

EFFECTS OF OXYPERTINE AND CHLORDIAXEPOXIDE ON HUMAN MOTOR CO-ORDINATION, P.A. Berry; D.J. Grubb, The Journal of International Medical Research, v2 n3 p177-88 (1974)

The performance of six normal healthy male volunteers aged 25 to 44 in three simple coordination tests was used to assess the effects of three doses of oxypertine and one dose of chlordiazepoxide on motor coordination. In the first part of the study, the effects of single doses of oxypertine (10 and 20 mg) were assessed on performance on a driving simulator. Both doses produced initial improvements in performance in the braking test, followed by deterioration. Performance four hours after 10 mg of oxypertine was normal when compared with the placebo response. Chlordiazepoxide (10 mg) produced a deterioration in performance. Statistical analysis of the braking reaction times revealed large subject-to-subject variations, and in only one case was a statistically significant difference between treatments demonstrated.

The second part of the study failed to confirm the improvements noted in the earlier study. No statistically significant changes in performance were detected following the first capsules of oxypertine (5 or 10 mg). Three and four hours after consuming the second 5 or 10 mg capsule, significant changes in braking performances were recorded at the 1% and 5% levels of significance respectively. Performance in the pursuit rotor test was enhanced following the ingestion of 5 mg of oxypertine, but was depressed after 10 mg of the drug; these observations were not statistically significant.

Dose related drowsiness was detected following oxypertine and although less obvious outwardly in later studies, it was still apparent in the performance scores of the subjects, particularly those who had consumed the higher (20 mg) dose of oxypertine.

The braking reaction time experiments suggest that dosage with oxypertine of a frequency of 10 mg every four hours or less may result in an accumulation of the drug and may significantly impair motor coordination. However, it seems unlikely that prolonged

dosage with the 5 mg dose of oxypertine will lead to accumulation of the drug and significantly impair motor coordination. (JA)

4 refs

KEYWORDS: Antidepressants: oxypertine. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. Experimentation: Acute Dosage Study. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Psychomotor Tests.

UM-75-D1049

KONTROLLIERTE PRUFUNG DES EINFLUSSES VON NEOSTON(R) AUF DAS REGELLEISTUNGSVERHALTEN, AUF DIE HERZFREQUENZ UND SINUSARRHYTHMIE UND AUF DAS SUBJECTIVE BEFINDEN GESUNDER VERSUCHSPERSONEN IN TRACKING TESTS, H. Strasser, Psychopharmacologia, v43 n1 p145-56 (10 Jan 1975)

The influence of Neoston(R)--a relatively new analgesic, antipyretic, and antiinflammatory agent -- on performance in different tracking tests, on heart rate, on sinus arrhythmia, and on subjective rating was measured objectively. Fifteen healthy male and female subjects, aged 19 to 27 years, took part in sessions lasting about two and one-half hours each. Two pills Neoston(R) (2 g) or a placebo were taken orally two and five hours before the tests.

Performance in tracking was poorer on the whole with Neoston(R) than with placebo, but only up to a maximum of 5%. Except for one of the ten measurement parameters, no differences between the tests with the active drug and placebo were statistically significant at the level of 5%. The relatively uniform trend suggests a small but definite impairing effect of Neoston(R). When relating the data of the second and third session to the data of the first session of each day, impairment was more obvious. Therefore the influence of Neoston(R) on tracking performance is statistically significant but is practically almost irrelevant. In physiological variables as well as in subjective ratings only small differences between the drugs and placebo condition were measured.

When relating the results to comparable research on the effects of alcohol, tranquilizers, and stimulants, it is concluded that Neoston(R), even in the relatively high dosage used here, has no real detrimental effects on traffic safety. English translation of title: [CONTROLLED RESEARCH OF THE INFLUENCE OF NEOSTON(R) ON TRACKING PERFORMANCE, HEART RATE, SINUS ARRHYTHMIA AND ON SUBJECTIVE RATING OF HEALTHY SUBJECTS] (JA)

24 refs German

KEYWORDS: Analgesics and Antipyretics: alclofenac. Experimentation: Acute Dosage Study. Physiological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1050

PHARMACOKINETIC STUDIES ON TOLERANCE TO SEDATIVE-HYPNOTICS IN A POLY-DRUG ABUSE POPULATION. I. SECOBARBITAL, T.P. Faulkner; J.W. McGinity; J.H. Hayden; M. Martinez; E.G. Comstock, Clinical Pharmacology and Therapeutics, v23 n1 p36-46 (Jan 1978)

Described here is a study attempting to determine whether tolerance to secobarbital exists and if so, its degree in a polydrug abusing population who considers it the primary drug of abuse, and to determine the contributions of the proposed mechanisms of tolerance. The study also investigated the relationship of the intensity and diversity of drug use to barbiturate tolerance.

Twenty-three patients from a polydrug abuse treatment program with a history of sedative-hypnotic abuse were titrated with secobarbital, their alleged drug of choice, to a minimal state of toxicity consisting of nystagmus, drowsiness, ataxia, and slurred speech. Seven volunteer control subjects underwent the same titration procedure. Blood level determinations were made, and several pharmacokinetic parameters were estimated in order to determine the nature and degree of tolerance in the patient population.

Results indicated that the patients tolerated a titration dose which was slightly, but significantly higher than that tolerated by the control group. Cellular tolerance could be demonstrated in terms of higher blood levels determined at 7.0 hours after the last dose but not at the onset of toxicity. A significantly greater beta-phase disposition constant and significantly smaller population suggested the contribution of drug

disposition tolerance. Statistical comparisons of these parameters were made between several subgroups of the patient population. The patients indicating a higher frequency of sedative abuse did not differ from their patient counterparts. Those patients with positive screens for barbiturates on admission provided similar results except for an apparently higher volume of distribution. Patients indicating concurrent alcohol use did not differ from the overall patient population; those also using amphetamines showed no sign of tolerance or increased elimination and were indistinguishable from control subjects. (JAM)

39 refs

KEYWORDS: Barbiturates: secobarbital*. Drug Concentrations in Body Fluids: Chronic Dose Study. Experimentation: Chronic Dosage Study. Pharmacokinetics: Chronic Dose.

UM-77-D1051

ALCOHOL, DRUGS AND DRIVING. Canberra, Austrailia: Commonwealth of Australia Government Printer (1977)

The purposes of this book are (1) to state the problems caused by persons who drive motor vehicles under the influence of alcohol and other intoxicating drugs; and (2) to describe the application of the laws of the Australian Capital Territory (A.C.T.) designed to control them. The A.C.T. laws are contrasted with those of other states of Australia and with those of countries overseas.

The present Ordinance provisions were introduced in 1971 following a Report by the Joint Parliamentary Committee on the Capital Territory. Under the new law, persons are not being prosecuted for alcohol concentration offenses unless the concentration of alcohol in the blood when tested exceeds 165 mg of alcohol per 100 mm of blood (0.165 g). This is the highest blood alcohol concentration tolerated in drivers by the law in any part of the world.

The book discusses a number of problems resulting from the new ordinance. The most controversial is whether "random" tests should be introduced in the Capital Territory. Recent developments in Victoria and reports from overseas lend support to those who would attach to the privilege of driving license the obligation, without cause, to submit to random breath tests by police. However, the Commission does not recommend this procedure. The reasons are rehearsed at length in the report. The report contains large numbers of alternative proposals to facilitate the work of the police in combating the problems of the intoxicated driver.

The report also discloses the growing problem of driving impaired by the consumption of drugs other than alcohol. New provisions are suggested for medical examinations and the taking of blood and other samples necessary to identify the presence of other intoxicating drugs. The report also suggests significantly increased penalties that bear some relationship to the gravity with which modern societies must come to view these offenses. New countermeasures are proposed, such as development in the Capital Territory of a system of referral centers for the treatment and rehabilitation of persons with a problem of alcohol or other drug dependence. (AAM)

The Law Reform Commission report no. 4

290 pages 290 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation. Review: Drugs and Highway Safety.

UM-78-D1052

ROAD ACCIDENTS: ARE DRUGS OTHER THAN ALCOHOL A HAZARD? British Medical Journal, v2 n6149 p1415-17 (1978)

Presented here is a brief review of several surveys that studied drug impairment in drivers. These studies showed that stimulants increase the risk of fatal accidents fourteen times and sedatives and antihistamines five times, but tranquilizers not at all.

In the second part of the article the author suggests some precautions to be taken while taking medication, the most important being that doctors and dentists should warn patients about possible side effects of the medicine they prescribe and increased driving risks.

The authors also suggest that although drug abuse does not appear to be a major cause of accidents, addicts should clearly be warned of the dangers of driving while under the influence of drugs and whenever possible, be individually discouraged from doing so. (HSRI)

11 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-79-D1053

DRIVING AFTER ANAESTHETICS [letter]. P. Baskett, British Medical Journal, v1 n6164 p686-7 (10 Mar 1979)

Presented here are two letters-to-the-editor debating the proper amount of time which must elapse before a patient who has been given a general anesthetic can drive unimpaired. In the first letter it is suggested that an arbitrary forty-eight-hour limit is unnecessary, and that the physician should instead take into account the specific drug administered, the dose, and the individual. There is no interval that can be unconditionally recommended for all situations.

The response to this letter, however, defends the forty-eight-hour interval in view of the fact that laboratory studies have indicated that drug concentrations can be identified in tissues for up to forty-eight hours after administration. Since no realistic tests of driving impairment from general anesthetics have been done, the physician must rely on these laboratory tests. Therefore, it is more prudent for the physician to err on the side of caution. (HSRI)

2 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-63-D1054

VERGLEICHENDE ELEKTRONYSTAGMOGRAPHISCHE UND PSYCHOPHYSISCHE UNTERSUCHUNGEN NACH INTRAVENOSEN KURZNARKOSEN MIT THIOPENTAL, METHOHEXITAL UND PHENOXYESSIGSAUREAMID, E. Haas; H. Kreuscher; M. Strickstrock, Der Anaesthesist, v12 n11 p345-49 (Nov 1963)

This study attempted to determine the effects of thiopental, methohexital, and Bayer 1420(R) on nystagmus, reaction time, and other psychophysical parameters. Electronystagmographic and psychophysical tests were performed on twenty volunteers after comparable intravenous anaesthesia of three to four minutes duration with thiopental, methohexital, and the phenoxyaceticacid derivative Bayer 1420(R).

Optico-kinetic and sight line nystagmus as well as rotatory stimulus threshold of the vestibular apparatus were tested after awakening until the preanesthetically ascertained norms were reached. Comprehension and reaction time were assessed by the "Fallstab" and Tachystoskop tests, while power of concentration and rapidity of motion were determined by the number and Bourdon test. Motor coordination impairment was judged by the shading and writing test.

An evaluation of these optico-vestibular reactions and psychophysical tests showed a significantly shortened recovery time after intravenous anesthesia with methohexital and Bayer 1420(R) in contrast to thiopental. There was, however, no significant difference in the postanesthetic phase after administration of methohexital as compared to Bayer 1420(R). English translation of title: [ELECTRO NYOSTAGMOGRAPHIC AND PSYCHOPHYSICAL PARAMETERS DURING ANAESTHESIA AFTER INTRAVENOUS INJECTION OF THIOPENTAL, METHOHEXITAL, AND A PHENOXYACETICACID DERIVATIVE] (JA)

50 refs German

KEYWORDS: Barbiturates: methohexital. General Anesthetics: propanidid. thiopental. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Psychomotor Tests. Tests of Sensory Function.

UM-78-D1055

FOUR DEATHS RESULTING FROM ABUSE OF NITROUS OXIDE, V.J.M. DiMaio; J.C. Garriot, Journal of Forensic Sciences, v23 n1 p169-72 (Jan 1978)

Only rarely does abuse of nitrous oxide result in death. Reported here are four case histories of victims of the gas. Methods for the detection of nitrous oxide concentrations in blood samples are briefly described. Also provided is a brief history of the use of nitrous oxide from its discovery in 1776 to the present. (HSRI)

4 refs

KEYWORDS: Gases: nitrous oxide*. General Anesthetics: nitrous oxide*. Hallucinogens and Related Agents: nitrous oxide*. Drug Concentrations in Body Fluids: Acute Dose Study. Experimentation: Acute Dosage Study.

UM-79-D1056

MARIJUANA: A REVIEW OF RECENT PSYCHOSOCIAL RESEARCH, R. Jessor, Handbook On Drug Abuse, R.I. Dupont; A. Goldstein; J. O'Donnell, p337-57, Washington, D.C.: U.S. Government Printing Office (Jan 1979)

This article reviews the main findings of recent epidemiological research on marijuana. It discusses a variety of dimensions of use including frequency, recency, amount used per occasion, and the simultaneous use of other drugs.

The research of the past five years is organized under six different headings. The first concerns current epidemiology of marijuana use-- its extent, distribution, and the change in prevalence that has characterized the recent past. The second, third, and fourth sections focus respectively on environmental, personality, and behavioral factors associated with marijuana use. The fifth section deals with current developmental research on marijuana use. The final section considers some implications of current findings for further research and for a possible initiative in the direction of the prevention of marijuana abuse. (HSRI)

126 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Review: Drug Use.

UM-77-D1057

IMPAIRED DRIVING [letter], H.M. Simpson, Canadian Medical Association Journal, v116 n2 p121-2 (22 Jan 1977)

This editorial urges researchers to identify the precise elements of the problem of impaired driving. The author presents statistics on impaired driving, information on current programs of rehabilitation, and countermeasures aimed at secondary and tertiary prevention. He concludes that a fresh realistic appraisal of impaired driving and of the development of countermeasures is needed. More effort needs to be directed toward the development of primary preventive measures (those directed at the time before drinking and driving). Such developments can occur only when definition of the problem is adequate. (HSRI)

8 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-76-D1058

LONG-TERM LITHIUM TREATMENT: EFFECT ON SIMULATED DRIVING AND OTHER PSYCHOLOGICAL TESTS, P. Bech; J. Thomsen; D.J. Rafaelsen, European Journal of Clinical Pharmacology, v10 n5 p331-35 (1976)

The effects of lithium on simulated car driving and psychological test scores were studied over six months in patients with Meniere's disease. The dose of lithium was adjusted every two weeks to maintain a serum level between 0.7 and 1.0 mmol/liter. The trial was double-blind and cross-over in type, the effect of lithium being compared with a placebo. The subjects were within the normal range of Beck's depression scale and Marke-Nyman's temperament scale. Lithium was found neither to influence the simulated driving nor to effect the scores in the two rating scales. The only specific complaints observed during lithium treatment were tremor and increased thirst. Therefore, six months of treatment with lithium had no detectable influence on psychic or psychomotor functions in these patients. (JA)

18 refs

KEYWORDS: Antidepressants: lithium. Other CNS Agents: lithium. Clinical Study. Driving Simulator. Experimentation: Chronic Dosage Study. Psychological Testing.

UM-78-D1059

EFFECT OF ACTIVE METABOLITES OF CHLORDIAZEPOXIDE AND DIAZEPAM, ALONE OR IN COMBINATION WITH ALCOHOL, ON PSYCHOMOTOR SKILLS RELATED TO DRIVING, E.S. Palva; M. Linnoila, European Journal of Clinical Pharmacology, v13 n5 p345-50 (1978)

This study attempted to investigate the effects of oxazepam, methyloxazepam, N-desmethyldiazepam, and chlordiazepoxide lactam, alone or in combination with alcohol, on psychomotor skills. Seventeen healthy males and twenty-three healthy females, 20-29 years of age, were administered the drugs for two-week periods. One group of twenty subjects received oxazepam (15 mg), methyloxazepam (20 mg), and placebo, each three times daily. The other group received N-desmethyldiazepam (5 mg), chlordiazepoxide lactam (10 mg), and placebo, each three times daily. Thirty minutes before each test the subject was given alcohol (0.5 g/kg) or a placebo drink together with the drug capsules.

The variables measured in this study were choice reaction time and accuracy, eye-hand coordination, divided attention, flicker fusion, proprioception, and nystagmus. Results of the tests indicate that chlordiazepoxide lactam, methyloxazepam, and oxazepam significantly enhanced the alcohol-induced impairment of psychomotor skills, whereas N-desmethyldiazepam did so only exceptionally in certain subjects in the choice reaction test.

It is concluded that the diazepam-alcohol interaction on psychomotor skills is mainly due to the parent compound. No correlation between the serum level of the agents and the impairment of skills was found. Finally, it seems probable that chlordiazepoxide lactam significantly contributes to a mild chlordiazepoxide-alcohol interaction during prolonged administration of the drug. (JAM)

14 refs

KEYWORDS: Metabolites of Drugs and Other Agents: oxazepam. N-desmethyldiazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. methyloxazepam. oxazepam. N-desmethyldiazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests.

UM-79-D1060

STUDIES OF CLOBAZAM AND CAR-DRIVING, B. Biehl, British Journal of Clinical Pharmacology, v7 suppl n1 p85s-90s (1979)

This paper compares the effects of clobazam with those of diazepam and placebo on driving performance in everyday traffic conditions. The methodology used in studies to assess the effects of drugs on car driving performance is also reviewed. Clobazam (20 mg), diazepam (10 mg), or placebo were administered daily for three days to twenty-four male students with high neuroticism scores. Car driving performance was assessed on the second day in real traffic conditions; tests of attention and concentration and subjective assessment were made on the third day.

Diazepam (10 mg) significantly impaired braking reaction time in comparison with clobazam (20 mg) and placebo ($P<0.01$). Subjects also reported feeling more "depressed" and lethargic after diazepam. Clobazam, on the other hand, seems to have had no detrimental effects on subjects with high neuroticism scores either subjectively or in any of the performance tests. (HSRI)

9 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): clobazam. diazepam. Muscle Relaxants (Central): diazepam. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Open Road Driving. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-74-D1061

NYSTAGMUS AND DISTURBANCES IN PSYCHOMOTOR FUNCTIONS INDUCED BY PSYCHOTROPIC DRUG THERAPY, A. Penttila; H. Lehti; J. Lonnqvist. Psychiatria Fennica, p315-26 (1974)

The purpose of this paper was to report the results of a survey of the effects of long-term drug therapy on psychomotor functions of 100 patients treated in a psychiatric hospital. Phenothiazine, benzodiazepine, and tricylic antidepressants were most often used in medication. Most of the patients had combined therapy. The clinical examination included: walking tests, the Romberg tests, counting backwards, finger-to-finger test, collection of small objects, nystagmus tests, Bender tests, measurement of pupils, pupillary reflex to light, and presence of tremor in the hands.

The error scores of the tests increased with the number of drugs used and the relative strength of medication. An interesting and unexpected finding was the nystagmus phenomena induced by psychotropic drugs. In 73% of the patients, the presence of finely-divided nystagmus was found, and in 17%, coarsely-divided nystagmus was found. In six cases the coarsely-divided nystagmus was positive after both rotation and lateral gazing. This kind of side effect of psychotropic drugs has not been previously mentioned in the literature.

The present results are consistent with earlier observations that the effects of psychotropic drugs and drug combinations on different clinical performances show great individual variation. The authors conclude that use of this clinical examination system is valuable for the assessment of persons using drugs when driving, especially in view of the fact that interpretation of the effects of drugs on the basis of blood or urine samples alone is beset with difficulties. The observations also indicate that the blood alcohol standardized clinical examination system for suspected drunken drivers is also applicable for clinical use in estimating the side-effects of psychotropic drug therapy. (JAM)

28 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Antidepressants: amitriptyline. doxepin. imipramine. lithium. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. haloperidol. thioridazine. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. meprobamate. *oxazepam.* Muscle Relaxants (Central): diazepam. Other CNS Agents: lithium. Antidepressants. Minor Tranquilizers (Anti-Anxiety and Ataractics). Clinical Study. Experimentation: Chronic Dosage Study. Psychological Testing. Psychomotor Tests. Tests of Sensory Function.

UM-74-D1062

EFFECTS OF SECOBARBITAL AND D-AMPHETAMINE ON TRACKING PERFORMANCE DURING ANGULAR ACCELERATION, D.J. Schroeder; W.E. Collins; G.W. Elam. Ergonomics, v17 n5 p613-21 (1974)

Recent studies have shown that the deleterious effects of alcohol and other drugs on psychomotor performances in the laboratory are more pronounced during angular motion than under stationary conditions. The purpose of this study was to investigate the interaction of tracking performance, angular acceleration, and drugs, particularly secobarbital and d-amphetamine.

Thirty male college students ranging in age from 20 to 30 years were randomly assigned in equal numbers to one of the following groups: placebo (lactose); secobarbital (100 mg); or d-amphetamine (10 mg). The drugs or placebo were administered in capsules in a double-blind procedure following practice at a tracking test and baseline determinations of tracking performance levels in both static (stationary) and dynamic (angular acceleration) conditions. Tests were scheduled one, two, and four hours after capsule ingestion; all tests were conducted inside a Stille-Werner rotator and were in total darkness with the exception of the illuminated tracking display.

With the rotator stationary, d-amphetamine subjects performed significantly better than controls during the two-hour and four-hour postdrug sessions; no other static differences among the groups were significant. However, during angular acceleration, secobarbital subjects made significantly more tracking errors and had significantly more vestibular nystagmus than both the control and the d-amphetamine groups for all postdrug sessions.

These findings agree with previous studies of alcohol effects: depressant drugs may have little or no deleterious influence on tracking performance in static environments, but may produce marked performance degradation during angular motion. The primary cause of

this impairment appears to be a vestibulo-ocular one; the ability to inhibit vestibular nystagmus by visual fixation is impaired. (JAM)

12 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Barbiturates: secobarbital. Stimulants: dextroamphetamine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Physiological Testing. Psychomotor Tests. Tests of Sensory Function.

UM-73-D1063

THE PSILOCYBIN-INDUCED "STATE OF DRUNKENNESS" IN NORMAL VOLUNTEERS AND SCHIZOPHRENICS, A.J. Parashos, Behavioral Neuropsychiatry, v8 n1-12 p83-6 (Apr 1976)

This report is a clinical-experimental investigation which attempted to investigate the psilocybin-induced psychoneurotoxic syndrome and its psychopathologic differences from functional and organic psychoses. The effects of 6 g psilocybin, a psychomimetic substance, on mental functioning were investigated in 32 normal volunteers and in 104 schizophrenics. The disturbances induced by psilocybin constitute a psychoneurotoxic syndrome--"a state of drunkenness"--of about four hours duration which develops in three distinct phases.

The basic mental symptoms of this syndrome consist of disturbances of the apperception, sensory perception, and emotion. A moderate impairment of ego-functioning or reality appraisal and an inability to integrate different mental processes are also observed. The psychomotor behavior is mainly harmonized to the prevailing emotional state and in a lesser degree, to the experiences caused by perceptual alterations.

These changes, according to the author's observations, are more severe and more "psychotic-like" in schizophrenics than in normals. Psychopathological analysis of these changes proves that the syndrome cannot be considered to be related to the spontaneously triggered functional psychoses or to the organic ones. Therefore, the term "model-psychosis" is unsatisfactory. (AAM)

23 refs

KEYWORDS: Hallucinogens and Related Agents: psilocybin. Metabolites of Drugs and Other Agents: psilocybin. Clinical Study. Experimentation: Acute Dosage Study. Other Factors Influencing Drug Effects. Psychological Testing.

UM-76-D1064

L'INFLUENCE DES AFFECTIONS CARDIO-VASCULAIRES ET DE LEUR TRAITEMENT SUR LA CONDUITE AUTOMOBILE [THE INFLUENCE OF CARDIO-VASCULAR DISEASES AND THEIR TREATMENT ON DRIVING], P. Fortin, Annales de Medicine des Accidents et du Traffic, n10 p7-11 (1976)

This paper questions the validity of claims that the influence of cardiovascular disease on traffic safety is very slight. Driving an automobile provokes in coronary patients an acceleration of the pulse rate, a small elevation in blood pressure, and a pathological electroencephalogram, indicating a state of emotional stress with a discharge of catecholamines.

Proposed official prohibitions for cardiac patients are also discussed. The author believes, however, that the problem will best be solved by the physician, who must ensure that each cardiovascular patient is informed about the dangers of both the disease and the treatment. (EMM)

0 refs French

KEYWORDS: Review: Drugs and Highway Safety.

UM-78-D1065

DRUGGED DRIVERS, Autocar, v149 n4269 p19 (2 Sep 1978)

This brief article summarizes a recent article in the Drug and Therapeutics Bulletin which claimed that many doctors do not always warn their patients of the possible adverse effects of seemingly innocuous drugs on driver performance. Because it is an offense to drive while one's ability is impaired by drugs, a doctor should be familiar

not only with driving license regulations, but also with any possible reactions or interactions of the drugs he prescribes.

Drivers have a statutory duty to inform the licensing authority of any medical condition or medication likely to cause danger while driving and to last more than three months. If the patient refuses to do this, the physician may have to go so far as to inform the licensing authority without the patient's permission.

It is suggested that physicians should give even stricter advice to professional drivers. Also, pharmacists who already put labels on antihistamines warning that these can cause drowsiness and can affect driving should extend the practice to other medications when appropriate. (HSRI)

0 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-79-D1066

DRUGS AND DRIVING, G. Beaumont, Traffic Safety, v79 n2 p14-5 (Feb 1979)

This article discusses the laws in Great Britain concerning drugs and driving. It claims that the law has been, for the most part, unconcerned with the effect of drugs on driving. No legal limit has been set for any drug concentration other than alcohol because no blood test is yet available that can identify any and every drug and indicate the plasma concentration.

Every effort must be made to make laws forbidding driving under the influence of drugs more enforceable both legally and scientifically. Manufacturers must be forced to test their drugs in the driving situation and make appropriate recommendations. Doctors who prescribe drugs must advise their patients about drinking, driving, and taking drugs. Finally, if a drug has been tested and cautionary advice has been given, the patient who drives anyway ought to be punished in the same way as the driver who drinks. (HSRI)

0 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation. Review: Drugs and Highway Safety.

UM-78-D1067

VERIFICATION OF PENTOBARBITAL INDUCED SEDATION BY A NEW REAL TIME METHOD OF EEG COMPUTER ANALYSIS, A.J. Lim; K.S. Kott; C.H. Teitel; W.D. Winters, Proceedings of the Western Pharmacology Society, v21 n3 p31-5 (1978)

Described here is a method for detection of the sedative effect of pentobarbital using a three-dimensional representation of the electroencephalogram (EEG). The system is incorporated into a laboratory computer system and used in interpreting drug induced changes in the EEG. The analytical system operates on one channel of EEG and consists of a minicomputer, a storage screen graphics display terminal, and a specially designed detector interface.

The method is applied in this paper to the study of pentobarbital induced sedation in the cat. A cat implanted with chronic brain electrodes was given a sedative dose of pentobarbital sodium (10 mg/kg, s.c.). Recordings of brain waves were made from the electrodes. The state of sedation, however, was difficult to detect because it occurred irregularly and with only brief episodes of 10-16 H_Z bursts. (HSRI)

3 refs

KEYWORDS: Barbiturates: pentobarbital. Animal Research.

UM-78-D1068

PHENCYCLIDINE INTOXICATION: A LITERATURE REVIEW, L.J. Sioris; E.P. Krenzelok, American Journal of Hospital Pharmacy, v35 n11 p1362-67 (Nov 1978)

The history, symptoms, diagnosis, and treatment of phencyclidine hydrochloride (PCP) intoxication and the pharmacology of PCP are reviewed in an effort to increase the

pharmacist's awareness of the problem of PCP abuse and to demonstrate the unique toxicity of the drug for those who are in direct contact with the overdose victim.

Intoxication with low to moderate doses of PCP (5-20 mg) resembles an acutely confused state generally lasting four to six hours. High doses (greater than 20 mg) may cause serious neurologic and cardiovascular complications, and the patient is often comatose for several days. Treatment involves supportive psychological and medical measures. Evacuation of the stomach with activated charcoal and a saline cathartic may be indicated. Succinylcholine chloride may ease intubation. Diazepam and chlorpromazine may be used to control the combative patient and the "PCP psychosis" patient, respectively. Antihypertensive agents are not usually needed, but diazoxide and hydralazine hydrochloride have been used to treat hypertensive crises. Diazepam and phenytoin have been used to treat seizures.

Ion-trapping by continuous gastric suctioning and by urine acidification with ammonium chloride may increase clearance of PCP. Forced diuresis with furosemide in conjunction with acidification may further increase PCP clearance. Use of physostigmine is based on conjecture.

Diagnosis of PCP intoxication is made difficult owing to the ever increasing variety of abused drugs. However, several key signs may be of assistance in arriving at the final diagnosis; horizontal and vertical nystagmus, increase in blood pressure to moderately hypertensive levels, excessive secretions, muscle rigidity, and prolonged coma all would lead one to suspect PCP exposure in the agitated, catatonic, or comatose patient. Furthermore, improved analytical techniques in the toxicology laboratory now provide the ability to arrive at a definitive diagnosis.

The authors conclude that continued research is needed to determine the drug's mechanism of action and to further document the efficacy of ion-trapping methods and the possible role of charcoal hemoperfusion. (JAM)

64 refs

KEYWORDS: Hallucinogens and Related Agents: phencyclidine. Review. Review: Drug Use.

UM-77-D1069

THE BEHAVIORAL TOXICITY OF MONOAMINE OXIDASE-INHIBITING ANTIDEPRESSANTS, D. L. Murphy, Advances in Pharmacology and Chemotherapy, v14 p71-105 (1977)

This review considers the nature and incidence of adverse effects reported for a major class of drugs used primarily as antidepressant and antihypertensive agents--the monoamine oxidase (MAO) inhibiting drugs. For comparative purposes, several other drugs with some antidepressant properties such as the tricylic antidepressants, lithium carbonate, amphetamine, L-trytophan, and L-dopa are also considered briefly. The specific sections of the paper review case histories illustrating iproniazid-related adverse behavioral changes; phenelzine-related adverse behavioral changes; tranylcypromine-related behavioral changes; adverse behavioral changes associated with other monoamine oxidase-inhibiting antidepressants; comparison of adverse behavioral effects during monoamine oxidase inhibitor treatment with those during treatment using other antidepressant drugs; behavioral effects of monoamine oxidase-inhibiting drugs in animals of possible relevance to their behavioral toxicity in man; and biochemical effects of monoamine oxidase-inhibiting drugs in animals and man of possible relevance to their behavioral effects.

It is concluded that the MAO inhibitors very clearly induce some behavioral changes in nonpsychiatric patients, including normal volunteers and patients with tuberculosis, hypertension, and cancer. The predominant behavioral changes observed in these individuals are similar to those observed in the psychiatric patient groups, including hypomania or mania, euphoria, irritability, hallucinations, and paranoid episodes. Direct relationships between adverse behavioral effects and drug dosage were observed with several of these MAO-inhibiting antidepressants. (HSRI)

140 refs

KEYWORDS: Antidepressants: phenelzine. tranylcypromine. Antidepressants. Review: Drug Effects.

UM-70-D1070

REACTION-TIMES OF METHADONE TREATED EX HEROIN ADDICTS, N.B. Gordon, Psychopharmacologia, v16 n4 p337-44 (1970)

This paper reports on reaction times of eighteen male and nine female former heroin addicts who were being treated with an average daily dose of 100 mg of methadone. Three different reaction time tests were used: (1) simple visual; (2) simple choice and multiple discrimination; and (3) multiple choice reaction time. The addicts' scores were compared to the scores of a similar group of control subjects who were either nondrug users or had been recently withdrawn from narcotic drugs.

The median reaction times of subjects tolerant to average doses of 100 mg of methadone per day were either equal to or shorter than those of control subjects. In fact, methadone patients appear to have superior simple reaction times. The author speculates that both male and female methadone subjects as well as heroin addicts in general may consist of individuals who are more reactive than the general population. It is also possible that prolonged use of narcotic drugs may lead to increased levels of arousal. Analysis of the data indicate that the source of reaction time differences may be ascribable to superior signal detection or decision time (premotor components) rather than to limb transport time components of the total reaction time. The results of this study suggest the need to investigate further the nature of reaction time performance as a function of prolonged tolerance to narcotic drugs. (HSRI)

13 refs

KEYWORDS: Opiates and Related Agents: methadone. Experimentation: Chronic Dosage Study. Psychomotor Tests.

UM-64-D1071

A COMPARATIVE EVALUATION OF THE ACTION OF DEPRESSANT AND STIMULANT DRUGS ON HUMAN PERFORMANCE, B. Blum; M.H. Stern; K.I. Melville, Psychopharmacologia, v6 p173-777 (1964)

This study investigates the effects of low doses of alcohol; of the depressant pentobarbital; of two stimulants, amphetamine and caffeine; and of the combined action of a low dose of alcohol and psychic distraction on motor and intellectual performance.

Seventy-two healthy male and ten healthy female medical students were randomized and by a double blind procedure were individually tested before and at varying times after drug intake. The following drug dosages were administered: (1) 10 ml alcohol; (2) 20 ml alcohol; (3) 150 mg pentobarbital sodium; (4) 100 mg caffeine; (5) 200 mg caffeine; (6) 7.5 mg d-amphetamine; or (7) placebo. Tasks representing motor and intellectual functions included (1) speed of tapping; (2) visual reaction time; (3) digit symbol substitution; and (4) serial additions.

Pentobarbital was found to depress all of these tests, whereas the other drugs showed differential actions. Alcohol increased errors in the serial addition test at doses not affecting other intellectual tasks or motor performance. Amphetamine and caffeine decreased errors on mental tasks while not affecting the motor tasks. Distraction acted in these individuals as a stimulant, decreasing errors apparently by raising the level of alertness. Distraction also counteracted the deleterious effects of alcohol on these tasks. (HSRI)

14 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Barbiturates: pentobarbital. Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: caffeine. dextroamphetamine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests.

UM-72-D1072

RESIDUAL EFFECTS OF HYPNOTICS, A.J. Bond; M.H. Lader, Psychopharmacologia, v25 n1 p117-32 (1972)

Described here is an experiment in which a battery of psychological and physiological tests was used to assess the residual effects of the barbiturate butobarbitone sodium and the nonbarbiturate hypnotic nitrazepam when caffeine was not withheld. Five healthy male and five healthy female subjects aged between 21 and 34 years were tested on a

large battery of physiological and psychological tests twelve hours after a hypnotic dose of butobarbitone sodium (100 or 200 mg) or nitrazepam (5 or 10 mg) and compared with a placebo. The subjects received all five treatments in a balanced design. The tests used included self-ratings, an electroencephalogram, the auditory electroencephalographic evoked response, reaction time, tapping, card-sorting, and the digit symbol substitution test.

Results show that both drugs were effective hypnotics but butobarbitone had more subjective "hangover" effects the following morning. The electroencephalogram showed significant changes after both drugs but the evoked response was affected most by 10 mg nitrazepam. Bioassay statistics suggested that with respect to these residual effects the relative potency of nitrazepam to butobarbitone was 27:1.

Several of the behavioral tests were affected by the drugs. In general, simple motor tasks of a repetitive nature were severely impaired. Speed and reaction time were impaired. However, cognitive measures were not affected. It seems, therefore, that the residual effects of hypnotics do not affect cognition as much as they affect simple motor performance. It is essential that people taking sleeping tablets occasionally are warned of these unavoidable residual effects on motor skills. (JAM)

21 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): nitrazepam*. Barbiturates: butabarbital. Nonbarbiturates: nitrazepam*. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Physiological Testing. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-79-D1073

THE EFFECTS OF CARBON MONOXIDE ON DUAL-TASK PERFORMANCE, V.R. Putz, Human Factors, v21 n1 p13-24 (1979)

This study attempted to determine whether carbon monoxide levels producing 5% COHb adversely affect performance on a dual-task when compared to effects on performance with levels of 1% and 3% COHb, and whether this effect is evident only under conditions of high frequency tracking as opposed to low frequency conditions. Thirty adult nonsmokers were exposed for four hours to one of three concentrations of CO: 5 ppm; 35 ppm; and 70 ppm to produce blood levels of either 1%, 3%, or 5% carboxyhemoglobin. After the third hour of exposure, performance in the double-blind study was assessed by a tracking task paired with a peripheral monitoring task, each possessing two levels of difficulty.

The results indicated that visual-manual tracking was significantly impaired by about 30% during the fourth hour of exposure to 70 ppm of CO when 5% COHb was reached, as compared to performance at 5 ppm and 35 ppm. The impairment occurred only during the high frequency tracking condition. Response times of subjects to the peripheral light-intensity changes also increased during the third and fourth hours. These findings suggest that an assessment of the effects of low-level CO on human performance should include an analysis of the demand characteristics of the task as well as data on concentration and exposure duration. Task-demand characteristics can serve to exacerbate conditions of toxic stress and must be considered in assessing those situations. The significance of these findings to safe job performance by workers remains to be determined. (JAM)

27 refs

KEYWORDS: Gases: carbon monoxide*. Experimentation: Acute Dosage Study. Experimentation: Dose-Effect Study. Psychomotor Tests.

UM-78-D1074

DRUGS AND DRIVING, A. Hecht, Food and Drug Administration Consumer, p17-19 (Sep 1978)

Presented here is a broad overview of the dangers of mixing drugs with driving. The paper warns that many medicines can interfere with a person's ability to drive because they can cause drowsiness, dizziness, lightheadedness, or blurred vision. Such side effects might be expected from prescription drugs, but are often overlooked as a possibility in over-the-counter products such as cough and cold remedies. Many daytime sedatives taken to relieve "simple nervous tension" can also cause drowsiness that can impair driving. Various studies of the effects of diazepam(R), the most popular of all prescription drugs, on driving and related skills show that there is an increased risk of accident that lasts many hours after a single dose. Antidepressant drugs such as the

phenothiazines or haloperidol cause deterioration of psychomotor skills during the first few days while the patient is getting used to the drug. Barbiturates can impair efficiency for as long as fourteen hours. These drugs can become even more dangerous to health and safety when combined with alcohol. Some combinations can be lethal.

The paper concludes with several recommendations for the patient taking drugs. (HSRI)

0 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-78-D1075

COCAINE PLASMA CONCENTRATION: RELATION TO PHYSIOLOGICAL AND SUBJECTIVE EFFECTS IN HUMANS, J.I. Javaid; M.W. Fischman; C.R. Schuster; H. Dekirmenjian; J.M. Davis, Science, v202 n4364 p227-8, (13 Oct 1978)

This study attempted to correlate physiological and subjective effects with the plasma concentration of cocaine in ten volunteer subjects who had histories of intravenous cocaine use. Subjects were tested daily with either intravenous cocaine (16 or 32 mg), saline, or intranasal cocaine (16, 64, or 96 mg).

Results showed a positive relationship between peak plasma concentration, physiological and subjective responses, and dose administered. After intravenous injection the cardiovascular and subjective effects occurred almost immediately, when the plasma concentration was also maximum. The rate of cocaine disappearance after intravenous administration paralleled the drop in physiological and subjective drug effects. Plasma levels of the drug remained fairly elevated after sixty minutes when subjective and cardiovascular effects had approached base line. After intranasal administration, blood levels remained elevated for a considerably longer period. Also, after intravenous administration the cardiovascular effect disappeared slightly faster than cocaine disappeared from plasma. These data suggest that in subjects showing an initial response to cocaine administration, compensatory mechanisms are triggered, resulting in a faster decline of both cardiovascular and subjective effects than of plasma cocaine concentration. (HSRI)

6 refs

KEYWORDS: Local Anesthetics: cocaine*. Stimulants: cocaine*. Drug Concentration-Effect Study: Clinical Research. Drug Concentrations in Body Fluids: Acute Dose Study.

UM-75-D1076

EFFECTS OF DIFFERENT DOSAGES OF ANTICONVULSANT DRUGS ON MENTAL PERFORMANCE IN PATIENTS WITH CHRONIC EPILEPSY, A.S. Dekaban; E.J.B. Lehman, Acta Neurologia Scandinavica, v52 n4 p319-30 (1975)

This study attempted to assess the effects of anticonvulsant drugs on mental performance and to evaluate the psychological tests used in this assessment.

Fifteen epileptic patients had their dose of anticonvulsant drugs changed twice, each time by thirty to fifty per cent of the initial medication. Before the dose change, the patients were given six mental performance tests designed to measure vigilance, reaction time, and certain aspects of memory. Serum drug levels were also monitored.

The main results showed the following: 1) Vigilance and reaction time tests were the most useful in evaluation of effects of various doses of the medication; the memory tasks showed similar, but less definite trends; and rote calculation and block design were of no particular value in this study. 2) On the tests for vigilance and reaction time, the greatest number of patients performed best on the lowest dose of their medication, the respective percentages being 45.8 and 56%. By comparison, fewest patients performed best on their highest dose, the percentage being 16.7 for vigilance and 12.5 for reaction time; while the percentages for medium dose were 37.5 and 31.2 on the respective tests. The authors conclude that use of well-standardized, yet simplified mental performance tests in combination with changes in the dosage of medication can help in reaching a compromise between acceptable seizure control and avoidance of excessive slowing of mental activity. (JAM)

34 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics). Experimentation: Dose-Effect Study. Psychological Testing. Psychomotor Tests.

UM-76-D1077

EFFECTS OF ETHOSUXIMIDE UPON PSYCHOMOTOR RESPONSES AND ELECTROMYOGRAPHIC PARAMETERS OF HEALTHY INDIVIDUALS, I. Kastner; N. Roth; A. Wagner, Acta biologica et medica Germanica, v35 n6 p763-72 (1976)

The purpose of this paper was to investigate the effects of the anticonvulsant ethosuximide (800 mg) upon physiological parameters, psychomotor reactions, and electromyographic criteria in eight healthy subjects aged 21 to 31. Ethosuximide increased choice reaction time in most subjects, often provoked a greater amount of errors during choice reactions, and decreased the average heart frequency. The functional activation during the tasks was diminished. The EEG showed no marked qualitative or quantitative changes.

Ethosuximide reduced the maximum conduction velocity of the motor nerve and changed the action potential duration but not the action potential shape. There is no exact parallelism between the increase in reaction time and decrease of nerve conduction velocity. The drug effect upon psychomotor reactions seems to be caused by reduction of vigilance and an inhibitory effect upon the individual's motor responsiveness. Like other anticonvulsants, ethosuximide may alter the electrical properties of all excitable membranes and, by this ubiquitous site of action, exerts the described effects. (JA)

45 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): ethosuximide. Experimentation: Acute Dosage Study. Physiological Testing. Psychomotor Tests.

UM-77-D1078

AMPHETAMINE-INDUCED CATECHOLAMINE ACTIVATION IN SCHIZOPHRENIA AND DEPRESSION: BEHAVIORAL AND PHYSIOLOGICAL EFFECTS, D.P. Van Kammen; W.E. Bunney; J.P. Docherty; D.C. Jimerson; R.M. Post; S. Siris; M. Ebert; J.C. Gillin, Advances in Biochemical Psychopharmacology, v16 p655-9 (1977)

The purpose of this article is to describe the similarities and differences in the behavioral and physiological effects of a single intravenous infusion of 20 mg d-amphetamine between and within groups of twenty schizophrenics and eight depressed patients. Subjects were assessed by the Brief Psychiatric Rating Scale and a modified Bunney-Hamburg Global Psychosis test before and after infusion. Serial vital signs, blood samples, and EEG recordings were obtained for two nights before and two nights after administration.

Some of the results were as follows: Both depressed and schizophrenic patients showed an activating effect of amphetamine as measured by decreases in the retardation-withdrawal item on the Brief Psychiatric Rating scale. Placebo infusions were associated with little physiological or behavioral effect in either the schizophrenic or the depressed patients. There was a significant increase in pulse in the schizophrenic patients but not in the depressed patients, who responded more like normals while receiving d-amphetamine. Both groups showed significant and similar increases in systolic and diastolic blood pressure. Similarly, total sleep, REM time, and percent of REM time decreased in both patient groups. Amphetamine blood levels peaked at approximately 15 minutes; there was no significant difference in blood levels between the two diagnostic groups.

The overall findings involved an increase in psychosis in the group of schizophrenic patients in contrast to the depressed patients. However, seven schizophrenic patients improved on amphetamines. These findings highlight an emerging area of paradoxical effects--that the same drugs may have opposite effects in different patients while drugs with apparently opposite pharmacological effects produce similar ones.

In conclusion, it is clear that as a group, schizophrenics respond to amphetamines differently than depressed patients. This suggests that they may have a specific vulnerability to increases in psychosis with catecholamine release. (HSRI)

24 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Stimulants: dextroamphetamine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Acute Dosage Study. Physiological Testing. Psychological Testing.

UM-78-D1079

TEENS, DRUGS AND ALCOHOL: ON THE ROAD AGAIN, Journal of American Insurance, v54 n3 p1-4 (1978)

This paper presents a broad overview of the problem of teenage use of alcohol and drugs while driving. While a great deal of data exists for the effects of alcohol use on driving behavior, very little is known about how many drivers are under the influence of licit or illicit drugs and whether their driving ability is diminished because of drug use. Knowledge of the effects of marijuana, one of the most common illicit drugs used by teens, has so far eluded scientists. No test has yet been developed that can detect whether the person is intoxicated or whether he has ingested only a small amount of marijuana. There are no tests for detection of marijuana thus far that are practical for roadside use, since all take several hours to perform in a laboratory.

Research has proven that marijuana adversely affects driving ability immediately after use and increases the user's chances of being involved in an auto accident. It has also been shown to cause attention lapses. What is more insidious about the effects of marijuana is that the driver is usually not aware of his impairment as he might be after having several drinks. However, very few teenagers realize the potential adverse effects of marijuana on driving ability. Only 19% of teenagers regularly involved with alcohol thought there was any likelihood of drunk teenaged drivers being involved in an auto accident resulting in death or crippling injury. Marijuana, which more teenagers use on a daily basis than alcohol, is even less understood in terms of its effects on driving ability.

It is concluded that a realistic educational approach concerning drugs and driving is necessary. These programs should give a straightforward warning about the dangers of driving under the influence of any mood altering drug. They showed stress that teenagers know both the limits of their tolerance and the risks they take if they decide to drive while under the influence. (HSRI)

0 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Review: Drugs and Highway Safety.

UM-78-D1080

EFFECT OF PAIN ON HUMAN PSYCHOMOTOR PERFORMANCE, K. Korttila; T. Seppala, Acta Anaesthesiologia Scandinavica, v22 n3 p334-8 (1978)

The effect of pain on human psychomotor performance was measured in seven healthy male volunteers after an intramuscular injection of vitamin B or saline using a controlled cross-over method. Vitamin B, causing moderate to severe pain, or painless saline was injected after an intravenous injection of diazepam (0.3 mg/kg). The subjects' psychomotor performance was tested before and 2, 3, and 4 hours after diazepam (before, 15 minutes, and 75 minutes after the Vitamin B and saline injections). The effects of the Vitamin B injection on the subjects' divided attention, reaction time, coordination skills, and their ability to discriminate the fusion of flickering light did not differ from the corresponding effects of the saline injection.

The results suggest that pain as such does not have any major influence on human psychomotor performance. Furthermore, the results demonstrate that experiments on the effects of intramuscularly administered local anaesthetics on healthy volunteers are not invalidated by the presence or absence of pain at the injection site. (AAM)

16 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Vitamins: vitamin B complex. Experimentation: Acute Dosage Study. Psychomotor Tests.

UM-77-D1081

PSYCHOTROPIC DRUGS AND ROAD ACCIDENTS [letter], D. Wheatley, British Medical Journal, v2 n6079 p126-7 (9 Jul 1977)

The author of this letter points out that while the side effects of psychotropic drugs can impair driving and that patients should be made aware of this, psychotropic drugs in most cases improve the ability of the person under treatment when administered properly. This author contends that the hazards of treatment with psychotropic drugs are far outweighed by the hazards of leaving untreated those illnesses that might impair the judgment or coordination of the driver. (HSRI)

0 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-78-D1082

SOME CLINICAL PHARMACOLOGICAL STUDIES WITH TERFENADINE, A NEW ANTIHISTAMINE DRUG, V.K. Kulshreshtha; P.P. Gupta; P. Turner; J. Wadsworth, British Journal of Clinical Pharmacology, v6 n1 p25-9 (1978)

A double-blind cross-over trial was performed to determine and compare the CNS and autonomic effects of single and multiple doses of terfenadine with those of chlorpheniramine and placebo using a battery of objective and subjective tests. The study also compared the sensitivity of the tests used to detect CNS activity.

Twelve healthy male volunteers aged twenty-one to twenty-five years received the following treatments in random order based on a 3x4 design with an interval of at least five days between treatments: (1) terfenadine (120 mg) and chlorpheniramine placebo; (2) chlorpheniramine (12 mg) and terfenadine placebo; and (3) chlorpheniramine placebo and terfenadine placebo. Subjects were tested just before drug administration and at two and four hours after. Critical flicker frequency, pursuit rotor performance, reaction time, salivary volume, and pupil size were assessed. Subjects were also required to assess the effect of the treatments on their concentration, mood, and degree of sedation using an analogue rating scale.

In the objective tests of critical flicker frequency, pursuit rotor, reaction time, salivary volume, and pupillary diameter, no statistically significant difference was observed between the treatments. However, chlorpheniramine produced a statistically significant ($P<0.05$) degree of sedation and impaired concentration as compared to placebo and terfenadine. The results obtained in the subjective analogue rating scales were not normally distributed. Therefore, the authors strongly advocate use of nonparametric statistical methods for analysis of such data. (HSRI)

10 refs

KEYWORDS: Antihistamine Agents: chlorpheniramine. terfenadine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Physiological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-79-D1083

INFLUENCES OF ALCOHOL, INTERPERSONAL FEEDBACK, AND DRINKING EXPERIENCE UPON PERFORMANCE AND JUDGMENT, R.A. Lubin, Perceptual and Motor Skills, v48 n1 p95-104 (Feb 1979)

This study examined influences of alcohol, social feedback, and drinking experience upon performance, performance awareness, and awareness of intoxication. Twenty-four subjects were selected on the basis of drinking experience. All subjects consumed either a placebo or an alcoholic beverage for a target blood-alcohol concentration of .05% or .10% prior to each of three experimental sessions. Within groups, subjects were paired and completed a series of cognitive and psychomotor tasks. During each session subjects evaluated both their own and their partner's performance and degree of intoxication. A series of correlations between performance or measures of blood-alcohol concentration and judgments determined relative awareness.

Alcohol significantly impaired performance, with inexperienced drinkers being significantly more impaired than experienced drinkers. All groups overestimated their blood-alcohol concentration, but inexperienced drinkers evaluated themselves as most highly intoxicated. Subjects generally underestimated alcohol impairment, and correlations showed that awareness decreased as blood-alcohol concentration increased.

The implications of this research to the drinking and driving problem are discussed. (JA)

22 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Experimentation: Dose-Effect Study. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1084

THE THEORETICAL IMPLICATIONS OF CHLORPROMAZINE AS A SENSORY INTEGRATIVE THEORY, J.S. Saffir, American Journal of Occupational Therapy, v32 n7 p460-6 (Aug 1978)

In order to evaluate the influence of antipsychotic drugs used in the treatment of schizophrenia on therapy based on sensory integrative theory, this study, developed through library research, explores the theoretical bases for these two modes of treatment. Studies of chlorpromazine, a protctypical antipsychotic drug, show that its local action on the neurotransmitters of the brain may explain in theory its therapeutic efficacy. By citing evidence of sensory processing deficits in schizophrenic patients, a theoretical basis for the use of a sensory integrative approach to therapy is established. A comparison of these theories leads to the conclusion that a sensory integrative approach can serve as an important reinforcer of the therapeutic actions of chlorpromazine. Implications for treatment and research are considered. (JA)

35 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Review: Drug Effects.

UM-77-D1085

THE EFFECTS OF PSYCHOTROPIC DRUGS UPON HUMAN BEHAVIOUR, K. Wesnes, Modern Problems in Pharmacopsychiatry, v12 p37-58 (1977)

Presented here is a review of effects of psychotropic drugs on attention, human performance, perception, memory, learning, and sleep and dreaming. The paper discusses methods for testing these effects such as reaction time tests, vigilance tests, the digit symbol substitution test, the Stroop Color test, tapping tests, pursuit rotor tests, and critical flicker frequency. For each test or area of testing, drugs affecting that test are discussed. Some of the drugs discussed in greater depth include marijuana, hyoscine, diazepam, and alcohol. (HSRI)

117 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Mydriatics: scopolamine. Nonbarbiturates: ethanol (ethyl alcohol). Parasympatholytic (Cholinergic Blocking) Agents: scopolamine. Review: Drug Effects.

UM-77-D1086

PSYCHOMOTOR SKILLS DURING ACUTE AND TWO-WEEK TREATMENT WITH MIANSERIN (ORG GB 94) AND AMITRIPTYLINE, AND THEIR COMBINED EFFECTS WITH ALCOHOL, T. Seppala, Annals of Clinical Research, v9 p66-72 (1977)

The purpose of this investigation was to compare the acute and subacute effects of mianserin (ORG GB 94) and amitriptyline with and without alcohol on psychomotor skills related to driving. Fourteen healthy men and six healthy women (mean age 21.1 years) took a placebo, 10 mg of mianserin, or 25 mg of amitriptyline three times daily for two weeks each in a double-blind cross-over design, with one week between treatment sessions. Several psychomotor tests measuring eye-hand coordination, acoustic and visual reaction time, attention, proprioception, and central visual processes were performed on the first, seventh, and fourteenth days of each period after either 0.5g/kg alcohol or a placebo drink.

Coordination, reaction time, and critical flicker frequency were affected by all drug combinations while attention was slightly impaired only after amitriptyline alone or mianserin together with alcohol. Drug actions and drug-alcohol interactions were most obvious on the first day but declined toward the end of the drug periods. After mianserin the skills were impaired on the first day only, but after amitriptyline

impairment continued up to the seventh day in most of the tests. Both drugs seemed to interact additively with alcohol. Impairment of flicker fusion by the amitriptyline-alcohol combination remained constant over the whole two-week period.

The author concludes that both amitriptyline and mianserin in small doses may have a harmful effect on psychomotor function in the initial phase of therapeutic treatment. The combined effects of these antidepressants and 0.5g/kg ethanol impair driving skills. (HSRI)

31 refs

KEYWORDS: Antidepressants: amitriptyline, mianserin. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects. Tests of Sensory Function.

UM-79-D1087

THE CALCIUM CARBIMIDE-ETHANOL INTERACTION: EFFECTS OF ETHANOL DOSE, J.F. Brien; J.E. Peachey; C.W. Loomis; B.J. Rogers, Clinical Pharmacology and Therapeutics, v25 n4 p454-63 (Apr 1979)

The purpose of this study was to examine the effects of ethanol on the intensity of the calcium carbimide (CC)-ethanol interaction. Experiments were conducted to determine the effect of ethanol dose on blood ethanol and acetaldehyde levels, heart rate, and blood pressure during the CC-ethanol interaction, and to determine whether blood acetaldehyde levels correlate with the changes in heart rate and blood pressure. Five male alcoholic volunteers aged twenty-three to forty-four were given placebo or 0.7 mg/kg of calcium carbimide followed twelve hours later by 0.125, 0.25, or 0.5 g/kg ethanol.

The intensity of the interaction, as measured by blood acetaldehyde, heart rate, and blood pressure, increased with increasing ethanol dose but was not subjectively apparent at the 0.125 g/kg level. At the two higher levels, the interaction commenced within thirty minutes of the ethanol dose and lasted thirty to sixty minutes. At the 0.5 g/kg dose the blood ethanol level rose from 0.67 mg/ml (with placebo) to 0.88 mg/ml; the acetaldehyde level rose from 2.49 ug/ml to 10.76 ug/ml. With the criterion of heart rate above 100 as indicative of the CC-ethanol interaction, the onset of interaction was 0.25 and 0.38 hours for the 0.5 and 0.25 gm/kg ethanol doses; the duration of the interaction was 1.0 and 0.38 hours respectively.

There was appreciable individual variability in the intensity and duration of the interaction. The authors conclude that an approximate dose of 50 mg CC would provide alcohol aversion feedback for twelve hours for any dose of alcohol exceeding 0.25 mg/kg. However, the legal implications of the raised blood ethanol level would have to be considered. A dose of ethanol that normally would give a blood ethanol level of less than 0.80 mg/ml could lead to a blood concentration above 0.80 mg/ml in the presence of calcium carbimide, which is the legal limit for blood alcohol content in Canada. (HSRI)

27 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Unclassified Agents: calcium carbimide*. Experimentation: Study of Combined Effects of Drugs. Physiological Testing.

UM-77-D1088

EFFECTS OF HALAZEPAM AND DIAZEPAM ON THE MOTOR COORDINATION OF GERIATRIC SUBJECTS, M.A. Gagnon; Y. Langlois; D.R. Boghen; M. Verdy, European Journal of Clinical Pharmacology, v11 n6 p443-8 (1977)

The purpose of this study was to establish a safe dose range for halazepam, a new benzodiazepine, in older subjects, especially with regard to its effects on motor coordination. Two doses of halazepam, 20 and 40 mg, were compared to diazepam (5 mg) and placebo in this double-blind, parallel experiment. The medications were administered three times a day during the first three days and twice daily during the following eleven days. Their effects were measured on the tandem walking ability and manual dexterity of fifty-nine elderly female subjects. Most volunteers had some walking difficulty prior to the study and twenty-one suffered from some illness.

With the higher dose of halazepam, a statistically and clinically significant impairment of motor coordination was observed. Halazepam (40 mg), at the regimen above mentioned,

should therefore not be used in elderly persons. This is substantiated by the results of testing all pertinent variables: tandem walk, manual dexterity, side effects, and compliance to the drug regimen; indeed, only five subjects out of fifteen could tolerate halazepam (40 mg) twice daily. With the manual dexterity test, significant effects of diazepam (5 mg) and halazepam (20 mg) were also observed. This test as well as the analysis of the side effects shows that the lower dose of halazepam is well tolerated when compared to diazepam (5 mg). The authors conclude that doses of halazepam for geriatric patients should not exceed 20 mg daily. (JAM)

5 refs

KEYWORDS: Major Tranquilizers (Antipsychotics and Neuroleptics): halazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study.

UM-78-D1089

ALCOHOL AND ROAD SAFETY: GEELONG EXPERIENCE 1967 TO 1978, V.D. Plueckhahn, Medical Journal of Australia, v2 n14 p615-6, 625, 630 (30 Dec 1978)

This paper reviews the role of alcohol in motor vehicular fatalities in Geelong, Victoria and the surrounding district between January 1967 and June 1978. There were 344 persons aged seventeen years and older who died within four hours of the motor accident. Of the 147 driver fatalities aged seventeen to fifty years, 54% had a blood alcohol concentration (BAC) greater than 0.1 g/100 ml (22 mmol/l) at autopsy. Of thirty-five male pedestrians, 60% had a BAC greater than 0.15 g/100 ml (33 mmol/l) at autopsy; 80% of such accidents occurred between 6 p.m. and 10 p.m. A high degree of sobriety was noted among all female road traffic victims. The increasing road toll related to motorcycle accidents and the problems of legal and illegal drug use are also briefly discussed. (JAM)

10 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-78-D1090

CENTRAL NERVOUS SYSTEM DEPRESSANT ACTIONS OF CLONIDINE AND UK-14, 304: PARTIAL DISSOCIATION OF EEG AND BEHAVIOURAL EFFECTS, H. Ashton; M.D. Rawlins, British Journal of Clinical Pharmacology, v5 n2 p135-40 (1978)

This investigation attempted to compare the sedative and hypotensive effects of clonidine and the imidazole derivative UK-14,304 in normal subjects. The effects of a single oral dose of 300 micrograms clonidine, 75 micrograms UK-14,304, and placebo were studied double-blind in five male volunteers aged twenty to twenty-five years on three occasions a week apart. Contingent negative variation, reaction time, blood pressure, and heart rate were compared over six hours, as well as the subjects' ratings of their alertness and drowsiness.

Results of the tests showed that there was a fall in systolic and diastolic blood pressure and in heart rate. These changes were maximal between two and four hours and were greater after clonidine than after UK-14,304. There was a progressive increase in subjective ratings of sleepiness after both drugs, commencing at one hour and maximal between two and four hours. This effect was more pronounced after clonidine than after UK-14,304. There was a close correlation between the fall in blood pressure and the change in subjective rating for sleepiness after both drugs. Behavioral sleep also occurred after both drugs.

Compared with placebo there was a decrease in CNV magnitude at two and four hours after both drugs, associated with a lengthening of reaction time and consistent with the subjective behavioral changes. Depression of CNV magnitude was more pronounced after clonidine than after UK-14,304. In some subjects after both drugs there was an initial increase in CNV magnitude at 1.5 hours, occurring at the same time as behavioral sleep and subjective ratings of sleepiness.

The authors conclude that UK-14,304 causes less central nervous system depression than clonidine at the dosage studied, but also has a less marked hypotensive effect. (JAM)

13 refs

KEYWORDS: Hypotensive (Antihypertensive) Agents: clonidine. Unclassified Agents: UK-14,304. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Physiological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-77-D1091

TANDAMINE--A NEW NOREPINEPHRINE REUPTAKE INHIBITOR: CLINICAL, PSYCHOMETRIC AND QUANTITATIVE EEG STUDIES IN DEPRESSED PATIENTS, B. Saletu; P. Krieger; J. Grunberger; H. Schanda; I. Sletten, International Pharmacopsychiatry, v12 n3 p137-52 (1977)

Tandamine (AY 23,946)--a new norepinephrine reuptake inhibitor with practically no serotonin potentiation, MAO inhibition, or anticholinergic activity--was administered in doses from 75 to 200 mg to a group of twenty hospitalized depressed patients. Weekly clinical evaluation, which included the ECDEU global score, Hamilton score, and Zung self-rating score, demonstrated a slight improvement which became statistically significant between the first and second weeks of therapy. While the thymoleptic properties of the drug were weak, a pronounced stimulating effect of the drug was noted. Psychometric tests showed an increase in attention, concentration, and psychomotor activity as well as an improvement in the personality dimensions "depression" and "inhibition." Digital computer period analysis of the EEG demonstrated (six hours after oral administration of 50 mg tandamine) a decrease of slow waves, a significant increase of fast activity, and a significant attenuation of the amplitude variability. Such changes are reminiscent of the pharmaco-EEG profile of psychostimulatory drugs and may represent the neurophysiological correlate for the activating and stimulatory properties of tandamine. These findings suggest that this well-tolerated drug may be of some benefit for retarded depressions. (JA)

31 refs

KEYWORDS: Antidepressants: tandamine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-77-D1092

DRUG EFFECTS ON EEG FREQUENCY SPECTRA AS A FUNCTION OF INTERSTIMULUS INTERVAL, A.W.K. Gaillard, Electroencephalography and Clinical Neurophysiology, v42 n3 p417-20 (1977)

This study investigates the change in EEG background activity as a function of interstimulus interval (ISI) by comparing conditions in which ISI is either constant or variable. Prolonged experimental sessions were used to induce fatigue in the subjects. The activation level of the subject was manipulated by administering four different drug treatments: (1) 20 mg phentermine HCL; (2) 600 mg hexobarbital sodium; (3) a suppository placebo; and (4) a nonsuppository control. Sixteen male subjects aged twenty to thirty years worked for three hours at a serial simple reaction time task under each of the four drug conditions. Their EEGs were recorded bipolarly.

The main finding of this study was that, as a function of ISI, similar changes occurred in the EEG frequency spectrum under both the constant and variable ISI conditions. The percentage of power in the alpha and theta bands increased with longer ISIs, while the delta activity decreased. The increase in alpha activity with longer ISI conditions was larger after barbiturate than after placebo, while it remained constant after amphetamine treatment.

Contrary to expectation, no systematic changes in alpha activity were found during the three-hour session for any of the treatments. It is suggested that the background EEG during the foreperiod of a reaction time task mainly reflects phasic arousal. The characteristics of the background EEG in this study are quite different from those in previous studies because it was not done under relaxed no-task conditions. (AAM)

11 refs

KEYWORDS: Anorectic (Appetite Control) Agents: phentermine. General Anesthetics: hexobarbital. Sympathomimetic (Adrenergic) Agents: phentermine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Physiological Testing. Psychomotor Tests.

UM-77-D1093

IMPAIRMENT OF VIGILANCE AND PERFORMANCE UNDER LITHIUM-TREATMENT. B. Muller-Oerlinghausen; H. Bauer; W. Girke; S. Kanowski; N. Goncalves, Pharmakopsychiatrie Neuro-Psychopharmakologie, v10 n2 p67-78, (1977)

This study attempted to objectively determine whether lithium increases fatigue, loss of concentration and memory, and temporary physical weakness, all of which are common complaints of long-term lithium patients. Before and after one week of lithium application EEG was recorded in eighteen female outpatients under long-term lithium treatment for manic depression (aged 28 to 65 years) and in ten normal matched volunteers. Performance and psychophysiological tests were also carried out which measured reaction time, fine hand tremor, and critical flicker fusion. Lithium was determined in the serum and red blood cells, and plasma cortisol was determined by radiommunoassay.

Results of the psychometric testing indicated that lithium impaired performance considerably in both patients and in normal volunteers. The EEG data in both groups suggest reduced vigilance. Critical flicker fusion frequency was significantly elevated only during the first days of lithium application in the normal volunteers. Whereas EEG changes persisted, other symptoms such as critical flicker fusion frequency reduction, fine hand tremor, or reduced performance resolved at least partially seven days after lithium withdrawal in normal volunteers.

The authors conclude that from this single study that it is difficult to determine whether the low performance of the lithium-treated patients is a real drug effect or whether it is related to the underlying disease. (JAM)

52 refs

KEYWORDS: Antidepressants: lithium*. Other CNS Agents: lithium*. Experimentation: Chronic Dosage Study. Physiological Testing. Psychomotor Tests.

UM-77-D1094

VALPROATE SODIUM: EVALUATION OF SO-CALLED PSYCHOTROPIC EFFECT. A CONTROLLED STUDY, K.W. Sommerbeck; A. Theilgaard; K.E. Rasmussen; V. Lohren; L. Gram; K. Wulff, Epilepsia, v18 n2 p159-67 (1977)

Described here is a controlled study using a triple-blind crossover design and placebo techniques in which the effect of the antiepileptic valproate sodium (VPA) on some simple and complex cognitive and motor functions in twenty hospitalized, previously therapy-resistant epileptics was investigated with an extensive psychological test battery. In addition, the combined effects of VPA and clorazepam were studied. Subjects were eighteen females and two males ranging in age from 13 to 63 years, and were randomly chosen to start on VPA or placebo. Serum VPA concentrations varied from 84 to 301 micromoles/liter. Drug effects were assessed with eleven tests: (1) Bourdon's test; (2) Visual Gestalt test; (3) verbal substraction; (4) Stroop's Color Naming test; (5) simple reaction test; (6) paired-associate learning; (7) learning and reproduction of visuospatial material; (8) digit span; (9) tapping test; (10) hidden patterns test; and (11) time estimation test.

Test results showed few significant differences between performance during VPA and placebo periods, the differences found indicating decreased performance during VPA treatment. The majority of other observed differences showed trends in the same direction. In particular VPA reduced psychomotor tempo and, to a lesser degree, inhibited visuospatial analytic and synthetic functions. Other cognitive functions investigated remained unaffected. Objective psychological assessment of patients' condition during VPA treatment showed a slight degree of deterioration.

Concurrent treatment with VPA and clonazepam (Rivotril(R)) inhibited even further patients' psychomotor tempo, and objective psychological assessment supported the impression of this further deterioration in comparison to VPA treatment alone.

The psychological test results did not correlate with (1) frequency of seizures, (2) EEG evaluations from VPA and placebo treatment periods, or (3) serum VPA level. (JAM)

19 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): clonazepam. valproate sodium*. Clinical Study. Experimentation: Chronic Dosage Study. Psychological Testing. Psychomotor Tests.

UM-76-D1095

THE EFFECTS OF CHLORDESMETHYLDIAZEPAM ON BEHAVIORAL PERFORMANCE AND SUBJECTIVE JUDGMENT IN NORMAL SUBJECTS, C. Zimmermann-Tansella; M. Tansella; M. Lader, Journal of Clinical Pharmacology, v16 n10 pt 1 p481-8 (Oct 1976)

This study investigated the effects of chlordesmethyldiazepam on behavioral performance and subjective judgment in normal subjects. Eight normal healthy males aged 25 to 31 years were tested on four consecutive weekly occasions, receiving one of the following drug treatments on each occasion: (1) 1 mg chlordesmethyldiazepam; (2) 2 mg chlordesmethyldiazepam; (3) 100 mg amylobarbitone sodium; and (4) placebo. Before drug ingestion, subjects were administered several personality assessments. Twelve hours after drug ingestion subjects were tested for auditory choice reaction time, simple auditory reaction time, card sorting, digit symbol substitution, symbol copying, motor speed, coordination, numerical reasoning, and tapping rate. After completing each behavioral test the subject rated himself on his test performance.

Residual effects were definitely detectable after the 2 mg dose of benzodiazepine with both behavioral impairment and subjective hangover. Both the 1 mg dose and the amylobarbitone sodium were almost devoid of such effects. Very few drug effects on test anxiety and performance judgment were discerned. Plasma concentrations of amylobarbitone were related to decreases in test anxiety and of chlordesmethyldiazepam to increased sleepiness. (HSRI)

14 refs

KEYWORDS: Barbiturates: amobarbital*. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordesmethyldiazepam*. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1096

A REPEATED DOSE COMPARISON OF THE SIDE EFFECTS OF FIVE ANTIHISTAMINES ON OBJECTIVE ASSESSMENTS OF PSYCHOMOTOR PERFORMANCE, CENTRAL NERVOUS SYSTEM AROUSAL AND SUBJECTIVE APPRAISALS OF SLEEP AND EARLY MORNING BEHAVIOUR, I. Hindmarch; A.C. Parrott, Arzneimittel Forschung/Drug Research. v28 (I) n3 p483-6 (1978)

The side effects of five antihistamines (chlorpheniramine maleate, mebhydrolin, clemastine hydrogen fumarate (Tavegil(R)), ketotifen, and promethazine hydrochloride) were measured on subjective assessments of sleep and objective assessments of complex psychomotor behavior and central nervous system arousal. Fifty consenting volunteers aged twenty to fifty years each received one of the five preparations for a period of four days with the subjective effects being reported on a set of 10 cm line visual analogue scales and the objective assessments being made via a computer assisted reaction time task and critical flicker fusion thresholds. The following dosages were used: (1) chlorpheniramine maleate (4 mg t.d.s.); (2) mebhydrolin (50 mg t.d.s.); (3) clemastine hydrogen fumarate (1 mg b.d.); (4) ketotifen (1 mg b.d.); and (5) promethazine hydrochloride (25 mg nocte.).

Chlorpheniramine, (4 mg t.d.s. for four days) produced a significant impairment in critical flicker fusion thresholds with respect to pretreatment baselines but none of the preparations showed any significant impairment in complex reaction time assessments. The subjective assessments of sleep and early morning hangover showed mebhydrolin and clemastine to be free from detrimental side effects, but promethazine and chlorpheniramine to produce significant impairments in the integrity of early morning behavior. The authors conclude that clemastine and mebhydrolin show no evidence of any impairment of psychomotor behavior or subjective aspects of sleep following repeated doses of the drugs and can safety be prescribed for drivers. Ketotifen produces no impairment of psychomotor behavior while at the same time promotes and improves the quality of sleep. (JAM)

10 refs

KEYWORDS: Anti-Emetics: promethazine. Antihistamine Agents: chlorpheniramine, clemastine, ketotifen, mebhydrolin. Major Tranquilizers (Antipsychotics and Neuroleptics): promethazine. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects. Tests of Sensory Function.

UM-78-D1097

MARIJUANA: DOSE EFFECTS ON PULSE RATE, SUBJECTIVE ESTIMATES OF INTOXICATION, FREE RECALL AND RECOGNITION MEMORY, L.L. Miller, T.L. Cornett, Pharmacology Biochemistry and Behavior, v9 p573-7 (1978)

The effects of marijuana on memory as measured by free recall and recognition, pulse rate, and self-ratings of intoxication was evaluated in sixteen males, aged 21 to 28, all of whom were moderate users of marijuana. Marijuana containing 0, 5, 10, or 15 mg delta-THC was administered to all subjects by smoking in four sessions separated by a one-week interval. Pulse rate measures were taken before smoking and fifteen, fifty, and ninety minutes following smoking. Subjects were assessed for immediate free recall, delayed recall, and delayed recognition using eight forty-item work lists. At the end of testing each subject rated the intensity of his high and its pleasantness.

Results of the test showed that free recall was reduced in a dose-related manner by the drug, but recognition memory was unaffected. A two-second word presentation rate produced inferior recall in comparison to a four-second rate, but this variable did not interact with drug condition. Intrusion errors increased following intoxication but this effect was not systematically related to dosage of delta-9-THC. Both pulse rate and self-ratings of intoxication increased with dosage.

The authors conclude that the actions of marijuana on memory might be best described in terms of retrieval deficit from episodic memory which is due to impaired encoding operations involving semantic and cognitive integration. (JAM)

34 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Experimentation: Acute Dosage Study. Experimentation: Dose-Effect Study. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-77-D1098

THE EFFECTS OF FOUR ANTIHYPERTENSIVE AGENTS ON THE STROOP COLOUR-WORD TEST IN NORMAL MALE VOLUNTEER SUBJECTS, P.G. Harvey; A.B. Clayton; T.A. Betts, Psychopharmacology, v54 n2 p133-8 (1977)

Presented here is a report of a study investigating the effects of four antihypertensive agents, namely, atenolol, methyldopa, propanolol, and reserpine, on the Stroop Color-Word Test in normal subjects. Sixty healthy male volunteers (aged 18 to 29 years) were randomly assigned to one of six treatment groups on a double-blind basis: (1) atenolol, 50 mg t.d.s.; (2) methyldopa, 250 mg t.d.s.; (3) propanolol, 40 mg t.d.s.; (4) reserpine, 0.2 mg t.d.s.; (5) placebo; and (6) control (no tablets). Prior to drug administration all subjects completed an Eysenck Personality Inventory and mood rating scale, and heart rate and blood pressure were monitored. Before treatment, two hours after the first dose, after seven doses, and after twenty-one doses, subjects were administered a kinetic visual acuity test followed by the Stroop Test. Subjects' performance was assessed in terms of word reading speed and an interference score based on the difference between the incongruous color word and color card reading speed.

Results indicate that the drugs used had no central effects as measured by the Stroop Color-Word Test. Propanolol was found to have no effect on a primarily cognitive task; however, there were slight suggestions of adverse effects on cognitive tasks for methyldopa. Some personality and drug interactions were found, particularly in the reserpine group. (HSRI)

33 refs

KEYWORDS: Anti-Anginal Agents: propranolol. Anti-Arrhythmia Agents: propranolol. Hypotensive (Antihypertensive) Agents: methyldopa, propranolol, reserpine. Major Tranquilizers (Antipsychotics and Neuroleptics): reserpine. Sympatholytic (Adrenergic Blocking) Agents: atenolol. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing.

UM-76-D1099

THE EFFECTS OF LOW DOSES OF AMYLOBARBITONE SODIUM AND DIAZEPAM ON HUMAN PERFORMANCE, J. Hart; H.M. Hill; C.E. Bye; R.T. Wilkinson; A.W. Peck, British Journal of Clinical Pharmacology, v3 n2 p289-98 (1976)

The effects of diazepam (2.5 and 5 mg) and amylobarbitone sodium (50 and 100 mg) on mental performance and subjective effects were assessed in twelve healthy subjects under standardized conditions. Treatments were administered orally at weekly intervals according to a balanced design and under double-blind conditions. Tests administered to the subjects measured auditory vigilance, short-term memory, auditory reaction time, visual search ability, tapping speed, and digit symbol substitution.

The tests of performance most sensitive to drug effects in these healthy subjects were those that were either prolonged and monotonous and gave the subject no feedback on performance, or that required short-term memory for efficient execution. Auditory vigilance was significantly impaired ($P<0.05$) between 45 and 105 minutes after all drug treatments except amylobarbitone sodium (100 mg) compared with performance after lactose. At the same time false reports were significantly increased after amylobarbitone sodium (100 mg) compared with all other active drugs but not with lactose. These effects disappeared by five hours after drug administration. Short-term memory was impaired 105 minutes after all treatments and impairment was dose related. No significant effects occurred after five hours postdrug.

Simple auditory reaction time was prolonged up to two hours after the highest doses of amylobarbitone sodium and past five hours after treatment with 50 mg amylobarbitone. Digit symbol substitution was impaired by amylobarbitone sodium (50 and 100 mg) and diazepam (5 mg) up to nearly three hours. No significant changes in visual search or tapping occurred after active drugs compared with lactose.

Subjective ratings indicated both mental and motor impairment 165 minutes after all active preparations compared with scores after lactose. Both correct detections and false reports in auditory vigilance tended to fall over the six separate days of testing, indicating an increase in caution. Visual search, short-term memory, tapping, and digit symbol substitution significantly improved with time, but there was no change in reaction time.

From the limited information obtained by sampling blood at three and six hours, no relationship between change in performance and plasma level was found in these subjects. (JAM)

22 refs

KEYWORDS: Barbiturates: amobarbital*. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam*. Muscle Relaxants (Central): diazepam*. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects. Tests of Sensory Function.

UM-78-D1100

EMPIRICAL SEPARATION OF PHYSIOLOGIC AND EXPECTED EFFECTS OF ALCOHOL ON COMPLEX PERCEPTUAL MOTOR PERFORMANCE. R.E. Vuchinich; M.B. Sobell. Psychopharmacology, v60 n1 p81-5 (1978)

The role of expectancy in producing perceptual motor-performance deficits following alcohol consumption was investigated in a 2 x 2 factorial experiment. Forty male normal drinkers (1) either were or were not administered 0.414 g ethanol/kg body weight; and (2) either were or were not instructed they were consuming an alcoholic beverage (regardless of actual beverage content). Performance on a divided-attention task requiring simultaneous pursuit rotor tracking and choice reaction-time responding provided the main dependent measures.

Alcohol disrupted tracking performance and interacted with instructions regarding beverage content to influence choice reaction-time performance. Results confirmed previous reports of divided-attention task performance deficits induced by a low alcohol dose, but more importantly, indicated that subjects' expectancies also influence performance levels. These findings demonstrate the importance of controlling for expectancy effects in alcohol research, and suggest that alcohol and expectancy may influence perceptual motor performance through different processes. (JA)

21 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Acute Dosage Study. Other Factors Influencing Drug Effects. Psychomotor Tests.

UM-77-D1101

EEG, BLOOD LEVEL, AND BEHAVIORAL EFFECTS OF THE ANTIDEPRESSANT MIANSERIN (ORG GB-94), M. Fink; P. Irwin; M. Gastpar; J.J. de Ridder, Psychopharmacology, v54 n3 p249-54 (1977)

A pharmacokinetic analysis of a new antidepressant drug, mianserin (ORG GB-94), was undertaken in four male volunteers, aged 21 to 33, each of whom received 15 mg mianserin on two occasions. The study attempted to determine the EEG profile, plasma levels, and effects on behavior of single doses, and to relate the response measures to the plasma and urine levels.

Plasma levels were found to peak at two hours with a median level of 11.0 ng/ml, a median beta-phase half-life of 10.0 hours, and a median apparent volume of distribution of 3.3×10^3 liters. EEG profile analysis showed mianserin to increase frequencies below 6 Hz, decrease those from 7.5 to 15 Hz, and increase frequencies above 18 Hz, a pattern similar to amitriptyline. Peak EEG effects ranged from two to five hours with a pattern of measured changes that paralleled plasma levels with varying latency. Decreases in vigilance measures and in critical flicker-fusion frequency showed a similar time course.

The results of the study show that mianserin is a putative thymoleptic on EEG profile analysis with high cerebral penetrance. (JAM)

24 refs

KEYWORDS: Antidepressants: mianserin*. Pharmacokinetics: Acute Dose. Physiological Testing. Psychological Testing.

UM-78-D1102

EFFICACY AND SIDE EFFECTS OF FLURAZEPAM, FOSAZEPAM, AND NITRAZEPAM AS SLEEPING AIDS IN PSYCHOGERIATRIC PATIENTS, M. Viukari; M. Linnoila; U. Aalto, Acta Psychiatricia Scandinavica, v57 n1 p27-35 (1978)

The purpose of this study was to investigate the relative efficacy and side effects of different benzodiazepine hypnotics. It also attempted to formulate a description of groups of elderly psychiatric patients particularly sensitive to these drugs. Seventeen psychogeriatric patients (fourteen female, three male) whose mean age was 77.4 years and who had trouble sleeping were administered 15 mg flurazepam, 60 mg fosazepam, 5 mg nitrazepam, or placebo in a randomized, double-blind, crossover design. Each patient received an active treatment for the first, third, and fifth weeks of the five-week experiment and placebo for the second and fourth weeks. Drug effects on the following variables were assessed on the seventh day of each treatment: (1) short-term memory; (2) long-term memory; (3) automated series; (4) handgrip; (5) tapping speed; (6) coordination; and (7) sleep quality. In addition, serum levels of fosazepam and N-desmethyldiazepam were measured with high-pressure liquid chromatography.

Results of the study showed an overall tendency toward a reduced number of awakenings during the night when the benzodiazepines were used. There was no significant decline in sleep quality after flurazepam and fosazepam. However, after nitrazepam, the number of awakenings was significantly higher. It also induced a rebound insomnia after withdrawal. Neither long- nor short-term memory was significantly affected by the benzodiazepines in most patients, nor were handgrip or coordination. Tapping speed was slowed significantly by nitrazepam and fosazepam.

All hypnotics lost some of their efficacy toward the end of seven days of drug use. Patients with evident cerebrovascular disease were vulnerable to the side effects of the benzodiazepine hypnotics. The side effects did not correlate with the age of the patient. In addition, no correlations were found between the serum levels of fosazepam or its main metabolite and the side effects.

The authors conclude that in short-term therapy of insomnia in psychogeriatric patients, flurazepam is more advantageous than fosazepam and nitrazepam. (HSRI)

15 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): nitrazepam. Metabolites of Drugs and Other Agents: N-desmethyldiazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): N-desmethyldiazepam. Nonbarbiturates: flurazepam, fosazepam*, nitrazepam. Clinical Study. Epidemiologic Research: Drug Concentrations in Body Fluids. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests.

UM-76-D1103

PSYCHIATRIC SEQUELAE OF PHENCYCLIDINE ABUSE, B. Faumen; G. Aldinger; M. Fauman; P. Rosen, Clinical Toxicology, v9 n4 p529-38 (1976)

Presented here is a review of the psychiatric aftereffects of phencyclidine (PCP) abuse or overdose. Seven cases of PCP overdose are presented. The paper describes the objective and subjective effects of the drug and the difficulties encountered in assessing psychedelic drug effects. Psychiatric, emotional, and social characteristics commonly found in PCP abusers are discussed and compared to those in amphetamine, LSD, and marijuana users. Particular emphasis is given to psychosis stemming from PCP abuse.

Phencyclidine use has been noted to produce a psychosis of several weeks' duration in a small fraction of users. Descriptions of the premorbid personalities of those who became psychotic resemble descriptions of LSD and marijuana users who experience prolonged psychiatric difficulty. In addition, the psychosis produced can often be recognized as a "hallucinogen" psychosis. Certain features of the phencyclidine psychosis, namely the neurologic abnormalities, dose-related severity of symptoms, and regularity of the length of illness, are not noted with other psychedelic drugs, leading to the conclusion that PCP psychosis is a drug effect rather than a brief functional psychosis precipitated by the disintegrating PCP experience. However, the infrequent occurrence of psychosis in the (apparently) large exposed population still suggests that this is a combination of drug effect and vulnerable, pathologic personality. (AAM)

24 refs

KEYWORDS: Hallucinogens and Related Agents: phencyclidine. Review: Drug Effects.

UM-77-D1104

GLUTETHIMIDE AND 4-OH GLUTETHIMIDE: PHARMACOKINETICS AND EFFECT ON PERFORMANCE IN MAN, J.W. Crow; P. Lain; F. Bochner; D.W. Shoeman; D.L. Azarnoff, Clinical Pharmacology and Therapeutics, v22 n4 p458-64 (1977)

This study was designed to investigate the pharmacokinetics of multiple therapeutic doses of glutethimide and 4-OH glutethimide (4-HG) in plasma and effects on selected performance tests in normal volunteers. The subjects were four males and three females aged twenty-four to twenty-nine. Subjects received four doses of 500 mg glutethimide within twenty-four hours. Blood samples were taken just prior to administration of the last dose and hourly thereafter. Performance on a digit symbol substitution test, finger tapping task, card sorting task, subtraction test, and a computer generated tracking test was evaluated just before the last dose and every two hours thereafter for ten hours.

Linear, log-linear, and log-log relationships were investigated for each test. No trend in drug level versus performance was found except for tracking. There was excellent positive correlation between plasma level and tracking errors. The metabolite 4- hydroxyglutethimide did not contribute significantly to the effect of glutethimide administered in therapeutic doses.

When the volunteers were divided into smokers and nonsmokers, glutethimide decreased tracking ability to a greater extent in smokers than in nonsmokers. (HSRI)

19 refs

KEYWORDS: Metabolites of Drugs and Other Agents: 4-hydroxy-2-ethyl-2-phenylglutarimide*. Nonbarbiturates: glutethimide*. Drug Concentration-Effect Study: Driving Skill Impairment. Pharmacokinetics: Chronic Dose. Psychological Testing. Psychomotor Tests.

UM-75-D1105

EFFECTS OF NITROUS OXIDE ON DECISION-STRATEGY AND SUSTAINED ATTENTION, J.M. Garfield; F.B. Garfield; J. Sampson, Psychopharmacologia, v42 n1 p5-10 (1975)

This study attempted to determine whether decision-making ability and sustained attention are impaired by a 30% concentration of nitrous oxide. Effects of 10, 20, and 30% nitrous oxide on decision-making strategy, reaction times, sustained attention, the Digit Symbol Substitution Test (DSST), short-term memory, and the Clyde Mood Scale were assessed in twelve male test subjects aged 18 to 25.

Decision-making strategy, as measured by two-choice probability-learning, was unaffected by 30% nitrous oxide once a strategy had been formulated, but reaction-times were increased. Sustained attention was significantly affected in 33% of the subjects, whereas performance on the DSST and on the short-term memory task was impaired in virtually all subjects. Changes were noted in several mood-scale factors with 30% nitrous oxide. No residual drug effects were found. The authors conclude that those tasks that are most complex in terms of stimulus complexity, response complexity, or both, may be most affected by nitrous oxide. It is probable that nitrous oxide at subanesthetic concentrations does not first depress the newest phylogenetic areas of the brain, but instead selectively affects areas of the central nervous system mediating attention and motor expression. (JAM)

24 refs

KEYWORDS: Gases: nitrous oxide. General Anesthetics: nitrous oxide. Hallucinogens and Related Agents: nitrous oxide. Experimentation: Dose-Effect Study. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1106

THE INTERACTION BETWEEN ETHANOL AND ANTIHISTAMINES, 1: DEXCHLORPHENIRAMINE, H.M. Franks; V.R. Hensley; W.J. Hensley; G.A. Starmer; R.K.C. Teo, Medical Journal of Australia, v1 n7 p449-52 (22 Apr 1978)

This paper investigates the acute interaction of a therapeutic dose of dexchlorpheniramine and a moderate dose of ethanol on human performance measures, particularly perceptual, cognitive, and motor functions. Nine males and four females aged eighteen to twenty-seven years were orally administered placebo, ethanol (0.75 g/kg), and dexchlorpheniramine (4 mg/70 kg) alone and in combination. Subjects were tested before treatment and twenty minutes after for standing steadiness, simple auditory and visual reaction time, complex reaction time, manual dexterity, perceptual speed, and various parameters using the Vienna Determination Apparatus. Plasma ethanol and glucose concentration and whole blood lactate concentration were also determined.

Results of the tests showed that 0.75 g/kg alcohol induced a significant impairment in most of the performance tests. When administered alone, dexchlorpheniramine (4 mg/70 kg) was found to decrease standing steadiness and to reduce performance on the Vienna Determination Apparatus.

Although a synergistic effect of dexchlorpheniramine with ethanol was observed in only some of the tests, a delayed recovery from the effects of the combination was noted. Subjective data indicated that the sedative effects of dexchlorpheniramine were more pronounced in the presence of ethanol. It is possible that since the subjective feeling of impairment after taking ethanol with an antihistamine is greater than the actual decrement in performance, this combination could be more beneficial than detrimental to traffic safety due to the fact that the driver will often attempt to compensate for his impairment. (HSRI)

12 refs

KEYWORDS: Antihistamine Agents: dexchlorpheniramine. Nonbarbiturates: ethanol (ethyl alcohol)*. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-77-D1107

BEHAVIORAL AND ELECTROENCEPHALOGRAPHIC CORRELATES OF THE CHRONIC USE OF MARIJUANA--A REVIEW, P.A. Fried, Behavioral Biology, v21 p163-96 (1977)

Research and discussion related to the behavioral and electroencephalographic effects of long-term use of marijuana or its constituents are reviewed. It is concluded that tolerance develops to the behavioral and electroencephalographic depressant aspects of the cannabis drugs but little attentuation develops to the stimulant effects. The rate of tolerance development is considerably influenced by learning factors such as the opportunity or necessity to make behavioral responses that counteract the decrements in performance resulting from the drug's influence. Evidence is presented indicating that the animal and human literature are in considerable agreement concerning chronic use of marijuana and tolerance to it if socially acquired cues and expectancies and dosage/ frequency parameters are taken into consideration.

In conclusion, it is evident that many of the acute effects of cannabis or its constituents are altered after chronic use. (JA)

191 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-8-tetrahydrocannabinol, delta-9-tetrahydrocannabinol, marijuana. Review: Drug Effects.

UM-78-D1108

WIRKUNGEN UND NEBENWIRKUNGEN DER STIMULANTIENBEHANDLING BEI KINDERN [EFFECTS AND SIDE EFFECTS IN THE TREATMENT OF CHILDREN WITH STIMULANTS], C. Klicpera, Fortschritte der Neurologie und Psychiatrie und Ihrer Grenzgebiete, v46 n7 p392-414 (1978)

This article reviews the results of controlled studies published so far on the effects of stimulants on children with disordered behavior patterns. These effects are subdivided into short-term and long-term effects. Three types of effects are examined and demonstrated in the short-term group: (1) behavioral; (2) psychological; and (3) psychophysiological. Besides providing a survey of the side effects of stimulating medicaments, the article discusses studies comparing treatment with stimulants to treatment with other medicaments and to behavioral therapy measures.

A review of the results of these studies shows that the effect of stimulants is mainly seen in an inhibition of maladjusted, impulsive behavior, and in improved attentiveness. To the observer, this effect seems to be represented by decreased motor activity, but this is actually seen in only a few children. Treatment with stimulants is the drug treatment of choice for hyperactive children with regard to effectivity and side effects. However, juvenile reaction to stimulants is subject to greater variation than their reaction to other kinds of drug therapy. In many children the short-term effect can be considered as favorable even when compared with the results obtained via behavioral therapy. However, medicaments seem to exercise little influence on long-term prognosis. The fact that side effects occasionally occur should prompt the physician to exercise particular caution with regard to the indication and to ensure good medical and psychological supervision during the treatment. (JA)

129 refs German

KEYWORDS: Stimulants. Review: Drug Effects.

UM-77-D1109

EFFECT OF ALCOHOL AND BENZODIAZEPINES ON PERFORMANCE AS RELATED TO PERSONALITY CHARACTERISTICS. PERSONALITY CHARACTERISTICS AMONG HEALTHY "PLACEBO REACTORS" AND NONREACTORS, M. Linnoila; R. Liljequist; J. Olkoniemi; I. Saario, Pharmakopsychiatrie Neuro-Psychopharmakologie, v10 n4 p246-63 (1977)

This study attempted to measure personality factors associated with placebo reactors as opposed to placebo nonreactors. At the same time an attempt was made to determine the effect of alcohol and benzodiazepines on performance as related to personality characteristics.

Subjects were thirty-seven male and three female moderate alcohol users between twenty and twenty-three years of age. Drugs were administered t.i.d. for two weeks in a double-blind, crossover design. Twenty subjects received chlordiazepoxide and placebo; twenty received diazepam and placebo. The following treatments were used: (1) placebo capsules plus placebo drink; (2) either 5 mg diazepam or 10 mg chlordiazepoxide plus placebo drink; (3) placebo capsules plus .5 g/kg body weight alcohol; and (4) either 5 mg diazepam or 10 mg chlordiazepoxide plus .5 g/kg body weight alcohol. Before treatment, subjects were assessed with Eysenck's EPIC-NESI, Taylor's Manifest Anxiety Scale, and Lattell's 16 PF inventory.

On the fourteenth day of each treatment, thirty minutes after drug administration, the subjects were given a choice reaction test, two coordination tests, and an attention test. After the tests the subjects rated the quality of their treatment as placebo, tranquilizer, or stimulant.

A multiple regression analysis was computed that showed that benzodiazepines impaired most the performance of subjects having a high ego strength and paranoid tendencies and who were self-sufficient. Most of the significant correlations between personality factors and drug effects on performance were observed after the benzodiazepines in the attention test. The results indicate a weaker personality-drug interaction on

performance after the benzodiazepines in combination with alcohol treatment than after the benzodiazepines alone. The authors conclude from these results that certain personality factors have more effect on performance changes after benzodiazepines than do drug serum levels.

The study also found that about half of the subjects were placebo reactors. The traits common to the placebo reactors reflected tendencies to feel guilt and to have protected emotional sensitivity and a high superego strength. (HSRI)

27 refs

KEYWORDS: Metabolites of Drugs and Other Agents: N-desmethyldiazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide*. diazepam*. N-desmethyldiazepam. Muscle Relaxants (Central): diazepam*. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Personality and Drug Effects. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1110

EFFECT OF DIAZEPAM AND CHLORPROMAZINE ON MEMORY FUNCTIONS IN MAN, R. Liljequist; M. Linnoila; M.J. Mattila, European Journal of Clinical Pharmacology, v13 n5 p339-43 (1978)

This study was performed to obtain information about the action of diazepam on different phases of memory functions in man and to analyze possible state-dependency effects. Chlorpromazine was used as a reference drug since previous research shows it does not affect human memory. Ten females and ten males were given a single daily oral dose of 10 mg diazepam for nineteen days, and eleven females and nine males were given 25 mg chlorpromazine daily for five days. All subjects were between nineteen and twenty-five years of age. Forty minutes after treatment each subject was evaluated with Kahn's Test for symbol arrangement and a paired association-learning task in order to assess drug effects on acquisition, storage and retrieval, and state-dependency effects. A flicker fusion test, two coordination tests, and a choice reaction task were used to evaluate alertness in the subjects.

Results of the tests showed that diazepam significantly impaired acquisition, but slightly facilitated recall. Reaction time was shortened after acute diazepam treatment and coordination was impaired after two weeks treatment with diazepam. Acute treatment with chlorpromazine did not change memory or psychomotor performance. (JAM)

21 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests.

UM-77-D1111

EFFECTS OF D-AMPHETAMINE ON SPEAKING IN ISOLATED HUMANS, M.L. Stitzer; R.R. Griffith; I. Liebson, Pharmacology Biochemistry and Behavior, v9 n1 p57-63 (1977)

The effects of oral d-amphetamine (5-20 mg) were studied in isolated humans who produced speech monologues during experimental sessions. Drug effects were studied under double-blind conditions by making repeated observations within each subject after placebo or active drug.

In the first study, d-amphetamine (15 mg) was studied in four isolated subjects who had received instructions that they should talk some of the time during experimental sessions. All subjects spoke more after active drug than after placebo.

In the second experiment, d-amphetamine (5-20 mg) was studied in four subjects who were instructed to talk, but who also earned points under a fixed interval five-minute schedule by speaking (i.e., by closure of a voice operated relay).

Point delivery did not generally influence patterns of speech over time. Reliable drug-produced increases in amount of talking were observed in three of four subjects. Adjective checklist self-report scores indicating a stimulant drug effect were also sensitive to effects of d-amphetamine.

Under controlled laboratory conditions, an increase in speaking is a reliable behavioral effect of d-amphetamine in isolated humans producing speech monologues. (JA)

14 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Stimulants: dextroamphetamine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Acute Dosage Study. Psychological Testing.

UM-75-D1112

DIE BEWERTUNG VON ARZNEIMITTELNEBENWIRKUNGEN [EVALUATION OF SIDE EFFECTS], K. W. von Eickstedt, Arzneimittel Forschung, v25 n7a p1223-6 (1975)

This paper discusses the benefit-risk ratio of drugs in terms of degree of severity of side effects. A method for calculation of this ratio is presented. The author discusses particularly those side effects which are difficult to evaluate because of their complexity. The "Stufen Plan" is described which is used for the coordination of necessary preventive measures when side effects of drugs become evident. (JAM)

10 refs German

KEYWORDS: Review: Drug Effects.

UM-78-D1113

EFFECTS OF ALCOHOL ON PSYCHOMOTOR PERFORMANCE OF MEN AND WOMEN, M. Linnoila; C.W. Erwin; W.P. Cleveland; P.E. Logue; W.D. Gentry, Journal of Studies on Alcohol, v39 n5 p745-58 (1978)

This study was designed to investigate possible sex-dependent effects of alcohol on a psychomotor test battery. Particular attention was given to: (1) selecting tests that differentially challenge tracking skills and sensory processing requiring both verbal and spatial judgments which are possibly related to the functions of the dominant and nondominant hemispheres of the brain; (2) studying the development of tolerance to alcohol; and (3) studying the relationships between alcohol effects and circadian rhythms.

Ten men and ten women between the ages of twenty-one and twenty-six were administered alcohol at 0, 0.5, 0.8, or 1.2 g/kg body weight. Following consumption, subjects were tested with a simple reaction time test, a subcritical continuous tracking task, a continuous performance task, and a visual vigilance task. After testing, the subjects rated their performance.

Test results indicated that reaction times were not greatly affected by alcohol dosage, although there was a slight tendency for men to have longer reaction times at the highest alcohol dose. In the continuous tracking task some of the subjects' performance, both male and female, declined at higher doses of alcohol. There was no sex-dependent variation in performance patterns after different doses of alcohol. The same was true for the continuous performance task.

The data on psychomotor performance in the sober condition showed that women had slower reaction times than men. When the effect of alcohol was superimposed, both sexes were affected in a similar manner. The results of the reaction time tests suggest that verbal information processing ability is not affected significantly by alcohol. Results also show that alcohol may preferentially affect the function of the nondominant hemisphere of the brain. Acute habituation to alcohol among moderate drinkers of either sex is probably not significant.

The authors conclude that the degree of impairment observed in subjects after alcohol suggests that current BAC limits concerning drinking and driving are conservative. Further studies in homogeneous populations are necessary to elucidate factors related to the large individual variation in sensitivity to the effects of alcohol. (HSRI)

22 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Acute Dosage Study. Experimentation: Dose-Effect Study. Gender and Drug Effects. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-75-D1114

SCOPOLAMINE EFFECTS ON VISUAL DISCRIMINATION: MODIFICATIONS RELATED TO STIMULUS CONTROL, H.L. Evans, Journal of Pharmacology and Experimental Therapeutics, v195 n1 p105-13 (1975)

This study attempted to determine the extent to which drug effect resembles a reduction in stimulus control resulting from manipulation of a physical property of the stimulus. Stumptail monkeys performed a discrete trial, three-choice visual discrimination. The discrimination behavior was controlled by the shape of the visual stimuli. Strength of the stimuli in controlling behavior was systematically related to a physical property of the stimuli, luminance.

Low luminance provided weak control, resulting in a low accuracy of discrimination, a low response probability, and maximal sensitivity to scopolamine (7.5-60 ug/kg). In contrast, high luminance provided strong control of behavior and attenuated the effects of scopolamine. Methylscopolamine had no effect in doses of 30 to 90 ug/kg.

Scopolamine effects resembled the effects of reducing stimulus control in undrugged monkeys. Since behavior under weak control seems to be especially sensitive to drugs, manipulations of stimulus control may be particularly useful whenever determination of the minimally-effective dose is important, as in behavioral toxicology. Present results are interpreted as specific visual effects of the drug, since nonsensory factors such as base-line response rate, reinforcement schedule, training history, motor performance, and motivation were controlled. Implications for state-dependent effects of drugs are discussed. (JAM)

38 refs

KEYWORDS: Mydriatics: scopolamine. Parasympatholytic (Cholinergic Blocking) Agents: methscopolamine. scopolamine. Animal Research.

UM-75-D1115

UNE DIMENSION PARTICULIERE DE L'USAGE NON MEDICAL DES DROGUES [A PARTICULAR DIMENSION OF THE NONMEDICAL USAGE OF DRUGS], R. Dugal; M. Bertrand; C. Vaziri; G. Sanchez; S.F. Cooper, L'Union Medicale du Canada, v104 n6 p944-52 (Jun 1975)

This paper reviews the practice of administration of drugs to athletes to enhance performance in sports. After a brief description of the ethical and social repercussions of this practice, the physiological effects caused by physical exertion are examined. Special emphasis is given to the efficacy and dangers of amphetamines and anabolic steroids, two groups of drugs commonly used to enhance performance, suppress psychological symptoms of fatigue, and decrease the physiological modification associated with violent muscular efforts. Finally, the paper discusses various means of curtailing drug abuse in sports. (JAM)

36 refs French

KEYWORDS: Androgens. Stimulants. Review. Review: Drug Effects.

UM-79-D1116

SOLVENT ABUSE: A REVIEW, G.E. Barnes, International Journal of the Addictions, v14 n1 p1-26 (1979)

In this paper the literature on solvent abuse is reviewed. Methods of use, symptoms of use, and effects of long-term solvent abuse are discussed. Several surveys on solvent use are summarized.

The highest prevalence of solvent abuse seems to occur in native peoples undergoing periods of cultural change. Environmental conditions that are postulated as leading to psychological vulnerability and solvent abuse include low social assets, parental drug use, peer and sibling influence, and acculturative stress. Solvent abuse seems to provide a pharmacological way out of a stressful environment for people who feel helpless to improve their situation in other ways. Methods of intervention thus far employed generally have not been evaluated in any systematic fashion. Suggestions for future research are provided. (JA)

7 refs

KEYWORDS: Volatile Solvents. Review.

UM-79-D1117

DIMENSIONS OF THE SUBJECTIVE MARIJUANA EXPERIENCE, R.O. Pihl; D. Shea; L. Costa, International Journal of the Addictions, v14 n1 p63-71 (1971)

The purpose of the present study is threefold: (1) given the same geographic environment, to ascertain whether differences in marijuana intoxication experiences may occur over a period of time; (2) to look for a possible replication of the more stable factors in marijuana intoxication; (3) to describe a specific subject population in terms of drug history variables and patterns of drug use.

A drug history questionnaire and a marijuana effects questionnaire were completed by ninety-one male volunteers who were experienced marijuana smokers. A factor analysis was performed on the frequency of occurrence data concerning marijuana effects.

The resultant factors were similar to those reported previously in the literature supporting the existence of a stable, verbally definable marijuana experience. In comparison to the drug history variables of marijuana smokers in the late 1960s, this population showed increased multiple drug use, an earlier age of introduction to cannabis, and heavier use of cannabis. An analysis of the interaction of drug history variables with experienced marijuana effects suggested that the more frequently one uses cannabis, the less pronounced the experienced effects tend to be. (JAM)

7 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Epidemiology: Regional or Local Survey of Drug Use Patterns. Other Factors Influencing Drug Effects.

UM-79-D1118

COCAINE: MAGICAL DRUG OR MENACE? D.J. Egan; D.O. Robinson, International Journal of the Addictions, v14 n2 p231-41 (1979)

This paper reviews the available evidence concerning cocaine's physiological and psychological safety. Few deaths are attributed to cocaine, but its use is presently restricted by very limited supplies. Use of the drug may possibly result in liver and respiratory problems and may lead to paranoid psychotic conditions.

On the one hand cocaine has been acclaimed as a "magical drug" with a wide range of therapeutic and social uses. On the other hand the drug has been declared a menace, and the elimination of its use has been an urgent priority for law enforcement agencies. Although attempts to curb cocaine use by legal controls appear to be at an all time high, there is also a trend toward the endorsement of its use.

This paper examines evidence that both supports and refutes the position that cocaine is the most benign of illicit drugs currently in widespread use and points to gaps in existing knowledge. (JAM)

25 refs

KEYWORDS: Local Anesthetics: cocaine. Stimulants: cocaine. Review.

UM-77-D1119

ADVERSE BEHAVIORAL EFFECTS OF BENZODIAZEPINES, S. Zisook; R.A. DeVaul, Journal of Family Practice, v5 n6 p963-6 (1977)

This paper examines three myths of benzodiazepine safety: nondependence, consistent tranquilization, and low suicidal potential. Each of these myths at least partially accounts for the widespread use and abuse of benzodiazepines. In reality, the adverse effects of benzodiazepines include the risk of dependency, an increase in hostile-aggressive feelings and behavior, and suicidal depression.

Physiologic dependence on benzodiazepines has been documented not only in patients taking very high doses over extended periods of time or who have "high addictive potential", but also in healthy adults taking therapeutic doses for twenty or more weeks. Increase in hostility-aggression, originally considered a paradoxical drug effect, has been repeatedly demonstrated to be associated with diazepam and

chlordiazepoxide. There is even some evidence that this ought to be considered a true drug effect rather than a paradoxical effect occurring in a substantial proportion of the people taking these drugs.

Depression, with or without suicidal intentions, is another potentially hazardous effect of benzodiazepines. A specific syndrome of ego-alien suicidal ideation has been identified and reported.

The risks of dependency, hostility, and depression are markedly attenuated by the physician's awareness and acknowledgment of these adverse effects. Thus far, the literature on the potentially hazardous effects has not seemed to have substantially influenced clinical practice, but as benzodiazepine use continues to proliferate, the need for careful monitoring of effects also increases. (HSRI)

36 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics). Review.

UM-78-D1120

THE EFFECTS OF TWO ANTIDEPRESSANT AGENTS ON PERFORMANCE ON THE STROOP COLOUR-WORD TEST IN NORMAL MALE VOLUNTEER SUBJECTS, P.G. Harvey; A.B. Clayton, T.A. Betts, British Journal of Clinical Pharmacology, v5 n4 p305-12 (1978)

In this study, a new compound, viloxazine hydrochloride (Vivalen(R)), was compared with imipramine (Tofranil(R)). Viloxazine hydrochloride has a novel profile of neuropharmacological activity that has similarities to both amphetamine and the tricyclic antidepressants. Imipramine is a well-established member of the tricyclic family of antidepressant drugs.

Healthy male volunteers were given imipramine (25 mg three times a day), viloxazine hydrochloride (50 mg 3 times a day), placebo, or no tablets on a double-blind basis. Subjects took the tablets for seven days and were tested before treatment and then after one, seven, and twenty-one doses. The Stroop Colour-Word test was used to assess performance.

While no significant drug effects were found, it is suggested that some of the trends shown are indicative of a slight worsening of performance with imipramine and a slight improvement with viloxazine hydrochloride after seven doses. (JAM)

26 refs

KEYWORDS: Antidepressants: imipramine. viloxazine. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing.

UM-78-D1121

EFFECTS OF AMITRIPTYLINE AND MIANSERIN ON PSYCHOMOTOR SKILLS AND MEMORY IN MAN, M.J. Mattila; R. Liljequist; T. Seppala, British Journal of Clinical Pharmacology, v5 suppl p53s-55s (1978)

Twenty volunteers (fourteen men and six women aged 20 to 23 years) were tested with amitriptyline (25 mg), mianserin (10 mg), and placebo three times daily for two weeks each in a double-blind, cross-over study. Tests of psychomotor function and of learning and memory were carried out after consumption of alcohol or a placebo drink at intervals during each treatment period.

Coordination and reaction skills were affected by mianserin on the first day only, but were affected by amitriptyline up to day seven in most of the tests. Both drugs seemed to interact additively with alcohol. Amitriptyline improved short-term memory span and acquisition, and alcohol enhanced these effects. Mianserin did not interact with alcohol in this respect. The differing effects of amitriptyline and mianserin are considered in relation to anticholinergic properties.

It may be concluded from these experiments that both amitriptyline and mianserin exhibit a central sedative effect manifested in psychomotor activities such as those used in driving. In the acute phase of treatment, this sedation may be significant, and the concurrent use of these drugs with alcohol would probably increase accident risk in traffic. (JAM)

5 refs

KEYWORDS: Antidepressants: amitriptyline. mianserin. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Psychological Testing. Psychomotor Tests.

UM-78-D1122

PERFORMANCE STUDIES WITH ANTIHISTAMINES, C.H. Clarke; A.N. Nicholson, British Journal of Clinical Pharmacology, v6 n1 p31-5 (1978)

The effects of four antihistamines, chlorpheniramine (4 mg), clemastine (1 mg), promethazine (10 mg), and terfenadine (60 mg) on visuo-motor coordination and on subjective assessments of performance and well-being were compared with placebo in six healthy females (aged 19 to 32) from 0.5 to 7.0 hours after morning ingestion of each drug. The study was double-blind, and the doses used were believed to be equally potent in their antihistaminic activity.

Results showed impaired performance 1.5 hours ($P<0.01$) after chlorpheniramine, 3.0 hours ($P<0.05$) and 5.0 hours ($P<0.01$ after clemastine, and 3.0 hours ($P<0.01$) and 5.0 hours ($P<0.0001$) after promethazine. It was not possible to establish effects on performance after ingestion of terfenadine. Subjective assessments of performance were not altered.

The subjects as a group reported improved alertness ($P<0.05$) and improved wakefulness ($P<0.05$) 0.5 hours and 3.5 hours respectively after ingestion of terfenadine, and were less energetic ($P<0.05$) 7.0 hours after ingestion of chlorpheniramine. There were no other consistent changes in assessments of well-being. The authors conclude that the appearance of central effects varies considerably between antihistamines. With most antihistamines some impairment of performance is likely, though persistence and severity of the impairment is likely to be different between drugs. Impairment may not be detected by the drug user. (JAM)

10 refs

KEYWORDS: Anti-Emetics: promethazine. Antihistamine Agents: chlorpheniramine. clemastine. terfenadine. Major Tranquilizers (Antipsychotics and Neuroleptics): promethazine. Experimentation: Comparison of Different Drugs. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1123

IMMEDIATE AND RESIDUAL EFFECTS IN MAN OF THE METABOLITES OF DIAZEPAM, C.H. Clarke; A.N. Nicholson, British Journal of Clinical Pharmacology, v6 n4 p325-31 (1978)

Immediate and residual effects of diazepam and its metabolites on visuo-motor coordination were studied in six healthy males aged 23 to 43 years. Performance was observed from 10.0 - 16.0 hours after overnight ingestion of diazepam (5 and 10 mg), tenazepam (10, 20 and 30 mg), oxazepam (15, 30, and 45 mg), and nordiazepam (5 and 10 mg), and from 0.5 - 6.5 hours after morning ingestion of diazepam (10 mg), tenazepam (20 mg), oxazepam (30 mg), and nordiazepam (5 and 10 mg). Immediate and residual effects of diazepam and tenazepam were also studied on a choice response time test.

Visuo-motor coordination was not impaired after the overnight ingestion of the following dosages: 5 and 10 mg diazepam; 10, 20, and 30 mg tenazepam; 15 and 30 mg oxazepam; and 5 and 10 mg nordiazepam. However, there was a trend of impaired performance over the dose range used with tenazepam 10.0 hours after ingestion. With 45 mg oxazepam performance at 10.0 hours was impaired compared with performance at 14.0 ($P<0.01$) and 16.0 hours ($P<0.001$). Performance on the choice response time test was not impaired after the overnight ingestion of 5 and 10 mg diazepam and 10, 20, and 30 mg tenazepam.

With morning ingestion visuo-motor coordination was impaired at 0.5 ($P<0.01$) and 2.5 hours ($P<0.05$) after 10 mg diazepam, at 0.5 hours $P<0.001$) after 20 mg tenazepam, and at 2.5 ($P<0.01$) and 4.5 hours ($P<0.05$) after 30 mg oxazepam. Performance 6.5 hours after 10 mg nordiazepam was impaired compared with performance 0.5 and 2.5 hours ($P<0.01$) after ingestion. Performance on the choice response time test was impaired 1.0 hour after ingestion of 10 mg diazepam ($P<0.01$) and 20 mg tenazepam ($P<0.05$).

It is concluded that diazepam (5-10 mg), tenazepam (10-20 mg), and oxazepam (15-30 mg) would be useful hypnotics within the dose ranges indicated, at least for occasional use, when impaired performances the next day would be unacceptable. The studies with nordiazepam suggest that, though this drug may have limited effects on performance, it may have persistent effects on behavior consistent with its clinical use as an anxiolytic. (JA)

13 refs

KEYWORDS: Metabolites of Drugs and Other Agents: oxazepam, temazepam, N-desmethyldiazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam, oxazepam, temazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): N-desmethyldiazepam. Muscle Relaxants (Central): diazepam. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Psychomotor Tests.

UM-78-D1124

SPEECH BLOCKAGE: A TRICYCLIC SIDE EFFECT, A.F. Schatzberg; J.O. Cole; D.P. Blumer, American Journal of Psychiatry, v135 n5 p600-1 (May 1978)

This paper discusses five patients who developed speech blockage when they were treated with a tricyclic antidepressant. Three patients had been treated with amitriptyline and two with imipramine, with a minimum time on the drug of eighteen days and minimum dosages of 150 mg a day. "Speech blockage" was defined as a delay in thinking and speech in which the patient has difficulty conceiving or transferring the next logical thought into words.

In all cases, the symptom had not been present before treatment with the tricyclic and disappeared promptly within four days of a decrease in the tricyclic dosage. The authors believe that the symptom reflects an untoward reaction to the tricyclic. (HSRI)

10 refs

KEYWORDS: Antidepressants: amitriptyline, imipramine. Antidepressants. Experimentation: Chronic Dosage Study. Experimentation: Dose-Effect Study. Psychological Testing.

UM-79-D1125

BENZODIAZEPINES IN THE TREATMENT OF AGGRESSIVE PATIENTS, J.R. Lion, Journal of Clinical Psychiatry, v40 n2 p70-71 (Feb 1979)

A double-blind, controlled clinical trial of chlordiazepoxide, oxazepam, and placebo was conducted in sixty-five outpatients aged 20 to 58 with past histories of temper outbursts, assaultive behavior, and impulsiveness associated with anxiety, irritability, and hostility. Patients were randomly assigned to one of three treatments: (1) 240 mg oxazepam; (2) 200 mg chlordiazepoxide; and (3) placebo. A psychiatric evaluation and psychological data were obtained at baseline and after two and four weeks. Tests included were the Scheir Cattell Anxiety Scale, the Buss-Durkee Hostility Scale, and the Physician's Target Symptom Scale.

Of those tests showing statistically significant results, there was a tendency for oxazepam to be somewhat more effective in the reduction of anxiety than chlordiazepoxide. Oxazepam was also superior to the latter on one subscale of tests used to measure hostility. No paradoxical rage responses were noted. (JAM)

11 refs

KEYWORDS: Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. oxazepam. Clinical Study. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing.

UM-77-D1126

PSYCHOLOGIC AND NEUROENDOCRINE RESPONSE TO METHYLPHENIDATE, W. A. Brown, Archives of General Psychiatry, v34 n9 p1103-8 (Sep 1977)

Presented here is a strategy for examining the interface between neurochemical activity, psychological state, and neuroendocrine regulation. The value of neuroendocrine techniques for providing information regarding the pathophysiology of psychotic disorders is largely dependent on clarification of the relationships among psychologic state, neural activity, and neuroendocrine regulation.

Psychologic state, serum growth hormone (GH), and cortisol were monitored following administration of methylphenidate hydrochloride, a drug that appears to preferentially affect central dopamine regulation. Subjects were seventeen healthy males, aged 21 to 37 years, and were randomly assigned to one of three drug groups on a double-blind

basis: (1) 10 mg methylphenidate hydrochloride; (2) 20 mg methylphenidate hydrochloride; and (3) placebo.

While individuals varied in both their endocrine and psychologic responses to methylphenidate, the general effects were GH elevation, euphoria, and activation with elation, the most pronounced psychologic effect. Subjects who showed GH elevation became elated while those who did not show a GH response did not become elated. The author concludes that elation and GH release following administration of methylphenidate may be mediated by the same neurochemical events. The data collected in this study suggest an approach through which the neuroendocrine system may provide information regarding neurophysiologic processes relative to pathologic and normative changes in the psychologic state. (JAM)

23 refs

KEYWORDS: Stimulants: methylphenidate. Experimentation: Dose-Effect Study. Pharmacokinetics: Acute Dose. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1127

ARE PROPHYLACTIC ANTIPARKINSON DRUGS NECESSARY? A. Rifkin; F. Quitkin; J. Kane; F.Struve; D.F. Klein, Archives of General Psychiatry, v 35 n4 p483-9 (Apr 1978)

This article reports on a placebo-controlled, double-blind study of adjunctive procyclidine in outpatient psychotics previously routinely treated with a combination of antipsychotic and antiparkinson (AP) medications for months--most for more than a year. Also offered is data focusing on the difficult problem of the differential diagnosis of akinesia.

Of fifty-five aftercare patients receiving long-term treatment with antipsychotic and antiparkinson drugs, thirty-seven were switched to placebo, and eighteen remained on a regimen of procyclidine hydrochloride. The dose of antipsychotic was kept constant.

After three weeks, extrapyramidal side effects (EPS) developed in 54% of the patients receiving placebo and in none of those receiving procyclidine ($P<.002$). Twenty-seven percent of the placebo group had EPS without akinesia, and in the same percentage akinesia developed ($P=.003$). It is believed the risk-benefit ratio favors the routine use of AP drugs for prophylaxis and maintenance so as to avoid misdiagnosing as psychopathology unspontaneity due to akinesia, and to reduce unreliable pill-taking due to EPS. (JAM)

23 refs

KEYWORDS: Anti-Parkinsonism Agents: procyclidine. Parasympatholytic (Cholinergic Blocking) Agents: procyclidine. Anti-Parkinsonism Agents. Experimentation: Chronic Dosage Study. Psychomotor Tests.

UM-76-D1128

RESIDUAL EFFECTS OF HYPNOTIC DRUGS: EVIDENCE FOR INDIVIDUAL DIFFERENCES ON VIGILANCE, A.W. Peck; R. Adams; C. Bye; R.T. Wilkinson, Psychopharmacology, v47 n2 p213-6 (1976)

The main purpose of this study was to examine the residual effects of butobarbitone and nitrazepam using the Wilkinson Vigilance Test (1970), a test which has been shown to be a particularly sensitive indicator of impaired behavioral function due to disturbed sleep.

Nine healthy female and three healthy male volunteers aged 21 to 44 years were given butobarbitone (100 and 200 mg), nitrazepam (5 and 10 mg), and two lactose dummy treatments at 23.00 hours at weekly intervals over six weeks according to a balanced design and using a double-blind procedure. Performance was studied between 09.00 hours and 17.00 hours the following day.

Significant ($P<0.05$) impairment of tapping rate and digit symbol substitution occurred. No significant differences occurred between performance after active drug and dummy in auditory vigilance or subjective effects. Examination of individual differences in the response of subjects to the four hypnotic drug treatments, compared with their responses after dummy, indicated that the subjects could be divided into two groups. One group consistently rated themselves as more alert after hypnotics and their vigilance performance improved. The other group consistently was more drowsy after hypnotics and had impaired performance. It is suggested that the improvement in the first group

resulted from improved sleep quality sufficient to counteract the residual effect of the hypnotic, whereas the second group merely showed the residual effects of the drugs. Further research concerning individual differences in residual effects of hypnotics is needed. (JAM)

18 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): nitrazepam. Barbiturates: butabarbital. Nonbarbiturates: nitrazepam. Sedatives and Hypnotic Agents. Experimentation: Acute Dosage Study. Experimentation: Dose-Effect Study. Other Factors Influencing Drug Effects. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-76-D1129

DRUG-RELATED TEST PATTERNS OF DEPRESSED PATIENTS, J.F. Legg; M.P. Stiff, Psychopharmacology, v50 n2 p205-10 (1976)

This study investigates that aspect involving specific effects that tends to differentiate one particular drug from another. It compares the effects of an antidepressant (imipramine), a phenothiazine (chlorpromazine), and placebo on the performance of depressed patients on a wide range of psychological tests.

Several types of drugs reportedly have been useful in treating depressions but the specific effect of these drugs on functioning remain unclear. Forty-nine hospitalized depressed patients between the ages of 16 and 70 years were randomly assigned on a double-blind basis to an imipramine (300 mg), chlorpromazine (600 mg), or placebo group. Psychological test performance was compared after three weeks of in-hospital drug treatment. Some of the tests used were information processing, digit span, picture completion, and the Benton Visual Retention Test.

Neither drug produced impairment on most measures of intellectual functioning. The results suggest that imipramine may impair ability to assimilate and retain information, and that chlorpromazine may impair sustained attention. The differential effects are discussed in relation to symptoms and to hypotheses about the relationships between arousal and chlorpromazine and between retardation and imipramine in the treatment of depression. (JAM)

29 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Antidepressants: imipramine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Clinical Study. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing.

UM-78-D1130

PRL-8-53: ENHANCED LEARNING AND SUBSEQUENT RETENTION IN HUMANS AS A RESULT OF LOW ORAL DOSES OF NEW PSYCHOTROPIC AGENT, N.R. Hansl; B.T. Mead, Psychopharmacology, v56 n3 p249-53 (1978)

The effect of 3-(2-benzylmethylaminoethyl) benzoic acid methyl ester hydrochloride (PRL-8-53) on learning and retention of verbal information on human subjects was investigated. Forty-seven normal healthy volunteers received either placebo or 4 mg PRL-53 two hours before testing. Using the serial anticipation testing under double-blind conditions, it was found that PRL-8-53 causes slight improvement of acquisition. Retention of verbal information was found improved to a statistically significant degree (most P values better than 0.01, some better than 0.001). No significant changes were found for either visual reaction time or motor control after drug when compared with placebo values. The authors conclude that this drug can promote an optimal balance of conductive systems in the central nervous system, and can possibly modulate the existing balance in a given individual. (JA)

20 refs

KEYWORDS: Other CNS Agents: 3-(2-benzylmethylaminoethyl) benzoic acid methyl ester hydrochloride (PRL-8-53). Experimentation: Acute Dosage Study. Psychological Testing. Psychomotor Tests.

UM-78-D1131

OPIATES, CATECHOLAMINES, BEHAVIOR, AND MOOD, R.E. Meyer; J.J. Schildkraut; S.M. Mirin; P.J. Orsulak; M. Randall; M. McDougle; P.A. Platz; E. Grab; T. Babor, Psychopharmacology, v56 n3 p327-33 (1978)

Indirect evidence has linked opioid reinforcement with changes in noradrenergic metabolism secondary to drug administration. Methodological precedents for biobehavioral correlations in depressive illness have suggested an important association between changes in mood and biogenic amine excretion patterns in the urines of patients during depression and recovery. This paper presents preliminary data on the possible relationship between observed changes in catecholamine excretion and the changes in behavior, mood, psychiatric status, and cardiorespiratory physiology secondary to heroin administration and methadone-assisted withdrawal. This study focuses on the urinary excretion of MHPG, since an appreciable fraction of this metabolite is probably derived from norepinephrine originating in the brain.

The study showed that subjective changes in mood associated with heroin use, the decrease in respiratory rate, and the behavioral and mental status effects associated with opiate intoxication were observed only in the individuals whose MHPG excretion increased during the period of opiate administration. (JA)

32 refs

KEYWORDS: Opiates and Related Agents: heroin. Opiates and Related Agents. Drug Concentrations in Body Fluids: Chronic Dose Study. Physiological Testing. Psychological Testing.

UM-78-D1132

COMPARISON STUDIES OF CHLORAZEPATE ADMINISTERED AS A DIVIDED DAILY DOSE AND AS A SINGLE DOSE AT NIGHT, I. Dureman; H. Malmgren; B. Norrman, Psychopharmacology, v57 n2 p123-6 (1978)

The residual effects of dipotassium chlorazepate administered as either a single daily dose of 20 mg at bedtime or a divided daily dose (5+5+10 mg) were studied in a placebo-controlled, double-blind trial comprising twelve male outpatients aged 19 to 30 years. About eight hours after bedtime administration, the following tests were used to determine changes in perceptual wakefulness, performance ability, fine motor skills, and coordination: critical flicker fusion test, car driving in a simulator, and the "bead and needle" tests. In addition, the patients underwent a clinical assessment and also filled out a self-rating scale for judging factors related to the tests.

No significant differences were found between the dosage schedules or between the active medication and the placebo. The clinical results were not dependent on the dosage schedule. Furthermore, results of the study indicate that dipotassium chlorazepate elicits only nominal perceptual hangover effects. (JAM)

9 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): clorazepate. Clinical Study. Driving Simulator. Experimentation: Chronic Dosage Study. Experimentation: Dose-Effect Study. Psychomotor Tests.

UM-78-D1133

PARADOXICAL EFFECTS IN SLEEP AND PERFORMANCE OF TWO DOSES OF CHLORPROMAZINE, L. Hartley; J. Couper-Smartt, Psychopharmacology, v58 n2 p201-5 (1978)

This report concerns the effects of the phenothiazine chlorpromazine on rapid eye movement (REM) sleep and some measures of performance in man. The experiment, which consisted of giving placebo, 25 mg chlorpromazine, and 75 mg chlorpromazine on three separate occasions to twenty-four young male subjects, attempted first to confirm the paradoxical effect of low and high doses of chlorpromazine on REM duration and to relate this to the period of the REM/non-REM cycle, and second to discover if there was a dose-related difference in behavior during wakefulness. Three behavioral tests measured waking efficiency in perceptual input, response selection, and cognitive speed in human volunteers.

Time of administration of the drug, a potentially important variable in EEG response, was controlled.

The REM sleep of two groups of subjects was recorded. One group of subjects received the drug in the morning fourteen hours before they slept, and the second group received the drug only one hour before they retired.

The low dose of drug shortened the REM|non-REM cycle length in comparison to the high dose, and placebo values were intermediate. In performance tests, visual integration time was impaired by the high dose of the drug. Logical reasoning was slowed by the high dose of the drug in comparison to the low dose, while placebo values intermediate between the two. The authors conclude that a low dose of chlorpromazine has an effect more similar to that of a stimulant than to that of a high dose of chlorpromazine, and is thus more likely to reflect heightened arousal than tranquilization. (HSRI)

15 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Experimentation: Acute Dosage Study. Experimentation: Dose-Effect Study. Physiological Testing. Psychological Testing.

UM-78-D1134

PROPRANOLOL IN EXPERIMENTALLY INDUCED STRESS, S. Nakano; H.K. Gillespie; L.E. Hollister, Psychopharmacology, v59 n3 p279-84 (1978)

The aim of the present study was to determine the effect of d,l-propranolol on the central manifestations of anxiety using subjects with high trait anxiety in an experimentally induced stress situation. The beta-adrenergic receptor-blocking drug d,l-propranolol was compared with placebo for relief of experimentally induced anxiety in twenty-four male subjects aged 18 to 30 years with high levels of trait anxiety. Stress was induced experimentally by the mirror drawing test and by the Stroop Color-Word Test.

Single 40 mg doses of propranolol significantly slowed the heart rate, suggesting a satisfactory pharmacologic effect of the drug. The treatment was not superior to placebo, however, in any other measure, including relief of anxiety. The experimental model used had previously clearly demonstrated an antianxiety effect of single 5 mg doses of diazepam. Propranolol at the dose used had little effect on psychic anxiety as determined by this model. The authors conclude the effects of propranolol are primarily on the somatic rather than the psychic aspects of anxiety. This limited action may make the drug less acceptable as an antianxiety agent than the benzodiazepines. (JAM)

41 refs

KEYWORDS: Anti-Anginal Agents: propranolol. Anti-Arrhythmia Agents: propranolol. Hypotensive (Antihypertensive) Agents: propranolol. Experimentation: Acute Dosage Study. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-74-D1135

CARDIOVASCULAR VARIABLES, SKIN CONDUCTANCE AND TIME ESTIMATION: CHANGES AFTER THE ADMINISTRATION OF SMALL DOSES OF NICOTINE, C. Ague, Psychopharmacologia, v37 n2 p109-25 (1974)

This experiment attempted to study various psychophysiological and biochemical parameters after the smoking of tobacco cigarettes with varying nicotine contents. Three tobacco cigarettes with known content of nicotine and one lettuce-leaf cigarette were smoked by twenty-four male habitual smokers aged 17 to 24 at different times of day and at fixed rates of smoking. Changes in various psychophysiological parameters were automatically recorded during the sixty minutes following smoking.

These parameters included heart rate, skin temperature, forearm blood flow, and skin conductance. Subjects were also tested for time estimation ability.

Heart rate and forearm blood flow increases were found to be dose dependent, the latter occurring only after smoking at the fast rate. Their duration was simultaneous to the presence of active nicotine in the organism. Skin vasoconstriction, as measured by decreases in temperature, showed itself more reactive to environmental stimuli than to drug effect. Significant increases in skin conductance levels lasting throughout the experimental session occurred immediately after smoking, although they were not related to drug effects. Diphasic effects of nicotine were, however, obtained with the two largest doses, at different times of day. This finding is discussed in relation to possible "unspecific" nicotine effects upon a preexisting level of "activation". Nicotine did not influence subjective time estimates. However, a specific pattern of

responses occurred. This is discussed in terms of "disruption" of the timing task and a gradual reorganization towards presmoking estimates. The value of psychophysiological indices in relation to drugs of habitual use is questioned. (JAM)

32 refs

KEYWORDS: Ganglionic Blocking and Stimulating Agents: nicotine. Stimulants: nicotine. Experimentation: Dose-Effect Study. Physiological Testing. Psychological Testing.

UM-78-D1136

COMBINED EFFECTS OF FENMETOZOLE AND ETHANOL, L.C. Griffis; T.P. Bright; B.J. Cerimele; R.B. Forney, Clinical Pharmacology and Therapeutics, v24 n3 p350-3 (1978)

The purpose of this study was to investigate the effect of fenmetozole alone and in combination with ethanol on human performance and subjective symptoms. Eight male subjects 22 to 25 years of age took 0 mg or 200 mg fenmetozole one hour before drinking a beverage containing 0 ml or 50 ml/70 kg ethanol. Tests designed to measure mental and motor performance were administered two hours after fenmetozole ingestion. The test battery included the following objective and subjective tests: (1) stability of stance as measured by the Wobble Board; (2) attentive motor performance as measured by a Pursuit Meter; (3) manual dexterity as measured by pegboard tests; (4) mental performance, measured by several reasoning tasks; and (5) subjects' subjective assessment of symptoms using the Modified Cornell Medical Index.

Fenmetozole alone impaired standing steadiness but improved mental performance in one test. Fenmetozole did not antagonize the decrement in performance induced by this amount of ethanol. In combination, the subjective symptoms caused by fenmetozole were additive with those of ethanol. However, their combination did not result in a greater decrement of performance than that caused by ethanol alone. (JAM)

12 refs

KEYWORDS: Other CNS Agents: fenmetozole. Experimentation: Acute Dosage Study. Experimentation: Study of Combined Effects of Drugs. Psychological Testing. Psychomotor Tests.

UM-77-D1137

EFFECTS OF TRITHIOZINE ON PSYCHOMOTOR SKILLS RELATED TO DRIVING: A COMPARISON WITH DIAZEPAM AND INTERACTIONS WITH ALCOHOL, M.J. Mattila; E. Palva; T. Seppala; I. Saario, Current Therapeutic Research, v22 n6 p875-84 (Dec 1977)

Effects of trithiozine, a new gastric antisecretory drug, on psychomotor skills related to driving were studied in paid healthy student volunteers. The effects of oral trithiozine (200 and 400 mg), alone and in combination with 0.5 g/kg of ethyl alcohol, were compared in two double-blind cross-over trials against oral diazepam (10 mg), alcohol (0.5 g/kg), and lactose placebo. Reactive and coordinative skills, attention, flicker fusion, proprioception, nystagmus, Maddox wing, and subjective estimation were assessed.

The study was conducted in two parts. In the first trial the acute effects of two doses of trithiozine were measured and compared with the effects of diazepam. In the second trial, the multiple-dose effects of trithiozine and also its interaction with alcohol were studied. The single-dose trial using four females and eight males aged 21 to 27 years revealed that neither trithiozine nor diazepam modified attention. Diazepam impaired reactive skills whereas coordinative skills remained largely influenced by diazepam or trithiozine. Both trithiozine and diazepam impaired leg proprioception.

In the multiple-dose trial with one female and eleven males aged 19 to 24 years, trithiozine (400 mg) alone did not differ from placebo as to its effects on coordinative skills, while both diazepam alone and trithiozine (400 mg) in combination with alcohol impaired coordination somewhat more than alcohol did. Both diazepam and, to a lesser extent, trithiozine (400 mg) impaired flicker fusion. Alcohol antagonized rather than enhanced this effect of trithiozine (400 mg). Some acute tolerance developed to the diazepam action on coordinative skills but not to its action on flicker fusion. None of the drugs impaired manual proprioception. A slight impairment of foot proprioception by trithiozine (400 mg) was, strangely enough, antagonized rather than enhanced by alcohol.

It is concluded that trithiozine, having mild central sedative effects usually equal to or lower than those of 10 mg diazepam, could be a good and safe substitute for

combinations of anticholinergics and tranquilizers. At the doses employed in this study, trithiozine alone or in combination with low doses of alcohol cannot be considered dangerous for traffic and occupational life. (JAM)

21 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Unclassified Agents: trithiozine. Experimentation: Acute Dosage Study. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests. Tests of Sensory Function.

UM-78-D1138

THE ASSOCIATION BETWEEN CHRONIC CANNABIS USE AND COGNITIVE FUNCTIONS, R. Ray; G.G. Prabhu; D. Mohan; L.M. Nath; J.S. Neki, Drug and Alcohol Dependence, v3 n5 p365-8 (1978)

The cognitive functions of thirty chronic cannabis users were compared with those of fifty nonusers from the same population.

The following tests were used: (1) digits backwards test; (2) serial addition of 3's; (3) serial subtraction of 3s; (4) color cancellation test; (4) visuo-motor coordination tests; and (5) tests of memory functions. The tests did not reveal any significant differences between the two groups in respect to memory, attention, concentration, and percepto-motor functions. (JAM)

21 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Experimentation: Chronic Dosage Study. Psychological Testing.

UM-76-D1139

EEG AND TASK PERFORMANCE AFTER $ACTH_{4-10}$ IN MAN, W.G. Sannita; P. Irwin; M. Fink, Neuropsychobiology, v2 n5-6 p283-90 (1976)

Effects of the heptapeptide $ACTH_{4-10}$ (Org OI-63) on EEG, memory, and behavior were examined in twelve normal male volunteers under thirty years of age. An intravenous dose of 60 mg was compared to placebo in a latin square design in order to see whether the $ACTH_{4-10}$ could enhance sustained attention and improve learning ability. At 60 and 120 minutes after drug or placebo administration a battery of tests was administered: backward digit span; digit symbol substitution; first and last name test; and the Benton visual retention test. EEG was recorded for two hours after administration of $ACTH_{4-10}$ or placebo and was quantified by power spectral density analysis. Drug differences were tested by analysis of variance and coordinance.

No statistical drug effect was seen on the EEG or behavioral measures. Of the psychological tests, only the digit span test showed a decrease in number of errors with $ACTH_{4-10}$ ($P \leq 0.05$). These results are consistent with previous studies and suggest that an intravenous dose of $ACTH_{4-10}$ has a limited effect on the brain functions tested. (JAM)

17 refs

KEYWORDS: Pituitary: $ACTH_{4-10}$ (Org OI-63). Experimentation: Acute Dosage Study. Physiological Testing. Psychological Testing.

UM-78-D1140

SOME PSYCHOLOGICAL CORRELATES OF LONG-TERM HEAVY CANNABIS USERS, S.S. Mendhiratta; N.N. Wig; S.K. Verma, British Journal of Psychiatry, v132 p482-6 (1978)

Fifty persons who had all been heavy cannabis users for a several years were given psychological tests measuring psychomotor, perceptual, and other variables. Half of these persons were "Charas" smokers, half "Bhang" drinkers. The duration of cannabis use ranged from four to ten years, with an average daily dose of 150 mg tetrahydrocannabinol. A matched control group of twenty-five persons was given the same tests.

These tests included digit span tests, a recognition test, a pencil tapping test, a speed and accuracy test, a time perception test, reaction time tests, the Bender Visuo-

Motor Gestalt test, and a size estimation test. Compared with the control group, the cannabis users were found to react more slowly, to be poorer in concentration and time estimation, to have higher neuroticism, and to have greater perceptuo-motor disturbance. The Charas smokers were the poorest performers and also showed poor memory, lowered psychomotor activity, and poor size estimation. (JAM)

11 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Experimentation: Chronic Dosage Study. Psychological Testing. Psychomotor Tests.

UM-77-D1141

THE PSYCHOTROPIC EFFECTS OF ATENOLOL IN NORMAL SUBJECTS: PRELIMINARY FINDINGS, T.A. Betts; A. Blake, Postgraduate Medical Journal, v53 supp 3 p151-6 (1977)

This study attempted to assess both objectively and subjectively the effects of atenolol on mood, arousal, and anxiety in comparison to the effects of placebo and the conventional tranquilizing drug chlordiazepoxide. Thirty-six normal female medical students were randomly assigned to three drug groups: (1) atenolol (50 mg t.i.d.); (2) chlordiazepoxide (10 mg t.i.d.); and (3) placebo (one capsule t.i.d.). Subjects were tested before drug administration and two hours after the final (seventh) dose with a visual analogue scale and a kinetic visual acuity test. Blood pressure and heart rate were recorded. Each subject also underwent a five-minute videotaped interview concerning work, interests, family, and relationships.

Results showed that after seven doses, subjects in both the atenolol and chlordiazepoxide groups felt significantly less anxious; placebo had no such effect. Atenolol had no effect on measures of arousal, whereas chlordiazepoxide had an adverse effect on subjective feelings of arousal. After seven doses of active drugs there was little effect on subjective reports of mood. The interviewers' observations confirmed the results of the subjective assessments. Subjects who had taken the active drugs were rated as significantly calmer and less aggressive.

The authors conclude from the results of this study that atenolol makes normal subjects feel calmer (after a week) and increases feelings of well-being without producing any evidence of sedation. It has many of the beneficial effects of a conventional tranquilizer without any of the penalties. It is, therefore, of potential value for treatment of chronic anxiety. It is suggested that atenolol may be particularly suitable for the symptom-free hypertensive patient. Further studies should be undertaken into whether it has a central action in the nervous system and into its effects on clinically anxious patients. (HSRI)

11 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. Sympatholytic (Adrenergic Blocking) Agents: atenolol. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Physiological Testing. Self-Evaluation of Drug Effects by Subjects. Tests of Sensory Function.

UM-78-D1142

ESSAI DE TRAITMENT, DE L'AGITATION ET DE L'AGRESSIVITE DE L'OLIGOPHRENE PAR LE TIAPRIDE [THE TREATMENT WITH TIAPRIDE OF THE AGITATION AND AGGRESSIVITY OF OLIGOPHRENIC PATIENTS], Y. Garnier, Semaine des Hopitaux, v54 n37-40 p1149-50 (1978)

Tiapride, which is a medication for the treatment of agitation and psychomotor excitation, was studied in mentally retarded patients--nine severe and three moderate--suffering from bouts of agitation and excitation, aged eighteen to forty years.

The dosage was 400 mg daily by intramuscular injection in acute agitation (two cases), six tablets (600 mg) daily in moderately severe cases, and four tablets (400 mg) daily in milder cases (four).

Very good results were obtained in three patients and good results in six others, while no effect was noted in three patients. Tolerance was excellent in all cases.

The author concludes that tiapride can be used to fill the therapeutic gap that exists today in the treatment of the agitation and aggressivity of oligophrenia. (JAM)

4 refs French

KEYWORDS: Anti-Emetics: tiapride. Major Tranquilizers (Antipsychotics and Neuroleptics): tiapride. Experimentation: Chronic Dosage Study. Psychological Testing.

UM-77-D1143

PROPRANOLOL FOR THE CONTROL OF BELLIGERENT BEHAVIOR FOLLOWING ACUTE BRAIN DAMAGE. F.A. Elliott, Annals of Neurology, v1 n5 p489-91 (May 1977)

The belligerence of seven patients who had suffered an acute brain insult was effectively controlled by propranol in doses of 60 to 320 mg per day. Of the seven patients, three were treated in the acute stage--one after a stroke, one after a severe closed head injury, and one after a gunshot wound of the brain, respectively. A chronic postconcussion syndrome associated with chronic irritability was present in two, and two were not chronically irritable but suffered from intermittent attacks of explosive rage in response to minor irritations. In all instances the belligerent behavior was controlled without inducing general sedation. The fact that propranolol prevented angry, aggressive behavior implies that it has a direct action on the brain. In view of the side effects of propranolol, it must be used with caution in patients with cardiac failure, nonallergic bronchospasm, and brittle diabetes. (JAM)

10 refs

KEYWORDS: Anti-Anginal Agents: propranolol. Anti-Arrhythmia Agents: propranolol. Hypotensive (Antihypertensive) Agents: propranolol. Clinical Study. Experimentation: Chronic Dosage Study. Psychological Testing.

UM-77-D1144

EEG PROFILE AND BEHAVIORAL CHANGES AFTER A SINGLE DOSE OF CLOZAPINE IN NORMALS AND SCHIZOPHRENICS, J. Roubicek; I. Major, Biological Psychiatry, v12 n5 p613-33 (1977)

Clozapine, a powerful neuroleptic with unique clinical efficacy (and without parkinsonic side effects), has been shown to have an unusual EEG profile. The EEG changes after clozapine, especially when instrumentally quantified, demonstrate the predictive value of EEG. The similarities of the EEG profile of clozapine with the profile of thymoleptic compounds indicate its possible thymoleptic effect. This has proven to be the case with therapeutic studies in depression. The EEG profile of clozapine in volunteers is similar to the EEG profile in schizophrenics (with appropriately higher doses). Instrumental quantification performed with spectral and iterative interval analysis is described to show the advantages of each method and also the complimentary value of both of them. (JAM)

20 refs

KEYWORDS: Major Tranquilizers (Antipsychotics and Neuroleptics): clozapine. Review.

UM-78-D1145

DEXTROAMPHETAMINE: COGNITIVE AND BEHAVIORAL EFFECTS IN NORMAL PREPUBERTAL BOYS, J.L. Rapoport; M.S. Buchsbaum; T.P. Zahn; H. Weingartner; C. Ludlow; E.J. Mikkelsen, Science, v199 p560-3 (3 Feb 1978)

The behavioral, cognitive, and electrophysiological effects of a single dose of dextroamphetamine (0.5 mg per kg of body weight) or placebo was examined in fourteen normal prepuberta1 boys (mean age, ten years, eleven months) in a double-blind study. When amphetamine was given, the group showed a marked decrease in motor activity and reaction time and improved performance on cognitive tests. The similarity of the response observed in normal children to that reported in children with "hyperactivity" or minimal brain dysfunction casts doubt on pathophysiological models of minimal brain dysfunction which assume that children with this syndrome have a clinically specific or "paradoxical" response to stimulants. (JAM)

23 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Stimulants: dextroamphetamine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Acute Dosage Study. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1146

THE BEHAVIORAL TOXICOLOGY OF METALS, B. Weiss, Federation Proceedings, v37 n1 p22-7 (Jan 1978)

Many metals express their toxic actions through behavioral disturbances. Such disturbances most often reflect impairment of central nervous system function, but also may arise from deleterious effects on other systems. Numerous factors influence behavioral toxicity. Uptake into brain obviously is important; the chemical form of the metal (e.g., inorganic versus organic) and route of exposure are key determinants of brain penetration. Species differences in toxicity may arise from differences in kinetics (e.g., blood-brain ratio) and affinity to target brain structures. Developmental stage is still another crucial variable, but the young organism is not necessarily the most susceptible, and nutritional considerations compound the standard paradigms. Furthermore, parametric variations of behavioral functions can no more be ignored than dose-effect functions, a principle exemplified in research on methylmercury. Unwarranted loyalties to traditional psychological tests may be one source of the current dispute about safe levels of lead simply because parametric variations of clearly specified functions are beyond the scope of such instruments. (JAM)

35 refs

KEYWORDS: Heavy Metals and Heavy Metal Antagonists. Review.

UM-77-D1147

ETHANOL AND DELTA-9-TETRAHYDROCANNABINOL: INTERACTIVE EFFECTS ON HUMAN PERCEPTUAL, COGNITIVE AND MOTOR FUNCTIONS. II, G.B. Cheser; H.M. Franks; D.M. Jackson; G.A. Starmer, R.K.C. Teo, Medical Journal of Australia, v1 n14 p478-81 (1977)

Fifteen paid student volunteers aged 18 to 32 (ten male, five female) were used in a double-blind crossover experiment to further investigate the effects of delta-9-tetrahydrocannabinol (THC) alone and in combination with ethanol on perceptual, cognitive, and motor functions. Both ethanol (0.54 g/kg) and THC (15 mg/70 kg) were given orally. Subjects were tested for standing steadiness, manual dexterity, simple auditory and visual reaction times, complex reaction time, perceptual speed, numerical reasoning, and various parameters measured by the Vienna Determination Apparatus.

Ethanol was not very effective in influencing performance at the dose given, but this dose of THC produced marked decrements, predominantly in the latter part of the experiment (after 100 minutes postdrug). When they were given together, an early additive effect was apparent, but later, there was a suggestion of antagonism in that subjects who received the drug combination performed better than those who were given THC alone. It is concluded that the interaction between THC and ethanol is very complex and warrants further research. (JAM)

13 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Acute Dosage Study. Experimentation: Study of Combined Effects of Drugs. Psychological Testing. Psychomotor Tests.

UM-78-D1148

DER EINFLUSS VON TRAMADOL AUF DIE PHYSISCHE UND DIE PSYCHOMOTORISCHE LEISTUNGSFAHIGKEIT DES MENSCHEN [THE EFFECT OF TRAMADOL ON PSYCHIC AND PSYCHOMOTOR PERFORMANCE IN MAN], W. Muller-Limmroth; H. Krueger, Arzneimittel-Forschung, v 28 n1A p179-80 (1978)

This paper discusses the effect of tramadol on psychic and psychomotor performance in man. Two major conclusions were drawn: (1) 1-(methylphenyl)-2-(dimethylaminoethyl)-cyclohexan-1-ol [tramadol; Tramal(R) (75 mg)] did not affect the physical working capacity as measured by means of bicycle ergometer in healthy volunteers. (2) Tramadol also had no effect on psychomotor performance in the eye-hand coordination test. (JAM)

4 refs German

KEYWORDS: Analgesics and Antipyretics: tramadol. Experimentation: Acute Dosage Study. Psychomotor Tests.

UM-79-D1149

INCIDENCE OF MARIJUANA IN A CALIFORNIA IMPAIRED DRIVER POPULATION, V. Reeve (Jul 1979)

This report summarizes information arising from an Office of Traffic Safety funded project that examined the forensic blood samples of a randomly selected California impaired driving population for the presence of marijuana. This impaired driving population consisted of 1,792 subjects whose blood samples were submitted by the California Highway Patrol to thirteen Department of Justice criminalistics laboratories.

A specific, sensitive, and inexpensive radioimmunoassay was used to analyze hemolyzed blood samples of drivers for delta-9-THC. Correlations of a number of variables such as age, sex, and geography with the use of marijuana were also examined.

The research yielded significant information regarding the use of marijuana by California impaired drivers. There was a 16% overall incidence of delta-9-THC in the blood of the sampled impaired driving population. Where no alcohol was present in the blood samples (185 of the total 1,792 samples), the incidence of delta-9-THC rose to 24% in that particular subpopulation. The study indicated that marijuana use widely crosses age brackets. It was confirmed by controlled delta-9-THC administration to volunteer subjects that the detectable presence of delta-9-THC is associated with significant driving impairment.

The author concludes that the 16% incidence of delta-9-THC in the impaired driving population is a conservative figure, due to the fact that delta-9-THC rapidly drops below detectable limits in the blood. Consequently only high dosages were detected in this study. He recommends legislation giving the arresting officer authority to give the suspect a breath test. When no alcohol is present, or with low legal levels of alcohol, the arrested person should be required to provide a blood sample. He also recommends the establishment of forensic programs for the detection and analysis of marijuana. (AAM)

State of California Department of Justice;

143 pages 15 refs

National Highway Traffic Safety Administration contract OTS 087705

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Nonbarbiturates: ethanol (ethyl alcohol)*. Epidemiologic Research: Drug Concentrations in Body Fluids. Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-77-D1150

L'INFLUENCE DES MEDICAMENTS SUR LA CONDUITE AUTOMOBILE [INFLUENCE OF MEDICATIONS (DRUGS) ON AUTOMOBILE DRIVING], P.H. Muller, Annales de Medicine des Accidents et du Traffic, n13-14 p41-4 (1977)

This paper reviews several aspects of the drug and driving problem. There is no doubt that this problem exists when one considers the number of people who drive and the large percentage of those who are under medication. The author begins his discussion by summarizing the qualities necessary for safe driving. These qualities include vigilance, alertness, and good social interaction.

Also discussed are medications which may have an effect on driving. At this point it is difficult to determine how much drug use impairs driving since in one case a drug might have a therapeutic affect beneficial to safe driving while in another case the same drug might impair skills related to driving. This determination of whether the therapeutic benefit outweighs the impairment must be made for both psychotropic and nonpsychotropic drugs.

The review concludes with a study of drug interactions, particularly those involving alcohol. (HSRI)

0 refs French

KEYWORDS: Review: Drugs and Highway Safety.

UM-74-D1151

PLACE DU SULPIRIDE EN PSYCHOPATHOLOGIE COURANTE [PLACE OF SULPIRIDE IN ROUTINE PSYCHOPATHOLOGY], M.C. Largeteau, De Medicine et de Chirurgie Pratiques, v 145 n6 p104-18 (1974)

This paper discusses the use of sulpiride in psychopathology. In contrast to many psychotropic medications, sulpiride does not affect vigilance and other driving-related abilities. Therefore it is a potentially valuable drug.

The action of sulpiride was studied in forty-nine women aged sixteen to seventy-seven, thirty-four men aged eighteen to seventy-two, and four children, all of whom were being treated with sulpiride. In sixty-five percent of these cases the dosage was 150 mg spread out over a period of five to thirty days. In all of the patients sulpiride significantly improved health without adverse side affects. The author concludes that greater use should be made of sulpiride in situations indicating its use. (HSRI)

0 refs French

KEYWORDS: Major Tranquilizers (Antipsychotics and Neuroleptics): sulpiride. Experimentation: Chronic Dosage Study.

UM-78-D1152

A STUDY OF THE EFFECTS OF GONADOTROPIN-RELEASING HORMONE ON HUMAN MOOD AND BEHAVIOR, B.C. McAdoo; C.H. Doering; H.C. Kraemer; N. Dessert; H.K.H. Brodie; D.A. Hamburg, Psychosomatic Medicine, v40 n3 p199-209 (1978)

This study attempts to identify behaviors, moods, and various psychological parameters that might be affected by the administration of gonadotropin-releasing hormone (GnRH).

GnRH in doses up to 500 mg was administered to twelve healthy male volunteers. Luteinizing hormone and testosterone levels increased subsequent to GnRH administration. No immediate effects of GnRH on mood and behavior were noted, though an increase in alertness, a decrease in anxiety and fatigue, and an increased speed of performance on automatized motor tasks were noted several hours after GnRH administration. The authors conclude that the trends seen in this laboratory environment suggest that GnRH administration does have some subtle effects. Longer term administration of the hormone in a more natural setting might well unmask these effects. (JAM)

34 refs

KEYWORDS: Androgens: testosterone*. Pituitary: luteinizing hormone (LH)*. Drug Concentrations in Body Fluids: Chronic Dose Study. Experimentation: Dose-Effect Study. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1153

EFFET D'UN PLACEBO ET DE FAIBLES DOSES D'UN BETA INHIBITEUR (OXPRENOLOL)ET D'ALCOOL ETHYLIQUE, SUR LA PRECISION DU TIR SPORTIF AU PISTULET [EFFECT OF A PLACEBO AND OF SMALL DOSES OF OXPRENOLOL AND ALCOHOL ON THE PRECISION OF PISTOL SHOOTING], J.J. S'Jongers; P. Willain; J. Sierakowski; P. Vogelaere; G. Van Vlaenderen, M. DeRudder, Bruxelles-Medical, v58 n8 p395-9 (Aug 1978)

This study compares the effects of placebo, a low dose of alcohol (30 microliters), and oxprenolol (40 micrograms) on accuracy as measured by a pistol shooting test. Results of the test indicated that all three treatments enhanced significantly the precision of pistol shooting. This improvement was about equal for all treatments, including placebo. The authors conclude, therefore, that the improvement in precision was probably due to the placebo effect rather than to the individual effects of the drugs.

Literature concerning the effects of oxprenolol is also discussed, particularly the literature illustrating the enhancing effects of oxprenolol on psychomotor performance even in small doses. (HSRI)

24 refs French

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Vasodilating Agents: oxprenolol. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Psychomotor Tests.

UM-77-D1154

A REPEATED DOSE COMPARISON OF DICHLORALPHENAZONE, FLUNITRAZEPAM AND AMYLOBARBITONE SODIUM ON SOME ASPECTS OF SLEEP AND EARLY MORNING BEHAVIOR IN NORMAL SUBJECTS, I. Hindmarch; A.C. Parrott; L. Arenillas, British Journal of Clinical Pharmacology, v4 n2 p229-33 (Apr 1977)

Seven normal subjects (four female, three male aged 18 to 27 years) were given three different hypnotics in order to investigate their effects on sleep. The following drug treatments were given double-blind: flunitrazepam (1 mg); amylobarbitone sodium (100 mg); and dichloralphenazone (1300 mg) for four consecutive nights each.

All three substances resulted in improved subjective assessments of the ease of getting to sleep. Flunitrazepam was rated as better than either dichloralphenazone or amylobarbitone sodium in this respect. The perceived quality of induced sleep was not altered by any of the preparations. There was a disturbance of the subjective ratings of getting to sleep following cessation of treatment with dichloralphenazone, giving tentative support to the existence of a "rebound" effect. Dichloralphenazone produced an impairment in psychomotor performance as measured on a complex reaction time test following four night's medication with the drug. (JAM)

8 refs

KEYWORDS: Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-77-D1155

EFFECTS ON CAFFEINE AND CYCLIZINE ALONE AND IN COMBINATION ON HUMAN PERFORMANCE AND SUBJECTIVE RATINGS, M. Clubley; T. Henson; A.W. Peck; C. Riddington, British Journal of Clinical Pharmacology, v4 n5 p652 (1977)

Combined effects of caffeine, a stimulant, and cyclizine, known to produce drowsiness, are reported in this study. Two studies were performed, both on twelve volunteers. All treatments were administered in identical capsules under double-blind conditions. In Trial 1 the treatments were: caffeine (75, 150, and 300 mg); cyclizine (25 and 50 mg); and placebo. In Trial 2 they were: caffeine (100 mg); cyclizine (150 and 100 mg); caffeine (100 mg) plus 50 mg cyclizine; and caffeine (100 mg) plus 100 mg cyclizine. All doses of caffeine (75, 150, and 350 mg) improved auditory vigilance. In Trial 2 no treatment produced any changes in vigilance differing from lactose.

In conclusion, caffeine improved auditory vigilance, reaction time, and tapping rate, but cyclizine up to 100 mg produced no significant difference from lactose except reduced arithmetic skills at five hours. Cyclizine tended to impair performance, and differences between the two active drugs were frequent. Similar changes occurred in subjective ratios of alertness. Combination of the two drugs gave either intermediate values not differing from lactose, or values similar to caffeine given alone, but never similar to those of cyclizine. (HSRI)

4 refs

KEYWORDS: Anti-Emetics: cyclizine. Antihistamine Agents: cyclizine. Stimulants: caffeine. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-77-D1156

COMPARATIVE EFFECTS OF D-AMPHETAMINE, L-AMPHETAMINE, AND METHYLPHENIDATE ON MOOD IN MAN, R.C. Smith; J.M. Davis, Psychopharmacology, v53 n1 p1-12 (1977)

The comparative effects of d-amphetamine, l-amphetamine, and methylphenidate on mood and motor activity were assessed in sixteen normal subjects (twelve males and four females aged 21 to 35) using a double-blind, crossover, placebo-controlled design. Drug doses were the following: d-amphetamine (10 or 20 mg); l-amphetamine (10 or 20 mg); and methylphenidate (10 or 20 mg).

Within the dose range tested, the efficacy ratio of d-amphetamine: l-amphetamine was about 2:1. Graph-presentation of dose response scores indicated a relatively small difference in potency between the amphetamine isomers. Methylphenidate was intermediate in efficacy between d-amphetamine and l-amphetamine. The efficacy ratios for d-

amphetamine: l-amphetamine on increasing euphoric mood in man were similar to the previously reported ratios of these two isomers in inducing or exacerbating psychosis in humans. (JAM)

38 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. levamphetamine. Stimulants: dextroamphetamine. levamphetamine. methylphenidate. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-77-D1157

PRIMATE INFORMATION PROCESSING UNDER SODIUM PENTOBARBITAL AND CHLORPROMAZINE: DIFFERENTIAL DRUG EFFECTS WITH TACHISTOSCOPICALLY PRESENTED DISCRIMINATIVE STIMULI, R.T. Bartus; H.R. Johnson, Psychopharmacology, v53 n3 p249-54 (1977)

Sodium pentobarbital and chlorpromazine (CPZ) were evaluated for the degree to which they differentially reduce the speed or efficiency with which sensory information can be processed. Rhesus monkeys were tested under comparable doses of sodium pentobarbital and CPZ on a visual discrimination problem with varying durations of tachistoscopically presented stimulus information. When unlimited stimulus information was available, no effects of the two drugs were observed at the doses used, but as the duration of stimulus presentation was progressively decreased, the effect of sodium pentobarbital became more severe, whereas CPZ did not differ from the saline control at any presentation duration.

While previously published literature indicates that CPZ impairs performance by intermittently blocking sensory input or transmission, the present data provide the first direct behavioral confirmation that barbiturates impair performance by retarding the rate at which sensory stimuli can be processed and utilized. (JA)

29 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Barbiturates: pentobarbital. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Animal Research.

UM-78-D1158

A SURVEY STUDY OF THE USE OF ELECTROPUPILLOGRAM IN PREDICTING RESPONSE TO PSYCHOSTIMULANTS, V. Bhatara; L.E. Arnold; W. Knopp; D.J. Smeltzer, Psychopharmacology, v57 n2 p185-7 (1978)

To confirm the conclusions from a previous study supporting the usefulness of the electropupillogram in predicting clinical response, data from three separate studies with hyperkinetic and learning disabled children treated with stimulants were surveyed. Change in extent of pupillary contraction after a test dose of stimulant as measured by electropupillogram did not correlate significantly with actual clinical rating change (with one exception out of fourteen correlations calculated). These negative results are reported with a reservation regarding their validity because of technical difficulties in data collection. (JA)

11 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. levamphetamine. Stimulants: dextroamphetamine. levamphetamine. methylphenidate. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Physiological Testing.

UM-78-D1159

MARIJUANA, ALCOHOL, AND COMBINED DRUG EFFECTS ON THE TIME COURSE OF GLARE RECOVERY, A.J. Adams; B. Brown; G. Haegerstrom-Portnoy; M.C. Flom; R.T. Jones, Psychopharmacology, v56 p81-6 (1978)

This study attempted to determine whether marijuana retards glare recovery in dose-related fashion and whether glare recovery changes produced with a combined dose of alcohol and marijuana reflect a drug interaction. Ten male subjects (twenty to thirty-two years), all of whom were regular users of alcohol and marijuana, were given a placebo, 0.75 ml/kg of 95% ethanol, 8 or 15 mg of delta-9-THC, or 0.75 ml/kg of 95%

ethanol together with 15 mg of delta-9-THC in a double-blind, 5x5 Latin square experiment. Blood alcohol levels were measured and subjects were tested for glare recovery by assessment of contrast sensitivity 40, 120, and 300 minutes after administration of the drug treatment. Subjective ratings of level of intoxication were also ascertained.

Results of the tests showed that the time course of light adaptation after intense light exposure was significantly delayed by alcohol, marijuana, and the combined dose of alcohol and marijuana. The marijuana-induced delay in glare recovery was found to be dose related. Both alcohol and marijuana delayed recovery for at least two hours after drug ingestion. The combined alcohol and marijuana treatment produced little more than the effect produced by either drug alone, suggesting some antagonism between the drugs. This theory is supported by a significantly lower blood alcohol level for the alcohol dose when combined with marijuana than when taken alone. (HSRI)

11 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Nonbarbiturates: ethanol (ethyl alcohol)*. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Experimentation: Study of Combined Effects of Drugs. Self-Evaluation of Drug Effects by Subjects. Tests of Sensory Function.

UM-77-D1160

BEHAVIORAL TOXICITY AND EQUIVOCAL SUICIDE ASSOCIATED WITH CHLOROQUINE AND ITS DERIVATIVES, M.I. Good; R.I. Shader, American Journal of Psychiatry, v134 n7 p798-80 (Jul 1977)

Although the antimalarial agents chloroquine, hydroxychloroquine, and amodiaquine are widely used to treat a variety of medical conditions, their behavioral toxicity and lethality are not generally recognized. Therapeutic doses sometimes cause psychosis, delirium, personality change, and depression. Since moderately low overdoses of chloroquine can result in rapid death, such behavioral effects could lead to accidental or state-dependent overdosage and death.

It is recommended that the mental status of the patient be evaluated before administration of chloroquine and related drugs and periodically during their use, and that there be more detailed investigation of the nature and cause of antimalarial overdosage. (JAM)

61 refs

KEYWORDS: Analgesics and Antipyretics: hydroxychloroquine. Plasmodicides: amodiaquine. chloroquine. hydroxychloroquine. Review: Drug Effects.

UM-78-D1161

USEFULNESS OF LITHIUM FOR AGGRESSIVENESS [letter], J.P. Tupin, American Journal of Psychiatry, v135 n9 p1118 (Sep 1978)

Lithium has been found to be effective in preventing aggressive outbursts among several populations with a variety of disorders that cause aggression and violence.

This author suggests that there is a common underlying neuropsychological disturbance in all of these groups which is behaviorally manifested in the following ways: 1) extreme stimulus sensitivity; 2) the inability to reflect on the meaning or intent of the stimulus, i.e., the lack of reflective, introspective review to assess accidental or purposeful attack; and 3) maximal response--little capacity to modulate the expression of anger.

He suggests that these characteristics be investigated further in the way of being useful in identifying these individuals with explosive violence who might benefit from lithium. (HSRI)

3 refs

KEYWORDS: Antidepressants: lithium. Other CNS Agents: lithium. Review: Drug Effects.

UM-77-D1162

INFLUENCE OF MOBILETTEN(R) ON THE EFFECT OF ALCOHOL DRINKING IN MAN, R. Kraemer; H.J. Mallach; G. Raff; H. Schulz, International Journal of Clinical Pharmacology and Biopharmacy, v15 n7 p301-9 (1977)

This study attempted to determine the influence of Mobiletten(R), a drug being promoted as having the ability of decreasing the detrimental effects of alcohol, on the ethanol effect, especially on breath ethanol content. Fifteen healthy male subjects aged twenty to thirty-five were given an average of 180 mg of 32% ethanol or 20 g of Mobiletten(R) on several days in changing order, either separately or together. Blood samples were taken 15, 30, 45, 60, 90, 120, 180, 240, 300, and 360 minutes after consumption. The ethanol content of these samples was determined by gas chromatography. The urinal ethanol elimination of each subject was determined hourly, also by gas chromatography. Finally, the gross amount of ethanol content in the subjects' expired air was measured.

Results indicated that the maximal ethanol concentrations in blood were significantly decreased and delayed by Mobiletten(R) while ethanol elimination remained unchanged. Ingestion of Mobiletten(R) resulted in a remarkable decrease of the urine volume; however the quantitative determination of the ethanol content in the expired air was not significantly affected.

The authors conclude that the effects of Mobiletten(R) are limited to the resorption phase; that is, Mobiletten(R) does not influence ethanol metabolism but does delay ethanol resorption, therefore, using Mobiletten(R) as a "sobering method" is ineffective. (HSRI)

39 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Unclassified Agents: Mobiletten(R). Drug Concentration-Effect Study: Clinical Research. Drug Concentrations: Comparison of Body Fluids. Experimentation: Chronic Dosage Study. Experimentation: Study of Combined Effects of Drugs. Physiological Testing.

UM-77-D1163

PSYCHOTROPIC DRUGS: INFLUENCE ON RESPIRATORY FUNCTION, L. Casali; E. Pozzi; C. Rampulla; R. Serra, International Journal of Clinical Pharmacology and Biopharmacy, v15 n10 p480-4 (1977)

This study investigated in twenty-two normal subjects and twenty-two bronchopneumopathic patients the action of two anxiolytic drugs on ventilatory functions and on the associated respiratory function. The following treatments were administered to each patient: 50 mg trazodone; 10 mg diazepam; and 55 ml alcohol.

The analyses carried out before drug administration and one, two, and six hours later showed that while trazodone did not cause any important variation in the ventilatory parameters and oxygen uptake either in healthy subjects or in patients, the diazepam clearly reduced the ventilatory efficacy and oxygen uptake.

This behavior was quite evident at two hours after the administration of the drug while after six hours the parameters returned to the initial values. Simulated driving tests demonstrated that the second anxiolytic drug provoked a standard depression unevenly distributed like that obtained after the ingestion of a fixed dose of an alcoholic drink. The data from this study indicate that two drugs having the same anxiolytic properties such as diazepam and trazodone can induce quite different reactions on respiratory activities. (JA)

15 refs

KEYWORDS: Antidepressants: trazodone. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. trazodone. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Driving Simulator. Experimentation: Comparison of Different Drugs. Physiological Testing.

UM-73-D1164

A COMPARISON OF THE EFFECTS OF 1-BENZYLPIPERAZINE AND DEXAMPHETAMINE ON HUMAN PERFORMANCE TESTS, C. Bye; A.D. Munro-Faure; A.W. Peck; P.A. Young, European Journal of Clinical Pharmacology, v6 n3 p163-9 (1973)

The effects of dexamphetamine (1 mg to 7.5 mg) and 1-benzylpiperazine (20 mg to 100 mg) on performance tests and cardiovascular responses were measured in two groups of twelve normal subjects aged 21 to 47 years. Drugs and dummy control were administered orally under double-blind conditions at weekly intervals according to a balanced design. Drug effects were assessed by an addition test, a hand steadiness test, a tapping test, and an auditory vigilance test.

Significant ($p<0.05$) improvement occurred in the auditory vigilance test following both drugs, and this test was sufficiently sensitive to detect the changes produced by dexamphetamine (1 mg) at the time of peak drug action. Subjective effects were only detected by the subjects after dexamphetamine (7.5 mg) and 1-benzylpiperazine (100 mg). Significant changes attributable to drug treatment were not found in tests of short duration such as tapping rate, hand steadiness, and arithmetic. Both drugs produced significant increases in heart rate and systolic blood pressure. It is concluded that 1-benzylpiperazine has psychomotor stimulant activity similar to dexamphetamine and that this is most reliably detected by using a prolonged signal detection test. (JA)

16 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Stimulants: dextroamphetamine. 1-benzylpiperazine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests. Tests of Sensory Function.

UM-77-D1165

THE EFFECT OF DIPHENHYDRAMINE ALONE AND IN COMBINATION WITH ETHANOL ON HISTAMINE SKIN RESPONSE AND MENTAL PERFORMANCE, R. Baugh; R.T. Calvert, European Journal of Clinical Pharmacology, v12 p201-4 (1977)

The effects of diphenhydramine hydrochloride (DPHA) on histamine skin response and mental performance when taken alone and in combination with ethanol were investigated in a group of twelve male volunteers, aged 22 to 33. Each volunteer received one of the following treatments: 0.5 g/kg ethanol plus placebo; 0.5 g/kg ethanol plus 75 mg DPHA; or 75 mg DPHA plus placebo ethanol. The study used a double-blind, Latin square design. Treatments were at weekly intervals for three weeks.

Subjects were tested before treatment and 1, 2, 4, and 6.5 hours after drug administration for the following parameters: histamine skin response; serial seven subtraction; digit symbol substitution; and tracking ability.

Results of the testing indicated that a significant impairment of histamine skin response was caused by DPHA. This response was unaffected by ethanol. Ethanol improved performance with a tracking test compared with diphenhydramine alone; the effect was not potentiated by the combination. None of the treatments had a significant effect on the digit symbol substitution test. However, diphenhydramine impaired performance in the serial seven subtraction test, particularly when combined with alcohol.

The authors conclude that DPHA can cause impairment of mental performance, and that this impairment is potentiated by ethanol. Therefore people purchasing diphenhydramine for self-administration should be warned not only that the drug causes drowsiness, but also that the depressant action of the drug on mental performance may be enhanced when combined with alcohol. (HSRI)

5 refs

KEYWORDS: Antihistamine Agents: diphenhydramine. Nonbarbiturates: diphenhydramine. ethanol (ethyl alcohol). Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Physiological Testing. Psychological Testing.

UM-77-D1166

PEOPLE'S VIEWS ON MARIHUANA, DRUGS, AND DRIVING: A CHANGING SCENE, D.M. Grilly, Journal of Psychedelic Drugs, v9 n4 p311-16 (Oct-Dec 1977)

This article reports the results of two surveys of college students' views of the effects of marijuana and other drugs on driving skills. Students in a state-supported urban university in Ohio were asked to anonymously answer twenty-eight questions pertaining to their age, sex, drug and driving experiences, and their views of the effects of commonly used amounts of various drugs on their driving skills and other

people's driving skills. The first survey conducted in 1975 questioned 376 students, and 401 students were surveyed in 1977, approximately one year after Ohio decriminalized the possession of marijuana.

The results of these surveys indicate that people's perceptions about the effects of drugs on driving depend a great deal on whether they are talking about themselves or other people and, in the case of marijuana, how frequently they use it. The more frequently a person uses marijuana the less he or she tends to believe that marijuana may adversely affect driving.

One argument that is often made is that decriminalization of marijuana will lead to more frequent use and therefore higher accident rates. However, the present surveys do not support this argument because it appears that decriminalization, at least in Ohio, has not led to more frequent use of the drug. (HSRI)

18 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Epidemiology: Self-Reported Drug Use by Drivers.

NTSB-HAR-79-6

UM-79-D1167

HIGHWAY ACCIDENT REPORT--FORD COURIER PICKUP TRUCK FIXED OBJECT COLLISION PATUXENT ROAD NEAR CROFTON, MARYLAND APRIL 23, 1979, National Transportation Safety Board Highway Accident Report (Sep 1979)

Presented here is a report of a fatal accident in which ten out of the twelve passengers of a compact pickup truck were killed when the driver failed to negotiate a curve in the road while traveling between 64 and 78 mph. The National Transportation Safety Board concluded that the probable cause of this accident was high speed and reckless driving of the vehicle by a driver who was under the influence of marijuana and alcohol, since witnesses reported seeing the driver drink alcoholic beverages and smoke marijuana immediately prior to the accident. According to blood tests, the driver could have had a blood alcohol level as high as 0.135%. Contributing to the severe consequences of the accident was the presence of passengers in the open bed of the pickup truck, an area that offered no crash protection. (HSRI)

0 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Crash Investigation. Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-76-D1168

DRUG EFFECTS ON HEART RATE AND HEART VARIABILITY DURING A PROLONGED REACTION TASK, A.W.K. Gaillard; D.A. Trumbo, Ergonomics, v19 n5 p611-22 (1976)

The effects of an amphetamine and a barbiturate on heart rate were investigated during long-term performance and compared with effects of task difficulty. Sixteen male subjects aged 20 to 30 years were administered rectally the following treatments at weekly intervals with a different treatment at every session: (1) 20 mg phentermine; (2) 600 mg hexobarbital sodium; (3) a suppository placebo; and (4) a no-suppository control. One hour after treatment subjects began working for three hours on a serial reaction test, which included blocks with variable or constant interstimulus intervals (ISI).

Besides the interbeat interval (IBI), derived from the successive R-peaks of the ECG, the variability of IBI was scored in three ways. Each of these scores increased as a function of time-on-task, indicating a gradually decreasing activation level during the three-hour session.

Amphetamine had an activating effect, decreasing both IBI and ISI variability; the barbiturate effect on the other hand was paradoxical: Hexobarbital tended to increase IBI variability but to decrease IBI.

The IBI changes between constant and variable blocks were negligible after amphetamine, while these changes were pronounced after barbiturate treatment. IBI variability was reduced during blocks with variable ISI, where mental effort was assumed to be maximal. This reduction in variability was larger for amphetamine and tended to be smaller for barbiturate as compared to the placebo condition. The results of this study indicate that amphetamines seem to influence control and autonomic activation (as measured by the

heart rate) in the same direction, while barbiturates seem to have no direct effect on the heart rate. Several possible explanations for this are discussed. (JA)

16 refs

KEYWORDS: Anorectic (Appetite Control) Agents: phentermine. General Anesthetics: hexobarbital. Sympathomimetic (Adrenergic) Agents: phentermine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Physiological Testing.

UM-78-D1169

STIMULUS PROPERTIES OF INHALED SUBSTANCES, R.W. Wood, Environmental Health Perspectives, v26 p69-76 (Oct 1978)

This paper discusses techniques suitable for characterizing the behavioral significance of airborne contaminants as stimulus events that can control behavior.

Inhaled substances can modify behavior by their toxic action, or because they are discriminable events, or because they can support or suppress behavior. They can be used as discriminative stimuli at concentrations above the olfactory thresholds. Inhalants can also elicit unconditioned reflexes. As aversive stimuli, they can be studied in respondent conditioning experiments (e.g., conditioned suppression), in punishment paradigms, or as negative reinforcers in escape paradigms. Inhalants can also be positive reinforcers; their intoxicating properties have engendered patterns of chronic self-administration (solvent abuse). Such stimulus properties should be considered in industrial hygiene and environmental quality decisions. (JAM)

81 refs

KEYWORDS: Other Toxicants. Volatile Solvents. Review: Drug Effects.

UM-78-D1170

EXPOSURE TO XYLENE AND ETHYLBENZENE: III. EFFECTS ON CENTRAL NERVOUS FUNCTIONS, F. Gamberale; G. Annwall; M. Hultengren, Scandinavian Journal of Work Environment and Health, v4 n3 p204-11 (1978)

The effect of exposure to the solvent xylene on performance of tests of numerical ability, reaction time (simple and choice), short-term memory, and critical flicker fusion was studied in two separate laboratory series. In the first series, fifteen healthy male subjects aged 21 to 33 were studied individually on three separate occasions with exposure to 435 and 1,300 mg/m^3 xylene in inspired air and under control conditions. In a second series, eight of the subjects were exposed to 1,300 mg/m^3 xylene in inspired air. This exposure period began with thirty minutes of work on a bicycle ergometer and continued during the behavioral tests. The procedure was the same under control conditions. Each exposure period lasted seventy minutes. At certain times during exposure, samples of the subjects' alveolar air were collected.

Exposure to xylene did not cause any noticeable change in performance during the first laboratory series during which the subjects' total uptake of xylene was estimated to be on an average 180 and 540 mg respectively. In the second series, the physical work induced an increase in the total uptake up to an average of 1,200 mg. In this series of experiments clear evidence of performance decrement was observed in three of the performance tests. The results of these experiments support the argument for the urgent need for biological values in the evaluation of current-threshold limit values for solvents in inspiratory air. (JAM)

19 refs

KEYWORDS: Volatile Solvents: ethylbenzene. xylene. Experimentation: Dose-Effect Study. Psychological Testing. Psychomotor Tests. Tests of Sensory Function.

UM-78-D1171

NEUROPHYSIOLOGICAL EFFECTS OF LONG-TERM EXPOSURE TO A MIXTURE OF ORGANIC SOLVENTS, A.M. Seppalainen; K. Husman; C. Martenson, Scandinavian Journal of Work Environment and Health, v4 n4 p304-14 (1978)

Neurophysiological effects of long-term exposure to a mixture of organic solvents were studied among 102 car painters from twenty-seven car repair garages in Helsinki. The

reference group consisted of 102 age-matched railroad engineers from the Finnish State Railways. The mean age was thirty-five years and the exposure time ranged from one to forty years (mean 14.8).

According to measurements the mean concentration of the solvent mixture was relatively low in the garages, being only 31.8% of the Finnish threshold limit value (TLV). The range of separate components varied from 4 to 212% of their respective TLVs. The main components of about twenty organic solvents of the mixture were toluene, xylene, butyl acetate, and white spirit.

Electroencephalograms (EEGs) of all the 102 exposed and 102 nonexposed subjects were studied, but electroneuromyographic measurements were made of only 59 car painters and 53 referents with a similar age distribution. Motor (MCV and CVSF) and sensory conduction (SCV) velocities, as well as motor distal latencies, were recorded from nerves in the upper and lower extremities. Abnormal EEGs were encountered in 32 car painters and 37 referents. The frequency of abnormal EEGs was in both groups higher than expected on the basis of EEG literature (about 10%). Twenty-six car painters had a complex of four common symptoms of disturbances in the central nervous system: the same symptom complex was found in 12 engineers. Forty-six percent of the car painters with this symptom complex had an abnormal EEG, while only 26% of those without this symptom complex had an abnormal EEG. Railroad engineers did not show such a tendency. Abnormally slow MCVs or SCVs and prolonged motor distal latencies or both were found in 12% of the 59 car painters but in none of the 53 engineers studied.

Previous studies have shown that many solvents primarily cause neuropathy, while objective signs of central nervous involvement have been minor, if any. The findings of this study are similar; they showed slight positive signs of slowed nerve condition velocities among the car painters and no increase in EEG abnormalities in comparison to the reference group of railroad engineers. (JA)

48 refs

KEYWORDS: Volatile Solvents. Experimentation: Chronic Dosage Study. Psychological Testing.

UM-78-D1172

EVALUATION OF WORKERS EXPOSED TO ELEMENTAL MERCURY USING QUANTITATIVE TESTS OF TREMOR AND NEUROMUSCULAR FUNCTIONS, G.D. Langolf; D.B. Chaffin; R. Henderson; H.P. Whittle, American Industrial Hygiene Association Journal, v39 n12 p976-84 (Dec 1978)

The major objective of this study was to determine if objective evidence of mercury related behavioral effects could be found in a group of 130 workers subjected to good contemporary hygiene controls resulting in an average urinary mercury level of 0.24 mg/L. Effects of mercury exposure were assessed in the following parameters: tremor activity under both heavy and light muscular loading; electromylogram; and myotatic reflex speed. Several psychomotor tests were also administered which included choice reaction, rapid pointing, finger tapping, Michigan maze, and tracking tests.

Overall, the results of testing indicate that functionally significant effects were indeed absent in the exposed workers. While test results showed some statistically significant trends related to urine mercury, the mercury-related changes were themselves far smaller than the natural background variability among individuals. These small but statistically significant trends occur in EMG, tremor, finger tapping, and eye-hand coordination results. Thus, these correlations confirm the basic usefulness of mercury determinations in gauging workers' exposure and in preventing adverse neurological effects. (HSRI)

14 refs

KEYWORDS: Heavy Metals and Heavy Metal Antagonists: mercury*. Experimentation: Chronic Dosage Study. Physiological Testing. Psychological Testing. Psychomotor Tests.

UM-79-D1173

MORPHINE-INDUCED HYPEREXCITABILITY IN MAN, R.E. Berryhill; J.L. Benumof; D.S. Janowsky, Anesthesiology, v50 n1 p65-6 (Jan 1979)

The case reported here documents the occurrence of a stimulatory effect of morphine in man, and although the mechanism underlying this phenomenon is speculative, its occurrence may serve as a link in relating animal data to human physiology. The

description of morphine-induced hyperactivity in man alerts physicians to a new, possibly adverse reaction to morphine. (HSRI)

15 refs

KEYWORDS: Opiates and Related Agents: morphine. Experimentation: Acute Dosage Study. Physiological Testing.

UM-78-D1174

BEHAVIORAL EFFECTS OF ESTROGEN IN THE HUMAN FEMALE, A. A. Ehrhardt, Pediatrics, v62 n6 pt 2 s1166-9 (1978)

This paper reviews the behavioral effects of estrogen in the human female. Since estrogen plays different roles at different ages, this review of its behavioral effects is divided on the basis of different age periods. Before birth or neonatally, various sex hormones have long-term and permanent effects on behavior. In contrast, hormones in adulthood affect reversible changes in behavior.

Several specific topics are reviewed in this paper: (1) the role of estrogen in brain differentiation; (2) prenatal steroidal effects on human female behavior; (3) estrogen treatment in patients with Turner's Syndrome; and (4) estrogen effects on the behavior of women, particularly as they relate to menstruation, oral contraception, and menopause. (HSRI)

14 refs

KEYWORDS: Estrogens: estrogen. Review: Drug Concentration-Effect Relationships. Review: Drug Effects.

UM-78-D1175

BEHAVIORAL EFFECTS OF ESTROGEN TREATMENT IN HUMAN MALES, H.F.L. Meyer-Bahlburg, Pediatrics, v62 n6 pt 2 s1171-7 (1978)

The author reviews the behavioral effects of estrogen treatment in human males during three different age periods: (1) prenatally (a) when the pregnant mother continues to ingest certain contraceptive steroids and (b) when she is administered estrogen for pregnancy maintenance; (2) in adolescence or adulthood when treated (a) for the control of deviant sexual behavior or (b) for demasculinization and feminization in the case of transsexualism; and (3) in midlife or later, when treated for androgen-dependent cancer, especially of the prostate .

Some of the topics discussed are estrogen's effect on sex-dimorphic behavior, intelligence, and general psychopathology and its use in controlling sexually deviant behavior. Negative side effects as well as therapeutic uses are discussed. (HSRI)

43 refs

KEYWORDS: Estrogens: estrogen. Review: Drug Concentration-Effect Relationships. Review: Drug Effects.

UM-76-D1176

UNDER THE INFLUENCE, Medical Journal of Australia, v1 n8 p215-16 (1976)

This article discusses the extent to which individuals drive while under the influence of drugs in North America, England, and Australia. Also reported are the results of an Australian investigation attempting to determine the effects of drugs and alcohol on driving.

The investigation led to the following conclusions: (1) A "blanket warning" on antihistamine usage may not be appropriate, since each individual antihistamine has different effects. (2) Patients receiving diazepam should be warned of the dangers of driving, especially when combining the drug with alcohol, since diazepam is synergistic with alcohol and combination of the two can cause significant psychomotor impairment. (3) No evidence exists supporting the belief that coffee or fructose decreases blood alcohol levels. (4) The role of drugs combined with alcohol in the causation of traffic accidents in Australia has yet to be established. (HSRI)

1 ref

KEYWORDS: Review: Drugs and Highway Safety.

UM-77-D1177

ALTERED HEMISPHERIC FUNCTIONING UNDER ALCOHOL, B.C. Chandler; O.A. Parsons, Journal of Studies on Alcohol, v 38 n3 p381-91 (1977)

This study tested the hypothesis that single doses of alcohol produce greater impairment of functions associated with right hemispheric control or dominance than of functions controlled primarily by the left hemisphere. Forty right-handed males, aged 21 to 30 years and light to moderate drinkers, were assigned to four groups: (1) no delay-alcohol; (2) no delay-placebo; (3) delay-alcohol; and (4) delay-placebo. Subjects in the two alcohol groups received 1.04g alcohol per kg body weight, which produced a peak BAC of 0.10%.

To test the hypothesis that alcohol would produce greater impairment of right hemisphere functions, Teuber's technique was modified to include verbal and nonverbal stimuli of known association value. This technique permits examination of the effect of alcohol on information processing as a function of the two types of stimuli as well as of the left and right visual areas, and thus allows inferences as to functioning of the left and right hemispheres. Subjects were required to find a matching pattern for a target among an array of shapes. The target was a circular area in the subject's control vision and was either filled (no delay) or blank (delay).

Although in the predicted directions, neither of the specific interactions was significant, but when the interaction involving all three variables (groups, visual area, and stimulus content) was examined, it was clear that a selective effect of alcohol was present. (HSRI)

17 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Acute Dosage Study. Psychological Testing. Tests of Sensory Function.

UM-78-D1178

BEHAVIORAL TOXICOLOGY--HEAVY METALS AFFECTING BEHAVIOR, C.C. Pfeiffer; I.A. Michaelson; L.S. Rafales; R.L.Bornschein; R.K. Loch; O.J. David; S. Hoffman; A. Koltun; et al., Psychopharmacology Bulletin, v14 n3 p47-61 (1978)

Presented here is a collection of five papers dealing with the behavioral effects of overexposure to heavy metals. Heavy metal excess as it reaches the brain can interfere with the essential trace metals and produce convulsions, mental retardation, hyperactivity, or psychosis. The metals most commonly causing adverse effects on the brain are copper, lead, aluminum, cadmium, mercury, bismuth, and silver.

These adverse effects are discussed in the studies presented here. The following topics are discussed: (1) hyperactivity in animals as a result of exposure to lead; (2) the need for early and accurate diagnosis and treatment of lead poisioning, particularly in children; (3) the adverse effects of high serum zinc levels in female patients with anorexia nervosa; (4) the sedative or antianxiety effects of single doses of trace elements in both normal and schizophrenic subjects; and (5) the effects of high copper levels on behavior and learning in autistic and hyperactive children. (JAM)

39 refs

KEYWORDS: Heavy Metals and Heavy Metal Antagonists: copper*. lead*. zinc*. Vitamins: copper*. zinc*. Compilation.

UM-78-D1179

STIMULANT DRUG THERAPY IN CONTROL OF ON-TASK BEHAVIOR: A CASE STUDY, E.D. Fahrmeier, Psychological Reports, v42 pt 2 p1285-6 (1978)

While the use of stimulant drugs such as methylphenidate (Ritalin(R)) for the treatment of hyperactivity in children is common in the U.S., present assessment of the value of this treatment suggests that much more research is needed before unequivocal positive recommendations for drug treatment of these cases can be made. Concerns are possible

side effects from extended use and a determination of actual effectiveness on classroom behavior.

In order to evaluate the effectiveness of Ritalin(R) or similar drugs, the author suggests that the child be observed in his school environment under double-blind conditions, both after administration of drug and placebo. A trained behavioralist should observe the child in several types of activities. In the case described here, this method indicated that Ritalin(R) was having no effect on the child's behavior. Therefore, the drug was discontinued and other nondrug approaches were used to curb his hyperactivity. The author concludes that stimulant drugs should not be arbitrarily administered to all hyperactive children. (HSRI)

2 refs

KEYWORDS: Stimulants: methylphenidate. Stimulants. Experimentation: Acute Dosage Study. Psychological Testing.

UM-76-D1180

"SIDE" EFFECTS: A MISNOMER. C.R.B. Joyce, Journal of Medical Ethics, v2 n3 p112-7 (1976)

This paper discusses the results of the tragic side effects of thalidomide and discusses the possibility of similar problems with other drugs. Despite extensive clinical trials before drugs are made available to the prescribing doctor, side effects cannot be entirely anticipated or eliminated. However, it is important, the author argues, for information obtained by the doctor from the patient and by the manufacturers from the doctor to be collected and evaluated. Only in this way can effects of drugs other than those intended be drawn to the notice of the manufacturer.

The article is followed by a commentary which critiques the preceding article. The authors lament the lack of reliable drug information disseminated by the pharmaceutical industry. They recommend that a national committee be established to assess and reassess medicines. Such a committee would be useful in both protecting the public from adverse drug effects and in preventing needless alarm about drug effects. (JA)

21 refs

KEYWORDS: Review.

UM-78-D1181

CLINICAL PHARMACOLOGY AND THERAPEUTICS OF BENZODIAZEPINES, E.M. Sellers, Canadian Medical Association Journal, v118 p1533-8 (24 Jun 1978)

This article presents a broad overview of the clinical pharmacology and therapeutics of the benzodiazepines, which are among the most commonly prescribed drugs in the world. In spite of their extensive use, the therapeutic indications and potential of benzodiazepines are limited. This paper reviews some of these limitations. The author draws several conclusions about the use of benzodiazepines: (1) Benzodiazepines should be prescribed only when clearly indicated and only for the minimum time necessary. (2) Diazepam and chlordiazepoxide should not be given intramuscularly. (3) Persons more than seventy years old should receive initial doses of benzodiazines which are no more than half of those prescribed for younger persons. Persons with cirrhosis should receive no more than one-third that amount. (4) Barbiturates should not be prescribed for any condition for which benzodiazepines are effective.

Also briefly reviewed in this paper are the absorption, protein binding, biotransformation, and distribution of the benzodiazepines. Clinical effects such as sensitivity to benzodiazepines, tolerance, dependence, withdrawal, drug interaction, and negative side effects are also discussed. (HSRI)

36 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): clonazepam. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. clorazepate. diazepam. lorazepam. oxazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: flurazepam. Review.

UM-77-D1182

MARIJUANA-PRODUCED IMPAIRMENTS IN FORM PERCEPTION: EXPERIENCED AND NON-EXPERIENCED SUBJECTS, K. MacCannell; S.L. Milstein; G. Karr; S. Clark, Progressive Neuro-Psychopharmacology, v1 p339-43 (1977)

This study attempted to examine and compare the effect of marijuana on tactual form perception in cannabis-experienced and naive subjects. Sixteen male and sixteen female subjects, half of whom were regular users of marijuana and half of whom were nonusers, received 600 mg of 1.3% delta-9-THC and placebo double-blind on two different occasions seven days apart. The two groups were matched for age, sex, and education. Subjects were tested before drug administration and fifteen minutes after for form perception ability and size estimation ability. Three subjective measures of intoxication were also employed: (1) an evaluation of subject intoxication by the drug administrator on the basis of conjunctival redness, memory lapse, and ability to converse; (2) the Primary Affect Scale, which assesses anger, arousal, depression, fear, and happiness; and (3) *a posteriori* drug identification by the subject.

Results of testing showed a 52% impairment in form perception under the marijuana condition. Although there was no statistically significant interaction between the drug effect and previous experience, there was a definite trend toward greater impairment for the experienced compared to the naive group. The results on the Primary Affect Scale indicate that marijuana produces an increase in happiness in both the experienced and inexperienced groups. The ability to make a posteriori identification of the drug condition appears to be related to previous cannabis experience. The experienced group correctly identified the marijuana condition more often than did the inexperienced group. The authors conclude that a moderate dose of marijuana can produce an acute impairment in form perception for both experienced and inexperienced subjects. (HSRI)

8 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Experimentation: Acute Dosage Study. Psychological Testing. Tests of Sensory Function.

UM-78-D1183

HYPNOTIC ACTIVITY OF DIPHENHYDRAMINE, METHAPYRILENE, AND PLACEBO, A. Sunshine; I. Zighelboim; E. Laska, Journal of Clinical Pharmacology, v18 n8-9 p425-31 (Aug-Sep 1978)

The purpose of this study was to determine if methapyrilene, one of the major components of the over-the-counter preparation Exedrin PM(R), has hypnotic properties as compared to diphenhydramine and placebo. Graded doses of each drug were used to determine a dose-response curve so that relative potency estimates could be obtained.

91,295 consecutive postpartum patients on the obstetrical service in a large hospital were given a single administration of one of the following seven randomly selected treatments if they complained of a sleep problem: (1) diphenhydramine hydrochloride, 12.5 mg.; (2) diphenhydramine hydrochloride, 25 mg.; (3) diphenhydramine hydrochloride, 50 mg.; (4) methapyrilene fumarate, 36 mg.; (5) methapyrilene fumarate, 72 mg.; (6) methapyrilene fumarate, 144 mg.; and (7) placebo.

Two methods were used to estimate the efficacy of the treatments. One was based on objective observations carried out by a nurse every fifteen minutes for three hours to determine how long after drug administration it took the subject to fall asleep. The second was based on a subjective interpretation by the patients elicited during an interview.

Results of both the subjective and objective estimates show that methapyrilene and diphenhydramine at all doses were found to be effective hypnotics in comparison to placebo based on assessment of sleep latency, sleep duration, awakening in the night, global evaluation, and morning alertness. Increasing the dose of these drugs produced only a minimal increase in effectiveness. No significant adverse effects were noted in any of the patients. (HSRI)

10 refs

KEYWORDS: Antihistamine Agents: diphenhydramine. methapyrilene. Nonbarbiturates: diphenhydramine. Clinical Study. Experimentation: Dose-Effect Study. Physiological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-78-D1184

EFFECTS OF CANNABINOID COMPOUNDS ON AGGRESSIVE BEHAVIOR, E.A. Carlini, Modern Problems in Pharmacopsychology, v13 p82-102 (1978)

This review analyzes existing available data on cannabis and aggressive behavior and discusses some conflicting results in the literature. First the concept and theory of aggression is discussed. This is followed by a review of several studies investigating acute and chronic cannabis effects in animals. Finally the effects of cannabis on human aggression are discussed.

Results of the animal studies indicate that cannabis, when administered in an acute dosage, has a suppressive effect on aggressive behavior in the nonstressed animal. However, if animals receive marijuana chronically, aggressive behavior becomes evident after the development of tolerance to the depressant effect of the drug. Therefore, cannabis has a dual action on aggression in the nonstressed animal: it blocks aggressiveness after acute dosage and induces or increases it with chronic administration.

In studies with stressed or manipulated animals, both acute and chronic administration of marijuana can also generate aggressive behavior. In spite of the relationship between marijuana ingestion and aggression in rats and other animals, no link has yet been found between cannabis use and aggression or crime in humans. The author suggests that more research be done in this area, particularly on the subject of the possible interaction between stress and cannabis in humans. (HSRI)

121 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Review: Drug Effects.

UM-77-D1185

SOME CURRENT RESEARCH IN BEHAVIORAL PHARMACOLOGY, A. McKim, Modern Problems in Pharmacopsychiatry, v12 p77-87 (1977)

The purpose of this chapter is to present summaries of eight papers dealing with a variety of current research problems in different fields of behavioral pharmacology. Dr. M. Burns addressed the problem of whether impairments seen after administration of alcohol and marijuana to human subjects are a result of the drug's action on the same system or different processes. Dr. Moskowitz's paper was primarily concerned with alcohol-produced deficits in visual search behavior and their role in alcohol-related driving accidents. Dr. G. Lowe's paper was concerned with the significance of sensory stimulation, particularly the reinforcing value of stimulus change. He concluded from the findings that hallucinogenic drugs alter the significance of sensory stimulation and that in these circumstances the actions of drugs cannot properly be understood without assessing the existing arousal level of the animal and the ways in which it can be modified. Dr. Warburton's research was concerned with exploring the role of cholinergic mechanisms in discrimination performance based upon multiple stimuli. Dr. Heise attributed scopolamine-produced deficits in rat's performance to information-processing mechanisms rather than sensory reception and transduction. His paper was specifically directed at discovering how changes in delay between the presentation of stimuli and the opportunity to respond and stimuli complexity effect scopolamine-produced disinhibition. Dr. McKim reviewed data showing that many drugs have stimulus properties. Dr. Sanger's paper was concerned with a more complete understanding of the processes involved in benzodiazepine-produced increases in behavior normally supressed by electric shocks. Dr. E.T. Uyeno reported on an improved method of drug self-administration which he has developed.

Two encouraging aspects that can be noted from the papers are that 1) drug effects on behavior are being studied using a great variety of techniques and from a diversity of theoretical positions; and 2) in spite of the variability in approaches and techniques, consistencies in data are starting to appear. (HSRI)

20 refs

KEYWORDS: Compilation.

UM-78-D1186

SUBMISSION BY THE COMMONWEALTH DEPARTMENT OF TRANSPORT TO THE STANDING COMMITTEE ON ROAD SAFETY INQUIRY INTO ALCOHOL, DRUGS, AND ROAD SAFETY, Melbourne, Victoria: Australian Commonwealth Department of Transport (Aug 1978)

Presented here is a government report on the problem of alcohol, drugs, and traffic safety in Australia. This report summarizes the nature and magnitude of the problem, describes existing countermeasures and their effectiveness, and describes the roles of several governmental groups responsible for traffic safety. In Australia, about one-third of adults killed in road accidents and about one-fifth of adults injured have elevated blood alcohol concentrations. Alcohol is most often important in single vehicle accidents. Drinking drivers involved in accidents are almost always male, their accidents occur most frequently at night, especially on Fridays and Saturdays, and their blood alcohol concentrations are typically well above the legal limit, suggesting that many are heavy drinkers. Evidence concerning the involvement of alcohol in other types of trauma suggests that it may be more appropriate to view drinking and driving accidents as one aspect of the wider problem of alcohol abuse than to examine them in isolation.

The evidence that drugs other than alcohol increase the risk of accident involvement is not yet conclusive. Such evidence as does exist suggests that many drugs adversely affect driving and increase the risk of accident to some degree, particularly when combined with alcohol. It seems unlikely, however, that any drug carries as high a risk as alcohol. Available evidence suggests that drugs other than alcohol do not, at present, have a major impact on the road toll in Australia.

Present countermeasures against drinking while driving include prohibitive legislation, police detection and prosecution, court-imposed penalties, court-directed treatment, and education and publicity. Present countermeasures against driving under the influence of other drugs include prohibitive legislation and campaigns encouraging medical practitioners to inform patients of the likely effect on driving of any drug they prescribe.

There are no radically new countermeasures in sight. Very little is known about the effectiveness of measures currently in use or of the relationships between them. There is an urgent need to evaluate existing measures and to examine the way they interact through the application of a systems approach. In this way it may be possible to identify factors that prevent current measures from working as efficiently as they might and to enable the system to be streamlined. Some worthwhile gains may be possible by designing or modifying the road and roadside environment to be more forgiving of the errors alcohol-affected road users make. It is also possible that a breakthrough in the design or use of ignition interlocks will enable their potential to be realized. (AAM)

61 pages 53 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Countermeasure Concepts. Countermeasure Development, Testing, and Evaluation. Epidemiology: National Survey of Drug Use Patterns.

UM-78-D1187

THE ANTIAGGRESSIVE EFFECTS OF LITHIUM, E.P. Worrall, Lithium in Medical Practices, F.N. Johnson; S. Johnson, eds., p69-77, Lancaster, England: MTP Press (1978)

This paper discusses evidence in recent studies in which lithium is shown to have a general antiaggressive effect in man and reviews the problems in proving that lithium has this effect. Four major problems exist: (1) The aggressive behavior in question must be defined and measured. (2) There must be reasonable proof that the patients studied are not manic depressive. (3) It must be shown that any antiaggressive effect is not just part of a toxic effect. (4) Subjects must be free from all other psychotropic drugs.

These problems are discussed in the context of a study investigating the antiaggressive effect of lithium in eight severely mentally retarded inpatients. These patients were studied over sixteen weeks receiving lithium or placebo alternately for intervals of four weeks. The nursing staff observed and reported the patients' aggressive behavior for three four-hour time periods per day.

Because of the problems mentioned above, no accurate assessment of lithium effects could be made in these patients. However, results of their observation scores indicated that three patients were less aggressive while on lithium, two were more aggressive, and three were unchanged. The variability in response to lithium suggests that there are underlying patient characteristics that determine the antiaggressive response. (HSRI)

23 refs

KEYWORDS: Antidepressants: lithium. Other CNS Agents: lithium. Clinical Study. Experimentation: Chronic Dosage Study. Psychological Testing. Review: Behavioral Research Methodology.

UM-68-D1188

1968 ALCOHOL AND HIGHWAY SAFETY REPORT, Washington, D.C.: Government Printing Office (Aug 1968)

Presented here is a report on the relationship between the consumption of alcohol and highway safety. Various aspects of the alcohol problem are discussed. These include: (1) alcohol and the human body; (2) alcohol in crashes and violations; (3) experiments on alcohol and driving; (4) countermeasures and their effectiveness; (5) public opinion concerning drinking while driving; and (6) legal approaches to the problem of the drinking driver. The discussion of each of these topics is supported by a great deal of statistical information from both experimental and epidemiological research. The report concludes with suggestions for educational programs about alcohol and highway safety. (HSRI)

Department of Transportation

182 pages 0 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-75-D1189

AN OVERVIEW OF THE DRUG/DRIVING PROBLEM, G. Milner, Drug/Driving Research Review Symposium, chap 3 p18-34, Bloomington, Indiana: Indiana University (Apr 1975)

Presented here is a general review of the drug and driving problem, particularly as it relates to Australia. A brief summary of drug use in Australia is presented, and these statistics are compared to statistics of drug use in the United States.

The author strongly believes that drugs other than alcohol present a real driving hazard that warrants extensive study. However, several problems hamper research at this point. These include: (1) stereotyping of individuals, i.e., ignoring the complexities of society; (2) the tendency of researchers to concentrate only on fatal accidents and to disregard minor accidents where drug usage is probably more common; (3) emotional reactions that prevent objectivity; and (4) the funneling of nearly all research money into alcohol studies to the exclusion of drug studies.

The article concludes with a discussion of seven possible societal responses to the drug and driving problem. The following are evaluated by the author: (1) laissez faire; (2) taking advantage of the profit from drug sales; (3) legislation of measures to curtail or prevent substance use; (4) punishment; (5) treatment; (6) alteration of the environment through education or advertising; and (7) adopting an attitude of inquiry, that is, investigating the actual state of affairs. The author sees this last response, which has been the most neglected response, as the most important. The author concludes that in view of the complex interactions between drug, individual, and environment, simplistic solutions to the drug and driving problem must be avoided. (HSRI)

0 refs

NHTSA DOT-HS-4-00994

KEYWORDS: Review: Drugs and Highway Safety.

UM-75-D1190

DRUGS AND PERFORMANCE AS RELATED TO DRIVING, M.H. Orzack, Drug/Driving Research Review Symposium, chap 5 p66-80, Bloomington, Indiana: Indiana University (Apr 1975)

The purpose of this paper is to review recent experimental studies on the effects of drugs which are related to driving skills.

A summary of experimental studies on each class of psychotropic drugs is presented and examples are given which are illustrative of the general types of performance changes

characteristically brought about by particular agents. The drugs included in these experiments are hypnotics and depressants; antipsychotics; hallucinogens; stimulants; antidepressants; antihistamines; antianxiety agents; and inhalants.

Several conclusions can be drawn from this study. First, the problem of mixing one or more psychotropic agents together is of paramount importance. Frequently the effect is more than additive, especially if the second drug is alcohol. Secondly, a pure and simple predictive measure of drugs on performance cannot be obtained. The literature is extensive on drug effects on performance tasks, but while drug effects can be defined operationally, confounding variables such as motivation, set, and setting are modifying influences on the stability of such tests, and may actually obscure the "true" drug effects. In short, while partial indicators may be obtained from the use of performance tests, a measure of driving ability is best obtained in a real life driving situation. (HSRI)

47 refs

NHTSA DOT-HS-4-00994

KEYWORDS: Review: Drugs and Highway Safety.

UM-75-D1191

THE PROBLEMS OF DRUGS AND DRIVING: AN OVERVIEW OF CURRENT RESEARCH AND FUTURE NEEDS, R.G. Smart, Drug/Driving Research Review Symposium, chap 12, p218-32, Bloomington, Indiana: Indiana University (Apr 1975)

Discussed here are both some general issues in the area of the effect of drugs on driving and some specific issues such as risk identification, behavioral measurement of impairment, legal and practical constraints, drug measurement in the body, and countermeasures development.

These issues are discussed in the context of several experimental and epidemological studies which are described and evaluated by the author.

Several recommendations are also presented: (1) Research should be concentrated on the major psychoactive and hallucinogenic drugs such as tranquilizers, antidepressants, and cannabis. (2) More research is needed at the level of drugs in various nonaccident populations and among accident-involved pedestrians and passengers. (3) More studies are needed involving behavioral impairment from drugs in older subjects, female subjects, patients, and nonexperienced drivers, preferably in real life driving situations and after varying intervals after drug ingestion. (4) Of utmost importance is the development of simple, inexpensive methods of detecting cannabis and LSD in body fluids. (HSRI)

21 refs

NHTSA DOT-H-4-00994

KEYWORDS: Review: Drugs and Highway Safety.

UM-HSRI-78-5

UM-78-D1192

ALCOHOL AND HIGHWAY SAFETY 1978: A REVIEW OF THE STATE OF KNOWLEDGE, R.K. Jones; K.B. Joscelyn, Ann Arbor, Mich: University of Michigan Highway Safety Research Institute (Jan 1978)

This report presents the results of a comprehensive review and analysis of the problem of alcohol and highway crashes in the United States. Both the nature of the alcohol-crash problem and societal responses to that problem are treated. Epidemiologic studies, experimental studies, and countermeasure programs are examined in the review. The short-term future of the alcohol crash problem is projected and conclusions and recommendations relative to future research and action programs are developed. In order to develop more effective programs for dealing with the alcohol crash problem, the authors recommend that research be concentrated in the following areas: (1) analysis of targets of possible alcohol-safety programs; (2) identification of deterrent threats, treatment, and rehabilitation regimens most appropriate to drinking drivers; (3) greater understanding of the principal elements of public information and education relative to modifying drinking-driving behavior; (4) development of technologies that could be used to support legal, health, and other approaches to controlling alcohol-crash losses; (5) application of the systems approach to the design, management, and evaluation of alcohol

safety programs; (6) development of better techniques and methodologies for evaluating alcohol-safety programs and for applying the results of such evaluations to the design and operation of new programs. (AAM)

207 pages 324 refs

NHTSA DOT-HS-5-01217

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Review: Drugs and Highway Safety.

UM-HSRI-78-9 UM-78-D1193

ALCOHOL AND HIGHWAY SAFETY 1978: A REVIEW OF THE STATE OF KNOWLEDGE: SUMMARY VOLUME, R.K. Jones; K.B. Joscelyn, Ann Arbor, Mich.: University of Michigan Highway Safety Research Institute (Jan 1978)

This report summarizes the results of a comprehensive review and analysis of the problem of alcohol and highway crashes in the United States. Both the nature of the alcohol-crash problem and societal responses to that problem are treated. Epidemiologic studies, experimental studies, and countermeasure programs are examined in the review. The short-term future of the alcohol-crash problem is projected and conclusions and recommendations relative to future research and action programs are developed. (AA)

113 pages 324 refs

NHTSA DOT-HS-5-01217

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Review: Drugs and Highway Safety.

UM-77-D1194

CHANGES IN REACTION TIME AND DRUG PLASMA CONCENTRATIONS AFTER NITRAZEPAM AND GLUTETHIMIDE, S.H. Curry; R. Whelpton; D.F. Scott, British Journal of Clinical Pharmacology, v4 n2 p229-33 (Apr 1977)

This study attempted to determine the relationship of plasma concentration of nitrazepam and glutethimide to reaction time. The effects of placebo on reaction time were also studied.

The subjects were five healthy adult volunteer medical students, one female and four males, ranging in age from 19 to 21 years. They were given five treatments according to a latin square design: (1) nitrazepam, (5 mg); (2) nitrazepam, (10 mg); (3) glutethimide, (250 mg); (4) glutethimide, (500 mg); and (5) placebo. Treatments were given double-blind in matching capsules one week apart. Subjects were tested for reaction times five times at thirty-minute intervals after drug administration. After each test session a venipuncture was taken and plasma was separated by centrifugation of the blood into heparinized tubes. Nitrazepam and glutethimide were assayed by gas chromatography.

Results showed that with glutethimide in all five subjects and with nitrazepam in four subjects, larger doses led to higher concentrations in plasma and to greater increases in reaction time. The relationship between change in reaction time and plasma concentration appears to be mainly a within-subject dose-effect relationship, with the peak concentration in plasma as the dose and the area under the reaction time curve as the effect. (JAM)

10 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): nitrazepam*. Nonbarbiturates: glutethimide*, nitrazepam*. Drug Concentration-Effect Study: Driving Skill Impairment. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Psychomotor Tests.

AM 64-18 UM-64-D1195

PHYSIOLOGICAL RECORDINGS FROM PILOTS OPERATING AN AIRCRAFT SIMULATOR, C.E. Melton, Oklahoma City, Oklahoma: FAA Civil Aeromedical Institute (Sep 1964)

This study attempted to determine whether or not therapeutic doses of two commonly used drugs, a tranquilizer and an antihistamine, cause decrements in the operating deficiency

of pilots and whether these drugs have measurable effects on selected physiological functions. Six healthy pilots aged 37 to 42 years were given for four days each meprobomate (400 mg four times daily), chlorpheniramine (4 mg four times daily), or placebo in a double-blind procedure. Before and after drug administration ten physiological measurements were assessed in the subjects while performing on a C-97 aircraft simulator. Records were made of electrocardiogram, heartrate, respiratory rate, galvanic skin response, electroencephalogram (parietal-occipital and frontal-central), and lateral eye movements.

Results of the tests indicated that neither of the drugs had any effect on the physiological parameters measured under these experimental conditions. The authors stress, however, that the negative findings in this study are not to be interpreted as expressing or implying that tranquilizers or antihistamines can safely be used in an actual flight situation. Flight activities should remain suspended for twenty-four hours after ingestion of the standard dose of either meprobomate or chlorpheniramine. The authors conclude that the present study is valuable in that it demonstrates the feasibility of obtaining reliable physiological records from patients in a work situation such as flying or driving. (HSRI)

5 refs

KEYWORDS: Antihistamine Agents: chlorpheniramine. Minor Tranquilizers (Anti-Anxiety and Ataractics): meprobamate. Driving Simulator. Experimentation: Chronic Dosage Study. Physiological Testing.

AM 69-9

UM-69-D1196

EFFECTS OF TWO COMMON MEDICATIONS ON COMPLEX PERFORMANCE, W.D. Chiles; H.L. Gibbons; P.W. Smith, Oklahoma City, Oklahoma: FAA Civil Aeromedical Institute (Jun 1969)

The purpose of this research was to examine the effects of normal, clinical dosages of Donnatal(R) (phenobarbital) and chlorpheniramine maleate on the performance of complex tasks of the sort involved in aircraft and air traffic control operations. The performance of ten college students was measured over three four-hour periods following the administration of 16.2 mg phenobarbital, 4 mg chlorpheniramine maleate, or placebo in a double-blind experiment. Prior to the experiment the subjects had been given extensive training on the battery of tests used. The subjects were tested as two five-man crews on tasks which were designed to assess psychological functions of the kind involved in aircraft operations. Included were measures of reaction time, monitoring, mental arithmetic, problem solving, and visual discrimination.

Results of the tests show that while performance under the chlorpheniramine maleate condition was "numerically" inferior, no effects were found that could be statistically attributed to the drugs administered. The major qualification of this conclusion lies in the fact that only ten subjects were tested. Although this number is adequate for the purposes of establishing average effects, it does not permit detailed examination of individual differences in relation to the possible occurrence of idiosyncratic reactions of particular subjects. (AAM)

1 ref

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital. Antihistamine Agents: chlorpheniramine. Barbiturates: phenobarbital. Parasympatholytic (Cholinergic Blocking) Agents: Donnatal(R) (phenobarbital + atropine sulfate + hyoscine HBr + hyoscyamine sulfate). Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests. Tests of Sensory Function.

FAA-AM-73-12

UM-73-D1197

FLYING HIGH: THE AEROMEDICAL ASPECTS OF MARIHUANA, M.F. Lewis, D.P. Ferraro, Oklahoma City, Oklahoma: FAA Civil Aeromedical Institute (Dec 1973)

A summary of the discussions and papers presented at the June 1972 Symposium on Aeromedical Aspects of Marihuana at the Civil Aeromedical Institute in Oklahoma City is presented. The panel, consisting of representatives from the aviation community, discussed the legal aspects of using marijuana while flying, the frequency of use in military aviation, and the acute and chronic effects of the drug.

The panel made several recommendations: (1) No radical changes in FAA policy with respect to marijuana use are necessary at this time. (2) A twelve- to sixteen-hour

period between marijuana use and aviation work is advisable. (3) The FAA should conduct research on the aeromedical aspects of marijuana since the academic community is not equipped to research this area of interest. (HSRI)

8 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Review: Drugs and Highway Safety.

FAA-AM-75-6 UM-75-D1198

INTERACTION BETWEEN MARIHUANA AND ALTITUDE ON A COMPLEX BEHAVIORAL TASK IN BABOONS, M.F. Lewis; D.P. Ferraro; H.W. Mertens, J.A. Steen, Oklahoma City, Oklahoma: FAA Civil Aeromedical Institute (Aug 1975)

Marijuana, or its principal active ingredient, delta-9- tetrahydrocannabinol, impairs performance on complex behavioral tasks in animals and man. Although there exists some evidence that altitude-induced hypoxia potentiates the physiological effects of marijuana, the interaction between altitude and marijuana on behavioral tasks has not been established. In the absence of evidence that use of marijuana is less frequent among members of the aviation community than among the general population, it was necessary to evaluate the effects on performance of any interaction between hypoxia and marijuana.

Two baboons were trained to perform on a delayed matching-to-sample task at ground level and altitudes of 8,000 and 12,000 feet. The animals were orally administered doses of delta-9-THC ranging from 0.25 to 2.0 mg/kg two hours prior to experimental sessions at each altitude.

No effects on accuracy of matching performance were observed for any of the drug doses or altitudes used. Amount of work output, as measured by number of trials completed and speed of responding, was not affected by delta-9-THC at ground level but was markedly reduced by the 8,000 and 12,000 feet altitudes. This interaction suggests that the behavioral impairment produced by marijuana can be potentiated by hypoxia. (AA)

9 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Animal Research.

FAA-AM-75-14 UM-75-D1199

THE EFFECTS OF DEXTROAMPHETAMINE ON PHYSIOLOGICAL RESPONSES AND COMPLEX PERFORMANCE DURING SLEEP LOSS, E.A. Higgins; W.D. Chiles; J.M. McKenzie, P.F. Iampietro; J.A. Vaughan; G.E. Funkhouser; M.J. Burr; A.E. Jennings; G. West, Oklahoma City, Oklahoma: FAA Civil Aeromedical Institute (Nov 1975)

The purpose of this experiment was twofold: First, it attempted to identify and clarify possible differences between the subject's appraisal of his performance of a complex task and objective test scores while under the influence of dextroamphetamine sulfate by relating test scores to physiological responses. Secondly, it attempted to evaluate the subject's performance for several hours after withdrawal of the drug as well as during the use of it. On two separate occasions, performance of ten male subjects aged 20 to 28 was measured on the Civil Aeromedical Institute Multiple Task Performance Battery at four-hour intervals for a period of twenty-four hours without sleep. Each subject received a capsule at four-hour intervals beginning at 2000. On one occasion, the first three doses contained 5 mg each of dextroamphetamine sulfate followed by placebos for the remaining three capsules. On the other occasion, all capsules were placebos.

Results of the experiment demonstrated that the dextroamphtamine sulfate sustained a high level of proficiency and alertness and delayed the effects of fatigue for eight to twelve hours after the ingestion of the third and final drug capsule. Heart rate, rectal temperature, and urinary excretion rates of catecholamines were elevated with this drug. Neither the subjects' feelings of fatigue nor the accuracy of their estimates of performance capabilities differed significantly in these two test conditions.

The authors stress that the results of this study should not be interpreted to suggest that detrimental effects of sleep loss can be prevented by the administration of dextroamphetamine sulfate. However, it may be concluded that performance can be maintained at a higher level under dextroamphetamine than without it. Also, since dextroamphetamine is generally regarded as one of the most effective stimulants, more

common legal stimulants such as caffeine cannot be assumed to insure satisfactory performance levels under conditions of sleep loss. (JAM)

15 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Stimulants: dextroamphetamine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Physiological Testing. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

FAA-AM-77-17

UM-77-D1200

EFFECTS OF LITHIUM CARBONATE ON PERFORMANCE AND BIOMEDICAL FUNCTIONS, E.A. Higgins; W.D. Chiles; J.M. McKenzie; A.W. Davis, G.E. Funkhouser; A.E. Jennings; S.R. Mullen; P.R. Fowler, Oklahoma City, Oklahoma: FAA Civil Aeromedical Institute (Jul 1977)

The effects of a single 600 mg dose of lithium carbonate were evaluated in a study of fifteen healthy, normal male subjects aged 19 to 27 years. Subjects were studied on two occasions by utilizing a double-blind design, once receiving the lithium carbonate and once receiving a lactose placebo. Measurements were made of (i) complex performance, using the CAMI Multiple Task Performance Battery; (ii) hand steadiness, using the steadiness tester of the Motor Steadiness Kit; (iii) heart rate; (iv) the urinary excretion of 17-ketogenic steroids, epinephrine, and norepinephrine; and (v) short-term memory, as measured by the Wechsler Memory Scale.

The only statistically significant effect due to the drug was on short-term memory, in which scores of subjects taking the placebo were higher than scores of those taking the lithium carbonate. (JA)

22 refs

KEYWORDS: Antidepressants: lithium. Other CNS Agents: lithium. Experimentation: Acute Dosage Study. Physiological Testing. Psychological Testing. Psychomotor Tests.

UM-78-D1201

ROAD RESEARCH: NEW RESEARCH ON THE ROLE OF ALCOHOL AND DRUGS IN ROAD ACCIDENTS, Paris: OECD (1978)

This report contains a state-of-the-art review of alcohol and drugs in relation to traffic safety. This report has four objectives: (1) to review existing scientific literature and other available information on the role of alcohol and drugs in traffic accidents; (2) to examine information related to impaired driving countermeasures and evaluate their effectiveness; (3) to identify the research results obtained from successful programs that can be recommended for general and immediate application elsewhere; and (4) to indicate priority needs for research in the fields of alcohol, drugs, and traffic safety and to outline possible future international cooperative activities.

The report includes six chapters. Following an introductory chapter on drugs and driving, the report examines the general methodological approaches that have been taken in research on alcohol and drugs in relation to driving. Limitations on expanding this area of research are discussed. The next chapter discusses the alcohol problem--its extent, nature, and possible countermeasures. The subsequent chapter on drugs examines the kinds of substances that have a possible influence on traffic safety. Public information programs concerning drug effects, education, treatment, and rehabilitation are discussed.

The report concludes by suggesting several recommendations concerning the implementation in OECD countries of an epidemiological research program which would attempt to evaluate and control the alcohol and drug/driving problem as well as develop more sensitive and practical assay techniques. (HSRI)

Organisation for Economic Co-operation and Development

317 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Anesthetics. Antidepressants. Hallucinogens and Related Agents. Opiates and Related Agents. Sedatives and Hypnotic Agents. Stimulants. Tranquilizers. Countermeasure Concepts. Review: Behavioral Research Methodology. Review: Drug

Analysis Methodology. Review: Drug Effects. Review: Drug Use. Review: Drugs and Highway Safety. Review: Survey Methodology.

UM-78-D1202

SUICIDES, HOMICIDES, AND FATAL ACCIDENTS, P.W. Haberman; M.M. Baden, Alcohol, Other Drugs and Violent Death, P.W. Haberman; M.M. Baden, p75-93, New York: Oxford University Press (1978)

This chapter discusses the roles that alcohol and other drugs play in suicides, homicides, traffic fatalities, and other fatal accidents. Reported here is a New York study of the incidence of drugs and alcohol in victims of violent deaths. The study found that 28% of all motor vehicle fatalities were alcoholics, narcotic abusers, or both. Many perpetrators of homicides are narcotics addicts or are intoxicated when committing the murder. In fact, well over one-half of all homicides of adults in New York City may involve substance abusers as either victims, perpetrators, or both. It is very difficult to estimate how often alcohol or other drugs influence the perpetrator of a homicide or survivor at fault in an accidental death because the living are not subject to the same immediate toxicologic testing as the dead, for legal or temporal reasons. (HSRI)

28 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents. Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-78-D1203

RESEARCH ISSUES UPDATE, 1978, G.A. Austin; M.A. Macari; D.J. Lettieri, eds., NIDA Research Issues 22 (1978)

The issues of psychosocial drug use and abuse have generated many volumes of research conducted in many disciplines and from many different points of view. This volume attempts to bring together and make accessible the results of these research investigators by collecting, summarizing, and disseminating this large body of literature. Included are such areas as family and peer influence, attitudes toward drug use, personality of the drug user, psychopathology, addict lifestyles, employment of drug users, criminal behavior, and pregnancy. Also included is a section on the driving behavior of drug users. Studies summarized in this section study the interaction between drug use and driving, particularly those psychomotor and perceptual functions related to driving performance.

Within each section entries are arranged alphabetically by author. For each entry the purpose of the article is stated and the methodology and results are summarized. Major conclusions are also stated. Only literature published between 1974 and 1977 in the English language is included. Most studies are taken from the professional literature and focus on American drug issues. (HSRI)

308 pages 136 refs

U.S. Department of Health, Education and Welfare publication no. (ADM) 79-808

KEYWORDS: Compilation.

UM-79-D1204

DRUGS AND DRIVING: INFORMATION NEEDS AND RESEARCH REQUIREMENTS, K.B. Joscelyn; R.K. Jones; R.P. Maickel; A.C. Donelson (Apr 1979)

This report presents the results of a comprehensive review and analysis of the relationship between drugs (other than alcohol alone) and highway safety. The report identifies research to define the problem of drugs and driving. Epidemiologic and experimental studies are examined in the review. Also reviewed is literature on approaches to countermeasures in this area of highway safety. Methodologic issues, problem areas, and information needs in drug and driving research are extensively discussed. Conclusions and recommendations for near-term research are developed, and a systematic program of research is suggested for implementing the recommendations. (AA)

398 pages 422 refs

National Highway Traffic Safety Administration technical report DOT-HS-804-774

KEYWORDS: Countermeasure Development, Testing, and Evaluation. Review: Drugs and Highway Safety.

UM-78-D1205

MARIJUANA UPDATE 78, Focus on Alcohol and Drug Issues, v1 n2 p5-30 (Mar-Apr 1978)

This periodical issue deals in its entirety with marijuana. It contains nontechnical articles on several aspects of marijuana. These include therapeutic uses of marijuana; medical effects; marijuana and taxes; penalties for use and possession in each state; marijuana laws in other lands; brain damage; international agreements concerning the drug; and marijuana use by motorists.

The article concerning marijuana use and driving discusses a California study of the use of marijuana by drivers. Initial results of the study indicate that of 291 blood samples drawn from suspected drunken drivers, 22% contained varying amounts of marijuana. Many of the blood samples containing marijuana came from middle-income motorists in their thirties who were generally well-educated. (HSRI)

0 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Other Sociolegal Study. Review: Drug Analysis Methodology. Review: Drug Effects. Review: Drug Use. Review: Drugs and Highway Safety.

UM-78-D1206

HUMAN POLYDRUG USE: MARIHUANA AND ALCOHOL, N.K. Mello; J.H. Mendelson; J.C. Kuehnle; M.L. Sellers, Journal of Pharmacology and Experimental Therapeutics, v207 n3 p922-35 (Dec 1978)

This report describes an attempt to examine the effects of concurrent availability of marijuana and alcohol on drug use patterns under clinical research ward conditions. The study was designed to explore patterns of polydrug abuse involving marijuana and alcohol.

Patterns of drug use during ten days of concurrent access to marijuana and alcohol were compared with consecutive five-day periods when only alcohol or only marijuana was available. Sixteen adult male volunteers (aged 21 to 29) with a history of concurrent alcohol and marijuana use were studied in a clinical research ward for thirty-four days. Subjects could earn money (50 cents) or marijuana (a 1 g cigarette) by working at a simple operant task on a fixed interval one-second schedule of reinforcement for thirty minutes. Alcohol (30 ml) was available as wine, beer, or distilled spirits for fifteen minutes of operant work.

Fourteen of the sixteen subjects drank less alcohol when marijuana was concurrently available ($P<.01$), and alcohol consumption remained depressed throughout this period. Within-subject analysis showed that seven subjects drank significantly less alcohol ($P<.05$) in comparison to the period when only alcohol was available. Trend analysis of group data indicated a progressive increase in marijuana smoking over the fifteen days when marijuana was available ($P<.001$). Twelve subjects smoked slightly more marijuana when alcohol was also available ($P<.05$), and the magnitude of the increase was significant in two instances. Only two subjects increased consumption of both alcohol and marijuana during the concurrent access condition. Although alcohol and marijuana were usually used together, there were no instances of adverse reactions or other evidence of toxic drug interactions.

Temporal patterns of operant work were similar across conditions. Subjects worked at the operant task more than nine hours each day and earned an equivalent number of purchase points during alcohol, marijuana, and concurrent drug use. All subjects earned more points for money than for drugs. Heavy drinkers earned fewer total purchase points throughout the study than moderate or light drinkers ($P<.05$). The total number of purchase points earned by the entire group tended to decrease over the course of the study ($P<.025$).

The data obtained were not consistent with the hypothesis that simultaneous availability of marijuana and alcohol will lead to significant increase in use of both drugs. Rather, marijuana use tends to increase through time, independently of concurrent

alcohol availability. Alcohol consumption decreases when marijuana is also available. (JAM)

32 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-D1207

DISULFIRAM IN THE TREATMENT OF ALCOHOLISM: A REVIEW, J. Kwentus; L.F. Major, Journal of Studies on Alcohol, v40 n5 p428-46 (1979)

This report reviews the complex pharmacological and psychological parameters that must be considered in the use of disulfiram, a drug often used in the treatment of alcoholism. Although most alcohol-disulfiram reactions are not serious, a certain number of patients will develop a shock-like syndrome. In a few patients, a dangerous delayed reaction may develop. This reaction can produce vasodilation, hypotension, and ECG changes. Other complications of therapy include hemiplegia, myocardial infarction, esophageal rupture, and death.

Disulfiram also has been found to have significant effects on the central nervous system. Side effects include fatigue, morning drowsiness, inability to rise, seizures, disturbed EEGs, and most significantly, development of psychosis in some patients.

Since disulfiram is an inhibitor of many enzymes, it has the capability of either altering the effect or interfering with the metabolism of many common drugs, especially medications which contain alcohol.

This report also discusses strategies of disulfiram administration and the physical and psychological consequences of treatment. Although the strategy of administration is a crucial factor in successful disulfiram therapy, the proper choice of patients is also important. Patients who are prone to depression, who are fairly young, or who have had a rapid progression of their alcoholism are poor risks. (HSRI)

112 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Unclassified Agents: disulfiram. Review. Review: Drug Effects.

UM-79-D1208

INFORMATION CONCERNING DRUGS AND DRIVING RECEIVED BY CUSTOMERS OF PHARMACIES, M. Maki; M. Linnoila; J. Idanpaan-Heikkila; J. Isomeri, Accident Analysis and Prevention, v11 n2 p117-24 (Jun 1979)

This epidemiological study attempted to determine the prevalence of the use of various drugs having the potential to impair driving skills among drivers purchasing drugs in pharmacies in Finland. Patterns of alcohol use within the sample and the relative number of accidents among drivers purchasing various drugs were also studied. In the first part of this study, pharmacists recorded prescription and over-the-counter drugs bought by their customers. In addition, 1,942 questionnaires were completed by oral prescription drug customers assessing whether they possessed a driver's license and whether their physician had informed them concerning the effects of their drugs on driving skills. In the second part of the study 984 pharmacy customers were asked about their possession of a driver's license, their use of drugs, consumption of alcohol, and whether their physician had informed them concerning drug side effects and the possible interaction of their drugs with driving.

In urban areas, the combined use of alcohol and drugs was associated with an increased involvement in traffic accidents. Results of this study also indicated that about 60% of pharmacists' customers having a driver's license purchased drugs which may have deleterious effects on driving skills. Only 20% of these subjects had received information concerning drugs and driving from their physicians. The authors believe that the large number of subjects uncertain whether they received such information reflects insufficient communication between physicians and patients. They suggest that information concerning drugs and driving and general side-effect information be distributed by pharmacies to their customers. (HSRI)

12 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Epidemiology: Record-Based Survey. Epidemiology: Regional or Local Survey of Drug Use Patterns. Epidemiology: Self-Reported Drug Use by Drivers.

UM-78-D1209

EFFECTS OF TERFENADINE AND DIPHENHYDRAMINE ALONE OR IN COMBINATION WITH DIAZEPAM OR ALCOHOL ON PSYCHOMOTOR PERFORMANCE AND SUBJECTIVE FEELINGS, L. Moser; K.J. Huther; J. Koch-Weser; P.V. Lundt, European Journal of Clinical Pharmacology, v14 n6 p417-23 (18 Dec 1978)

Terfenadine, a new histamine H-receptor antagonist, has been found to be free of central nervous system side effects in pharmacological, toxicological, and clinical studies. To evaluate further the lack of action of terfenadine on the central nervous system, this study compared the effects of single oral doses of terfenadine, diphenhydramine, and placebo, alone and in combination with diazepam or alcohol, on psychomotor skills and subjective feelings.

Twenty normal healthy male volunteers aged 21 to 29 years were tested in three sessions. In session I subjects received one of the following treatments: placebo; 100 mg diphenhydramine; 60 mg terfenadine; 120 mg terfenadine; or 240 mg terfenadine. In session II, the drug treatments were: 10 mg diazepam plus placebo; 10 mg diazepam plus 100 mg diphenhydramine; or 10 mg diazepam plus 120 mg terfenadine. In session III, treatment consisted of placebo plus 0.75g/kg alcohol; 100 mg diphenhydramine plus 0.75 g/kg alcohol; or 120 mg terfenadine plus 0.75g/kg alcohol, all alcohol being given one hour after drug administration.

Testing took place before and two and four hours after drug administration. Psychomotor performance was assessed by the Vienna Determination Apparatus, the Vienna Reaction Apparatus, the Ball Cylinder Test, critical flicker frequency, letter tachyscope, and an alertness test. Subjective feelings were also assessed.

Results showed that terfenadine at doses of 60, 120, and 240 mg had no effect on psychomotor skills and subjective feelings. Terfenadine (120 mg) did not influence the adverse effects of oral diazepam (10 mg) or of alcohol (0.75 g/kg) on psychomotor performance and subjective feelings. In contrast, diphenhydramine (100 mg) significantly enhanced these effects of diazepam and alcohol.

The authors conclude that this study confirms the failure of terfenadine to impair psychomotor performance or adversely affect subjective feelings. (HSRI)

34 refs

KEYWORDS: Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-79-D1210

EFFECTS OF ATENOLOL AND PROPRANOLOL ON HUMAN PERFORMANCE AND SUBJECTIVE FEELINGS, A.A. Landauer; D.A. Pocock; F.W. Prott, Psychopharmacology, v60 n2 p211-15 (1979)

The experiment described here had several purposes: (1) to determine psychological and behavioral effects during periods of moderate plasma concentration of atenolol and low plasma concentration of propranolol; (2) to determine changes in subjective self-ratings after administration of atenolol and propranolol; and (3) to compare the effects of atenolol and propranolol on heart rate and blood pressure.

In a double-blind, double crossover experiment, eighteen healthy male volunteers aged 18 to 33 received over three-day periods either 100 mg atenolol, 80 mg propranolol, or placebo. Eighteen hours after the last dose had been taken, subjects underwent various motor and cognitive tests which assessed concentration, digit substitution ability, tracking ability, sustained attention (by use of a driving simulator), peripheral vision, choice reaction, short-term memory, critical flicker fusion, blood pressure, and pulse. Four questionnaires were also administered which assessed subjective feelings, health, and mood.

Results of the tests show that propranolol significantly increases variability of a choice reaction-time task. Scores on various subjective rating scales show that propranolol had a larger mood elevating effect than atenolol. Heart rate and blood

pressure were significantly reduced twenty-four hours after atenolol medication; these effects were absent or reduced after propranolol medication.

The authors conclude that the variance of response time after propranolol ingestion is a typical effect and is indicative of behavioral impairment: subjects are at some times slower in responding while at other times they compensate for their delay. The general absence of subjective effects after atenolol administration even when plasma levels are high indicates that this drug has far fewer central effects than does propranolol. (HSRI)

17 refs

KEYWORDS: Anti-Anginal Agents: propranolol. Anti-Arrhythmia Agents: propranolol. Hypotensive (Antihypertensive) Agents: propranolol. Sympatholytic (Adrenergic Blocking) Agents: atenolol. Driving Simulator. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Physiological Testing. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-79-D1211

ALCOHOL-DRUG INTERACTIONS, FDA Drug Bulletin, v9 n2 p10-12 (Jun 1979)

This article reviews interactions between alcohol and several classes of widely prescribed drugs. Drug classes discussed include analgesics, antialcohol preparations, antianginal and antihypertensive agents, anticoagulants, anticonvulsants, antidepressants, stimulants, antihistamines, antidiabetic agents, antibiotics, barbiturates, minor tranquilizers, major tranquilizers, and narcotics.

Also included in the article is the Surgeon General's Advisory concerning drug-alcohol interactions. This advisory urges medical professionals to pay greater attention to the possible dangers of prescribing certain drugs, many of them widely used, to alcohol users. One of these dangers is impairment of driving skills. The frequent combined use of minor tranquilizers and other central nervous system depressants with alcohol may impair performance of tasks requiring alertness such as driving, thereby increasing the likelihood of injury and even death. (HSRI)

24 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Analgesics and Antipyretics. Anti-Anginal Agents. Anti-Coagulants. Antibiotics. Anticonvulsants (Anti-Epileptics). Antidepressants. Antihistamine Agents. Barbiturates. Hypotensive (Antihypertensive) Agents. Insulins and Anti-Diabetic Agents. Opiates and Related Agents. Stimulants. Tranquilizers. Review: Drug Effects.

UM-79-D1212

DRUGS, ALCOHOL AND DRIVING, T. Seppala; M. Linnoila; M.J. Mattila, Drugs, v17 p389-408 (1979)

This article reviews the potential effects of drugs and alcohol on driving skills and driving behavior by discussing available data from both epidemiological and laboratory studies. It also discusses the limitations and methodological difficulties of these studies.

Alcohol is the most common single cause of traffic accidents. A progressively increased risk with increasing blood alcohol levels is well documented: fatigue and drugs increase this risk. Drugs are related much more infrequently to traffic accidents, although on the basis of statistics, there is a potential risk with drug use. However, drugs alone are not as important as alcohol.

Drugs presenting the greatest risk of driving impairment are certain antianxiety agents, hypnotics, stimulants, hallucinogens, marijuana, lithium, narcotic analgesics, ganglionic blocking agents, insulin, and sulphonylurea derivatives. Patients should not drive after taking these drugs until they are objectively fully alert and capable. Anticholingerics, antihistamines, antidepressants, antipsychotics, phenylbutazone, indomethacin, a-methyldopa, and beta-blockers may in some cases cause central side effects such as drowsiness strong enough to affect driving performance. After starting therapy with these drugs or after a significant change in dose, driving should be avoided until it is known that unwanted effects do not occur. Psychotropic drugs may enhance the deleterious effect of alcohol, and with most hypnotics there is still an effect the next morning.

Some drugs, for example anticonvulsants or antiparkinsonian drugs, may make driving safer, but the disease (epilepsy, Parkinsonism, cardiovascular diseases, psychic disorders) often precludes driving. Clinicians should warn their patients about an impairment of driving skills if this is likely to occur due to the drug or the illness concerned. (JAM)

181 refs

KEYWORDS: Antidepressants: lithium. Cannabis Sativa L. and Related Agents: marijuana. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Other CNS Agents: lithium. Analgesics and Antipyretics. Anesthetics. Anti-Anginal Agents. Antibiotics. Anticonvulsants (Anti-Epileptics). Antidepressants. Antihistamine Agents. Hallucinogens and Related Agents. Hypotensive (Antihypertensive) Agents. Insulins and Anti-Diabetic Agents. Major Tranquilizers (Antipsychotics and Neuroleptics). Muscle Relaxants (Central). Parasympatholytic (Cholinergic Blocking) Agents. Sedatives and Hypnotic Agents. Stimulants. Review: Drug Effects. Review: Drugs and Highway Safety.

UM-79-D1213

MARIJUANA AND DRIVING: THE SOBERING TRUTH, P. Mann, Reader's Digest, v114 p106-110 (May 1979)

This brief article discusses the dangers of marijuana use while driving. Studies are cited and discussed which address the following issues: (1) How much does marijuana contribute to traffic accidents and fatalities? (2) How does marijuana affect driving abilities? (3) How long after use does marijuana continue to affect driving skills? (4) Do marijuana users recognize the dangers of driving while drug intoxicated?

The author concludes that the United States is both unaware of the impending marijuana highway crisis and unprepared for it. She suggests that state legislatures should immediately pass laws imposing a high fine or stiff penalty for possession of marijuana in any type of motor vehicle. Secondly, there must be a coordinated effort by governmental agencies, insurance companies, private groups, and especially high school and driver training instructors to provide educational programs that inform the public of the dangers of driving while marijuana intoxicated. Thirdly, brochures should be distributed to motorists from toll booths, gas stations, and garages. These measures can alleviate the problem until a roadside kit for testing THC levels is developed and laws based on drug levels are enacted. (HSRI)

0 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Review: Drugs and Highway Safety.

UM-79-D1214

DRIVING STONED, J.E. Rood, Driver, v12 n9 p1-8 (Feb 1979)

This nontechnical article discusses the effects of marijuana on psychomotor skills, perception, and driving behavior. It attempts to persuade its audience (primarily young people) of the dangers of driving while marijuana intoxicated. It is illustrated by cartoons and is based on epidemiological and experimental literature. (HSRI)

13 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Review: Drugs and Highway Safety.

UM-77-D1215

EFFECTS OF AMPHETAMINE ON SOCIAL BEHAVIORS OF RHESUS MACAQUES: AN ANIMAL MODEL OF PARANOIA, S. Haber; P.R. Barchas; J.D. Barchas, Animal Models in Psychiatry and Neurology, I. Hanin; E. Usdin, eds., p107-15, Oxford: Pergamon Press (1977)

Past studies have indicated that chronic use of amphetamine is capable of producing a paranoid syndrome, and that vulnerability to this amphetamine-induced paranoid syndrome is not limited to particular individuals. In view of the fact that amphetamine behaviors in animals are very similar to those in humans, this study attempted to develop an animal model of amphetamine-produced paranoia. It attempted to investigate

whether a perceptual system distorting danger and threat underlies paranoid behaviors, and whether chronic doses of amphetamine elicit species-specific behavior in the primate which are consistent with perception of a threat in his environment.

The behavior of ten rhesus monkeys was studied before and during amphetamine administration (0.1 mg/kg daily). Results of the observation showed that amphetamine administration caused a significant decrease in the time spent eating, huddling, and sleeping. The most dramatic result was the great increase of agonistic encounters. The dominant animals of the colony, especially, increased their threatening.

The authors conclude that three major amphetamine-induced alterations in the behavior of the monkeys were clearly compatible with those reported in humans. First, a monkey treated with amphetamine appears more tense in posture and shows an increased orientation to noises and movements of other animals. Secondly, the animal increases his association with one member of the colony and isolates himself from remaining members. Finally, consistent with his behavior patterns but inappropriate to the cues of his environment, the animal displays marked increases in agonistic behaviors. Each of these changes may be interpreted as consistent with a distorted perception of threat or danger in a neutral environment. This evidence suggests that amphetamine administration coupled with ethological methods provides a means to elicit and observe an animal analogue of a fundamental feature of human paranoia. (HSRI)

19 refs

KEYWORDS: Stimulants: amphetamine. Animal Research. Experimentation: Chronic Dosage Study.

UM-74-D1216

METAKVALON--HISTORIEN OM ETT SOMNMEDEL [METHAQUALONE--REPORT ON A SEDATIVE], G. Alvan; B. Holmstedt; J. Lindgren, Lakartidningen, v71 n40 p3777-80 (1974)

This article describes analytical tests of methaqualone and discusses its pharmacokinetics. After single oral doses to volunteers, the plasma disposition could be interpreted according to a two-compartment open model. The terminal log linear elimination phase had a half-life of twenty to forty-two hours in five investigated subjects. The administration of methaqualone to three subjects once every night for sixteen days produced equilibrium concentrations, as implied by the half-life of the drug.

Steady state levels are discussed in relation to the case of a man accused of driving under the influence of methaqualone. Unspecific analysis revealed a high concentration of the drug. The man stated that he had taken no more tablets than had been prescribed by his doctor. He had been using methaqualone regularly against insomnia for two to three months.

The plasma concentrations determined may well reflect equilibrium concentrations of multiple doses. It has been found that ultraviolet spectrophotometry gives much higher and varying concentration values than a specific gas chromatographic assay. (JA)

20 refs

KEYWORDS: Nonbarbiturates: methaqualone*. Drug Concentrations in Body Fluids: Chronic Dose Study. Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-80-D1217

ACCIDENT RECORDS OF SELF-REPORTING MEDICALLY IMPAIRED DRIVERS, M.K. Janke, Sacramento, Ca.: Department of Motor Vehicles (Feb 1980)

In this study a comparison was made between the accident records of drivers reporting themselves on the California license application form as having some physical or mental impairment and the records of a random sample from the entire California driving population. For a six-and-one-half-month period from May 14, 1979 through December 31, 1979 all application forms for original or renewal licenses on which impairment was indicated were collected, resulting in a total sample of 579, 321 (55%) of which were men and 258 (45%) of which were women. The median age of the sample was 37.3 years. The accident records for these subjects for the three years prior to their application were determined and compared with the records of a randomly selected group of 12,436 drivers, 53% (6,579) of whom were men. Median age of the comparison sample was 37.8 years.

Analysis of the data showed that the medically impaired drivers had worse accident involvement records than the comparison group had. Of the 579 impaired drivers, the 276 who reported themselves as having had a recent lapse of consciousness had accident involvement even greater than that for the impaired group as a whole. This difference was statistically highly significant.

The author concludes that since drivers reporting their medical impairment on their application showed an accident-involvement rate higher than the rate of the general population, identification of such drivers by means of a medical impairment question on a license application has a beneficial traffic-safety effect and should be continued. (HSRI)

4 pages 2 refs

KEYWORDS: Epidemiology: Record-Based Survey.

UM-77-D1218

DRUG THERAPY FOR PATIENTS IN RENAL FAILURE [letter], W.R. Barclay, Journal of the American Medical Association, v237 n24 p2635 (13 Jun 1977)

This letter-to-the-editor informs the reader of three articles in Journal of American Medical Association that provide in tabular form information about drugs helpful to physicians treating patients with compromised renal function. These tables provide information about route of excretion, normal half-life, dosage intervals for varying degrees of renal failure, significant dialysis of the drug, and major toxic effects. This information is provided for antimicrobial agents, analgesics, antihistamines, narcotics, narcotic antagonists, sedatives, hypnotics, tranquilizers, cardiovascular drugs, antihypertensive agents, diuretic agents, and some miscellaneous drugs. These tables can be extremely helpful to the clinician, especially when the difference between a therapeutic level and a toxic level is small and the physician lacks the laboratory methods necessary to measure serum drug levels. (HSRI)

0 refs

KEYWORDS: Drug Concentrations in Body Fluids: Tabulated Data.

UM-78-D1219

LEAD AND HUMAN BEHAVIOUR, H.A. Waldron, Journal of Mental Deficiency Research, v22 pt 1 p69-78 (1978)

This article reviews the effects of lead ingestion on human behavior, particularly in children. The article discusses the following topics: the effects of lead in asymptomatic children; sequelae of clinical intoxication in children; lead and mental retardation; and epidemiological studies of blood lead levels.

Several conclusions are drawn from the research. There is little evidence that blood lead levels below about 2.0 micromol/liter cause any profound neuropsychiatric effects. With blood lead levels in excess of 3.0 miromol/liter, and particularly with prolonged exposure, neuropsychiatric effects are always evident, increasing in frequency the closer the child is towards developing clinical signs of obvious intoxication and encephalopathy. Any child who has symptoms which may be caused by lead absorption obviously needs treatment even if his blood lead value is not markedly elevated. Mentally retarded children are very likely to ingest lead from their surroundings and elevate their blood lead concentration.

The author concludes that there is a need to investigate the possibility that intrauterine exposure to lead may be causally related to the development of mental retardation. It is also necessary to begin epidemiological research in order to establish whether blood levels below 2.0 micro mol/l are hazardous or not. (HSRI)

42 refs

KEYWORDS: Heavy Metals and Heavy Metal Antagonists: lead*. Review: Drug Concentration-Effect Relationships. Review: Drug Effects.

UM-70-D1220

A COMPARATIVE STUDY OF PSYCHOMOTOR EFFECTS OF INTRAVENOUS AGENTS USED IN DENTISTRY, M.G. Newman; N. Trieger; W.J. Loskota; A.W. Jacobs, Oral Surgery, Oral Medicine and Oral Pathology, v30 n1 p34-40 (Jul 1970)

In this study, four sedative agents administered intravenously were studied for their effects on sixty dental patients scheduled for molar extractions. It also attempted to demonstrate the usefulness of a new test. Each patient was randomly assigned to one of six drug groups: (I) 2.5 ml lidocaine (control group); (II) 79.3 mg meperidine (mean dose); (III) 10.5 mg diazepam plus 54.5 mg meperidine; (IV) 52.8 mg hydroxyzine plus 63.9 mg meperidine; (V) 56.9 mg pentobarbital plus 69.4 mg meperidine; (VI) 132.2 mg methohexital plus 38.2 mg meperidine plus 53.5 mg hydroxyzine. Before drug administration, immediately following the operation, and upon discharge, subjects took the Trieger test, a modified Bender Motor Gestalt Test. This test requires subjects to connect dots in a figure and measures recovery from anesthesia since it demands fine motor coordination and perception, two behaviors affected by depressant drugs.

The results of the tests for each drug group were as follows: (1) Groups I and II had no significant changes in performance. Recovery times from anesthesia were less than five minutes for both groups. (2) Groups III and IV showed a minor impairment of performance. Recovery times were 60 and 75 minutes, respectively. (3) Group V showed a moderate effect on performance, and recovery time was 85 minutes. (4) Group VI showed profound impairment of performance. Recovery time was 80 minutes.

The authors conclude that the Trieger test is a valuable tool for measuring recovery from general anesthesia in patients in ambulatory offices and clinics. (HSRI)

6 refs

KEYWORDS: Anti-Arrhythmia Agents: lidocaine. Antihistamine Agents: hydroxyzine. Barbiturates: methohexital. pentobarbital. Local Anesthetics: lidocaine. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. hydroxyzine. Muscle Relaxants (Central): diazepam. Nonbarbiturates: hydroxyzine. Opiates and Related Agents: pethidine. Clinical Study. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests.

UM-79-D1221

MEDICAL COMPLICATIONS OF DRUG ABUSE, C.E. Becker, Advances in Internal Medicine, v24 p183-202 (1979)

The purpose of this chapter is to discuss how drugs cause medical complications and to stress the importance of the physical examination for clues to drug abuse behavior. Special emphasis is given to more recently recognized complications of drug abuse. The medical complications of drug abuse affect almost all organ systems, and may result acutely from overdose or may not become apparent until after prolonged or recurrent use. Special emphasis has been placed on recognizing the key points of the physical examination in the overdose setting and in the driving patient using drugs that will give clues as to the nature and degree of the drug abuse. It is not clear whether drug abuse causes behavioral problems or vice versa. Special attention is called to several drug abuse problems: complications associated with phencyclidine, amyl nitrate, and layman's remedies; acute and pulmonary complications; rhabdomyolysis; the brown heroin syndrome; and methylphenidate abuse. (HSRI)

45 refs

KEYWORDS: Review: Drug Effects.

UM-78-D1222

KOLA NUT AND ROAD TRAFFIC ACCIDENTS IN NIGERIA [letter], S.E. Asogwa, American Journal of Public Health, v68 n12 p1228-9 (December 1978)

This letter to the editor discusses road traffic accident rates in Nigeria, which are higher than those in both the industrialized and developing countries of the world. It is suggested in this letter that the extensive use of kola nut as a stimulant by drivers, especially those traveling long distances, is a significant factor in the toll on Nigerian roads. An inquiry of 555 drivers involved in road accidents in Nigeria showed that while 7.74% admitted having drunk alcohol, 12.25% had eaten kola nut, a

stimulant and appetite depressant. The author stresses the need for investigation of the interaction of kola nuts with alcohol and other drugs. (HSRI)

12 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: kola. Epidemiology: Self-Reported Drug Use by Drivers.

UM-77-D1223

LITHIUM AS A DRUG OF ABUSE [letter], B. Lipkin, British Medical Journal, v1 n6073 p1411-2 (28 May 1977)

The purpose of this letter is to alert the reader to the increasing abuse of lithium and serious consequences of the ingestion of large amounts of lithium in any form whatsoever. It warns all doctors that in a case of lithium intoxication a sodium-depletive diuretic is contraindicated. It is advised to induce an osmotic diureses by an intravenous infusion of one-sixth molar lactate solution for treatment of lithium intoxication. (HSRI)

1 ref

KEYWORDS: Antidepressants: lithium. Other CNS Agents: lithium. Review: Drug Use.

UM-76-D1224

ACUTE EFFECTS OF CANNABIS ON COGNITIVE, PERCEPTUAL, AND MOTOR PERFORMANCE IN CHRONIC HASHISH USERS, R. L. Dornbush, A. Kokkevi, Annals of the New York Academy of Sciences, v282 p313-22 (1976)

This study investigated and compared the acute effects of various cannabis preparations on mental functioning in American short-term users of marijuana and Greek long-term hashish users in order to better understand long-term effects of cannabis. Twenty Greek subjects with an average of 25.8 years of hashish use received five cannabis preparations on five different days. These preparations consisted of the following: (1) 0 mg delta-9-THC; (2) 78 mg of American delta-9-THC; (3) 90 mg delta-9-THC (Greek hashish); (4) 100 mg delta-9-THC (liquid); and (5) 180 mg of delta-9-THC (Greek hashish). Psychological tests were administered thirty and seventy minutes postdrug. These tests assessed memory, alertness, time sense, mental coordination, and motor performance.

There was no simple dose-response relationship for cannabis substances in the tasks on which there was a drug effect. Hashish (180 mg), with the largest quantity of THC, usually resulted in the greatest impairment. Assays of American marijuana and Greek hashish indicated that marijuana contained less cannabidiol and cannabinoids than did hashish. Therefore marijuana may represent a qualitatively different and new substance for Greek subjects, which might explain the absence of predictable dose-response effects.

The authors conclude that after an average of 25.8 years of cannabis use, Greek subjects evidenced a similar pattern response on these tests of mental functioning after administration of doses that ranged from 78 to 180 mg of delta-9-THC as did American short-term users who consumed up to 25 mg of THC. Performance on simple tasks such as digit span was unaffected, while performance on more complex tasks such as time estimation was impaired. Therefore, the heavy long-term use of cannabis does not appear to qualitatively change the general patterns of response in acute use that are exhibited by occasional short-term users. (HSRI)

25 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. hashish. marijuana. Experimentation: Dose-Effect Study. Other Factors Influencing Drug Effects.

UM-78-D1225

THE EFFECT OF LITHIUM AND OTHER IONS ON AGGRESSIVE BEHAVIOR, M. H. Sheard, Modern Problems in Pharmacopsychiatry, v13 p53-68 (1978)

Presented here is a review of the effects of lithium and other ions on aggressive behavior. A study of human clinical studies and animal models of aggressive behavior

reveals that lithium can inhibit many types of aggressive behavior. An examination of the evidence suggests that the antiaggressive action of lithium is not due to toxic, motor, sensory, placebo, or endocrine effects. Moreover, it is not due entirely to atypical manic-depressive psychosis. It may be, on the other hand, that a common constitutional background with a possible genetic basis becomes manifest in several different forms. For example, an uncontrolled, easily aggravated, impulsive individual given to chronic episodic patterns of behavioral oppression is one possibility. Another is the classic manic-depressive disorder. (JAM)

63 refs

KEYWORDS: Antidepressants: lithium. Other CNS Agents: lithium. Review: Drug Effects.

UM-72-D1226

ABBOTT-35616 (TRANXENE) DEVELOPMENTAL STUDY: SIMULATED AUTO DRIVING, V. S. Ellingstad; D. L. Struckman; F. U. Sebring, Vermillion, South Dakota: Human Factors Laboratory, University of South Dakota (October 1972)

This investigation examined the effects of Abbott-35616 (Tranxene(R)) and diazepam on selected elements of the driving task and compared these effects with a control or no-drug condition. Subjects were thirteen male and sixteen female volunteers between the ages of 18 and 59. All were chronically anxious, but were not taking any central nervous system drugs at the time of the experiment.

Nine subjects were treated with Abbott-35616 (Tranxene(R)), ten subjects were treated with diazepam, and ten subjects were treated with a placebo preparation. All subjects were tested on a driving performance battery before and after treatment. The battery included a driving simulation task, a film passing simulation task, and a choice reaction time task.

Results indicated no differences in performance between groups on the driving simulation task and the passing simulation task, but a significant difference in the groups for the choice reaction time task. Both the placebo treatment group and the Tranxene(R) treatment group showed a slight decrease in reaction time, whereas the diazepam treatment group showed a significant increase in reaction time. The results of the study are considered to be a first step in the area of determining effects of psychotropic drugs on driver behavior, and further research is suggested. (JAM)

9 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): clorazepate. diazepam. Muscle Relaxants (Central): diazepam. Driving Simulator. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychomotor Tests.

UM-77-D1227

DRIVERS IN ALBERTA WITH PREVIOUS IMPAIRED DRIVING RECORDS RESPONSIBLE FOR FATAL HIGHWAY ACCIDENTS: A SURVEY, 1970-1972, G. Bako: W.C. Mackenzie; E.S.O. Smith, Canadian Journal of Public Health, v68 n2 p106-10 (Mar-Apr 1977)

This paper presents survey data which reveal the seriousness of recidivism (role of recurrent offenders) in road safety. The survey discussed here presents convincing evidence for the need of immediate measures to curb this factor in traffic risk.

This survey of highway accidents is based on data collected from the files of the Chief Coroner of Alberta. Using the epidemiological approach, 64 variables were coded for each person killed in a motor vehicle crash and for all culpable drivers who survived the accident. 742 of the 854 culpable drivers were investigated for previous records of impaired driving.

11.1% of Alberta drivers found to be responsible for fatal crashes had previous records for impaired driving and had been charged one or more times before the fatal crash. 87% of tested recidivists were again legally impaired at the time of the accident. 112 persons were killed in crashes caused by recidivist drivers, mostly in head on collisions with other motor vehicles and in run-off road and overturn crashes.

47 of the 82 investigated recidivist drivers survived the fatal accident and are probably still driving on the highways in addition to the large group of recidivists who have not yet been involved in a fatal crash. The magnitude of the risk to highway

safety created by recidivist drivers should be of great concern to legislators and highway authorities. (HSRI)

6 refs

KEYWORDS: Crash Investigation.

UM-74-D1228

THE ROLE OF THE DRINKING DRIVER IN TRAFFIC ACCIDENTS (THE GRAND RAPIDS STUDY), R.F. Borkenstein; R.F. Crowther; R.P. Shumate et al., Blutalkohol, v11 suppl p1-131 (1974)

Presented here is a description of an in-depth epidemiological survey of the role of the drinking driver in traffic accidents. The paper discusses the objectives, philosophy, methodology, results, and conclusions of the well-known Grand Rapids survey. The study found that blood alcohol concentrations (BACs) over 0.04% are definitely associated with an increased accident rate. The probability of accident involvement increases rapidly at BACs over 0.08% and becomes extremely high at BACs over 0.15%. When drivers with BACs over 0.08% have accidents, they tend to have more single-vehicle accidents, more severe accidents (in terms of injury and damage), and more expensive accidents than sober drivers. BACs of 0.04% and below apparently are not inconsistent with traffic safety.

Many factors other than alcohol are related to the probability of accident involvement. The driver classes with the worst accident experience, in addition to the alcohol-impaired, are the young or very old, the inexperienced, and those with less formal education. Persons with the most education, those with better jobs, and the middle-aged have better than average accident experience. The effects of alcohol are consistent within the various socioeconomic classes considered. High BACs are always associated with bad accident experience. At the higher BACs, the difference in the accident potential between the various classes of drivers is unimportant.

An important aspect of the applied survey technique is that it is adaptable to assessing the effect of various policies directed at the drinking driver. Drinking and driving is clearly associated with the frequent use or abuse of alcohol. Many drivers overestimate the number of drinks that it is safe to have before driving. The tendency to drive after drinking is related significantly to the socioeconomic categories appearing most frequently in the drinking driver class. (JAM)

25 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Crash Investigation. Epidemiology: Analysis of Driver Body Fluids for Drugs. Epidemiology: Self-Reported Drug Use by Drivers.

UM-79-D1229

TRAFFIC FATALITIES IN LUSAKA, ZAMBIA, N.S. Patel, Medicine Science and the Law, v19 n1 p61-5 (1979)

From January 1, 1974 to December 31, 1976 a total of 1,746 medicolegal postmortems were done by the Department of Forensic Medicine, University Teaching Hospital, of Lusaka, Zambia Out of these 630 (36%) were traffic fatalities -- 516 (82%) were males and 114 (18%) were females. More than half of the victims -- 375 (59.5%) -- were between twenty--one and forty years of age; 292 (46%) were pedestrians; 121 (19%) were drivers; 173 (27%) were passengers; and 44 (7%) were on two-wheelers. 201 (40%) accidents occurred between 18.00 and 24.00 hours; 131 (21%) occurred between 12.00 and 18.00 hours. 418 (65%) victims died on the spot, 18 (3%) died on the way to the hospitals, and 127 (20%) died within 24 hours of the accident. 407 (65%) had chest injuries, 301 (47%) had head injuries, 233 (37%) had abdominal injuries, and 220 (35%) received injuries to the limbs. Of 121 drivers, 43 (35.5%) died due to chest injuries (steering wheel impact injuries) and out of 292 pedestrians, 49 (17%) died of head injuries only. 107 (64.5%) pedestrians, 61 (66%) drivers, 64 (56%) passengers, and 15 (52%) on two-wheelers were under the influence of alcohol at the time of the accident. 95 (57%) pedestrians, 52 (56.5%) drivers, 46 (40%) passengers, and 12 (41%) two-wheeler drivers had more than 100 mg% of alcohol in their blood. 427 (68%) died of head injuries, 55 (9%) died of chest injuries, 27 (4%) died of injuries to the abdomen, and the other 44 (7%) died of complications. (JAM)

13 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Crash Investigation.

UM-76-D1230

SURVEY OF IMPAIRED DRIVERS, FATALLY INJURED OR SURVIVING, WHO CAUSED FATAL HIGHWAY ACCIDENTS IN ALBERTA IN 1970-72, G. Bako; W.C. Mackenzie; E.S.O. Smith, Canadian Medical Association Journal, v115 n9 p856-7 (6 Nov 1976)

Reported here are the results of a survey of impaired drivers who caused fatal highway accidents in Alberta from 1970 to 1972. 456 (53.4%) of 854 drivers responsible for a motor vehicle accident in which either they or other persons were killed had been drinking beforehand. Of surviving culpable drivers tested for blood alcohol concentration. Only 24.8% of these drivers were tested with a blood alcohol test. 81.7% of these 99 tested were found to be legally impaired. 233 (51.3%) of the fatally injured drivers were tested. Because surviving culpable drivers pose a possible future hazard to highway safety, it is important that data on this group be collected and analyzed. Data on survivors may be helpful in establishing a more realistic account of the accident situation.

The author concludes that such data may indicate that alcohol-related fatal accidents may be more frequent than is recognized from fatality statistics alone. (JAM)

2 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Crash Investigation. Epidemiology: Record-Based Survey.

UM-78-D1231

PRESCRIPTION DRUGS, ALCOHOL, AND ROAD FATALITIES [LETTER], A.W. Missen; W.T. Cleary; K.S. McDonald, New Zealand Medical Journal, v88 n624 p418-9 (22 Nov 1978)

This letter concerns analyses of 302 blood samples taken from fatally injured road users between April 1977 and March 1978. Drugs were identified in 15 cases while alcohol was detected in 185 cases. Methods used did not detect the illicit drugs (with the exception of methadone). The identified drugs were diazepam, phenylbutazone, analgesic diphenylhydantoin, and primidone, all taken with alcohol. Only quinine and amitriptyline were found in two pedestrians who had zero blood alcohol levels.

In conclusion, prescription drugs play, at present, a minor role in New Zealand road fatalities. The major role is still played by alcohol. (HSRI)

0 refs

KEYWORDS: Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-79-D1232

MINOR TRANQUILLISERS INCREASE THE RISK OF A SERIOUS ROAD ACCIDENT, D.C.G. Skegg, British Medical Journal, v1 n917 (7 Apr 1979)

There was a highly significant association between use of minor tranquilizer and the risk of a serious road accident (relative risk estimate 4.9) in a prospective study of 43,117 people registered with sixteen general practitioners over a two-year period. Prescriptions issued during that time were linked with records of hospital admissions and deaths. The medicines dispensed to fifty-seven people injured or killed while driving cars, motorcycles, or bicycles in the three months prior to their accident were compared to medicines dispensed to 1,425 matched controls.

Eleven percent of the fifty-seven fatally injured drivers had received a sedative or tranquilizer during the three months before the accident in contrast to 2.5% of the controls. The relative risk associated with use of sedatives and tranquilizers was estimated as 5.2. Five drivers had received minor tranquilizers such as benzodiazepines. The relative risk associated with their use was estimated as 4.9. It is not yet known whether the increased risk associated with tranquilizers is due to the effects of the drugs themselves or the conditions being treated. Nevertheless, patients given tranquilizers should at least be warned that they are at special risk. (JAM)

0 refs

KEYWORDS: Tranquilizers. Epidemiology: Record-Based Survey.

UM-79-D1233

CLASSIFICATION OF MEN ARRESTED FOR DRIVING WHILE INTOXICATED, AND TREATMENT IMPLICATIONS, R.A. Steer; E.W. Fine; P.E. Scoles, Journal of Studies on Alcohol, v40 n3 p222-9 (1979)

This study attempted to identify by cluster analysis the patterns of alcohol impairment and neuroticism in a sample of 1,500 men arrested for DWI in Philadelphia. The study also attempted to differentiate types of offenders according to psychosocial characteristics and drinking histories and to suggest how distinct types of DWI offenders could be treated in the existing judicial, educational, and clinical framework. Three subjective measures and one measure of psychoneuroticism were used for diagnosis: (1) the alcohol quantity-frequency index, which measures the amount of alcohol ingested in one day in any form; (2) a self-report of problems attributed to excessive drinking in the past month; (3) a Breathalyzer reading of blood alcohol concentration at the time of arrest; and (4) the Psychoneuroticism-Stability Scale of the Eysenck Personality Inventory.

The results of the clustering indicated that there were seven predominant types of male DWI offenders. These groups are described in terms of history of drug and alcohol use, race, family characteristics, and test scores. Treatment for each group is suggested. The finding that thirty-seven percent of the sample had levels of alcohol impairment and psychoneuroticism below the grand means of the variables may indicate (1) that a high proportion of the men were really social drinkers or, (2) that many of the men were disclaiming alcohol misuse or psychoneurotic symptoms. (HSRI)

11 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Epidemiology: Analysis of Driver Body Fluids for Drugs. Epidemiology: Self-Reported Drug Use by Drivers.

UM-79-D1234

ALCOHOL--SOCIAL, MEDICAL AND LEGAL ASPECTS OF ITS USE, Lectures on Forensic Medicine and Pathology 3rd ed., V.D. Plueckhahn, p261-84, Melbourne: University of Melbourne (1979)

Presented here is a review of social, medical, and legal aspects of alcohol use in Australia. Statistics are provided for Australian consumption of alcohol, number of alcoholics, deaths directly attributable to alcohol from 1965 to 1974, and traffic accidents in which alcohol was involved. Australian state laws concerning the use of motor vehicles by persons who have consumed alcohol or drugs are discussed, and means of ascertaining BAC are described including screening tests, breath analysis tests, blood tests, and urine analysis. Alcohol effects on driving skills are discussed, as well as the relationship between BAC and accident risk.

Also discussed is the role of drug use in traffic accidents. The author contends that although the effects of drugs on the skills used in driving are not nearly as well documented as are those of alcohol, definite scientific evidence exists indicating that a wide variety of drugs, including both prescription and illegal drugs, can considerably impair the skills necessary for safe driving, especially when combined with alcohol. Studies have shown that up to 15% of accident-involved drivers have either taken a medically prescribed psychotropic or an illegally obtained hallucinatory drug alone or in combination with alcohol prior to driving.

Research indicates that cannabis use, too, is positively associated with the road toll. In both controlled laboratory studies and closed course driving studies marijuana has been shown to adversely affect perception, coordination, braking time, mood, and judgment, as well as other skills and factors related to driving. At this point in time the degree to which marijuana is involved in traffic accidents can not be determined; however, marijuana does appear to be a causative factor, especially when combined with alcohol. (HSRI)

24 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Review: Drug Concentration-Effect Relationships. Review: Drug Effects. Review: Drug Use. Review: Drugs and Highway Safety.

UM-78-D1235

MINNESOTA ALCOHOL AND TRAFFIC SAFETY PROGRAM, St. Paul, Minn.: Office of Traffic Safety (1978)

This report is an update of information related to the role of alcohol in traffic crashes in Minnesota. It is the third in a series first published in 1970 to provide legislators, professionals, and the general public with a comprehensive picture of this complex and serious traffic safety problem. Data are provided for drinking driver fatalities in the state, DWI clinics, liquor consumption in Minnesota, clinical testing programs, and the Hennepin County Alcohol Safety Action Project. Also discussed are the Minnesota DWI Statutes--their history, current status, and proposed legislation concerning the statutes.

A particular concern of the state of Minnesota is the increasing use of drugs by the driver, especially tranquilizers, narcotics, antihistamines, barbiturates, and amphetamines. These drugs, when taken with alcohol or in combination with each other, can produce a dangerous potentiating or synergistic effect. This report discusses the effects of these drugs on psychomotor skills related to driving. It also summarizes the Minnesota Statutes concerning the operation of a motor vehicle while under the influence of a narcotic drug or a controlled substance which impairs the ability to drive. Special attention is given to "Pharm 41," a rule set forth by the State Board of Pharmacy which states that drugs classified as controlled substances must be labelled with the following warning: "Caution: Taking this drug alone or with alcohol may impair your ability to drive." The authors believe that the promulgation of this rule is a significant step in educating the driving public on the potential hazards of certain prescription drugs. However, it is urgent that measures also be taken to warn the public about the danger of illicit drugs in traffic safety, especially marijuana. (HSRI)

Minnesota Department of Public Safety

66 pages 0 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Local Anesthetics: cocaine. Nonbarbiturates: ethanol (ethyl alcohol)*. Opiates and Related Agents: heroin. morphine. Stimulants: amphetamine. cocaine. Antihistamine Agents. Barbiturates. Tranquilizers. Other Sociolegal Study. Review: Drug Effects. Review: Drugs and Highway Safety.

SCNAC-96-1-7

UM-79-D1236

HEALTH CONSEQUENCES OF MARIHUANA ABUSE: RECENT FINDINGS. HEARINGS BEFORE THE SELECT COMMITTEE ON NARCOTICS ABUSE AND CONTROL, HOUSE OF REPRESENTATIVES. 96TH CONGRESS, 1ST SESSION. JULY 17 AND 19, 1979, Washington, D.C.: U.S. Government Printing Office (1979)

These hearings before the House Select Committee on Narcotics Abuse and Control focus on the potential health hazards of using marijuana and attempt to determine the extent, adequacy, and reliability of present knowledge about marijuana. Experts from various health fields address several aspects of health effects of marijuana use which include the following: the pharmacokinetics of marijuana; quantification and identification in body fluids; effects of cannabinoids on cellular metabolism, the lungs, and the reproductive system; effects on the brain and behavior; therapeutic uses such as treatment of glaucoma and asthma; embryotoxicity; effects when combined with alcohol; pulmonary and immune system effects; marijuana and driving; and psychological effects. From this testimony, eight major conclusions were drawn: (1) pregnant women should not use marijuana; (2) driving under the influence of marijuana can be hazardous; (3) young people should be discouraged from using the drug; (4) individuals with lung disease should avoid using marijuana because of its irritating effect; (5) people with heart disorders may be further impaired because of the increase in heart rate brought on by use of the drug; (6) preschizophrenic and schizophrenic people may develop or exacerbate a psychotic break in connection with the effects of THC; (7) infrequent use (less than once a week) will probably not result in ill effects in adults unless the smoker experiences one of the uncommon acute reactions; (8) the therapeutic potential of marijuana, particularly for the management of nausea and for wide-angle glaucoma, should be studied further.

Of special interest is the effect of marijuana on driving skills. Studies indicating impairment of driving skills are cited and discussed. Special attention is given to a study in which experienced pilots showed marked deterioration in performance under flight-simulated test conditions while intoxicated by marijuana. Driving after marijuana use is dangerous not only because skills and perception are impaired, but also

because the impairment can last for several hours and the driver is often unaware of the degree of impairment. (HSRI)

156 pages

KEYWORDS: Review: Drug Effects. Review: Drugs and Highway Safety.

UM-70-D1237

MARIJUANA--THE NEW PROHIBITION, J. Kaplan, New York: World Publishing (1970)

Presented here is a lengthy argument for the decriminalization of marijuana in the United States. The author believes that in view of increased knowledge concerning the effects of marijuana and more importantly, the enormous costs to society of the present marijuana law, the American public cannot delay facing the issue. The only responsible course of action within the framework of a democratic society is a liberalization of the marijuana law so extensive as to constitute an abandonment of primary reliance on criminal law in this area.

The book attempts to answer two major questions that must be faced by legislators in evaluating the present marijuana law: (1) what are the total social and financial costs attributable to the present law? and (2) what are its benefits? In attempting to answer these questions, the following aspects of marijuana are discussed: (1) benefits of the present marijuana laws; (2) the cost of marijuana laws in terms of effects upon offenders, costs of prosecuting offenders, and societal hostility directed at police; (3) the subjective and objective effects of the ordinary use of marijuana; (4) the extent to which marijuana causes its users to commit violent and aggressive crimes; (5) the types and degrees of harm that the drug may inflict upon its users; (6) the connection between the use of marijuana and the use of more dangerous drugs such as amphetamines, barbiturates, hallucinogens, and heroin; (7) an analysis of the similarities and differences between alcohol and marijuana; (8) alternatives to criminalization that would eliminate many of the costs of marijuana laws; and (9) obstacles to reaching a more rational solution of the marijuana problem.

The author contends that in spite of the fact that marijuana use may impair driving, its possible hazardous effects are no grounds for the criminalization of its use. The advocates of marijuana criminalization assume that alcohol and marijuana are equally dangerous, and justify their very different legal treatment on the grounds that there are presently no blood or urine tests for the driver under the influence of marijuana. It is probable, however, that alcohol is considerably more dangerous than marijuana for the automobile driver, especially when one considers how many traffic fatalities are due to alcoholism and not simply to social drinking.

The author concludes that the costs of marijuana laws far outweigh their benefits, and that a drastic change of approach is needed to avoid a national tragedy. (HSRI)

402 pages 40 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: hashish. marijuana. Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Other Sociolegal Study. Review: Drug Effects. Review: Drug Use.

UM-79-D1238

SOME RECENT ADVANCES IN THE STUDIES OF CANNABIS, G.B. Cheser; R. Malor; P. Scheelings, Research paper 6 (1979)

This review paper discusses the chemistry and general pharmacology of cannabis in animals and in man. Three major areas are discussed. Following a brief introduction discussing basic properties of delta-9-tetrahydrocannabinol (the major active substance in cannabis) and its pharmacological classification, the chemistry of cannabis is discussed. This section also discusses the botanical classification of cannabis and methods of identification and analysis of cannabinoids.

The next section evaluates recent world literature on the biochemistry of cannabis. Particular emphasis is placed on laboratory studies in experimental animals, especially those in vitro biochemical investigations which have been searching for clues to the mechanisms of action of the cannabinoids at cellular levels. Studies such as these pose particular difficulties, both methodological and interpretive, and the implications of these studies are discussed.

The final section deals with the clinical pharmacology of cannabis, that is, the recent literature on the effects of the drug in man. The problems and benefits of drug interactions, as well as recent experimental data on the effects of the drug on the endocrine system and the role of neurotransmitters are also addressed. (AAM)

142 pages 620 refs

Commission into the Non-Medical Use of Drugs, South Australia

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabichromene. cannabicyclol. cannabidiol. cannabielsoic acid. cannabigerol. cannabinol. delta-9-tetrahydrocannabinol. delta-9-trans-tetrahydrocannabinol. marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Pharmacokinetics: Acute Dose. Pharmacokinetics: Chronic Dose. Review: Drug Analysis Methodology. Review: Drug Concentration-Effect Relationships. Review: Drug Effects.

DOT-HS-801 267 UM-74-D1239

A PSYCHOSOCIAL ANALYSIS OF OPERATORS INVOLVED IN FATAL MOTOR VEHICLE ACCIDENTS. FINAL REPORT, R.S. Sterling-Smith, Springfield, Va.: National Technical Information Service (Nov 1974)

Presented here are preliminary results collected by the Boston Special Study Accident Investigation Team that has been researching motor vehicle accidents resulting in a fatality since September 1971. This report presents data from the first 175 cases of the total 300 cases to be studied concerning the human factors associated with the most responsible operators involved in fatal motor vehicle accidents. Each operator was investigated in depth from historical and focal perspectives; the empirical and clinical data were recorded using the Human Factor Index. Pathology reports, toxicity reports, probation and registry histories, reports of social and medical professionals, and media reports were used to collect 278 variables on each subject. This data included basic demographic information, psychosocial history, physical health history, alcohol and other drug use, legal and arrest history, and focal accident data.

Three dominant themes emerge from the findings of this study: (1) The operator who strikes and kills a pedestrian is very different from the operator who is responsible for a vehicular occupant fatality. He generally takes less risks, is better able to handle the effects of drugs and alcohol, and is less likely to have used drugs or alcohol before the accident. (2) Fatal motor vehicle operators who survive are younger, have more psychiatric problems, smoke more marijuana more frequently, and are more willing to take risks than either fatal motor vehicle operators who were killed or operators of a vehicle in which a pedestrian was killed. (3) It appears that the operator most likely to be involved in an alcohol-related fatal motor vehicle accident can be identified in advance by analyzing violation and accident records.

The author concludes that in spite of the large numbers of drivers who smoke marijuana, very little public research has been done to investigate the effects of marijuana intoxication on the operator of a motor vehicle. There is an urgent need for such research as well as for a method for determining the level of marijuana in a driver and the extent of impairment this level produces. (HSRI)

41 pages 4 refs

National Highway Traffic Safety Administration contract no. DOT-HS-310-3-595

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Epidemiology: Analysis of Driver Body Fluids for Drugs. Epidemiology: Record-Based Survey. Epidemiology: Self-Reported Drug Use by Drivers.

UM-78-D1240

TRAFFIC SAFETY AND THE LONG DISTANCE TRUCK DRIVER, D.R. Linklater, research report 8/78, New South Wales: Traffic Accident Research Unit, Department of Motor Transport (Oct 1978)

Reported here are the results of analysis of data from a survey comparing the driving records of truck drivers to those of other motorists on major New South Wales roadways during May 1976. This study particularly attempted to explain why long-distance truck drivers report experiencing more traffic crashes than do other motorists.

The study found that the outstanding difference between the two samples was the greater amount of time spent behind the wheel by truck drivers; this was found to be the most important predictor of traffic crash frequency. The long-distance truck driver is exposed or vulnerable to traffic crashes for longer periods of time than other motorists and thus is likely to experience more crashes. However, the long-distance truck driver in this survey reported having fewer crashes than other motorists sampled at the same time and general locations.

When the exposure factor was controlled, most other factors were shown to be unrelated to traffic crash frequency with the exception of age, which was found to be important in the crash prediction of the general population. Some evidence was found indicating that use of stimulants, while showing no direct relationship to crash frequency, could detract from the ability of truck drivers to interact safely with others in the traffic system. The significant relationships demonstrated between use of stimulants and both aggression and experiencing hallucinations suggest that drug users may be endangering both their own road safety and that of others.

The author concludes that further research into the practice of truck drivers to work excessively long hours is indicated. If truck drivers were to drive for less than fifty-five hours per week, driving fatigue and the need to use stimulants would likely be reduced below the critical level at which crash probability is increased. (AAM)

45 pages 22 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: amphetamine. Crash Investigation. Epidemiology: Record-Based Survey. Epidemiology: Self-Reported Drug Use by Drivers.

UM-79-D1241

TRUCK DRIVERS IN AMERICA, D.D. Wyckoff, Lexington, Mass.: Lexington Books (1979)

This chapter examines the reactions of truck drivers to the physically and emotionally demanding task of truck driving and their attempts to cope with these conditions. Of particular interest is their attitude toward and use of drugs and alcohol, both while driving and during leisure time. These data are based on responses to questionnaires from 9,630 truck drivers in the United States, as well as several personal interviews.

Although frequent use of various types of stimulants and pills to stay awake has commonly been reported by truck drivers in the past, the author concludes from the data collected that the heaviest use of drugs of all kinds is among drivers who regularly exceed the ten-hour driving limitation. Data show a slightly higher level of abstention from alcoholic beverages among truck drivers of all types. However, the willingness of drivers, particularly those under 25 years of age, to operate their trucks immediately after or within one hour of drinking shows a high potential for drunk driving among truck drivers.

Data also revealed that some use of marijuana and narcotics while driving does occur. Again, the greatest use of marijuana was among drivers under age 25. Among these drivers, 23% admitted to having used marijuana while driving, and 4.3% admitted regular use. Marijuana use by truck drivers while not driving appears to be comparable to that of the overall population.

Approximately 39% drivers under age 25 reported using amphetamines while driving, compared to about 28% of drivers 25 to 50 and 10% of drivers over 50. Narcotic use was seldom reported by drivers of any age.

In general, drivers carrying hazardous materials demonstrate better driver records and more closely adhere to safety regulations pertaining to hours of service and the use of drugs and alcohol. The author concludes that use of amphetamines presents the greatest hazard since their use is often coupled with abuse of the ten-hour driving limitation. (HSRI)

160 pages 12 refs

KEYWORDS: Ganglionic Blocking and Stimulating Agents: nicotine. Local Anesthetics: cocaine. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Stimulants: amphetamine. cocaine. nicotine. Opiates and Related Agents. Epidemiology: Self-Reported Drug Use by Drivers.

UM-79-D1242

CALIFORNIA RESEARCHES HAZARDS OF MARIJUANA AND DRIVING, V.C. Reeve. National Traffic Safety Newsletter, p14-16 (Nov-Dec 1979)

Since marijuana, even at low doses, impairs a wide variety of functions important to safe driving, an important objective of any traffic safety program should be to develop programs of controls, standards, and countermeasures that reduce the incidence of driving impairment caused by marijuana use. This paper summarizes the findings of a California Department of Justice study investigating the incidence of marijuana in a California impaired driving population and makes recommendations for similiar studies and road safety programs concerned with drugs.

Essential to a marijuana traffic safety program are reliable tests for delta-9-THC that can be used for small amounts of hemolyzed blood and are capable of processing at least 10,000 cases a year. Legislation allowing law enforcement officials to insist on blood samples from impaired drivers where breath demonstrates a low or no blood alcohol level is critical. There is also a critical need for roadside tests to screen out marijuana-impaired drivers from drivers impaired by other drugs or alcohol for special treatment and handling.

Also crucial to a successful marijuana countermeasure program is experimentation with human subjects to develop behavioral patterns and blood levels which correlate with driving performance. This is necessary for courtroom interpretation, being similar to blood alcohol limits. This driving experimentation should include the evaluation of the effects of marijuana in combination with ethyl alcohol and other drugs.

Also necessary is the establishment of greater confidentiality for human experimentation with a greater nondisclosure privilege in order to legally protect the volunteer human subjects who participate in driving experiments. Finally, educational programs are needed for both the public and the criminal justice system that would dramatically reinforce facts about the hazards of marijuana and driving. (HSRI)

0 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Review: Drug Use.

UM-78-D1243

ZUR WIRKUNG DES ANTIDEPRESSIVUMS VILOXAZIN AUF DAS HIRNELEKTRISCHE VERHALTEN UND DIE OPTIMIERUNG DES SYSTEMS FAHRER-FAHRZEUG-STRASSE [ON THE EFFECT OF THE ANTIDEPRESSANT VILOXAZIN ON EEG AND OPTIMIZATION OF THE SYSTEM DRIVER-VEHICLE-ROAD], D. Bente; P. Chenchanna; W. Scheuler; P. Sponagel, Arzneimittel Forschung, v28 n8 p1308-10 (1978)

The effects of a single dose of 100 mg 2-[(o-ethoxyphenoxy)-methyl]-morpholine hydrochloride (viloxazin) on EEG and optimizing control behavior of drivers were investigated under double-blind conditions in five male subjects with many years of driving experience. The study was carried out on a special test course using a car equipped with measuring devices. The following parameters were assessed: EEG and EOG, driving speed, steering torque, steering angle and angle rate, longitudinal and lateral acceleration, and yaw rate. As evaluated by means of spectral analysis with a subsequent principal component analysis, the EEG showed an increase of the power in alpha and beta frequencies indicating a drug-induced decrease of EEG vigilance. Furthermore, the optimization of the system driver-vehicle-road was reduced after drug intake, indicating an impairment of the driver's control behavior. (JA)

13 refs German

KEYWORDS: Antidepressants: viloxazine. Closed Course Driving. Experimentation: Acute Dosage Study. Physiological Testing.

UM-79-D1244

DER EINFLUSS VON KOFFEIN AUF DIE MOTORISCHE REAKTIONS-UND DIE VISUELL-MENTALE VERARBEITUNGSZEIT [THE EFFECT OF CAFFEINE ON MOTOR-REACTION TIME AND VISUAL-MENTAL PROCESSING TIME], H. Krueger; J. Zulch; M. Gandorfer, Zeitschrift fur Ernahrungswissenschaft, v18 n1 p51-61 (1979)

The effect of coffee with caffeine (200mg) and without caffeine on psychomotor performance was compared in five females and seven males, aged 22 to 32 years, in a

double-blind crossover study. Subjects were tested both in an "awake" condition (in the morning) and in a "fatigued" condition (at night) for motor reaction time, visual-mental processing time, reading speed, and reading accuracy. Further, tests under conditions of strong acoustical disturbances were also carried out.

Results showed that in the awake condition caffeine increased the efficiency of all parameters except reading accuracy. In the fatigued condition the effects of caffeine on the parameters tested were insignificant. In a few subjects, caffeine actually decreased the speed of reading and increased the number of errors.

The authors conclude that under the test conditions in this study, in which there were strong acoustical disturbances, caffeine does not improve efficiency when compared with caffeine-free coffee, nor does it impair performance. (JAM)

12 refs German

KEYWORDS: Stimulants: caffeine. Experimentation: Chronic Dosage Study. Psychological Testing. Psychomotor Tests.

UM-77-D1245

THE IMPAIRED-DRIVER PROBLEM VS THE IMPAIRED PROBLEM-DRIVER, H.M. Simpson, Association of Life Insurance Medical Directors of America. Transactions, v61 p178-92 (1977)

Set forth in this article is the proposition that the drinking driver problem is much more complex than previously envisaged by law and policy makers. The author believes that there is no such thing as "the impaired driver." Rather there are different types of drivers who are at different levels of risk, whether impaired or not. Alcohol exacerbates the level of risk for different types of drivers, but it does so differentially.

Within the population of impaired drivers are vastly distinct subgroups with at least two important defining attributes: (1) Not all impaired drivers are at equal risk of collision, and the difference in levels of risks are substantial; (2) not all impaired drivers crash for the same reason--that is, alcohol must be recognized as a causal variable in some cases, but as only a correlated or associated variable in other cases. This latter distinction is crucial, since failure to recognize it will result in the futile expenditure of time and money to treat the symptoms while the disease becomes worse.

In order to develop this argument, the author has organized the paper into three sections. Part I defines the drinking driver problem by providing some descriptive statistics on alcohol in fatal traffic crashes. Part II compares these data to data on the general driving population at risk in an effort to identify relative risks for various age groups of drivers. Finally, having established such risk estimations, some of the paradoxical elements of control mechanisms are explored. For example, it is suggested that the driver at greatest risk of collision may, in fact, be the driver most infrequently on the highway, and thus, least capable of control by the usual methods of police detection.

The author concludes that unless impaired driving is recognized as a complex, multidimensional phenomenon, massive countermeasure efforts including legislative controls, educational approaches, information and media campaigns, and rehabilitative programs will continue to produce disappointing results. (HSRI)

0 refs

KEYWORDS: Barbiturates: amobarbital. Nonbarbiturates: ethanol (ethyl alcohol)*. Review: Drugs and Highway Safety.

UM-79-D1246

HIGHWAY SAFETY RESEARCH, DEVELOPMENT, AND DEMONSTRATION: CONFERENCE PROCEEDINGS. FINAL REPORT, Washington, D.C.: Transportation Research Board (Dec 1979)

This report contains the proceedings of the 1979 Conference on Highway Safety Research, Development, and Demonstration held in Chantilly, Virginia in April 1979. This conference was held to review proposed activities to be undertaken by the National Highway Traffic Safety Administration over a five-year period, FY1980-FY1984. In addition to specific program elements, the report reviews issues related to program

priorities, the basis for their selection, the transfer of program results, and their responsiveness to the needs of the national highway safety community.

Program plans reviewed include the following: 55 mph noncompliance and other unsafe driving acts; occupant restraints; pedestrians and bicyclists; public transportation; driver licensing; motorcycle and moped safety; young drivers; emergency medical services; state traffic records; state program management; traffic law adjudication; police traffic services; motor vehicle registration, titling, and antitheft; and the National Driver Register.

The proposed plans for studying and dealing with alcohol and drugs as they relate to highway safety were also specifically reviewed in a workshop on alcohol and drugs. Some of the specific areas of the alcohol and drug problem discussed were surveys of high-risk drivers, general deterrence projects, public information and education strategies, roadside countermeasures, and priorities for National Highway Traffic Safety Administration projects.

Several recommendations were made by the committee: (1) NHTSA should expand its driver-background survey to investigation of driver characteristics as a function of BAC and inclusion of seriously injured drivers. (2) Some method is needed for capturing secondary data on drunk drivers processed by the courts; similar data might be available in drug cases. (3) Research to establish the incidence of drug presence among drivers should be given top priority in NHTSA's plans; the current plan to determine the possibilities for adjusting drug dosages to reduce impairment should be dropped. (4) In general, NHTSA should concentrate its alcohol and drug efforts more on a few important projects rather than diffusing its program over a large number of small projects. (HSRI)

Steering Committee for the Conference on Highway Safety Research, Development and Demonstration

129 pages 0 refs

National Highway Traffic Safety Administration contract no. DOT-HS-9-02113

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Countermeasure Concepts. Review: Drugs and Highway Safety.

UM-77-D1247

CANNABIS AND ALCOHOL: EFFECTS ON CLOSED-COURSE DRIVING BEHAVIOUR, S. Casswell, paper presented at the Seventh International Conference on Alcohol Drugs and Traffic Safety, Melbourne, 1977. (1977)

This study investigated the effects of cannabis, alcohol, and a combination of the two on perceptual and decision-making abilities and concurrent use of vehicle controls in a closed-course driving situation. Subjects were thirteen male volunteers between the ages of 20 and 30 years. Average years of driving was 8.2; average number of moving violations was 1.8; average number of accidents was also 1.8. All subjects were regular alcohol and cannabis users.

The performance of each subject was compared after six drug treatments administered during three sessions. In the first session alcohol (BAC = .10%) and a placebo were administered first, followed by a second treatment of alcohol (BAC = .10%) plus 500 mg cannabis. In the second session the first treatment consisted of a placebo drink and a placebo cigarette; the second treatment consisted of a placebo drink plus 500 mg cannabis. In the third session, the first treatment was alcohol (BAC = .05%) plus 250 mg cannabis; the second was alcohol (.10%) plus 250 mg cannabis.

Thirty minutes after drug ingestion driving began; subjects were scored for coarse and fine steering reversals, deviation of vehicle position on the track, speed control, decision making, passing time, speed during the overtaking maneuvers, and reaction time to auditory and visual signals.

Steering control was impaired most by alcohol. There was a significant decrease in fine steering wheel movements after alcohol alone and after the three combined doses. Deviations of the vehicle position were also most common after alcohol. Marijuana alone did not significantly increase the variability of the vehicle's path. There was a consistent tendency for speeds to be significantly faster after alcohol and combined treatments and to be slower after marijuana alone.

There was a significant difference in passing time between treatments. Passing times in the alcohol conditions, especially alcohol combined with marijuana, were significantly shorter than the other treatments. Reaction times to auditory signals showed highly significant increases, following the treatments involving the high dose of marijuana.

The author concludes from these test results that the drug treatments administered may have had different effects upon performance measures indicative of the driver's perception or tolerance of risk. The pattern of driving following marijuana alone (consistently slower speeds) suggests that in a self-paced driving task drivers compensate for what they perceive as adverse effects on driving ability by maintaining control and attempting to reduce the rate of required information processing by driving more slowly. By contrast, the alcohol-related speed increases and changes in steering control provide confirmation of the disinhibitory effect on driving performance indicated by previous epidemiological studies of alcohol and road accidents. The effects of the combination treatments suggest the potential for increased accident risk if social use of the two drugs simultaneously increases. The results of these tests indicate the need for countermeasures before the pattern of combined use becomes more widespread. (HSRI)

15 pages 23 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Closed Course Driving. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Experimentation: Study of Combined Effects of Drugs.

UM-78-D1248

HEROIN ADDICTION AND ROAD TRAFFIC ACCIDENTS [letter], G. Edwards; P.J. Quartaro, British Medical Journal, v2 n6153 p1710 (16 Dec 1978)

Research on the role of heroin in traffic accidents has been sparse and contradictory. This letter-to-the-editor briefly reviews some of these studies and reports the results of a survey of 100 heroin addicts concerning their driving and road traffic accidents. Eighty-seven addicts stated that they drove; of these, 69 (82.1%) admitted driving while under the influence of drugs. Fifty-three had had an accident at some time, the average number per addict being 1.9. Of those who had accidents, 18 (34%) said that they occurred while under the influence of drugs.

These data indicate that, in view of the fact that 35-50% of the general population drives after using a drug, heroin addicts probably drive under the influence of a drug more often than the average person. Because opiates decrease reaction time, one can conclude that they run a greater than average risk of an accident. The fact that over one-third of the heroin addicts in this study, who were from a state (New Jersey) having one of the three lowest accident rates in the United States, admitted having accidents while under the influence of drugs, supports this conclusion. (HSRI)

6 refs

KEYWORDS: Opiates and Related Agents: heroin. Epidemiology: Self-Reported Drug Use by Drivers.

UM-79-D1249

DIE AUSWIRKUNGEN EINES BETA-REZEPTORENBLOCKERS AUF DIE KRAFTFAHREIGNUNG [THE EFFECT OF A BETA-ADRENERGIC BLOCKING AGENT ON DRIVING CAPABILITY], L. Moser; U. Schmidt; P.V. Lundt, Medizinische Klinik, v74 n30 p1134-9 (17 July 1979)

This study investigated the effect of Betadrenol(R), a beta-adrenergic blocking agent, on driving capability over a period of thirteen days. Twenty-nine male patients suffering from cardiovascular disorders and aged 29 to 60 years performed traffic psychology tests while under the influence of the drug. After a seven-day washout period, each subject received either placebo or 100 mg Betadrenol(R) three times daily for three days. This short-term, double-blind study revealed no impairment of driving performance.

On each of the following ten days, each patient was given 100 mg Betadrenol(R) three times daily. The results of this study showed significant improvements in test performance, especially in concentration and speed of reaction. (JAM)

28 refs German

KEYWORDS: Anti-Anginal Agents: bupranolol. Experimentation: Chronic Dosage Study. Psychological Testing. Psychomotor Tests.

UM-79-D1250

NITROUS OXIDE EXHAUST FROM CRYOSURGICAL UNITS MAY AFFECT PHYSICIAN PERFORMANCE, E.R. Gonzalez, Journal of the American Medical Association, v242 n22 p2379 (30 Nov 1979)

Discussed here are the hazards involved in the use of cryosurgical probes that employ nitrous oxide, particularly the hazards to physicians working in treatment rooms with suboptimal ventilation and air recirculation. Cryosurgical probes, although they are usually operated for ten minutes or less, exhaust many liters more of nitrous oxide per minute than other anesthetic equipment.

Nitrous oxide can cause a temporary decrement in psychomotor performance. Research indicates that persons exposed to more than 50 ppm of nitrous oxide may suffer impaired motor and audiovisual skills, diminished dexterity, impaired cognition, and other neurological deficits, all of which can seriously impair performance on the part of the surgeon and endanger the lives of his patients. In order to prevent overexposure to nitrous oxide, the cyrosurgical unit must be scavenged and the exhaust vented outdoors. Nitrous oxide concentrations in the operating room should not exceed a 25 ppm time-weighted average. (HSRI)

0 refs

KEYWORDS: Gases: nitrous oxide. General Anesthetics: nitrous oxide. Hallucinogens and Related Agents: nitrous oxide. Review: Drug Effects.

UM-79-D1251

AD HOC TECHNICAL GROUP ON THE INFLUENCE OF ALCOHOL AND DRUGS ON DRIVING, MONACO, 30 OCTOBER - 2 NOVEMBER 1978. SUMMARY REPORT, Journal of Traffic Medicine, v7 n3 p51 (3 Sept 1979)

Presented here is a preliminary summary report of the conference of the Ad Hoc Technical Group on the Influence of Alcohol and Drugs on Driving held in Monaco, October 30-November 2, 1978. This meeting brought together professionals from the medical and other health professions to examine the role of drug abuse in traffic accidents. The following topics were discussed: behavioral indicators of drug abuse; classification of psychotropic drugs and specification of drugs with a potentiating effect on alcohol; a comparison of alcohol and road accident prevention in various countries; epidemiologic studies and issues; psychosocial aspects of drug use while driving; and evaluation of legislation concerning drugs and driving.

The committee made several recommendations on the basis of the data collected. They recommend that research on the determination of blood-alcohol concentration be intensified, especially techniques for random roadside tests. Clinical pharmacological research should also be intensified to identify adverse effects of alcohol and drugs. The committee stresses the urgent need to develop national guidelines on safe driving and drugs, especially for prescribing physicians and road safety authorities. Medical, legal, and social measures directed toward different types of drivers must also be developed as soon as possible. These measures must be very consistently and strictly enforced. The success of these programs depends a great deal on the development and application of specific and inexpensive techniques for determining levels of drugs in the body fluids of drivers and the corresponding levels of impairment. (HSRI)

0 refs

KEYWORDS: Review: Drugs and Highway Safety.

UM-79-D1252

DRUGS: THE HIGHWAY MENACE THAT WON'T GO AWAY, B. Swart, Fleet Owner, v4 p94-96 (April 1979)

This article summarizes a report presented at a private carrier conference concerning illegal drug use by truck drivers in the United States. Drug use by truck drivers is extensive and in spite of public information campaigns, is as high as it ever was, if not higher. Many truck stops sell amphetamines, barbiturates, glue, and hallucinogens

to truck drivers who pay for them by selling spare tires, using credit cards dishonestly, or adding their cost to minor repair bills.

The article also describes several drug groups and discusses their special hazards when used by truck drivers. Stimulants, depressants, tranquilizers, marijuana, and alcohol are discussed in terms of their effects and extent of use. (HSRI)

0 refs

KEYWORDS: Barbiturates: secobarbital. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: amphetamine. Review: Drugs and Highway Safety.

UM-75-D1253

CLINICAL AND EXPERIMENTAL COMPARISON OF DIAZEPAM, CHLORAZEPATE AND PLACEBO, I. Dureman; B. Norrman, Psychopharmacologia, v40 p279-284 (1975)

This study attempted to investigate the extent to which diazepam, chlorazepate, and placebo differ in their clinical profiles. Subjective drug effects were studied in thirty-four neurotic patients aged 29 to 31, and drug effects on simulated driving tests were assessed in forty-two healthy volunteers aged 19 to 29. In the second experiment, drug effects on heart rate, respiratory rate, and skin conductance were also assessed.

In the clinical study, each patient received diazepam (5 mg x 3), chlorazepate (10 mg x 3), and placebo for one week in a double-blind, randomized sequence. All patients were assessed for muscular weakness, anxiety and restlessness, muscular tension, fatigue, gastrointestinal effects, irritability, and sleep disturbances.

Results of this study showed that in nearly all of the patients, both active drugs were better than placebo in relieving symptoms of anxiety. Comparison of the two drugs showed chlorazepate to be better than diazepam in reducing anxiety and restlessness, muscular tension, and gastrointestinal disturbances. Both drugs were equally effective with respect to fatigue, irritability, and sleep disturbances.

In the simulated driving test, the forty-two healthy volunteers were premedicated for two days before the test with the same drug they had randomly been allocated to, namely, diazepam (5 mg x 3), chlorazepate (10 mg x 3), or placebo. One hour before testing they received 5, 10, or 20 mg diazepam, or 10, 20, or 40 mg chlorazepate, or placebo. During a three-hour driving period steering precision, brake reaction time, heart rate, respiratory rate, and skin conductance level were continuously recorded.

Results indicated that even at the highest dose levels of either drug the subjects failed to show any statistically significant impairment of steering precision or brake reaction time when compared to placebo. Heart rate and skin conductance level recordings demonstrated a higher psychophysiological effect at all dose levels of diazepam as compared with chlorazepate. (HSRI)

11 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): clorazepate, diazepam. Muscle Relaxants (Central): diazepam. Clinical Study. Driving Simulator. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Physiological Testing. Psychological Testing. Self-Evaluation of Drug Effects by Subjects.

UM-79-D1254

SOME ASPECTS OF THE EFFECTS OF CLOBAZAM ON HUMAN PSYCHOMOTOR PERFORMANCE, I. Hindmarch, British Journal of Clinical Pharmacology, v7 p77s-82s (1979)

The three experiments reported here are investigations of the effects of clobazam on human psychomotor performance. The results of the experiments provide a profile of the action of clobazam on human psychomotor performance in a variety of task situations under both acute and chronic regimens with subjects with differing trait anxiety scores.

The first experiment compared the effects of acute nighttime doses of 20 mg clobazam, 100 mg amylobarbitone sodium, 5 mg nitrazepam, and placebo on choice reaction time, critical flicker fusion, and stabilometer performance in ten male and ten female volunteers whose mean age was twenty-eight. Clobazam was found to improve early morning

performance on a choice reaction test, in contrast to amylobarbitone sodium and nitrazepam.

In the second experiment, repeated doses of 10 mg clobazam t.i.d., 10 mg chlordiazepoxide t.i.d., and 5 mg diazepam t.i.d. were given for five days to eighteen male and twelve female volunteers whose mean age was thirty-one. Again clobazam did not produce any impairment of psychomotor performance; clobazam did, however, noticeably increase critical flicker fusion thresholds.

In the third experiment the effects of an acute nighttime dose of 20 mg clobazam on psychomotor performance (choice reaction) the morning after nighttime medication were correlated with the neuroticism scores (EPI) of eight male and twelve female subjects whose mean age was thirty-four. Clobazam was found to have a different effect on psychomotor performance dependent on the basic personality trait.

The author concludes from these three experiments that clobazam seems to differ significantly from the 1,4-benzodiazepines in that although it reduces anxiety it does so without any apparent impairment of psychomotor performance. Thus, it can be assumed that the anxiety-reducing mechanism of the drug is not caused by sedation, but rather its ability to increase cortical arousal and central integrating processes. (JAM)

30 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): nitrazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. clobazam. diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: nitrazepam. Experimentation: Acute Dosage Study. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects. Tests of Sensory Function.

UM-79-D1255

MEDICIN, ALKOHOL OG KULILTE HOS TRAFIKDRAEBTE [DRUGS, ALCOHOL AND CARBON MONOXIDE IN VICTIMS OF FATAL TRAFFIC ACCIDENTS], B. Kaempe; J.B. Dalgaard, Ugeskrift fur Laeger, v141 n15 p1036-1040 (1979)

Postmortem examinations and chemical analyses were performed on 283 victims of fatal traffic accidents. Men accounted for 82% (232) of the victims; analysis of age distribution revealed a slightly higher than average age among the victims.

Blood alcohol levels of over .02% were found in 26% of all cases; 20% of these victims showed positive findings of drugs in addition to alcohol. Alcohol was found most frequently in the younger age groups, whereas drugs were found more frequently in elderly individuals.

In victims of traffic accidents in whom alcohol was found, 65% had BACs over the legal limit of .08%; 50% had BACs over .12%, only three of whom were women. Alcohol was found most frequently in men aged 15 to 39, especially in motorcyclists, followed by motorists, pedestrians, and bicyclists.

Alcohol was without doubt the most important factor in the majority of accidents in this study. In isolated cases drugs other than alcohol, especially barbiturates, were probable or possible causes of the accident. In two cases amphetamine and in one case pethidine may have been responsible.

Positive chemical findings increased with age and reached a maximum in the 60 to 69 age group. No marked differences in use were found among the various traffic groups. Women with positive chemical findings were more common (27%) than men (19%). Carbon monoxide was found in two cases, neither showing significant amounts. P It is concluded that further studies be done on the hazards of drugs in traffic, a problem of increasing significance. (JAM)

23 refs

KEYWORDS: Analgesics and Antipyretics: antipyrine. propoxyphene. Anti-Anginal Agents: propranolol. Anti-Arrhythmia Agents: chinidine. propranolol. Antidepressants: amitriptyline. imipramine. Gases: carbon monoxide. Hypotensive (Antihypertensive) Agents: propranolol. Major Tranquilizers (Antipsychotics and Neuroleptics): thioridazine. Minor Tranquilizers (Anti-Anxiety and Ataractics): meprobamate. Nonbarbiturates: ethanol (ethyl alcohol). glutethimide. Opiates and Related Agents: ketobemidone. pethidine. Oral Hypoglycemics: tolbutamide. Skin and Mucous Membrane

Preparations: salicylic acid. Stimulants: amphetamine. Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-76-D1256

A COMPARISON OF THE EFFECT OF IMIPRAMINE, NOMIFENSINE, AND PLACEBO ON THE PSYCHOMOTOR PERFORMANCE OF NORMAL MALES, J.R. Wittenborn; C.F. Flaherty; W.E. McGough; K.A. Bossange; R.J. Nash, Psychopharmacology, v51 p85-90 (1976)

Although antidepressant drugs, particularly imipramine, are widely used in the outpatient treatment of depressed individuals, little is known of the initial detraction effects of a usual regimen of divided dosage. This investigation attempted to assess the effect of a one-day t.i.d. regimen of 50 mg imipramine, 50 mg neomifensine, or placebo on ninety male students over twenty-one years of age. Medication in indistinguishable capsules was administered after the first, fourth, and seventh testing session to the three different medication groups, each containing thirty subjects. The testing session was repeated at hourly intervals for eleven hours and included the following sequence: (1) digit symbol substitution; (2) numerical ability; (3) perception; (4) time estimation; (5) simple vigilance (continuous performance); and (6) complex vigilance (continuous performance).

Results of the testing showed that with the exception of the numerical ability test, the following trends were evident: (1) Relative to placebo and nomifensine, imipramine revealed a persisting pattern of impaired performance. (2) In some tests nomifensine showed evidence of impairment relative to placebo, but significant impairment was not manifested as frequently in the nomifensine group as in the imipramine group. (3) In most respects, the performance of the nomifensine group seemed to be more similar to that of the placebo group than to that of the imipramine group. (4) Sleepiness was reported by seventeen of the thirty subjects receiving imipramine in contrast to only seven subjects receiving nomifensine and six subjects receiving placebo.

The authors conclude that the contrasts revealed by this study are favorable to nomifensine and are of considerable clinical interest particularly in the care of outpatient depressives who must continue to meet the requirements of routine daily tasks. Imipramine, however, may result in sufficient initial psychomotor impairment to require precautionary measures and restriction of normal activities. (HSRI)

18 refs

KEYWORDS: Antidepressants: imipramine, nomifensine. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects.

UM-79-D1257

PSYCHOMOTOR CHANGES DURING INITIAL DAY OF BENZODIAZEPINE MEDICATION, J.R. Wittenborn; C.F. Flaherty; W.E. McGough; R.J. Nash, British Journal of Clinical Pharmacology, v7 p69s-76s (1979)

The purpose of this study was to investigate the extent of initial impairment of psychomotor skills caused by treatment with benzodiazepines, drugs which are principally used in outpatient management of anxiety. The impairing psychomotor effects of diazepam (5 mg three times daily) and clobazam (10 mg three times daily) were compared with placebo effects over the course of the initial day of medication in ninety male volunteers over twenty-one years of age. Alternative medications were assigned on a predetermined double-blind randomized basis with thirty subjects in each treatment group. Tests were administered at hourly intervals for eleven hours and included the following: (1) digit symbol substitution; (2) numerical ability; (3) perception; (4) balance beam equilibrium; (5) time estimation; (6) simple vigilance; and (7) complex vigilance. Data from the tests were analyzed from the standpoint of contrasts at each session and from the standpoint of trends that accrued during the course of the day.

Test results of the digit symbol substitution test and numerical ability tests did not show any significant differences between treatment groups. Diazepam impaired both perception and balance beam equilibrium when compared to clobazam. The effect of 5 mg diazepam three times daily in this study appeared to be cumulative through the course of the initial day and was reflected in significant verges in trend lines.

Clobazam, in contrast to diazepam, may have an enhancing effect on certain aspects of psychomotor function. In the present study, clobazam was associated with relatively few

missteps on the balance beam and relatively short sequences of errors in the continuous vigilance test.

The authors conclude that 5 mg three times daily may be near the threshold for psychomotor impairment during the initial day of diazepam and that 10 mg clobazam three times daily has no appreciable detracting effects, and in fact may have some enhancing effects. (HSRI)

19 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): clobazam. diazepam. Muscle Relaxants (Central): diazepam. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Psychological Testing. Psychomotor Tests.

UM-78-D1258

DRIVING UNDER THE INFLUENCE OF MEDICINE: CRIMINAL POLITICAL VIEWS ON THE SIGNIFICANCE OF MEDICINE AS A FACTOR IN TRAFFIC ACCIDENTS (SUMMARY), A. Solarz (trans. P. Jones), Stockholm: National Laboratory for Forensic Chemistry (1978)

Presented in this report are the results of a study investigating (1) drug consumption among 6,725 drivers suspected of drunken driving and (2) drugs used by 1,529 drivers admitting combining drug use with alcohol. In addition, a control of 283 drivers suspected of driving a motor vehicle under the influence of alcohol only was studied for purposes of comparison. Police reports, drug and alcohol analyses, court records, and questionnaires were examined.

The report is divided into five parts. The sociological and legal background of existing legislation concerning driving under the influence of drugs is described in Part I. Part II describes the methodology used in the survey. Part III reports the findings of the survey. Part IV reports the findings of a survey of drivers concerning their attitudes toward driving while under the influence of drugs. Part V critically evaluates existing drug and driving laws and offers several conclusions and recommendations.

Several major findings of the study are discussed and analyzed: (1) The use of drugs by automobile drivers has increased from 12% in 1965 to 23% in 1976. (2) One out of four drivers suspected of drunk driving also uses drugs while driving. (3) The percentage of drivers in this study who used drugs and was involved in traffic accidents and traffic accident risks was as high as in those drivers suspected of drunken driving. (4) 90% of those drivers using drugs while driving use them in combination with alcohol. (5) Use of drugs while driving is most frequent in the male aged 20-29 years who owns his own car and has a high number of previous sentenced crimes.

The study concludes with a discussion of the implications of these results for future research, the medical profession, the pharmaceutical industry, and Swedish law. (HSRI)

96 pages 111 refs

Swedish Councils for Crime Prevention Social Science project no. UE 12/76

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Analgesics and Antipyretics. Sedatives and Hypnotic Agents. Stimulants. Epidemiology: Analysis of Driver Body Fluids for Drugs. Epidemiology: Record-Based Survey.

UM-79-D1259

THE EFFECTS OF MARIJUANA AND ALCOHOL USAGE ON HANDWRITING, R.G. Foley; A. L. Miller, Forensic Science International, v14 p159-164 (1979)

In this study the handwriting of five females and seven male marijuana users between the ages of 18 and 29 who were under the influence of marijuana, alcohol, and a combination of the two was compared with control samples.

Signatures and handwriting control samples were taken prior to the consumption of marijuana and alcohol. Comparison samples were taken between thirty and sixty minutes after use of the drugs. Between one and five marijuana cigarettes of unknown delta-9-THC content were smoked prior to the final sampling. (Alcohol levels were not stated in the study.) To determine drug effects, the test and control handwriting were compared for speed, letter forms, proportions, height ratio, size, slant, and alignment.

Comparison of the control samples with those taken after the smoking of one marijuana cigarette revealed little or no change in handwriting. After three marijuana cigarettes, some handwriting changes were observed, especially in subjects with little previous experience with marijuana.

Comparison of the control samples with samples taken after the consumption of three twelve-ounce cans of beers showed significant changes which were very similar to those produced by three cans of beer plus three marijuana cigarettes.

The CNS depressant activity of alcohol appears to be most responsible for the marked effect on handwriting. Previous research suggests that while marijuana does affect the CNS, it does not greatly depress the CNS activity used to direct manipulative functions such as handwriting. This may explain why the individuals in this study experienced a high and yet were able to write without the significant departure from normal handwriting seen during alcohol intoxication. (HSRI)

23 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests.

UM-79-D1260

SELF-ADMINISTERED ANALGESIA WITH NITROUS OXIDE: ADJUNCTIVE AID FOR EMERGENCY MEDICAL CARE SYSTEMS, E.R. Thal; S.J. Montgomery; J.M. Atkins; B.G. Roberts, Journal of the American Medical Association, v242 n22 p2418-19 (30 Nov 1979)

This study was undertaken to evaluate the analgesic effects of self-administered nitrous oxide in a 50:50 oxygen mixture (Nitronox(R)) in emergency medical care systems. A Nitronox(R) unit was evaluated for analgesic effects, ease of use by both patient and paramedic, and adverse side effects in forty-seven emergency cases where patients suffered from musculoskeletal trauma; abdominal pain, acute urinary retention, burns, and kidney stones, 98% of whom complained of moderate to severe pain. Each patient was instructed to hold the face mask and establish a tight seal around the nose and mouth.

The use of Nitronox(R) was extremely well-accepted by the patients, paramedics, and physicians in this study. The majority of the patients were alert on arrival at the hospital. Virtually all patients experienced some relief of pain, and more than 50% of those with severe pain reported complete relief. Nausea and vomiting were not a major problem. Blood pressures remained unchanged in every case but one.

The authors conclude that Nitronox(R) appears to be a safe analgesic that is particularly well-suited to the alleviation of pain in emergency conditions. It serves as an additional adjunct to safe and improved medical care. (HSRI)

4 refs

KEYWORDS: Gases: nitrous oxide. oxygen. General Anesthetics: nitrous oxide. Hallucinogens and Related Agents: nitrous oxide. Clinical Study. Experimentation: Acute Dosage Study. Self-Evaluation of Drug Effects by Subjects.

UM-79-D1261

TESTING FOR SEDATIVE-HYPNOTIC DRUGS IN THE IMPAIRED DRIVER: A SURVEY OF 75,000 ARRESTS, J.M. White; G.C. Brouillette; D.O. Clardy; M.H. Graves; M.C. Kuo; B.J. McDonald; D.S. Pearce; S.J. Wiersema, paper presented at the 31st Annual Meeting of the American Academy of Forensic Sciences, 12-17 February 1979, Atlanta, Georgia (1979)

Presented here are data from a six-year study done by the Orange County Sheriff-Coroner Criminalistics Laboratory investigating blood levels of sedative-hypnotic drugs in persons arrested for impaired driving. This study, begun in 1973, tested blood samples (approximately 75,000) of all impaired drivers with BACs less than 0.10% for alcohol, barbiturates, methaqualone, benzodiazepines and other sedative-hypnotics, PCP, and morphine. Each year approximately 12% of the arrests met the criterion for drug screening. Drug positive cases were 282 of 723 in 1973, 520 of 1,191 in 1974, 639 of 1,374 in 1975, 586 of 1,316 in 1976, 570 of 1,693 in 1977, and 714 of 1,819 in 1978.

Ultraviolet spectrophotometry and a combination of paper, thin-layer, and gas chromatography were used to detect sedative-hypnotic drugs. Radiomimmunoassay

techniques were used to detect barbiturates, and gas chromatography-mass spectrometry was used to detect PCP.

Selected findings in 1978 were as follows: (1) 538 of 1,819 specimens (29.6%) tested positive for sedative-hypnotics; (2) 154 (8.5%) tested positive for methaqualone; (3) 140 (7.7%) tested positive for benzodiazepines; (4) 82 (4.5%) specimens contained combinations of these drugs; (5) 32 (1.8%) tested positive for other sedative hypnotics; (6) 125 (6.9%) tested positive for PCP; and (7) morphine was found in 51 (2.8%) of the 1,819 samples where the blood alcohol level was below 0.10%.

Several trends in drug use are evident from this data. In 1973 barbiturates alone contributed 70% of the drug positive cases; in 1977 this percent decreased to 44%. Methaqualone, however, rose to 33% of the drug positive findings in 1977 from 8% in 1973. (HSRI)

0 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital. Barbiturates: amobarbital. butalbital. pentobarbital. phenobarbital. secobarbital. General Anesthetics: hexobarbital. Hallucinogens and Related Agents: phencyclidine. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. meprobamate. oxazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol)*. ethchlorvynol. glutethimide. methaqualone. Opiates and Related Agents: morphine. Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-80-D1262

MARIJUANA, OTHER DRUGS AND THEIR RELATION TO HIGHWAY SAFETY. A REPORT TO CONGRESS, Washington, D.C.: National Highway Traffic Safety Administration (Feb 1980)

Presented here is the report to Congress by the Department of Transportation concerning efforts to detect and prevent marijuana and other drug use by operators of motor vehicles. This report includes information concerning the frequency of marijuana and other drug use by drivers, capabilities of law enforcement officials to detect the use of marijuana and drugs by drivers, and a description of federal and state projects undertaken to investigate methods of detection and prevention. A review of recent literature concerning frequency of use of marijuana and other drugs in drivers and a summary of current knowledge about drugs and driving gained from both experimental and epidemiologic studies are presented. Also included are recommendations both for legislation and for specific programs aimed at reducing marijuana and other drug use by motor vehicle operators.

Several major conclusions emerged from the study: (1) With the exception of alcohol, no drug has been established to be a high priority highway safety concern. (2) The frequency with which drug-impaired drivers drive, are arrested, or are involved in crashes is not known. (3) Drugs which may impair driving and which are used by drivers include prescription and over-the-counter drugs as well as illicit drugs. (4) The information on marijuana and driving is incomplete and does not support arguments either for or against establishing marijuana as a high priority highway safety concern. (5) The magnitude and scope of the highway safety problem due to inappropriate use of drugs by drivers cannot be adequately determined without roadside surveys to determine the nature and extent of drug use by drivers who are not involved in accidents or suspected of impaired driving.

On the basis of these conclusions the following recommendations are made: (1) No federal legislation concerning drugs and driving is recommended at this time. (2) States are encouraged to revise existing laws dealing with drugs and driving to allow law enforcement to act in conformance with the Uniform Vehicle Code with regard to use of chemical tests and the definition of driving under the influence of alcohol, drugs, or both. (3) The federal government should develop an information and education program on the potential impairing effects of drugs on driving. (4) The federal government should continue epidemiological, experimental, and behavioral research on drugs and driving. (5) A study must be done to examine the feasibility of developing and implementing practical and reliable chemical analyses and also legal countermeasures. (HSRI)

46 pages 52 refs

National Highway Traffic Safety Administration report DOT-HS-805-229

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam.

Nonbarbiturates: ethanol (ethyl alcohol). flurazepam. Countermeasure Development, Testing, and Evaluation. Other Sociolegal Study. Review: Behavioral Research Methodology. Review: Drug Analysis Methodology. Review: Drug Effects. Review: Drug Use. Review: Drugs and Highway Safety. Review: Survey Methodology.

UM-78-D1263

INDUCTION OF ALCOHOL WITHDRAWAL SYMPTOMS BY NALORPHINE IN CHRONIC ALCOHOLIC PATIENTS, H.G. Markley; E. Mezey, International Journal of the Addictions, v13 n3 p395-402 (1978)

Presented here is an investigation of the effect of the narcotic antagonist nalorphine on eliciting either narcotic or alcohol withdrawal symptoms in chronic alcoholic patients ingesting alcohol. Subjects were five male chronic alcoholic patients aged 32 to 60 who had abused alcohol (more than 200 g daily) from four to thirty-three years. After a detoxification period of six to sixteen days, the patients received either nalorphine in sequentially increasing amounts (3.0, 5.0, and 8.0 mg) every thirty minutes, or isotonic saline (0.6, 1.0, and 1.6 ml). Treatments were administered double-blind in both the sober and alcohol state. The doses of ethanol given were 30 ml of 95% ethanol in eight daily doses two hours apart and were increased to 40 ml in three doses every two hours. Each patient was observed for development of nalorphine effects and for symptoms of narcotic and alcohol withdrawal. Respiratory rate, pulse rate, blood pressure, and pupil size were recorded before and every fifteen minutes for six hours after nalorphine or saline administration.

Results of the study showed that administration of saline to the patients when sober had no effect, however, it resulted in mild sedation in three patients and nausea in two during the alcohol state. Nalorphine administration to sober subjects resulted in sedation in four, dizziness in three, miosis in three, euphoria in one, and nausea in one. Pulse rate decreased in sober patients after nalorphine administration but increased in patients in the alcohol state.

The administration of nalorphine resulted in symptoms of either narcotic or alcohol withdrawal in the patients when ingesting ethanol, but not when sober. The following characteristic withdrawal symptoms were observed: lacrimation in one patient; weakness in two; anorexia in two; insomnia in two; disorientation in one; perspiration in one; tremor in two; restlessness in one; and headache in two.

The authors conclude that the induction of symptoms of alcohol withdrawal with nalorphine in patients ingesting ethanol suggests that an accumulation of morphine-like alkaloid compounds may play a role in the mediation of alcohol withdrawal symptoms in chronic alcoholic patients. More research in this area is needed to develop the potential therapeutic role of narcotic antagonists in addict treatment programs. (HSRI)

13 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: nalorphine. Experimentation: Chronic Dosage Study. Experimentation: Study of Combined Effects of Drugs. Physiological Testing.

UM-78-D1264

APOMORPHINE REVIVED: FORTIFIED, PROLONGED, AND IMPROVED THERAPEUTICAL EFFECT, K.A. Lock-Halvorsen; O. Martensen-Larsen, International Journal of the Addictions, v13 n3 p475-84 (1978)

This study of the therapeutic effects of apomorphine has two parts. The first part presents a historical literature review of the evolution of the clinical use of apomorphine for treatment of alcohol and drug addicts. Recent literature indicates that there might exist a close relationship between abstinence and craving symptoms in drug and alcohol addicts, and that anxiety, depression, and tremor symptoms in Parkinsonism (and dementive senilis) are due to disturbances of the same (mainly dopaminergic) pathways in the central nervous system.

The second part of the paper describes a study in which the synergistic effect of small amounts of apomorphine, L-dopa, and decarboxylase inhibitor administered orally was used with considerable therapeutic effect in drug addicts. The paper describes the therapeutic results of the various combinations of apomorphine, Benserazid(R), L-dopa, ascorbic acid, or carbidopa which were used to determine the optimal combination. Of a group of fifty drug addicts receiving this preparation intensely for four weeks and at monthly intervals thereafter, fifteen remained free of drugs one year after commencement of treatment, fifteen had partially relapsed, using a very reduced consumption of

morphine, and twenty had totally relapsed. Thirty-eight addicts (76%) found the craving for morphine totally blocked or greatly reduced.

Also reported is a case history of a Parkinsonism patient severely afflicted with the disease and addicted to diazepam and ketogen who was treated with the preparation. Treatment resulted in almost complete remission of the disease. This case, which is probably the first known successful treatment of Parkinsonism complicated by drug addiction, illustrates the stimulation of the endocrine system due to increased production of releasing hormones from the hypothalamus, which stimulates the hypophysis, after treatment with apomorphine and L-dopa. (HSRI)

39 refs

KEYWORDS: Emetics: apomorphine. Opiates and Related Agents: apomorphine. morphine. Clinical Study. Experimentation: Chronic Dosage Study. Review: Drug Effects.

UM-79-D1265

THE EFFECTS OF COMBINED ALCOHOL-DRUG ABUSE ON HUMAN BEHAVIOR: A REVIEW OF THE LITERATURE, S. Cohen, Drug Abuse and Alcoholism Review, v2 n3 p1,3-13 (1979)

This paper reviews the current literature on alcohol and other drug interactions in humans. The psychophysiologic effects of specific drug combinations are discussed, and the impact of multiple drug use on certain behaviors is described to the extent possible. Literature on the following drug combinations is discussed in terms of tolerance, cross tolerance, physical dependence, synergism, antagonism, additive effects, and supraadditive effects: alcohol-narcotic; alcohol-sedative; alcohol-minor tranquilizer; alcohol-marijuana; alcohol-stimulant; alcohol-antidepressant; alcohol-antihistamine; and alcohol-nicotine.

Patterns of multiple drug abuse as determined by the National Drug/Alcohol Collaborative Project (NDACP), the Drug Abuse Reporting Program (DARP), and the Drug Abuse Warning Network (DAWN IV) are also reported. Some of their major conclusions are these: (1) Alcohol is the substance abused most often by both single and multiple drug abusers. (2) Marijuana is the drug most commonly combined with alcohol, followed by minor tranquilizers, heroin, amphetamines, and barbiturates. (3) Suicidal attempts are the most common cause of patients who have taken alcohol in combination with other drugs appearing at crisis centers, emergency rooms, and morgues.

The author concludes that in view of the large number of bio- and sociobehavioral problems resulting from polydrug use, pharmacists, physicians, and clinic personnel must be prepared to advise their clients or patients on the possible ill effects of combined substance use. More importantly, they should stress that the combination of two or more mind-altering agents produces not only successively greater impairments, but also tends to increase the unpredictability of effect. (HSRI)

74 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Ganglionic Blocking and Stimulating Agents: nicotine. Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: nicotine. Antidepressants. Antihistamine Agents. Minor Tranquilizers (Anti-Anxiety and Ataractics). Opiates and Related Agents. Sedatives and Hypnotic Agents. Stimulants. Review.

UM-80-D1266

EFFECTS OF CIGARETTE SMOKING ON IMMEDIATE MEMORY AND PERFORMANCE IN DIFFERENT KINDS OF SMOKER, D.G. Williams, Journal of Psychology, v71 pt 1 p83-90 (Feb 1980)

This study investigated the immediate effects of the first cigarette of the day on memory and mental performance in forty-eight male smokers aged 20 to 46 years who were classified both by daily consumption and by relative desire for smoking in high or low arousal situations. Subjects were classified as light smokers (less than fifteen cigarettes per day), medium smokers (sixteen to twenty-five cigarettes per day), or heavy smokers (more than twenty-five per day). Subjects were further equally divided into those who preferred to smoke in low arousal situations, and those who preferred to smoke in high arousal situations.

Subjects completed a questionnaire on smoking habits, the Eysenck Personality Questionnaire, and the Frith Situational Smoking Questionnaire. Each subject took one of four treatments each of the four days: (1) sham smoking of an unlit cigarette; (2)

actual smoking of a cigarette containing 0.6 mg nicotine and 7 mg tar; (3) actual smoking of a cigarette containing 1.3 mg nicotine and 19 mg tar; and (4) actual smoking of a cigarette containing 1.8 mg nicotine and 27 mg tar. All four sessions followed the same procedural order: letter cancellation test, an immediate memory test, paced cigarette smoking, another immediate memory test, and a final letter cancellation test. All testing was completed within fifteen minutes after termination of smoking.

Analyses of the test scores showed that with increasing cigarette strength there were gains in letter cancellation speed compared to presmoking scores. However, immediate memory accuracy progressively deteriorated once presmoking performance was controlled for. Smokers with greater desire to smoke in low arousal situations appeared to react more strongly to cigarettes and showed superior gain in cancellation speed after smoking.

The author concludes that there are important contrasts to be found in smoking effects in different smoker types and that such distinctions between smokers should be included in future research. (HSRI)

38 refs

KEYWORDS: Ganglionic Blocking and Stimulating Agents: nicotine. Stimulants: nicotine. Experimentation: Acute Dosage Study. Experimentation: Dose-Effect Study. Psychological Testing.

UM-78-D1267

CAFFEINISM COMPLICATING HYPERSOMNIC DEPRESSIVE EPISODES, J.F. Neil; J.M. Himmelhoch; A.G. Mallinger; J. Mallinger; I. Hanin, Comprehensive Psychiatry, v19 n4 p377-85 (Jul-Aug 1978)

Reported here are the findings of a study investigating the confounding effects of self-medication with caffeine in a group of 31 anergic, hypersomnic unipolar depressives. Self-reported quantification of caffeine consumption in the form of coffee, tea, cola beverages, and prescription drugs was obtained from 186 psychiatric outpatients and a total daily caffeine dosage estimated for each patient. Data from the 31 patients whose diagnosis was primary anergic hypersomnic depression (unipolar II) were compared to data from 47 patients whose diagnosis was primary agitated hyposomnic depression (unipolar I) and from 62 patients whose diagnosis was bipolar affective disorder. The initial clinical state of the unipolar II cases was analyzed for the presence of mixed affective features, agitation, hyposomnia, and the effects of caffeine abstinence or reduction on clinical presentation and treatment outcome. Data was collected using a self-administered questionnaire. The data were analyzed and used to test the hypothesis that unipolar II depressives who show mixed affective features or who are initially mistaken for unipolar I depressives might be abusing caffeine, and that reduction of caffeine intake might clear up clinical quandaries as well as aid in the design of more effective treatment.

At the time they entered treatment, 16% of the unipolar II patients met the criteria for mixed affective states, while another 19% showed superimposed features of agitated hyposomnic depression that were not consistent with previous anergic affective episodes and cleared after a period of caffeine abstinence. The mean daily caffeine intake of these patients was found to be significantly higher than that of a group of more typical unipolar II depressives. Moreover, the estimated dosage range for caffeine consumption in a group with mixed states was consistent with that reported in previous reports of caffeinism associated with psychiatric symptomology.

The authors conclude that self-medication with large doses of caffeine is a likely response to the anergia and hypersomnia experienced during certain types of depression, and that self-medication often leads to initial diagnostic confusion and a complicated course of pharmacotherapy. In addition to the diagnostic confusion resulting from self-medication with caffeine, there may also be therapeutic implications. Some evidence exists indicating that concurrent caffeine use renders anxiolytic and antipsychotic medications less effective. Enhanced toxicity may result when high doses of caffeine and therapeutic doses of MAOI are combined. Potentiation of caffeine may also occur during administration of lithium salts. Therefore, it is necessary to achieve caffeine abstinence in patients with a unipolar II depressive profile before therapy is begun. (HSRI)

31 refs

KEYWORDS: Stimulants: caffeine. Clinical Study. Experimentation: Chronic Dosage Study. Psychological Testing.

UM-79-D1268

BEHAVIORAL EFFECTS OF CARBON MONOXIDE ON ANIMALS AND MAN, V.G. Laties; W.H. Merigan, Annual Review of Pharmacology and Toxicology, v19 p357-92 (1979)

Presented here is a review of experimental laboratory studies investigating the behavioral effects of relatively low levels of carbon monoxide (CO) in both humans and animals. In the first part of the paper, literature concerning effects in animals is surveyed. To date, this literature has clearly demonstrated response-rate-decreasing effects of CO and suggests an approximate range of minimally effective CO concentrations. However, other major issues have scarcely been broached in animal studies. Further research is needed to determine the differential sensitivity of various types of behavior to disruption by CO. Research is also needed to determine the relative importance of various parameters of CO exposure (concentration, duration, COHb level) in determining the extent of behavioral impairment. Further research is also needed to investigate the behavioral consequences of prenatal exposures to CO. Existing research suggests that the developing organism may face grave risks when the mother is exposed to CO.

The literature on CO effects on human behavior is extremely contradictory. Some researchers report that low levels of CO influence some aspects of human behavior, whereas others report opposite results. However, several general conclusions can be drawn: (1) There are without doubt interactions between the effects of CO and various characteristics of the particular behavior under study. (2) Most CO effects appear to be marginal, that is, CO probably does not have large and consistent effects upon behavior when given for short periods at low levels. In human studies levels high enough to produce unambiguous effects are rarely used. (3) The dose-effect and time-effect relationships for CO may not be monotonic. Several studies report CO effects that appeared only transiently, diminishing in magnitude or disappearing completely as exposure continued. Other studies report reversals, with higher exposure levels apparently producing less effect than lower ones. (4) Since the behavioral effects of CO are usually studied in healthy young subjects, judicious extrapolation is needed in using these results for the establishment of permissible exposure levels for the general public. CO effects may be exaggerated in utero, in the elderly, or in persons with cardiovascular or respiratory insufficiency.

It is concluded that although the literature on behavioral effects of CO includes a wide range and variety of experiments, the majority of these report only isolated observations. Future experimental work should emphasize parametric investigations of those variables that appear to be the most crucial contributors to the behavioral toxicity of carbon monoxide. (HSRI)

120 refs

KEYWORDS: Gases: carbon monoxide. Review.

UM-79-D1269

EFFECTS OF AZATADINE MALEATE ON SUBJECTIVE APPRAISAL AND PSYCHOMOTOR FUNCTIONS RELEVANT TO DRIVING PERFORMANCE, B. Biehl, Current Medical Research and Opinion, v6 n1 p62-9 (1979)

Studies were carried out in normal healthy male subjects aged 18 to 25 to assess the effects on psychomotor functions and subjective ratings of performance after acute administration of azatadine maleate, a potent antihistamine with additional antiserotonin activity. In the first trial, 2 mg azatadine was compared with another new antihistamine, Sch 12169 (2 mg), and placebo in twenty-seven subjects. In a second trial, higher doses of azatadine (4 mg and 8 mg) were compared with dexchlorpheniramine (4 mg) and placebo in thirty-two subjects. Both trials were of a double-blind randomized Latin square design and subjects were assessed using a battery of tests after administration of each trial drug.

The following tests were included in the test battery: self-assessment of mood; subjective self-assessment of test performance; assessment of speed of visual perception using a tachistoscope; the Dueker and Lienert concentration test; a coordination test; reaction test; a complex reaction test; a tapping test; and a two-hand coordination test. The time and sequence of tests were standardized, with a one-week interval between test sessions.

The results showed that azatadine did not produce significant impairment of psychomotor functions at either the standard 2 mg or the maximum recommended 4 mg per day dosage level. Performance was only significantly impaired when compared with placebo at the 8

mg dose level, and was of a similar order to that observed after dexchlorpheniramine at the usual 4 mg dosage. It is suggested, therefore, that at the normal recommended dosage of 2 mg per day, azatadine is not likely to impair driving ability. (JAM)

12 refs

KEYWORDS: Antihistamine Agents: azatadine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Psychological Testing. Psychomotor Tests. Self-Evaluation of Drug Effects by Subjects. Tests of Sensory Function.

UM-79-D1270

TRANQUILLISERS AND ROAD ACCIDENTS [editorial]. New Zealand Medical Journal, v89 n636 p387 (23 May 1979)

Presented here is a brief, general review of the drug-driving problem. While it appears that many drugs may impair driving skill and cause accidents, their precise role in traffic safety is difficult to assess. The significance of tranquilizers, in particular, has not been proven, in spite of several studies investigating their role. However, that the benzodiazepines are associated with an increased risk of road accident appears to necessarily follow from their pharmacological actions. The risk factor is greatly potentiated by alcohol, a fact which drug users must be made aware of. It is concluded that since tranquilizers do appear to increase accident risk, the continuing and frequent prescribing of these drugs should be critically scrutinized. (HSRI)

3 refs

KEYWORDS: Tranquilizers. Review: Drugs and Highway Safety.

UM-79-D1271

A COMMENT ON KOLA NUTS AND TRAFFIC ACCIDENTS [letter], S.P. Bohrer, American Journal of Public Health, v69 n7 p723-4 (Jul 1979)

This letter-to-the-editor responds to an earlier letter (D1222) suggesting that kola nut consumption in Nigeria may contribute to the high traffic accident rate in Nigeria. The present letter argues that the 12.25% of Nigerian drivers involved in road accidents who admitted to having recently eaten kola nuts is probably no higher a percentage than one would find among comparable Nigerians not involved in road accidents, since the habit is a common one. The accident rates of kola nut users must be compared to those of control groups before the effect of kola nuts on driving can be established. (HSRI)

0 refs

KEYWORDS: Stimulants: kola. Epidemiology: National Survey of Drug Use Patterns. Epidemiology: Self-Reported Drug Use by Drivers.

UM-78-D1272

POLYDRUG ABUSE, J.M. Foxworth, Psychiatric Forum, v7 n2 p17-22 (Spring 1978)

Presented here is a general review of polydrug abuse. Special attention is given to the clinical complications and problems which result from polydrug abuse. Also discussed are motivation for polydrug abuse, the current status of polydrug abuse, types of polydrug abuse, and symptoms.

There are several areas of clinical concern related to polydrug abuse which medical personnel must be aware of: (1) The pure classical pictures of single drug abuse will likely be mixed and obscured. (2) Evaluation will often reveal numerous physical problems aside from the short-term toxic effects of the drugs. These include such conditions as hepatitis, endocarditis, and pneumonia. (3) Severe polydrug intoxication or overdose requires both knowledge of the differential effects of single drugs as well as drug interactions. (4) Specific drug antagonists are limited in number, and polydrug abuse often limits or compromises the use of these and other less specific medications. (5) Detoxification or withdrawal requires special considerations since certain combinations of drug produce significant abstinence syndromes. (6) Polydrug abuse is often a symptom of severe psychiatric pathology, requiring more than just physical treatment. (HSRI)

16 refs

KEYWORDS: Review.

UM-78-D1273

PSYCHOANALYTIC OBSERVATIONS ON MARIJUANA USE, L. Wallace, American Journal of Psychiatry, v135 n8 p990-1 (Aug 1978)

Presented here is an in-depth study of a regular user of marijuana. It focuses primarily on the immediate aftereffects of marijuana. A case study of a thirty-two-year-old male psychiatric patient is described. Two consequences of marijuana use were observed in this patient. First, the immediate high contributed an intense quality to his daydreaming that substituted for the pursuit of satisfaction in reality and provided a temporary escape from internal conflict. Second, there were aftereffects which lasted for twenty-four hours after drug use. The immediate postintoxication period was characterized by fatigue, lethargy, and boredom. The next day there was a noticeable consistent tranquilizing effect; all other effects were diminished. This tranquilizing effect, sometimes lasting two or three days, was an important reason for this patient's regular use of marijuana.

The patient suffered withdrawal symptoms which reached a peak in four days and tapered off over the period of a week. This withdrawal raises a question regarding possible addictive effects of marijuana use.

The author suggests that psychoanalytic observation of patients in whom regular use of marijuana is an incidental observation can be a potentially valuable source of data concerning marijuana effects and reasons for use. However, it must be remembered that the focus on therapeutic goals has limiting effects on data collection and the analysis may influence responses to the drug. These limitations must be kept in proper focus. (HSRI)

1 ref

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Clinical Study.

UM-78-D1274

THE NEUROLOGICAL MANIFESTATIONS OF CHRONIC INHALATION OF LEADED GASOLINE, S.S. Seshia; K.R. Rajani; R.L. Boeckx; P.N. Chow, Developmental Medicine and Child Neurology, v20 n3 p323-34 (June 1978)

Chronic inhalation of leaded gasoline is a common form of solvent abuse among young people in native Indian communities. This paper reports the neurological manifestations of chronic gasoline inhalation in fifty children and adolescents and discusses the pathophysiology of these manifestations. Special attention is given to the clinical neurotoxicity associated with this practice and the use of chelation therapy in the management of those abusing this solvent. Subjects were thirteen males and four females aged four to ten, and twenty-seven males and six females aged ten to twenty who had been sniffing leaded gasoline for periods ranging from six months to over five years. Frequency of inhalation ranged from twice a day to three times a week.

Standard techniques of neurological examination were followed including assessment of deep reflexes, encephalopathy, and postural tremor. Blood lead (Pb) and erythrocytic delta aminolevulinic acid dehydratase (ALAD) were determined. Urine lead level was determined using twenty-four-hour samples of urine. Other investigations included nerve conduction velocity determination, blood count, renal and hepatic function, EEG, and ECG.

Forty-six (92%) of the subjects had abnormal neurological signs at the time of first assessment. There was a significant relationship between blood Pb and ALAD levels and several reflexes, tremors, stance, and gait. Forty-nine had blood lead levels greater than 40 micrograms per deciliter. Over half had abnormally brisk deep reflexes, indicating dysfunction of corticospinal and corticobulbar components and contributing to impairment of skilled movement and dysarthria. A highly significant number of patients also had intention tremor, adiadochokinesis, and ataxia of speech, stance, gait, and tandem walking, suggesting involvement of cerebellar structure and its connections. EEGs were abnormal in twenty of the forty-six patients who had EEGs taken, the records being of very low voltage and containing an excess of diffuse slow activity.

The patients were given one of five treatment regimens based on their clinical presentations. Various combinations of dimercaprol, calcium disodium edatate (CAEDTA), and d-penicillamine were administered. After eight weeks of treatment, only one subject still had symptoms of neurological dysfunction.

The authors conclude that chelation therapy has an important place in the management of those abusing leaded gasoline. (HSRI)

44 refs

KEYWORDS: Heavy Metals and Heavy Metal Antagonists: lead*. Volatile Solvents: gasoline. Clinical Study. Drug Concentration-Effect Study: Clinical Research. Physiological Testing. Psychomotor Tests.

UM-79-D1275

INDIVIDUAL AND GROUP EFFECTS OF 10 MG DIAZEPAM ON DRIVERS' ABILITY, CONFIDENCE AND WILLINGNESS TO ACT IN A GAP-JUDGING TASK, A. Wetherell, Psychopharmacology, v63 p259-67 (1979)

It has been suggested that an increasing number of people are driving after taking diazepam, and while the clinical use of anxiolytics is expected to improve the patients' everyday level of performance, experimental studies of the effects of diazepam on driving have variously indicated performance decrements, no effects, or performance increments. Possible reasons for this inconsistency are variations between and within subjects and differential effects of the drug on the various components of task performance. These factors were investigated by an experiment designed to compare the effects of a single 10 mg oral dose of diazepam between and within groups and between and within individuals, and to examine effects of the drug on separate behavioral components of a driving task. Twenty drivers took part in the study which assessed their ability, their degree of confidence in their ability, and their willingness to drive through various sizes of gap. The drivers were divided into two groups of ten, and were tested individually on each of two days. Group 1's treatment was placebo-diazepam, and group 2's was placebo-placebo.

When analyzed by group, the results showed a significant increase ($P<0.01$) in group 2's willingness and a significant decrease ($P<0.001$) in group 1's willingness to attempt gaps, which suggests greater caution under diazepam treatment. There was no change in either group's confidence, but group 1 showed a significant increase ($P<0.05$) in their ability variance. When analyzed by individual, a wide variety of significant changes ($P<0.05$ or better) was found in ability and confidence for group 1 individuals, some changing for better and some for worse under diazepam treatment. No significant changes in ability or confidence were found for group 2 individuals. All group 1 individuals were less willing to attempt gaps under diazepam treatment, while all group 2 individuals were more willing to attempt gaps under continued placebo treatment.

The validity of these findings is discussed in terms of real-life driver behavior, and it is concluded that there may be a wide interindividual variation in the effects of diazepam not necessarily apparent in grouped data, and that diazepam may have differential effects on the decision-making and perceptual-motor components of driver behavior in a gap-judging task. (JA)

18 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Closed Course Driving. Experimentation: Acute Dosage Study.

UM-79-D1276

HUMAN BEHAVIORAL PHARMACOLOGY: METHODS AND ISSUES, E.H. Uhlenhuth; C.R. Schuster; M.W. Fischman, Psychopharmacology Bulletin, v15 n2 p21-3 (Apr 1979)

Briefly described here are several laboratory studies illustrating how important the reinforcing factor is in evaluating the results of common performance tests in human subjects, both in studies using drugs and in those not using drugs. On speed and accuracy tests, subjects reinforced only for accuracy tended to have relatively low stable error rates and high, variable reaction times. Subjects reinforced for accuracy and speed tended to have relatively high variable error rates and relatively low, stable reaction times. In a tapping test reinforcement was able to reverse the impairing effect of diazepam.

It appears that the effects of the contingencies of reinforcement on common human test performances are similar in magnitude to the effects of psychotropic drugs within an acceptable dose range. The effects of contingencies may compete with drug effects and largely reverse them. Behaviors not under schedule control may show high levels of random variation well within the range of change produced by acceptable doses of psychotropic drugs. These observations suggest that optimal structuring of contingencies of reinforcement is a crucial part of experimental design in evaluating the effects of psychotropic drugs on commonly used performance tests. (HSRI)

2 refs

KEYWORDS: Review: Behavioral Research Methodology.

UM-80-D1277

MARIJUANA FOR DRUG-INDUCED NAUSEA AND VOMITING [editorial], D.L. Sweet, Journal of the American Medical Association, v243 n12 p1265 (28 March 1980)

This editorial proposes that marijuana has great potential as an antiemetic for drug-induced nausea and vomiting and for treating a variety of other diseases. It briefly discusses several studies of marijuana's effects on cancer patients receiving chemotherapy.

Many studies provide evidence that THC may effectively alleviate the nausea and vomiting induced by certain cancer chemotherapies substantially more than legal, clinically acceptable drugs such as prochlorperazine. Although THC produces minor to serious side effects, the patient who suffers severe nausea from cancer chemotherapy often finds THC's effects more tolerable. These side effects include dizziness, somnolence, and feelings of euphoria or dysphoria. Less common side effects include feelings of intense anxiety or panic, hallucinations, memory loss, blocked speech, and loss of motivation.

Some studies have shown that the antiemetic effect of THC varies with the drug that is causing the vomiting. The mechanism of action for the antiemetic and other effects of THC is not yet clear. Marijuana possesses adrenergic activity and may depress prostaglandin activity. Further research is needed to realize the potential of this drug. (HSRI)

6 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Review: Drug Effects.

UM-80-D1278

DELTA-9-TETRAHYDROCANNABINOL FOR REFRACTORY VOMITING INDUCED BY CANCER CHEMOTHERAPY, V.S. Lucas; J. Laszlo, Journal of the American Medical Association, v243 n12 p1241-3 (28 March 1980)

The purpose of this study was to determine whether orally administered delta-9-tetrahydrocannabinol (THC) is an effective and practical antiemetic for the control of chemotherapy-induced nausea and vomiting in patients who are unresponsive to conventional antiemetics. Fifty-three patients receiving antineoplastic chemotherapy who had experienced severe vomiting and nausea refractory to standard antiemetic agents were given THC before, during, and after chemotherapy. Two dosage schedules were used: (1) nine patients received 15 mg per square meter THC orally every six hours, starting one hour before chemotherapy administration and continuing every six hours for four doses; (2) the remaining patients received THC orally at doses of 5 mg per square meter every four hours, starting eight to twelve hours before chemotherapy and continuing for twenty-four hours after. Patients' responses were evaluated first by taking a history of past nausea, vomiting, and antiemetic therapy for comparison and secondly, by observation during treatment.

Results showed that ten patients (19%) had no further nausea or vomiting; twenty-eight (53%) had at least a 50% reduction of nausea and vomiting compared to previous courses with the same agents. No appreciable reduction of nausea and vomiting was seen in fifteen patients (28%). Toxic reactions were generally mild, with only four patients experiencing reactions that necessitated stopping THC therapy.

The authors suggest that since THC is a useful antiemetic agent in patients having refractory chemotherapy-induced vomiting, existing restrictions prohibiting its therapeutic use should promptly be eased. (JAM)

8 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Clinical Study. Experimentation: Chronic Dosage Study. Experimentation: Other Multiple-Drug Studies. Other Factors Influencing Drug Effects.

UM-78-D1279

COCA LEAF AS A THERAPEUTIC AGENT, A.T. Weil, American Journal of Drug and Alcohol Abuse, v5 n1 p75-86 (1978)

Presented here is a discussion of the use of coca as a therapeutic agent. It is based on the author's own clinical experience with the drug and on accounts of its use in both the historical and current scientific literature. The following aspects of coca are discussed: its nature, effects, historical medicinal uses, possible uses in modern therapeutics, pharmacology, forms of administration, potential for abuse, legal status, and availability.

The author proposes that coca is a safe and useful drug. Its lack of toxicity, safety, acceptability by patients even in crude form, and its favorable side effects make it a potentially valuable therapeutic drug. Among its uses in modern therapeutics are the following: (1) to relieve painful and spasmodic conditions of the entire gastrointestinal tract; (2) as a substitute stimulant for coffee in persons who consume much coffee and suffer gastrointestinal irritation; (3) as a fast-acting antidepressant; (4) as a treatment for acute motion sickness; (5) as adjunctive therapy in programs of weight reduction and physical fitness; (6) to give energy to persons engaged in strenuous physical activity; (7) asymptomatic treatment of toothache and sores in the mouth; (8) as a laryngeal tonic; and (9) as a substitute stimulant to wean users of amphetamines and cocaine.

Coca users do not experience the extreme mood changes of cocaine users. Coca is chewed, thus causing a very gradual increase in blood levels of cocaine. Furthermore, much of the cocaine in coca enters the body as ecgonine, a less toxic alkaloid.

Coca users show no signs of physical deterioration attributable to the leaf, nor any physiological or psychological dependence on coca. Life-long chewers seem to get the desired effect without having to increase the dose overtime; there is no development of tolerance and no withdrawal syndrome upon abrupt cessation of use.

The author favors the therapeutic use of coca. It could be administered as a chewing gum which would contain a whole extract of the leaf, including alkaloids, natural flavors, and several nutrients. This would allow the drug to enter the body slowly, providing a natural safeguard against abuse. (HSRI)

17 refs

KEYWORDS: Local Anesthetics: coca. Stimulants: coca. Review.

UM-78-D1280

DRUG ABUSE AND SUICIDE, S. Saxon; E. Kuncel; S. Aldrich, American Journal of Drug and Alcohol Abuse, v5 n4 p485-95 (1978)

The purpose of this paper is to examine the occurrence of past suicidal behavior and past self-destructive behavior within a group of drug abusers. During August of 1976, all of the 114 persons who requested drug abuse services from the Orange County Department of Mental Health were interviewed according to a defined protocol to determine their histories of self-destructive behaviors. The following variables were assessed: primary drug of abuse, treatment program requested, arrests for driving under the influence of drugs or alcohol, auto accidents in which the subject was the driver, and nonsuicidal overdoses.

The data collected during the interviews showed that the primary drug of abuse for the 114 patients (76 males and 38 females) was as follows: heroin, 60%; marijuana, 22%; cocaine and/or amphetamines, 7%; alcohol, 5%; barbiturates, 3%; PCP, 2%; and diazepam, 1%. Thirty-seven percent of the subjects (27 males and 15 females) indicated one or more arrests for driving under the influence of drugs or alcohol. Almost half the subjects (38 males, 17 females) had been involved in an auto accident as a driver, and 47% reported having had suicidal thoughts. Fifty-two percent indicated having experienced at least one suicidal overdose, with 23% reporting three or more nonsuicidal

overdoses. For the 13 subjects who attempted suicide by overdosing, 5 did so with barbiturates, 2 with heroin, 1 with aspirin, and 5 with unspecified drugs.

Analysis of the data indicates that 19% of the sample had made a suicide attempt, a rate 12 to 152 times greater than that expected in the general population. No evidence was found indicating that drug abusers making a suicide attempt do so with their primary drug of abuse. A high correlation exists between suicidal thoughts and suicide attempts; about half of the sample reported having suicidal thoughts.

Considering the nonsuicidal overdose rate, the arrests for driving under the influence of drugs or alcohol, and the suicide attempt rate, it appears that this drug abusing sample contains a definite high suicide risk population.

The paper concludes with a discussion of the implications of these results and the roles of depression and self-destruction in suicide. (HSRI)

9 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Local Anesthetics: cocaine. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Stimulants: cocaine. Barbiturates. Stimulants. Epidemiology: Self-Reported Drug Use by Drivers.

UM-79-D1281

MINOR TRANQUILLISERS AND ROAD ACCIDENTS, D.C.G. Skegg; S.M. Richards; R. Poll, British Medical Journal, v1 n6168 p917-19 (7 Apr 1979)

According to prescription records, approximately 19% of the British population fifteen years or older uses psychotropic drugs within the period of one year. This study attempted to determine whether such patients are at an increased risk of having traffic accidents. For each of 43,117 patients included in the study, demographic characteristics, prescription use, and hospital records were collated. This study investigated this information for fifty-seven drivers who had been included in the study for at least twelve months before their accident. Included were twenty-one car drivers, twenty-two motorcyclists, and fourteen cyclists. For each of the patients, twenty-five controls were selected at random from the total population who: (1) had been treated by the same physician; (2) were of the same sex; (3) had the same or an adjacent year of birth; and (4) had also been included in the study for at least twelve weeks before the accident. Patients injured in road accidents and their matched controls were compared with respect to the drugs that had been prescribed for them and dispensed to them during the three months before each accident.

Of the fifty-seven drivers, six (11%) had received a sedative or tranquilizer during the twelve months prior to the accident. Of the 1,425 controls, thirty-six (2.5%) had received such a drug. The relative risk associated with use of sedatives and tranquilizers was estimated to be 5.2. Five (8.8%) of the drivers had received minor tranquilizers such as benzodiazepines compared to 2.2% of the controls; the relative risk associated with use of these drugs was estimated to be 4.9. There was also a significant association between use of antihistamines (chlorpheniramine and mebhydroline) and motorcycle accidents.

The authors conclude that drivers taking minor tranquilizers are at a substantially increased risk of having a road accident. Whether or not this risk is due to the drug effects or to the condition being treated was not able to be ascertained by this study. Nevertheless, the increased risk has implications for the safety of the other road users as well as the patient himself. (HSRI)

17 refs

KEYWORDS: Analgesics and Antipyretics. Antacids and Adsorbants. Antihistamine Agents. Diuretics. Minor Tranquilizers (Anti-Anxiety and Ataractics). Oral Contraceptives. Penicillins. Sedatives and Hypnotic Agents. Tetracyclines. Epidemiology: National Survey of Drug Use Patterns. Epidemiology: Record-Based Survey.

UM-79-D1282

DRIVING AFTER ANAESTHETICS [letter], W.D.A. Smith, British Medical Journal, v1 n6169 p1016 (14 Apr 1979)

This letter-to-the-editor emphasizes the residual effects of general anesthetics, particularly nitrous oxide, on behavior. Subjective and objective changes in mood and behavior induced by nitrous oxide may outlast retention of appreciable quantities of the gas. A lunch-time inhalation of 80% nitrous oxide, for example, up to the point of no response to repeated auditory stimuli may leave the individual subjectively aware of slight difficulty in assessing traffic speed in the evening. In nine out of eighty-one patients anesthetized for orthopedic procedures, nausea and vomiting developed, usually precipitated by the automobile trip home. Several of the patients felt ill for up to three days.

The author urges further research on the effects of nitrous oxide on driving, particularly as it relates to stimulation of the semicircular canals. (HSRI)

1 ref

KEYWORDS: General Anesthetics: nitrous oxide. Hallucinogens and Related Agents: nitrous oxide. Anesthetics. Review: Drug Effects. Review: Drugs and Highway Safety.

UM-79-D1283

DRIVING AFTER ANAESTHETICS [letter], D.G. Moyes; P. Cleaton-Jones; T. Lelliott, British Medical Journal, v1 n6175 p1425 (26 May 1979)

This letter-to-the-editor briefly describes a study of the effects of nitrous oxide on driving ability. Driving ability following fifteen minutes of inhalation of air, 50% nitrous oxide in combination with 50% oxygen, or 70% nitrous oxide in combination with 30% oxygen was studied in student volunteers using a driving simulator.

A slight but definite impairment in driving ability was found up to thirty minutes following inhalation of the nitrous oxide-oxygen mixtures.

The authors conclude that caution should be exercised by drivers after even a short exposure to nitrous oxide. (HSRI)

0 refs

KEYWORDS: General Anesthetics: nitrous oxide. Hallucinogens and Related Agents: nitrous oxide. Driving Simulator. Experimentation: Acute Dosage Study. Review: Drugs and Highway Safety.

UM-79-D1284

DIAZEPAM AND TRAFFIC ACCIDENTS [letter], A. Landauer, British Medical Journal, v2 n6183 p207 (21 July 1979)

This letter-to-the-editor contends that no detrimental effect of diazepam on driving ability has been established. While there is considerable evidence that critical flicker fusion frequently is reduced by small doses of diazepam and that reaction time is altered, no relationship between these laboratory measures and actual driving has been determined.

Existing studies investigating the effects of diazepam on driving ability fail to distinguish between the effects of the drug and the condition being treated.

The author concludes that as a general rule, it is preferable that anxious, aggressive, and depressed patients do not drive; with diazepam driving safety could deteriorate, remain unchanged, or improve. (HSRI)

3 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Review: Drug Effects. Review: Drugs and Highway Safety.

UM-79-D1285

BENZODIAZEPINES AND TRAFFIC ACCIDENTS [letter], I. Hindmarch, British Medical Journal, v2 n6191 p671 (15 Sep 1979)

This letter responds to an earlier letter-to-the-editor contending that diazepam has not been directly linked to impaired driving. This author states that all 1,4-

benzodiazepines, not just diazepam, have been shown to possess sedative activity which can severely impair the regulation and performance of the sensory-motor tasks undertaken by patients during the course of their everyday behavior.

Laboratory assessments of performance do relate to the real life situation if appropriate measures are used. Both critical flicker fusion and reaction time have been shown to be analogues of real life performance where coordination of eye, hand, and brain is important. Laboratory results have been supplemented by tests of actual car driving performance. The impairment of performance shown in laboratory tests following the administration of lorazepam has been mirrored in the reduced performance on actual car driving tests of brake reaction, steering, width estimation, parking, and garaging undertaken by the same subjects in a placebo controlled study. One can only conclude from these studies that the administration of 1,4-benzodiazepines produces an increased risk of accident in situations where the integrity of the sensory and motor systems is an essential prerequisite for the safe performance of the task. (HSRI)

6 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam, lorazepam. Muscle Relaxants (Central): diazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics). Review: Drug Effects. Review: Drugs and Highway Safety.

UM-79-D1286

PSYCHIATRISCHE KRANKHEITEN UND FAHRTAUGLICHKEIT [PSYCHIATRIC DISEASES AND DRIVING FITNESS], H. Hippius, Munchener Medizinische Wochenschrift, v121 n41 p1322-5 (12 Oct 1979)

Mental factors frequently play a decisive role in the conditional setup of accidents. Analyses of the mental factors determining the cause of accidents show these to be by far more often mental factors of a nonpathological nature, such as personality factors, disordered concentration and alertness in conflict situations, overstrain, and fatigue, than factors conditioned by illness, for example, as associated with depression or schizophrenia. Psychological alterations in subjects of advanced age constitute a border area of high significance in medical science concerned with traffic safety. In the consulting room, particular attention should be paid to the recognition of potential risk constellations in traffic precipitated by alcohol or drugs. (JA)

0 refs German

KEYWORDS: Review.

UM-79-D1287

DIE WIRKUNG VON ALKOHOL UND COFFEIN AUF DEN DURCH LANGERE FAHRT ERMUDETEN KRAFTFAHRER. EINE UNTERSUCHUNG AM FAHRSIMULATOR [EFFECT OF ALCOHOL AND CAFFEINE ON THE DRIVER FATIGUED BY A LONG TRIP. A STUDY ON A DRIVING SIMULATOR, E. Schuller; G. Drasch; L. von Meyer; D. Anselm, Beitrage zur Gerichtlichen Medizin, v37 p219-22 (1979)

The effects of alcohol and caffeine on driving fatigue were investigated in ten subjects using a driving simulator. After driving for two and one-half hours a significant impairment was evident for blood alcohol concentrations greater than .05%. The average decrease in performance rate was 32%.

When the subjects were administered coffee with 100 mg caffeine, an increase in driving ability and a decrease in reaction time was observed in most subjects. Caffeine decreased impairment from 32% (alcohol alone) to 20%. However, there was a great deal of variability among subjects in their driving performance under both drug conditions.

A break of thirty minutes resulted in an average improvement in performance of 20%. (JAM)

8 refs German

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: caffeine. Driving Simulator. Experimentation: Acute Dosage Study. Experimentation: Study of Combined Effects of Drugs.

UM-79-D1288

PROCEEDINGS OF THE SEVENTH INTERNATIONAL CONFERENCE ON ALCOHOL, DRUGS AND TRAFFIC SAFETY, I.R. Johnston, ed., Canberra: Australian Government Publishing Service (1979)

The excessive use of alcohol remains the single most important factor contributing to the incidence of serious crashes on Australian roads. These proceedings of the Seventh International Conference on Alcohol, Drugs and Traffic Safety held 23-28 January 1977 in Melbourne review progress in worldwide efforts to reduce the role of alcohol and other drugs in traffic accidents. Possible countermeasures are examined and directions for future research and action are indicated.

The following major topics are addressed by papers dealing with both alcohol and other drugs: (1) problems and methodological issues in epidemiologic studies, particularly in identification of high risk groups; (2) pharmacological and behavioral issues; (3) methodology for measuring the presence of alcohol; (4) evaluation of countermeasure strategies; (5) legislation, enforcement, and deterrence; and (6) education and information.

The volume concludes with a list of conference resolutions for both policy and research in the area of alcohol, drugs, and traffic safety. The specific areas covered by the resolutions include community attitudes and public education; legislation, courts, and clinics; police enforcement strategies; the nature and effects of legal sanctions; modification of vehicles and environments; rehabilitation of the drinking driver; and detection and quantification of drugs and alcohol in the body fluids of drivers. (HSRI)

712 pages

KEYWORDS: Anti-Emetics: chlorpromazine. Antidepressants: imipramine. viloxazine. Barbiturates: amobarbital. Cannabis Sativa L. and Related Agents: marijuana. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Nonbarbiturates: ethanol (ethyl alcohol). Compilation.

UM-79-D1289

ANALYTIC ISSUES IN STUDYING THE INTERACTION OF ALCOHOL AND OTHER DRUGS AND HIGHWAY CRASHES, J.A. Waller, Proceedings of the Seventh International Conference on Alcohol, Drugs, and Traffic Safety, I.R. Johnston, ed., p15-23, Canberra: Australian Government Publishing Service (1979)

This paper attempts to review, describe, and correlate previous and current epidemiologic and sociologic studies of drugs and highway safety. The epidemiological method is described and related to other methods of studying injury events for purposes of establishing countermeasures. These broad concepts are then applied more specifically to alcohol, other drugs, and highway crashes.

Some of the major problems in epidemiologic studies of drug use and driving are the following: (1) noncomparability of collection methods; (2) inaccuracies in drug analyses methods; (3) inability to assess the actual role of drugs in driving-related performance; (4) lack of objective measures of drug impairment and of drug concentrations in biofluids; (5) failure to use comparison samples of driving without crash samples. The author believes that none of the epidemiologic studies existing, as carried out, suggest an increase in crash risk involving the drugs identified.

The author suggests several areas needing further research that involve epidemiologic issues: (1) In order to identify minimal impairment, it is necessary to develop a standardized split task format to use for comparing effects of individual drugs or of drug combinations. (2) Standard characterization and division of individuals according to age, sex, drug experience, driving experience, and health status is necessary to ensure that these variables have been taken into consideration. (3) There is a need to identify the extent to which psychotherapeutic drugs for alcoholism modify the behavior patterns of the alcoholic after ingestion of alcohol. (4) More information is needed to determine whether all persons with alcoholism are equally at high risk of crashing after heavy drinking. (5) More exploration is needed to investigate the differences in drug effects among individuals and the role of these effects in highway safety. (6) Preplanning of the evaluation, adequate collection of baseline data, and use of comparison samples must be included in every epidemiologic study if it is to be of any value. (HSRI)

27 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Review: Survey Methodology.

UM-79-D1290

PROBLEMS OF DRUG ANALYSIS, A.E. Robinson, Proceedings of the Seventh International Conference on Alcohol, Drugs and Traffic Safety, I.R. Johnston, ed., p95-9, Canberra: Australian Government Publishing Service (1979)

Presented here is a review of problems in drug analysis and an evaluation of several studies using analysis to determine drug use in drivers. Toxicological analysis is often limited by the nature and volume of the available blood, bile, saliva, or urine samples. While 100 ml urine and blood samples usually allow the analyst to identify and quantify most psychotropic drugs, often they are unavailable. Some samples which are ordinarily adequate in volume are unsuitable because of the drug involved; for example, a very large saliva sample is necessary to detect amylobartitone because of the low ratio of saliva:serum concentrations reported after administration of amylobarbitone.

Drug analysis can also be limited by the metabolic changes undergone by the drug in the body. Diazepam, for example, metabolizes to N-desmethyldiazepam which is hydroxylated to form oxazepam, all of which can impair driving. This results in continued impairment well after diazepam plasma levels have peaked. Accumulation of metabolites during chronic drug administration is also common. Such metabolic reactions must be taken into account in interpreting serum levels.

Another problem of drug analysis in drivers is the lack of a practical, inexpensive method for the identification of a drug. This has been true particularly for cannabinoids. The methods that do exist for quantititating these commonly used drugs are inadequate for routine screening. A closely related problem is the expense involved in analysis procedures for many commonly used drugs such as barbiturates.

Due to the complexities of individual variations in response to drugs, it is not practical to attempt to establish arbitrary blood levels for every known psychotropic drug. However, it is possible by analysis of body fluids to identify the driver who has taken a drug or drugs that may adversely influence performance. Further research is needed to determine whether the cost of legislation utilizing drug analysis in drivers would be justified in terms of improved traffic safety. (HSRI)

35 refs

KEYWORDS: Review: Drug Analysis Methodology.

UM-79-D1291

DRUG-ALCOHOL INTERACTION AND DRIVING--AN EFFECTIVE LEGISLATION, D.G. Wilson, Proceedings of the Seventh International Conference on Alcohol, Drugs and Traffic Safety, I.R. Johnston, ed., p100-3, Canberra: Australian Government Publishing Service (1979)

Presented here is a discussion and evaluation of existing drug-driving legislation in Queensland, Australia and recommendations for more effective legislation. The history of legislation since 1968 concerning the use of alcohol, drugs, or both while driving is presented. The suspected driver is now required to provide a specimen of his breath, blood, or urine, or all three, and trained police officers are permitted to perform breath analysis. If his BAC, as measured by a Borkenstein Breathalyzer, is incompatible with his behavior pattern, blood and urine samples are collected and the driver is examined by a medical officer. Qualitative and quantitative analyses of the blood sample are done, or if the drug is unknown, the urine sample is screened by thin-layer chromatography. However, only blood analyses are used as court evidence.

The author concludes that the full effect of drugs alone or in combination with other drugs or alcohol cannot be determined until objective methods of measuring blood alcohol levels become available. He suggests an educational rather than legislative approach to the problem. These programs should be directed primarily at the prescriber of the drug--the physician. It must be the duty of every physician to fully understand the properties of each drug he prescribes and to warn his patient about drug effects on driving, operating machinery, and drinking alcohol. Pharmaceutical manufacturers should also take responsibility by attaching appropriate warning labels to each package of drugs acting on the central nervous system. (HSRI)

5 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Countermeasure Development, Testing, and Evaluation. Other Sociolegal Study.

UM-79-D1292

DETERMINANTS AND MODIFIERS OF THE EFFECTS OF DRUGS ON DRIVING ABILLITY AND BEHAVIOR, J.G. Rankin, Proceedings of the Seventh International Conference on Alcohol, Drugs and Traffic Safety, I.R. Johnston, ed., p217-29. Canberra: Australian Government Publishing Service (1979)

The purpose of this paper is to examine the various factors that determine or modify the effects of alcohol and other drugs on driving. The implications of these factors are discussed as they relate to countermeasures aimed at preventing accidents due to alcohol or drug impairment.

The following topics are discussed: (1) individual variations in the relationship between drug dose and drug effects; (2) modifiers of drug effects on driving behavior and ability such as age, sex, disease, inheritance, and prior drug use; (3) drug interactions such as antagonism, synergism, or summation; (4) effects of ethanol and its interactions with other drugs; and (5) alcohol, age, and the total impairment risk factor.

Some drugs are much more likely to cause serious traffic injury; this fact must be taken into account when countermeasures are developed. Alcohol is undoubtedly the greatest threat to traffic safety. Other drugs which could impair driving, due to their high rate of usage and potential for abuse, include benzodiazepines, barbiturates, nonbarbiturate sedatives, tricyclic antidepressants, and neuroleptics. These drugs are particularly dangerous when combined with alcohol or with each other.

The author concludes that present knowledge concerning how drugs alone or in combination with one another or alcohol affect driving ability and behavior is significantly deficient. He suggests that for legal purposes the combined use of alcohol plus any one of certain other specified drugs might be defined as unsafe even when the blood alcohol limit is below present legally defined limits. Diagnosis of combined alcohol and drug use would be based on the qualitative detection of alcohol and one of these other substances and not require quantitative estimations. The taking of drugs alone or in combination without alcohol presents a more complex problem because of the lack of a clear understanding of the relationship between drug effects on driving and plasma levels. Given the number of drugs involved, the variations in their toxicological properties, and the problems of quantitative analysis, it would be impossible to establish a legal limit for drugs as exists for alcohol. (HSRI)

23 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Antidepressants. Autonomic Nervous System (ANS) Agents. Barbiturates. Minor Tranquilizers (Anti-Anxiety and Ataractics). Sedatives and Hypnotic Agents. Countermeasure Concepts. Review: Drugs and Highway Safety.

UM-79-D1293

THE EFFECT OF SEDATIVE DRUGS ON HUMAN PERFORMANCE, J.G. Manton, Proceedings of the Seventh International Conference on Alcohol, Drugs and Traffic Safety, I.R. Johnston, ed., p247-55, Canberra: Australian Government Publishing Service (1979)

The purpose of the two experiments reported here was to measure the effect of outpatient doses of sedative drugs on human performance. Special attention is given to the problem of isolation of a sensitive performance parameter. The study attempted to determine: (1) whether a measure of selective attention was sensitive to therapeutic doses; and (2) whether the effect of drug action on the structure of attention is a multicomponent, complex task.

Four healthy students were administered double-blind each of seven treatments at weekly intervals: (1) placebo; (2) 2.5 mg diphenylpryaline; (3) 5.0 mg diphenylpryaline; (4) 50 mg amylobarbitone; (5) 100 mg amylobarbitone; (6) 20 mg chlorpromazine; (7) 40 mg chlorpromazine. One and five hours after drug ingestion the subjects performed a tracking task and a peripheral detection task.

Results of the test scores indicated that the 100 mg dose of amylobarbitone and both doses of chlorpromazine caused impairment in tracking ability. In the peripheral signal detection test, nearly all drugs (except for placebo) impaired detection of signals at 20 degrees but improved detection of signals at 80 degrees. Chlorpromazine impaired performance over all stimulus positions.

Two general conclusions were drawn from this study: (1) sedation causes a reduction in selectivity of attention; and (2) sedation does not lead to unsystematic changes in selectivity. Relative performance appeared to be related to some phenomenal priorities across the multicomponent task.

In order to refine these conclusions further a second experiment was conducted. This experiment manipulated arousal by using the stimulant caffeine and the sedative action of amylobarbitone. The peripheral detection task was modified so that the parameters derived from signal detection theory (SDT) and information theory (IT) could be analyzed.

Subjects were seven male students. They were administered double-blind each of seven drug treatments: (1) placebo; (2) 75 mg caffeine; (3) 150 mg caffeine; (4) 300 mg caffeine; (5) 50 mg amylobarbitone; (6) 75 mg amylobarbitone; (7) 125 mg amylobarbitone. Procedures and tests were identical to those used in the previous experiment.

In the tracking test, 300 mg caffeine significantly improved tracking performance, while 125 mg impaired performance. In the peripheral detection task significant results were found for the largest doses of each, with caffeine improving performance and amylobarbitone impairing performance.

Results of the two experiments are analyzed, and possible drug-arousal level interactions are discussed. Several models of arousal and attentional selectivity are evaluated using the test results.

The author concludes that a simple model of attentional selectivity based on arousal levels is inappropriate for evaluation of drug effects on performance. A more appropriate model should include parameters of task complexity. (HSRI)

22 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Antihistamine Agents: diphenylpyraline. Barbiturates: amobarbital. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Stimulants: caffeine. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Psychological Testing. Psychomotor Tests. Tests of Sensory Function.

UM-79-D1294

DRIVING TESTS UNDER THE EFFECTS OF BETA RECEPTOR BLOCKING DRUGS, B. Friedel, Proceedings of the 23rd Conference of the American Association for Automotive Medicine, p90-103, Morton Grove, Ill.: AAAM (1979)

Twenty healthy subjects were used in a double-blind study to test the two beta receptor blocking drugs propranolol and pindolol with respect to their effects on drivers and driver behavior. The driving tests were conducted on a test ground. In addition to several psychophysiological parameters and psychomental performance tasks, driver behavior was studied by means of special auxiliary driving tasks.

In a completely randomized crossover test, ten males and ten females with a mean age of 25.4 years were administered oral doses of 5 mg pindolol, 40 mg propranolol, and/or placebo three times daily for six days. On the sixth day subjects were tested ninety minutes after their last dose.

In addition to the effects on the heart and circulation system predicted on the basis of the pharmacodynamics of beta blockers, a clear change in psychophysiological reactions was established. The effect of beta blockers on psychomotor coordination and reactivity was negative. These results, together with the sedative side effects reported by many subjects, indicate that a general reduction of psychomotor activity results from the ingestion of beta blockers. (JAM)

6 refs

KEYWORDS: Anti-Anginal Agents: propranolol. Anti-Arrhythmia Agents: propranolol. Vasodilating Agents: pindolol. Closed Course Driving. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs.

UM-79-D1295

THE EFFECT OF A SINGLE ACUTE DOSE OF DIAZEPAM ON DRIVING-RELATED SKILLS PERFORMANCE, H. Moskowitz; S. Sharma; K. Ziedman, Proceedings of the 23rd Conference of the American Association for Automotive Medicine, p277-89, Morton Grove, Ill.: AAAM (1979)

This study used three measures of skills performance to assess the effects of a single dose of diazepam on driving-related skills performance over a twenty-four-hour period. Subjects were eight males aged 21 to 28 who were medically and psychologically normal. They were tested in five experimental sessions: three times under active diazepam levels of .031 mg/kg body weight, .063 mg/kg, and .126 mg/kg; once under placebo; and once without any treatment. Mean doses of diazepam were 2.27 mg, 4.54 mg, and 2.27 mg and were administered double-blind as Valium tablets. At each treatment session performance was examined at twelve time points within twenty-three hours after treatment. Visual search, visual search and tracking in a divided-attention situation, and information processing rate were assessed.

Results of the tests demonstrate that diazepam has a detrimental effect on the performance of the complex tasks examined in this study. All three tasks showed statistically significant degrees of impairment which were dose-related, albeit often nonlinearly. Impairment persisted up to eight hours postdrug.

When compared to a similar study of the effects of 0.58 mg/kg alcohol (producing a blood alcohol level of 0.07%) on the same test measures, the following results were found: (1) Tracking ability under this alcohol dose was impaired to roughly the same extent as the 0.063 mg/kg diazepam dose. (2) The 0.126 mg/kg diazepam dose produced twice the level of tracking impairment as the alcohol dose. (3) Impairment on the rate of information processing resulting from this dose of alcohol was roughly midway between the impairments produced by the 0.063 mg/kg and 0.126 mg/kg doses of diazepam. (4) Response times and the combined error scores in the visual search task under alcohol were larger than under the 0.126 mg/kg diazepam dose. Clearly, the pattern of behavioral impairment produced by diazepam differs from that produced by alcohol. The temporal duration of diazepam impairments is longer than that produced by the alcohol treatment.

The authors conclude that the magnitude and duration of the effects of diazepam suggest that driving or the operation of machinery under the influence of diazepam presents possible dangers to the user. (HSRI)

8 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Tests of Sensory Function.

UM-79-D1296

EFFECTS OF ALCOHOL AND DIAZEPAM, SINGLY AND IN COMBINATION, ON SOME DRIVING PERFORMANCES, R.G. Mortimer; P.R. Stubing; P.A. Howat; D.B. Stone, Proceedings of the NCA Alcohol and Traffic Safety Session. 1979, p321-41, Washington, D.C.: NHTSA (Aug 1979)

The study described here had three objectives: (1) to develop relevant driving tasks and evaluate them in terms of the degree to which they reflected changes in steering task difficulty as speed was increased and in terms of how they were affected by drugs; (2) to evaluate how alcohol and diazepam, singly and in combination, affected the driving task; and (3) to investigate interindividual differences among subjects in terms of drug effects on driving performance.

Seven male and seven female moderate alcohol drinkers aged 21 to 32 were administered one of four drug treatments in four testing sessions: (1) pure ethanol in orange juice to produce a BAC of 0.08%; (2) .05 mg diazepam per pound of body weight; (3) diazepam and alcohol in combination; (4) placebo.

The tests were performed on an airport runway in a fullsize passenger car. The tests consisted of steering through a serpentine course at 25 to 40 mph; lane changing and braking accuracy involving speeds of 25 to 40 mph; and a speed reproduction and maintenance task in which drivers had to attain a speed between 25 and 40 mph and maintain it as steadily as possible without the use of the speedometer.

Results of the study showed that (1) steering tests were clearly affected by variations in task difficulty and driving speed; (2) subjects varied considerably in driving performance and in effects of alcohol and diazepam; (3) diazepam and alcohol, singly and in combination, impaired ability to perform evasive maneuvers and to steer in the

serpentine course; (4) neither diazepam nor alcohol had a significant effect upon speed reproduction, speed maintenance, or controlled braking performance; and (5) there was no significant interaction of alcohol with diazepam.

Several conclusions were drawn from these results. Therapeutic doses of diazepam can impair the patient's abilities to control a vehicle on the road and to steer evasively. Moderate doses of alcohol (0.08% BAC) can have similar effects. Alcohol also leads to impaired subjective judgment of driving performance. Both alcohol and diazepam alone and in combination can cause drowsiness which can increase several hours after ingestion. Finally, combining alcohol with diazepam does not result in increased impairment of driving skills. (HSRI)

31 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Closed Course Driving. Experimentation: Acute Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs.

UM-59-D1297

PANEL ON INTERPRETATION AND MEDICAL ASPECTS, L. Goldberg, Proceedings of the Symposium on Alcohol and Road Traffic, R. A. Myren, ed., p165-229, Bloomington, Ind.: Indiana University (1959)

This chapter includes the presentations of a panel on interpretation and medical aspects of drugs, alcohol, and driving which were presented at the 1959 Symposium on Alcohol and Road Traffic. The major part of the discussion focuses on the medical, pharmacological, social, and psychological aspects of alcohol use and abuse and the effects of alcohol on skills related to driving. Some discussion on the effects of drugs is included, and effects of drugs on nystagmus are briefly reviewed. In one study, a drug which, although it relieved vomiting and nausea in alcoholics, also added to the other effects of alcohol, is briefly discussed.

Also reported in the panel discussion was a double-blind study of the effects of several drugs on driving ability as measured by a driving simulator. The drugs used were 300 mg phenaglycodal, 400 mg meprobamate, 50 mg chlorpromazine, and 100 mg secobarbital, all of which were clinical dosages. When compared to placebo, phenaglycodal produced no measurable effect. Meprobamate showed no effect after the first hour, but showed a significant affect after the second hour and an even greater effect after the second dose. Chlorpromazine had a delayed onset of action; no significant effect was evident until the second dose, but by the sixth hour postdrug performance was significantly impaired.

Also presented are the responses of several members of the panel to a question concerning the effects of tranquilizers on driving and chemical testing methods for detection of tranquilizers. Most panel members agreed that tranquilizers are similar to alcohol in that they dull the senses and lull the driver's sense of responsibility. Some felt that tranquilizers probably impair driving, especially when combined with alcohol. Most also agreed that the presence of drugs can be detected by chemical analysis, and that the presence of tranquilizers does not interfere with chemical tests for alcohol. (HSRI)

0 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Minor Tranquilizers (Anti-Anxiety and Ataractics): meprobamate. phenaglycodol. Tranquilizers. Compilation.

UM-70-D1298

ANTAGONISM TO INTRAVENOUSLY ADMINISTERED ETHANOL BY CHLORDIAZEPOXIDE (LIBRIUM), J.W. Dundee; M. Isaac, Internationalen Konferenz uber Alkohol und Verkehrssicherheit, I.37-I.42, Freiburg im Breisgau: Hans Ferdinand Schulz Verlag (1970)

This study compares the effects of chlordiazepoxide to those of pentobarbitone on anesthesia induced by intravenously administered alcohol to investigate whether chlordiazepoxide increases difficulties in achieving sleep. Findings are reported for 142 patients who received varying doses of chlordiazepoxide (50 mg, 100 mg, or 140 mg) or diazepam (10 mg or 30 mg) as premedication; for a control group of 40; and for a comparison group treated with 200 mg pentobarbitone. All of the 222 female

gynecological patients were infused with 10% v/v (44-55 g) pure alcohol over five minutes to induce anesthesia and with 0.6 mg atropine to prevent excess salivation during surgery.

Results indicate that 100 mg chlordiazepoxide, but not the 50 mg dose, makes induction of anesthesia more difficult. Not only were fewer patients asleep after the 550 ml solution, but the quality of anesthesia was less satisfactory than in the control group, with patients moving more upon stimuli. It was not possible to induce sleep with this amount of ethanol after 140 mg chlordiazepoxide.

There was no evidence of this antagonism after 10 mg diazepam. Barbiturate premedication augmented the effect of ethanol slightly, although it had no obvious effect on the dose required to produce loss of consciousness.

Mechanisms possibly involved in this chlordiazepoxide-induced resistance to ethanol are discussed, and further studies investigating these possible mechanisms are described. Studies of blood levels show that the resistance of chlordiazepoxide to the soporific effects of alcohol are not associated with a more rapid breakdown of ethanol, but with increased tolerance of the brain to its action. It is concluded that the prior administration of chlordiazepoxide appears to induce a state of cerebral resistance to ethanol in which higher blood levels of alcohol are required to produce sleep.

English translation of source title: [Alcohol and Traffic Safety. Proceedings of the International Conference on Alcohol and Traffic Safety, 22-27 September 1969] (HSRI)

0 refs

KEYWORDS: Barbiturates: pentobarbital. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Experimentation: Acute Dosage Study. Experimentation: Other Multiple-Drug Studies. Physiological Testing.

UM-80-D1299

BLOOD SERUM LEVELS OF DELTA-9-TETRAHYDROCANNABINOL (DELTA-9-THC) AND THE ROADSIDE SOBRIETY TEST (PRELIMINARY REPORT), V. Reeve, paper presented at the American Academy of Forensic Sciences 32nd Annual Meeting, 20-23 February 1980, New Orleans, La. (1980)

This pilot project was conducted to determine the feasibility and to assist in the design of a sophisticated double-blind placebo study which will correlate blood delta-9-THC levels and blood delta-9-THC/alcohol levels with the ability of the arresting officer or the trained drivers license examiner to judge impairment. It attempted to ascertain the range of delta-9-THC levels that are associated with observable impairment in the general driving population.

Experienced California Highway Patrol officers interviewed and tested for sobriety thirty-nine male and twenty-two female subjects aged 21 to 52. Four of the subjects were marijuana experimenters, fifteen were occasional users, twenty-seven were moderate users, and fifteen were heavy users. Subjects were administered enough 18-mg NIDA marijuana cigarettes to achieve a comfortable high. Blood samples were withdrawn just prior to smoking and 5, 30, 90, and 150 minutes after. The subject then completed a roadside test after which he was asked to evaluate his performance. The officer also assessed the subject's performance.

Peak mean plasma concentrations of delta-9-THC assessed during the roadside sobriety test by smoking habits five minutes after smoking were the following: heavy users, 84.1 ng/ml; medium users, 61.2 ng/ml; light users, 46.7 ng/ml. Both observed and self-assessed impairment were greatest in the first 30 minutes after administration. Impairment was still apparent 150 minutes after administration, although subjects consistently judged themselves less impaired than the observers did. General impairment versus drug concentration for each type of drug user and general impairment versus serum THC were also calculated. A considerable range of THC concentrations was demonstrated (0-18 ng/ml). Despite this, the majority of subjects were rated impaired by observers.

Analysis of the data collected demonstrated that general impairment as judged by the officers and trained observers correlates with delta-9-THC blood levels. It is concluded that roadside sobriety tests correlated with THC levels and compared to independent ratings of drivers license examiners need to be performed to document the ability of the trained law enforcement officer to detect marijuana-impaired drivers with measured THC blood levels. Furthermore, a full scale study of the effects of marijuana on driving behavior is imperative since impaired subjects do not rate themselves as under the influence when they are judged to be so by impartial observers. (HSRI)

9 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol*. Drug Concentration-Effect Study: Driving Skill Impairment. Epidemiology: Analysis of Driver Body Fluids for Drugs. Self-Evaluation of Drug Effects by Subjects.

UM-63-D1300

EFFECTS OF ALCOHOL ON PERSONS USING TRANQUILLIZERS, T.A. Loomis, Alcohol and Road Traffic.Proceedings of the Third International Conference on Alcohol and Road Traffic, September 3-7, 1962, J.D.J. Havard, ed., p119-22, London: British Medical Association (1963)

This article discusses some experimental evidence reported in the literature regarding the effects of combinations of sedative drugs on performance under simulated driving conditions. A review of the literature yielded only two studies specifically dealing with sedatives. Both of these studies concluded that under the conditions of the dosages (2 oz. 100 proof whiskey with 400 mg oxanamide four times daily, and 2 oz. 86 proof whiskey with 800 mg meprobamate) and time intervals (thirty to sixty minutes) involved in these studies, the drug had no greater effect than that produced by placebo plus alcohol as measured on the AAA Driver Trainer.

Also discussed are the results of studies done by the author himself. These studies investigated the effects of various doses of alcohol, secobarbital, meprobamate, and chlorpromazine, alone and in combination on driving simulator performance. These tests indicated the following: (1) The drugs investigated produce measurable impairment of performance if given in sufficient dosages. (2) Providing the dose is large enough, the drug-induced impaired performance will at least summate with the effects of alcohol. (3) Ordinary clinical doses of some of the drugs under consideration do not produce measurable impairment of function and do not appear to increase the simultaneous effects of alcohol. (HSRI)

0 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Barbiturates: secobarbital. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Minor Tranquilizers (Anti-Anxiety and Ataractics): meprobamate. oxanamide. Nonbarbiturates: ethanol (ethyl alcohol). Driving Simulator. Experimentation: Acute Dosage Study. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Study of Combined Effects of Drugs.

UM-63-D1301

EFFECTS AND AFTER-EFFECTS OF ALCOHOL, TRANQUILIZERS AND FATIGUE ON OCULAR PHENOMENA, L. Goldberg, Alcohol and Road Traffic. Proceedings of the Third International Conference, J.D.J. Havard, ed., p123-35, London: British Medical Association (1963)

This paper surveys a series of studies on the possible effects and aftereffects of various alcoholic beverages on the following parameters: (1) ocular phenomena, including positional alcohol nystagmus (PAN) and roving ocular movements (ROM) as recorded by electro-oculography (EOG); (2) cortical activity, recorded by EEG; (3) standing steadiness; (4) time course of blood alcohol, as influenced by tranquilizers, fatigue, food intake, high temperature, and humidity; and (5) subjective estimates of mood variables.

Subjects were 250 moderate drinkers. Various amounts and types of alcohol were administered double-blind in single, two-dose, or multiple doses. The following drugs were also tested, alone and in combination with alcohol: Series I consisted of 50 mg buclozine, 10 mg chlorpromazine, 25 mg hydroxyzine, 400 mg meprobamate, and 300 mg phenaglycodole given the night before testing, the same morning, and at noon immediately before alcohol intake, and then at four-hour intervals. In this series alcohol was administered in several doses at twenty-minute intervals. Series II tested .5 g acetylsalicylic acid plus .01 g codeine, 20 mg chlordiazepoxide, and 500 mg meprobamate administered orally before a single dose of alcohol and four hours after.

The following major results emerged from the study: (1) Objective and subjective effects and aftereffects were present many hours after alcohol had left the blood. These were especially noticeable for PAN, ROM, standing steadiness, and fatigue. (2) The addition of various drugs such as tranquilizers modified the objective and subjective effects and after-effects in various quantitatively different ways for the various drugs. (3) The intake of food, even after the alcohol had left the blood, increased the intensity of

ROM, impaired standing steadiness, and increased drowsiness and fatigue. (4) The procedure used in this study allows the action of tranquilizers, stimulants, and other drugs on the effects and after-effects of alcohol to be tested objectively. (HSRI)

20 refs

KEYWORDS: Analgesics and Antipyretics: salicylate. Anti-Emetics: buclizine. chlorpromazine. Antihistamine Agents: hydroxyzine. Expectorant and Cough Preparations (Antitusive Agents): codeine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Minor Tranquilizers (Anti-Anxiety and Ataractics): buclizine. chlordiazepoxide. hydroxyzine. meprobamate. phenaglycodol. Nonbarbiturates: ethanol (ethyl alcohol)*. hydroxyzine. Opiates and Related Agents: codeine. Experimentation: Acute Dosage Study. Experimentation: Chronic Dosage Study. Experimentation: Comparison of Different Drugs. Experimentation: Dose-Effect Study. Experimentation: Study of Combined Effects of Drugs. Self-Evaluation of Drug Effects by Subjects. Tests of Sensory Function.

UM-63-D1302

THE FORENSIC MEDICAL DEMONSTRATION OF THE PRESENCE OF ALCOHOL AND CLINICAL INTOXICATION IN FINLAND, A. Alha, Alcohol and Road Traffic. Proceedings of the Third International Conference, J.D.J. Havard, ed., p293-8, London: British Medical Association (1963)

Reported here are the results of investigations performed by the Helsinki Department of Forensic Medicine from 1952 to 1961 to determine the alcohol content of blood samples taken in cases of drunken driving and drug content in urine samples in suspected narcotics cases. Of the more than 21,000 cases examined by the Division of Forensic Chemistry since 1952, 4 to 5% of the cases indicated no alcohol (BAC<.015%). In 16 to 20% of the cases, alcohol was present in an amount less than 0.12%. In over 75% of the cases the blood alcohol level exceeded .12%.

Among the 21,000 cases were many in which clinical examination demonstrated considerable intoxication although the blood alcohol level was below .08%. After brain and other injuries have been eliminated there has, in the remaining cases, been an above-average incidence of the examinee being under twenty or over sixty years old or occurrence of drug ingestion. This was established chemically from urine samples, although this was the case only in those few instances where the clinical examination had primarily aroused suspicion of the use of narcotics or drugs. In 1961, twenty-one urine samples were investigated, twenty of which contained various drugs. The most commonly encountered drugs were PAS and isonicotinyl hydrazide, taken by tuberculous patients. Analysis of the data indicates that the general use of drugs, especially antipyretics, sedatives, hypnotics, ataracts, tranquilizers, antidepressants, and antihistamines has increased during recent years. In 1952 16.2% of the cases examined for drugs indicated drug use; in 1956 the percent increased to 23.9; in 1961 26.2% (194) indicated drug use. Of the 194 drug cases investigated in 1961, the substance involved in 73% of the cases was a mixture of various antipyretics, sedatives, and ataracts used against general aches or pains or for sedation and mostly obtainable without prescription. (HSRI)

0 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-76-E0075

EFFECTS OF LABELING THE "DRUG-ABUSER": AN INQUIRY, J.R. Williams, ed., NIDA Research Monograph 6 (Mar 1976)

This monograph explores what is known about the effect of arrest and official identification of the adolescent "drug abuser" or "addict" on his or her self-image and subsequent behavior. The perspective of labeling dealing specifically with the impact of societal reaction to deviance on the person designated as "deviant" is discussed in detail. Other broad areas discussed are self-concept, effects of official apprehension, juvenile delinquency, symbolic interactionism, and adolescent behavior. These topics are discussed in terms of how they individually or in combination contribute to understanding the problem of labeling the drug abuser.

Two empirical studies were reviewed. One explored the impact of apprehension for delinquent behavior on subsequent delinquent behavior. The other explored the relationships between perception of self as delinquent with self-esteem and official apprehensions.

Subsequent delinquent behavior was found to be increased by arrests. The perception of self as delinquent was found to be weakly related to official apprehension (positive correlation) and to self-esteem (negative correlation). The reported weak effect of official labeling on the perception of self as delinquent was lessened by parental and peer support. The self-esteem of those who accepted the delinquent label, as well as those who were insulated against it, was essentially unaffected.

These results, however, do not explain how apprehension for a drug law violation effects adolescent psychological development. Ideally, self-concept should be measured prior to the onset of drug abuse, during the abuse phase, and prior to arrest. Self-concept should be measured again after apprehension, along with some measure of postapprehension drug abuse. (HSRI)

39 pages 379 refs

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-320

KEYWORDS: Review: Behavioral Research Methodology. Review: Drug Use.

UM-77-E0076

THE EPIDEMIOLOGY OF HEROIN AND OTHER NARCOTICS, J.D. Rittenhouse, ed., NIDA Research Monograph 16 (Nov 1977)

This monograph reports the work of the Task Force on the Epidemiology of Heroin and Other Narcotics. Four issues are addressed by contributed papers: (1) the spectrum of heroin use and its diversity; (2) the methodologies for measurement of use; (3) the contributions of treated prevalence to epidemiology; and (4) consequences of use. Each of the major papers is critiqued and evaluated.

The editor concludes the work by stating that scientific inquiries in the area of heroin epidemiology cannot be defined narrowly. No successful investigation can have as its goal merely a count or number of heroin addicts; rather, an attempt must be made to understand developmental processes in drug use and the antecedent and consequent correlates that characterize drug use. One of the areas of the greatest concern is the relationship between heroin experience and the use of other illicit drugs; namely, is heroin use the endpoint of a developmental sequence of drug use?

One theme recurrent in these papers is the complexity of the heroin experience to a degree much greater than thought before. It appears that the term "heroin user" can apply to experiences that are both isolated and reversible. Surveys have confirmed each other in the conclusion that self-reported mild use without social or health problems is more common that had been suspected a few years ago. (HSRI)

249 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 78-559

KEYWORDS: Opiates and Related Agents: heroin. Opiates and Related Agents. Compilation. Review: Drug Effects. Review: Drug Use. Review: Survey Methodology.

UM-78-E0077

SELF-ADMINISTRATION OF ABUSED SUBSTANCES: METHODS FOR STUDY, N.A. Krasnegor, ed., NIDA Research Monograph 20 (Jul 1978)

This monograph is the first in a series of related volumes addressing different aspects of "substance abuse", included in which are excessive caloric intake and excessive use of ethanol, illicit drugs, and tobacco. The papers in this volume attempt to determine empirically whether there are commonalities among the several substance abuse behaviors. Specifically, this monograph was organized to provide the reader with an appreciation of the methods used by behavioral scientists to observe and study the self-administration of cigarettes, alcohol, food, and illicit drugs by humans under controlled laboratory conditions. Some of the topics discussed which deal with excessive use of drugs and ethanol are experimental drug self-administration, therapeutic self-medication, drug abuse research in outpatient clinics, heroin and sedative self-administration, and social reactions to drug self-administration. (HSRI)

246 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 78-727

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Sedatives and Hypnotic Agents. Compilation. Review: Behavioral Research Methodology. Review: Drug Use.

UM-78-E0078

PHENCYCLIDINE ABUSE: AN APPRAISAL, R.C. Petersen; R.C. Stillman, eds., NIDA Research Monograph 21 (Aug 1978)

Phencylidine (PCP) abuse has only recently emerged as a problem of widespread proportions. Because of this, knowledge of the drug remains fragmented and unreliable. This volume is comprised of papers presented by experts on the drug at a conference in February 1978 that attempted to update present knowledge of PCP. Some of the topics covered in this volume are the neurobiology of phencyclidine, its neurochemical pharmacology, phencyclidine use among youth, epidemiology of multiple drug use involving phencyclidine, the psychiatric aspects of chronic use, and phenomenological aspects of phencyclidine abuse among ethnic groups in Hawaii. Also discussed are the pharmacokinetics of PCP in overdosage, overdosage treatment, clinical observations during PCP intoxication, treatment based on ion-tapping, PCP's effect on criminal behavior and diminished capacity, and control of drug self-administration. Extensive references, tables, and graphs are included for each paper. (HSRI)

313 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 78-728

KEYWORDS: Hallucinogens and Related Agents: phencyclidine*. Compilation. Review: Drug Concentration-Effect Relationships. Review: Drug Effects. Review: Drug Use.

UM-75-E0079

PREDICTING ADOLESCENT DRUG ABUSE: A REVIEW OF ISSUES, METHODS AND CORRELATES, D.J. Lettieri, ed., NIDA Research Issues 11 (Dec 1975)

This volume is comprised of some of the most recent research on the problems and intricacies surrounding the prediction of drug-abusing behaviors. Most of the papers focus specifically on adolescent drug abuse; consequently much of the discussion is about marijuana use.

The articles are organized into several categories: general conceptual issues; nosological and clinical approaches; methodological strategies; intrapersonal, behavioral, and interpersonal variables and correlates; longitudinal designs; and developmental models.

Some of the specific topics discussed are speculations on possible changes in youthful lifestyle between the 1960s and 1970s; computer interview questionnaires for drug use and abuse; self-esteem as a predictor of adolescent drug abuse; ego mechanisms and marijuana usage; and behavioral and demographic correlates of drug use in junior high school and high school students. (HSRI)

361 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-299

KEYWORDS: Compilation. Review: Drug Use. Review: Survey Methodology.

UM-76-E0080

DRUG ABUSE INSTRUMENT HANDBOOK: SELECTED ITEMS FOR PSYCHOSOCIAL DRUG RESEARCH, M.A. Macari; D.J. Lettieri; A. Nehemkis, eds., NIDA Research Issues 12 (1976)

Identifying, acquiring, or developing valid and reliable instruments to measure drug use are major problems facing researchers who study psychosocial drug use and abuse. This handbook is designed to help eliminate these problems. It is intended to serve as a basic tool for the researcher in identifying existing instruments and in suggesting items for the creation of new instruments. Over two thousand items from forty instruments are included, categorized according to the areas they assess. These items are categorized into four major divisions and approximately forty subcategories. The major divisions are: (1) demographic variables; (2) interpersonal variables; (3) intrapersonal variables; and (4) drug variables. Descriptive summaries of each

instrument and how each has been used in drug research are provided. The summary provides information concerning the developer, title, and copyright or publication date. Also provided is information concerning the specific drugs assessed by the instrument, the age range for which the measure was intended, the general areas or variables that the instrument assesses, design features, and administration.

Abstracts follow, containing when available such specific information as major purposes and concerns of the instrument. They also provide information concerning assessed, related, or derivative instruments; reliability or validity data; development and use history; and existing evaluations and analyses. Reports in which the instrument is discussed or in which results obtained from its use are noted or cited, and information on availability of the instrument and usage charges where applicable is provided.

The intent of the summaries is to permit researchers to make an initial determination of the appropriateness and merit of an instrument for the researcher's individual purposes. (AAM)

331 pages

U.S. Department of Health, Education and Welfare publication no. (ADM) 79-394

KEYWORDS: Review: Behavioral Research Methodology. Review: Survey Methodology.

UM-76-E0081

DATA ANALYSIS STRATEGIES AND DESIGNS FOR SUBSTANCE ABUSE RESEARCH, P.M. Bentler; D.J. Lettieri; G.A. Austin, eds., NIDA Research Issues 13 (Dec 1976)

This volume contains ten original papers discussing methodologies applicable to performing psychosocial research on substance abuse, particularly abuse with drugs. The intent of this collection is to permit increased methodological sophistication in the field of drug abuse by making available basic information on some of the latest and most relevant research techniques. Each of the papers has been written by a prominent methodologist. Each has been designed to assist drug researchers in the behavioral and social sciences who do not have an advanced background in research techniques and who are in need of introductory information.

Eight data analysis strategies are discussed by the authors: automatic interaction detection, actuarial prediction, cluster and typological analysis, path analysis, factor analysis, general multiple regression and correlation analysis, multivariate analysis of variance, and discriminant analysis. In addition, two relevant research designs are dealt with: single-organism designs and longitudinal designs.

Each paper includes a description of the rationale, procedures, assumptions, advantages, and disadvantages of the methodology. Practical illustrations show how the method has been applied in both nondrug and drug-related situations. References are provided to existing computer programs for performing the analyses, as well as to relevant documents for additional reading. These citations include more detailed discussions of mathematical derivations and descriptions of both drug and nondrug research that have employed the methodology. (AAM)

226 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 78-389

KEYWORDS: Compilation. Review: Behavioral Research Methodology. Review: Survey Methodology.

UM-76-E0082

DRUGS AND PERSONALITY: PERSONALITY CORRELATES AND PREDICTORS OF NON-OPIATE DRUG USE, G.A. Austin; C. Phil; D.J. Lettieri, eds., NIDA Research Issues 14 (Jul 1976)

This volume presents abstracts of current research papers and theoretical studies that explore various aspects of the relationship between nonopiate drug use and personality. The volume focuses particularly on personality predictors and correlates of adolescent drug use. The fifty-nine studies abstracted in this volume discuss such subjects as self-image and attitude towards drugs; drug use and achievement; drug use in juvenile prisoners; predicting adolescent drug abuse; the correlation between drug abusers and suicide; and the relationship of social class to drug abuse in high school students.

Each abstract is intended to be a faithful representation of the original study, conveying what was done, why it was done, what methodology was employed, what results were found, and what conclusions were derived from the results. (AAM)

121 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-390

KEYWORDS: Compilation. Review: Drug Use.

UM-77-E0083

DRUGS AND PSYCHOPATHOLOGY, G.A. Austin; M.A. Macari; P. Sutker; D.J. Lettieri, eds., NIDA Research Issues 19 (Jun 1977)

The fifty-seven studies summarized in this volume deal with experimental and epidemiological aspects of both opiates and nonopiates, and include all age groups. Each summary states the purpose of the article, provides a contents summary of the article, and states the major conclusions.

This volume reveals a variety of methodologies for collecting information on drug abuse psychopathology including use of case histories, clinical observations, administrations of psychological instruments, experimental manipulations in controlled situations, and other potentially replicable techniques. In most of these studies, however, investigators have relied upon psychiatric interviews and clinical observations or upon data yielded by objective personality tests.

Some of the areas of research summarized include investigation of the psychological correlates and sequelae of drug-induced states in controlled environments; the interaction of personality and sociocultural variables in accounting for drug abuse behavior; the characteristics of special drug-abusing subpopulations such as women, adolescents, servicemen, and addict physicians; and the results of treatment efforts among drug abuse groups. (HSRI)

140 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 79-509

KEYWORDS: Compilation.

UM-77-E0084

DRUGS AND MINORITIES, G.A. Austin; B.D. Johnson; E.E. Carroll; D.J. Lettieri, eds., NIDA Research Issues 21 (Dec 1977)

This volume contains summaries of the latest research focusing on the extent of drug use and abuse among racial and ethnic minorities and the factors influencing it. Included are research reports that deal specifically with the topic of minority drug use and that seek to examine different racial and ethnic patterns. Also included are reports of research examining drug abuse within a minority population without seeking to examine minority drug use per se. Finally, a sample of studies examining the extent and patterns of drug use within a general population has been included in order to provide a better understanding of the proportion of minorities among all drug users.

Studies included discuss the psychosocial aspects of addiction, differential patterns of drug abuse among white activists and nonwhite militant college students, onset of marijuana and heroin use among Puerto Rican addicts, the Chinese narcotic addict in the U.S., black narcotic addicts, and patterns of drug abuse among military inductees.

The following general conclusions can be derived from these studies: (1) Whites have been at least as likely as black and other minorities to be multiple drug users and to use all drugs except for heroin and cocaine. Racial differences in cocaine and heroin use seem to be diminishing. (2) Opiate addicts are disproportionately black and Hispanic when compared with the general population. (3) American Indians are more likely to use drugs than whites or blacks. (4) Drug arrests may be more a reflection of political pressures and enforcement policies than a true indication of the white and black narcotic-using population. (HSRI)

210 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 78-507

KEYWORDS: Compilation.

UM-77-E0085

GUIDE TO THE INVESTIGATION AND REPORTING OF DRUG-ABUSE DEATHS, L.A. Gottschalk; F.L. McGuire; E.C. Dinovo; H. Birch; J.F. Heiser, eds. (1977)

This guide attempts to describe the current state-of-the-art of the investigation and reporting of drug deaths, to alert medical examiners to certain problems involved, to encourage medical examiners to adopt more consistent methods of investigation and reporting, and finally, to provide accurate data for use by persons working in the field of drug abuse deaths.

The chapters of this volume were organized roughly in the order in which events occur when a drug abuse death is investigated and reported. Some of the topics discussed are the initial onsite investigation, the postmortem examination, consideration of the varied evidence and situations determining cause, the procedures necessary for a valid, reliable toxicological analysis, the psychological autopsy, certification by the medical examiner, compilation of data into record-keeping systems, and provision of testimony by the medical-legal examiner. Included in the appendices is a table of therapeutic and toxic concentrations of more than one hundred toxicologically significant drugs in blood, plasma, or serum. (HSRI)

151 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 77-386

KEYWORDS: Review.

UM-74-E0086

THE EPIDEMIOLOGY OF PSYCHOACTIVE AND HALLUCINOGENIC DRUG USE, G.W. Mercer; R.G. Smart, Research Advances in Alcohol and Drug Problems, R.J. Gibbins; et al., v1 p303-54, New York: John Wiley and Sons (1974)

Recent epidemiologic literature on marijuana, amphetamine, tranquilizers, barbiturates, and other psychoactive drugs is reviewed. Topics include the following: the methodological difficulties associated with drug epidemiology research; the reported morbidity and mortality associated with the use of these drugs; and the reported nature, extent, and trends of their use. Finally, the conclusions that can be drawn from these studies are presented, and future directions for epidemiologic studies are suggested. Epidemiological studies grouped according to geographical areas are summarized. These groupings are the Americas (Canada and the United States, Mexico, Chile); Europe (Britain, France, Scandinavia, Switzerland, Holland, Germany, Czechoslovakia); Africa; Asia and Asia Minor; and Australia. Because of the large number of studies done in the United States and Canada, this subsection is further divided into sections covering secondary school studies, university and college studies, and studies of other population groups (i.e., normal adults, hippies, soldiers in Vietnam, and miscellaneous adult populations). The Canadian and United States studies that dealt with school samples are each considered with regard to interdrug use and drug use trends, year of study, geographical variables, gender, multiple drug use, grade average, social variables, and the user's personality. The authors conclude that, although many valuable and worthwhile studies have been done, there is now a desperate need for improvement in the design and coordination among epidemiological studies. Emphasis on theory dealing with rates and patterns of use is also needed.

The editors of Research Advances in Alcohol and Drug Problems are R.J. Gibbins; Y. Israel; H. Kalant; R.E. Popham; W. Schmidt; R.G. Smart (HSRI)

294 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Hallucinogens and Related Agents. Review: Drug Use.

UM-77-E0087

PHENCYCLIDINE (PCP): A LOCAL AND NATIONAL PERSPECTIVE, D.B. Graeven, Addictive Diseases: An International Journal, v3 n2 p243-52 (1977)

This paper reviews current studies of PCP use in the United States and presents the results of an exploratory study of a local outbreak. A brief history of the drug from its discovery in the late 1950s is presented as well as a description of its effects.

PCP has a high potential for negative effects due to the fact that it is easy to synthesize and difficult to control because the precursors are easy to obtain. DAWN (Drug Abuse Warning Network) data show that increased PCP episodes in emergency rooms and hospitals have changed PCP from the twenty-third most frequently observed drug in 1973 to sixteenth in 1975. One explanation for the increase in PCP use is the change in the mode of administration from pills to smoking. At present PCP does not seem to be a major drug of choice when used in pill form; however, use of PCP seems to increase when smoked.

The profile of the PCP user provided by DAWN data shows that the PCP user who enters the DAWN system is most likely to have used PCP alone (78%) rather than with one or more other drugs; most likely to come into a crisis center (63%) rather than an emergency room (34%) or inpatient facility (3%); and most likely to be young (48% are 10-19 years old), white (79%), and male (69%).

The results from an exploratory study based on interviews with twenty-five PCP users (three of whom were dealers), probation and police officers, emergency room staff, and local drug crisis programs are also provided. One of the major findings of the study is the high rate of behavioral toxicity of PCP. In the interviews conducted almost all of the interviewees had either been in an automobile accident or had a friend who was in an accident as a result of PCP use. (HSRI)

6 refs

KEYWORDS: Hallucinogens and Related Agents: phencyclidine. Epidemiology: National Survey of Drug Use Patterns. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0088

THE PAIN-PILL-PLEASURE MODEL AND ILLICIT DRUG CONSUMPTION, T. A. Shimp; R. F. Dyer, Journal of Consumer Research, v6 n1 p36-46 (June 1979)

The primary objective of this article is to discuss and further stimulate research on the potential effects of over-the-counter drug advertising on illicit drug use. The secondary objective is to encourage consumer researchers to go beyond the advertising controversy and to undertake research involving the more general issue of problem consumption behavior, including such behavior as problem drinking and narcotics use by adolescents.

The article begins with a review of the relevant literature, which is very limited. Next, these studies are critically evaluated in terms of sample selection, variable specification, validity and reliability assessment, research designs, and theoretical framework.

The paper then describes a model of the factors influencing drug consumption. This model suggests that young people's illicit drug use or potential use results from a lifetime exposure to drug related information. It depends on the values inculcated by these sources, and is largely predetermined by family socialization and peer influence. It proposes further that drug-related information processing and behavior are initiated and directed by personality characteristics and that situational factors moderate drug use.

The authors conclude that there is a great need for further research in this area. Such studies should include longitudinal research and experimental designs, superior sampling procedures that focus on preteens rather than high school and college students, and control for individual differences. Psychological mediators should be used as criterion variables rather than focusing exclusively on error-prone, self-reported behavioral measures. (HSRI)

72 refs

KEYWORDS: Review: Drug Use.

UM-74-E0089

MULTIDRUG USE: SUPPLEMENTARY PERSPECTIVES, P.C. Whitehead, International Journal of the Addictions, v9 n2 p185-204 (Apr 1974)

This paper investigates the hypothesis that users of any one drug are more likely to use other drugs than those who do not use that drug. 1,606 students from grades 7, 9, 11, and 12 in Halifax, Nova Scotia completed a questionnaire concerning their use of drugs. Of the 1,606 students, 704 did not admit to use of tobacco, alcohol, solvents, LSD, tranquilizers, stimulants, marijuana, barbiturates, other hallucinogens, or opiates during the six months prior to the survey. Of the 902 drug users, tobacco was used by 85%. More smokers had used LSD and barbiturates than nonsmokers. Two to three times as many alcohol users as nonusers had also used stimulants, tranquilizers, solvents, and marijuana. Alcohol users used hallucinogens, LSD, and barbiturates about five times as much as nonusers. Fifteen percent of the students had used solvents. The use of opiates among these users was almost fourteen times as frequent as it was among nonusers of solvents. Thirteen times as many solvent users as nonusers had used barbiturates; almost eight times as many had used stimulants or other hallucinogens.

Data are also provided for the comparison of rates of drug use between users and nonusers of LSD, tranquilizers, stimulants, barbiturates, and opiates.

The data presented in this study provide substantial support for the hypothesis that users of most drugs are more likely to use almost any other drugs than are nonusers. Not all drugs, however, have the same etiological significance in terms of multidrug use. There is a sizeable association between the use of such drugs as stimulants, opiates, marijuana, and LSD, and multidrug use. This association is much greater than that between alcohol and tobacco use, and multiple drug use. The results also suggest that the use of a drug that was not formally part of one's drug repertoire tends to have a cumulative rather than a replacement effect relative to other drugs. Therefore efforts designed to change some drug using practices must take into account the potential impact of such changes on other drug using practices. (HSRI)

15 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Ganglionic Blocking and Stimulating Agents: nicotine. General Anesthetics: thiopental*. Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Nonbarbiturates: ethanol (ethyl alcohol). Stimulants: nicotine. Unclassified Agents: tobacco. Barbiturates. Hallucinogens and Related Agents. Opiates and Related Agents. Stimulants. Tranquilizers. Volatile Solvents. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-E0090

THE ETIOLOGIC RELATIONSHIP BETWEEN DRUG USE AND CRIMINALITY, W.H. McGlothlin, Research Advances in Alcohol and Drug Problems, Y. Israel; F.B. Glaser; H. Kalant; et al., v4 p367-94, New York: Plenum Press (1978)

This paper provides a selective review of the literature concerning the relation between drug use and criminal behavior. The literature review is organized in three sections: (1) studies dealing with evidence that drug use contributes to crime as a direct result of the pharmacological effects; (2) studies dealing primarily with nonaddictive drug use; and (3) studies dealing primarily with addictive use of drugs--primarily heroin.

Several conclusions can be drawn from this review of the literature: (1) There is some evidence that drug use other than alcohol causes crimes directly as a result of reduced impulse control, paranoia, and negligence; however, the overall contribution is quite small when compared to that of alcohol use. (2) There is a clear association between crime and even modest use of nonaddictive drugs; however, prospective longitudinal studies have found no evidence that nonaddictive drug use leads to crime. The available data do not preclude the possibility that heavy involvement may contribute to crime for some individuals. (3) Criminality generally precedes narcotic addiction and typically increases following the onset of the behavior. (4) On the basis of arrest data, narcotic addicts show a lower ratio of violent to nonviolent crimes than do nonaddicted criminals; however, no information is available concerning the absolute frequency of crime types for the two groups. A relatively high proportion of addicts is involved in robberies at some time, although this source represents a very small percentage of the total criminal income. (5) There is fairly strong evidence that narcotic addiction causes an increase in the amount of income-generating crime for those individuals using this means of acquiring heroin. (AAM)

121 refs

Addiction Research Foundation, University of Toronto, Ontario, Canada

KEYWORDS: Opiates and Related Agents. Review.

UM-74-E0091

DRUG ABUSE IN EUROPE, International Hospital Review, v11 n2-3 p21-4 (1974)

Presented here are brief descriptions of the patterns of drug abuse other than the abuse of alcohol in several European countries. Major epidemiological studies are summarized for the Netherlands, Denmark, Sweden, and the United Kingdom.

The author also briefly discusses the problem of drugs and driving. Whereas the behavior of drinking drivers can be influenced by legal restrictions, parallel action in regard to the misuse of other drugs is beset by difficulties, not the least of which is concerned with the application of simple, reliable screening tests. Laboratory studies investigating the effects of drugs on driving skills are fraught with serious methodological problems since it is impossible to be certain that the performance under examination is relevant to an accident situation. Furthermore, the effects of many drugs are cumulative, and may vary considerably from individual to individual. Therefore only limited information is available on the relationship of drugs other than alcohol to accident involvement. (HSRI)

0 refs

KEYWORDS: Review: Drug Use. Review: Drugs and Highway Safety.

UM-78-E0092

A SURVEY OF DRUG USE AMONG PROBATIONERS IN THE LOS ANGELES AREA IN 1976, N.C. Jain; R.D. Budd; T.C. Sneath; B. Olson; W.J. Leung; D. Chinn, The International Journal of The Addictions, v13 n8 p1319-25 (1978)

This paper reports the results of a study analyzing more than ten thousand urine specimens from Los Angeles County probationers in early 1976 for the following drugs: amphetamine, methamphetamine, allylbarbital, amobarbital, butabarbital, pentobarbital, phenobarbital, secobarbital, morphine, codeine, methadone, primary metabolite of methadone, cocaine, benzoylecgonine, propoxyphene, norpropoxyphene, methaqualone, and phencyclidine. Analyses were made by radioimmunoassay, enzyme multiplied immunoassay techniques, gas-liquid chromatography, and thin-layer chromatography.

The results of the analyses indicated that 27.2% of the probationers' urine specimens contained confirmable levels of one or more of the eighteen drugs. Nearly 33% of those urine samples found positive contained more than one drug. Seven specimens contained as many as five different drugs.

Opiates and barbiturates made up nearly 60% of the drugs detected, morphine being most common. This is probably due to its greater use, slow excretion from the body, and metabolism from codeine. Methadone, phenobarbital, codeine, and propoxyphene were also found quite frequently. The significant amount of methadone found indicates treatment of opiate dependency with this drug, but may also indicate some illegal diversion of methadone for street use.

These data indicate a trend of continued drug use by many Los Angeles County probationers originally associated with drug problems. Although some drug use is undoubtedly by legitimate prescription, much of it is illicit and thus represents violation of probationary conditions. (JAM)

5 refs

KEYWORDS: Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-E0093

THE ROLE OF THE FORENSIC PATHOLOGIST IN THE INVESTIGATION OF FATAL TRAFFIC ACCIDENTS--THE FINNISH SYSTEM, K. Karkola, Forensic Science International, v12 p203-6 (1978)

This paper discusses the provincial boards used to investigate serious accidents in Finland. About one-half of the fatal traffic accidents are investigated by these special boards of inquiry. These boards consist of a police officer, a motor vehicle inspector, a traffic safety engineer, and a physician, usually a pathologist. On the basis of the evidence collected from police, on-the-scene reporters, relatives, friends, and medical personnel, each board formulates a final report that describes the events preceding the accident, the causes of the accident, the injuries and their causes, the safety equipment of the vehicle and its effect, the chances that the accident could have been avoided, and other traffic aspects to be taken into account. The cumulating data is useful for multidisciplinary sciences, juridical and insurance purposes, and legislation. The participating physicians also benefit from the systematic work of the boards in many ways. As an example of the type of data collected and analyzed, a list of causes of accidents is shown. (HSRI)

2 refs

KEYWORDS: Crash Investigation.

UM-79-E0094

YOUTHFUL DRUG USE, R. Blum; L. Richards, Handbook On Drug Abuse, R.I. Dupont; A. Goldstein; J. O'Donnell, eds., p257-71, Washington, D.C.: U.S. Government Printing Office (Jan 1979)

This article deals with drug prevalence--why and how young people use drugs; changes in behavior patterns brought about by effects of drugs; trends in youthful drug use; and treatment. Particular attention is given to TASC (Federal Treatment Alternative to Street Crime). The authors suggest that religion may serve as both a preventive measure and a therapeutic measure for drug abuse. They also make recommendations for action in treatment, prevention, policy, statistics, and basic research. (HSRI)

65 refs

KEYWORDS: Epidemiology: National Survey of Drug Use Patterns.

UM-79-E0095

DRUG MISUSE BY THE ELDERLY, C. Eisdorfer; M.M. Basen, Handbook On Drug Abuse, R.I. Dupont; A. Goldstein; J.O'Donnell; eds., p271-7, Washington, D.C.: U.S. Government Printing Office (Jan 1979)

This article discusses the serious biopsychosocial problems that the elderly face that often cause them to resort to taking drugs for relief. It also cites studies that have investigated this topic and arrives at the conclusion that primarily health, as well as knowledge of resources, perceived abilities of other older adults, and self-perceived physical disability are the major predictors of prescription drug use. For OTC medications, age, poor health, and less satisfaction with life as well as lack of knowledge of resources are additional predictor variables of heavy OTC drug use in the elderly. Among the topics of concern are implications for clinical care and biological issues concerning drug use among the aged.

The authors urge that new knowledge be brought to bear on the array of issues affecting drug use and misuse among the elderly. Data ranging from the somatic changes accompanying age and their influence on drug metabolism and efficacy to the effective and safe ranges of drug dosage are lacking. (HSRI)

36 refs

KEYWORDS: Review. Review: Drug Use.

UM-77-E0096

CASE-CONTROL STUDY OF RECIDIVIST DRIVERS INVOLVED IN FATAL HIGHWAY ACCIDENTS IN ALBERTA IN 1970-72, G. Bako; W.C. Mackenzie; E.S.O. Smith, Canadian Medical Association Journal, v116 n2 p149-51 (22 Jan 1977)

This study attempted to determine if differences in previous driving records existed between culpable recidivist drivers and innocent drivers without previous records, and what human factors are most important in fatal highway accidents. The authors compiled the findings of a three-year epidemiologic study of fatal motor vehicle accidents

conducted by the Alberta Task Force on Highway Accidents. It was found that 11.1% of culpable drivers had been convicted of driving while impaired by alcohol on at least one occasion prior to the fatal accident, while only 3.3% of exonerated drivers had previous records. This significant difference led to a cause-control study which demonstrated that the recidivist drivers differed significantly in a number of aspects from the innocent drivers--notably age, sex, frequency of drinking before the accident, blood alcohol concentration, ethnic distribution, class of accident, and type of collision. Thus the recidivist driver is a greater threat to highway safety than the innocent driver and needs special attention by legislators and law enforcement agencies. (JAM)

3 refs

KEYWORDS: Crash Investigation. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0097

STUDY FINDS SLEEPING PILLS OVER-PRESCRIBED, R.J. Smith, Science, v204 p287-88 (20 Apr 1979)

This article summarizes the findings of the Institute of Medicine (IOM) on sleeping pills. According to their report, they are more dangerous and less useful than either physicians or patients realize; hazards associated with the most common drugs are particularly unrecognized. At the same time little evidence exists that sleeping pills control insomnia.

The IOM report concludes that although barbiturates are hazardous, the chief alternative, benzodiazepines, may be just as risky and in some ways may be even riskier than barbiturates. The most common benzodiazepine, flurazepam, under the trade name of Dalmane(R), accounts for 53% of total sleeping pill prescriptions. Studies have shown, however, that after being used consecutively for seven nights, the effects of the drug are increasingly felt during the day, contributing to greatly diminished alertness and hand-eye coordination, which may be important for driving.

The panel also discovered that an increasing proportion of drug-related deaths involve alcohol; because both barbiturates and benzodiazepines are lethal in combination with alcohol, Dalmane(R) offers no significant advantage in diminishing the overall number of deaths related to sleeping pills in spite of its not being lethal by itself in overdose.

In light of these results, the panel criticizes the barbiturates ban, and opts instead for corrections to generic problems in the medical and pharmaceutical communities. It extends its criticism to the FDA and suggests that the FDA can perform its watchdog role only if it gets more outside advice, particularly from experts not connected with the drug industry. However, the panel does not suggest that either barbiturates or benzodiazepines be more tightly controlled by the federal government. Instead the IOM panel of physicians suggests that the medical profession heal itself by reducing dosages and number of prescriptions. (HSRI)

0 refs

KEYWORDS: Nonbarbiturates: flurazepam. Barbiturates. Review: Drug Effects.

UM-79-E0098

THE EPIDEMIOLOGIC TRADITION, M. Terris, Public Health Reports, v94 n3 p203-9 (May-June 1979)

This paper consists of a lecture presented to the Epidemiology Section at the annual meeting of the American Public Health Association concerning the epidemiologic tradition. The lecture begins with a discussion of the essence of epidemiology--what it is, its nature, and its relation to medical science. This is followed by a history of epidemiology of both infectious and noninfectious diseases in which the leaders of the field are identified and their dedication to epidemiology illustrated. The author goes on to lament the shift of the epidemiologic tradition from the practical to the academic. He concludes by stating the two major tasks confronting epidemiologists in the future. The first is to extend epidemiology further into the unsolved problems of infectious and noninfectious diseases by carrying out major work in the occupational diseases, by developing serious research in the epidemiology of health, and by studying the effects of public health and medical care services on disease and its outcomes. The second major task is the control of noninfectious diseases and accidental injury. (HSRI)

12 refs

KEYWORDS: Review.

UM-78-E0099

THE DRUG ATTITUDES SCALE (DAS): ITS DEVELOPMENT AND EVALUATION, M.S. Goodstadt; G. Cook; S. Magid; V. Gruson, The International Journal of The Addictions, v13 n8 p1307-17 (1978)

This paper evaluates five studies employing three independent samples of high school students conducted to develop and assess the reliability and validity of a Drug Attitudes Scale. Each of the studies is summarized here in terms of format, presentation, procedure, and results. The Drug Attitude Scale, consisting of sixty attitude items dealing with drugs and drug use, is comprised of ten six-item subscales referring to tranquilizers, barbiturates, heroin, opiates other than heroin, "speed", alcohol, cannabis, hallucinogens, tobacco, and general drug use.

The results of these studies indicate the potential utility of the Drug Attitude Scale. Its uses could include assessment for educational and research purposes in order to identify and discriminate target populations, to establish preprogram base lines, and to evaluate program impact. As with all such instruments, it would be necessary to establish the scale's cross-cultural validity before its true value could be determined. All samples, to date, have been from a single Canadian province; samples with other demographic backgrounds are needed to be employed as well. (HSRI)

8 refs

KEYWORDS: Epidemiology: Regional or Local Survey of Drug Use Patterns. Review: Survey Methodology.

UM-79-E0100

GINSENG ABUSE SYNDROME: PROBLEMS WITH THE PANACEA, R.K. Siegal, Journal of the American Medical Association, v241 n15 p1614-5 (13 Apr 1979)

This paper describes a study investigating the effects of long-term use of ginseng in 133 regular ginseng users. Subjects used a wide variety of commercial ginseng preparations, including roots, capsules, tablets, teas, cigarettes, and candies, usually orally.

After an initial interview and drug-history questionaire, subjects were given physical and psychological examinations, including a subjective drug-effects questionnaire for ginseng. These examinations were repeated at six-month intervals for two years. Results of the study indicated that most subjects experienced symptoms of central nervous system (CNS) excitation and arousal. Ten percent of the subjects experienced Ginseng Abuse Syndrome (GAS), defined as hypertension together with nervousness, sleeplessness, skin eruptions, and morning diarrhea. The average daily dosage for the GAS subjects was 3g of root material.

The most common psychological finding among these subjects was an elevation of mood. Ten GAS subjects became euphoric, restless, agitated, and insomniac. High doses (15g) resulted in feelings of depression, depersonalization, and confusion for four subjects.

These effects of GAS mimic those of corticosteroid poisoning, strongly suggesting a steroid mechanism of action operating through the adrenal cortex or pituitary. Treatment of patients with GAS should include withdrawal from ginseng and other stimulants while monitoring for possible hypotensive crises. (HSRI)

14 refs

KEYWORDS: Unclassified Agents: ginseng. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0101

MMPI PROFILES OF MEN ALCOHOLICS, DRUG ADDICTS AND PSYCHIATRIC PATIENTS, D. Lachar; C.L. Gdowski; J.F. Keegan, Journal of Studies on Alcohol, v40 n1 p45-56 (1979)

Described here is a study investigating personality differences between alcoholics, heroin addicts, and polydrug users using the Minnesota Multiphasic Personality Inventory (MMPI). Because these three populations typically differ in age, education, and race, all demographic factors that affect MMPI scores directly, a matched psychiatric sample was collected to document the relative psychopathology of these different groups. The study also evaluated the influence of demographic variables on profile configuration to determine whether alcohol and drug users differing in demographic characteristics can be directly compared with accuracy.

The MMPI protocols of both the patients and the controls were scored for twenty-nine scales including the standard thirteen clinical scales and the thirteen Wiggins Content Scales. In addition, profiles of the alcohol and drug users and the controls were classified into five code type categories. Mean scale differences between the groups were tested by univariable analyses of variance, posthoc analyses, and chi-square.

Results of the study suggest that polydrug users tend to describe themselves in more psychopathological terms than do alcoholics or heroin addicts. They evidenced more dysphoria, somative concern and complaints, antisocial characteristics, and social alienation, and had poorer family relations. However, posthoc analysis indicated no significant differences between the heroin addicts and alcoholics. Comparisons of the alcoholics, heroin addicts, and polydrug users with psychiatric controls suggest that alcoholics were the least pathological of the three groups.

The analysis also suggests that although the effects of demographic variables are quite evident in a general psychiatric population, the experience of alcohol or drug misuse has a greater effect on the MMPI profile and overrides the effects often found to be related to age and race. (HSRI)

21 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-77-E0102

A SUICIDE BY THIOPENTONE INJECTION, A.M. Bruce; J.S. Oliver; H. Smith, Forensic Science, v9 n3 p205-7 (1977)

Described in this paper are ultraviolet and gas chromatographic methods used to find the concentrations of thiopentone in human tissue obtained at the postmortem examination of a thiopentone suicide victim. The drug was administered by injection.

The thiopentone concentrations were found to be 0.6 mg/100 ml of blood and 2.6 mg/100 g of tissue. These values are consistent with those reported for deaths where only thiopentone and other anesthetic agents were present. The gas chromatographic method gives more accurate results with tissues than does ultraviolet spectrometry. (JAM)

1 ref

KEYWORDS: Drug Concentrations in Body Fluids: Acute Dose Study. Specific Drug Screening: Gas Chromatography. Specific Drug Screening: Optical Techniques.

UM-78-E0103

THE USE OF BENZODIAZEPINES IN PRISON POPULATIONS, C.R. Brown, Journal of Clinical Psychiatry, v39 n3 p219-22 (1978)

This paper presents past experiences with tranquilizing drugs such as Valium(R) and other benzodiazepines among violent, hostile prisoners at the Utah State Prison. In view of recent literature that the drug oxazepam or Serex(R) has all of the beneficial effects of Valium(R), Librium(R), and other benzodiazepines without the incidence of paradoxical rage reactions or increased hostility associated with them, approximately half of the prisoners being treated with diazepam were switched to treatment with oxazepam. Preliminary observations show that oxazepam substantially relieved anxiety, depression, hostility, and aggression.

The author concludes that in view of the fact that approximately seventy percent of criminals in the Utah State Prison are incarcerated because of drug or alcohol related crimes, it is imperative that strict guidelines be set up for the use of tranquilizers in this type of personality. (HSRI)

11 refs

KEYWORDS: Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. oxazepam. Muscle Relaxants (Central): diazepam. Review: Drug Effects. Review: Drug Use.

UM-76-E0104

CURRENT TRENDS IN PRESCRIBED PSYCHOTROPHIC DRUG USE, R. Cooperstock, Research Advances in Alcohol and Drug Problems, R.J. Gibbins; et al., v3 p297-316, New York: John Wiley and Sons (1976)

This paper attempts to indicate the magnitude of increase in the use of prescription drugs, particularly psychotropics. Several Western industrialized countries are compared for their use of psychotropics.

Various factors influence the use of drugs. The ratio of general practitioners to specialists influences prescribing rates since general practitioners are more likely to write prescriptions for psychotropic drugs than specialists are. Other factors that influence the magnitude of drug use are the following: the ratio of physicians to patients; the cost and method of payment; the number of pharmaceutical preparations available; the ratio of urban population to rural; national preferences regarding the form of medications; the differences in availability of drugs to the public; and the number of controls on the manufacture, import, and sale of pharmaceutical products.

Psychotropics are more popular in the United States than in other countries. North Americans, particularly those in the United States, consume more prescribed drugs than do other nationals. Europeans consume antianxiety agents and sedatives, however, at a rate equal to that of the United States population.

In Canada, a number of clear trends in patterns of prescribing have emerged. The prescription levels of major tranquilizers and antidepressants have remained relatively stable. The sedative and hypnotic drugs have shown a slight decline in recent years, a decline largely accounted for by barbiturates. Nonbarbiturates have shown a steady increase since 1970, most of which can be attributed to increased use of methaqualone. Currently, the minor tranquilizers, particularly the benzodiazepines, are the most commonly prescribed class of drugs.

In 1970, the National Health Service (NHS) in England spent 170 million British pounds on pharmaceuticals at manufacturers' prices. The NHS market for pharmaceuticals has been growing at about 10.5% per year and it is estimated that the growth of the industry from 1970 to 1980 will be between 55 and 70%. From 1961 to 1971 total prescriptions increased 30%, from 205.0 million to 266.5 million. During this same period the number of prescriptions for psychotropics rose from 32.2 to 47.8 million prescriptions, thus increasing by 48%. By 1973, psychotropics had reached 49.6 million prescriptions.

The editors of Research Analysis in Alcohol and Drug Problems are R.J. Gibbins; Y. Israel; H. Kalant; R.E. Popham; W. Schmidt; R.G. Smart (HSRI)

55 refs

KEYWORDS: Central Nervous System (CNS) Agents. Epidemiology: National Survey of Drug Use Patterns.

UM-78-E0105

COLLEGE DRINKING AND OTHER DRUG USE, B. A. Rouse, J. A. Ewing, Drinking: Alcohol in American Society--Issues and Current Research, J. A. Ewing; B. A. Rouse, eds., p171-202, 309-404, Chicago: Nelson-Hall (1978)

Presented here is data drawn from national representative samples and other in-depth scientific studies concerning alcohol and other drug use by college students. Much of the paper reports the results of a series of studies conducted in a large coeducational state university between 1969 and 1972 investigating drug and alcohol use. In addition to the usual demographic variables of interest, specific variables such as risk-taking, driving under the influence, alienation, and serious suicidal thoughts were also examined. The students were administered a comprehensive, standardized questionnaire in a confidential interview situation.

Results of the study indicated that 93% of the students drank and 30% had tried marijuana at least once. Seventy percent of the total sample of men admitted that they

drove after drinking, 26% admitted driving after using marijuana, 20% after alcohol and marijuana, and 5% after alcohol with amphetamines. Most of the students admitted that the drugs used had an adverse effect on their driving. Those who had used marijuana, especially those who used it almost daily, were more likely to drive after drinking and after using combinations of drugs. (HSRI)

64 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Ganglionic Blocking and Stimulating Agents: nicotine. Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Stimulants: nicotine. Unclassified Agents: tobacco. Barbiturates. Hallucinogens and Related Agents. Stimulants. Epidemiology: Regional or Local Survey of Drug Use Patterns. Epidemiology: Self-Reported Drug Use by Drivers.

FAA-AM-78-81

UM-78-E0106

AGRICULTURAL AVIATION VERSUS OTHER GENERAL AVIATION: TOXICOLOGICAL FINDINGS IN FATAL ACCIDENTS, D. J. Lacefield; P. A. Roberts; C. W. Blossom, Oklahoma City, Oklahoma: FAA Civil Aeromedical Institute (September 1978)

This study reports results of research activities attempting to identify and determine the magnitude of toxicological factors in fatal air carrier and general aviation accidents, particularly those involving agricultural aviation. Results from a toxicological study of samples from 174 pilots killed while engaged in agricultural aviation and samples from 2,449 other general aviation pilots were compared. The incidence of alcohol in specimens was similar for agricultural pilots and other general aviation pilots but the blood levels of alcohol tended to be lower in the agricultural pilots. Carbon monoxide as an incapacitating agent did not appear to be a factor in aerial application operations. Evidence of the use of drugs or medications was less in agricultural pilots than in other general aviation pilots.

Over half of the agricultural pilots had below normal cholinesterase levels, suggesting a continuing problem of acute or chronic toxicity from the pesticides being applied by agricultural aircraft. This finding suggests that better educational efforts could reduce the accident rate in agricultural aviation. (AAM)

2 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Herbicides. Pesticides. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-E0107

PERSPECTIVES ON THE HISTORY OF PSYCHOACTIVE SUBSTANCE USE, G. A. Austin, NIDA Research Issues 24 (1978)

This volume contains thirty-four separate studies that individually summarize significant developments in the history of psychoactive substance use in developed countries since the sixteenth century. The primary intent of the volume is to provide a greater awareness of the ubiquity of drug use in the past and of the complex and varied factors that have influenced its spread and society's response, as well as the effects of that response.

The studies cover a wide range of countries, eras, and drugs. Substances discussed include tobacco, coffee, alcohol, cannabis, cocaine, opium, and the opiates. Each study is divided into four sections: (1) background--an introductory section reviewing major points of interest and providing an overview to the topic; (2) chronology--an annotated and referenced review of some of the most relevant or interesting developments in the history of the substance; (3) commentaries or summaries of previous researchers' points of view, interpretations, or conclusions regarding the topic; and (4) a bibliography with short citations of the sources used in each study. In addition, a complete bibliography with full citations is included at the end of the volume. (AAM)

280 pages 381 refs

U.S. Department of Health, Education, and Welfare publication no. (ADM) 79-809.

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Ganglionic Blocking and Stimulating Agents: nicotine. Local Anesthetics: cocaine. Nonbarbiturates: ethanol

(ethyl alcohol). Opiates and Related Agents: opium. Stimulants: caffeine. cocaine. nicotine. Unclassified Agents: tobacco. Opiates and Related Agents. Compilation.

UM-77-E0108

INCIDENCE OF FIRST USE OF A DRUG: SIGNIFICANCE AND INTERPRETATIONS, L.G. Hunt, Addictive Diseases: An International Journal, v3 n2 p177-86 (1977)

Data on incidence of first use of a drug have frequently resulted in an incidence curve which rises and falls in a regular pattern rather than fluctuating randomly. This paper discusses the properties, significance, and possible interpretations of an incidence curve for first use of a drug. The theory of contagious transmission and the simple epidemic model are discussed. The author suggests that new drug use spreads in a fashion similar to the way diseases and rumors spread, starting slowly at first, then increasing rapidly until most of the group is exposed, then finally dying out. Drug use, it is argued, is contagious in that initiation of illicit and nonmedical drug users is usually by friends, peers, or family members, who also act as suppliers of drugs during early use.

Empirical incidence data showing typical peaks appears to be a reflection of a contagious process, that is, the peaks are evidence that a drug is spreading among peers by interpersonal contact. This process is called contagious transmission.

The author also describes iatrogenic introduction, which produces random incidence patterns, in contrast to regular peaked incidence curves resulting from contagious transmission.

It is concluded that the most striking property of incidence of first-use curves for treated users -- sharp peaks of new use -- probably reflects contagious spread of use among peer groupings, since a one-at-a-time introduction by physicians cannot cause such temporal clustering. (HSRI)

12 refs

KEYWORDS: Review: Survey Methodology.

UM-78-E0109

INTERNATIONAL DRUG USE, G. A. Austin; M. A. Macari; D. J. Lettieri, eds., NIDA Research Issues 23 (1979)

This volume contains ninety-five summaries of research conducted on drug use in countries other than the United States. It is neither a comprehensive nor a representative survey of drug use throughout the world, but rather an introductory collection of readings designed to provide a basic familiarity with some of the major differences and similarities between drug use in the United States and elsewhere. Each summary is intended to be a faithful representation of the original study. The purpose of the volume is to alert drug specialists and lay readers to pertinent research that has been conducted and to direct them to the original documents for further examination.

The first section of this volume contains twenty-three studies on the United Kingdom, principally Great Britain. The second consists of seventy-two studies dealing with other foreign countries which are organized by major geographic area (Continental Europe, Scandinavia, Africa and the Near East, Asia, Latin America, and the Caribbean), and then by individual country. The studies in each section are cited alphabetically in the list of studies; the table of contents provides an overview of the geographic arrangement of the countries and the drugs discussed. A supplementary bibliography of additional readings in the areas covered is included at the end of the volume. Several indexes are also provided, designed to meet the needs and interests of drug researchers.

The studies themselves cover a wide range of topics. A great many are purely epidemiological: they describe the incidence and prevalence of drug use in a country as a whole or among a particular population within that country. Other articles focus on specific aspects or issues involved in use, such as personality or background characteristics of users, crime, and law enforcement. (AAM)

199 pages 78 refs

U.S. Department of Health, Education, and Welfare publication no. (ADM) 79-809

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: methaqualone. Opiates and Related Agents: opium. Analgesics and Antipyretics. Opiates and Related Agents. Stimulants. Compilation.

UM-79-E0110

THE AGING PROCESS AND PSYCHOACTIVE DRUG USE, B. Piland; R. Prentice; J. Gollub, NIDA Services Research Monograph Series (1976)

This monograph attempts to systematically organize, analyze, and evaluate available data on the drug use problems of the elderly. It is composed of three separate reports. Part I examines the literature on the physiological and psychological changes of the aging processes and the relationship of these changes to drug use.

Part II attempts to identify and synthesize information on the patterns of use of psychoactive drugs by the elderly.

From the few data that are available, it is difficult to conclude that there is a substantial problem of drug misuse or abuse by the elderly. However, available data do indicate that the elderly are a major group in the consumption of prescription and over-the-counter drugs, and that particular characteristics of the elderly make them prone to drug misuse. Thus, the findings on use of psychomotor drugs by the elderly warrant a closer examination of the appropriations of that use.

Part III identifies current operating programs that have been established to prevent or treat the problem of drug misuse or abuse by the elderly. The study found few active programs in the area of specific intervention and treatment of the elderly psychoactive drug user.

The study concludes with two appendices, one containing a list of researchers working in the area of drug abuse by the elderly, the other containing a list of programs attempting to alleviate the problem. An annotated bibliography is also provided. (AAM)

91 pages 34 refs

U.S. Department of Health, Education, and Welfare publication no. (ADM) 76-392

KEYWORDS: Review: Drug Use.

UM-76-E0111

THE LIFESTYLES OF NINE AMERICAN COCAINE USERS: TRIPS TO THE LAND OF COCKAIGNE, J.V. Spotts; F.C. Shontz, NIDA Research Issues 16 (1976)

Representative case methods were used to examine in detail the relationship between cocaine use and life style, as well as to obtain information about the physiological and psychological effects of this drug. Nine male drug users, all of whom strongly preferred cocaine, participated in the project as expert consultants. The men selected varied widely in type and effectiveness of life adjustment and also in overall level of cocaine consumption.

All participants were interviewed at length and in depth about their life histories and usage of drugs. They were also examined with standard psychological tests of intelligence and personality as well as with specially constructed and individualized morphogenic and semimorphogenic instruments. Data from several of the morphogenic and semimorphogenic measures were obtained at least three times from all but one participant (who was killed) at intervals of at least one month between testings. Each participant also described in detail all of his daily activities for a full two-week period of time.

The results showed clearly that each participant had a unique life style and personality. This was most persuasively demonstrated by the fact that attempts to summarize the findings by conventional statistical methods proved unsatisfactory. Overall level of drug usage was found to be the most appropriate variable around which to organize the findings. Characteristics associated with relatively low levels of usage are use of cocaine to enhance sensory pleasures, to make the real world seem like an imaginary paradise, and to help the user compensate for inability or unwillingness to accept the responsibilities and the problems of life. Characteristics associated with relatively higher levels of usage are use of cocaine to provide necessary support for the self-concept, or (at higher levels) as a means to provide the drive and energy needed to succeed in a tough, competitive world, or (at the highest level) as a way of inducing a state of blissful oblivion to overwhelming life problems. At the higher

levels of usage, sensory pleasure is present, but it is counter-balanced by highly adverse effects such as increased tension, anxiety, paranoia, and in the extreme, hallucinations and fear of overdose and subsequent death. At these levels of usage, pleasure seeking does not provide a major incentive for taking the drug.

To further knowledge of drug-use patterns, additional studies using representative case methodology are needed that examine similar persons who take and prefer relatively large amounts of other drugs, such as amphetamines, barbiturates, heroin, and alcohol, as well as individuals who use no drugs to excess. (JA)

571 pages 0 refs

Department of Health, Education and Welfare publication no. (ADM) 76-392

KEYWORDS: Local Anesthetics: cocaine. Stimulants: cocaine. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-75-E0112

TIME PERSPECTIVE CORRELATES OF COLLEGIATE MARIJUANA USE, M.R. King; G.J. Manaster, Journal of Consulting and Clinical Psychology, v43 n1 p99 (Feb 1975)

This study attempted to determine whether marijuana users differ from nonusers in their orientation toward past, present, and future. Sixty-four female and twenty-two undergraduate students completed a Time Reference Inventory demographic data sheet dealing with the extent of marijuana use. Fifty-six percent (forty-eight) of the subjects reported never having used marijuana.

Results of analyses by nondirectional univariate F tests indicated that marijuana users were significantly more oriented toward the past than were nonusers; no significant differences were found on measures of present or future orientations.

These data suggest that a significant relationship exists between marijuana use and past orientation; however, this study does not indicate whether greater orientation to the past is an antecedent or a resultant factor associated with continued use of marijuana. (HSRI)

4 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0113

INHALANT USE AND TREATMENT, T. Mason, NIDA Services Research Monograph Series, Rockville, Md.: National Institute on Drug Abuse (1979)

This report presents the findings from an exploratory study designed to assess the patterns of inhalant use in six communities, the problems and treatment needs presented by inhalant abusers, the types of services sought by and provided for inhalant abusers, and the general response of the health delivery systems to individuals who abuse inhalants. The data for this study were collected from the following sources: (1) eighty-eight client interviews; (2) examination of 117 clinical records; (3) fifty interviews of treatment staff; (4) secondary analyses of existing data sets, such as the Client Oriented Data Acquisition Program (CODAP) and the Drug Abuse Warning Network (DAWN); and (5) review of the psychosocial literature.

Results of the study indicated that inhalants were not the drugs of choice for 77% of the inhalant users interviewed. Marijuana was most often reported to be the drug of choice; it was the second most widely used drug after inhalants. Approximately 40% of the inhalant abusers reported no secondary drug use.

Inhalant abusers tend to be young, male, Mexican American or white, and from large, low income families. However, recent studies suggest that inhalant users are becoming more commonly found among different ethnic groups and socioeconomic levels, and that greater proportions of females are using inhalants.

Inhalant abusers do not generally respond well to treatment. The inhalant abuser has been described as psychologically maladjusted, mentally slow, withdrawn, disruptive, uncooperative, and of low self-esteem with an exceptionally high expulsion rate and a higher than average dropout rate.

The author concludes that inhalant abusers are younger than other drug abuse populations, are more likely to be disruptive and delinquent, and appear to suffer from low self-esteem and a lack of motivation more than other drug abusers; therefore, traditional treatment programs geared to more stable adult populations are not well-equipped to deal with inhalant abusers. The author recommends several general methods for successful treatment of inhalant abusers. (HSRI)

62 pages 69 refs

DHEW Publication No. (ADM) 79-783

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Other Toxicants: glue (model builder's). paint, spray. Stimulants: amphetamine. Volatile Solvents: gasoline. Barbiturates. Opiates and Related Agents. Countermeasure Development, Testing, and Evaluation. Epidemiology: National Survey of Drug Use Patterns. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-77-E0114

CAFFEINE, TOBACCO, ALCOHOL AND DRUG CONSUMPTION AMONG MEDICAL STUDENTS IN BARCELONA, J.R. Laporte; J. Cami; R. Gutierrez; J. Laporte, European Journal of Clinical Pharmacology, v11 n6 p449-453 (July 1977)

This study investigated nonmedical use of caffeine, alcohol, tobacco, and drugs among 515 male and 293 female medical students at the University of Autonoma de Barcelona in 1974. Out of 1,029 students, 808 (78.5%) returned properly completed questionnaires. These showed that mean caffeine consumption was 8.3 g per month and increased with the length of stay at the university. Tobacco consumption (general mean, 190 cigarettes per month--216 for males and 150 for females) and alcohol consumption (8.8 litres per year for males and 4.1 litres per year for females) also increased with time spent at the university. Alcohol consumption was not as high as in the general population. Amphetamine consumption was very high; 22% of the students had taken amphetamines on more than one occasion in the six months prior to the survey. Marijuana and hashish were by far the most commonly used drugs (9.6%), the use of these drugs being much less common than at other European universities. The use of "harder" drugs was very limited. Reappraisal of alcohol, tobacco, and amphetamine abuse countermeasures is necessary in view of the high rate of use. (JAM)

6 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: hashish. marijuana. Ganglionic Blocking and Stimulating Agents: nicotine. Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Local Anesthetics: cocaine. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. morphine. Stimulants: amphetamine. caffeine. cocaine. nicotine. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0115

ACUTE DRUG REACTIONS IN A HOSPITAL EMERGENCY ROOM, J.A. Inciardi; B.R. Russe; A.E. Pottieger; D.C. McBride; K.S. Wells; H.A. Siegal, NIDA Services Research Report Series, Rockville, Md.: National Institute on Drug Abuse (1979)

This report presents data collected by the Acute Drug Reactions Project, a five-year program initiated at the University of Miami School of Medicine in May 1972 to determine the extent to which the hospital emergency room might be utilized for the identification and analysis of drug abuse. The project attempted to determine the demographic and social characteristics of the substance-abusing population coming into the emergency room, to examine the nature of drug use resulting in emergency room appearances, to determine whether the kinds of drugs and the characteristics of the populations using them are changing over time, and to determine what proportion of these drug emergency patients are not coming to the attention of local drug treatment programs.

Several major conclusions emerged from the data: (1) Drug emergency patients are most often white females under age 35. (2) The emergency room drug-abusing population is getting older. (3) Legally manufactured and distributed drugs are the primary substances presented in the hospital emergency room. (4) Attempted suicides and accidental overdoses are the primary causes of a drug emergency, but these have decreased during recent years while panic and psychotic reactions have significantly increased. (5) Acute alcohol reactions are the major problem presented in the emergency room; this is an essentially older male population. (6) Intervention in the emergency

room setting appears to be an effective technique for initiating treatment. Furthermore, emergency room data can be used to examine trends in drug use and to isolate the fads and fashions in drug use over time. (HSRI)

48 pages 33 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Local Anesthetics: cocaine. Opiates and Related Agents: heroin. methadone. Stimulants: amphetamine. cocaine. Analgesics and Antipyretics. Barbiturates. Hallucinogens and Related Agents. Opiates and Related Agents. Other Toxicants. Sedatives and Hypnotic Agents. Tranquilizers. Volatile Solvents. Countermeasure Development, Testing, and Evaluation. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-74-E0116

MARIHUANA-HASHISH EPIDEMIC AND ITS IMPACT ON U.S. SECURITY. HEARINGS, Subcommittee to Investigate the Administration of the Internal Security Act, and Other Internal Security Laws of the Committee on the Judiciary, United States Senate, 94th Congress, 2nd Session, May 9, 16, 17, 20, 21, and June 13, 1974, Washington, D.C.: U.S. Government Printing Office (1974)

Presented here are the hearings before the Subcommittee to Investigate the Administration of the Internal Security Act and Other Internal Security Laws of the Senate Committee on the Judiciary concerning the marijuana-hashish epidemic and its impact on United States Security held in May and June 1974. Speakers on the issue were several scientists internationally known for their research on cannabis and other drugs.

Several topics are presented in the hearings concerning marijuana use in the United States. These include the extent of the marijuana epidemic in the United States today, social consequences of the marijuana epidemic, the epidemic potential of marijuana combined with alcohol, the myth of the harmlessness of marijuana, decriminalization of marijuana and related laws, and the need for a national education program.

Special attention is given to the scientific findings concerning alcohol. Evidence for the following conclusions is presented: (1) THC tends to accumulate in the brain and gonads and other fatty tissues in the manner of DDT. It persists in the body for as long as a week after ingestion. (2) Marijuana, even when used in moderate amounts, causes massive damage to the entire cellular process. These changes include reduction of DNA and RNA synthesis, reduction in lymphocyte production, and production of cells with defective chromosome complements. (3) Marijuana inflicts irreversible damages on the brain, including brain atrophy, when used in a chronic manner for several years. (4) There is a growing body of evidence that marijuana adversely affects the reproductive process in a number of ways, and that it poses a serious danger of genetic damage and even of genetic mutation. (5) Chronic cannabis smoking can produce serious respiratory difficulties in a year or less, as opposed to ten or twenty years of cigarette smoking to produce comparable complications. (6) Cannabis smoke is far more damaging to lung tissues than tobacco smoke alone, the damage being described as precancerous. (7) Chronic cannabis use results in deterioration of mental functioning, pathological forms of thinking resembling paranoia, and a lack of motivation--the so-called "amotivational syndrome." (HSRI)

430 pages

KEYWORDS: Cannabis Sativa L. and Related Agents: hashish. marijuana. Compilation. Epidemiology: National Survey of Drug Use Patterns. Other Sociolegal Study. Review: Drug Effects. Review: Drug Use.

UM-75-E0117

MARIHUANA-HASHISH EPIDEMIC AND ITS IMPACT ON UNITED STATES SECURITY. HEARINGS, Subcommittee to Investigate the Administration of the Internal Security Act and Other Internal Security Laws of the Committee on the Judiciary, United States Senate, 94th Congress, 1st Session, Part 2. May 8, 1975, Washington, D.C.: U.S. Government Printing Office (1975)

Presented here are the hearings before the Subcommittee to Investigate the Administration of the Internal Security Act and Other Internal Security Laws of the Senate Committee on the Judiciary held in May 1975 concerning the continuing escalation of the marijuana-hashish epidemic and its impact on United States security.

The evidence presented at this hearing concerns the escalation of the cannabis epidemic qualitatively as well as quantitatively. Until 1970, most of the marijuana consumed in the United States was of domestic origin and low in THC content--less than .2%--which contributed to the widespread myth of its harmlessness. However, in 1974 Jamaican and Columbian marijuana with a THC content of 3 to 4% began to enter the country in increasing quantities. Mexican marijuana, with a THC content of 5% or more, is now appearing in the country. At this time it appears that this potency escalation will continue at an increasing rate.

The escalation in potency has been paralleled by a continuing and massive escalation in the quantities of marijuana getting into the United States and being consumed. National consumption of marijuana in 1974 is estimated to have been between 6 billion and 9.5 billion joints. This tremendous consumption increase over the past few years can be explained by the great increase in the number of daily marijuana smokers, particularly among young people, and by the fact that daily smokers have now graduated to much higher levels of daily consumption.

In the light of the evidence produced at this hearing it is concluded that any changes made in existing laws concerning marijuana be made only after careful examination of the available scientific evidence. Any changes made now in the light of incomplete knowledge may prove difficult if impossible to reverse if future scientific evidence should reinforce what appears to be an emerging consensus that marijuana is a seriously dangerous and debilitating drug. (HSRI)

96 pages

KEYWORDS: Barbiturates. Cannabis Sativa L. and Related Agents: hashish. marijuana. Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Stimulants: amphetamine. Compilation. Epidemiology: Regional or Local Survey of Drug Use Patterns. Other Sociolegal Study. Review: Drug Effects. Review Drug Use.

UM-78-EO118

ALCOHOL AND ILLICIT DRUG USE: FOLLOW-UP STUDY OF TREATMENT ADMISSIONS TO DARP DURING 1969-197?, D.D. Simpson; M.R. Lloyd, American Journal of Drug and Alcohol Abuse, v5 n1 p1-22 (1978)

This paper reports a study of alcohol use and its relationship to illicit drug use and treatment. The study was based on follow-up data on 1,409 persons interviewed four to six years after admission to drug treatment in the Drug Abuse Reporting Program (DARP). The admissions to DARP occurred from 1969 to 1971, and for most persons the follow-up data included three or more years after termination of DARP treatment. The data in this study were obtained from client reports submitted by DARP treatment agencies from 1969 to 1974 and from follow-up interviews conducted in 1975 and 1976. Two sets of analyses were done on the data: (1) the Since DARP period, from DARP termination up to the follow-up interview; and (2) the At Interview data, which focused on the two months immediately preceding the follow-up interview.

The major findings of the study were that: (1) substitution of use occurred between alcohol and opioid drugs for a small segment of the sample; (2) persons who returned to drug treatment after DARP generally tended to use less alcohol than persons who did not; and (3) the use of alcohol tended to accompany the use of nonopioid drugs (particularly marijuana), but not opioid drugs.

Persons who did not return to treatment after DARP termination had lower opiate drug use, but slightly higher alcohol consumption, than those who did reenter treatment. The use of marijuana and other nonopioid drugs also tended to be associated with higher drinking rates.

Although excessive drinking may eventually become a problem for some persons following a drug use career and treatment, the data from this study suggest that its probability is not as great as sometimes expected. The data further suggest that drinking and illicit drug use do not occur independently of other life events.

The authors conclude that further research is needed to investigate the relationship of substance abuse to other behavioral indices and life events. (HSRI)

19 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-EO119

ILLICIT DRUG USE AND RETURN TO TREATMENT: FOLLOW-UP STUDY OF TREATMENT ADMISSIONS TO DARP DURING 1969-1971, L.J. Savage; D.D. Simpson, American Journal of Drug and Alcohol Abuse, v5 n1 p23-38 (1978)

The present study was based on follow-up data for 1,409 persons interviewed four to six years after admission to drug treatments in the Drug Abuse Reporting Program (DARP). The admissions to DARP occurred from 1969 to 1971, and for most persons the follow-up data included three or more years after termination of DARP treament. The focus of this study was on illicit drug use of former DARP clients, taking into account if and when they reentered drug treatment after termination of DARP treatment.

The results showed that a significant drop in opioid and nonopioid (but not marijuana) drug use generally occurred upon entry into other post-DARP treatments, and that these beneficial effects of treatment tended to continue beyond the end of treatment. Overall, 42% of the sample had no further drug treatment during the first three years after DARP, and almost half (42%) of this group used no opioid or nonopioid drugs at all during this time. Comparisons between DARP treatment groups also indicated that therapeutic community clients had the lowest rate of return to post-DARP treatments. (JA)

11 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Opiates and Related Agents. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-EO120

METHADONE AND CRIMINALITY: A SUBURBAN PERSPECTIVE, P.E. Jacobs; E.B. Doft; J. Koger, American Journal of Drug and Alcohol Abuse, v5 n1 p51-8 (1978)

This study attempted to determine whether entering a methadone maintenance treatment program results in a reduction in crime. A study was made of 80 patients who allowed the researchers to examine police records of their arrests before and after methadone treatment. These 80 patients were similar to the total clinic population of 226 in a suburban methadone program in terms of demographic variables, arrest record, and addiction history.

For these 80 patients both the rate of arrest and the number of patients arrested declined in association with entering methadone maintenance treatment. The decline was statistically significant for drug-related offenses but not for nondrug-related offenses. Overall, the decline in both rate of arrest and number of patients arrested was significant, but this was due to the decrease in drug-related arrests.

Drug-related arrests play a dominant role in the criminality of the suburban patients in this study. Because of this, the reduction in drug-related arrests is more significant for this group of patients than it would have been for an inner city patient population.

This study indicates that methadone maintenance is more effective with suburban patterns of addiction than previously thought, especially when compared to its effect on inner city addicts. (JAM)

9 refs

KEYWORDS: Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-EO121

PARSIMONY IN DESIGNING A DRUG USE SURVEY: A METHODOLOGY STUDY, D.V. Babst, American Journal of Drug and Alcohol Abuse, v5 n4 p441-54 (1978)

The purpose of this paper is to show how the responses to one question frequently reveal as much about a student's involvement in drug use as do responses to a complex attitudinal index built on many items. It illustrates how many surveys have many more questions per attitudinal dimension than may be necessary.

The study is based on the responses of a representative sample of 8,553 students in the seventh through twelfth grades in the public secondary schools in New York State. The questionnaire inquired about five major attitudinal areas--school, family, friends' use of drugs, risk-taking, and opinions about drugs. The data collected was analyzed and compared to data collected concerning actual drug use. The study attempted to determine how well individual items relate to drug use by ranking them as to their relationship (gamma) to drug use, with the most related item in each category at the top.

It was observed that the most related item in each category generally was associated with drug use more than the entire index of questions in that category. When multiple regression analyses were done, it was found that the items providing data about drug abuse were not only related to drug involvement, but also to each other.

The author concludes that it is economically and practically feasible, when planning surveys, to first carry out small pilot studies to determine which individual items can best measure each major attitudinal area of interest. The more items a questionnaire has, the more it taxes the patience of the respondent. Furthermore, it rapidly increases the cost of printing, administering, and processing, tempting the researcher to leave out crucial areas of interest. (HSRI)

7 refs

KEYWORDS: Review: Survey Methodology.

UM-78-EO122

PHYSICAL ILL-HEALTH AND PSYCHOTROPIC DRUG PRESCRIPTION--A REVIEW, P. Williams, Psychological Medicine, v8 n4 p683-93 (Nov 1978)

This literature review attempted to determine how often patients with physical health problems are prescribed psychotropic drugs. It investigated the proportion of psychotropic drugs prescribed for physical illness, which psychotropic drugs are most frequently prescribed, which physical illnesses are most frequently treated with psychotropic drugs, and reasons for this practice. In the studies reviewed, three methods of measuring physical health were used: prescriber's diagnosis, patient self-report, and independent assessment.

In order to determine the proportion of drugs prescribed for physical illness, community and hospital surveys of prescribers' diagnoses and studies using patient self-report as the measure of physical health were reviewed and found to have widely varying results. These inconsistencies were often due to lack of standard reporting procedures, inconsistent sample sizes, different methodology, and differing disease and drug classification systems. Therefore, no proportion of psychotropic drugs prescribed for physical evidence could be estimated.

The literature indicated that antidepressants generally are the least likely to be prescribed for a physical problem. Between 35 and 70% of the major tranquilizers and 40 to 90% of minor tranquilizers are prescribed for physical disorders. Psychotropic drugs are most often prescribed for cardiovascular disorders, respiratory disorders, obesity, CNS disorders, neoplasms, and gastrointestinal disorders.

A number of factors may contribute to the prescription of a psychotropic drug for a patient with physical illness: (1) secondary properties of psychotropic drugs which are unrelated to psychological functioning; (2) the coexistence of physical and psychiatric disease; and (3) psychic components of somatic disease.

In conclusion, this review of the literature reveals evidence of substantial physical morbidity in patients who receive psychotropic drugs. It is suggested that future epidemiological studies of psychotropic drug prescribing should give due attention to physical morbidity as a variable and should ascertain the precise reasons for the prescription of these drugs in patients with physical illness. (HSRI)

38 refs

KEYWORDS: Antidepressants. Minor Tranquilizers (Anti-Anxiety and Ataractics). Sedatives and Hypnotic Agents. Tranquilizers. Epidemiology: National Survey of Drug Use Patterns. Review: Drug Use.

UM-79-E0123

ESTIMATION OF NONRESPONDENT BAC USING A PRIORI JUDGEMENT, W.L. Carlson, Accident Analysis and Prevention, v11 n1 p35-41 (March 1979)

Two methods of adjusting for nonparticipation bias in roadside breath testing surveys are compared. Method 1 uses the assumption that the probability of measured BAC level conditional on a priori judgement of drinking is the same for respondents and nonrespondents. Method 2 uses the assumption that the probability of a priori judgement of drinking conditional on BAC level is the same for respondents and nonrespondents. Method 2 yields substantially larger estimated probabilities of high BAC for nonrespondents. Both methods can be supported by sound logical arguments. Method 2 is shown to yield negative probabilities when applied to a large roadside survey sample, and is thereby rejected. (JA)

4 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Review: Survey Methodology.

UM-79-E0124

RECENT TRENDS IN CANNABIS USE IN CANADA, I. Rootman, Drug and Alcohol Dependence, v4 n5 p425-34 (Sep 1979)

Reported here are the results of a nationwide survey of cannabis use conducted to determine current cannabis use among adult Canadians. A total of 1,057 adults, eighteen years and older, were interviewed in their homes to provide data on whether they had ever used marijuana or hashish, use in the last twelve months, frequency of use in the last thirty days, and year of first use. In addition, respondents were asked questions concerning age, sex, occupation, mother tongue, region of residence, community size, education, and income. The sample was representative of the adult Canadian population in most respects.

The following conclusions were drawn from the study: (1) 17.2% of the sample reported that they had used marijuana or hashish at some time in their lives. (2) 9.7% reported that they had used cannabis in the past twelve months. (3) 3.6% reported that they had used cannabis more than once a week in the past thirty days. (4) The period 1970-73 was most often reported as the time of initiation of cannabis use, followed by the period 1974-77. (5) Significant differences in patterns of cannabis use between regional and social groups were evident. Residents of British Columbia, young people, males, laborers, persons whose mother tongue was English, residents of larger communities, and those with university education reported more marijuana use.

The author concludes that there has been an increase in cannabis use in Canada over the past decade, the exact magnitude of which is unknown and probably unknowable given the limitations of previous research. The available data do suggest, however, that the rate of increase may have slowed in the past few years. (HSRI)

10 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Epidemiology: National Survey of Drug Use Patterns.

UM-79-E0125

LOXAPINE FATALITIES, P.C. Reynolds; C.W. Som; P.W. Herrmann, Clinical Toxicology, v14 n2 p181-5 (Feb 1979)

Although loxapine has been available for clinical use in the United States for two to three years, the literature reports very few overdose cases involving this drug. Reported here are the findings from two cases of apparent suicidal ingestion of loxapine.

Blood, urine, and liver samples were examined for the presence of volatiles and acidic, neutral, and basic drugs using a combination of gas chromatography and ultraviolet spectrophotometry; analysis indicated the presence of loxapine. Quantitative estimation of loxapine in urine, blood, and liver was accomplished by gas-liquid chromatography.

In these two cases the ingestion of loxapine was found to be approximately 2,500 mg and 2,900 mg, indicating that death in both cases was the result of suicidal loxapine intoxication. Recommended doses of loxapine are 250 mg or less per day. (HSRI)

7 refs

KEYWORDS: Major Tranquilizers (Antipsychotics and Neuroleptics): loxapine*. Epidemiologic Research: Drug Concentrations in Body Fluids.

UM-79-E0126

SELF-POISONING WITH OVER-THE-COUNTER HYPNOTICS, M.D. Allen; D.J. Greenblatt; B.J. Noel, Clinical Toxicology, v15 n2 p151-8 (Sep 1979)

This study investigated the incidence and consequences of over-the-counter (OTC) hypnotic overdosages in cases aged fifteen years and older admitted to Massachusetts General Hospital between 1962 and 1975. Out of a total of 97,994 admissions, 0.8% (773) were attributable to accidental or deliberate overdosage with a psychotherapeutic drug. Of these, 21 had ingested OTC preparations. Thirteen were female and eight were male, their ages ranging from 17 to 82 years with a mean of 29.5. Preparations ingested included Dormirex(R), Sominex(R), Sleep Eze(R), Nytol(R), Napkaps(R), Rexall(R), and Sleeptite(R). Ten of twenty-one cases had manifestations of central anticholinergic toxity (atropine-like psychosis) such as hallucinations, delirium, and confusion. Seven displayed tachycardia and three developed mild hypertension. However, all patients recovered rapidly and without sequelae. Specific therapy (i.e., physostigmine) was rarely required. Thus, OTC hypnotic overdosage commonly produces "toxic psychosis". Intoxication is usually of short duration and relatively benign. Several deaths have been attributed to methapyrilene in the literature, but in general fatal poisoning due to OTC hypnotics is rare. (HSRI)

16 refs

KEYWORDS: Sedatives and Hypnotic Agents. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0127

SCREENING FOR DRUG AND ALCOHOL ABUSE IN A GENERAL MEDICAL POPULATION, F.S. Tennant; C.M. Day; J.T. Ungerleider, Journal of the American Medical Association, v242 n6 p533-5 (10 Aug 1979)

The purpose of this study was to determine whether use of a simple questionnaire or personal inquiry in conjunction with a routine physical examination could serve as an effective and efficient tool for the screening of drug and alcohol abuse in the general medical population. One hundred and fifty consecutive, first-visit, general medical patients without psychiatric complaints completed a one-page questionnaire about drug, alcohol, and tobacco use. During the examination, each patient was examined for various physical signs frequently associated with drugs of abuse such as constricted or dilated pupils, sedation, and abnormal reflexes. Each patient was specifically asked if he abused alcohol or used any illegal psychoactive drugs, and if so, how much and for how long. If abuse was verified, treatment was offered.

Results of this screening method indicated that seventeen patients (11.3%) currently used one or more psychoactive drugs; three patients (2.0%) stated that they had an alcohol problem. Seven patients (4.7%) abused one or more drugs on most days during the preceding ninety days.

Of the seventeen drug users, fourteen (82.4%) either admitted on the questionnaire that drug abuse was a problem for them or listed by name the psychoactive drugs they used. The other three readily admitted to their problem when asked.

The results of this study are similar to other studies of drug use in the general medical population. Ten (6.7%) of one hundred and fifty patients were found to abuse drugs or alcohol. Seventy percent of the drug and alcohol abusers recognized by this simple screening method voluntarily entered treatment.

The authors conclude that general medical patients can be screened effectively and inexpensively for drug and alcohol abuse in a way which does not interfere with the normal routine of clinical practice, and once recognized, most patients will enter treatment. (HSRI)

18 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-E0128

PSYCHOPATHOLOGY AND NONMEDICAL DRUG USE: A COMPARISON OF PATIENT AND NONPATIENT DRUG USERS, A.S. Carlin; E. Detzer; F.F. Stauss, International Journal of the Addictions, v13 n3 p337-48 (Apr 1978)

This study attempted to determine whether all heavy drug users are mentally ill or whether it is possible for drugs to be used heavily for recreational purposes without the presence of profound psychopathology. Eleven heavy drug users not being treated for drug abuse, all of whom were males between twenty and thirty years of age, were compared to a group of eleven patients matched for sex, age, and lifestyle who were seeking treatment for drug abuse. All subjects were administered the Current and Past Psychopathology Scales (CAPPS) and the Minnesota Multiphasic Personality Inventory (MMPI).

Analysis of the comparison indicated that although both groups used drugs with high frequency, actual patterns of drug use differed. Nonpatients preferred stimulants and hallucinogens, whereas the patient group preferred alcohol and sedatives. Both the MMPI and CAPPS scores indicated that the patient sample was experiencing more guilt, lower morale, more tension, and more anxiety than nonpatients, which manifested itself in somatic symptoms and concerns. Patients under treatment had a greater incidence of marriage and separation and used drugs to self-medicate their psychological distress. Nonpatients used drugs in a way less likely to disrupt their lives and less likely to develop dependence.

The authors conclude from these results that despite the fact that drug users are as heterogeneous a group as any other, there exist two distinct groups of substance abusers; those who are experiencing psychological distress, and those who, although deviant, are not in psychological distress. It appears, therefore, that drugs may be used in various contexts and may provide different functions for different users. Since individuals who use drugs heavily are not necessarily in psychological distress, it is necessary to determine the individual's psychological state before treatment for drug abuse. Psychologically based treatment may not be effective for all drug users. (HSRI)

14 refs

KEYWORDS: Clinical Study. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-E0129

DEATHS OF DRUG ADDICTS IN LONDON DURING 1970-4: TOXICOLOGICAL, LEGAL, AND DEMOGRAPHIC FINDINGS, B.C. Stevens, Medicine, Science and the Law, v18 n2 p128-37 (1978)

This paper describes the toxicological, legal, and demographic aspects of 138 deaths due to drug addiction in London from January 1970 through December 1974. The deaths of the 107 male and 31 female addicts, all aged between 15 and 50 (Sample A), were compared to a 10% simple random sample of all unnatural deaths in London over the same time period, including road traffic accidents, murders, and suicides. Twenty-nine drug addicts (Sample B) were found by this sampling technique, representing approximately 290 addicts dying of causes not directly related to their addiction.

Results of the comparison indicate that drug addicts appear more likely to die a sudden death unrelated directly to their addiction than to die of a cause directly attributable to drug abuse. In deaths caused by drug abuse, barbiturates were the main drug causing death (52.2% in sample A, 55.2% in sample B). Postmortem records showed that one-third of the deaths in sample A were due to inhalation of vomit. One-fifth of sample B died of road traffic accidents, falls, or burns in which toxicological analysis of peripheral blood demonstrated drugs usually below the lethal level. The most significant variable differentiating sample A from sample B is the greater number of deaths caused by intravenous drug administration in sample A (80.6%) compared to sample B (17.2%). (HSRI)

33 refs

KEYWORDS: Barbiturates. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-77-E0130

POLYPHARMACY AMONG PSYCHIATRIC PATIENTS, E. Hemminki, Acta Psychiatrica Scandinavica, v56 n5 p347-56 (Nov 1977)

The purpose of this study was to determine the frequency of polypharmacy among 694 psychiatric patients. Patients from three major mental hospitals and four psychiatric outpatient centers in Helsinki were diagnosed according to the following categories: psychoses, mental retardation, neurologic disease, alcoholism and drug abuse, and neuroses. Records of the drugs prescribed on one selected day were examined and drugs were categorized as follows: (1) proper psychotropic drugs, including hypnotics, ataractics, antipsychotics, and antidepressants; (2) neurologic drugs, including those used for treatment of migraine, epilepsy, convulsions, vertigo, nausea, emesis, and obesity, and centrally acting muscle relaxants; (3) hidden psychotropic drugs, that is, drugs which contain not only a psychotropic agent, but also other active ingredients; and (4) psychotropic drugs, which comprise the three above classes combined. For each patient the number of different drugs in the above categories was calculated.

More than two-thirds of the patients (69%) received more than one psychotropic drug in the same day. Sixty-one percent received more than one proper psychotropic drug, with 22.1% receiving three or more, up to a maximum of five. On the average there were 1.7 different proper psychotropic drugs per patient. The average number of all drugs, both psychotropic and nonpsychotropic, was three; the maximum number was eleven.

Very few patients were treated without psychotropic drugs, and most of these were children or adolescents. Psychotropic polypharmacy was very rare among patients under twenty years (0.30 drugs per patient) and those over seventy years (1.6 drugs per patient). The highest number of drugs was among those between fifty and sixty (2.4 drugs).

The most frequent drug combinations among the general patient population as well as among patients with alcoholism, psychoses, and mental retardation were antipsychotic drugs and antiparkinson drugs. Alcoholics also frequently combined antipsychotics and hypnotics. The combination of antipsychotics and neurologic drugs was most frequent among patients with neurologic diseases. Among patients with neuroses, the combination of antipsychotics and ataractics was most frequent.

These results are evaluated in the light of the results and conclusions of fourteen controlled clinical trials investigating the efficiency of polypharmacy reported in the literature. Most of these studies failed to find any benefit in combining several proper psychotropic drugs. Therefore the number of psychotropic drugs prescribed for most psychiatric patients should in all probability be reduced. (HSRI)

30 refs

KEYWORDS: Anti-Emetics: chlorpromazine. Antidepressants: amitriptyline. clomipramine. desipramine. doxepin. imipramine. lithium. protriptyline. Antihistamine Agents: hydroxyzine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. fluphenazine. perphenazine. thioridazine. trifluoperazine. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. hydroxyzine. oxazepam. Nonbarbiturates: flurazepam. hydroxyzine. Other CNS Agents: lithium. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-E0131

NORMATIVE AND ATTITUDINAL CONTROL AS MODERATING INFLUENCES ON MARIJUANA USE, W.O. Bearden; A.G. Woodside, Journal of Health and Social Behavior, V19 p199-204 (1978)

This paper contends that there are two types of individuals who use drugs: (1) those under attitudinal control, that is, whose drug use is governed by individual attitudes and beliefs; and (2) those under normative control, that is, whose drug use is governed by normative and social concerns. Consequently, individuals concerned with marijuana usage and seeking to affect pending legislation regarding the legalization of marijuana should consider differences between these groups and adapt communication strategies accordingly.

The intent of this study was to assess the degree and direction of differences between consumers under attitudinal or normative control along a number of belief, situational, or usage dimensions of marijuana consumption. Specifically, differences in consumption and intentions to use marijuana within a variety of anticipated situations were examined, as were respondent perceptions concerning the likely influences of intervening and unexpecting events affecting marijuana-usage behavior. Differences in respondent evaluations concerning salient beliefs underlying individual attitudes and consumer normative beliefs reflecting the influence of social norms were also examined across both groups. In order to do this, a questionnaire designed to assess belief, behavioral, and situational dimensions underlying marijuana consumption was administered

to 251 college students aged 19 to 26, all of whom reported prior trial use, current use, or personal observation of friends using marijuana.

Sample respondents were categorized into two groups based upon the weights assigned by the individuals to normative and attitudinal components. Significant differences were found between the groups for a number of dimensions underlying marijuana usage. Individuals comprising the group under attitudinal influence were found to be heavier consumers of marijuana and more likely to consume marijuana in all situations than individuals under normative influence. Individuals under attitudinal control feel less apprehensive about the physical and legal consequence of the drug's use and are less negative about the perceived beliefs of others toward their use of marijuana.

These results have significant implications for the development of further communications concerning marijuana usage and provide helpful insight into policy decisions regarding drug legalization and use. Promotional programs for or against marijuana consumption stressing solely social appeals or drug-attribute concerns are unlikely to reach both audience segments effectively. (HSRI)

10 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Countermeasure Concepts. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-78-E0132

A SYSTEMATIC STUDY OF THE PREVALENCE OF DRUG USE IN FRESHMAN COLLEGE STUDENTS, J.D. Rimmer; J.A. Halikas; M.A. Schuckit, Comprehensive Psychiatry, v19 n3 p253-6 (May-June 1978)

This paper reports student drug use in a randomly selected sample of a college freshman student population, with information obtained from 97% of a selected sample of 158 students. The study attempted to ascertain what proportion of students uses drugs, how often, which drugs, what changes in student drug use occur during the freshman year, and in which ways users differ from nonusers. The data were collected by means of an annual systematic structural interview.

Results of the study indicated that 46% (70) reported drug use prior to their freshman year. Sixty-six percent of the students (101) reported some drug use during their freshman year, including 20% (31) who used drugs for the first time. Of the 101 students who reported drug use, 67% reported only marijuana. The drugs used most frequently were, in descending order, marijuana, mescaline, LSD, amphetamines, various hallucinogens, speed, barbiturates, cocaine, and opiates.

The thirty-one students who reported drug use for the first time during the freshman year were compared to the forty-six consistent never-users, using twenty-three variables frequently examined in the literature representing student social background, life events, and academic ability. New drug users reported more conflicts with parents and perceived themselves as having less ability to fit into society than never-users. New users also reported higher occupational status for the father and more frequently had a nonworking mother. Drug users in general reported greater ease in forming relationships than nonusers, and had had sexual intercourse prior to arrival at college more frequently.

The authors conclude that the drug use rate is higher in this study than that reported in most other studies. Methodological considerations possibly relating to this finding are discussed. (HSRI)

7 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). mescaline. Local Anesthetics: cocaine. Stimulants: cocaine. Barbiturates. Opiates and Related Agents. Stimulants. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0133

DELTA-9-TETRAHYDROCANNABINOL LEVELS IN STREET SAMPLES OF MARIJUANA AND HASHISH: CORRELATION TO USER REACTIONS, R.S. Ritzlin; R.C. Gupta; G.D. Lundberg, Clinical Toxicology, v15 n1 p45-53 (Aug 1979)

Reported here are the results of a six-year study done by the Los Angeles County University of Southern California Medical Center Street Drug Identification Program investigating the potency of street samples of marijuana and hashish in terms of their delta-9-tetrahydrocannabinol content and effects. In this study, 3,624 samples voluntarily and anonymously submitted were analyzed using gas chromatography. Information was collected regarding alleged contents, reactions, price, general location and date acquired, and amount of drug sample.

Marijuana accounted for 12.4% (449) of the samples, hashish for 1% (36), and hash oil for 0.7% (26). Over 94% of alleged marijuana, hashish, and hash oil samples were uncontaminated by other pharmacological agents. The amount of delta-9-THC per sample varied from 1.5 to 144.9 mg, with higher concentrations being found in the more expensive imported varieties. Adverse reactions occurring in nonadulterated samples of marijuana were not associated with high potencies. Headache and anxiety were most commonly reported. Some strange tastes and smells were also reported. (HSRI)

12 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. hashish. marijuana. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-80-E0134

THE DRUG ABUSE WARNING NETWORK (DAWN) PROGRAM: TOXICOLOGIC VERIFICATION OF 1,008 EMERGENCY ROOM 'MENTIONS', J.T. Ungerleider; G.D. Lundberg; I. Sunshine; C.B. Walberg, Archives of General Psychiatry, v37 n1 p106-9 (Jan 1980)

One thousand eight emergency room patient records from which reports were contributed to the federal Drug Abuse Warning Network (DAWN) system from the Los Angeles County/ University of Southern California Medical Center in 1977 were studied. The drugs reported to DAWN for these patients were compared with the available toxicology laboratory reports for some of these same patients. The purpose was to test the validity of the data reported to DAWN.

Toxicologic analyses had been performed on only 528 patients (52%) of the entire sample. Eighty percent of these tested patients had some positive toxicology result. The DAWN reports were verified in 20% of the tested sample, found to be incorrect in 11%, and partially correct or partially incorrect in 69%. Drugs identified toxicologically had varied concentrations, some below or within therapeutic range and some at toxic levels. This study suggests that the reliability of DAWN reports should be tested prospectively in an unbiased definitive material study. (JA)

7 refs

KEYWORDS: Barbiturates: Tuinal(R) (amobarbital sodium + secobarbital sodium). Hallucinogens and Related Agents: phencyclidine. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0135

MANAGEMENT INFORMATION SYSTEMS IN THE DRUG FIELD, G.M. Beschner; N.H. Sampson; C. D'Amanda, eds., NIDA Research Monograph Series, Rockville, Md.: National Institute on Drug Abuse (1979)

This monograph describes the role of management information systems (MIS) in the drug abuse field, particularly as it is illustrated by various existing programs. The following topics are presented: (1) a state-of-the-art review of MIS in drug abuse programs, which reviews design characteristics, sources of information, data collection procedures, utilization of data, information gaps, and staff attitudes and capability; (2) a state-of-the-art review of drug abuse MIS in single state agencies and a select number of county agencies which discusses such problems as inadequate state support, inappropriate or insufficient staffing, lack of leadership, organizational barriers, and financial constraints; (3) a discussion of how MIS can assist managers of drug abuse programs in procuring, allocating, and deploying limited resources; (4) a discussion of some of the strategies required to elicit staff cooperation and support, which is a prerequisite to a successful information system; (5) an overview of the development and utilization of computer software, particularly the instructions and programming developed to handle large arrays of date; (6) an explanation of some of the steps and functions involved in data processing such as the collection, input, manipulation,

storage, and output of data as well as factors of availability, reliability, security, turnaround time, software suitability, and flexibility; and (7) a discussion of some factors that should be considered by drug treatment managers in establishing an MIS such as identifying information needs, classifying information, developing a format to capture and display the data, and establishing procedures for collecting and processing data. (HSRI)

214 pages 35 refs

National Institute on Drug Abuse, DHEW Publication No. (ADM) 79-836

KEYWORDS: Review: Survey Methodology.

UM-79-E0136

DRUGS AND THE CLASS OF '78: BEHAVIORS, ATTITUDES, AND RECENT NATIONAL TRENDS, L.D. Johnston; J.G. Bachman; P.M. O'Malley, Rockville, Md.: National Institute on Drug Abuse (1979)

Presented here are detailed statistics on the prevalence of drug use among American high school seniors in 1978 and on trends in those figures since 1975. The volume also assesses current attitudes and beliefs concerning drug use and the extent to which drugs are available to high school youth. Information on the following eleven separate drugs or classes of drugs is provided: marijuana (including hashish), inhalants, hallucinogens, cocaine, heroin, natural and synthetic opiates other than heroin, stimulants, sedatives, tranquilizers, alcohol, and cigarettes.

The basic research design of the series of studies of which this study is a part involves annual data collection from high school seniors during the spring of each year, beginning with the class of 1975. Each data collection takes place in approximately 125 public and private high schools selected to provide an accurate cross-section of high school seniors throughout the United States.

Data were collected and analyzed for the following aspects of drug use; prevalence of lifetime, daily, monthly, and annual drug use according to sex and drug; differences in prevalence related to college plans; regional differences in rates of drug use and types of drugs used; differences related to population density; use at earlier grade levels; and degree of highs. The data collected are analyzed and evaluated, and several major conclusions are drawn. (HSRI)

335 pages 28 refs

National Institute on Drug Abuse, DHEW Publication No. (ADM) 79-877

KEYWORDS: Anti-Anginal Agents: amyl nitrite. Cannabis Sativa L. and Related Agents: hashish. marijuana. Hallucinogens and Related Agents: phencyclidine. Local Anesthetics: cocaine. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Other Toxicants: butyl nitrite. Stimulants: cocaine. Unclassified Agents: tobacco. Vasodilating Agents: amyl nitrite. Hallucinogens and Related Agents. Opiates and Related Agents. Other Toxicants. Sedatives and Hypnotic Agents. Stimulants. Tranquilizers. Volatile Solvents. Epidemiology: National Survey of Drug Use Patterns.

UM-79-E0137

A COMPARISON OF MENTAL HEALTH TREATMENT CENTER AND DRUG ABUSE TREATMENT CENTER APPROACHES TO NONOPIATE DRUG ABUSE, NIDA Services Research Report, Research Triangle Park, N.C.: Research Triangle Institute (1979)

The purpose of this study was to obtain information about the types of treatment available to persons who abuse drugs other than opiates, to describe the treatment programs and the clients in these programs, and to identify critical needs in nonopiate drug abuse treatment. It provides a description and comparison of incidence rates, demographic variables, and treatment of the nonopiate abuser population in three types of settings: the freestanding drug abuse clinic (Type I); drug abuse units in community mental health centers (Type II); and community mental health centers without separate facilities for drug abusers (Type III). Findings are based on a sample of 1,113 clients from the overall population of twelve clinics--four of each type--which included 281 nonopiate abusers. Data were obtained from staff interviews and client records.

In the sample as a whole (N=1,113), the majority of clients were male (56 percent), white (65 percent), unmarried (72 percent), young (mean age 26.4), and unemployed (63 percent). Typically, Type I programs treated young male opiate addicts with limited education and low-status jobs who were frequently referred by the criminal justice system. Type II clients were more often diagnosed as having personal or emotional difficulties than were Type I clients. Type III clients were more likely to be older and female; many of these clients had been diagnosed as psychotic and were of daycare status. In Type I programs, 73 percent of clients received diagnoses of drug addiction, while only 26 percent in Type II and less than 1 percent in Type III were so diagnosed. Drug problems of any type, including alcohol abuse, were reported in case records of 97 percent of the Type I sample, and 44 percent and 15 percent, respectively, of the Type II and III samples.

A subsample of those persons with primary problems of nonopiate drug abuse (N=281) was selected and the data gathered were analyzed in greater detail. The selected nonopiate sample was 62 percent male, 83 percent white, and 80 percent neither married nor living together. In Type I clients (N=138), less than half mention drugs in presenting complaints, and only 4 percent complain specifically of nonopiate use. This suggests that these clients do not consider or choose to acknowledge drug abuse as the sole, or even primary, problem for them. Diagnoses given Type I clients, in addition to that of drug abuse, tend to be transient situational disturbances and personality disorders.

Nonopiate abusers in Type II clinics (N=98) tend to be older than the Type I clients, and also better educated, with higher status of employment. They are more often self-referred. Two-thirds mention drugs in presenting complaints, and 12 percent specifically seek treatment for their nonopiate drug use.

The Type III nonopiate addicts (N=45) tend to be the oldest, best educated clients with the highest unemployment rates. They are most often referred by professionals or institutions. Half mention no presenting complaint at all, and those who do usually describe emotional difficulties. Psychosis is the most common diagnosis, followed by personality disorder or neurosis.

Date were collected on treament modality, medication, and supportive services for the nonopiate sample, but are extremely sparse. Clinics of Type I and II provided clients with drug-free treatment (their only available service), and Type III provided daycare. Individual therapy was the most common technique in all clinics. Some differences in treatment depending on drug of primary abuse were noted, however.

The records on treatment outcome were also extremely limited, demonstrating the need for developing a standardized and informative data bank in community mental health centers if useful comparative data is to be obtained in the future. Average overall stay is 40 weeks, Type III having the longest average stay. Type I clients more often completed treatment, and those who completed their treatment in this modality stayed a shorter time than Type II or III completers. Clients in Types II and III were longer-term, and more were still in treatment at the time of the study. This may reflect the more serious emotional problems of these clients, or differences in treatment philosophy. (AAM)

0 refs

National Institute on Drug Abuse, DHEW Publication No. (ADM) 79-879

KEYWORDS: Opiates and Related Agents: heroin. Countermeasure Development, Testing, and Evaluation. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-79-E0138

HEROIN INDICATORS TREND REPORT--AN UPDATE 1976-1978, Heroin Indicators Task Force, Rockville, Md.: National Institute on Drug Abuse (1979)

This report provides a brief and objective assessment of heroin in the United States for the years 1976 to 1978. The information was obtained from a variety of sources which are probably associated with trends in drug use. The changes in the value of these indicators are seen to be relative measures of the changes in drug use. These indicators include heroin-related deaths, heroin-related emergency room visits, average price and purity of heroin, heroin treatment admissions, household surveys, high school surveys, and estimates of heroin prevalence.

All national heroin indicators uniformly showed declining trends for 1976 through 1978. The number of heroin-related deaths in 1978 was less than half of the number reported in 1976. Emergency room visits in 1977 had also declined from the number noted in 1976.

The average retail price of heroin increased substantially, while the average purity of heroin decreased. Both price and purity trends indicated diminished availability of heroin. The total number of heroin treament admissions to drug abuse treatment programs as well as the percent of heroin admissions declined noticeably between the two years. Although not statistically significant, there were inclines in lifetime prevalence of heroin use as indicated by the 1977 National Household Survey.

National trends are a composite of the trends for various parts of the United States. When the local trends were examined, a few different patterns emerged. Some Standard Metropolitan Statistical Areas (SMSAs) showed an increase in the number of heroin-related emergency room visits or deaths, while others showed a decrease. Those with increases were San Francisco, Miami, and Philadelphia. These increases may possibly be due to the poor quality of local heroin.

Some SMSAs exhibited a cyclical trend with peaks occurring in the summer months and lows in the winter months; these were Detroit, Boston, and Washington, D.C. An increase was noted in 1978 for these SMSAs but the increase is thought to be attributable to seasonal factors. (AAM)

19 pages 3 refs

National Institute on Drug Abuse, DHEW Publication No. (ADM) 79-892

KEYWORDS: Epidemiology: National Survey of Drug Use Patterns.

UM-79-E0139

1979 HIGHLIGHTS. DRUGS AND THE NATION'S HIGH SCHOOL STUDENTS. FIVE YEAR NATIONAL TRENDS, L.D. Johnston; J.G. Bachman; P.M. O'Malley, Rockville, Md.: National Institute on Drug Abuse (1979)

This report is the third in a series reporting drug use and related attitudes of U.S. high school seniors of the 1975 through 1979 classes. Emphasis is placed on the current prevalence of drug use and trends in use since 1975. Also reported are data on grade of first use, intensity of drug use, attitudes and beliefs among seniors concerning various types of drug use, and their perceptions of certain relevant aspects of the social environment. These data are provided for the following eleven drugs and drug classes: (1) marijuana and hashish; (2) inhalants, particularly amyl and butyl nitrites; (3) hallucinogens, particularly PCP; (4) cocaine; (5) heroin; (6) natural and synthetic opiates other than heroin; (7) stimulants; (8) sedatives; (9) tranquilizers; (10) alcohol; and (11) cigarettes. The 1979 data collection took place in 111 public schools and 20 private schools chosen to provide an accurate cross section of high school seniors throughout the United States.

The following conclusions emerged from results of the questionnaire: (1) 65% of high school seniors report illicit drug use at some time in their lives. (2) Marijuana is by far the most widely used illicit drug, with 60% reporting some use in their lifetime. It is followed by stimulants, which are used at least once by 24%. (3) Marijuana is used daily by 10.3% compared to 6.9% using alcohol. (4) Marijuana use among high school seniors has increased from 47% in 1975 to 60% in 1979. Increased marijuana use has been largely responsible for the increase in overall illicit drug use. (5) The illicit drugs used have changed since 1975 with cocaine, amyl and butyl nitrites, and stimulants becoming more popular and sedatives, heroin, and tranquilizers declining in popularity. (6) Daily marijuana use has increased from 6.0% in 1975 to 10.3% in 1979. (7) The greatest portion of marijuana users usually stays high for one to two hours, followed by those who stay high for three to six hours. (8) Regular use of marijuana is judged to involve great risk by 42% of the sample. Only 14% thought there was much risk in using marijuana occasionally. (9) 62% favor legally prohibiting marijuana use in public places despite the fact that the majority have used marijuana themselves. In addition, the great majority believe that the use in public of illicit drugs other than marijuana should be prohibited by law. (10) 32% believe marijuana use should be entirely legal; 30% feel it should be treated as a minor crime. (11) The respondents predict that they would be little affected by the legalization of the sale and use of marijuana. 50% said they would not use the drug even if it were legal; 29% said they would use it about as often as they do now. (HSRI)

80 pages 0 refs

National Institute on Drug Abuse, DHEW Publication No. (ADM) 80-930

KEYWORDS: Anti-Anginal Agents: amyl nitrite. Cannabis Sativa L. and Related Agents: hashish. marijuana. Hallucinogens and Related Agents: phencyclidine. Local

Anesthetics: cocaine. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Other Toxicants: butyl nitrite. Stimulants: cocaine. Unclassified Agents: tobacco. Vasodilating Agents: amyl nitrite. Hallucinogens and Related Agents. Opiates and Related Agents. Other Toxicants. Sedatives and Hypnotic Agents. Stimulants. Tranquilizers. Volatile Solvents. Epidemiology: National Survey of Drug Use Patterns.

UM-78-E0140

STREET HEROIN POTENCY AND DEATHS FROM OVERDOSE IN SAN ANTONIO, D.P. Desmond; J.F. Maddux; A. Trevino, American Journal of Drug and Alcohol Abuse, v5 n1 p39-49 (1978)

This study attempted to determine the role that fluctuation in street heroin potency plays in the frequency of death from heroin overdose. This relationship was studied over a five-year period in San Antonio, Texas using drug data from heroin mixtures purchased or seized by San Antonio police officers and mortality data from the records of the county medical examiner's office.

Frequent and marked fluctuations in the potency of heroin available to the San Antonio consumer were found during the period studied. The mean monthly dose of heroin in street package varied from 9 to 110 mg. However, only a small, nonsignificant correlation (r=+.13) between monthly mean heroin dose and monthly number of heroin overdose deaths was found. Furthermore, no significant correlation was found between the variability of dose and deaths, nor between the monthly maximum dose and deaths.

The low correlation between dose and deaths in San Antonio highlights the need to investigate the role of other factors in these fatalities, especially that of alcohol and similar CNS depressants. Suicide and lack of tolerance may also contribute to heroin overdose deaths.

These findings neither confirm nor refute the pharmacologic overdose hypothesis of heroin-related death. It is concluded that heroin overdose deaths may best be understood by studying not only the pharmacological properties of the drug itself, but the social context of heroin addiction and the psychosocial characteristics of heroin users as well. (HSRI)

23 refs

KEYWORDS: Opiates and Related Agents: heroin. Epidemiology: Regional or Local Survey of Drug Use Patterns.

UM-73-E0141

TOP 200 DRUGS. 7-YEAR RISE IN GENERICS BEATS INCREASE RATE FOR ALL RXS BY OVER 2 TO 1, Pharmacy Times, v39 n4 p29-33 (April 1973)

This brief analysis of written prescriptions in the past seven years, based on National Prescription Audit Data, provides statistics on sales by retail pharmacies. It includes such information as the ranking of the top 200 drugs newly prescribed in 1972; percentages of new generically written prescriptions; statistics on specific drugs, both generic and brand name; frequency of prescription for the top 200 drugs; total number of prescriptions in 1972; and average price for all prescriptions. (HSRI)

0 refs

KEYWORDS: Epidemiology: National Survey of Drug Use Patterns.

UM-74-E0142

TOP 200 DRUGS. NEW GENERIC RXS CONTINUE TO RISE IN 1973, ACCOUNTING FOR 10.6% OF NEW PRESCRIPTIONS, Pharmacy Times, v40 n4 p35-41 (Apr 1974)

This article contains an analysis of prescriptions based on data from the National Prescription Audit for the past seven years. The article includes information for 1973, ranking the top 200 drugs by number of prescriptions written; it also includes information on the number of prescriptions for generic drugs among the top 200 drugs. It also provides information on the total number of prescriptions written in 1973, the percentage of new and refill prescriptions, and the average price for new prescriptions, both generic and brand name. (HSRI)

0 refs

KEYWORDS: Epidemiology: National Survey of Drug Use Patterns.

UM-75-E0143

TOP 200 DRUGS. 1973 vs. 1974: 4.3% DECLINE IN REFILLS SPAWNS 0.9% DIP IN OVERALL Rx VOLUME, Pharmacy Times, v41 n4 p39-46 (1975)

Reported in this paper are the results of 1974 National Prescription Audit. The 200 drugs most commonly prescribed are ranked, and various other statistics are presented, such as prescription prices and number of generic vs. brandname drugs dispensed.

In 1974, the total number of prescriptions filled by retail pharmacists fell slightly to 1,504,535,000--a 0.9% drop from 1973. Most of this decrease was due to a 4.3% drop in refills--from 797,926,000 in 1973 to 763,528,000 in 1974. Various reasons for this decline are discussed.

Two hundred drugs accounted for more than two out of three prescriptions in 1974. Heading the list were Valium(R), ampicillan, Darvon(R), Librium(R), Premarin(R), and tetracycline. The top fifty drugs accounted for 37% of all prescriptions. The average price for new prescriptions in 1974 was $4.70, compared to $4.45 in 1973. This represented a 5.6% increase. Brandname drugs averaged $4.81, and generic drugs averaged $3.75. (HSRI)

0 refs

KEYWORDS: Epidemiology: National Survey of Drug Use Patterns.

UM-76-E0144

THE TOP 200 DRUGS, 1974 VS. 1975: GENERICS RISE BY 3.2% DESPITE 1% DIP IN TOTAL RX VOLUME, Pharmacy Times, v42 n4 p37-4 (Apr 1976)

This article is another in the series of annual reports published in Pharmacy Times that provides statistics on written prescriptions from 1966 through 1975. It provides statistics on the top 200 drugs; the decline in the total number of prescriptions filled in retail pharmacies in 1974 and 1975; year by year increases in generically written prescriptions, both new and refills; and other trends concerning written prescriptions as reflected in the data collected by the National Prescription Audit. (HSRI)

0 refs

KEYWORDS: Epidemiology: National Survey of Drug Use Patterns.

UM-79-E0145

1978: TOP 200 DRUGS, TOTAL NUMBER OF PRESCRIPTIONS DECLINES BY 1.1%, Pharmacy Times, v45 n4 p29-37 (Apr 1979)

This article, based on the annual National Prescription Audit, provides information about the top 200 drugs sold in the United States. The total number of prescriptions filled by retail pharmacies fell in 1978 by 15,769,000 to 1,396,888,000. This drop, which represents a 1.1% decrease from 1977, occurred despite the fact that the percentage of generically written prescriptions increased by 8.7%. The decline in prescriptions represents the fifth year in a row that prescription volume dropped in retail pharmacies.

The 200 drugs most commonly prescribed are ranked both numerically and alphabetically here. Valium(R) was the drug most frequently purchased, followed by ampicillin, Inderal(R), Lasix(R), and Tylenol/Codeine(R). The top generically prescribed drugs were ampicillan (#2), tetracycline (#7), erythromycin (#19), and penicillin VK (#20).

The article also provides information about prescription prices. The average price for a brand name prescription drug was $6.69 in 1978, compared with $6.18 in 1977, an 8.3% increase. The average price for a generic prescription was $4.81 in 1978, up 5.9% from $4.54 in 1977. (HSRI)

0 refs

KEYWORDS: Epidemiology: National Survey of Drug Use Patterns.

UM-76-EO146

FACTORS INFLUENCING DRUG PRESCRIBING--INQUIRY INTO RESEARCH STRATEGY, E. Hemminki, Drug Intelligence and Clinical Pharmacy, v10 n6 p321-9 (Jun 1976)

This review analyzes published studies of doctors' prescribing habits, particularly emphasizing the problems involved in such studies. Sixty-four studies in English, Scandinavian languages, and Finnish from the last fifteen years are examined.

Many factors affecting prescribing have never been studied. There are very few studies, for example, of two potentially important factors--education and control measures. Studies that question doctors for their opinions are unreliable because the real effects of the factors influencing doctors' prescribing habits are not known to the doctors themselves. Studies in which information was collected from doctors frequently failed to cover a representative sample and may have been biased. When studying the effect of a factor on prescribing, conclusions were often drawn without using control groups or taking into consideration possibly confounding factors present.

Studying the factors affecting prescribing also has a number of inherent difficulties. To measure the effect of a factor, the result in terms of number and type of prescr:ptions written by the individual physician should be known. In most Western countries these figures are not publicly available. The drug industry, one of the most important influences on prescribing, is often unwilling to let outsiders study its activities. The industry is also uncooperative in giving information, discouraging researchers from studying prescribing habits. For these reasons most studies of physicians' prescribing habits have been narrow in scope and inadequate. New and more suitable studies might be made by comparing prescribing habits in different countries and correlating these differences with various factors that might be causing those differences. (AAM)

65 refs

KEYWORDS Review.

UM-76-EO147

PHYSICIAN PRESCRIBING PATTERNS--THERAPEUTIC CATEGORIES AND AGE CONSIDERATIONS, J.E. Knoben; A.I. Wertheimer, Drug Intelligence and Clinical Pharmacy, v10 n7 p398-401 (Jul 1976)

The purpose of this report is to delineate the different therapies prescribed in the outpatient setting for various age groups in the population. The data were derived from a special tabulation of unpublished figures by the National Disease and Therapeutic Index. Data are provided for the volume of drug use by age groups. Also presented is a list of the "one hundred most frequently prescribed" drugs. Additionally, a more refined picture of differences among age groups by therapeutic category is presented.

Many studies show that trends are discernible in the types of prescription for various age groups. Age-specific utilization rates of drugs generally rise with age; the predominant preparations prescribed in the over sixty-five group were cardiovascular drugs in contrast to the thirty to thirty-nine years of age group, which used most heavily psychotropic drugs. For the under nine years of age group, cough and cold preparations represent over twenty per cent of the prescriptions. Certain therapeutic categories of drugs are not seen at all in some age groups. (JAM)

8 refs

KEYWORDS: Analgesics and Antipyretics. Anorectic (Appetite Control) Agents. Antibiotics. Antidepressants. Antihistamine Agents. Cardiovascular Agents. Diuretics. Hormones, Synthetic Substitutes, and Antagonists. Insulins and Anti-Diabetic Agents. Sedatives and Hypnotic Agents. Tranquilizers. Epidemiology: National Survey of Drug Use Patterns.

UM-77-EO148

INCREASED PRESCRIBING OF VALIUM, LIBRIUM, AND OTHER DRUGS--AN EXAMPLE OF THE INFLUENCE OF ECONOMIC AND SOCIAL FACTORS ON THE PRACTICE OF MEDICINE, I. Waldron, International Journal of Health Services, v7 n1 p37-62 (1977)

This paper discusses the causes and consequences of the rapidly growing use of prescription drugs in the United States, particularly Librium(R) (chlordiazepoxide) and Valium(R) (diazepam). Drug prescriptions per capita in the United States have more than doubled since 1950 without a commensurate improvement in health. Drugs are often prescribed for clinical conditions in which the risk of adverse drug reactions outweighs the therapeutic benefits. Deaths due to adverse drug reactions are roughly as frequent as deaths due to automobile accidents.

Valium(R) and Librium(R) are the first and fourth most commonly prescribed drugs in the U.S., used by one in ten adults each year. The rapid rise in use of these drugs has occurred during a period of rising social stress as indicated by increases in alcohol consumption, suicide, and homicide. Valium(R) and Librium(R) are frequently prescribed for patients who go to doctors with social or other nonmedical problems, often in lieu of attempts to resolve these underlying problems.

Overprescribing occurs because the decision to prescribe is influenced not only by consideration of therapeutic factors, but also nonmedical factors. One of these is the widespread expectation by both patient and doctor that the doctor will always provide a drug or some other technological treatment. Prescribing decisions are also influenced by the profit-motivated activities of drug companies, including the expenditure of almost one-quarter of every sales dollar on drug promotion. The most widely used source of drug information for doctors is the industry-sponsored Physicians' Desk Reference which overrates the therapeutic value of Valium(R) and Librium(R) as compared to disinterested medical sources. Drug companies also contribute to overprescribing by introducing numerous minor variants of existing drugs. The therapeutic benefits of such new drugs are often overestimated in the early years of use when adverse side effects are not well known and apparent efficacy is enhanced by placebo effects in uncontrolled observations.

Specific solutions proposed to solve the problem of medically unjustified prescribing have for the most part failed. The author concludes that given the extent to which the problem of drug prescribing is embedded in the structure of the U.S. medical system and society in general, it seems probable that fundamental solutions will depend on more far-reaching restructuring of the system. (JAM)

123 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. Muscle Relaxants (Central): diazepam. Review: Drug Use.

UM-55-F0037

THE POWERFUL PLACEBO, H.K. Beecher, Journal of the American Medical Association, v15 n17 p1602-6 (24 Dec 1955)

Presented here is an overview of the placebo. The reasons for use, its therapeutic effect, toxic and subjective side effects, and objective effects are discussed. The placebo has in the past been used as a psychological instrument in the therapy of certain ailments arising out of mental illness, as a resource of the harassed doctor in dealing with the neurotic patient, as a method to determine the true effect of drugs apart from suggestion in experimental work, and as a device for eliminating bias not only on the part of the patient but also, when used as an unknown, on the part of the observer. This author sees the most important use of the placebo to be its ability to get at certain fundamental mechanisms of the actions of drugs, especially those designed to modify subjective responses. Evidence is presented to support the view that a major part of the action of several classes of drugs is on the reaction or processing component of suffering as opposed to the original sensation.

It is concluded, in view of the literature reviewed here, that placebos have a high degree of therapeutic effectiveness in treating subjective responses. Decided improvement was produced in 35% of the cases in fifteen studies in which over one thousand patients were studied. These patients suffered from a wide variety of ailments including wound pain, the pain of angina pectoris, headache, nausea, phenomena related to cough, drug-induced mood changes, anxiety, tension, and the common cold, all of which are influenced by subjective factors. Analysis of these studies indicates that placebos are most effective when the stress is greatest, supporting the concept of the reaction phase as an important site of drug action.

Placebos have not only remarkable therapeutic power, but also toxic effects which are both subjective and objective. The reaction (psychological) component of suffering has power to produce gross physical change. It is plain not only that the therapeutic power

of a drug under study must in most cases be hedged about by laboratory controls but also that studies of side-effects must also be subjected to stringent controls. (HSRI)

9 refs

KEYWORDS: Review.

UM-71-F0038

THE PLACEBO--A POORLY UNDERSTOOD AND NEGLECTED THERAPEUTIC AGENT, H.R. Bourne, Rational Drug Therapy, v5 n11 p1-6 (Nov 1971)

This paper discusses the therapeutic effect of the placebo, particularly regarding the great variability among patients. Compared to the present knowledge of drugs and mechanisms of disease, information documenting the importance of the individual patient as a variable in therapeutics appears relatively meager. There is no doubt, however, that in many clinical situations the patient himself makes an important contribution to the therapeutic result, either in his capacity to develop a significant placebo response or in the degree to which he adheres to a prescribed medical regimen. The data suggest that a great deal of the success of treatment depends on effective communication between the physician and the patient. Such communication increases the likelihood that the patient will understand, accept, and take the medicine he needs. Similarly, a placebo response need not be the result of cynical deception, but should in most cases be the result of planned, straightforward communication between doctors and patients.

The article also discusses the mechanism of the placebo effect, indications for placebo, and toxic side effects of placebo. (AAM)

0 refs

KEYWORDS: Review.

UM-75-F0039

AMINERGIC HYPOTHESES OF BEHAVIOR: REALITY OR CLICHE B.K. Bernard, ed., NIDA Research Monograph 3 (Nov 1975)

The central problem addressed in this monograph concerns the status of the current views on the relation between the function of the brain monoamines and their effect on behavior. Several papers are presented in this volume. They are arranged in an order such that the monograph progresses along a continuum of behaviors from those which are well-defined as causally related to the brain amines to others in which such a relationship is still highly speculative. Interspersed between the general topic articles are papers which are narrower in scope and of a more technical nature. Some of the topics discussed are brain monoamines and Parkinsonism, supersensitivity to dopaminergic agonists induced by haloperidol, the role of serotonin and norepinephrine in sleep-waking activity, and the effects of heroin on catecholamine metabolism in man.

Several conclusions can be derived from these papers. First, there are several hypotheses of behavior, not all of which are complementary or consistent. Secondly, these hypotheses vary greatly with regard to presently available supporting data and the breadth of behavior each hypothesis encompasses. Thirdly, with only a few exceptions, these theoretical constructs concerning the role of the brain monoamines are based upon correlations obtained from highly specific experimental manipulations, the results of which are difficult to apply to other aminergic research. (AAM)

148 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 78-295

KEYWORDS: Antidepressants: lithium. Major Tranquilizers (Antipsychotics and Neuroleptics): haloperidol. Neurochemicals, Neurotransmitters, and Neurohormones: levarterenol. serotonin. Opiates and Related Agents: heroin. Other CNS Agents: lithium. Sympathomimetic (Adrenergic) Agents: dopamine. levarterenol. Unclassified Agents: disulfiram. Neurochemicals, Neurotransmitters, and Neurohormones. Sympathomimetic (Adrenergic) Agents. Compilation.

UM-77-F0040

PSYCHODYNAMICS OF DRUG DEPENDENCE, J.D. Blaine; D.A. Julius, eds., NIDA Research Monograph 12 (May 1977)

This monograph attempts to identify key personality traits which may be involved in drug abuse and to investigate the role of psychodynamics in drug dependence. In the past, research in drug dependence has focused primarily on the pharmacokinetics, biochemical structure, and physiological effects of individual drugs. Very little research has been done at the level of the individual or which is focused on the structure and dynamics of the total personality. What is needed is research at this level in order to identify high risk traits that signal predilection to drug dependence, to organize traits for diagnosis, and to indicate differential treatment regimens. This monograph is a collection of available research on these issues. Some of the topics discussed in the papers presented are psychodynamics in compulsive drug use; self- and object-representation in alcoholism and other drug dependence; theoretical and treatment considerations of the Ego, the Self, and opiate addiction; transference phenomena in the treatment of addictive illness; implications of psychodynamics for therapy in heroin use; and ego functions in drug users.

The editors conclude by stressing the potential of psychodynamic psychology as a powerful tool in the training, treatment, and prevention of drug abuse. (HSRI)

187 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 78-470

KEYWORDS: Compilation.

UM-78-F0041

BEHAVIORAL TOLERANCE: RESEARCH AND TREATMENT IMPLICATIONS, N.A. Krasnegor, ed., NIDA Research Monograph 18 (Jan 1978)

The role played by nonpharmacologic factors in tolerance to the effects of abused substances has become an area of increasing research interest and potential clinical importance. At present, very little agreement exists on the mechanisms underlying behavioral tolerance. This volume is comprised of past and present research findings on behavioral tolerance in substance abuse. Theoretical and experimental approaches to investigation in this field are contrasted and compared, and an attempt is made to develop a working definition of behavioral tolerance as it applies to substance abuse. Possible new initiatives for investigating the concept within clinical research and experimental treatment research settings are also discussed.

Behavioral tolerance is discussed in terms of abuse of narcotics, ethanol, marijuana, stimulants, and depressants. Some of the topics discussed are narcotic tolerance and operant behavior, conditioning effects of narcotics, environmental influences on marijuana tolerance, and behavioral tolerance to cocaine. (HSRI)

151 pages

U.S. Department of Health, Education, and Welfare publication no. (ADM) 78-551.

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital. Barbiturates: phenobarbital. Cannabis Sativa L. and Related Agents: marijuana. Local Anesthetics: cocaine. Opiates and Related Agents: morphine. Stimulants: cocaine. Opiates and Related Agents. Compilation.

UM-79-F0042

AUTOMOBILE RESEARCH SIMULATORS--A REVIEW AND NEW APPROACHES, R.W. Allen; R.H. Klein; K. Ziedman, 58th Annual Meeting of the Transportation Research Board, Washington, D.C. 15-19 Jan. 1979 (1979)

As evidenced by an increasing number of successful research driving simulator systems and applications over the last few years, driving simulation technology is rapidly expanding. This paper reviews current driving simulator state of the art, and presents examples of two simulators with advanced visual display capabilities, one using hybrid simulation, the other using digital computer generated imagery.

The hybrid approach is useful in that the electronic display generator can present symbols at a high update rate (about 100 samples per second) and can accommodate complex features such as curves, obstacles, and dashed lines with simple commands. The generator places no computational load on the other simulation elements and requires only relatively low frequency commands from the equations of motion or other controlling elements. Vehicle motions can be computed in real time without computational delay.

The digital approach uses general purpose computational power rather than special purpose components. A great deal of flexibility concerning the roadway situation is possible with this type of system. Performance measures can be calculated and printed immediately after each run. Results can be stored along with the raw data for later statistical analysis or possible future reanalysis.

The simulator has several advantages over other types of experimental approaches used to measure driving ability. Among these are safety, its relatively low cost, its ability to allow the control of experimental conditions over a wider range than in field tests, flexibility, and its ability to effectively measure, store, and analyze data.

Some potential roles for simulators are investigation of high accident risk situations, driver education and training, and driver licensing. An effective simulator should provide visual display, motion, auditory cues, and an active control feel system. (HSRI)

120 pages 30 refs

KEYWORDS: Review: Behavioral Research Methodology.

UM-79-F0043

BEHAVIORAL ANALYSIS AND TREATMENT OF SUBSTANCE ABUSE, N.A. Krasnegor, ed., NIDA Research Monograph 25, Rockville, Md.: National Institute on Drug Abuse (June 1979)

This monograph presents a variety of views on methods of both behavioral treatment and analysis of addictive behaviors. It focuses on four behavioral patterns which have been shown to contribute significantly to chronic disease and rising health costs in the United States--overeating, cigarette smoking, alcohol abuse, and drug abuse. The papers included in this volume were presented by scientists working in the area of substance abuse at a conference assessing past and present research and research needs of the future.

The monograph is divided into four parts: Part I discusses drugs. A set of experiments to measure behavioral aspects of the addictive personality is detailed. Also described is the use of behavior therapy in connection with narcotic antagonist therapy. A behavioral analysis of methadone detoxification failures based on the concept of anxiety and a behavioral method to treat this problem are outlined. Two behavioral programs are described as well as the use of contingency management to achieve abstinence from drug use and methodological, conceptual, and practical issues in this research area.

Part II includes papers on research issues related to cigarette smoking. An overview of research on behavioral methods employed to achieve cessation is presented. The relevance of social learning to smoking is discussed, as well as a treatment approach utilizing controlled smoking. Also presented is a paper on the commonalities inherent in substance abuse behavior.

Part III is devoted to alcohol abuse. Behavioral and psychophysical methods for treatment of problem drinkers are described. Also presented is an overview of abstinence across the various types of substance abuse. A cognitive behavioral model that can guide research designed to determine how to maintain abstinence once it has been achieved is presented.

Part IV deals with obesity. Current literature on the topic is reviewed, especially that dealing with conceptual and therapeutic issues. A central issue in the treatment of obesity, compliance, is discussed. Finally, a provocative study containing counterintuitive data-based findings concerning obesity is presented that challenges traditional conceptions of behavioral disorders. (HSRI)

256 pages

National Institute on Drug Abuse, DHEW Publication No. (ADM) 79-839

KEYWORDS: Barbiturates: pentobarbital. Ganglionic Blocking and Stimulating Agents: nicotine. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. naltrexone. Stimulants: nicotine. Compilation.

UM-69-F0044

EVALUATION OF LABORATORY METHODS FOR THE STUDY OF DRIVER BEHAVIOR: THE RELATION BETWEEN SIMULATOR AND STREET PERFORMANCE. FINAL REPORT, D.S. Edwards; C.P. Hahn; E.A. Fleishman, Silver Springs, Md.: American Institutes for Research (May 1969)

This report describes a study designed to compare on-the-road performance of drivers with their performance in a controlled laboratory setting on simulated driving tasks and driving related perceptual-motor tasks. The study involved comparisons between road performance, simulator performance, perceptual-motor skill performance, biographical factors, and officially recorded accidents and violations during a five-year period.

The population consisted of approximately 300 taxi operators from the Washington, D.C. area. Road performance data were obtained by pairs of trained observers using behavioral checklists. Simulator performance data were obtained from the scoring apparatus of one device widely used in high school driver education courses and from another device used for driver improvement activities relating to experienced commercial drivers. Perceptual-motor data were obtained from three devices originally developed in the U.S. Air Force Program. Violation and accident data were obtained from both the Motor Vehicle Department and the Police Department.

None of the component or total scores from the simulators were correlated with road performance. It was found that checklist methods developed from motion picture techniques were feasible for use in direct observation by auto passengers. There is, however, a need for further determination of ride-reride reliability under these conditions. Questions about the generality of simulator measures were raised by the lack of obtained relationships between scores designated to measure presumably the same function.

Perceptual motor performances were not correlated with road perfomances. Some significant relations between perceptual-motor performance and simulator performance were found. Although not high, these relations tended to be higher than those between performance on the two simulators. Age and driving experience were the most consistent predictors of simulator performance. Relations between officially recorded accident and violation data and all performance measures used were low. Some significant predictors of certain classes of violations were achieved from road performance measures. (AA)

43 pages 8 refs

KEYWORDS: Driving Simulator. Epidemiology: Record-Based Survey. Open Road Driving.

UM-79-F0045

A NONLINEAR MODEL DESCRIBING DRIVER BEHAVIOR ON STRAIGHT ROADS, J. Baxter; J.Y. Harrison, Human Factors, v21 n1 p87-97 (1979)

The purpose of this paper is to describe the experimental derivations of a nonlinear mathematical model which describes the driver's behavior during the driving task, in particular the generation of self-induced disturbance.

Experiments on a CRT driving simulator were used to develop a closed-loop human operator model for straight road driving in the absence of any externally applied disturbance such as side wind gusts or road roughness. It is shown that a significant portion of the driver's control characteristics can be represented by a stationary, nonlinear system with a single visual input. The driver's visual input is considered to be the angle subtended between the heading axis and a line connecting a point on the lane center at a preview distance with his eyes. An optimization procedure is used to evaluate the the model parameters, and it is found that the driver's action can be best represented by a pure time delay cascaded with a classical hysteresis nonlinearity. The self-excited limit cycle frequency and amplitudes of this model system are shown to agree closely with respective quantitative aspects of the experimental data confirming the validity of the model.

It is concluded that the nonlinear model provides a better fit to the experimental data then does the linear model; and it is found to be a useful tool in the quantitative understanding of driving behavior. The author hopes that the model optimization technique based on the cross correlation coefficient proposed in this study will prove

beneficial in the relative evaluation of any driver models developed in the future. (JAM)

24 refs

KEYWORDS: Review: Behavioral Research Methodology.

UM-71-F0046

VISION AND DRIVING: A REPORT ON RESEARCH, A. Burg, Human Factors, v13 n1 p79-87 (1971)

Reported here is a description of a long-range, large scale study of the relationship between visual ability, as measured on several standard and nonstandard screening tests, and driving performance, as reflected in driving records. Information on vision test performance and personal and driving habits was obtained for 17,769 California drivers and was compared with their driving records, i.e., accidents and convictions for traffic citations. The vision tests utilized in the study were dynamic visual acuity, static visual acuity, lateral visual field, lateral phoria, low-illumination vision, glare recovery, and sighting dominance. Of the vision tests evaluated, dynamic visual acuity was by far the one most closely related to driving record, followed by static visual acuity, visual field, and night vision.

Results also indicate that conviction experience is a much more stable and hence predictable characteristic than is accident experience. Age and mileage were found to be the two most important nondriving record variables in the prediction of driving record. Accidents and convictions generally decrease with increasing age and increase with increasing mileage, but not linearly.

The relationships between variables were found to vary both qualitatively and quantitatively between males and females. In general, driving record variables are not as predictable for females as for males. Males have higher accident and conviction frequencies than do females.

Based on the study findings, a number of recommendations are made: (1) A compact, reliable, and inexpensive multipurpose tester should be developed for testing of static acuity, dynamic acuity, and night vision. (2) A complete and detailed driver record file should be established at the federal level containing basic data on every conviction and every reported accident. (3) A cost benefit analysis is necessary before long-term decisions regarding vision screening for license applicants are made. (HSRI)

13 refs

KEYWORDS: Crash Investigation.

UM-77-F0047

RISK-TAKING RELATED TO DRUG USE: AN APPLICATION OF THE SHIFT-TO-RISK DESIGN, S. Deren; D.C. Des Jarlais, American Journal of Drug and Alcohol Abuse, v4 n3 p391-9 (1977)

The purpose of this paper was to investigate the utility of the shift-to-risk (the effect of group influence on decisions involving risk-taking) design for studying the influence of peer groups on drug taking. Two studies related to drug use using this design were conducted, each study providing different levels of information about the safety of a drug. Subjects were from two college classes consisting of twenty-six and twenty-eight students. Each group was presented with a problem for which they had to come to a collective decision from a list of probability choices.

Results indicated that the specification of possible harmful drug effects which were somewhat minimal led to a significantly greater willingness to recommend trying the drug. In addition, a tendency for a shift-to-caution was found. It is concluded that the shift-to-risk design is useful for studying decision-making regarding drug use, and that both users and nonusers of drugs should be included in future research. (JAM)

15 refs

KEYWORDS: Other Sociolegal Study.

UM-79-F0048

PERIPHERAL VISION AND TRACKING PERFORMANCE UNDER STRESS, J.M. Bermudez; D.A. Harris; J.C.H. Schwank, Compass for Technology. Proceedings of the Human Factors Society, 23rd Annual Meeting, C.K. Bensel, ed., p402-6, Santa Monica, Ca.: Human Factors Society (1979)

The complexity of modern aircraft systems places substantial information processing loads on the pilot. These loads are exacerbated during periods of cognitive and emotional stress such as during emergency landing situations. Physiological and behavioral evidence for two human visual systems that may differ in susceptibility to psychological stress suggests the possibility of a natural stress resistant information channel that could be used to input information during stressful flight situations. It follows that the extreme peripheral visual fields could be a possible location for adjunct visual displays that serve to orient expeditiously the pilot's focal vision and attention to critical instrument displays during emergencies or other situations.

This report presents data on two follow-up experiments involving forty-six male cadets. The data concern the effects of three types of instrument displays used under varying levels of stress during a simulated instrument landing. Stress was defined as demand for primary task-related cognitive activity. A modified Sternberg memory probe technique was used to impose these demands.

Subjects were less prone to compensatory tracking errors when directional information was not combined with rate information ($p<.003$). Focal viewing was found to be more sensitive to information about pitch, whereas peripheral viewing was found to be more sensitive to information about roll ($p<.003$). Reaction time data and memory probe data provided support for the use of a secondary task involving the modified Sternberg item recognition paradigm to increment levels of stress ($p<.005$) in future experiments. (JA)

7 refs

KEYWORDS: Driving Simulator. Psychological Testing. Tests of Sensory Function.

UM-77-F0049

METHODS FOR THE ASSESSMENT OF PSYCHOTROPIC DRUG EFFECTS IN HEALTHY VOLUNTEERS, K. Taeuber; G. Gammel; A. Gordon; D. Koeppen, Modern Problems in Pharmacopsychiatry, v12 p23-36 (1977)

An examination of recent pharmacopsychological experiments reveals a remarkable lack of systematic methodology: rather than developing their own methodology tailored to suit their specific problems, pharmacopsychologists tend to adopt methods and techniques from other scientific fields for the sake of convenience. This paper outlines current deficiencies in pharmacopsychology and recommends means to correct these deficiencies.

The most basic deficiency in methodology is the lack of clearly defined objectives. Objectives and hypotheses of each trial should mention the practical and theoretical progress expected to be gained from the findings.

Another deficiency has been the inappropriate selection of independent variables. Independent variables should be selected carefully. Drug plasma levels should be considered rather than the dose administered. Nondrug factors (e.g., personality or situation) should be controlled in multifactorial designs.

Dependent variables in past research have overemphasized drug influence on performance. Methods and techniques should be developed or further improved for the assessment of drug-induced changes in mood state, social behavior, cognitive functions, personality traits, and other parameters. Interdisciplinary approaches using psychological variables together with neurophysiological or biochemical measurements are necessary.

The experimental subject sample must always be thoroughly described. Subjects should be selected for their pertinent characteristics. These should either serve as second-order independent variables or as criteria for the selection of "symptomatic volunteers".

Finally, appropriate experimental designs must be used and statistical procedures be further developed to suit the relatively complex designs, the nature of the variables measured, and the sample sizes. (JAM)

59 refs

KEYWORDS: Review: Behavioral Research Methodology.

UM-79-F0050

COMPARISON OF FIVE MENTAL WORKLOAD ASSESSMENT PROCEDURES IN A MOVING-BASE DRIVING SIMULATOR, T.G. Hicks; W.W. Wierwille, Human Factors, v21 n2 p129-43 (1979)

This study investigated the relative ability of various techniques to measure mental workload and the degree to which each technique intruded on or disrupted the driving task. Five methods of measuring mental workload (secondary task performance, visual occlusion, cardiac arrhythmia,subjective opinion rating scales, and primary task performance) were compared for sensitivity to changes in operator loading. Each was used to differentiate among low, medium, and high levels of workload defined in terms of the application point of crosswind gusts in a driving task. Subjects were twenty-five males and five females ranging in age from 19 to 35 years, all of whom held valid driver's licenses.

The driving task was produced using an automobile driving simulator with a six-degree of freedom computer generated display, a four-degree of freedom physical motion system, and a four-channel sound system. Techniques of mental workload measurement that have shown promise in previous studies were used as a between-subjects factor, and subjects were presented with a within-subject factor of wind gust placement. Gusts at the front of the vehicle represented high workload levels, and gusts toward the center of the vehicle represented progressively lower levels of workload.

The results showed significant differences among workload levels for subjective opinion scales and primary performance measures of lateral deviation, yaw deviation, and steering reversals. A relative sensitivity estimate of these would be, from highest to lowest sensitivity, steering reversals and yaw deviation, rating scales, and lateral deviation. The techniques of occlusion, cardiac arrhythmia, and secondary performance yielded no significant workload effect. The authors conclude that primary task measures and rating scale measures should be used in assessing driver workload, particularly if it is of a psychomotor nature. These measures demonstrate greatest sensitivity and least intrusion. (JAM)

22 refs

KEYWORDS: Driving Simulator.

UM-77-F0051

THE CURRENT STATUS OF PHARMACOLOGY AND BEHAVIOR, J.R. Wittenborn, Modern Problems in Pharmacopsychiatry, v12 p88-95 (1977)

This paper summarizes the papers presented at a symposium on pharmacology and behavior that focused on the behavioral effects of pharmacological substances in "normal" man and laboratory animals.

The following topics were discussed at the symposium and are briefly summarized here: (1) lack of sensitivity of assessment devices to measure slight changes in mood; (2) use of theory in psychopharmacology; (3) methods of assessing psychotropic drug effects in normal subjects; (4)effects of psychotropic drugs on attention, performance, perception, memory, and learning in humans; (5) the present inability of researchers to draw any meaningful conclusions from the mosaic of experimental results; and (6) animal studies investigating the disinhibiting effect of chlordiazepoxide on behavior. (HSRI)

0 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. Compilation.

UM-79-F0052

A PSYCHOLOGICAL REFRACTORY PERIOD OR AN UNPREPARED PERIOD? R. Gottsdanker, Journal of Experimental Psychology: Human Perception and Performance, v5 n2 p208-15 (1979)

A massively replicated finding is that reaction time (RT) to a signal (S2) that is briefly preceded by a different signal (S1), typically one that requires its own response, is lengthened beyond its normal unpreceded value. The present study was designed as a crucial test to compare the two basic interpretations that have been made of this effect--the psychological refractory period and the unprepared period.

The concept underlying all the variants of a psychological refractory period (PRP) is that of an interval of time following the first signal, during which the producing of a response to a second signal is delayed because of the subject's involvement with the first signal. The unprepared period theory holds that reaction time to a second signal (RT2) is lengthened because the subject is unprepared. This will come about when the subject does not expect the second signal to occur when it does.

Twelve women 17 to 22 years of age were separated into experimental and control groups. Two tasks were employed, a choice response performed with the left hand to a visual signal (S1) and a response performed with the right hand to a tone (S2). Typical lengthening of reaction time to a second signal (RT2) occurred by using a constant intersignal interval and a psychological refractory period (PRP) procedural paradigm. However, RT2 was lengthened even more on occasional probe trials without Signal 1 (S1). Since, in the latter case, there was no possible involvement with S1, the lengthening is not attributable to a psychological refractory period. In view of previous evidence that a subject cannot be prepared simultaneously for optimal response to two stimuli, the effect would seem to be that of unpreparedness. More generally, any model of processing in reaction-time experiments must include the subject's state of preparation at the time the signal occurs. (JAM)

35 refs

KEYWORDS: Psychological Testing. Review: Behavioral Research Methodology.

UM-79-F0053

DIVIDED ATTENTION: THE WHOLE IS MORE THAN THE SUM OF ITS PARTS, J. Duncan, Journal of Experimental Psychology: Human Perception and Performance. v5 n2 p216-28 (1979)

This paper discusses and evaluates the traditional theory of divided attention and proposes a new, more complete theory. The author argues that the idea dominating the study of divided attention--that single tasks and single task processes compete for common resources--captures only part of the problem. He argues that a divided attention situation is more than the sum of its component single tasks. Emergent aspects of the whole situation must also be considered. Three examples illustrate this. (a) When several complex stimuli (e.g., letters) are identified at once, their perceived components or features must be appropriately bundled together. Otherwise, components of two different stimuli may appear combined. This emergent problem is shown to depend on attention to multiple stimuli, not simply their presentation. (b) In the psychological refractory period (PRP) situation, special difficulties arise when stimulus-response mappings are different for first and second reactions. It appears that for each reaction there is some emergent uncertainty over which mapping to use. This is only one of many possible emergent processes in the PRP situation. (c) When the two hands perform different actions (internally programmed sequences of taps) there is some tendency for each hand to carry out the action assigned to the other. This again is only a small part of the emergent problem of motor coordination. Thus, the simple idea of competition for limited resources captures only a part of the problem of divided attention. Performance under divided attention will reflect an interaction between resource limitation, single task processes, and emergent aspects of the whole situation. (JAM)

20 refs

KEYWORDS: Psychological Testing. Review: Behavioral Research Methodology.

UM-79-F0054

INFORMATION PROCESSING IN THE CEREBRAL HEMISPHERES: SELECTIVE HEMISPHERIC ACTIVATION AND CAPACITY LIMITATIONS, J. B. Hellige; P. J. Cox; L. Litvac, Journal of Experimental Psychology: General, v108 n2 p251-79 (1979)

Several previous experiments have found that concurrently maintaining verbal information in memory influences visual laterality patterns. The present article critically reviews existing experiments and reports five additional experiments designed to identify the mechanisms responsible for such effects. Experiment 1 demonstrates that laterality patterns are not influenced by a concurrent memory task that does not require verbal processing. Experiments 2 and 3 were designed to determine whether concurrent verbal memory primarily influences very early visuospatial processes or later processes such as those involved in visuospatial memory. In Experiment 2, observers indicated whether two simultaneously presented nonsense forms had the same shape. Observers held 0, 2, 4, or 6 words in memory during each shape judgment trial. Responses were faster when the

forms were presented to the left visual field-right hemisphere (LVF-RH) than to the right visual field-left hemisphere (RVF-LH). This effect did not interact with memory set size. In Experiment 3, observers indicated whether either of two simultaneously presented forms was identical to a target form held in memory. Observers held 0, 2, or 6 words in memory on each trial. On same-as-target trials, responses were faster on LVF-RH trials than on RVF-LH trials in the no-word memory condition; this difference was reversed in the two-word and six-word conditions. The combined results of Experiments 2 and 3 suggest that concurrent verbal memory influences stages of processing beyond the initial registration of visuospatial information.

Experiments 4 and 5 examined the influence of concurrent verbal memory on verbal laterality tasks. Observers indicated whether two simultaneously presented letters of different cases had the same name. In Experiment 4, different groups of observers held 0, 2, 4, or 6 words in memory on each letter-pair trial. In Experiment 5, memory set size was manipulated within subjects. On the same-pair trials of Experiment 4 and the first session of Experiment 5, responses in the no-memory condition were faster on RVF-LH trials than on LVF-RH trials; this difference was reversed in all of the word memory conditions. This shift is opposite to that found when the laterality task does not require verbal processing and further indicates that concurrent verbal memory influences processing stages beyond those that are common to the form-pair and letter-pair tasks.

Neither directness-of-pathway nor attention-gradient laterality models can explain the entire pattern of results from the present experiments. Rather, the results suggest that the left hemisphere functions as a typical limited-capacity information processing system that can be influenced somewhat separately from the right hemisphere system. (JAM)

62 refs

KEYWORDS: Psychological Testing.

UM-69-F0055

MEASURING RECOVERY FROM ANESTHESIA--A SIMPLE TEST, M. G. Newman; N. Trieger; J. C. Miller, Anesthesia and Analgesia . . . Current Researches, v48 n1 p136-40 (Jan-Feb 1969)

This paper describes the Bender Test, a simple, direct, self-administered objective test to measure recovery time from ambulatory anesthesia. The test measures sensory motor performance, a critical determinant. With the aid of this test, the patient's return toward his own preanesthetic baseline becomes more evident and objective.

Fifty-seven oral surgery patients participated in this study: 25 in the experimental sedation group; 12 in a local anesthesia control group; and 20 in a position-effect group. All patients received intravenous sedation consisting of either pentobarbital sodium or hydroxyzine and meperidine hydrochloride, with scopolamine hydrobromide or atropine sulfate separately or combined with general anesthesia (methohexital), in addition to a local anesthesia. The test was administered before drug administration, immediately after consciousness returned, ten minutes after return of consciousness, and upon discharge.

The authors conclude that the Bender Test provides a reliable and reproducible index of performance. Performance, in turn, is directly and significantly related to recovery. (JAM)

7 refs

KEYWORDS: Anti-Arrhythmia Agents: lidocaine. Antihistamine Agents: hydroxyzine. Barbiturates: methohexital, pentobarbital. Local Anesthetics: lidocaine. Minor Tranquilizers (Anti-Anxiety and Ataractics): hydroxyzine. Mydriatics: atropine sulfate. Nonbarbiturates: hydroxyzine. Opiates and Related Agents: pethidine. Parasympatholytic (Cholinergic Blocking) Agents: atropine sulfate. Experimentation: Study of Combined Effects of Drugs. Psychomotor Tests.

UM-78-F0056

IS THERE A PLACE FOR THE SIMULATOR IN DRIVER LICENSING? J. F. O'Brien, Traffic Safety, v78 n8 p8-10,34-5 (Aug 1978)

This article discusses the value of the driving simulator for testing the driving skills of driver's license applicants. A broad overview of driving simulators is presented, including their operation, their validity, advantages, and disadvantages.

Also reported are the results of a research project that attempted to determine whether a valid driving test can be administered on a simulator. Data concerning driving experience was collected from 1,061 subjects who were subsequently tested on a driving simulator. The study demonstrated that a driving simulator examination is a valid test of driving ability since in this experiment it was able to distinguish between groups of drivers with various driving experience.

The author concludes that driving simulators are of great potential value, especially in testing situations that would be too dangerous to attempt on public highways. An example of such a situation might be a research study of the effects of abusive and therapeutic drugs on traffic safety. (HSRI)

0 refs

KEYWORDS: Review: Behavioral Research Methodology.

UM-78-F0057

EYE MOVEMENTS BEHAVIOR WHILE DRIVING A CAR: A REVIEW, A.S. Cohen, Zurich: Swiss Federal Institute of Technology (May 1978)

The method of utilizing eye movements as a technique in investigating the input of visual information to a car driver is a relatively new one. Most of the research work has been carried out in the last ten years. The central goal of this paper is to review these studies. This review is devoted primarily to the description of empirical findings.

When using the term "eye movements," one does not only mean the saccading movement of the eye, but more importantly the eye's fixations during which the visual information is picked up. A further goal of this paper is to point out the general assumptions underlying the analysis of eye movement behavior. These considerations lead then to the determination of those conditions under which a reasonable use of this technique in analyzing car driver's information input can be incorporated as part of the experimental paradigm.

Other topics discussed include blood alcohol concentration; fatigue and sleep deprivation; information acquisition by peripheral vision; and vehicle characteristics. (JAM)

54 refs

KEYWORDS: Review: Behavioral Research Methodology.

UM-78-F0058

EFFECTS OF VISUAL DISTRACTION ON REACTION TIME IN A SIMULATED TRAFFIC ENVIRONMENT, C. J. Holahan; R. E. Culler; B. L. Wilcox, Human Factors, v20 n4 p409-13 (1978)

This study investigated the effect of visual distraction on reaction time to a target stimulus in a simulated traffic environment. Subjects viewed slides of simulated roadside signs, some of which included a traffic stop sign. Reaction time was measured to their "stop" or "go" response. As predicted, the number and color of distractors, as well as the proximity of distractors to the target stop sign, all had significant effects on reaction time. In addition, all two-way interactions between the distractor dimensions were statistically significant. Practical suggestions for reducing visual distraction in the traffic environment are discussed. (JA)

12 refs

KEYWORDS: Driving Simulator. Tests of Sensory Function.

UM-79-F0059

ALCOHOL-IMPAIRMENT TESTS FOR DWI ARRESTS, M. Burns; H. Moskowitz, 58th Annual Meeting of the Transportation Research Board Washington, D.C. Jan. 15-19, 1979 (1979)

The objective of this study was to develop and standardize an improved test battery for use by police officer in assessing a DWI suspect's level of alcohol-related impairment. In most states .10% is the BAC at which a driver is presumed DWI, but the mean BAC of arrested drivers is closer to .17%. This reflects the difficulty of the police

officer's task. First, he must detect a vehicle being operated by an impaired driver. Then he must assess the BAC level and decide to arrest or release the individual. Usually he administers sobriety tests at roadside to assist in making the decision.Tests for DWI arrest must be sensitive to alcohol impairment and meet the severe constraints imposed by limited time and the characteristics of the roadside environment.

Based on the literature, field observations, and pilot studies, six tests were selected for evaluation. Ten police officers administered the tests to 238 participants at 0-.15% BAC in a laboratory study. Based on the analysis of these data, a battery of three tests was selected: one-leg stand, walk-and-turn, and alcohol gaze nystagmus. It was possible to correctly classify 83% of the laboratory study participants as above or below .10% BAC using the officers scores for these three tests. Therefore the authors conclude that if balance and walking skills are examined and the eyes are checked for the jerking nystagmus by an officer trained to precisely administer, observe, and evaluate these tasks, the level of intoxication can be estimated quite accurately, routinely, and quickly. (AA)

9 pages 3 refs

National Highway Traffic Safety Administration, Contract no. DOT-HS-5-01242

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Epidemiology: Analysis of Driver Body Fluids for Drugs.

UM-79-F0060

TRAFFIC ACCIDENTS AND PROFESSIONAL DRIVER CHARACTERISTICS: A FOLLOW-UP STUDY, S. Hakkinen, Accident Analysis and Prevention, v11 n1 p7-18 (1979)

Presented here is a follow-up study of the driver group reported on in the 1958 study (F0032) investigating the consistency of individual differences in accident rates for 100 drivers. Sixty-six members of the driver group considered in the 1958 study continued working in the same company. In the present follow-up study, the exposure time (the exact time a man was working as a driver in this company) and the accident figures for the 66 drivers were collected. The total exposure time varied from 10.5 to 26.5 years with a mean of 16.6 years.

The constancy of the accident coefficients and the prediction power of the test variables were studied with correlations, factor analyses, and discriminant analyses. The correlation between the accident coefficient (accidents per man per year) of the basic eight-year period and the follow-up period of nine years (average) was 0.56, corresponding to a reliability of 0.72 for the total exposure time. Correlations between the test variables and accident coefficients for the follow-up period were almost the same size as in the basic period, even though the follow-up period ranged from one to twenty years after the time of testing. Multiple correlations, between the accident coefficient and eighteen test variables for the basic, follow-up, and combined periods were 0.75, 0.77, and 0.81, respectively. These and other analyses showed that the accident behavior of professional city drivers is very constant, and this behavior can be predicted with specially planned psychological tests. (JAM)

12 refs

KEYWORDS: Crash Investigation.

UM-79-F0061

CLASSIFICATION OF PLACEBO DRUGS: EFFECT OF COLOR, K.W. Jacobs; F.M. Nordan, Perceptual and Motor Skills, v49 p367-72 (1979)

This study investigated the extent to which placebo capsules are subjectively classified by the user according to major pharmacological action on the basis of the color of the capsule. Subjects were forty-one males and fifty-nine females with a mean age of 29.83 years. Subjects were presented with six plastic prescription bottles, each containing a different color capsule: red, yellow, green, blue, black, and white. They were asked to indicate what type of drug they thought each bottle contained: a depressant-tranquilizer, a stimulant-antidepressant, or a hallucinogenic drug.

Analysis of the responses of the 100 subjects indicted a nonrandom classification of three of the colored capsules. Blue was classified as a depressant-tranquilizer by 61%, while red and yellow were classified as stimulant-antidepressants. Black was frequently classified as a depressant. No specific effect was attributed to the white capsules.

The authors conclude that this study provides an empirical basis for selecting certain colors for use in creating or expanding upon the placebo effects of pharmacological or inert agents. The existing body of empirical studies on color can also be extended to include expectations of physiological effects due to the color of the medication. (HSRI)

7 refs

KEYWORDS: Other Factors Influencing Drug Effects.

UM-79-F0062

MENTAL AND PHYSICAL PRACTICE AND THE LEARNING AND RETENTION OF OPEN AND CLOSED SKILLS, E.R. McBride; A.L. Rothstein, Perceptual and Motor Skills, v49 p359-365 (1979)

Presented here is a study of the acquisition of motor skills under conditions of mental, physical, and mental with physical practice using open and closed tasks as variables. The study is unique in that it used a novel motor skill under open or closed environmental conditions and manipulated mental and physical practice to observe the effect upon acquisition and retention of accuracy. An open environment is one which is unpredictable, unstable, and which requires anticipation and prediction of moving objects, such as externally paced or open skills. A closed environment is one in which events are predictable, stable, fixed, and which involve stationary objects. Skills taking place in this environment are termed self-paced or closed skills.

Female high school students (N = 120) performed the task of hitting a solid whiffle golf ball with a paddle at a target in open and closed environments. Subjects practiced under mental, physical, or physical-mental conditions for three successive days, were tested on a fourth day, and took a retention test immediately, a day later, a week later, and a month later. Accuracy scores were recorded in blocks of ten trials during acquisition and in blocks of five trials during testing and retention. Mental practice required mentally hitting forty balls, physical practice actually hitting forty balls, and combined practice alternated actually hitting ten with mentally hitting ten until forty balls were hit.

All practice conditions led to improvement in accuracy; the combined treatment was most effective, the physical next, and the mental treatment least effective in terms of overall accuracy. All groups showed retention of accuracy regardless of the duration of retention interval. While evidence was produced for a differential effect of combined practice on skill performed in open and closed environments, the rapid improvement during early learning of accuracy and in the skill performed in the closed environment makes firm comparisons unwise. Suggestions for further research which will clarify the relationship between type of practice and type of environment are included. (JAM)

15 refs

KEYWORDS: Psychological Testing. Psychomotor Tests.

UM-79-F0063

MEASUREMENT OF WORKLOAD BY SECONDARY TASKS, G.D. Ogden; J.M. Levine; E.J. Eisner, Human Factors, v21 n5 p529-548 (1979)

Presented here is a survey of the post-1965 scientific literature on the use of secondary tasks in the assessment of operator workload. The survey also provides an organized overview of the types of secondary tasks used in research since 1967.

The secondary task technique is used to determine how much additional work the operator can undertake while still performing the primary task to meet system criteria. It is characterized by an experimental situation in which two discrete and separate tasks are performed concurrently with a clear emphasis on the performance of one of the tasks.

The results of the review of the literature indicate that research on the use of secondary tasks in the assessment of operator workload has not yet been focused upon a single type of secondary task. The most frequently used are choice reaction time, memory, monitoring, and tracking. Other tasks used include mental math, shadowing, classification, tapping, detection, reaction time, piano playing, problem solving, time estimation, identification, and task battery. A table is presented listing the findings of 144 studies investigating the effects of a secondary task on primary task performance.

The authors conclude that secondary tasks are suitable for evaluating operator workload provided they do not interfere with the primary task, they are simple to learn, are self-pacing, provide continuous scoring, and are compatible with the primary task. Further research must be done before any one secondary task can be chosen as the best. (HSRI)

159 refs

KEYWORDS: Review: Behavioral Research Methodology.

UM-79-F0064

VISUAL VS AUDITORY DISPLAYS FOR DIFFERENT TASKS OF A CAR DRIVER, D. Bouis; M. Voss; G. Geiser; R. Haller, Compass for Technology. Proceedings of the Human Factors Society, 23rd Annual Meeting, C.K. Bensel, ed., p35-9, Santa Monica, Ca.: Human Factors Society (1979)

The development of microprocessors, radar technology, new types of visual displays, and speech synthesizers on dashboards will not only provide the driver with more extensive information about his car and traffic conditions, but also may distract him. This paper describes several experiments assessing and comparing the effectiveness, distraction effect, and processing time of visual, auditory, and combined visual and auditory informa ion presentations. Both field and simulator tests are described.

On the basis of these studies the authors make several recommendations for automobile instrument panel design. For indications of the state of the automobile, (1) frequent, routine information should be presented by a visual, not auditory presentation; and (2) information concerning the state of the automobile that occurs only rarely (e.g., once a year) but that is critical and requires immediate response should be presented by a dynamic signal such as a blinking lamp or intermittent sound and lamp. Information pertaining to road guidance should be presented visually in pictorial form. Information which requires an immediate response should not be presented in words which must be read by the driver, since the reading process may delay a driver's reaction for up to three seconds; h wever, reaction to an unexpected event is only imperceptibly delayed by spoken te> tual information presentation.

Fina ,, information should be as concise as possible in all modes of information presentations. (HSRI)

3 refs

KEYWORDS: Driving Simulator. Open Road Driving.

UM-79-F0065

IS TIME-SHARING A GENERAL CAPABILITY? H.L. Hawkins; E. Rodriguez; G.M. Reicher, Compass for Technology. Proceedings of the Human Factors Society, 23rd Annual Meeting, C.K. Bensel, ed., p532-5, Santa Monica, Ca.: Human Factors Society (1979)

Human factors researchers have long believed that a general time-sharing ability is influential in tasks such as piloting, driving, and air-traffic control where high rates of information exchange are required between operator and environment. This belief has led to the development of a theory that one's time sharing ability is largely determined by the capacity of a single central processing structure through which most input-output transactions must be funneled. This paper tests an alternative theory--that time-sharing performance is governed not by a single general capacity, but by several more specific subcapacities, each associated with a particular structure within the information processing sequence.

The time-sharing ability of eighteen students was measured under eight separate dual-task conditions. Three distinct task characteristics were systematically varied across conditions in an effort to manipulate the nature of the specific time-sharing demands imposed. Each condition contained two of these characteristics in common with three of the remaining seven conditions, one of the characteristics in common with three others, and none in common with the last condition.

Time-sharing efficiency correlated across conditions that imposed similar processing demands on the individual, but not across conditions imposing relatively dissimilar demands. It is concluded that time-sharing performance under present conditions is determined by several poorly correlated, task-specific subcapacities rather than by a single general ability. (JAM)

9 refs

KEYWORDS: Psychomotor Tests. Tests of Sensory Function.

UM-80-F0066

DRIVING SIMULATION--REQUIREMENTS, MECHANIZATION AND APPLICATION, R.W. Allen; H.R. Jex, SAE Technical Paper Series, n 800448, Warrendale, Pa.: Society of Automotive Engineers (1980)

This paper discusses recent developments and applications of driving simulators. Simulation of driving via films has been used for a number of years as a driver education tool. More recently, interactive simulators have been developed for research and training applications. Improvements are accelerating due to a combination of ongoing research needs and general state-of-the-art advances in hardware and software technology.

Modern simulator requirements are reviewed from the point of view of both driver characteristics (vision, audition, proprioception, vestibular motion sensation) and task demands (e.g., steering and speed control, risk perception, decision-making, general workload level).

Several imulator applications are summarized and compared with subsequent field tests. These applications include studies involving drunk driving and risk-taking, reduced visibility and delineation, and signing. Possible future simulator developments and application are also discussed based on current research needs and applications and ongoing general developments in electronics and computer hardware and software. (AA)

39 refs

KEYWORDS: Review: Behavioral Research Methodology.

UM-80-F0067

PERCEP[illegible]L/COGNITIVE SKILLS AND DRIVING: EFFECTS OF BRAIN DAMAGE, M. Sivak; P.L. Olson; D.G. Kewman; H. Won; D.L. Henson, Ann Arbor, Mich.: University of Michigan (Jan 1980)

This study investigated the relationship between perceptual and cognitive skills and driving. It specifically attempted to determine whether brain damage results in impaired perceptual and driving skills and in impaired driving and what the relationship is between subjective evaluation of driving by a driver educator and an evaluation of selected driving actions. The subjects included twenty-three persons with brain damage, eight persons with spinal cord damage, and ten able-bodied controls. Twenty-seven of the total were males, aged 18 to 69, and fourteen were females, aged 20 to 64. Each subject was evaluated using a battery of perceptual and cognitive tests, a set of driving tasks in a parking lot, and actual in-traffic driving.

The main findings are as follows: (1) Driving performance was significantly correlated with perceptual and cognitive skills. The highest correlations were obtained for Picture Completion Test ($r = .71$), Picture Arrangement Test ($r = .58$), and Motor Free Visual Perception Test ($r = .57$). (2) The persons with brain damage performed significantly worse than the control subjects or people with spinal-cord damage on a range of perceptual and cognitive tests. (3) The persons with brain damage exhibited impaired driving performance in relation to the control subjects or people with spinal-cord damage. (4) The correlation between a subjective evaluation of driving potential by a driver trainer and an evaluation of selected driving actions proved to be rather high ($r = .81$). (5) The obtained high correlations between several perceptual/cognitive tests and driving suggest that these tests (if properly validated) could be used in a screening battery to detect potentially serious driving-related problems. (6) Statistical procedures indicate that the data are consistent with the following hypothesis: Brain damage affects perceptual and cognitive skills (including those evaluated by Symbol Digit Modalities Test, Picture Completion, and Picture Arrangement), which in turn affect driving performance. (AAM)

54 pages 123 refs

KEYWORDS: Closed Course Driving. Open Road Driving. Psychological Testing.

DOT-HS-6-01490

UM-78-F0068

DRIVER SCREENING--SIMULATOR EVALUATION PROGRAM. FINAL REPORT, L. Barker; J. Polson; P. DuPont (July 1978)

The object of this study was to determine whether or not there is a significant difference between the results of the driver screening simulator developed by the Oklahoma Department of Public Safety and the results of their current road test conducted for the issuance of driver licenses. Forty-six applicants were selected in four categories: (1) out-of-state transfers; (2) driver education graduates; (3) renewals of drivers with good driving records; and (4) problem drivers (nine or more points).

Applicants were tested by the same examiner on both the road test and the simulator test. They were also administered questionnaires prior to and after testing in order to obtain attitudinal data. The knowledge-vision-road test results, simulator test results, and questionnaires were then analyzed and evaluated.

The results of the data analysis and evaluation indicated that driver license applicants can approximate the results of a given road test with those of a driving simulator test. In many test categories where test results showed significance, the incomplete design contributed to operator performance. The response of the participants was, for the most part, favorable.

The authors conclude that the driving simulator screen used in this study can, with a few design corrections, be used for the purpose of screening driver applicants for road testing capability prior to actual road testing as well as for relicensing of applicants. (HSRI)

157 pages 0 refs

National Highway Traffic Safety Administration technical report DOT-HS-803-595

KEYWORDS: Driving Simulator. Open Road Driving.

UM-78-F0069

A REANALYSIS OF CALIFORNIA DRIVER VISION DATA: GENERAL FINDINGS, B.L. Hills; A. Burg, Transportation Research Record, n681 p47-50 (1978)

Visual performance and driving record data on over 14,000 California drivers were analyzed to explore how vision-driving relationships change with age, and to examine the feasibility of using these data to establish cut-off scores for driver vision screening. Four age groups were analyzed: under 25, 25-39, 40-54 and over 54.

No consistent vision-driving relationships were found for the first three age groups; for the oldest group, poor performance on tests of dynamic visual acuity (DVA) and static visual acuity (SVA) was related to high accident rates, but the accident prediction value of these tests for an individual driver was low. Breaking down the over 54 drivers into smaller age groups failed to define more precisely the age at which the DVA and SVA relationships develop.

The data did not support the use of visual field testing as a practical driver licensing tool, but did suggest that a glare recovery test might be of value in screening older drivers. Using the same nominal cut-off score, two tests of static acuity (Ortho-Rater and Snellen chart) did not fail the same number of drivers, suggesting the need to standardize test procedures as well as cut-off scores. The practical implications of various cut-off scores were investigated for each test, but the results did not justify recommendation of specific cut-offs. Finally, the use of perceptual rather than sensory tests is suggested as being more likely to produce valid criteria for driver screening. (AA)

18 refs

KEYWORDS: Tests of Sensory Function.

UM-80-F0070

REACTION TIME AS A FUNCTION OF THE CARDIAC CYCLE, V.T. Wynn, British Journal of Psychology, v71 pt1 p155-62 (Feb 1980)

Three experiments are described, all of which were part of a study to determine whether simple reaction time to auditory stimuli is a function of the cardiac cycle. In the first experiment the onset of the R wave was singled out from the ECG to act as a triggering point and reaction time was assessed; this was compared with the reaction time resulting when the stimulus was independent of the cardiac cycle. The daily mean of more than 300 responses was calculated for each set for seven weeks. The results of this study clearly indicate the presence of an approximately nineteen-day rhythm and suggest that the heart might play a fundamental role in perturbing the reaction-time responses.

The second experiment, which lasted for six weeks, measured simple reaction time responses, one of which was triggered by the onset of the R wave, another by the onset of the P wave, and the last in the middle of the T wave, with 240 responses per day for each trigger point. Analysis of the data showed that the R-triggered results produced a rhythmic fluctuation similar to that in the first experiment, although of a slightly shorter period (sixteen days). The P and T results produced a shorter eight-day rhythm.

The third study attempted to determine the extent of the heart's control over each rhythm, therefore the stimulus was triggered at different points throughout the cardiac cycle. More than 35,000 reaction times were recorded in separate four-hour sessions. The results of this study were generally consistent with the presence of three fixed intervals in the cardiac cycle in which the reaction time varied in a specific pattern.

The author concludes that although the presence of two cycles with different periods is indicated by the experiments, it is not possible to do more than conjecture on the mechanisms producing the rhythmic behavior. It appears that both the hormone and the cardiovascular systems are implicated in the perturbation process. Further research is needed, especially of the ECG. (HSRI)

11 refs

KEYWORDS: Tests of Sensory Function.

UM-79-F0071

THE EFFECTS OF DRIVING EXPERIENCE ON OBJECTIVE MEASURES OF DRIVING PERFORMANCE, D. Attwood, Compass for Technology. Proceedings of the Human Factors Society 23rd Annual Meeting, C.K. Bensel, ed., p277-81, Santa Monica, Ca.: Human Factors Society (1979)

The experiment described herein was conducted to develop a method of predicting driver ability based on objective measures of driving performance.

Fifteen subjects drove an instrumented vehicle in live traffic on two-lane and multi-lane road sections in and around the Toronto area. Eight of the subject drivers had at least five years driving experience and seven of them had less than two thousand miles driving experience.

On selected portions of the road course, subjects were instructed to maintain certain speeds or lanes. During these periods raw data were collected on vehicle velocity, lane position, steering wheel position, and accelerator pedal position. Using off-line computer programs, the data were transformed into a number of descriptive statistics which were analyzed using univariate and multivariate statistical techniques.

Results indicated that even though univariate analyses were generally unsuccessful in differentiating between the groups of experienced and inexperienced drivers, successful discrimination was achieved with combinations of variables.

Results suggest that it could be possible to employ on-line monitoring devices to determine whether a driver is capable of a minimum level of driving performance. Implications for the use of such a device in driver licensing and education are discussed. (JA)

12 refs

KEYWORDS: Open Road Driving.

UM-79-F0072

DIURNAL VARIATION IN SUBSIDIARY REACTION TIME IN A LONG-TERM DRIVING TASK, H.-O. Lisper; B. Eriksson; K.-O. Fagerstrom; J. Lindholm, Accident Analysis and Prevention, v11 n1 p1-5 (March 1979)

Traffic accidents show a marked diurnal rhythm, which is a seldom investigated phenomenon. One possible background factor examined in the present study is the biological circadian rhythm. Eight subjects drove for three hours beginning at 0300, 0900, 1500, and 2100. During each session a subsidiary reaction time task was used as an indirect measure of driving performance. Critical confounding factors, such as lighting conditions, traffic intensity, amount of sleep preceding the session, and temperature in the car were considered.

The results showed that there were small differences in the level of performance among the four sessions. However, differences in the rate of performance deterioration were not observed. From these results it was concluded that biological rhythm as a single variable has only a minor influence on this type of performance. Consequently the diurnal rhythm of traffic accidents must be attributed to other factors such as long hours of driving or sleep deprivation, which culminate during the morning hours. (JA)

29 refs

KEYWORDS: Open Road Driving.

TRRL Lab Report 920

UM-80-F0073

ASPECTS OF ROAD LAYOUT THAT AFFECT DRIVERS' PERCEPTION AND RISK TAKING, G.R. Watts; A.R. Quimby, Crowthorne, Berkshire: Transport and Road Research Laboratory (1980)

This study investigated the frequency of drivers' incorrect perception of environmental hazards by comparing subjective estimations of risk with objective accident data. The purpose of the study was to indicate problem situations for drivers, thus enabling the determination of more effective countermeasures.

Various road locations characterized by unusual or misleading environmental features were investigated by sixty drivers representative of the general driving population who were required to assess risk on a sixteen-mile route. The route included a wide range of road types and hazards such as rural two-lane highways, narrow suburban roads, and sharp hill crests. Each subject assigned a relative degree of risk to each of the specified locations. Data from the group as a whole were analyzed, and each location was ranked according to perceived risk level. The subjective risk ranking was compared with the ranking of objective risk obtained from actual accident and traffic flow data. Reported injury accidents occurring in daylight hours from 1973 through 1976 at or near the specified locations were used to calculate objective risk.

Analysis of the subjective data indicated that there was significant agreement between drivers in ranking the subjective risks of a range of road locations. Comparison of the relative and objective risk level rankings resulted in a small but significant association. However, at some locations there were wide discrepancies between subjective and objective risk levels. Possible reasons for these differences are discussed.

Also recorded were drivers' speeds on the route. A measure designated as safety margin, based on the difference between the distance ahead that was visible and the overall stopping distance as determined by speed, was also compared to subjective assessments of risk level. The strong association between rankings of perceived risk and those based on the measure of safety margin indicates that drivers were aware of the differences between forward visibility distances and their stopping distances. Countermeasures for problem situations are recommended, based on this data. (HSRI)

22 pages 22 refs

KEYWORDS: Open Road Driving. Review: Behavioral Research Methodology.

CAL-DMV-RSS-78-67

UM-78-L0116

MEDICALLY IMPAIRED DRIVERS: AN EVALUATION OF CALIFORNIA POLICY. FINAL REPORT, M.K. Janke; R.C. Peck; D.R. Dreyer, Sacramento: State of California Business and Transportation Agency Department of Motor Vehicles (Sep 1978)

The chapters in this report address a number of issues using an array of methods and study approaches. The following approaches were used: (1) a review of traffic safety literature comparing the driving records of groups of impaired drivers with each other and with the general driving population; (2) a compendium of medical opinion and data from secondary sources on conditions causing lapses of consciousness; (3) a review of laws and administrative policies in California, other states, and other countries

relating to impaired drivers; (4) a correlational study comparing physicians' and DIA's recommendations regarding the driving privileges of subjects with lapses of consciousness; (5) a presentation of statistics relating to the role of impairment in California accidents, and a determination of accident records of six physically or mentally impaired groups and selected groups of high-risk drivers without known impairment as compared with that of the general California driving population; (6) retrospective studies of the administrative process as it relates to several samples of impaired drivers; (7) an experimental study of the effect of three types of treatment (formal probation, informal probation, and no action) on accident records of physically and mentally impaired subjects with lapses of consciousness, other physical impairments, or mental impairments; and (8) opinion surveys of the general driving population and impaired drivers.

From the findings of these various studies, conclusions were drawn and recommendations were formulated. The findings of the present study relate only to drivers who are known to have physical or mental impairments. The severity of their conditions and their accident involvement are undoubtably greater, to an unknown extent, than the average for the totality of all drivers with medical conditions. (AAM)

218 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation. Epidemiology: Record-Based Survey.

UM-78-LO117

INFORMED CONSENT, C. H. Wecht, Forensic Science International, v12 p175-86 (1978)

This paper reviews the history of informed consent. Informed consent can be traced as far back as ancient Babylonian law in 2000 B.C. In 1914 Justice Benjamin Cardozo of New York made the following assertion: "Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault,...". This statement was one of the first to assert that a patient should decide what could be done with his body.

In 1957, the first "modern" informed consent case, Salgo v. Leland Stanford, University Board of Trustees, shifted the cause of action from battery to negligence and changed the concept of consent to informed consent. It was the first formal recognition that perhaps patients should participate in decisions concerning their medical treatment.

The article also discusses hospital liability, physician defenses, and protection. (HSRI)

15 refs

KEYWORDS: Informed Consent.

UM-79-LO118

INFORMED CONSENT MAY BE HAZARDOUS TO HEALTH, E.F. Loftus; J. F. Fries, Science, v204 n4388 p11 (6 Apr 1979)

Presented here is an argument for the withholding of detailed information from persons participating in experimental studies. Many studies concerning informed consent have found that in a surprisingly large number of cases, explicit suggestion of possible adverse effects causes subjects to experience these effects. Possible consequences of suggested symptoms range from minor annoyance to, in extreme cases, death.

If protection of the subject is the reason for obtaining informed consent, the possibility of iatrogenic harm to the subject as a direct result of the consent ritual must be considered. This cost must be weighed against the potential benefit of giving some people an increased sense of freedom of choice about the use of their bodies.

The authors suggest that detailed information concerning specific slight risks should be reserved for those who request it. When a specific risk is disclosed, it should be discussed in the context of placebo effects. A move in this direction may ensure that a subject will not be at a greater risk from self-appointed guardians than from the experiment itself. (HSRI)

0 refs

KEYWORDS: Informed Consent.

UM-75-LO119

ACCIDENT INVESTIGATION AND REPORTING, National Committee on Uniform Traffic Laws and Ordinances, Traffic Laws Commentary, v4 n2 p1-72 (Sep 1975)

This commentary deals with the legal framework for the accident analysis system. It reviews state laws current as of January 1, 1975 relating to accident reports and accident investigations in the context of comparable provisions of the Uniform Vehicle Code (1975 revision).

The paper begins with a discussion of what accidents are reportable. Required information exchange at the accident scene such as duty to stop and duty to provide information to police are specified. Notification of the police by the involved parties, by vehicle owners, and by service garages is also discussed, as well as police investigating and reporting regulations. This discussion is followed by regulations concerning written reports by involved parties, and includes a discussion of false reports and failure to report.

The provisions of the Uniform Vehicle Code and various state laws concerning special investigations such as coroners' reports and tests for alcohol and drugs are presented. A 1975 amendment to the Uniform Vehicle Code added a section providing for the withdrawal of a bodily substance from a driver or pedestrian killed in a vehicle accident and the analysis of the substance for alcohol by a medical examiner. One state does not specify that the purpose of the test is to determine the alcohol content of the blood; seven states specify that the test is to determine drug concentrations. The Code specifies that the results of the testing are to be used for statistical purposes that do not reveal the identity of the deceased person; however, test results are not privileged. The laws of various states pertaining to this provision are discussed.

The commentary concludes with several observations concerning trends and issues in police investigation, the writing of accident reports, and uniformity in accident laws. (HSRI)

64 refs

KEYWORDS: Other Sociolegal Study.

UM-77-LO120

THE CANADIAN APPROACH TO HEALTH POLICIES AND PROGRAMS, D.D. Gellman; R. Lachaine; M.M. Law, Preventive Medicine, v6 n2 p265-75 (1977)

The purpose of this paper is to review Canada's health insurance programs, recent initiatives in prevention, health promotion, and health care. "A new perspective on the health of Canadians" has become the major blueprint for the development of health policies at the federal level in Canada. Under this new perspective five strategies are proposed: (1) a health promotion strategy; (2) a regulatory strategy; (3) research strategy; (4) health care efficiency strategy; and (5) a goal-setting strategy.

Canada's national health policies and programs have developed as a result of joint efforts of the federal and provincial governments. A federal General Health Grant program, begun in 1948, assisted the provinces in upgrading hospital facilities, in training health professionals, in research, and in categorical programs to control such diseases as cancer, tuberculosis, and V.D. A universal program of insurance for hospital care was introduced in 1958 and was followed, ten years later, by universal insurance to meet the cost of physicians' services. Having taken care of the major "sickness" services, attention is now being turned to prevention, with particular emphasis on programs to improve the physical and social environment and to encourage such personal habits as careful driving, use of seat belts, exercising, not smoking cigarettes, moderation in the use of alcohol and food, and abstaining from using drugs except for medicinal purposes. (JAM)

13 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation.

UM-78-LO121

PLACEMENT OF N-ETHYL-1-PHENYLCYCLOHEXYLAMINE AND 1-(1-PHENYLCYCLOHEXYL) PYRROLIDINE INTO SCHEDULE I, Drug Enforcement Administration, Federal Register, v43 n186 p43295-6, (25 Sep 1978)

Presented here is a rule requiring that the manufacture, distribution, dispensing, importation, and exportation of PCE (N-ethyl-1-phenylcyclohexylamine) and PHP (1(1-phenylcyclohexyl)pyrrolidine) be subject to the regulations applicable to substances in schedule I of the Controlled Substance Act as of October 25, 1978. This was done on the basis of an investigation and review conducted by the Drug Enforcement Administration which found that (1) both drugs have a high potential for abuse; (2) neither substance has a currently accepted medical use in treatment in the United States; and (3) both drugs lack accepted safety for use under medical supervision.

Rules and regulations are stated for the registration, security, quotas, inventory, labeling and packaging, records, reports, order forms, importation and exportation, and criminal liability related to the two drugs. (HSRI)

0 refs

KEYWORDS: Hallucinogens and Related Agents: cyclohexamine (PCE). 1(1-phenylcyclohexyl) pyrrolidine. Other Sociolegal Study.

UM-71-LO122

THE POLICE OFFICER AND THE MEDICAL EXAMINER SYSTEM, I.M. Sopher; W.C. Masemore, Police, v16 n3 p23-6 (Nov 1971)

This article describes the operation and function of the medical examiner system and discusses how such a system relates to the daily duties of the police officer. The medical examiner system of Maryland is used as a model. The paper describes the state laws pertaining to this system, the size of the system, organization on the county level, and the annual workload.

Special emphasis is given to the role the law enforcement officer plays in the success of a medical examiner system. An accurate, thorough incident report by the investigating law enforcement officer may be the sole determining factor in the establishment of the manner of death. The facts or suspicions forwarded by the police officer often direct or redirect a search for a cause of death in a particular case. Instances involving deceased subjects often require the skillful employment of tact, ingenuity, and interrogative expertise on the part of the police officer. Competent investigation by the policeman coupled with data obtained from postmortem examinations by the forensic pathologist is necessary for an efficient medical examiner's system. (AAM)

0 refs

KEYWORDS: Other Sociolegal Study.

UM-77-LO123

EXAMENS MEDICAUX ET RETRAIT DE PERMIS [MEDICAL EXAMINATIONS AND THE SUSPENSION OF LICENSES], R. Vieville; H. Sapin-Jaloustre, Concours Medical, v99 n28-30 p4575-88 (25 Jun 1977)

This paper reports the results of a survey analyzing medical examinations of 1,300 drivers whose licenses had been suspended for impaired driving. Some of the major conclusions drawn from the survey were the following: (1) very few young drivers suffer from chronic alcoholism when compared to older drivers. (2) People suffering from diabetes, heart problems, neurological abnormalities, and psychiatric disorders were not overrepresented in drivers whose licenses were suspended. (3) The frequency of traffic accidents increases with alcohol use; that is, chronic drinkers are more likely to be involved in more serious and more frequent accidents. (HSRI)

0 refs French

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Epidemiology: Record-Based Survey.

AMA #1435

UM-63-LO124

DRIVER INTOXICATION AS A SOCIAL PSYCHOLOGICAL PROBLEM, I.H. Cisin, California School on Alcoholism Conference, June 20, 1963 (1963)

The author reviews the problems of driver intoxication both from the point of view of the individual driver and from the point of view of society. Several aspects of the problem are discussed: who the drinking driver is; why respectable, average members of society act so irresponsibly; why and how people drink; how society can effectively control drunk driving; and how society's attitude toward drinking can be modified.

The author recommends several solutions to the problem of drunk driving, none of which are without problems. These include more rigid enforcement of speed and other traffic laws, selective or differential licensing, self-evaluation devices to measure impairment, and development of drugs to counteract the effects of alcohol. (HSRI)

12 pages 0 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Review: Drugs and Highway Safety.

UM-72-LO125

A COMPENDIUM OF STATE MEDICO-LEGAL INVESTIGATIVE SYSTEMS, R.N. Kornblum; R.S. Fisher, Baltimore: Maryland Medical-Legal Foundation (May 1972)

This compendium represents an outline of the system of medico-legal death investigation in each state as it existed in 1971. The information was obtained by reviewing the state laws as well as annual reports of various offices and personal communications where these were available. Some of the information provided for each state includes qualifications of the county coroner, his duties, pathology or toxicology services, and structure of the medico-legal system on the county level. (JAM)

0 refs

KEYWORDS: Other Sociolegal Study.

UM-78-LO126

DEATH INVESTIGATION: AN ANALYSIS OF LAWS AND POLICIES OF THE UNITED STATES, EACH STATE AND JURISDICTION, A.P. Cleveland; R.E. Cook; R.W. Taylor; P.R. MacDonald; D.J. Scanlon, Rockville, Md.; Department of Health, Education, and Welfare (1978)

This study is designed to assemble and analyze existing state and territorial law, policies, and regulations governing medico-legal death investigation. Its purpose is to assist the Bureau of Community Health Services Office of Maternal and Child Health in developing a systematic surveillance of national medico-legal investigation of death in relationship to the sudden and unexplained death of infants.

In addition to the fifty states, this study covers the District of Columbia, American Samoa, Guam, Puerto Rico, Panama Canal zone, and the U.S. Virgin Islands. Local ordinances or regulations and policies adopted by governmental bodies below the state level are not included except in occasional instances where cited to clarify state law. (JA)

121 pages 0 refs

DHEW (HSA)78-5252

KEYWORDS: Other Sociolegal Study.

UM-75-LO127

AN OVERVIEW OF THE LEGAL ASPECTS OF HUMAN EXPERIMENTATION AND RESEARCH, J.W. Little, Drug/Driving Research Review Symposium, chap 9 p154-78, Bloomington, Indiana: Indiana University (Apr 1975)

This article examines the various theories of liability that researchers engaged in experimentation with human subjects need be aware of in designing their projects.

It also examines protective defenses including researcher privilege, informed consent, and ordinary care.

Of particular importance is the special dilemma posed by the seemingly irreconcilable duties to assure subjects of complete confidentiality as an element of informed consent on the one hand, and to produce all one's testimony and evidence in court on the other. The author suggests that the dilemma can be resolved by granting a researcher-subject testimonial privilege. This privilege is founded on the theory that it is better social policy to enable persons to disclose everything to the researcher without fear that the researcher will later be required to disclose the confidential information under court order than it is to require the production of every bit of evidence in every case. As of yet, this privilege has not been granted by the U.S. Supreme Court.

The author concludes that whether all research areas will qualify for this privilege or not may turn largely on the temper of the times. For researchers involved in research of the effect of drug and alcohol use on highway safety, researcher-subject privilege could conceivably be in the national interests of controlling drug use and preventing highway injuries. (HSRI)

47 refs

NHTSA DOT-HS-4-00994

KEYWORDS: Researcher Privilege. Right of Privacy/Confidentiality.

UM-74-L0128

DRUG LAWS: PERCEPTIONS OF ILLEGAL DRUG USERS, D.T. Jaffe, Drug Forum, v3 n4 p321-9 (Sum 1974)

This paper explores the consequences of the legal response to drug use on the attitudes of young drug users by analyzing accounts of their perspective on the drug laws at different stages of drug use. One hundred twenty-three middle-class young people (mean age 23) most of whom had some college experience and had used a variety of drugs, primarily marijuana and psychedelic drugs, were interviewed concerning their life history and drug use.

While it was difficult to separate the effect of the drug laws from simultaneous factors like personal and lifestyle changes on drug effects, the author concludes that the perspectives presented here represent consequences of the drug laws on a certain group more than they represent the effects of the drugs themselves or characteristics of the groups which take them.

It is concluded that drug use is not a static behavior that a group of people engage in unvaryingly, but rather part of a process of developing a conception of oneself in relation to a society which one does not entirely accept and agree with. The attitudes of young people toward law, as well as their use of drugs, change over time and develop along lines which parallel other development changes in values, attitudes, and behavior. (JAM)

6 refs

KEYWORDS: Other Sociolegal Study.

UM-79-L0129

DRUG OFFENDER DIVERSION: PHILOSOPHY AND PRACTICES, J.C. Weissman, Drug Abuse and Alcoholism Review, v2 n1 p1-8 (Spring 1979)

This paper attempts to clarify the function of and evaluate drug offender diversion, the policy of channeling or diverting drug abusers away from incarceration and into community treatment resources. Special emphasis is given to the origins of modern diversion programming, the policy base underlying the concept, prototype program models, available evaluative data, and anticipated future developments. Also presented is a historical review illustrating several policies used in twentieth-century American drug abuse prevention efforts. Primarily, the basic thrust has been and remains a criminal law approach.

In this writer's opinion, the present challenge is to reform diversion policies to effect a truly humane and enlightened approach toward the social treatment of drug use. Recreational and chronic drug use patterns must be distinguished. Reform strategies

must be advanced. Drug abuse professionals must emulate the pioneering social reform efforts in the alcohol abuse field. Rather than remaining a passive recipient of directives concerning the delivery of treatment services, drug abuse professionals must play a formative role in designing diversion policies. (HSRI)

26 refs

KEYWORDS: Countermeasure Concepts. Other Sociolegal Study.

UM-79-L0130

MARIJUANA AND HEROIN BY PRESCRIPTION: RECENT DEVELOPMENTS AT THE STATE AND FEDERAL LEVELS. S. L. Nightingale; S. Perry. Journal of the Americal Medical Association, v241 n4 p373-5 (26 Jan 1979)

This article explains the current legal and research status of marijuana, tetrahydrocannabinol, and heroin, and highlights some problems with state legislation concerning these substances for the medical profession as well as for state and federal government officials.

The authors believe that drug-specific legislation on the state level is neither practical nor theoretically sound. Where an attempt is made to approve a drug by state law, protection afforded the public by federal and state health regulatory bodies may be lost. These kinds of decisions should be made by public health officials on the basis of safety and efficacy considerations, not by legislators. Such legislation indicates to the public that these substances are safe and effective. Imparting an official governmental stamp of approval would undoubtedly increase the demand for these substances.

The authors conclude by stressing the importance of research with Schedule I substances such as marijuana. The demarcation between clinical research and treatment with approved drugs should remain distinct. (HSRI)

5 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. marijuana. Opiates and Related Agents: heroin. Other Sociolegal Study.

UM-78-L0131

IS THERE A SCIENTIFIC BASIS TO THE LEGISLATION OF MARIJUANA AS A MEDICANT? K. Green, Journal of Psychedelic Drugs, v10 n3 p217-26 (Jul-Sep 1978)

Presented here is a discussion of the legalization of marijuana as a clinically valuable drug in the treatment of various diseases. It specifically addresses marijuana's potential use in glaucoma treatment. While the scientific evidence for a reduction in intraocular pressure is substantial, there is a considerable body of evidence to indicate that marijuana can evoke alterations in short-term memory, driving ability, and other patterns of behavior. Knowledge concerning both short- and long-term effects of marijuana remains limited at this point because of the lack of control over test conditions and quality of marijuana. These factors inhibit the collection of scientifically sound information on which decisions can be made regarding potential legislation of marijuana.

This author believes that the retention of marijuana in Schedule I, a drug category that is defined as having no medical benefit, is appropriate at this time. A decision by the FDA to allow delta-9-THC and cannabidiol to be moved to Schedule II would be logical, but only after sufficient research is performed. Further research might discover different cannabinoids that affect specific disease entities but do not have the psychoactive effects of marijuana, effects that would place severe restrictions on the patients being treated by marijuana. (HSRI)

13 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabidiol. delta-9-tetrahydrocannabinol. marijuana. Cannabis Sativa L. and Related Agents. Other Sociolegal Study.

UM-78-LO132

POTENTIAL TAX REVENUES FROM A REGULATORY MARKETING SCHEME FOR MARIJUANA, A. S. Garber, Journal of Psychedelic Drugs, v10 n3 p217-26 (Jul-Sep 1978)

Presented here is an economic study of the potential revenue from marijuana in the form of taxes in the event that marijuana is legalized, assuming that it is sold in a regulatory marketing scheme. Based on NIDA surveys, Drug Abuse Council surveys, and several other reputable national surveys, the author calculates that the federal, state, and local governments would raise a minimum of 8 billion dollars in new, previously unforeseen revenues. This is more than five times what the Department of Health, Education and Welfare spent on drug abuse prevention in 1977.

The author concludes that in the event of legalization of marijuana and its subsequent taxation, the revenues should not go into a general fund. Rather, the money should be earmarked for some social project for the good of the citizens of the United States, for example, drug abuse treatment or cancer research. (HSRI)

16 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Other Sociolegal Study.

UM-78-LO133

RECOMMENDATIONS OF THE COMMITTEE ON ALCOHOL AND DRUGS 1936-1977, Chicago: National Safety Council (1978)

This report presents most of the recommendations, standards, and work of the Committee on Alcohol and Drugs since its inception in 1936. The Committee has been active in making recommendations for the control of the drinking-driving problem, including legislation, enforcement, education, chemical testing equipment, training of testing personnel, and other aspects of alcohol countermeasure programs, many of which are reported here in chronological order.

Several appendices are attached. These include: (A) A Model Program for the Control of Alcohol for Traffic Safety; (B) Recommendations of the Ad Hoc Committee on Quantitative Breath Alcohol Instrumentation; (C) Recommendations of the Ad Hoc Committee on Breath Alcohol Screening Tests; (D) Recommendations of the Ad Hoc Committee on the Report of Periodic Requalification and Continued Education and Training of Personnel Engaged in the Performance of Chemical Tests for Alcohol Influence; and (E) Special Report on the Blood/Breath Conversion Factor. (HSRI)

84 pages O refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol). Countermeasure Concepts.

UM-78-LO134

TASK PANEL REPORTS SUBMITTED TO THE PRESIDENT'S COMMISSION ON MENTAL HEALTH. VOLUME IV, APPENDIX, Washington, D.C.: U.S. Government Printing Office (1978)

This report analyzes and makes recommendations for several legal and ethical issues concerning mentally ill persons, mentally retarded and other developmentally disabled persons, children, the elderly, and various racial and cultural special populations. It encompasses such issues as education, employment, housing, federal benefits, confidentiality, guardianship, experimentation, and treatment (including the right to treatment and to protection from harm, the right to treatment in the least restrictive setting, the right to refuse treatment, and the regulation of treatment). Also discussed are civil commitment and the criminal justice system. Other sections discuss the need for advocacy and suggest structures for a patient's or consumer's bill of rights and the resolution of ethical dilemmas.

Of special interest is the report of the Liaison Task Panel on psychoactive drug use and abuse. The task panel stresses that the most important need in this area is the decriminalization of personal possession and use of small amounts of marijuana. Legislation should be developed to provide taxation regulation and control of marijuana. The task panel further believes that the social and personal costs of the continued criminalization for other psychoactive substances may outweigh the costs of the dysfunctional drug problems themselves. Therefore, public policy consideration should be devoted to the decriminalization of personal possession and private use of small amounts of other psychoactive substances. (HSRI)

781 pages

Task Panel on Legal and Ethical Issues

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: methadone. Opiates and Related Agents. Informed Consent. Other Sociolegal Study. Research with Human Subjects.

UM-79-LO135

FEDERAL STRATEGY FOR DRUG ABUSE AND DRUG TRAFFIC PREVENTION 1979, Washington, D.C.: U.S. Government Printing Office (1979)

Presented here is the 1979 Federal Strategy for Drug Abuse and Drug Traffic Prevention. This report represents a comprehensive approach to the nation's drug abuse problem and serves as the foundation from which the Federal Government can make serious attempts to reduce the serious effects of drug abuse in this country. Strategy 1979 has two main policy objectives: (1) to discourage all drug abuse, including the abuse of alcohol; and (2) to reduce to a minimum the health and social consequences of drug abuse when it does occur. It reflects a three-part program to reduce the negative effects of drug abuse: (1) treatment, rehabilitation, and prevention; (2) domestic drug law enforcement; and (3) international narcotics control. The overall program is intended to provide balanced and flexible means to reduce the supply of illicit drugs, discourage use, and make treatment available to drug abuse victims.

An underlying concept of Strategy 1979 is that domestic supply reduction efforts must be coupled with domestic treatment, rehabilitation, and prevention activities in order to be effective. Domestic supply reduction measures give priority to those drugs that are pharmacologically most dangerous or cause the most harm in the United States. International supply reduction is a critically important part of long-range strategy. (HSRI)

Strategy Council on Drug Abuse

70 pages 0 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Local Anesthetics: cocaine. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Stimulants: cocaine. Hallucinogens and Related Agents. Opiates and Related Agents. Other Toxicants. Sedatives and Hypnotic Agents. Stimulants. Tranquilizers. Volatile Solvents. Countermeasure Concepts. Other Sociolegal Study.

UM-78-LO136

CONTROLLING THE USE OF THERAPEUTIC DRUGS: AN INTERNATIONAL COMPARISON, W. M. Wardell, ed., Washington, D.C.: American Enterprise Institute for Public Policy Research (1978)

Presented here is an international comparison of measures controlling the use of therapeutic drugs. In recent years the United States has begun to move toward control of drug utilization on a large scale with two distinct aims: limiting costs and improving the quality of utilization. This book examines the public policy implications of these controls. It also explores the reasons for the trend toward control of drug utilization and the characteristics of the existing systems in various countries--their objectives, their performance measures against their goals, and their impact on the development of new therapies, as well as the costs and quality of utilization of existing ones.

Countries with different systems of utilization control were selected for examination on the basis of their importance for drug development or unique utilization control systems. Experts in these countries were asked to describe the systems from their own perspective. Each author was asked to cover certain points: the history of the system for regulating drugs; postgraduate education in clinical pharmacology and therapeutics; controls over access of drug to the market; controls over drug utilization after the point of marketing; bases for controls; specific avenues of control; performance of the system; contributions to the improvement of drug utilization; and features peculiar to the particular country or health service. In addition to summarizing these key public policy issues and the essential features of other systems, the book contains a chapter describing in some detail the background, mechanisms, and reasons for the systems currently being used or being proposed in the United States. (HSRI)

263 pages

KEYWORDS: Other Sociolegal Study.

UM-78-L0137

DRUG SCHEDULING--WHAT EFFECTS? (EVALUATION OF THE IMPACT OF THE CONTROL OF ABUSABLE DRUGS), D. L. Cosby; L. B. Burke; J.S. Kennedy, American Pharmaceutical Association Annual Meeting, Montreal, Canada, May 1978 (1978)

This study attempts to assess the impact of recent federal drug control and scheduling decisions on the use and abuse of some of the most widely prescribed psychoactive drugs in the United States. All the drugs selected for evaluation in this study were either scheduled or rescheduled between 1971 and 1976. The following drugs were analyzed: amphetamine, diazepam, flurazepam, methaqualone, propoxyphene, and secobarbital. The number, cost, and size of prescriptions were determined for all brands of each of these drugs from 1964 to 1977, and the patterns of use were compared to changes in the prescribing of all prescription drugs in general.

The data indicate that for most of the drugs studied there were no consistently remarkable or demonstrable effects of control from the parameters measured regardless of the degree of control imposed. However, a few trends are observable. All but one (flurazepam) of the six drugs showed a decrease in use from the time increased control was imposed. Every decrease was greater than the decrease in general prescription drug use over the same time period.

Wholesale prices did not seem to be affected by federal controls. Generally, it appears that controlling a drug in Schedule II has the effect of increasing average prescription size.

The authors conclude that the beneficial impact of more tightly controlling widely used prescription drugs to reduce abuse should be weighed against any potential negative impact on approved medical access to these substances. (HSRI)

0 refs

KEYWORDS: Analgesics and Antipyretics: propoxyphene. Barbiturates: secobarbital. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: flurazepam. methaqualone. Stimulants: amphetamine. Epidemiology: National Survey of Drug Use Patterns. Other Sociolegal Study.

UM-79-L0138

SLEEPING PILLS, INSOMNIA, AND MEDICAL PRACTICE, Washington, D.C.: National Academy of Sciences (1979)

This report contains the results of a study reviewing the safety and efficacy of hypnotic drugs, especially the barbiturates. The study also investigates physician prescribing practices with respect to these drugs.

Six major topics are discussed: (1) an overview of sleep and medication; (2) epidemiology of sleep complaints and prescribing practices; (3) public health problems associated with the use of hypnotic drugs; (4) insomnia-research findings, diagnostic approaches, and therapeutic options; and (5) sleep disturbance in the elderly.

The members of the study committee offer several recommendations concerning clinical practice, patient information, public health, professional education, use of benzodiazepines as an alternative to barbiturates, advertising and labeling, research needs, and coordination of federal efforts. Some of these specific recommendations include the following: (1) A thorough medical and psychosocial appraisal of the insomniac patient should be made before any decision is made to prescribe drugs for relief of the sleep complaint. (2) There should be close monitoring by the physician of all patients receiving hypnotic drugs. (3) More research must be initiated to study both nighttime and daytime effects. Assessing daytime effects, especially effects on psychomotor performance, is of special concern because of potential hazards in driving or in operating heavy machinery. Performance should be assessed by a standard test battery measuring gross motor coordination, fine motor coordination, cognition, perception, and memory. (4) All hypnotics should be tested for interaction with alcohol.

The report concludes with an appendix assessing the hazards and benefits of hypnotic drugs. (HSRI)

198 pages

Division of Mental Health and Behavioral Medicine, Institute of Medicine

KEYWORDS: Anticonvulsants (Anti-Epileptics): clonazepam. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. clorazepate. diazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): lorazepam. oxazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: flurazepam. Barbiturates. Sedatives and Hypnotic Agents. Countermeasure Concepts. Epidemiology: Regional or Local Survey of Drug Use Patterns. Other Sociolegal Study.

SCNAC-95-1-8

UM-77-LO139

DECRIMINALIZATION OF MARIHUANA. HEARINGS BEFORE THE SELECT COMMITTEE ON NARCOTICS ABUSE AND CONTROL, HOUSE OF REPRESENTATIVES, MARCH 14, 15, AND 16, 1977, 95TH CONGRESS, 1ST SESSION. Washington, D.C.: U.S. Government Printing Office (1977)

Presented here are the hearings before the House Select Committee on Narcotics Abuse and Control of the Ninety-fifth Congress, first session, held March 14, 15, and 16, 1977 concerning decriminalization of the use and possession of small amounts of marijuana under the Controlled Substances Act of 1970. The purpose of the hearings was to examine the methodology of decriminalization as it has been operating in California, Oregon, and six other states which have adopted decriminalization laws and to give both proponents and opponents of the legislation, both in and out of government, an opportunity to be heard. In addition, an examination was made of the circumstances surrounding the incarceration of some two hundred persons still in various state and federal institutions serving terms for possession or sale of small amounts of marijuana, in order to make appropriate recommendations concerning them.

The purpose of the hearings was not to debate over whether or not marijuana is more or less harmful than alcohol or whether or not sale of marijuana should be legalized, but rather to determine whether public attitudes toward decriminalization have changed, and if so, whether these changes are based upon public policy reasons. Also discussed was the cost-benefit ratio of decriminalization as it concerns public health, the criminal justice system, and the effects on the states of any serious movement toward decriminalization by the federal government.

Four major areas of the issue were presented at the hearings. (1) the current state of knowledge concerning the effects of marijuana use on human health and performance; (2) history of the origin of marijuana laws in the United States; (3) a review of the current knowledge as to whether the use of marijuana leads to the use of hard drugs, particularly heroin; and (4) the results of public opinion polls and other known public attitudes concerning criminal penalties for the use of small amounts of marijuana. The primary objective of the committee in gathering this information was to develop a record to enable the standing committees having legislative jurisdiction over decriminalization of marijuana to begin deliberations concerning the amendment of the Controlled Substances Act of 1970. (HSRI)

634 pages 0 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Compilation. Other Sociolegal Study. Review: Drug Effects. Review:Drug Use.

SCNAC-95-1-9

UM-77-LO140

CONSIDERATIONS FOR AND AGAINST REDUCTION OF FEDERAL PENALTIES FOR POSSESSION OF SMALL AMOUNTS OF MARIHUANA FOR PERSONAL USE., Washington, D.C.: U.S. Government Printing Office (1977)

Presented here is a report of the House Select Committee on Narcotics Abuse and Control of the Ninety-fifth Congress discussing considerations for and against the reduction of federal penalties for possession of small amounts of marijuana for personal use. These hearings were held to obtain testimony from federal, state, and local officials, citizens, and organizations holding widely divergent views on whether Congress should amend the Controlled Substances Act of 1970 to decriminalize the possession of small amounts of marijuana for personal use.

Both proponents and opponents of changing the amendment were given reasonable and equal opportunity to testify. Witnesses included not only federal, state, and local officials, but also medical experts, members of Congress, persons connected with drug abuse treatment programs, representatives of the organized bar and organized medicine,

representatives of jurisdictions which have reduced the penalties for the possession of small amounts of marijuana for personal use, and representatives of farm, veterans, and civil liberties organizations.

The report consists of the facts and opinions, both pro and con, produced by the witnesses and evaluated by the committee in accordance with existing scientific, legal, and sociological research. The committee made a qualitative analysis of the testimony and prepared statements of the witnesses based upon the following categories: federal policy considerations, legal considerations, medical considerations, law enforcement considerations, sociological considerations, public and private sector considerations, the California and Oregon experiences of decriminalization, and summaries of the opinions of opponents and proponents of decriminalization.

The complete title of this is CONSIDERATIONS FOR AND AGAINST THE REDUCTION OF FEDERAL PENALTIES FOR POSSESSION OF SMALL AMOUNTS OF MARIHUANA FOR PERSONAL USE. REPORT OF THE SELECT COMMITTEE ON NARCOTICS ABUSE AND CONTROL, HOUSE OF REPRESENTATIVES. 95TH CONGRESS, 1ST SESSION, MAY 1977. (AAM)

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Other Sociolegal Study. Review: Drug Effects. Review: Drug Use.

UM-78-L0141

THE NATION'S TOUGHEST DRUG LAW: EVALUATING THE NEW YORK EXPERIENCE. FINAL REPORT OF THE JOINT COMMITTEE ON NEW YORK DRUG LAW EVALUATION, Washington, D.C.: U.S. Government Printing Office (March 1978)

In 1973, New York State radically revised its criminal law relating to illegal drug use. The new law prescribed severe and mandatory penalties for heroin offenses at all levels and for most serious offenses involving many other drugs. Shortly after the 1973 law went into effect, the Association of the Bar of the City of New York and the Drug Abuse Council organized a committee to collect data about the 1973 law in a systematic function, to evaluate the law's effectiveness, and to identify any general principles or specific lessons that could be derived from the New York experience. The report presented here contains these findings and recommendations.

The committee reported the following findings: (1) Heroin use in New York City was as widespread in mid-1976 as it had been when the 1973 revision took effect and ample supplies were available. (2) The pattern of stable heroin use between 1973 and 1976 was not appreciably different from the average pattern in other East Coast cities. (3) The new law may have temporarily deterred heroin use, but there is no evidence of sustained reduction in heroin use after 1973. (4) Most evidence suggests that the illegal use of drugs other than narcotics was more widespread in 1976 than in 1973, and that in this respect New York was not unique among East Coast cities. (5) The recidivist sentencing provision of the 1973 law did not significantly deter prior felony offenders from committing additional crimes.

The report suggests that severe difficulties of administration were responsible for the disappointing results of the 1973 drug law. The criminal justice process as a whole did not increase the threat to the offender. The time required to process drug law cases lengthened dramatically. These court delays reduced the threat of the new law.

The committee suggests that the key lesson to be drawn from the experience with the 1973 drug law is that passing a new law is not enough. The efficiency, morale, and capacity of the criminal justice system is even more of a factor in determining whether the law is effectively implemented. The success of laws deterring antisocial behavior must rest upon swift and sure enforcement and a dramatic increase in the odds that violaters will be punished.

Supporting data for the committee's conclusions are presented in statistical graphs and tables. The major provisions of the 1973 New York State Drug Law are appended. (HSRI)

National Institute of Law Enforcement and Criminal Justice

162 pages

KEYWORDS: Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Opiates and Related Agents: heroin. methadone. Stimulants: methamphetamine. Hallucinogens and Related Agents. Sedatives and Hypnotic Agents. Stimulants. Epidemiology: Record-Based Survey. Other Sociolegal Study.

UM-78-L0142

THE NATION'S TOUGHEST DRUG LAW: EVALUATING THE NEW YORK EXPERIENCE. FINAL REPORT OF THE JOINT COMMITTEE ON NEW YORK DRUG LAW EVALUATION. EXECUTIVE SUMMARY. Washington, D.C.: U.S. Government Printing Office (March 1978)

This volume presents a summary of the conclusions of a three-year study of the impact of New York state's strict drug law enacted in 1973. The study was undertaken by the Joint Committee on New York Drug Law Evaluation, a committee established by the Association of the Bar of the City of New York and the Drug Abuse Council to evaluate the effects of the law and make recommendations for successful implementation of future laws dealing with drug abuse.

The committee concluded that in general, the law failed to result in a significant decrease in the abuse of narcotics and other drugs. Lack of enforcement, court congestion, and failure to convict offenders were some of the reasons for failure. The Commission suggests that the key lesson to be drawn from the 1973 drug law is that passing a new law is not enough. What criminal statutes say matters a great deal, but the efficiency, morale, and capacity of the criminal justice system is even more of a factor in determining whether the law is effectively implemented. (HSRI)

National Institute of Law Enforcement and Criminal Justice

48 pages

KEYWORDS: Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Opiates and Related Agents: heroin. methadone. Stimulants: methamphetamine. Hallucinogens and Related Agents. Sedatives and Hypnotic Agents. Stimulants. Epidemiology: Record-Based Survey. Other Sociolegal Study.

21CFR 1301.01

UM-79-L0143

CODE OF FEDERAL REGULATIONS 21: FOOD AND DRUGS, Part 1300 to end, Washington, D.C.: Office of the Federal Register National Archives and Records Service General Services Administration (1 April 1979)

Presented here is a codification of the general and permanent rules published by the Drug Enforcement Administration of the Department of Justice concerning food and drugs. Rules for the following aspects of drug regulation are provided: (1) registration of manufacturers, distributors, and dispensers of controlled substances; (2) labeling and packaging requirements for controlled substances; (3) quotas, both aggregate production and procurement; (4) records and reports of registrants regarding purchases, sales, and inventories; (5) order forms for the procurement of drugs; (6) the issuance, filling, and filing of prescriptions; (7) special exceptions for the manufacture and distribution of controlled substances; (8) disposal of controlled substances; (9) special exempt persons; (10) piperidine reporting and purchaser identification; (11) registration of importers and exporters of controlled substances; (12) importation and exportation of controlled substances; and (13) administrative functions, practices and procedures concerning inspections, protection of researchers and research subjects, enforcement proceedings, hearings, and seizure, forfeiture, and disposition of property.

Special attention is given to the scheduling of controlled substances. For each schedule (I-V) the included drugs are listed alphabetically. Excluded nonnarcotic substances, exempt chemical preparations, and exempt stimulant or depressant compounds are also listed. (HSRI)

188 pages 0 refs

KEYWORDS: Other Sociolegal Study.

UM-71-L0144

THE ROLE OF THE LAW IN DRUG CONTROL, J. Kaplan, Duke Law Journal, v1971 p1065-1104 (1971)

This article sets forth a logical argument for the decriminalization of possession of small amounts of marijuana. The author believes that marijuana is the key drug in present illegal drug use, and until substantial progress is made in controlling it, little real progress can be made in other areas of drug control.

The article has two main sections. In the first part the author discusses the difficulties and potentially dangerous results of legislating laws to prevent conduct which harms only the person committing the act or causes secondary harm, that is, indirect harm to the rest of society. Trying to legislate conduct in order to prevent secondary harm soon becomes more costly to society than beneficial.

In the second part of the article, these general arguments are extended and applied to drug use, particularly marijuana use. The author believes that in spite of some instance where drug use may endanger others, the overwhelming danger in drug use is the danger to the user himself. Six principles of drug control are set forth which must be kept in mind when enacting drug legislation: (1) It is hard, if not impossible, to justify a criminal law which punishes the drug user himself or tries to force a person to take better care of himself. (2) Drugs do people good as well as harm, and any legal measure attempting to reduce drug abuse will cause a corresponding reduction of their beneficial use. (3) An important factor in the success or failure of any method of drug control is the degree to which users want the drug. (4) The technology of drug production and consumption is an important factor in the success or failure of a drug control measure. Many illegal drugs can be produced without difficulty or detection. (5) The social cost of a drug control law can be staggering, especially if it is widely violated. (6) The central position of marijuana in the drug world makes it necessary to enact laws controlling its use as its use serves as a pattern and a starting point for other drug use.

In view of these principles, the author believes that short of a police state, it is impossible to enforce present marijuana laws. He concludes by presenting a plan for a licensing system for marijuana. This system, he admits, will not solve all of the problems caused by marijuana or other, more dangerous illegal drugs, but it will facilitate a beginning toward the application of rational principles of drug control to the generic problem of drug abuse. (HSRI)

141 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: marijuana. Nonbarbiturates: ethanol (ethyl alcohol). Opiates and Related Agents: heroin. Other Electrolytic, Caloric, and Water Balance Agents: cyclamate. Stimulants: amphetamine. caffeine. Antibiotics. Barbiturates Other Sociolegal Study.

UM-77-MO291

HIGH-PRESSURE LIQUID CHROMATOGRAPHIC-MASS SPECTROMETRIC DETERMINATION OF DELTA-9-TETRAHYDROCANNABINOL IN HUMAN PLASMA FOLLOWING MARIJUANA SMOKING, J.L. Valentine; P.J. Bryant; P.L. Gutshall; O.H.M. Gan; P.D. Lovegreen; E.D. Thompson; H.C. Niu, Journal of Pharmaceutical Sciences, v66 n9 p1263-6 (Sep 1977)

This paper describes a method for analyzing delta-9-tetrahydrocannabinol (THC), a psychotomimetic constituent found in marijuana smoke. The method utilizes a high-pressure liquid chromatographic (HPLC) gradient elution program to separate THC from the other major cannabinoids in marijuana smoke. To achieve the sensitivity required to detect THC in human plasma following marijuana smoking, a mass spectrometric quantification method was developed to analyze the HPLC eluant. To 1 ml of human plasma was added a known amount of internal standard, trideuterated THC. This stable isotope provided a check on extraction efficiency, a marker for ultraviolet monitoring of the HPLC effluent and subsequent collection, and a convenient mass for mass spectrometric quantification.

An ion-counting technique was used in conjunction with the peak matching accessory of the mass spectrometer to provide for a rapid comparison between molecular ions of THC and the internal standard. The method was linear, accurate, and reproducible over the concentration range expected for THC in plasma following marijuana smoking, with 2.5 ng/ml being the lower practical limit of detection.

Plasma from eleven male subjects was analyzed by the method at various intervals up to twenty-four hours after the smoking of a marijuana cigarette containing 10.8 mg of THC. Results demonstrated that levels of THC could be determined accurately in the plasma of marijuana smokers in the one-hour period following smoking.

This method, the authors conclude, is applicable to the study of other drug entities in biological fluids wherever low detection levels are required along with precise specificity. However, for such determination, the stable isotopic form of the drug is needed. (JAM)

12 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol*. Confirmatory/Quantitative Drug Analysis: Other Techniques.

UM-78-MO292

DRUG DETECTION IN URINE BY CHEMICAL IONIZATION MASS SPECTROMETRY, R. Saferstein; J.J. Manura; P.K. De, Journal of Forensic Sciences, v23 n1 p29-36 (Jan 1978)

Described here is a study concerned with determining the sensitivity of isobutane chemical ionization mass spectrometry (CIMS) for the detection of commmon drugs of abuse in urine. A simple and rapid extraction procedure was employed for removing drugs from a 10 ml sample of urine. The extract was subjected to chemical ionization mass spectral analysis via the direct probe. Limits of detection for the drugs studied in this manner were determined. The drugs studied included amobarbital, butabarbital, cocaine, glutethimide, meprobamate, methadone, methaqualone, pentobarbital, phenobarbital, and secobarbital. In general, the detection limit for most of these drugs was less than 0.5 micrograms per ml, except for phenobarbital, which was detectable at 3 micrograms per ml. Except for cocaine, and to a lesser extent, ecgonine, the drugs studied yielded sensitivities sufficient to detect therapeutic concentrations in urine.

Urine samples were obtained from normal healthy adults and analyzed to determine whether normal urinary constituents could yield interferences coinciding with chemical ionization of drugs. The results indicated that since the concentration of drugs encountered in overdose cases is generally significantly greater than any compound normally present in biological extracts, the problem of interfering ions is not a major concern. In conclusion, the sensitivity of the mass spectrometer combined with chemical ionization's ability to assay urine rapidly without prior chromatographic separation makes the technique extremely useful for the tentative identification of drugs and drug metabolites. (HSRI)

17 refs

KEYWORDS: General Drug Screening: Other Techniques.

UM-77-MO293

DRUG ABUSE PROFICIENCY TESTING, G.O. Guerrant; C.T. Hall, Clinical Toxicology, v10 n2 p209-19 (1977)

This paper describes the extensive drug abuse proficiency testing program of the Center for Disease Control in Atlanta. The history, objectives, and methods of the program are described. The paper evaluates the methods and results of the proficiency testing surveys from the first one in January 1972 to the most recent 1975 surveys. During this time period a significant improvement in the detection of drugs was observed in the participating laboratories. Some of the improvement may be due to advances in technology, as is probably the case with improvement in the detection of morphine and methadone. The improvement in the determination of methamphetamine within three surveys over six months can clearly be attributed to proficiency testing. In drug screening for cocaine abuse, the poor results in proficiency testing for the detection of the primary metabolite, benzoylecgonine, have clearly demonstrated that laboratories are not proficient in this screening. Further work is required in this area. (AAM)

10 refs

KEYWORDS: Proficiency Testing.

UM-77-MO294

PROFICIENCY ASSESSMENT PROGRAMS IN TOXICOLOGY, C.B. Walberg, Journal of Analytical Toxicology, v1 p105-8 (May-Jun 1977)

The current state of proficiency testing programs for clinical laboratories is discussed with special emphasis on those programs related to toxicology. The paper discusses the need for such programs, the reasons for their creation, the types of programs offered, and their administration. Federal and state laws pertaining to proficiency testing are also briefly described.

The demand for accurate and meaningful toxicologic analysis is ever increasing. To meet this demand there is a definite need for increasing the ability of the analyst and the efficiency of the laboratory. Clinical toxicology has now achieved the stature of a

separate and necessary laboratory function on an equal par with other disciplines of clinical laboratory technology. The author feels that the time has come for the establishment of a national organization of clinical toxicologists with its own program for education, certification, and review. Such an organization would go far in setting up its own committees to standardize methods, to work for appropriate legislation in certification and regulation of laboratories, to establish proficiency testing, to act as an organ for the dissemination of relevant information, and to uniformly review the credentials of personnel and proficiency of the laboratories. (HSRI)

2 refs

KEYWORDS: Review.

UM-78-MO295

HOMOGENEOUS ENZYME IMMUNOASSAY FOR CANNABINOIDS IN URINE, R. Rodgers; C.P. Crowl; W.M. Eimstad; M.W. Hu; J.K. Kam; R.C. Ronald; G.L. Rowley; E.F. Ullman, Clinical Chemistry, v24 n1 p95-100 (1978)

This paper describes a homogeneous enzyme immunoassay for measurement of cannabinoid metabolites and delta-9-THC-I in urine. Malate dehydrogenase from pig heart mitochondria was labeled with a derivative of THC-I. The compound used to calibrate the assay was the THC-I metabolite 11-nor-delta-9-THC-9-carboxylic acid (THC--II). With 15 micrograms of THC-II per liter of urine as the cutoff concentration, the assay can detect 25 micrograms of THC-II per liter with greater than 95% confidence.

A positive response was obtained for urine specimens assayed within thirty minutes after exposure to cannabinoids. Peak excretions of cannabinoids in clinical specimens occur from two to six hours after exposure. However, urinary cannabinoid excretion can remain high for more than twenty-four hours. It was also observed that frequent users of delta-9-THC (several exposures per week) have basal values for metabolites in their urine that exceed the peak values attained by relatively infrequent users. These data, and the fact that the period of intoxication lasts only from one to four hours, indicate that assay of delta-9-THC metabolites in urine is useful as an indicator of cannabis use but not as an indicator of intoxication. Quite possibly, concentrations of delta-9-THC and its metabolites in serum or saliva may more reliably indicate intoxication. Nevertheless, the method described as applied to cannabinoids combines rapid measurement with ease of sample manipulation, making it a valuable tool for toxicological laboratories. (JAM)

13 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabidiol*, cannabinol*, delta-9-tetrahydrocannabinol*, Specific Drug Screening: Immunoassay.

UM-76-MO296

METHODOLOGICAL PROBLEMS INHERENT IN THE DETERMINATION OF CERTAIN DRUGS IN BIOLOGICAL FLUIDS, J. de Graeve; P. Kremers; J. Van Cantfort; C. Heusghem, Drug Interference and Drug Measurement in Clinical Chemistry, G. Seist; D.S. Young, eds., Third International Colloquium on Prospective Biology, Pont-a-Mousson, 6-10 Oct. 1975 (1976)

The purpose of this paper is to indicate some of the difficulties which are often encountered in analytical methods for the quantification of drugs in plasma. These difficulties are illustrated in a discussion of the determination of the pharmacokinetic parameters of disopyramide and papaverine. Extraction of a drug and its metabolites from biological fluids presents a major problem in that the procedure should have as much selectivity and efficiency of extraction as possible. Furthermore, the procedure must remain simple and fast enough to be performed routinely in a laboratory and must be able to be utilized with small samples of blood. In this connection liquid-liquid extraction, salt-solvent pairs, and resins are discussed. Further problems include impurities in solvents and problems in separation and recovery procedures which can cause errors in analytical techniques.

In view of these problems the authors make two major conclusions: (1) It is essential to check carefully those methods that have limited specificity. No compounds, endogenous or exogenous, should interfere with the measurements, as can occur readily when using ultraviolet absorption or fluorescence with thin-layer chromatography assays and methods using total radioactivity measurements after administration of labelled drugs. (2) It is necessary to use the most sensitive and specific analytical techniques possible. Gas-liquid chromatography on open tubular glass capillary columns, for example, must be used

when using a flame ionization detector. Other techniques with high specificity can be used to validate other less specific analytical methods. Note: C. Heusghem; G. Olive; J.R. Royer, co-eds. (HSRI)

21 refs

KEYWORDS: Anti-Arrhythmia Agents: disopyramide. Vasodilating Agents: papaverine. Review: Drug Analysis Methodology.

UM-76-MO297

QUALITY CONTROL OF DRUG ESTIMATIONS, Drug Interference and Drug Measurement in Clinical Chemistry, A. Richens, G. Seist; D.S. Young, eds., p93-7, Basel, Switzerland: S. Karger AG. Third International Colloquium on Prospective Biology, Pont-a-Mousson, 6-10 Oct. 1975 (1976)

Many clinical chemistry and clinical pharmacology laboratories have set up methods for measurement of drugs that possess a narrow therapeutic ratio. However, very few laboratories have accurate methods for estimating antiepileptic drugs. This paper reports a quality control scheme for three antiepileptic drugs--phenytoin, phenobarbitone, and primidone. The quality control specimens were prepared by pooling serum from epileptic patients with high and low concentrations. The most useful function of this scheme has been to compare the accuracy of the various types of analysis, for example thin-layer and gas chromatography.

From the results of studies comparing these techniques, it appears that gas chromatography involving the use of a methylating agent has the most accurate results in estimating phenytoin and phenobarbitone, while spectrophotometric techniques have proved the most inaccurate.

The author concludes that quality control is essential if confidence is to be placed in the results of drug estimations in body fluids. Quality control of estimations of new drug undergoing controlled clinical trial is equally important. This responsibility should lie with the pharmaceutical company that is marketing the new drug. If they are themselves unable or unwilling to provide such a quality program, they should ensure that the laboratories estimating the new compound are doing so with precision by providing suitable quality control samples. Note: C. Heusghem; G. Olive; J.R. Royer, co-eds. (JAM)

14 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital. phenytoin. primidone. Barbiturates: phenobarbital. Review.

UM-76-MO298

GAS-LIQUID CHROMATOGRAPHY FOR THE ANALYSIS OF DRUGS OF ABUSE, D.T. Forman, Drug Interference and Drug Measurement in Clinical Chemistry, G. Seist; D.S. Young, eds., p136-45, Third International Colloquium on Prospective Biology, Pont-a-Mousson, 6-10 Oct. 1975 (1976)

Numerous procedures have been developed for the determination of drugs of abuse in serum and urine. This paper describes an analytical system for identifying and quantitating barbiturates, glutethimide, diazepam, meprobamate, methaqualone, methadone, diphenylhydantoin, primidone, morphine, amphetamine, and methamphetamine. This method involves several modifications of standard techniques in ultraviolet spectrophotometry (UV) and gas chromatography.

The procedure involves separation of the drugs from biological specimens by solvent extraction with chloroform after adding an internal standard together with either a buffer of pH 4.1 or 8.8. The drugs in the extract are concentrated by evaporation of the organic layer and identified and quantitated by ultraviolet spectrometry or gas-liquid chromatography (GLC) using a six-foot column containing 3% OV-17. GLC analysis times are kept below fifteen minutes by using temperature programming which allows good separations of drugs of varying volatilities.

In cases where the drug in question is specifically known, UV spectrophotometry may suffice to rapidly identify and quantify the substance. In cases of drugs with relatively weak UV absorption, GLC is the technique of choice.

Multiple drug intoxications require the application of GLC to identify and quantitate individual compounds. All calculations are based on peak heights. Losses of drugs during extraction and evaporation steps are compensated for by the use of internal standards. Actual extraction efficiencies of drugs from serum or urine range from 70 to 100%. The use of standards carried throughout the entire procedure provides reliable quantitation. Reproducibility of the GLC technique is approximately 5%. Note: C. Heusghem; G. Olive; J.B. Royer, co-eds. (AAM)

5 refs

KEYWORDS: General Drug Screening: Gas Chromatography. General Drug Screening: Systems.

UM-73-M0299

NEW METHODS FOR LABORATORY STANDARDIZATION, R.G. Hoffman, Reference Values in Human Chemistry. Effects of Analytical and Individual Variations, Food Intake, Drugs and Toxics, G. Seist, ed., p80-87, 2nd International Colloquium "Automatisation and Prospective Biology", Pont-a-Mousson, 10-14 Oct. 1972, Basel, Switzerland: S. Karger AG (1973)

This paper discusses problems of laboratory standardization and suggests recommendations for improvement. One problem is that even with widespread use of automated equipment throughout the world, surveys of laboratories show that there are differences among laboratories using the same methods and equipment. The author suggests that it is necessary to define and estimate for each laboratory standard clinical reference levels just as physical scientists do for many base units of measurement.

To become acquainted with the new clinical levels, laboratories should not estimate them solely from specimens drawn in their own laboratories. Rather they should study the new methods in small groups of two or three laboratories per group.

A few results from one study are presented by the author indicating that there is a very good correlation among tests from healthy girls and tests of patients. This indicates that much of the information needed to clinically standardize laboratories can be obtained from routine patients' tests.

The poor correlation between tests of actual cases and of reference samples indicates that this is an area that deserves more study. If laboratories attempt to standardize solely with reference samples, more harm than good could result in some instances.

It is almost useless to define quantities of the type given here unless a permanent, international organization is responsible for them. The author believes that at the present time, only one organization is suitable for this, namely the International Bureau of Standards. Steps should be taken to devise conceptually defined standards for clinical chemistry and to give the International Bureau of Standards responsibility for them. (AAM)

4 refs

KEYWORDS: Review.

UM-78-M0300

A MICROMETHOD FOR THE ISOLATION OF DRUGS FROM BLOOD USING AMBERLITE XAD-2, H.J. Schlicht; H.P. Gelbke, Zeitschrift fur Rechtsmedizin, v81 n1 p25-30 (1978)

The extraction of drugs from small blood samples (1 ml or less) for subsequent quantitative determination is described. Isolation was carried out by adsorption of the drugs to Amberlite XAD-2 resin utilizing a batch procedure that enabled the simultaneous extraction of up to 200 samples in approximately five hours. A new desorption technique yielded extracts of high purity that could be used directly for gas chromatographic or radioimmunological determinations, even if hemolyzed or putrid blood was to be examined.

The following twenty-six substances were quantitated after addition to postmortem blood specimens at concentrations of 1-10 mg/ml: tilidine, diphenhydramine, dibenzepine, imipramine, chlorpromazine, amphetamine, pentazocine, phenacetin, methaqualone, meprobamate, parathion, diazepam, digoxin, B-methyldigoxin, carbromal, glutethimide, amobarbital, pentobarbital, cyclobarbital, phenobarbital, diphenylhydantoin, carbutamide, tolbutamide, glycodiazin, tolazamide, and chlorpropamide. Recoveries of 60-100% were achieved. The reproducibility of the procedure was satisfactory as demonstrated by coefficients of variation of 3.7-8%.

The method presented here is time-saving and enables the isolation of a wide range of drugs from 1 ml or less of blood with high recovery and purity. It is a potentially valuable tool for the daily routine work of clinical or forensic toxicologists. (JAM)

18 refs

KEYWORDS: General Drug Screening: Other Techniques.

UM-78-M0301

SIMULTANEOUS TRACE ANALYSIS OF NITROUS OXIDE AND HALOTHANE IN AIR, L.A. Salamonsen; W.J. Cole; R.F. Salamonsen, British Journal of Anaesthesia, v50 n3 p221-7 (Mar 1978)

A gas chromatographic method for the simultaneous analysis of halothane and nitrous oxide in operating theatre atmospheres has been developed and evaluated. The flame ionization detector is suitable for the quantitative analysis of halothane in concentrations approaching one part per million. The frequency-modulated electron capture detector is highly sensitive to nitrous oxide; however, it was found to be nonlinear over the range 25-1000 ppm.

The overall reproducibility of the gas chromatographic method based on the dynamic technique of standard prepartion is approximately 4%. Effective exposure of personnel to pollutant anesthetics is assessed by the analysis of end-expired gas. (JA)

10 refs

KEYWORDS: Gases: nitrous oxide. General Anesthetics: halothane. General Anesthetics: nitrous oxide. Hallucinogens and Related Agents: nitrous oxide. Confirmatory/ Quantitative Drug Analysis: Gas Chromatography.

UM-78-M0302

PHOTOCHEMICAL DETECTION IN HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY AND ITS APPLICATION TO CANNABINOID ANALYSIS, P.J. Twitchett; P.L. Williams; A.C. Moffat, Journal of Chromatography, v149 p683-91 (1978)

A novel technique of on-line photochemical derivation is described that can enhance considerably both the sensitivity and specificity of detection in high-performance liquid chromatography (HPLC). Material eluting from the column is erradiated with a high flux of UV light, which may induce a reaction to form fluorescent or highly UV-absorbing products. The irradiated eluent then passes into a suitable detector. The photochemical reactor has a negligible effect on resolution, and reaction is achieved in one to five seconds.

An example of the use of this technique is in the detection of cannabinol (CBN), a component of cannabis, which is converted into a highly fluorescent compound on irradiation with UV light. Thus, if a sample containing CBN is chromatographed and the column eluent irradiated, CBN can be detected (as the fluorescent photoproduct) with a sensitivity of less than 1 ng. If the chromatogram is then repeated without UV irradiation, only naturally fluorescent products are detected. A comparison of the two chromatograms allows these to be eliminated and leads to a very high specificity for the method.

This approach is being developed as the basis of a rapid, sensitive, and specific method for the detection of cannabinoids in body fluids. It is expected that photochemical derivations will extend the use of HPLC to many substances that cannot be satisfactorily detected at present. (JA)

13 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabinol. Cannabis Sativa L. and Related Agents. Specific Drug Screening: Other Techniques.

UM-77-M0303

DETECTION OF DRUGS OF ABUSE IN BIOLOGICAL FLUIDS, C.W. Gorodetzky, Handbook of Experimental Pharmacology, v45 pt1 p319-409 (1977)

To assist in the diagnosis of medical emergencies involving possible drug overdose and to aid in the determination of cause of death, toxicology laboratories frequently

perform qualitative and sometimes quantitative analyses of body fluids and tissues for drugs. The major emphasis in this review is on qualitative screening methods for the detection of drugs of abuse. It examines the general principles and concepts of their use and interpretation, provides a comprehensive review of most commonly used methods, and evaluates the validity of these methods to detect drugs or their metabolites following ingestion by humans.

Some of the methods discussed include thin-layer chromatography; gas chromatography; fluorometry; immunoassays, including radioimmunoassay, homogeneous enzyme immunoassay, hemagglutination-inhibition immunoassay, and the free radical assay technique; paper chromotography; colorimetry; ultraviolet spectrophotometry; microcrystallography; mass spectrometry; gas chromatography/mass spectrometry; infrared spectrophotometry; and high-pressure liquid chromatography. The sensitivity, specificity, and socioeconomic parameters are discussed for each method. The validity of each method is discussed for narcotic analgesics and antagonists (especially heroin and morphine), sedative/hypnotics, stimulants, and other drugs such as LSD and quinine. (HSRI)

350 refs

KEYWORDS: Review: Drug Analysis Methodology.

UM-77-M0304

FALSE-POSITIVE FOR (+)-METHAMPHETAMINE, M.D. Solomon; J.A. Wright, Clinical Chemistry, v23 n8 p1504 (Aug 1977)

This letter-to-the-editor describes a case in which the user of a Vick's Inhaler was suspected of ingesting the widely abused anorexigenic and stimulant (+)-methamphetamine. A male subject in a drug surveillance program whose urine was repeatedly positive for methamphetamine vehemently denied any use of the drug. However, he did claim heavy use of the Inhaler, a product containing (-) methamphetamine, for a sinus disorder.

Analysis of two urine speciments showed that both were positive for (-) methamphetamine with no detectable (+) isomer. The implications of this finding are considerable with regard to forensic specimens. In the absence of an isomer identification, a defendent with methamphetamine in his urine could claim use of the legitimate (-) isomer even if he was actually using contraband (+) or racemic methamphetamine. (HSRI)

3 refs

KEYWORDS: Stimulants: methamphetamine. Specific Drug Screening: Gas Chromatography.

UM-77-M0305

HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC ANALYSIS OF METHADONE HYDROCHLORIDE ORAL SOLUTION, T.H. Beasley; H.W. Ziegler, Journal of Pharmaceutical Sciences, v66 n12 p1749-50 (Dec 1977)

Methadone hydrochloride is used widely in drug maintenance treatment programs, therefore, a rapid and simple analysis of methadone hydrochloride in a proprietary dosage form is desirable. This study describes such a direct and rapid high-performance liquid chromatographic assay for the drug in a flavored oral solution dosage form. A syrup sample, one part diluted with three parts of water, is introduced onto a column packet with octadecylsilane bonded on 10 um porous silica gel (reversed phase). A formic acid-ammonium formate-buffered mobile phase is linear programmed with acetonitrile. The absorbance is monitored continuously at 280 or 254 nm, using a flowthrough, UV, double-beam photometer. An aqueous methadone hydrochloride solution is used for external standardization. The relative standard deviation was not more than 1.0%. Drug recovery from a syrup base was better than 99.8%.

This method is a unique application on direct chromatography on a sample with little or no preparation, extraction, or derivatization. This technique may be applicable to other dosage forms such as cough-cold preparations. (JAM)

5 refs

KEYWORDS: Opiates and Related Agents: methadone. Confirmatory/Quantitative Drug Analysis: Other Techniques.

UM-78-M0306

IDENTIFICATION OF A STREET DRUG AS N-ETHYL-1-PHENYLCYCLOHEXYLAMINE, A PHENCYCLIDINE ANALOG, K. Bailey, Journal of Pharmaceutical Sciences, v67 n6 p885-6 (Jun 1978)

This paper reports the identification of N-ethyl-1-phenylcyclohexylamine (IV) also known as cyclohexamine, PCE, CL-45 and CI 400, in a street sample. This compound is said to have been available in California since about 1969, but information and descriptions suitable for identification have not been published.

Described here are spectroscopic and chromatographic properties of authentic material useful for its identification. (JAM)

14 refs

KEYWORDS: Hallucinogens and Related Agents: cyclohexamine (PCE). Specific Drug Screening: Other Techniques.

UM-77-M0307

THE IDENTIFICATION OF ORGANIC COMPOUNDS USING SPECTROSCOPIC INTERPRETATION AND A COMPUTER BANK OF MOLECULAR STRUCTURES STORED IN THE FORM OF THEIR WISWESSER LINE NOTATIONS, R.E. Ardrey; C. Brown, Journal of the Forensic Science Society, v17 n1 p63-71 (Jan 1977)

This paper describes a method of identification devised at Home Office Central Research Establishment (HOCRE) involving the searching of a data base of substructural information pertaining to compounds which are considered relevant but whose mass spectra are not readily available (for example, new drugs and metabolites). This system of identification enables information to be used which has been obtained not only from the mass spectrum, but also from supplementary spectroscopic evidence.

The system uses the Wiswesser Line Notation, which makes available information such as molecular weight, information on atoms with characteristic isotopic distributions, and substructural information. The present data base contains approximately 4,000 compounds of toxicological interest.

This system was not designed to provide an unambiguous identification in every case but rather to indicate possible solutions to the spectroscopist. In addition, the data base can generate a ring index, pick out compounds containing specific chemical moieties, and recognize synonymous pharmaceutical names, especially the correspondence of manufacturers' code names to eventual trademarks.

Some of the advantages of this system are the ability to use data from inaccessible compounds, the flexibility of the size of file, and the ability to use structural information from any source. Finally, the time required to enter a new record is very brief and no spectroscopic work is involved. (HSRI)

13 refs

KEYWORDS: General Drug Screening: Systems.

UM-77-M0308

EXTRACTION OF DRUGS FROM WHOLE BLOOD BY GEL FILTRATION, M.J. Malcolm, Journal of the Forensic Science Society, v17 n1 p57-62 (Jan 1977)

An ideal broad-spectrum screening procedure should have the following characteristics: it should isolate all compounds of toxicological interest from blood protein; it should provide yields of these compounds sufficient to permit their detection at significant levels; and it should use mild conditions in order to minimize destruction of drugs and tissue components. Earlier reports on the analysis of syringe washings and tissue extracts by the use of Sephadex gels suggested the possibility of their application in such a screening procedure. This paper reports the results of a study of the extraction of drugs from whole blood samples in order to determine the ability of a Sephadex column to isolate these drugs. Blood samples obtained from cases in which one or more drugs had been ingested were analyzed quantitatively following extraction by the Sephadex column and another selected extraction procedure. Yields obtained by these parallel determinations are reported.

Gel filtration, the author concludes, is capable of separating a wide range of drugs from blood protein, thus providing an extraction procedure which is potentially more exhaustive than any presently available. (JAM)

6 refs

KEYWORDS: General Drug Screening: Other Techniques.

UM-77-M0309

THE IMMUNOLOGICAL ASSAY OF DRUGS, V.P. Butler, Pharmacological Reviews, v29 n2 p103-84 (Jun 1977)

This review deals with the general principles of drug immunoassays; a description of each of the individual steps involved in the development of a drug immunoassay; a general consideration of the advantages, limitations, and applications of drug immunoassay procedures; and an individual consideration of specific drug immunoassay methods currently available for twenty-nine drug groups such as antibiotics, anticoagulants, bronchodilators, diuretics, narcotic antagonists, and sedatives and hypnotics. Immunoassay methods discussed include radioimmunoassay, enzyme immunoassay, spin label immunoassay, agglutination inhibition, viroimmunoassay, immunoradiometric assay, and other immunoassay methods. (HSRI)

738 refs

KEYWORDS: Review: Drug Analysis Methodology.

UM-77-M0310

THE DECOMPOSITION OF ACIDIC AND NEUTRAL CANNABINOIDS IN ORGANIC SOLVENTS, R.N. Smith; C.G. Vaughan, Journal of Pharmacy and Pharmacology, v29 n5 p286-90 (May 1977)

High-pressure liquid chromatography was used to study (a) the relative efficiencies of methanol, chloroform, light petroleum (B.P. 40-60 degrees) and methanol-chloroform (9:1) for extracting neutral and acidic cannabinoids from cannabis resin; (b) the decomposition patterns of the resulting solutions under various storage conditions; and (c) the cannabinoid profile of a cross section through a block of cannabis resin.

The results show that (a) methanol is the most effective extracting solvent of those tested; (b) acidic cannabinoids in solution decompose in darkness by varying amounts depending on the temperature, solvent, storage time, and particular cannabinoid; (c) neutral cannabinoids in solution are relatively stable in darkness; (d) daylight causes appreciable decomposition of both acidic and neutral cannabinoids in solution; and (e) the cannabinoid profile of resin is complex with lower levels of acidic material in the outer layers. (HSRI)

9 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabichromene. cannabichromenic acid. cannabidiol. cannabidiolic acid. cannabigerol. cannabigerolic acid. cannabinol. cannabinolic acid. delta-1-tetrahydrocannabinolic acid. delta-9-tetrahydrocannabinol. Metabolites of Drugs and Other Agents: delta-1-tetrahydrocannabinolic acid. Specific Drug Screening: Other Techniques.

UM-78-M0311

MARIHUANA METABOLITES IN THE URINE OF MAN, VIII. IDENTIFICATION AND QUANTITATION OF DELTA-9-TETRAHYDROCANNABINOL BY THIN-LAYER CHROMATOGRAPHY AND HIGH-PRESSURE LIQUID CHROMATOGRAPHY, S.L. Kanter; L.E. Hollister; K.O. Loeffler, Journal of Chromatography, v150 n1 p233-7 (1978)

The study attempted to combine the use of high-pressure liquid chromatography (HPLC) with the use of thin-layer chromatography (TLC) for the detection and quantification of THC or other cannabis metabolites in urine. Three young men were given single oral doses of 30 mg delta-9-THC. Urine specimens were collected during a twelve to twenty-four hour period prior to administration of the drug and at intervals of two, six, twelve, and twenty-four hours after. Delta-9-THC was detected in urine by TLC on silica gel G plates using 85:15 light petroleum diethyl ether (30-60 degrees) as the solvent. Delta-9-THC was then quantitated by high-pressure liquid chromatography on Spherisorb silica using 97:3 hexane-3% methanol in dichloromethane (97:3) at a flow rate of 1.6 ml/

min. for elution. Using this technique, approximately .003-.008% of delta-9-THC was recovered from urine after administration to the human volunteers.

Peaks coincident with the retention of THC were detected in the extracts of the zero-to-two-hour and two-to-six-hour postdrug urine samples. Equivalent peaks were not found in the predrug, the six-to-twelve-hour postdrug, and the twelve-to-twenty-four-hour postdrug urine samples.

The authors conclude that the use of HPLC is of great potential value in the detection of minute amounts of delta-9-THC in urine after social use. Further research is needed. (HSRI)

12 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol*. Confirmatory/Quantitative Drug Analysis: Other Techniques. Specific Drug Screening: Other Techniques.

UM-78-MO312

GAS-LIQUID CHROMATOGRAPHIC METHOD FOR THE ROUTINE ESTIMATION OF DISOPYRAMIDE IN PLASMA OR SERUM, A. Johnston; D. McHaffie, Journal of Chromatography, v152 n2 p501-6 (1978)

This paper describes a rapid, sensitive, and specific gas-liquid chromatographic method for the routine monitoring of plasma concentrations of the antiarrhythmic compound disopyramide. The procedure involves extraction of the drug from alkaline plasma into ether, purification of the extract, and gas chromatographic analysis using OV-101 liquid phase and flame ionization detection.

The results demonstrate the accuracy and reproducibility of the method. Replicate samples in the range 0.5 to 20 mg/ml gave coefficients of variation of less than 4%. In this study no drug being concurrently administered with disopyramide was found to interfere with the assay, the drugs tested including clofibrate, diazepam, digoxin, frusemide, salbutamol, and warfarin. Only one compound, di-2-ethylhexylphthalate, has been encountered that interferes with the assay. This compound is present in human blood stored in transfusion bags, therefore caution must be used when interpreting disopyramide levels obtained in patients who have recently received blood transfusions.

Contrary to a previous report, the present report shows that delay in separating plasma from erythrocytes does not affect disopyramide levels in plasma. (JAM)

14 refs

KEYWORDS: Anti-Arrhythmia Agents: disopyramide*. Confirmatory/Quantitative Drug Analysis: Gas Chromatography.

UM-78-MO313

SIMULTANEOUS GAS CHROMATOGRAPHIC DETERMINATION OF DIPHENYLHYDANTOIN, CARBAMAZEPINE (TEGRETOL), PHENOBARBITAL AND PRIMIDONE IN PRESENCE OF KEMADRIN (PROCYCLIDINE) AND PROLIXIN (FLUPHENAZINE) IN PLASMA OF PSYCHIATRIC PATIENTS, R. Varma, Journal of Chromatography, v155 n1 p182-6 (1978)

This paper describes a simple, rapid, and sensitive gas chromatographic procedure for simultaneous determination of the anticonvulsants diphenylhydantoin, carbamazepine, phenobarbital, and primidone in the presence of kemadrin and prolixin in human plasma as their methylated derivatives. This procedure overcomes the interference between primidone and kemadrin (which causes the two drugs to elute together as one peak) since primidone elutes just before kemadrin. In this method, the blood sample is extracted with methylene chloride and separated on a glass column packed with 3% OV-17 on chromosorb W HP using nitrogen as the carrier gas.

A recovery of 98-100% was observed. The limit of detection was approximately 0.5 micrograms/ml. This procedure is highly reproducible with variations from 0.5-1.3 micrograms/ml. No analytical interference was observed in psychiatric epileptic patients who are on prolixin therapy while also receiving diphenylhydantoin, carbamazepine, phenobarbital, and primidone.

An internal quality control program for the analysis of the four anticonvulsants is also described. (HSRI)

14 refs

KEYWORDS: Analgesics and Antipyretics: carbamazepine. Anti-Parkinsonism Agents: procyclidine. Anticonvulsants (Anti-Epileptics): carbamazepine. phenobarbital. phenytoin. primidone. Barbiturates: phenobarbital. Major Tranquilizers (Antipsychotics and Neuroleptics): fluphenazine. Parasympatholytic (Cholinergic Blocking) Agents: procyclidine. Confirmatory/Quantitative Drug Analysis: Gas Chromatography.

UM-79-MO314

THE SCREENING AND QUANTITATION OF DIAZEPAM, FLURAZEPAM, CHLORDIAZEPOXIDE, AND THEIR METABOLITES IN BLOOD AND PLASMA BY ELECTRON-CAPTURE GAS CHROMATOGRAPHY AND HIGH-PRESSURE LIQUID CHROMATOGRAPHY, M.A. Peat; L. Kopjak, Journal of Forensic Sciences, v24 n1 p46-54 (Jan 1979)

This report describes an analytical procedure involving both GLC-ECD (gas-liquid chromatography with electron-capture detection) and HPLC (high-pressure liquid chromatography) that can be used to identify, quantitate, and confirm the benzodiazepines (with the exeption of clonazepam) and their major metabolites in small-volume plasma and blood samples.

The screening method involves direct solvent extraction of a buffered sample followed by GLC-ECD analysis of a small aliquot of the unconcentrated solvent. The blood or plasma is then extracted with additional solvent, which is separated and concentrated. The residue is examined by HPLC to confirm the presence of the benzodiazepines. Quantitation is accomplished in either method by using flunitrazepam as an internal standard. The GLC-ECD method is used for diazepam, desmethyldiazepam, flurazepam, and desalkylflurazepam, and HPLC for chlordiazepoxide and desmethylchlordiazepoxide. Although the analytical procedure is described for 1 ml of whole blood or plasma in this paper, the GLC-ECD screening procedure can be applied to sample volumes as low as 50 micrograms if necessary. Use in these methods has resulted in an increase in detection of these drugs in both clinical and forensic toxicology cases. (AAM)

12 refs

KEYWORDS: Metabolites of Drugs and Other Agents: desmethylchlordiazepoxide. N-desme[illegible]diazepam. N-1-desalkylflurazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. N-desmethyldiazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: flurazepam. Confirmatory/Quantitative Drug Analysis: Other Techniques. Specific Drug Screening: Other Techniques.

UM-74-MO315

THE DETECTION OF SEDATIVE/HYPNOTIC DRUGS IN THE IMPAIRED DRIVER, J.M. White; M.H. Graves, Journal of Chromatographic Science, v12 n5 p219-24 (May 1974)

Reported here is the analytical procedure used in Orange County, California to screen all driving cases in which alcohol is absent or is present at levels of less than 0.10%. This procedure results in the detection of a number of commonly used compounds from a limited sample size (5 ml) within a reasonable amount of analytical time. All positive findings are confirmed with a second aliquot of the original sample. The procedure uses ultraviolet spectrophotometry and thin-layer chromatography.

The paper also describes the results of a study in which 705 blood samples from impaired drivers were screened using the analytical methods described. A higher incidence of drugs was found in those cases without alcohol. The incidence (18%) of drugs found in blood samples with alcohol levels below 0.10% supports the expansion of an analytical drug program to include these samples. In 29% of the drug-positive cases, a drug other than barbiturate was present.

Results of the study indicate changing patterns of drug use. Methaqualone, found frequently in early 1973, was encountered only twice in 1974. Another noticeable trend was the decline in barbiturates found, accompanied by an increase in other sedative/hypnotic drugs. Benzodiazepine use has also varied. In early 1973 diazepam was the only benzodiazepine encountered. The introduction of the phenobarbital/chlordiazepoxide preparation in late 1973 was coincident with an increase in blood samples containing chlordiazepoxide alone. (HSRI)

7 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital. Barbiturates: phenobarbital. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. clorazepate. diazepam. oxazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethchlorvynol. flurazepam. methaqualone. Barbiturates. Sedatives and Hypnotic Agents. Epidemiology: Analysis of Driver Body Fluids for Drugs. Specific Drug Screening: Other Techniques.

UM-78-MO316

COMBINED HIGH-PRESSURE LIQUID CHROMATOGRAPHY AND RADIOIMMUNOASSAY METHOD FOR THE QUANTITATION OF DELTA-9-TETRAHYDROCANNABINOL AND SOME OF ITS METABOLITES IN HUMAN PLASMA, P.L. Williams; A.C. Moffat; L.J. King, Journal of Chromatography, v155 n2 p273-83 (1978)

A high-pressure liquid chromatography-radioimmunoassay (HPLC-RIA) method for the measurement of cannabinoid levels in plasma is described. This method is capable of quantifying 0.1 ng of a cannabinoid in 1 ml of plasma. The experimental procedure consists of an initial separation of cannabinoids in a plasma extract by HPLC followed by collection of the HPLC eluate and radioimmunoassay. A chromatogram consisting of the cross-reacting cannabinoids in plasma can then be constructed. The plasma concentrations of cannabinoids with retention equivalent to those of delta-9-THC, cannabinol, and monohydroxylated metabolites were measured by this technique.

In conclusion, HPLC-RIA provides a convenient method for separating, identifying, and quantifying THC and some of its metabolites in plasma. It has the advantage over previously reported methods of needing only a small volume of sample to quantify simultaneously THC and some of its metabolites, making this method a potentially valuable tool for forensic examiners. (JAM)

20 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabidiol. cannabinol*. delta-9-tetrahydrocannabinol*. Cannabis Sativa L. and Related Agents. Confirmatory/Quantitative Drug Analysis: Other Techniques.

UM-78-MO317

SIMULTANEOUS DETECTION AND QUANTITATION OF DRUGS COMMONLY INVOLVED IN SELF-ADMINISTERED OVERDOSES, A.T. Howarth; G. Clegg, Clinical Chemistry, v24 n5 p804-7 (May 1978)

This paper describes a simple and inexpensive system for simultaneous detection and quantitation of tricyclic antidepressants, benzodiazepines, and other tranquilizers now commonly found in self-poisoning. The system described is designed specifically for laboratories which do not have access to the complex and expensive equipment necessary for gas-liquid chromatography or high-performance liquid chromatography.

An ether extract of serum is purified by acid transfer, back-extracted into ether, dried, and evaporated. The residue is run on a thin-layer plate against standards and inspected under 254 nm light. Depending on requirements, the amount of unknown may then be estimated or further chromatography performed in a different solvent. Quantification and further confirmation of identity by staining follow.

In this system serum, rather than urine or stomach contents, is the starting material. The present system works well for serum, and the results are more likely to be related to the clinical condition of the patient than would be the case for other starting materials since the amount of drug found is likely to be less than that found in either stomach contents or urine. The system is also adequately sensitive to measure the concentration of tricyclic antidepressants, benzodiazepines, and other tranquilizers in therapeutic doses. The much higher sensitivity used in the gas-liquid chromatographic detection of these drugs is superfluous and can introduce difficulties by producing numerous peaks of impurities which confuse the interpretation of the drug peaks being investigated, therefore this method is adequate.

The author concludes that this method is especially useful for large general hospitals since the equipment needed is very simple and many samples can be handled simultaneously and completed within a working day. (JAM)

2 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): nitrazepam. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide.

diazepam. oxazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: flurazepam. nitrazepam. Antidepressants, General Drug Screening: Systems.

UM-78-MO318

EVALUATION OF THE JET TECHNIQUE FOR EXTRACTING DRUGS FROM URINE, R.K. Lantz; R.B. Eisenberg, Clinical Chemistry, v24 n5 p821-4 (May 1978)

This paper describes and evaluates a new commercially available extraction technique preliminary to analysis for drugs in urine. In this method purified cellulose gauze is used as the adsorptive matrix. Extraction columns containing this purified cotton fiber (JETUBE) are shown to give high (90-97%) extraction efficiences for some commonly prescribed or abused drugs, notably phenobarbital, amphetamine, morphine, and methadone.

Two variations on the JET extraction method are described and evaluated in detail and compared to the XAD-2 method using resin columns. Analysis time, extraction efficiency, convenience, and eluate purity with the JET procedure are shown to be superior to results obtained with the XAD-2 method. (JAM)

8 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital. Barbiturates: phenobarbital. Opiates and Related Agents: methadone. morphine. Stimulants: amphetamine. General Drug Screening: Other Techniques.

UM-77-MO319

DIRECT EXTRACTION PROCEDURE FOR THE ANALYSIS OF NEUTRAL DRUGS IN TISSUE, L.J. Dusci; L.P. Hackett, Clinical Toxicology, v11 n3 p353-8 (1977)

Described here is a direct extraction method from postmortem tissue. This method involves a hexane/acetonitrile partitioning step which allows good recoveries of most of the neutral drugs as well as chromatograms that are free from extraneous peaks. The extracts are clean and are suitable for analysis by gas-liquid chromatography. Using this method, good recoveries of most neutral drugs at a concentration of 10mg/liter can be obtained. Notable exceptions are acetaminophen, caffeine, methyprylon, and primidone. Recoveries for the benzodiazepines, oxazepam, diazepam, and nitrazepam are acceptable. A number of acidic drugs also give good recoveries when subjected to the hexane/acetonitrile partition. (HSRI)

12 refs

KEYWORDS: Analgesics and Antipyretics: acetaminophen. phenacetin. Anticonvulsants (Anti-Epileptics): mephenytoin. nitrazepam. primidone. Hallucinogens and Related Agents: yohimbine. Metabolites of Drugs and Other Agents: oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. meprobamate. Minor Tranquilizers (Anti-Anxiety and Ataractics): oxazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: carbromal. glutethimide. methaqualone. methyprylon. nitrazepam. Stimulants: caffeine. Unclassified Agents: oxyphencycline. Specific Drug Screening: Gas Chromatography.

UM-78-MO320

DETERMINATION OF DRUGS OF ABUSE IN BODY FLUIDS BY RADIOIMMUNOASSAY, A. Castro; R. Mittleman, Clinical Biochemistry, v11 n3 p103-5 (Jun 1978)

Only recently has radioimmunoassay been used for the detection of drugs of abuse in body fluids. This paper reviews radioimmunoassay techniques specifically developed for measurement of drugs of abuse in humans. They are evaluated particularly in terms of their applicability to rapid drug screening. Drugs for which radioimmunoassays are evaluated in this paper are morphine, the barbiturates, amphetamine, lysergic acid diethylamide (LSD), methaqualone, benzoylecgonine, and methadone.

Several advantages are stated for these recently developed radioimmunoassay procedures. They are rapid and simple, and require a minimum quantity of blood or urine. They can be used not only for screening but for research into a better understanding of the physiological mechanisms and disappearance rates of these drugs and their metabolites. Another advantage to this type of assay is that a negative result reliably indicates that the drug in question is not present, thus avoiding more tedious procedures. Also,

since the radioimmunoassay procedures are highly sensitive, the drug in question can be detected for a longer time after administration than with other techniques. (HSRI)

28 refs

KEYWORDS: Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Metabolites of Drugs and Other Agents: benzoylecgonine. Nonbarbiturates: methaqualone. Opiates and Related Agents: methadone. morphine. Barbiturates. Stimulants. General Drug Screening: Other Techniques.

UM-78-M0321

COMPARISON OF GAS CHROMATOGRAPHY MASS SPECTROMETRY METHODS FOR THE DETERMINATION OF DELTA-9-TETRAHYDROCANNABINOL IN PLASMA, D. Rosenthal; T.M. Harvey; J.T. Bursey; D.R. Brine; M.E. Wall, Biomedical Mass Spectrometry, v5 n4 p312-16 (1978)

Reported here are the results of a study which attempted to develop a simple, reasonably fast, and accurate method to identify delta-9-THC by gas chromatography-mass spectrometry that could be used in forensic laboratories, hospitals, and pharmacology laboratories where equipment and experience might be limited. This method is compared with other techniques such as detection via thin-layer chromatography using tritium labeled delta-9-THC, a dual gas chromatographic method, and radioimmunoassay.

The gas chromatographic mass spectrometric (GCMS) method was found to be equal or superior to other techniques and has the added advantage of being highly specific for the compound analyzed. Except for the GCMS analysis, none of these methods provides the analyst with a method which gives positive identification of delta-9-THC. The GCMS procedure, since it makes use of the coincidence of a specific ion maximum with the precisely defined retention volume, is the method of choice where the ultimate reliability of identification, accuracy, and precision are required for delta-9-THC analysis.

Two general procedures for the determination of delta-9-THC by GCMS are described. The first consists of a direct method based on free delta-9-THC. It is suitable for electron impact analysis. This electron impact provides a highly reliable sensitive tool which is the procedure of choice where accurate data are required, particularly at pla levels less than 5 ng ml^{-1}. The method can be used either for specific determinations of unknown or as a comparison method to corroborate the data obtained by other techniques.

The second method makes use of the pentafluoropropionate derivative of THC and can be used for chemical ionization determination of delta-9-THC. (HSRI)

18 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Evaluation of Methods for Drug Analysis. Specific Drug Screening: Other Techniques.

UM-77-M0322

THE USE OF RADIOIMMUNOASSAY IN THE DETECTION OF URINARY CANNABINOIDS, J.D. Teale; J.M. Clough; D. Fry; C. Backhouse; V. Marks, Proceedings of the European Society of Toxicologists, v18 p252-4 (1974)

This study reports the development of a radioimmunoassay (RIA) for cannabinoids that satisfies the demand for an analytical method capable of measuring cannabis derivatives in biological fluids at the extremely low levels that often exist following normal usage. Several experimental studies are discussed to illustrate RIA's development and use. The paper focuses on a study in which this method was used to screen 1,002 urine samples, including 82 control specimens containing no cannabinoids. Approximately 30% of the specimens were positive for tetrahydrocannabinol-cross-reacting cannabinoids (THC-CRC).

Also reported is a case discussing a postmortem specimen of urine received from a driver involved in a motor accident. The level of THC-CRCs was 1,215 micrograms/l. No organic disease was found at autopsy, and screening for alcohol and other drugs was negative. No major mechanical defect was found on the driver's vehicle. Witnesses testified to the erratic nature of the subject's driving prior to his fatal accident. The urinary cannabinoid level detected was higher than any found in specimens from drug addicts. Therefore it appears that cannabis intoxication was a major contributory factor of the accident.

In conclusion, many samples can be rapidly and simply screened for specific cannabis use by means of RIA. The potential application of the method is in the mass screening of certain groups, for example, fatally injured drivers, to accumulate data on the incidence of use. (HSRI)

5 refs

KEYWORDS: Cannabis Sativa L. and Related Agents. Specific Drug Screening: Immunoassay.

UM-77-MO323

TOXICOLOGY: QUANTITATIVE ASPECTS, D.C.J. Horncastle, Medicine, Science, and the Law, v17 n1 p37-52 (Jan 1977)

Presented here is a broad overview of forensic methods for determining postmortem the drug content of blood, urine, and various organs as these methods developed through history. Historical treatment and evaluation is provided for the Stas-Otto extraction method, extraction methods for acidic and neutral drugs, and other methods of blood and urine analyses. Many newly developed methods are summarized and evaluated also. Special attention is given to the theory proposing that amounts of drugs found in body fluids and tissues at death are related to the time since ingestion and, within the limits of experimental error, obey Fick's law.

Five appendixes provide additional information in tabular and graphic form: (1) a detailed account of the methodology for general screening of urine samples for drugs; (2) details for the general screening of blood samples for drugs; (3) tables of the average weight of organs, recommended mean soft organ concentrations, and the overall percentage recoveries of various drugs after addition to viscera; (4) descriptions of an experimental methods for drug (ether) extraction and of an experimental methods for separation of acidic and neutral drugs (aqueous fraction); (5) thin-layer chromatography data for separation of acidic, neutral, and basic drugs. (HSRI)

19 refs

KEYWORDS: Review: Drug Analysis Methodology.

UM-78-MO324

THE ANALYSIS OF DRUGS IN BLOOD, BILE, AND TISSUE WITH AN INDIRECT HOMOGENEOUS ENZYME IMMUNOASSAY, E.L. Slightom, Journal of Forensic Sciences, v23 n2 p292-303 (Apr 1978)

Presented here is a study concerning the adaptation of the enzyme multiplied immunoassay technique (EMIT) drug abuse urine assay to the analysis of drugs in blood, bile, and tissues. EMIT is a homogeneous immunoassay designed to provide a direct and rapid method for the detection of antiepileptic drugs, primarily in urine and serum. This study attempts to extend the use of the EMIT serum assay to the analysis of whole blood, bile, and tissue through the sampling of reconstituted organic solvent extracts. This modification has the immediate advantages of controlling the concentration of the drug and providing a cleaner and more controlled matrix for analysis.

The indirect method of homogeneous enzyme immunoassay is described in detail in terms of the reagents and solutions used, the standard drug solutions used, equipment, and extraction procedure.

Results demonstrate the applicability of extending the EMIT assay to specimens other than urine through the analysis of reconstituted extracts. This may be useful for screening, confirming, and quantitation of drugs in biological specimens where other methods may be time-consuming, insensitive, or unavailable. Some of the advantages of this indirect method are these: (1) It extends the EMIT assay to more toxicologically significant specimens; (2) It concentrates the drug being analyzed, thereby increasing the sensitivity of the analysis; (3) It detects the presence of other drugs such as hydromorphone that may not be detected by more classical methods; (4) It separates certain cross-reacting drugs such as codeine and morphine; (5) It quantitates drugs, providing that the possibility of cross-reactivity can be overcome; (6) It requires minimal technical skill; (7) It gives rapid results compared to other methods.

Some of the disadvantages of this method are these: (1) It is not structurally specific and suffers from various degrees of cross-reactivity for certain structurally related molecules; (2) It increases the time of the EMIT assay; (3) It is limited in the number of drugs that can be analyzed; (4) The cost of instrumentation and reagents is relatively high. (HSRI)

15 refs

KEYWORDS: Analgesics and Antipyretics: propoxyphene. Anticonvulsants (Anti-Epileptics): phenobarbital. Barbiturates: pentobarbital. phenobarbital. Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Expectorant and Cough Preparations (Antitusive Agents): codeine. Local Anesthetics: cocaine. Metabolites of Drugs and Other Agents: N-desmethyldiazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. N-desmethyldiazepam. Muscle Relaxants (Central): diazepam. Opiates and Related Agents: codeine. hydromorphone. morphine. pethidine. Stimulants: cocaine. Barbiturates. General Drug Screening: Other Techniques.

UM-77-MO325

DETECTION OF TETRAHYDROCANNABINOL IN BLOOD AND SERUM USING A FLUORESCENT DERIVATIVE AND THIN-LAYER CHROMATOGRAPHY, J. A. Vinson; D. D. Patel; A. H. Patel, Analytical Chemistry, v49 n1 p163-5 (Jan 1977)

The purpose of this paper is to describe a thin-layer chromatographic (TLC) method suitable for routine use in the detection of THC in blood or plasma using a new derivatizing reagent, 2-p-chlorosulfophenyl-3-phenylindone (DIS-Cl). This reagent has been used for derivatizing amino acids, amino sugars, and vitamin B. DIS-Cl reacts with the phenolic group to form a derivative. Following extraction and clean up, the derivative is prepared and separated from the reagent and naturally occurring compounds by thin layer chromatography. The derivative is then detected by spraying the thin-layer plate with an alkoxide spray which produces a fluorescent spot visible under long wave ultraviolet light.

This method can detect 0.2 ng/ml of tetrahydrocannabinol in 5 ml of serum and is suitable for routine screening. It is comparable in sensitivity to sophisticated instrumental methods using gas chromatography or gas chromatography-mass spectrometry. Further work is being done to develop this procedure for use in detection of THC and its metabolites in urine and saliva and for quantitation of these compounds in biological fluids. (JAM)

16 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol. Specific Drug Screening: Thin-Layer and Paper Chromatography.

UM-78-MO326

ANALYSIS OF LSD IN HUMAN BODY FLUIDS BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY, FLUORESCENCE SPECTROSCOPY, AND RADIOIMMUNOASSAY, P.J. Twitchett; S.M. Fletcher; A.T. Sullivan; A.C. Moffat, Journal of Chromatography, v150 n1 p73-84 (1978)

A scheme of analysis of LSD is described in which the particular advantages of high-performance liquid chromatography (HPLC), fluorescence spectroscopy, and radioimmunoassay (RIA) are exploited to the greatest effect. This scheme was applied to samples of blood, urine, and stomach washings from seven people suspected of having taken LSD.

RIA affords a rapid and sensitive preliminary screening method, while the subsequent HPLC analysis using fluorometric detection yields quantitative chromatographic evidence together with characteristic fluorescence spectra. Fractionation of samples by HPLC followed by RIA of the fractions gives further confirmation of the presence of LSD and its metabolites.

This combined methodology can be applied to the analysis of LSD in body fluids for forensic and clinical purposes. Levels down to 0.5 ng of LSD per ml can be detected using the minimum of sample. (JAM)

18 refs

KEYWORDS: Hallucinogens and Related Agents: lysergic acid diethylamide (LSD)*. Specific Drug Screening: Other Techniques.

UM-78-MO327

ISOLATION OF DRUGS FROM BLOOD AND TISSUES WITH XAD-2 BAGS, M. Bogusz; J. Gierz; J. Bialka, Forensic Science International, v12 n1 p73-82 (19 Jun 1978)

The purpose of this paper is to evaluate a method of drug isolation from blood and tissues using XAD-2 resin extraction, a method which serves as a general toxicological screening procedure for forensic and clinical purposes. Nylon bags containing 2 g portions of Amberlite XAD-2 resin are used for systematic analysis of drugs in biosamples. The procedure requires 10 or less grams of material and two XAD-2 bags, and enables rapid and economical isolation of most common drugs. It can be routinely used in cases of fatal and nonfatal poisoning. This method is demonstrated in this paper on (1) autopsy blood spiked with nineteen of the most common drugs; (2) on heparinized blood samples taken from patients poisoned with diazepam and amitriptyline; and (3) on samples of autopsy blood and organs taken from subjects poisoned with chlorpromazine, barbiturates, glutethimide, oxazepam, chlorprothixene, endosulfan, and imipramine.

The procedure used appears to be more convenient than XAD-2 column extraction procedures. Classic solvent extraction methods were usually less efficient when compared to this method. (JAM)

27 refs

KEYWORDS: General Drug Screening: Other Techniques.

UM-78-M0328

ISOLATION OF DRUGS FROM AUTOPSY MATERIAL BY XAD-2 ADSORPTION-ELUTION TECHNIQUE. A ROUTINE PROCEDURE, M. Bogusz; J. Gierz; J. Bialka, Archives of Toxicology, v41 n2 p153-62 (1978)

This paper reports on an extraction procedure which enables a separation of acidic and basic drugs and assures good recoveries of both conjugated and protein-bound drugs in tissue due to an acid hydrolysis step before adsorption. This method of adsorption of drugs from autopsy specimens on Amberlite XAD-2 resin, followed by differential elution, was studied during one and one-half years of routine use.

The amounts of various drugs found in autopsy cases by the XAD-2 method were usually higher than those found by solvent extraction. The recovery of acid drugs from blood and liver, except phenacetin, was good. Poor yields were noted for phenothiazines, amitriptyline, and imipramine treated by differential elution scheme. Nevertheless, column extraction with XAD-2 resin is a valuable tool in forensic toxicology. This method requires small amounts of solvents (20 g of biofluid or tissue), and is moderately rapid and simple. (JAM)

20 refs

KEYWORDS: Analgesics and Antipyretics: methotrimeprazine. phenacetin. salicylate. Anti-Emetics: chlorpromazine. promethazine. Anticonvulsants (Anti-Epileptics): phenobarbital. Antidepressants: amitriptyline. imipramine. Barbiturates: phenobarbital. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. promethazine. Minor Tranquilizers (Anti-Anxiety and Ataractics): meprobamate. Nonbarbiturates: glutethimide. methaqualone. methotrimeprazine. General Drug Screening: Other Techniques.

UM-74-M0329

VERSUCHE ZUM NACHWEIS VON CANNABIS-INHALTSSTOFFEN IN DER AUSATEMLUFT, G. Hauck; H.R. Moll, Beitrage zur gerichtlichen Medizin, v32 p221-6 (1974)

Presented here is an evaluation of several different thin-layer and gas-liquid chromotographic methods for the detection of cannabis contents. The author believes that of the methods compared, the Von Lukowicz method was found to be the most sensitive and dependable. The gas-liquid chromatography method using the flame ionization detector was less favorable because of interferences with components of the solvent and the smoke of the tobacco. With the Von Lukowicz method, detection of cannabinol and tetrahydrocannabinol in the air of exhalation was possible up to eight minutes after smoking, and the detection of cannabidiol was possible up to fourteen minutes after smoking. (JAM)

20 refs German

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabidiol. cannabinol. delta-9-tetrahydrocannabinol. Evaluation of Methods for Drug Analysis.

UM-78-M0330

THE STABILITY OF DIAZEPAM IN PLASMA SAMPLES WHEN STORED UNDER VARYING CONDITIONS. P.J. Howard, Journal of Pharmacy and Pharmacology, v30 n2 p136 (Feb 1978)

Very little is known about the stability of diazepam when stored under varying temperature conditions. The study described here used morphine adsorbed on the glass of storage containers in order to investigate the stability of diazepam samples under temperatures ranging from -20(R) to 22(R). Statistical analysis was carried out on all groups, comparing results of analysis of drug concentrations in plasma before and after storage.

Diazepam concentrations in all stored samples except for those stored at room temperature for twenty days were not significantly different from the control values. The samples stored at room temperature showed evidence of decomposition of the plasma and had an offensive smell, but despite this the chromatograms were free of contaminant peaks.

These findings may be of significance in legal cases where it may be argued that the concentration of drug in the sample tested could be high or low because of the period of time between collection and analysis. With overdosage involving several drugs, a sample containing diazepam would remain virtually unchanged if stored over a period of time whereas other drugs may change significantly. (HSRI)

3 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Evaluation of Methods for Drug Analysis.

UM-79-M0331

STABLE SOLUTIONS FOR MARIJUANA ANALYSIS [letter], C.M. Bonuccelli, Journal of Pharmaceutical Sciences, v68 n2 p262-3 (Feb 1979)

This article describes research on the stability of synthetic and naturally occurring cannabinoids in chloroform and ethanol solutions. The researchers also studied extracts from plant material, continuing to investigate cannabidiol stability but giving primary consideration to the stability of the active constituent, tetrahydrocannabinol.

In conclusion, it is suggested that chloroform solutions of naturally occurring cannabinoids either be refrigerated at all times or, if substantial exposure to fluorescent or natural light cannot be avoided, that the combination of stabilizers sodium diethyldithiocarbamate and mercaptoethanol be added as a protective measure. The author believes that the stability of cannabinoid constituents in various solvents during analysis of actual plant material is of forensic importance. (HSRI)

4 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabidiol. delta-9-tetrahydrocannabinol. Review: Drug Analysis Methodology.

UM-78-M0332

ZUR VERWENDUNG VON FLUSSIG-FEST ELUTIONSVERFAHREN BEI DER CHEMISCH-TOXIKOLOGISCHEN URINUNTERSUCHUNG, L.V. Meyer; G. Drasch, Beitrage zur gerichtlichen Medizin, v36 p451-5 (1978)

The use of two commercially available liquid-solid elution methods for drug screening is described. The recovery rates of acid, neutral, and basic drugs are satisfactory (50-100%) in both systems. These results, which were obtained using the original procedure, might be improved with elution of more polar solvents, according to the authors.

The first procedure, the XAD-2 method, uses a nonionic resin for adsorption. In the second method, the Extrelut(R) procedure, the aqueous phase is adsorbed on a solid carrier, and during elution with organic solvents there is a quasi liquid-liquid extraction on the column.

The authors conclude that both systems are suitable for drug screening. They are more convenient than liquid-liquid extraction in the funnel, and are especially useful in laboratories with a large number of samples. (JAM)

9 refs German

KEYWORDS: Evaluation of Methods for Drug Analysis.

UM-78-MO333

EFFECT OF SPECIMEN STORAGE AND PRESERVATIOON ON TOXICOLOGICAL ANALYSES OF URINE, R.A. Rockerbie; D.J. Campbell, Clinical Biochemistry, v11 n3 p77-81 (Oct 1978)

In this investigation a study was made of the usefulness of various preservation methods and the effect of storage for up to thirty-six weeks on the reliability of specimens. Twenty-three drugs considered to be representative of drugs commonly abused were studied. Twenty-four-hour urine specimens were collected from subjects with known drug usage. Each urine specimen was divided into portions for storage under various controlled storage conditions. The effects on specimen preservation of refrigeration and of the addition of boric acid, chloroform, sodium fluoride, mercuric chloride, and buffers were assessed.

With the exception of flurazepam, glutethimide, and secobarbital, specimens were found to be able to be retained at room temperature for periods in excess of six weeks without deterioration.

The authors conclude that preservation by the addition of sodium fluoride (5 g/liter) followed by freezing, thawing, and filtration significantly prevents specimen deterioration, and may be used as the method of choice. (JAM)

15 refs

KEYWORDS: Quality Control.

UM-77-MO334

SOME CLINICAL AND PHARMACOLOGICAL APPLICATIONS OF HIGH-SPEED LIQUID CHROMATOGRAPHY, J.A. Nelson Advanced Chromatography, v15 p273-305 (1977)

This paper discusses the use of high-speed liquid chromatography in studies of purine and pyramide nucleotide metabolism, especially as it relates to clinical abnormalities and mechanisms of drug action. Examples are presented illustrating the utility of liquid chromatography in specific situations. Special emphasis is placed on separations using ion exchange because of their usefulness in the biomedical field.

Some of the clinical applications of high-speed liquid chromatography are (1) rapid, sensitive chemical analysis of enzymes responsible for disease; and (2) monitoring drug levels. Some of its pharmacological applications are (1) determining mechanisms of drug action; (2) measurement of enzyme reactions; and (3) separation of metabolites from parent compounds.

The author concludes that although high-speed liquid chromatography has a virtually unlimited ability to separate cellular metabolites and other organic compounds at present, there is a need for development of more selective, sensitive means of detection and positive identification of eluting components. (HSRI)

59 refs

KEYWORDS: Blood Derivatives: purine. pyrimidine. Review: Drug Analysis Methodology.

UM-77-MO335

USE OF SALIVA IN THERAPEUTIC DRUG MONITORING, M.K. Horning; L. Brown; J. Nowlin; K. Lertratanangkoon; P. Kellaway; T.E. Zion, Clinical Chemistry, v23 n2 p157-64 (1977)

Presented here is a suitable method for salivary drug analysis in a clinical chemistry laboratory. In this study concentrations of drugs in saliva and plasma were quantified by selected ion detection with a gas chromatograph-mass spectrometer computer (GC/MS/COM) system operated in the chemical ionization mode. Concentrations of phenobarbital, phenytoin, primidone, ethosuximide, antipyrine, and caffeine were measured in paired samples of saliva and plasma.

Mixed saliva was collected for the antipyrine and caffeine studies, while parotid saliva was collected for the phenobarbital, primidone, ethosuximide, and phenytoin studies.

The saliva/plasma (S/P) ratios (by weight) obtained by GC/MS/COM were: phenobarbital, 0.31-0.37; phenytoin, 0.11; ethosuximide, 1.04; antipyrine, 0.83-0.95; caffeine, 0.55. The S/P ratio obtained by enzyme immunoassay were: phenobarbital, 0.32; phenytoin, 0.12; primidone, 0.85. The concentrations of phenytoin, primidone, ethosuximide, and antipyrine in saliva corresponded very closely to the free fraction of the drug in plasma. When samples were analyzed containing phenobarbital or phenytoin (plasma or saliva) by both techniques, it was found that the enzyme immunoassay values were generally higher than GC/MS/COM values, suggesting that the metabolites as well as the parent drug were measured in the immunoassay.

The authors conclude that the two major advantages of the system described are its sensitivity and specificity of detection. Measurements in the picogram (>200pg) range can be done; analysis can be done on as little as 20 microliters of plasma or saliva. The system also provides information on the identity and homogeneity of the substance being quantified, and metabolites can be distinguished from the parent drug. (AAM)

46 refs

KEYWORDS: Analgesics and Antipyretics: antipyrine*. Anticonvulsants (Anti-Epileptics): ethosuximide*. phenobarbital*. phenytoin*. primidone*. Barbiturates: phenobarbital*. Stimulants: caffeine. Confirmatory/Quantitative Drug Analysis: Gas Chromatography-Mass Spectrometry. Evaluation of Methods for Drug Analysis.

UM-77-M0336

XAD-2 RESIN DRUG EXTRACTION METHODS FOR BIOLOGIC SAMPLES, A. Stolman; P.A.F. Pranitis, Clinical Toxicology, v10 n1 p49-60 (1977)

Presented here is a review of XAD-2 resin drug extraction methods for biologic samples, particularly urine samples. The paper describes the Amberlite XAD-2 nonionic resin and the columns used for XAD-2 chromatography. Also discussed are resin preparation methods as developed by various studies and differential elution of XAD-2 resins. Tables were compiled comparing percent recoveries of drugs from XAD-2 resin by several elution techniques. Some of the drugs for which these values are included are acetylsalicyclic acid, caffeine, cocaine, diphenylhydantoin, morphine, secobarbital, and thioridazine. Also provided is a table showing the effect of dilution on recovery of morphine, codeine, methadone, amobarbital, and phenobarbital from bile in terms of percent recovered.

The paper also reviews use of the XAD-2 extraction in biologic specimens other than urine. These techniques are being used for the differential elution of drugs from the resin into acid and basic drug fractions. These techniques vary from rapid, simple procedures for drugs of abuse in urine to more elaborate methods of extraction of autopsy material.

The authors conclude that the XAD-2 resin extraction procedure is flexible enough to suit the needs of most toxicology laboratories. (HSRI)

14 refs

KEYWORDS: Review: Drug Analysis Methodology.

UM-78-M0337

THE VALUE OF SERUM DRUG CONCENTRATION ASSAYS IN CLINICAL PRACTICE, N. Buchanan, South African Medical Journal, v53 n3 p103-5 (21 Jan 1978)

This paper discusses the value of serum drug assays in clinical practice. Serious problems can arise both in the clinical assessment of drug effects and in the measurement of drug concentration, and these problems are discussed here. Clinical application of assays of several drugs is discussed in some detail. These drugs include digoxin, quinidine, lignocaine, procainamide, the anticonvulsants, the tricyclic antidepressants, the antibiotics, and theophylline.

The author concludes that, in view of the problems and complexities involved in assaying drugs in serum, such assays are of little clinical value except in neonates, elderly persons, or patients with hepatic or renal dysfunction. However, many assays are important to research because the pharmacokinetic data obtained from the assays can be applied indirectly to clinical use and can provide data for the prescribing physician.

In summary, the author feels that clinical drug assays are still a luxury in a developing country such as South Africa is and should be restricted to teaching hospitals with a clinical pharmacology department. Even in an academic environment, serum assays should not replace clinical judgment. (HSRI)

20 refs

KEYWORDS: Anti-Arrhythmia Agents: lidocaine, procainamide, quinidine sulfate. Anti-Asthmatics: theophylline. Cardiac Glycosides: digoxin. Local Anesthetics: lidocaine. Stimulants: theophylline. Antibiotics. Anticonvulsants (Anti-Epileptics). Antidepressants. Review: Drug Analysis Methodology.

UM-77-MO338

A MICROCOMPUTER-DIRECTED MASS SPECTROMETER AS A COMPOUND-SELECTIVE DETECTOR FOR GAS CHROMATOGRAPHY, P.A. Strauss; R.H. Hertel, Journal of Chromatography, v134 n1 p39-48 (1977)

Determination and quantitation by mass spectrometry can be difficult for compounds in complex biological mixtures where chromatographic interferences are frequently encountered. This paper describes an instrument in which a form of selected ion monitoring, reverse search, and retention time screening are combined in order to automatically produce highly specific quantitation of mixtures. Computer control of instrument operation and data acquisition, analysis, and printout allows technologist operators to obtain highly reliable, precise quantitative results using relatively crude sample preparation procedures and short chromatographic times. The automatic quantitation of mixtures has made the approach particularly attractive in situations where assays are performed repetitively, where highly-trained personnel are not readily available for operation or interpretation, and where speed of analysis is important. Compared with usual chromatographic procedures, relatively simple extractions and short, incomplete separations are employed with excellent qualitative and quantitative results. This method can be particularly useful in toxicology and in the therapeutic monitoring of drugs. (JAM)

6 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital. Barbiturates: amobarbital, heptabarbital, phenobarbital, secobarbital. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide, diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: flurazepam, glutethimide, methaqualone. Confirmatory/Quantitative Drug Analysis: Gas Chromatography-Mass Spectrometry.

UM-77-MO339

AN ANALYTICAL APPROACH TO THE QUANTITATION OF KNOWN DRUGS IN HUMAN BIOLOGICAL SAMPLES BY HPLC, A. Bye; M.E. Brown, Journal of Chromatographic Science, v15 n9 p365-71 (Sept 1977)

Although many high-pressure liquid chromatography (HPLC) methods are available in the literature, only a fraction of them are applicable to the analysis of known drugs in human biological fluids. This paper presents the favored approach for a laboratory involved in the quantitative assay of drugs in man for the subsequent study of pharmacokinetics and bioavailability. It discusses the reasons for choosing HPLC for use, purification procedures for HPLC, and HPLC configurations commonly used. Four case histories are presented to illustrate the major points of this discussion which discuss analysis of allopurinol, oxipurinol, sulphamethoxazole, trimethoprim, and digoxin.

The authors conclude that the major problems for the analyst of drugs in biological fluids are low concentrations of the drug and the presence of numerous other compounds often at considerably higher concentrations than the drug. The problem of low concentration can be solved by concentrating outside the HPLC or injection of sufficient material into the HPLC to allow an adequate detector response for the drug. The problem of interfering compounds is best solved by either selective extraction or separation of the drug outside of the HPLC to minimize their influence. However, in some cases, injection of the drug together with other compounds into the HPLC is the only alternative. This latter approach requires that the full resolving power of HPLC be exploited but often lengthens the analysis time so as to be impractical for use in a clinical pharmacology laboratory. (AAM)

9 refs

KEYWORDS: Cardiac Glycosides: digoxin. Enzyme Inhibitors: allopurinol. oxypurinol. Other Anti-Infective Agents: trimethoprim. Sulfonamides: sulfamethoxazole. Uricosurics and Other Antigout Agents: allopurinol. Confirmatory/Quantitative Drug Analysis: Other Techniques.

UM-77-MO340

RADIOIMMUNOASSAYS OF DRUGS OF ABUSE IN HUMANS: A REVIEW, A. Castro; H. Malkus, Research Communications in Chemical Pathology and Pharmacology, v16 n2 p291-309 (Feb 1977)

This paper reviews specific radioimmunoassay methods, especially those methods applicable to rapid drug screening. The paper discusses radioimmunoassay of barbiturates, amphetamines, morphine, methadone, lysergic acid diethylamide, nicotine, methaqualone, and benzoylecogonine. Also described are combined radioimmunoassays, which involve simultaneous testing for drugs of two or more classes. The authors believe that combined radioimmunoassay for detection of two or more drugs promises to increase mass screening efficiency because a negative result will exclude the presence of more than one drug, and retesting will be necessitated only in the case of a positive result. Thus the quantity of tests can be greatly reduced. (HSRI)

30 refs

KEYWORDS: Ganglionic Blocking and Stimulating Agents: nicotine. Hallucinogens and Relatec Agents: lysergic acid diethylamide (LSD). Metabolites of Drugs and Other Agents: benzoylecgonine. Nonbarbiturates: methaqualone. Opiates and Related Agents: methadone. morphine. Stimulants: nicotine. Barbiturates. Stimulants. Review: Drug Analysis Methodology.

UM-78-MO341

ESTIMATION OF NITROUS OXIDE IN BLOOD, Y. Saloojee; P. Cole, Anaesthesia, v33 n9 p779-83 (Oct 1978)

While gas chromatography has proven to be a useful and accurate method for the estimation of minute quantities of gases dissolved in biological fluids, it has been difficult to apply this method to the extraction of nitrous oxide in a simple and reproducible manner within a reasonable amount of time. This paper reports the use of a modified vortex extractor technique designed to overcome these problems and to facilitate introduction of nitrous oxide into the chromatograph column.

Nitrous oxide from blood was estimated with one of two detectors: trace levels were measured with a microionization cross section detector to determine drug levels from 0.69-17.88 micromol/liter of blood; a thermal conductivity detector was used to determine nitrous oxide levels from 0.17-13.34 micromol/liter of blood.

The method uses a gas chromatograph with a steel column filled with Porapak Q. Helium was used as a carrier gas. The oven temperature was 60 to 90 degrees and the detector temperature was 100 degrees. The coefficient of variation was 1.3% for the thermal conductivity detector and 3.2% for the microionization cross section detector.

The authors conclude that this technique equals the precision of previously described methods but is considerably quicker. It appears to be suitable for use in the measurement of blood levels of nitrous oxide in both operating theatre personnel and in patients undergoing anesthesia. (HSRI)

5 refs

KEYWORDS: Gases: nitrous oxide*. General Anesthetics: nitrous oxide*. Hallucinogens and Related Agents: nitrous oxide*. General Drug Screening: Systems.

UM-78-MO342

EVALUATION OF WEIGHTED DISCRIMINATING POWER CALCULATIONS AS AN AID TO THE SELECTION OF CHROMATOGRAPHIC SYSTEMS FOR THE ANALYSES OF DRUGS, A.C. Moffat; P. Owen; C. Brown, Journal of Chromatography, v161 p179-85 (1978)

In toxicological analyses some chromatographic separations are more important than others. This paper examines the problem of choosing a thin-layer chromatography system for the routine screening for acidic drugs during toxicological analyses. It specifically examines two weighting methods in order to determine if the weighting of

the data confers any advantage to the calculation of discriminating power. The data were abstracted from a publication on the separations of acidic drugs on thin-layer chromatographic systems. When compared with nonweighted discriminating power calculations, those obtained with the weighting procedure did not give any advantage. (JA)

13 refs

KEYWORDS: General Drug Screening: Thin-Layer and Paper Chromatography.

UM-77-MO343

DIE RECHTSMEDIZINISCHE BEURTEILUNG VON DOSIS-WIRKUNGS-BEZIEHUNGEN BEI CANNABIS-MISSBRAUCH, M. Staak; A. Moosmayer; K. Besserer, Beitrage zur Gerichtlichen Medizin, v36 p443-9 (1977)

The problem of small amounts of cannabis as defined by the Narcotics Act (BtmG) is discussed in terms of the relation between dose and effect. On the basis of one relevant case, methods for analysis and computation are suggested. Compared to the present legally defined standards, qualitative and quantitative analyses of the cannabis component in given specimens plus conversion into dose and effect provide criteria for the medicolegal assessment of such circumstances which are considerably more exact and better founded scientifically. (JAM)

9 refs German

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol, marijuana. General Drug Screening: Other Techniques. Other Sociolegal Study.

UM-77-MO344

QUANTITATIVE MASS SPECTROMETRY IN BIOCHEMISTRY AND MEDICINE, W.D. Lehmann; H.R. Schulten, Angewandte Chemie International Edition in English, v17 n4 p221-38 (Apr 1978)

The current state of quantitative analysis using mass spectrometry in biochemistry and medicine is reviewed. The basic principles of mass spectrometry, its combination with chromatography, the development of sensitive, exact, and specific mass-spectrometric methods of detection, and the principle of dilution with stable isotopes are illustrated by descriptions of early investigations. The most important fields of application are clarification of the pharmacokinetics of drugs and active metabolites; investigation of metabolic pathways; supporting of medical diagnoses and enhancement of their specificity; and checking the quality of simpler quantitative processes of clinical chemistry.

The authors conclude that while the relatively high costs of the purchase and operation of a mass spectrometer can be a prohibiting factor, the expenditure is justified by the versatility of the technique, especially when combined with a data processing system. It allows the solution of many analytical problems in biochemistry and medicine that would otherwise be difficult or impossible to solve. (JAM)

291 refs

KEYWORDS: Review: Drug Analysis Methodology.

UM-77-MO345

SCREENING FOR TRICYCLIC ANTIDEPRESSANT DRUGS IN BIOLOGICAL SPECIMENS BY RADIOIMMUNOASSAY, B. Kaul; B. Quame; B. Davidow, Journal of Analytical Toxicology, v1 p236-43 (Sep-Oct 1977)

Described here is a radioimmunoassay method for the measurement of tricyclic antidepressants in urine and other biological specimens. This method can also be used, under controlled conditions, to monitor total tricyclics in the plasma.

Antisera to nortriptyline and desipramine were produced in rabbits against their succinylated derivatives conjugated to bovine serum albumin and bovine thyroglobulin, respectively. The antibodies thus produced were shown to be specific for tricyclic antidepressants. Some of the phenothiazines were found to cross-react in higher concentrations.

The assay was useful when either antibody was combined with generally or specifically tritium-labelled amitriptyline and nortriptyline.

The sensitivity of this assay is in the 2-5 nanogram range and is useful in screening for use and abuse of tricylics by man. Comparison of radioimmunoassay results with those of thin-layer and gas chromatography was made, and good agreement was reported. Combined with a thin-layer or gas chromatographic confirmation, the test is well suited for detection and exclusion of these components in biological specimens. (JAM)

33 refs

KEYWORDS: Analgesics and Antipyretics: carbamazepine. Anti-Emetics: chlorpromazine. prochlorperazine. promethazine. Anticonvulsants (Anti-Epileptics): carbamazepine. Antidepressants: amitriptyline. desipramine. doxepin. imipramine. nortriptyline. protriptyline. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. mesoridazine. prochlorperazine. promethazine. thioridazine. trifluoperazine. Metabolites of Drugs and Other Agents: desmethyldoxepin. Antidepressants. Specific Drug Screening: Immunoassay.

UM-77-MO346

A RAPID SCREENING TEST FOR DIAZEPAM IN SERUM, R.W. Samuels, Journal of Analytical Toxicology, v1 p208-10 (Sep-Oct 1977)

A simple, rapid procedure for the identification of diazepam in serum specimens is described. In order to determine the specificity of the procedure as a screening test for diazepam, powdered samples of several other benzodiazepines were also tested.

Of the benzodiazepines evaluated, only flurazepam and oxazepam gave any reaction product resembling the diazepam chromogen that was formed. The sensitivity of the screening test was determined by analyzing spiked serum specimens with varying concentrations of diazepam. A drug-free serum specimen was used as a negative control. The lowest level of diazepam that could be consistently identified was found to be approximately

.2 mg/dl.

This procedure demonstrates the presence of diazepam in serum specimens at high therapeutic levels by its reaction with m-dinitrobenzene and methanolic potassium hydroxide following its extraction on a celite column. The entire procedure takes approximately fifteen minutes. The procedure is potentially useful as a screening test in emergency toxicology analyses in cases of suspected diazepam overdose or abuse. Since any screening test is subject to interference by structurally similar compounds, confirmation of the presence of diazepam by more specific procedures such as ultraviolet spectrophotometry or gas liquid chromatography is strongly recommended. (AAM)

19 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Specific Drug Screening: Other Techniques.

UM-77-MO347

AN OXIDATIVE SCREENING PROCEDURE FOR NANOGRAM AMOUNTS OF BENZODIAZEPINES AND OTHER DRUGS IN BLOOD, A.W. Missen, Journal of Analytical Toxicology, v1 p224-6 (Sep-Oct 1977)

This paper describes a method for the sensitive detection of benzodiazepines and other drugs in blood. The procedure involves the extraction of 0.4 ml blood followed by chronic acid oxidation and analysis of the oxidized extract using electron capture gas-liquid chromatography.

This method was found to be suitable for a mass screening of blood samples for therapeutic and overdose levels of benzodiazepines. The oxidation procedure used is capable of detecting even low therapeutic levels of several benzodiazepines, except for clonazepam. While there is some degree of correlation between the amount of drug oxidized and the peak heights of the oxidation products observed, the unequal oxidation of most benzodiazepines and their metabolites precludes accurate quantitation. Nevertheless, the method is suitable for mass screening for benzodiazepines in blood. (HSRI)

19 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): nitrazepam. Metabolites of Drugs and Other Agents: oxazepam. N-desmethyldiazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. lorazepam. oxazepam. N-desmethyldiazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: flurazepam. nitrazepam. Specific Drug Screening: Gas Chromatography.

UM-78-M0348

A SIMPLE GAS CHROMATOGRAPHIC METHOD FOR ROUTINE DELTA-1- TETRAHYDROCANNABINOL ANALYSES OF BLOOD AND BRAIN, N.K. McCallum; E.R. Cairns; D.G. Ferry; R.J. Wong, Journal of Analytical Toxicology, v2 p89-93 (May-Jun 1978)

A rapid, sensitive, and specific method is presented for the quantification of delta-1-tetrahydrocannabinol in 1 ml of whole blood or in 0.5 g of brain tissue. This method utilizes a gas chromatographic method using an inexpensive detection device sensitive to phosphorus. The cannabinoids are detected as their diethyl phosphate esters. Detection limits are approximately 0.5 ng/ml of blood and 10 ng/g of brain.

This analytical technique fulfills the criteria necessary to make it suitable for routine toxicological use. The equipment is relatively inexpensive and is standard in many toxicological laboratories. The method can be used with most gas chromatographs equipped with alkali thermionic or alkali flame ionization detectors. The resolution and selectivity of detection of cannabinoids by this method is matched only by expensive and complex systems based on mass spectrometry, and it is superior to those based on immunoassay and TLC. The required sample sizes are much smaller than for all but immunoassay methods, yet excellent minimum levels of detectability are preserved. The limiting factor in the speed of analysis of large numbers of blood samples is the duration of each chromatogram. Even so, this speed can be matched only by other methods that lack the selectivity and specificity of this method. Therefore this method is particularly suitable for routine toxicological analyses of large numbers of blood samples. (AAM)

28 refs

KEYWORDS: Cannabis Sativa L. and Related Agents: delta-9-tetrahydrocannabinol*. Specific Drug Screening: Gas Chromatography.

UM-78-M0349

A NEW RAPID GAS CHROMATOGRAPHY METHOD FOR THE DETECTION OF BASIC DRUGS IN POSTMORTEM BLOOD, USING A NITROGEN PHOSPHOROUS DETECTOR. PART I. QUALITATIVE ANALYSIS, W.O. Pierce; T.C. Lamoreaux; F.M. Urry; L. Kopjak; B.S. Finkle, Journal of Analytical Toxicology, v2 p89-93 (May-Jun 1978)

This paper describes a new, rapid postmortem blood screening method for the detection of basic drugs such as phenothiazines, tricyclic antidepressants, antihistamines, analgesics, and other drug classes of toxicological interest. This method couples the clean extract characteristics of n-butyl chloride with the superior sensitivity and specificity capabilities of the nitrogen phosphorous detector. It involves a one-step extraction from 1.0 ml of postmortem blood buffered to pH 9.0-9.5 into n-butyl chloride. No back extraction or clean-up steps are required. Extracts are injected on 3% OV-1 and 3% OV-17 columns coupled to nitrogen phosphorus detectors.

For the nearly one hundred drugs and metabolites extracted and analyzed by this method, sensitivity limits in the range of 200-500 ng/ml were routinely achieved in this study. It was also found that twelve postmortem blood samples could easily be extracted in one hour, compared to only two samples per hour when gas chromatography was used. While this method has been developed for postmortem blood analyses, it could be useful in some clinical toxicology situations because of its rapidity and sensitivity. (JAM)

9 refs

KEYWORDS: Analgesics and Antipyretics: propoxyphene. Anti-Emetics: chlorpromazine. Antihistamine Agents: chlorpheniramine. diphenhydramine. Expectorant and Cough Preparations (Antitusive Agents): codeine. Hallucinogens and Related Agents: phencyclidine. Local Anesthetics: cocaine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. thioridazine. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: diphenhydramine. flurazepam. Opiates and Related Agents: codeine. pentazocine. pethidine. Plasmodicides: quinine. Stimulants: caffeine. cocaine. Analgesics and

Antipyretics. Antidepressants. Antihistamine Agents. General Drug Screening: Gas Chromatography.

UM-78-M0350

A NOVEL METHOD FOR THE ISOLATION AND QUANTITATIVE ANALYSIS OF NICOTINE AND COTININE IN BIOLOGICAL FLUIDS, M.P. Maskarinec; R.W. Harvey; J.E. Caton, Journal of Analytical Toxicology, v2 p124-6 (Jul-Aug 1978)

In spite of the widespread use of tobacco products, there exists no established, simple, quantitative method for the determination of nicotine and its major metabolite cotinine in body fluids. This paper describes a method for the estimation of nicotine and cotinine using high-performance liquid chromatography with ultraviolet detection and employing solvent partition for isolation. Isolation is accomplished by adsorption of the alkaloids on Amberlite XAD-2 resin and subsequent elution with chloroform and methanol. No solvent extraction or further purification is required. The final determination is made by high-performance liquid chromatography using ultraviolet detection.

Absolute recovery of nicotine was at least 80% in all samples. The accuracy of the method was estimated to be ± 5% on standard addition measurements. Detection limits of 2 ng/ml urine can be routinely obtained.

The simplicity and rapidity of the method allows up to forty samples per day to be conveniently run by one technician. Therefore, the method should find wide applicability in laboratories involved in nicotine screening on a routine basis. (JAM)

15 refs

KEYWORDS: Ganglionic Blocking and Stimulating Agents: nicotine. Stimulants: cotinine. nicotine. Specific Drug Screening: Other Techniques.

UM-78-M0351

A COMPREHENSIVE GC/MS DRUG SCREENING PROCEDURE, P.A. Ullucci; R. Cadoret; P.D. Stasiewski; H.F. Martin, Journal of Analytical Toxicology, v2 p33-8 (Mar-Apr 1978)

A comprehensive, rapid, and sensitive drug screening procedure employing gas chromatography/mass spectrometry (GC/MS) is presented. The method involves a series of four urine spot tests and a solid-buffer extraction technique to prepare acid and basic extracts for GC/MS analysis. Urine is analyzed for morphine, cocaine, and amphetamines by EMIT, with positives confirmed by GC/MS. The solid-buffer extraction technique uses a 5:1 urine-organic solvent ratio for extraction. After evaporation of the solvent, the residue is reconstituted with 50 microliters of methanol, and 2-3 microliters of it are injected into a Finnigan Model 3000D GC/MS. Mass spectra are recorded on a light beam oscillographic recorder, and the spectra are coded manually. Identification of unknown spectra is accomplished by a manual library search.

This procedure has been used for over 2000 drug screens at Rhode Island Hospital. This paper reports the results of its use. Recovery of drugs in urine was in the range of 78-100%, and sensitivity of the method ranged from 0.2-1.0 microgram per microliters of urine for those drugs studied. Some interesting drug ingestion cases are also discussed and the applicability of GC/MS as a routine drug screening method available on a twenty-four hour basis is demonstrated. (JA)

20 refs

KEYWORDS: Analgesics and Antipyretics: acetaminophen. phenacetin. propoxyphene. salicylate. Anti-Emetics: chlorpromazine. Anticonvulsants (Anti-Epileptics): phenobarbital. Antidepressants: amitriptyline. Antihistamine Agents: diphenhydramine. methapyrilene. Barbiturates: amobarbital. butabarbital. butalbital. pentobarbital. phenobarbital. secobarbital. Expectorant and Cough Preparations (Antitusive Agents): codeine. Hallucinogens and Related Agents: phencyclidine. Major Tranquilizers (Antipsychotics and Neuroleptics): chlorpromazine. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. meprobamate. Muscle Relaxants (Central): diazepam. Nonbarbiturates: diphenhydramine. ethchlorvynol. glutethimide. Opiates and Related Agents: codeine. Specific Drug Screening: Other Techniques.

UM-78-M0352

QUANTITATIVE TOXICOLOGY: INTERLABORATORY AND INTERMETHOD EVALUATION IN NEW YORK STATE, S.N. Buhl; P. Kowalski; R.E. Vanderlinde, Clinical Chemistry, v24 n3 p442-7 (1978)

Presented here is a report on intermethod and interlaboratory performance of a large number of toxicology laboratories that routinely perform drug assays. This paper describes the basis, operation, and results of a New York State proficiency-evaluation program in quantitative toxicology; the problems encountered in preparing test samples; and some observation on currently used methods for measuring barbiturates, phenytoin, procainamide, theophylline, and glutethimide in serum.

The New York State Department of Health has conducted a proficiency evaluation program in quantitative toxicology since 1974. Serum samples containing a barbiturate and phenytoin, together with either glutethimide, procainamide, or theophylline, are sent to participating laboratories quarterly for drug analysis. Within the first two years of the program the percentage of laboratories able to quantitate 75% of the test samples to within 25% of the gravimetric values increased from 25 (1974-1975) to 40% (1975-1976). This improvement was partly due to licensure requirements, improved technology for sample preparation and analysis, and the availability of better quality-control practices. Differences in results were most often due to lack of standardization of materials and methods, nonspecificity of analytic methods, and inaccurate calibration materials.

The authors conclude that although proficiency testing programs can lead to improvements in accuracy, improvement must begin with internal quality-control practices. (JAM)

35 refs

KEYWORDS: Anti-Arrhythmia Agents: procainamide. Anti-Asthmatics: theophylline. Anticonvulsants (Anti-Epileptics): phenytoin. Nonbarbiturates: glutethimide. Stimulants: theophylline. Barbiturates. Proficiency Testing. Quality Control.

UM-78-M0353

A RADIOIMMUNOASSAY FOR NORTRIPTYLINE (AND OTHER TRICYCLIC ANTIDEPRESSANTS) IN PLASMA, K.P. Maguire; G.D. Burrows; T.R. Norman; B.A. Scoggins, Clinical Chemistry, v24 n4 p549-54 (1978)

Measurement of tricyclic antidepressants in plasma is important in view of the conflicting evidence concerning their concentrations in plasma and therapeutic response. The recent availability of tritiated compounds with high specific activity has allowed the development of a rapid, simple procedure for measuring tricyclic antidepressants in plasma. This paper describes a radioimmunoassay for nortriptyline and other tricyclic antidepressants that can detect as little as 1 microgram/liter of plasma.

Within-day precision and day-to-day precision of this method were found to be ± 6 and ± 11%, respectively, over the concentration range 100-200 microgram/liter. The major metabolite hydroxy-nortriptyline did not cross react with the antiserum. These results correlated closely with results by a double-isotope derivative dilution technique.

The major advantages of this technique over currently available methods are its sensitivity, convenience (many samples can be processed in one day), simplicity, and cost. Furthermore, prior extraction of plasma samples is not required.

Cross-reactivity studies have been carried out with all other available tricyclic antidepressants. The antiserum has the ability to bind these drugs, thus radioimmunoassay for all the tricyclic antidepressant drugs can be set up because concurrent use of more than one of these drugs is rare. (JAM)

19 refs

KEYWORDS: Antidepressants: nortriptyline. Antidepressants. Specific Drug Screening: Immunoassay.

UM-78-M0354

PLASMA AND URINE CONCENTRATIONS OF DIAZEPAM AND ITS METABOLITES IN CHILDREN, ADULTS AND IN DIAZEPAM-INTOXICATED PATIENTS, J. Kanto; R. Sellman; M. Haataja; P. Hurme, International Journal of Clinical Pharmacology and Biopharmacy, v16 n6 p258-64 (1979)

Plasma and urine concentrations of diazepam and its metabolites after a single therapeutic dose of diazepam were measured in both children and adults and compared to drug concentrations in diazepam intoxicated patients who had taken huge doses of diazepam. The purpose of the study was to gain knowledge about the effect of dose size on the metabolism and excretion of diazepam.

The main diazepam metabolites in the urine of eight children aged from six days to six years after a single 0.5 to 10 mg dose of diazepam given orally, intramuscularly, or intravenously were conjugated oxazepam and N-demethyldiazepam. Conjugated N-methyloxazepam and free N-demethyldiazepam and diazepam were of minor importance. During the first twenty-four hours after administration, a mean of 11% of the single dose was excreted in the urine of the children.

The urinary metabolites in adult patients after toxic doses of diazepam were similar to those found in children after therapeutic doses. In healthy volunteers, after a single small oral dose (5 mg) the main diazepam metabolite in the urine was conjugated N-demethyldiazepam. Free and conjugated oxazepam was excreted in their urine in lower concentrations and no measurable levels of free or conjugated N-methyloxazepam, free N-demethyldiazepam, or diazepam were found. During twenty-four hours, a mean of 7% of the 5 mg oral dose of diazepam was excreted in the urine of the healthy volunteers. In the plasma of the volunteers or intoxicated patients, the main metabolite of diazepam was unconjugated N-demethyldiazepam. In contrast to the volunteers, free and conjugated oxazepam and N-methyloxazepam, as well as conjugated N-demethyldiazepam, were also found in the plasma of the intoxicated patients. The relative share of the hydroxylated diazepam metabolites N-methyloxazepam and oxazepam in the plasma and urine was more prominent after a high dose of diazepam in children and diazepam-intoxicated patients than in volunteers after a low dose.

In conclusion, the amount of diazepam administered to humans had an effect on the quality and quantity of its metabolites in the plasma and urine. The relative share of the hydroxylated metabolites N-methyloxazepam and oxazepam, as compared to that of N-demethyldiazepam, was more prominent after high doses of diazepam. (JAM)

17 refs

KEYWORDS: Metabolites of Drugs and Other Agents: oxazepam*. N-desmethyldiazepam*. Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam*. methyloxazepam*. oxazepam*. N-desmethyldiazepam*. Muscle Relaxants (Central): diazepam*. Pharmacokinetics: Acute Dose. Pharmacokinetics: Chronic Dose.

UM-79-MO355

MOLECULAR ANALYSIS BY MASS SPECTROMETRY, W.V. Ligon, Science, v205 n4402 p151-9 (13 Jul 1979)

This article discusses in detail how the special demands of molecular analysis have influenced spectrometer design and describes how modern mass spectrometers have dramatically influenced experimental methodology in a wide variety of fields. New ionization methods combined with powerful analyzers, detectors, and data systems have made mass spectrometry a versatile tool for molecular analysis. Samples consisting of nanogram quantities of hundreds of unique components are routinely analyzed. In favorable cases, samples as small as 2.5×10^{-14} gram and samples with masses of more than 3,000 atomic mass units have been successfully examined.

The author concludes that mass spectrometry is undergoing an extremely rapid development which shows little indication of abating either in the areas of instrument refinement or of extended applications. (JA)

47 refs

KEYWORDS: Review: Drug Analysis Methodology.

UM-77-MO356

APPLICATION OF POLAR STATIONARY PHASES OV-225 AND OV-275 IN THE DETECTION OF DRUGS IN URINE SAMPLES, G.L. Dadisch; W. Vycudilik; G. Machata, Forensic Science, v10 p205-16 (1977)

This paper describes a rapid procedure for the screening of drugs in urine samples using OV-225 and OV-275. This method, which uses thin-layer chromatography and gas chromatography equipped with a nitrogen phosphorous detector, enables detection of

therapeutic doses of drugs to be made in a short time. The thin-layer chromatography process detects drugs with a sequence of three reagents. Gas chromatography screening is carried out with a temperature programmed run of 30 degrees C/min up to 290 degrees C. For the determination of retention indices new polar phases with suitable thermal stabilities such as OV-225 and OV-275 are used.

This method is able to detect even small amounts of free drugs or metabolites. The efficiency depends only on the detection limits of thin-layer chromatography and gas chromatography; thin-layer chromatography detects concentrations down to 0.1 ppm and a gas chromatograph equipped with a nitrogen phosphorous detector detects concentrations down to 0.01 ppm. (JAM)

0 refs

KEYWORDS: Specific Drug Screening: Other Techniques.

UM-77-MO357

NEED FOR URINE DRUG TESTING [letter], K.K. Kaistha; R. Tadrus, Journal of Pharmaceutical Sciences, v67 n3 pIV (1977)

This letter evaluates the proposed elimination of all mandatory urine testing in government funded drug abuse treatment programs with the exception of the initial drug screening urinalysis. The authors claim that this proposal holds the potential for both counterproduction and retrogression against the goals of addict rehabilitation. They go on to list the advantages of mandatory urine testing, and conclude that the net result of this proposed elimination would be a deterioration in the effectiveness of methadone programs and other treament programs. (HSRI)

2 refs

KEYWORDS: Countermeasure Development, Testing, and Evaluation.

UM-77-MO358

A RANDOM SURVEY OF DRUG SCREENING PROFICIENCY, R.A. Rockerbie; D.J. Campbell, Clinical Biochemistry, v10 n3 p138-9 (1977)

The objective of this quality control survey was to illustrate the degree of error associated with toxicological analyses and thus encourage the use of controls to decrease the possibility of reporting erroneous findings. A 30 ml sample of urine with known amounts of salicylate, ethyl alcohol, and methamphetamine was submitted for analysis as a general unknown to each of twenty-two Canadian laboratories. Sixteen of the twenty-two laboratories failed to detect salicylate. Four reported no drugs. Five were able to make one correct drug identification, while only three were able to correctly identify two drugs. Fourteen laboratories had one or more false positives.

The most important finding of this study is the clearly illustrated need for a well-conceived program of proficiency testing in analytical toxicology, for upgrading the quality of the service, and for greater reliability in determining whether or not a particular drug may have contributed to the patient's abnormal condition. (HSRI)

3 refs

KEYWORDS: Proficiency Testing.

UM-77-MO359

RADIOIMMUNOLOGICAL SCREENING AND GAS CHROMATOGRAPHIC IDENTIFICATION OF DIAZEPAM IN BLOOD AND SERUM, H.P. Gelbke; H.J. Schlicht; G. Schmidt, Archives of Toxicology, v38 p295-305 (1977)

A radioimmunoassay for the determination of diazepam in human blood and serum is presented. Diazepam is separated from the bulk of the biological material by adsorption on Amberlite XAD-2 and subsequent desorption with ethyl acetate. The extract thus obtained can be used directly for the determination of diazepam by radioimmunoassay and gas chromatography with electron capture detection. For the combined radioimmunological and gas chromatographic determination, 0.5 ml of either blood or serum is necessary, the lower detection limit being approximately 5 ng/ml for both of these procedures. The

quantitative results obtained by radioimmunoassay and gas chromatography correspond well with each other.

The authors conclude that the radioimmunological procedure presented here enables the determination of diazepam in large numbers of serum and blood specimens with high reliability, accuracy, and practicability. The radioimmunological procedure enables the screening of more than 200 samples for diazepam by one technician within two working days. (JAM)

17 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam. Muscle Relaxants (Central): diazepam. Specific Drug Screening: Other Techniques.

UM-77-M0360

SIMPLIFIED RADIOIMMUNOASSAY OF URINARY DRUGS OF ABUSE ABSORBED ON ION-EXCHANGE PAPERS, G.J. Alexander; S. Machiz, Clinical Chemistry, v23 n10 p1921-4 (1977)

Described here is a convenient screening procedure for drugs of abuse in urine such as morphine, heroin, methadone, secobarbital, amphetamine, and methamphetamine. The procedure consists of two steps: (1) adsorption of the drugs from urine onto a paper loaded with a cation-exchange resin; and (2) detection of the adsorbed drugs by direct radioimmunoassay.

The first step can be performed at the point of the collection of the urine sample, the second, in a central laboratory. Storage and transport to the laboratory are simplified because specimens adsorbed on dried paper are stable and can be sent in letter-mail. In the laboratory a small disc of the ion-exchange paper is exposed to antigen and antibody, rinsed, and tested by radioactivity. Discs treated with positive urines are more radioactive than discs from negative urines. The simplicity of this procedure coupled with the convenience of the method of shipping samples makes it uniquely useful for adoption by central laboratories serving several satellite clinical units. (JAM)

8 refs

KEYWORDS: Barbiturates: secobarbital. Opiates and Related Agents: heroin. methadone. morphine. Stimulants: amphetamine. methamphetamine. Specific Drug Screening: Immunoassay.

UM-73-M0361

LYSERGIC ACID DIETHYLAMIDE: RADIOIMMUNOASSAY, A. Taunton-Rigby; S.E. Sher; P.R. Kelley, Science, v181 p165-6 (13 Jul 1973)

Described here is a method for producing antibodies to LSD and the development of a sensitive and specific radioimmunoassay capable of detecting picogram amounts of LSD. Antibodies to LSD were obtained by immunizing rabbits with a conjugate of LSD and human serum albumin. The antibody was found to be highly specific for LSD by competitive binding studies.

The radioimmunoassay has been used to detect the presence of LSD in urines from users of the drug. Results are reported for two studies in which urine samples from both normal subjects and from subjects given LSD were assayed. The data from these studies indicate that the radioimmunoassay can detect LSD and possibly closely related metabolites in urine. The assay can also be used to detect LSD in serum, bile, gastric fluids, and other biological material. It can detect as little as 20 picograms of LSD, making it a useful research tool. (HSRI)

4 refs

KEYWORDS: Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). Specific Drug Screening: Immunoassay.

UM-79-M0362

CANNABINOID ANALYSIS IN PHYSIOLOGICAL FLUIDS, J.A. Vinson, ed., ACS Symposium Series 98, Washington, D.C.: American Chemical Society (1979)

The analytical chemistry of marijuana has progressed from the analysis of tetrahydrocannabinol and other cannabinoids in plant material to the much more difficult problem of quantitation of tetrahydrocannabinol and its metabolites in physiological fluids. Recent advances in physiological fluid analysis were discussed in a symposium at the 173rd American Chemical Society National Meeting in New Orleans. This book offers representative papers from different analytical methods presented at that meeting from worldwide experts in the field. Following an introductory paper surveying metabolic transformation of delta 1-tetrahydrocannabinol, analytical methodologies using gas chromatography, mass spectroscopy, radioimmunossay, high-pressure liquid chromatography, and thin-layer chromatography are presented. (HSRI)

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabidiol*. cannabidiolic acid*. cannabigerol*. cannabigerolic acid*. cannabinol*. cannabinolic acid*. delta-8-tetrahydrocannabinol. delta-9-tetrahydrocannabinol*. marijuana. Cannabis Sativa L. and Related Agents. Compilation. Specific Drug Screening: Gas Chromatography. Specific Drug Screening: Immunoassay. Specific Drug Screening: Optical Techniques. Specific Drug Screening: Other Techniques. Specific Drug Screening: Thin-Layer and Paper Chromatography.

UM-78-M0363

THIN-LAYER DETECTION OF DIAZEPAM AND/OR CHLORDIAZEPOXIDE ALONE OR IN COMBINATION WITH MAJOR DRUGS OF ABUSE IN DRUG ABUSE URINE SCREENING PROGRAMS, K.K. Kaistha; R. Tadrus, Journal of Chromatography, v154 n1 p211-8 (Jul 1979)

Three extraction procedures for the detection of diazepam, oxazepam, chlorazepate, and chlordiazepoxide in human urines are presented. All three procedures are based on the acid hydrolysis of benzodiazepines or their conjugated metabolites to give the corresponding benzophenones. Procedure I involves the direct acid hydrolysis of raw urine and is recommended when the purpose is to test the abuse of benzodiazepine derivatives only. Procedure II is a two-step extraction method in which a wide variety of drugs of abuse including cocaine are extracted by the first step using paper loaded with cation-exchange resin. The benzodiazepines are then tested in the second step by the acid hydrolysis of the spent urine left after removing the ion-exchange paper. Procedure III involves the use of inert fibrous matrix and its acid hydrolysis.

The detection procedure is based on the identification of methylaminochlorobenzophenone (MACB) and aminochlorobenzophenone (ACB). MACB is detected as a yellow-colored compound while ACB is detected by spraying with Bratton-Marshall reagent. Specificity of detection of ACB has been achieved by the selection of a thin-layer developing solvent system in which sulfonamides with primary aromatic amino groups remain at the origin. (JA)

36 refs

KEYWORDS: Metabolites of Drugs and Other Agents: benzoylecgonine. oxazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. clorazepate. diazepam. Minor Tranquilizers (Anti-Anxiety and Ataractics): oxazepam. Muscle Relaxants (Central): diazepam. Specific Drug Screening: Thin-Layer and Paper Chromatography.

UM-78-M0364

ERRORS IN MEASURING DRUG CONCENTRATIONS, W. McCormick; J.A. Ingelfinger; G. Isakson; P. Goldman, New England Journal of Medicine, v299 n20 p1118-21 (16 Nov 1978)

Reported here are the results of a quality control investigation comparing the measurements of identical drug concentrations in six different laboratories. Simulated clinical specimens of digoxin, phenytoin, and phenobarbital were sent to each laboratory. Laboratories were also requested to measure drug concentrations of quality-control specimens.

Results showed that out of 190 clinical samples of digoxin, large errors occurred nine times, while large errors occurred only once in the 141 quality-control specimens. Five of the six mean values of the simulated clinical specimens fell outside the 90% confidence interval for the mean established by the measurement of designated quality-control specimens. Comparison of results from the phenytoin and phenobarbital studies indicated similar discrepancies.

The results of this investigation show that designated quality-control specimens do not reliably predict the measurement error that might be encountered in practice. Furthermore, even simulated clinical specimens do not measure all sources of error that

might be encountered in practice. The authors believe, however, that systems of quality-control based on simulated clinical specimens come much closer to measuring the errors present in clinical practice than do programs measuring only designated quality-control samples. (HSRI)

10 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenobarbital, phenytoin. Barbiturates: phenobarbital. Cardiac Glycosides: digoxin. Quality Control.

UM-78-MO365

COMPUTERIZED GAS CHROMATOGRAPHIC SCREENING OF VOLATILE STIMULANTS, SYMPATHOMIMETIC AMINES AND NARCOTIC ANALGESICS USING A NITROGEN SELECTIVE DETECTOR. R. Dugal; M. Bertrand; R. Masse, Farmaceutisch Tijdschrift voor Belgie, v55 n3 p55-83 (May-Jun 1978)

The primary purpose of this paper is to review some of the methodological aspects of the doping control analytical program at the Montreal Olympic Games, particularly gas chromatographic screening and preliminary identification of central nervous system stimulants, sympathomimetic amines, and narcotic analgesics (and their respective metabolites) extracted from urine. The complexities associated with such analyses are discussed and recent technological advances in the field of chromatographic signal detection and computer acquisition and reduction of data are presented. Pharmacokinetic data obtained with some typical urinary excretion studies are described to illustrate the necessity of obtaining such data in the construction of an adequate screening system. Finally, the feasability of screening for a large number of drugs and their metabolites is presented and discussed. (JA)

16 refs

KEYWORDS: Opiates and Related Agents. Stimulants. Sympathomimetic (Adrenergic) Agents. General Drug Screening: Other Techniques.

UM-79-MO366

DEVELOPMENT OF A LOW COST PORTABLE FLUOROMETRY TECHNOLOGY AND QUANTIFICATION OF CANNABINOIDS IN BODY FLUIDS, FINAL REPORT. J.L. Valentine; P.L. Gutshall; B.H.C. Niu; P.J. Bryant; O.H.M. Gan; P. Psaltis (Apr 1979)

Reported here are two methods developed for determining delta-9-tetrahydrocannabinol (delta-9-THC) and its major metabolite 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid (9-CO_2H-delta-9-THC) in human blood plasma utilizing high-pressure liquid chromatography (HPLC) and ultraviolet (UV) detection. The method developed for analysis of delta-9-THC was accomplished using an extraction of 1 ml of plasma with petroleum ether followed by normal phase HPLC analysis. With the method, the lower practical limit of quantification was found to be 10 ng/ml, but a detection limit of 5 ng/ml was readily achieved. Thus the method would be useful for quantifying delta-9-THC in the one-hour period following marijuana smoking.

For the analysis of 9-CO_2H-delta-9-THC, a HPLC-UV method was developed utilizing a reverse phase column. Although the lower practical quantification limit was found to be 10 ng/ml of plasma, the plasma levels determined in several marijuana smokers were found to give a response greater than that observed for a 100 ng/ml standard. The method was used to determine the plasma levels of 9-CO_2H-delta-9-THC in both marijuana smokers and in patients receiving delta-9-THC. Results indicated that 9-CO_2H-DELTA-9-THC does not give as smooth a plasma decay curve as delta-9-THC and that levels remain quite high for twenty-four hours following marijuana smoking. This assay method may be of practical value in identifying a marijuana user.

A third type of assay method was also developed during the study for one of the major constituents of marijuana, cannabinol (CBN). An assay was developed for saliva which allowed CBN present from marijuana smoking to be detected. A limited study was conducted using saliva from both marijuana smokers and nonsmokers as well as the saliva from nonsmokers to which 1 ng/ml of CBN was added. The results indicate that a marijuana smoker can be identified if at least 1 ng/ml of CBN is present in the saliva.

All three of the methods developed during the study represent an advance in reducing the complexity, time, and expense in assaying for marijuana use. (JAM)

10 refs

National Highway Traffic Safety Administration technical report DOT-HS-804-009

KEYWORDS: Cannabis Sativa L. and Related Agents: cannabinol*. delta-9-tetrahydrocannabinol*. Metabolites of Drugs and Other Agents: 11-nor-delta-9-THC-9-carboxylic acid*. Cannabis Sativa L. and Related Agents. Drug Concentrations in Body Fluids: Acute Dose Study. Specific Drug Screening: Other Techniques.

UM-78-M0367

INSTRUMENTAL APPLICATIONS IN FORENSIC DRUG CHEMISTRY. PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM, MAY 29-30, 1978, M. Klein; A.V. Kruegel; S.P. Sobol, eds., Washington, D.C.: U.S. Government Printing Office (1978)

The papers collected in this volume were presented at the International Symposium on Instrumental Applications in Forensic Drug Chemistry held in Arlington, Virginia on May 29 and 30, 1978.

The Symposium consisted of four sessions: Spectroscopy, Computer Applications, Chromatographic Advances, and Special Topics. It covered current methodology and approaches and also projected future needs and developments.

The Symposium presented twenty-four experts from eight countries. The current state-of-the-art in various countries is discussed, as well as instrumental advances encompassing spectrometry, computers, and chromatography. Also discussed are such topics as drug standards, scanning electron and light microscopy, immunoassays, and toxicology. This volume includes review papers in mass spectrometry and chemical identification processes as well as papers on the quantification of drugs by GC-MS-COM systems and negative ion mass spectrometry.

Techniques of Fourier transform infrared spectrometry and nuclear magnetic resonance and their possible future applications to the forensic sciences are discussed. The use of mass spectral computer systems in drug identification, and some computer programs in Federal, State and overseas facilities are described.

Many and varied applications of high-pressure liquid chromatography and gas chromatography, as well as improvements and capabilities of the instruments used in these techniques, are covered. Also, derivatization techniques, detection systems, and new approaches to the optimization of chromatographic systems are discussed. (AAM)

290 pages

KEYWORDS: Compilation. Review: Drug Analysis Methodology.

UM-77-M0368

DRUGS AND CHILDREN: METHODS FOR THERAPEUTIC MONITORING, K.B. Hammond, Clinical Toxicology, v10 n2 p159-83 (1977)

While many clinical laboratories monitor blood concentration of drugs to assess therapeutic efficacy and prevent toxicity in adults, they rarely meet the needs of pediatric patients because of special pharmacokinetic problems which must be taken into account when dealing with children. The purpose of this chapter is to describe a variety of analytical procedures which have particular value in monitoring drug therapy in children. Some of the methods of analysis include colorimetry, spectrophotometry, gas-liquid chromatography, and immunoassay. Standardization, quality control, and the need to establish therapeutic and toxic ranges are also discussed.

The major part of this chapter provides discussion and necessary information for the monitoring of specific blood drug concentrations. Among the drugs discussed are chloramphenicol, gentamicin, the sulfonamides, theophylline, phenobarbital, diphenylhydantoin, primidone, and carbamazepine.

The author concludes that there is a need for more investigation into the validity of procedures in current use for the determination of drug levels in biologic fluids and into the interpretation of the values they produce. Efforts must be made to define those drugs for which blood level information is needed and to develop rapid, sensitive, and accurate assays which can be performed by the routine clinical laboratory. (HSRI)

99 refs

KEYWORDS: Analgesics and Antipyretics: carbamazepine. Anti-Asthmatics: theophylline. Anticonvulsants (Anti-Epileptics): carbamazepine. phenobarbital. phenytoin. primidone. Barbiturates: phenobarbital. Other Antibiotics: chloramphenicol. gentamicin. Stimulants: theophylline. Sulfonamides. Review: Drug Analysis Methodology.

UM-77-MO369

GUIDE TO URINE TESTING IN DRUG ABUSE PREVENTION AND MULTIMODALITY TREATMENT PROGRAMS, K.K. Kaistha, Journal of Chromatography, v141 p146-96 (1977)

The need for a specific, sensitive, and versatile, as well as simple and inexpensive technique for measuring drugs of abuse has increased in recent years as drug usage rates continue to rise. This paper discusses one type of such a method--urinalysis. The paper attempts to provide information for physicians, therapists, program directors, and drug counselors on the following topics related to urine testing: (1) the purpose of urine testing; (2) basic knowledge about the dynamic nature of abused drugs in the body for correct interpretation of urinalysis data; (3) definitions of commonly used terms in urine analysis; (4) existing detection procedures pertaining to drugs of abuse and drugs used in drug abuse treatment; (5) setting up toxicology laboratory facilities; and (6) cost of analysis for testing more than one drug per urine specimen. A major objective of this study is to enable drug administrators and executive and clinical directors to make knowledgeable decisions in the choice of an appropriate toxicology laboratory facility, the type of drugs to be tested by urinalysis, drug abuse treatment monitoring efficac , and the need for additional treatment.

Drug dynamics and interpretation of urinalysis data are provided for eight major drugs and drug groups: (1) heroin; (2) codeine; (3) quinine and procaine; (4) cocaine; (5) central nervous stimulants; (6) sedative hypnotics including barbiturates, glutethimide, methyprylon, methaqualone, meprobamate, and ethchlorvynol; (7) drugs used in the treatment of psychoses, anxiety, and depression including phenothiazine derivatives, benzodiazepines, tricylic antidepressants, and psychotogenic and psychotomimetic drugs; and (8) miscellaneous analgesics and drugs used in the treatment of drug abuse.

Special attention is given to detection procedures in current use, especially criteria for evaluation of thin-layer chromatography, gas chromatography, gas-liquid chromatography, liquid chromatography, gas chromatography-mass spectrometry, spectrophotofluorometry, and immunoassays. The review concludes with some practical questions and answers on problems encountered in routine urinalysis. (HSRI)

292 refs

KEYWORDS: Analgesics and Antipyretics: cyclazocine. propoxyphene. Anticonvulsants (Anti-Epileptics): clonazepam. phenobarbital. Antidepressants: amitriptyline. desipramine. doxepin. imipramine. isocarboxazid. nortriptyline. phenelzine. tranylcypromine. Barbiturates: amobarbital. pentobarbital. phenobarbital. secobarbital. Cannabis Sativa L. and Related Agents: marijuana. Expectorant and Cough Preparations (Antitusive Agents): codeine. Ganglionic Blocking and Stimulating Agents: 2,5-dimethoxy-4-methylamphetamine (DOM) (STP). Hallucinogens and Related Agents: bufotenine. lysergic acid diethylamide (LSD). mescaline. methylenedioxyamphetamine (MDA). phencyclidine. psilocin. psilocybin. N,N-diethyltryptamine (DET). N,N-dimethyltryptamine (DMT). 2,5-dimethoxy-4-methylamphetamine (DOM) (STP). 3,4,5-trimethoxyamphetamine. 4-methoxyamphetamine (PMA). Local Anesthetics: cocaine. procaine. Metabolites of Drugs and Other Agents: oxazepam. psilocybin. Minor Tranquilizers (Anti-Anxiety and Ataractics): chlordiazepoxide. diazepam. meprobamate. oxazepam. Muscle Relaxants (Central): diazepam. Nonbarbiturates: ethchlorvynol. flurazepam. glutethimide. methaqualone. methyprylon. Opiates and Related Agents: codeine. heroin. l-alpha-acetylmethadol. methadone. naloxone. naltrexone. pentazocine. pethidine. Plasmodicides: quinine. Stimulants: amphetamine. cocaine. General Drug Screening: Gas Chromatography. General Drug Screening: Optical Techniques. General Drug Screening: Other Techniques. General Drug Screening: Thin-Layer and Paper Chromatography. Proficiency Testing. Review: Drug Analysis Methodology.

UM-76-MO370

POLAROGRAPHISCHE BESTIMMUNGEN DES EUHYPNICUMS FLURAZEPAM IN SEINEN ARZNEIFORMEN. 20. MITTEILUNG ARZNEIMITTELANALYSEN MITTELS POLARGRAPHISCHER METHODEN, H. Oelschlager; F. Druckrey; F.I. Senguen, Pharmaceutica Acta Helvetiae, v51 n12 p353-361 (1976)

This paper discusses drug analysis by polarographic methods, describing specifically analysis of flurazepam. Cathode ray polarography and differential pulse polarography were shown to rapidly assay flurazepam in commercial preparations to within a standard

deviation of ±3%. Also discussed in the paper is the stability of flurazepam in buffer solutions and its electro-analytical properties.

The English translation of the title of this paper is DRUG ANALYSIS BY POLAROGRAPHIC METHODS. PART 20. POLAROGRAPHIC ANALYSIS OF THE EUHYPNICUM, FLURAZEPAM, IN DRUGS. (JAM)

24 refs German

KEYWORDS: Nonbarbiturates: flurazepam*. Confirmatory/Quantitative Drug Analysis: Other Techniques.

UM-77-M0371

A SENSITIVE RADIOIMMUNOASSAY FOR FENTANYL. PLASMA LEVEL IN DOGS AND MAN. M. Michiels; R. Hendriks; J. Heykants, European Journal of Clinical Pharmacology, v12 n2 p153-8 (Oct 1977)

This paper reports development of a sensitive radioimmunoassay capable of measuring subnanogram levels of fentanyl in plasma. It also describes an investigation of the specificity of the fentanyl antiserum. The value of the assay for pharmacokinetic studies is demonstrated by measuring the plasma concentration of fentanyl in man and in dogs.

Antiserum to fentanyl was obtained in rabbits repeatedly injected with carboxyfentanyl conjugated to bovine serum albumin. Six healthy volunteers aged 21 to 35 years were injected intravenously with 0.2 mg and venous blood was collected in heparin before drug administration and at frequent intervals for up to six hours after administration. Three mongrel dogs weighing 22 to 24 kg were also treated, initially subcutaneously and, one week later, intravenously with 0.02 mg/kg fentanyl. Blood samples were collected at intervals for up to eight hours. Drug concentrations in the plasma samples were calculated from the degree to which an unknown amount of fentanyl inhibited the binding of ^{3}H-fentanyl to antibodies as compared to calibration curves obtained simultaneously for drug added either to control human or dog plasma.

Using the dextran-coated charcoal method of assay, it was possible to assay the drug directly in plasma in amounts as small as 30 picograms in 0.5 ml plasma. The antibody was highly specific for fentanyl and no cross-reaction was observed with its major metabolites. The plasma level of fentanyl could be followed for up to six hours after nine therapeutic doses in dogs and man.

The data obtained from this study, which used a limited number of subjects, indicate the range of plasma levels of fentanyl after a single therapeutic dose. The results demonstrate that this radiommunoassay is sufficiently sensitive and specific for study of the pharmacokinetics of this analgesic in man. (HSRI)

9 refs

KEYWORDS: Opiates and Related Agents: fentanyl*. Confirmatory/Quantitative Drug Analysis: Immunoassay. Pharmacokinetics: Acute Dose.

UM-78-M0372

THIN-LAYER DETECTION OF PENTAZOCINE, TRIPELENNAMINE, PHENCYCLIDINE AND PROPOXYPHENE ALONE OR IN COMBINATION WITH OPIATES IN DRUG ABUSE URINE SCREENING PROGRAMS, K.K. Kaistha; R. Tadrus, Journal of Chromatography, v155 n1 p214-17 (August 1978)

A simple, inexpensive, and reliable thin-layer chromatographic procedure is reported for detection of the widely abused pentazocine (Talwin(R)), tripelennamine (Pyribenzamine(R)), propoxyphene (Darvon(R)), and phencyclidine (PCP). This method is capable of detecting these drugs alone or in combination with opiates. Three commonly used antihistamines are also briefly discussed--methapyrilene, diphenhydramine, and chlorpheniramine.

The technique involves the use of paper impregnated with SA2 cation exchange resin to absorb the drug. The ion-exchange paper is soaked in 20-50 ml of fresh undiluted urine and shaken for thirty minutes. The paper is then removed, rinsed with water, and extracted at pH 10.1 using ammonium chloride-ammonium hydroxide buffer and chloroform-isopropanol. The lower organic layer is pipeted into a conical centrifuge tube containing 0.5% sulfuric acid in methanol and the solvent is evaporated in an oven. The residue along the sides of the tube is washed with methanol, vortexed, and again washed

with methanol, which is then evaporated to dryness. This residue is chromatographed on precoated silica gel glass microfiber sheets.

Two special detection procedures are described in addition to the basic procedure: the first is used if pentazocine, antihistamines, methadone, propoxyphene, or norpropoxyphene are to be detected; the second can be used to detect opiates in addition to the previously mentioned drugs. A technician can analyze 130 urine specimens per day for drugs using the first procedure, and 110 specimens for drugs included in both procedures. (HSRI)

7 refs

KEYWORDS: Analgesics and Antipyretics: propoxyphene. Antihistamine Agents: chlorpheniramine. diphenhydramine. methapyrilene. tripelennamine. Expectorant and Cough Preparations (Antitusive Agents): codeine. Ganglionic Blocking and Stimulating Agents: nicotine. Hallucinogens and Related Agents: phencyclidine. Nonbarbiturates: diphenhydramine. Opiates and Related Agents: codeine. methadone. morphine. pentazocine. Plasmodicides: quinine. Stimulants: nicotine. Specific Drug Screening: Thin-Layer and Paper Chromatography.

UM-78-MO373

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY IN CLINICAL TOXICOLOGY. I. GENERAL DRUGS, L.P. Hackett; L.J. Dusci, Clinical Toxicology, v13 n5 p551-6 (Dec 1978)

This paper describes high performance liquid chromatography (HPLC) methods for analysis of theophylline, acetaminophen, carbamazepine, indomethacin, and sulthiame. The object of this paper is to show that using a small sample size and an identical extraction procedure, these compounds may be analyzed rapidly by HPLC. The method of analysis is described in terms of the detector and solvents used, and the wavelengths and conditions used for the various compounds.

The recoveries obtained using this method were consistent and good. The use of a small sample volume, the rapidity of analysis, and the use of the same protein precipitation extraction procedure for these compounds allows accurate levels to be obtained when clinical or overdose levels are required urgently. The main advantage of this method is that it is possible to obtain accurate results using the same extract for a number of drugs that previously had required different extraction techniques or that had to be derivatized by different methods when being analyzed by gas-liquid chromatography. (HSRI)

10 refs

KEYWORDS: Analgesics and Antipyretics: acetaminophen. carbamazepine. indomethacin. Anti-Asthmatics: theophylline. Anticonvulsants (Anti-Epileptics): carbamazepine. sulthiame. Stimulants: theophylline. Specific Drug Screening: Other Techniques.

UM-79-MO374

THE 1978 COLLEGE OF AMERICAN PATHOLOGISTS THERAPEUTIC DRUG MONITORING INTERLABORATORY SURVEY PROGRAM, R. Juel, American Journal of Clinical Pathology, v72 n2 p306-19 (Aug 1979)

This paper describes and reports the results of the Therapeutic Drug Monitoring Interlaboratory Survey Program begun by the College of American Pathologists in 1978. The purpose of this program was to identify problems in monitoring plasma levels of therapeutic drugs. Fifty laboratories were included in the initial survey. Each participating laboratory received six vials of lyophilized serum specimens on two occasions approximately thirteen weeks apart which they were to analyze using a method of their own choosing. The specimens, all of which were prepared in an identical manner, contained various combinations of the following drugs (for which therapeutic monitoring of plasma levels is necessary) in subtherapeutic, therapeutic, and toxic concentrations: phenytoin, phenobarbital, primidone, ethosuximide, carbamazepine, digoxin, procainamide, N-acetylprocainamide, quinidine, theophylline, lithium, and gentamicin. Participants reported their results in a standardized form. These results were compared to target values established for each drug and statistically analyzed by computer.

For most of the drugs, results covered a wide range of concentrations; however, most results were closely grouped around the target value. In cases where there were

significant differences, these differences could often be attributed to the type of analysis used.

In general, the data from this survey suggest that interlaboratory variation for drug assays is greater than that seen in most other areas of the clinical laboratory. The author attributes these variations to four factors: (1) The results for the 1978 program were grouped and analyzed according to general methods, without taking into account modifications or variations used by the participating laboratories. (2) Standard reference materials in a biological matrix were not available for any of the drugs included in the 1978 survey program. (3) No internal quality control materials were available, so each laboratory was forced to prepare its own control materials. (4) Prior to this program there was no other method by which a laboratory could evaluate its performance in quantifying these drugs. (HSRI)

16 refs

KEYWORDS: Analgesics and Antipyretics: carbamazepine. Anti-Arrhythmia Agents: procainamide. quinidine sulfate. Anti-Asthmatics: theophylline. Anticonvulsants (Anti-Epileptics): carbamazepine. ethosuximide. phenobarbital. phenytoin. primidone. Antidepressants: lithium. Barbiturates: phenobarbital. Cardiac Glycosides: digoxin. Metabolites of Drugs and Other Agents: N-acetylprocainamide. Other Antibiotics: gentamicin. Other CNS Agents: lithium. Stimulants: theophylline. Proficiency Testing.

UM-80-M0375

IMMUNOFLUORESCENCE DETECTION OF DRUGS IN POSTMORTEM TISSUES: A NEW TECHNIQUE WITH POTENTIAL FOR ASSESSMENT OF DRUG INFLUENCE IN CAUSE OF DEATH, J. Balkon; J.H. Bidanset; V.D. Lynch, Journal of Forensic Sciences, v25 n1 p88-94 (Jan 1980)

This report describes a new immunofluorescence technique for the detection and possible characterization of drug content in postmortem tissues. By using antisera generated against a drug-protein conjugate, the stabilization of tissue-sequestered drug is accomplished by incubation of fresh frozen sections of tissue with dilute solutions of rabbit antidrug antibodies. Secondary incubation with a fluorescence-labeled antirabbit immunoglobulin labels these points of sequestration. Tissue sections so stained are examined by fluorescence microscopy. In studies with rats given graded doses of morphine sulfate, there were discernible differences in tissue binding of morphine in brain sections from animals treated "therapeutically," fatally, and chronically. Extension of these studies to human autopsy material is anticipated and potential problems are discussed. This technique offers the forensic toxicologist the potential for evaluating the drug content of tissues in situ. (JA)

5 refs

KEYWORDS: Opiates and Related Agents: morphine. Specific Drug Screening: Optical Techniques.

UM-79-M0376

SIMULTANEOUS DETERMINATION OF MORPHINE AND CODEINE IN BLOOD BY USE OF SELECT ION MONITORING AND DEUTERATED INTERNAL STANDARDS, D. Pearce; S. Wiersema; M. Kuo; C. Emery, Clinical Toxicology, v14 n2 p161-8 (Feb 1979)

Until recently, the only method available to provide chemical substantiation of heroin intoxication was analysis of urine samples for the presence of morphine, the major metabolite of heroin. For several reasons this method was unsatisfactory. Described here is a method for the simultaneous determination of morphine and codeine in blood. The procedure entails the use of gas chromatography-mass spectrometry coupled with a data system, and the use of deuterated morphine and codeine as internal standards. The time required for analysis of twenty samples, standard and blank, including sample preparation, hydrolysis, extraction, derivatization, and analysis, is approximately five hours. The method was applied to 1,025 blood samples. Blood morphine and codeine levels in the samples are discussed in terms of their ratios and sources.

The authors conclude that any correlation between morphine blood concentration with degree of intoxication is impossible at this point, since several discrepancies were found between plasma concentrations and observed levels of intoxication. Therefore, analysis of blood samples for the presence of morphine can determine the degree of heroin or morphine intoxication only when there is also a careful evaluation of the symptoms by a qualified and experienced observer. In the absence of this evaluation a

given morphine concentration is of limited significance to the issue of heroin or morphine intoxication. (HSRI)

14 refs

KEYWORDS: Expectorant and Cough Preparations (Antitusive Agents): codeine*. Opiates and Related Agents: codeine*. morphine*. Confirmatory/Quantitative Drug Analysis: Gas Chromatography-Mass Spectrometry. Epidemiologic Research: Drug Concentrations in Body Fluids.

UM-79-MO377

CALIFORNIA ASSOCIATION OF TOXICOLOGISTS PROFICIENCY TESTING PROGRAM, C.B. Walberg, Clinical Toxicology, v14 n2 p199-203 (Feb 1979)

A proficiency testing program instituted by the California Association of Toxicologists in 1968 is described. The purpose of the program is to permit a laboratory to evaluate its methodology and efficiency and to relate its results to other laboratories with whom it can communicate. The program is conducted on a volunteer basis with a sample containing an average of three drugs prepared by a different member each time. In 1968 one sample per year was sent to each participating laboratory; by 1974 the number of samples per year had increased to four. A wide range of drugs has been used in the samples including ethanol, diazepam, dephenylhydantoin, morphine, and several heavy metals.

After the sample is prepared, it is mailed, analyzed by the laboratory, and analysis results are returned anonymously to the person who prepared the sample. The results are collated and a compilation of all results mailed to each participant to allow the participant to reevaluate any discrepancy. The response to an individual sample appears to be related to the type of sample, the clarity and content of the description information, and the instrumentation and methodology required to perform the indicated assays. In general, urines for drugs of abuse had the highest response while those assays for heavy metals had the lowest response, indicating that many more laboratories screen for drugs of abuse than they do for heavy metals. (HSRI)

1 ref

KEYWORDS: Proficiency Testing.

UM-79-MO378

THE DETECTION OF SOME BASIC DRUGS AND THEIR MAJOR METABOLITES USING GAS-LIQUID CHROMATOGRAPHY, L.J. Dusci; L.P. Hackett, Clinical Toxicology, v14 n5 p587-93 (May 1979)

Described here is a rapid method for the extraction and detection of some basic drugs and their metabolites in urine using primarily gas chromatography and also some mass spectrometry. The retention times of several basic drugs and their metabolites on a 3% OV 17 gas chromatographic column are presented. Some of the drugs listed include chlormethiazole, ephedrine, pethidine, pheniramine, lignocaine, glutethimide, methapyrilene, methadone, propoxyphene, amitriptyline, nortriptyline, imipramine, methaqualone, desipramine, doxepin, pentazocine, procainamide, codeine, carbamazepine, chlorpromazine, promethazine, flurazepam, quinine, dextromonamide, and thoridazine.

This extraction method is rapid, allowing effective extraction of a large number of basic and neutral drugs as well as their metabolites. Certain drug ingestions result in characteristic patterns which can aid in the identification of drugs in cases of multiple drug overdosage. Therefore the method is beneficial in routine overdose screening since the characteristic gas chromatographic pattern can give more positive proof of the ingested drug than a single peak. (HSRI)

8 refs

KEYWORDS: General Drug Screening: Systems.

UM-79-MO379

COMPARISON OF SPECTROFLUOROMETRIC AND GC/MS PROCEDURES FOR THE QUANTITATION OF MORPHINE IN BLOOD AND BRAIN, D. Reed, Clinical Toxicology, v14 n2 p169-80 (Feb 1979)

The need for increased specificity as well as high sensitivity in detection of morphine and its derivatives, especially in forensic work, has resulted in greater use of gas-chromatography-mass spectrometry procedures (GC/MS) utilizing deuterated morphine as an internal standard. This paper presents comparative data based on the use of fluorometry and GC/MS in quantitation of morphine and its derivatives in fifty-five fatal cases.

For each case blood and brain morphine concentrations are presented as determined by both fluorometry and gas chromatography/mass spectrometry. Also provided for each sample is the ratio of spectrofluorometric procedure morphine values versus the nonhydrolyzed GC/MS values.

A comparison of the values obtained indicates that in both the blood and the brain tne spectrofluorometric morphine values were approximately one-half of those obtained by GC/MS. The lower values of fluorometry are probably due to its quenching interferences and the use of the internal standard in the GC/MS analysis which corrected for extraction variation. Therefore, GC/MS analysis is probably more accurate.

Of the thirty-eight cases analyzed by fluorometry, the morphine would have been missed in seven blood samples if the analyses had not been repeated by GC/MS. (HSRI)

14 refs

KEYWORDS: Opiates and Related Agents: morphine*. Confirmatory/Quantitative Drug Analysis: Gas Chromatography-Mass Spectrometry. Confirmatory/Quantitative Drug Analysis: Optical Techniques. Evaluation of Methods for Drug Analysis.

UM-78-P0047

USING PHARMACOKINETICS IN DRUG THERAPY II: RAPID ESTIMATES OF DOSAGE REGIMENS AND BLOOD LEVELS WITHOUT KNOWLEDGE OF PHARMACOKINETIC VARIABLES, G.E. Schumacher; J.C. Griener, American Journal of Hospital Pharmacy, v35 n4 p454-9 (Apr 1978)

The modification of the superposition method, which yields fast and reasonably accurate estimates of dosage regimens and steady-state maximum and minimum blood levels, is described.

In the modified superposition method, input data are obtained from the blood, plasma, or serum concentration versus time profile resulting from administration of a single dose of the drug. These estimates are valid only when the pharmacokinetics of the drug are linear and elimination from the body occurs according to first-order kinetics. Limitations of the method are discussed.

It is concluded that this is a rapid and clinically useful method for pharmacokinetic estimations. Using simple equations and a simple dose blood level versus time profile, estimates of the "true" steady-state levels are achieved without having to characterize the underlying pharmacokinetic variables. (AAM)

8 refs

KEYWORDS: Confirmatory/Quantitative Drug Analysis: Other Techniques. Pharmacokinetics: Acute Dose.

UM-78-P0048

USING PHARMACOKINETICS IN DRUG THERAPY III: ESTIMATING DOSAGE REGIMENS AND BLOOD LEVELS USING THE FRACTION-LOST METHOD, G.E. Schumacher, American Journal of Hospital Pharmacy, v35 n8 p955-7 (Aug 1978)

This paper describes the "fraction of drug lost during interval" method, a method that yields rapid estimates for drug dosage regimens and blood levels without tedious calculations. The necessary equations are presented and applied practically to problem situations.

The fraction-lost method has several limitations which must be taken into account: (1) The method requires that the pharmacokinetics of the drug are linear and that elimination from the body occurs as a first-order process. A change in the order of the elimination process during continued administration of the dosage regimen invalidates the use of the method. (2) The method requires that no changes occur in the pharmacokinetic values of the drug during continued administration. Changes in absorption or clearance, resulting from alterations in bioavailability or renal, hepatic, or distribution functions call for recalculation using the altered values. (3)

The method assumes that the blood level versus time profile for the drug is reasonably characterized by a one-compartment open kinetic model which provides estimates of body levels of the drug and dosage regimens of clinical use. When a multicompartment open kinetic model is more appropriate, then errors occur in the estimates. (4) Estimates of minimum and maximum blood, plasma, or serum concentrations of the drug at steady state reported in the literature will result in average estimates, and individual patient values may vary significantly from the average.

In spite of these limitations, the author highly recommends this method to practitioners for rapid estimates of steady-state drug levels and dosage regimens. (HSRI)

4 refs

KEYWORDS: Confirmatory/Quantitative Drug Analysis: Other Techniques. Pharmacokinetics: Acute Dose.

UM-78-P0049

SELF-INHIBITORY DOPAMINE RECEPTORS: THEIR ROLE IN THE BIOCHEMICAL AND BEHAVIORAL EFFECTS OF LOW DOSES OF APOMORPHINE, G. Di Chiara; G.U. Corsini; G.P. Mereu; A. Tissari; G.L. Gessa, Advances in Biochemical Psychopharmacology, v19 p275-92 (1978)

This article reviews biochemical and electrophysiological evidence for self-inhibiting dopamine receptors, kainic acid-induced destruction of postsynoptic dopamine receptors, functional changes induced by small doses of apormorphine in rodents, and sedation and sleep in rodents. The dopaminomimetric nature of the hypnotic effect of low dosages of apomorphine and whether this effect might be prevented by different neuroleptics such as pimozide, benzperidol, and sulpiride are also discussed. Other areas of concern are behavioral changes induced by small doses of apomorphine in humans, particularly sedation and sleep induced by nonemetic doses of apomorphine.

The major conclusions drawn from the study are the following: (1) Apomorphine causes a series of biochemical, neurological, psychological, and behavioral changes that are prevented by specific blockers of dopamine receptors, suggesting that these responses are mediated through stimulation of such receptors. (2) Some changes such as the decreased motor activity in rodents, the therapeutic effect of the drug in Huntington's chorea and tardive dyskinesia, and perhaps the antipsychotic effect might be due to a decreased dopaminergic transmission and therefore might result from stimulation of self- inhibitory dopamine receptors. (HSRI)

40 refs

KEYWORDS: Emetics: apomorphine. Opiates and Related Agents: apomorphine. Sympathomimetic (Adrenergic) Agents: dopamine. Animal Research.

UM-77-P0050

CONTINUOUS SAMPLING AS A PHARMACOKINETIC TOOL, B. Vogelstein; A.A. Kowarski; P.S. Lietman, Clinical Pharmacology and Therapeutics, v22 n2 p131-9 (1977)

Continuous sampling (CS) of blood through a nonthrombogenic catheter is presented as a tool for determining various pharmacokinetic parameters after a single injection of a drug. In addition to defining many of the usual parameters used in pharmacokinetic analyses, CS provides an accurate and direct determination of the total area under the plasma concentration curve. The theoretic background underlying the CS method is derived, and a practical formulation for its use in a clinical setting is described.

The aminoglycoside antibiotic amikacin was chosen to exemplify the use of this technique. The drug was administered to six children, and CS was used to define plasma and single organ (kidney) clearance, volume of distribution, half-life during the final elimination phase, the shape of the plasma concentration curve, and the exponential factorization of this curve for multicompartmental analysis.

The CS method has several theoretical and practical advantages over the usual technique of intermittent blood sampling such as accuracy in the determination of the plasma concentration-time curve integral, relative model independence, requirement for few samples, and ease in obtaining samples. (JA)

26 refs

KEYWORDS: Other Antibiotics: amikacin*. Pharmacokinetics: Chronic Dose. Variables Influencing Drug Concentration Data.

UM-77-P0051

MODELLENTWICKLUNG IN DER PHARMAKOKINETIK [MODEL BUILDING IN PHARMACOKINETICS/PART V: SIMULATION OF BLOOD LEVEL CURVES FOLLOWING REPETITIVE DOSING AND THEIR EXPERIMENTAL VERIFICATION], R. Hammer; G. Bozler; G. Heinzel; F.W. Koss. Arzneimittel Forschung, v27 (I) n4a p928-31 (1977)

An equation is given to describe the plasma level curve of linear compartment model following multiple dosing of various doses after various time intervals. The equation is especially suitable to be used with desk top computers equipped with a plotting device. A dosage regimen can be simulated using the parameters derived from single dose experiments. Experimental check-up of the predicted curves is necessary and illustrated by two examples. Systematic deviations from the prediction indicate changes in the biological system in absorption, in enzyme induction, in saturable processes, or in other variables. (JA)

15 refs German

KEYWORDS: Pharmacokinetics: Chronic Dose. Variables Influencing Drug Concentration Data.

UM-77-P0052

INVESTIGATING RELATIONSHIPS BETWEEN IN VIVO AND IN VITRO PHARMACOLOGICAL VARIABLES FOR THE PURPOSE OF PREDICTION, W.R. Fairweather, Journal of Pharmacokinetics and Biopharmaceutics, v5 n4 p405-18 (1977)

Consistency of effect in vivo is an important characteristic of a drug product, and great variation from lot to lot or between manufacturers is not desirable. The variation usually arises when some lots fail to meet minimum standards. It may then be necessary to develop a procedure for detecting and screening out these defective lots. A new, heuristic approach is presented for evaluating procedures in which screening is to be based on in vitro measurements rather than on more costly in vivo measures. A quantification of risks is defined from which a minimum risk procedure may be selected from a set of candidate procedures. This approach is shown to be more appropriate than those based on correlational techniques. (JA)

5 refs

KEYWORDS: Variables Influencing Drug Concentration Data.

UM-78-P0053

THE UPTAKE AND ELIMINATION OF CHLOROFORM IN MAN, N. Poobalasingham; J.P. Payne, British Journal of Anaesthesia, v50 n4 p325-9 (1978)

The rate of alveolar uptake of chloroform was studied in sixteen patients aged 28 to 68 years during general anesthesia. Eight patients breathed chloroform spontaneously at concentrations of 2-2.5% and in eight the lungs were ventilated with a 1% concentration. Elimination was studied after thirty and sixty-five minutes of exposure to the anesthetic. The arterial and venous blood concentrations of chloroform plotted against time during the early phase of equilibration showed that the initial uptake of chloroform was rapid, approaching a plateau after forty to fifty minutes. In patients breathing spontaneously the arterial concentration of chloroform, which averaged 17.28 ± 4.1 mg dl^{-1}, did not exceed 25% equilibration with the inspired concentration, whereas under controlled ventilation with 1% chloroform the mean concentration was 10.14 ± 3.30 mg dl^{-1}, which amounted to an equilibration of approximately 41%. The elimination of chloroform from the body was rapid, so that recovery was not prolonged.

The authors conclude that, contrary to current practice, chloroform does not deserve to be abandoned as a surgical anesthetic. (JAM)

10 refs

KEYWORDS: Volatile Solvents: chloroform*. Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-78-P0054

LA BIODISPONIBILITE, UN FAUX PROBLEME [BIODISPOSITION, A FALSE PROBLEM], P. Biron, L'Union Medicale du Canada, v107 n12 p1179-83 (Dec 1978)

This paper discusses the determinants of adequate plasma levels of drugs, the prescription of proper dosages, and the compliance of patients with regards to drug consumption. It also discusses the relative importance of bioavailability, and compares placebo effects compared to pharmacological actions. (JA)

2 refs French

KEYWORDS: Review: Drug Concentration-Effect Relationships.

UM-79-P0055

ALTERED DRUG BINDING DUE TO THE USE OF INDWELLING HEPARINIZED CANNULAS (HEPARIN LOCK) FOR SAMPLING, M. Wood; D.G. Shand; A.J.J. Wood, Clinical Pharmacology and Therapeutics, v25 n1 p103-7 (1979)

This study examines the effects on drug binding of administering heparin, which is likely to be used during multiple blood sampling in order to prevent clots forming in the cannula.

In this study the effect of the use of the so-called heparin lock for blood sampling on the binding of propranolol was studied in seven healthy males aged 25 to 31 and a cumulative dose-response curve to heparin constructed. The use of this method of blood sampling introduced considerable artifactual changes into the measurement of propranolol's plasma binding. The free fraction rose from 9.9% to 13.4% after only 50 units of heparin was used to flush the cannula. The increase in the free fraction of propranolol showed excellent correlation with the increase in free fatty acid levels ($p<0.001, r = 0.996$). The importance of ensuring that sampling techniques do not introduce artifactual changes in pharmacokinetic studies is emphasized. (JAM)

9 refs

KEYWORDS: Anti-Anginal Agents: propranolol. Anti-Arrhythmia Agents: propranolol. Anti-Coagulants: heparin*. Hypotensive (Antihypertensive) Agents: propranolol. Variables Influencing Drug Concentration Data.

UM-77-P0056

ISOLATION AND IDENTIFICATION OF MORPHINE 3- AND 6-GLUCURONIDES, MORPHINE 3,6-DIGLUCURONIDE, MORPHINE 3-ETHEREAL SULFATE, NORMORPHINE, AND NORMORPHINE 6-GLUCURONIDE AS MORPHINE METABOLITES IN HUMANS, S.Y. Yeh; C.W. Gorodetzky; H.A. Krebs, Journal of Pharmaceutical Sciences, v66 n9 p1288-93 (Sep 1977)

This paper reports the isolation and identification of morphine 3- and 6-glucuronides, morphine 3,6-diglucuronide, morphine 3-ethereal sulfate, normorphine, normorphine 6-glucuronide, and normorphine 3-glucuronide from the urine of morphine-dependent human subjects being maintained on morphine sulfate at a dose of 240 mg per day. Subjects were four postaddict males in good health between the ages of twenty-seven and forty-one.

These metabolites were isolated and identified in the subjects' urine by free phenol and glucuronide tests, enzymatic hydrolysis, gas-liquid chromatography, thin-layer chromatography, ultraviolet spectroscopy, and gas-liquid chromatography-mass spectrometry.

The implications of the results of the analysis are discussed as they relate to previous research. (HSRI)

29 refs

KEYWORDS: Metabolites of Drugs and Other Agents: morphine 3-ethereal sulfate. morphine 3-glucuronide. morphine 3,6-diglucuronide. morphine 6-glucuronide. normorphine. normorphine 6-glucuronide. Opiates and Related Agents: morphine. normorphine. Pharmacokinetic Factors: Drug Metabolism. Pharmacokinetics: Chronic Dose. Specific Drug Screening: Other Techniques. Specific Drug Screening: Thin-Layer and Paper Chromatography.

UM-78-P0057

SIGNIFICANCE OF ERROR ASSOCIATED WITH USE OF THE ONE-COMPARTMENT FORMULA TO CALCULATE CLEARANCE OF THIRTY-EIGHT DRUGS, B.H. Dvorchik; E.S. Vesell, Clinical Pharmacology and Therapeutics, v23 n6 p617-23 (Jun 1978)

A survey of the literature was performed to gather information on the magnitude of the error introduced into calculating drug clearance by using a one-compartment formula for drugs whose dispositions follow multicompartment kinetics. Sufficient data to permit quantitation of this error were found for thirty-eight drugs. The magnitude of the error varied widely depending on the initial distribution of the particular drug. Antipyrine and such commonly used drugs as amobarbital, chlordiazepoxide, nortriptyline, pentobarbital, phenytoin, sulfisoxazole, theophylline, tolbutamide, and warfarin had errors of 8% or less, thereby permitting utilization of the one-compartment formula for determination of drug clearances without much loss of accuracy. However, twenty-two drugs exhibited errors ranging from 12% to 196%; for these drugs, the one-compartment formula introduced considerable inaccuracy. The errors for diazepam, meperidine, and propranolol, when administered to patients with hepatic cirrhosis or to hypertensive patients, were 4%, 5%, and 6% respectively, whereas in normal subjects the errors were 18%, 14%, and 21%. Thus, the clinical status of the subject may influence the choice of the model used.

On the basis of these data the authors conclude that for some commonly used drugs the one-compartment formula is acceptable for determining drug clearance, loading dose, or maintenance dose. (JA)

41 refs

KEYWORDS: Variables Influencing Drug Concentration Data.

UM-77-P0058

DIAZEPAM ACTIONS AND PLASMA CONCENTRATIONS FOLLOWING ETHANOL INGESTION, S.M. MacLeod; H.G. Giles; G. Patzalek; J.J.Thiessen; E.M. Sellers, European Journal of Clinical Pharmacology, v11 n5 p345-9 (1977)

This study attempted to determine whether there is a significant influence of ethanol upon the absorption or distribution of diazepam by assessing motor performance and plasma concentrations with and without ethanol pretreatment. Eight male subjects aged 18 to 25 were given 10mg diazepam orally alone or in combination with 0.5 g/kg ethanol. Blood samples were taken hourly for eight hours and subjects were tested for pursuit rotor performance at 30, 60, 90, 120, 240, and 360 minutes after drug.

In all of the volunteers, the combination of ethanol and diazepam produced a greater decrease in motor performance on the pursuit rotor than diazepam alone. The pharmacologic effect of diazepam was enhanced by 73% and this potentiation was associated with significantly greater diazepam concentrations ($P<0.01$) than after diazepam alone. The failure to observe any increase in the concentrations of the principal metabolite N-desmethyl diazepam during the period of enhanced pharmacologic effect precludes any change in the demethylating metabolic process as being responsible.

The data suggest ($0.10>P>0.05$) a trend to the smaller volume of distribution of diazepam when ethanol is administered prior to diazepam ingestion. The subjects showed acute tolerance to the effects of diazepam. Lower plasma concentrations on the descending side of the plasma diazepam concentration versus time profile were linked with the same pharmacologic responses associated with a greater drug concentration on the descending portion of the same curve. (JAM)

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam*. Muscle Relaxants (Central): diazepam*. Nonbarbiturates: ethanol (ethyl alcohol)*. Drug Concentration-Effect Study: Driving Skill Impairment. Experimentation: Acute Dosage Study. Experimentation: Study of Combined Effects of Drugs. Pharmacokinetics: Acute Dose. Psychomotor Tests.

UM-78-P0059

CRITICAL EVALUATION OF THE POTENTIAL ERROR IN PHARMACOKINETIC STUDIES OF USING THE LINEAR TRAPEZOIDAL RULE METHOD FOR THE CALCULATION OF THE AREA UNDER THE PLASMA LEVEL-TIME CURVE, W.L. Chiou, Journal of Pharmacokinetics and Biopharmaceutics, v6 n6 p539-46 (1978)

The purpose of this article is to critically evaluate potential sources of error when using the conventional linear trapezoidal rule method for various pharmacokinetic studies. A simple system of the one-compartment open model with first-order absorption and first-order elimination kinetics is used for illustration.

The linear trapezoidal rule method is commonly used for the estimation of the area under the plasma level-time curve. Error analyses are performed when the method is used in first-order absorption and first-order elimination kinetics in the one-compartment system. This study found that significant underestimations and overestimations in area during the absorption phase and postabsorption phase, respectively, can occur when the method is improperly used. During the exponential postabsorption phase the relative error is only a function of the ratio (n) of the time interval over the half-life of the two plasma data points in the interval. The error from the linear trapezoidal rule method at n=0.5 is about 1%. The error increases to 15.5% and 57.1% when n is increased to 2 and 4, respectively. It is recommended that for most absorption studies the linear trapezoidal method be used for prepeak and plateau plasma data and the logarithmic trapezoidal method for postpeak plasma data. (JAM)

11 refs

KEYWORDS: Variables Influencing Drug Concentration Data.

UM-77-P0060

COMPARATIVE BIOAVAILABILITY OF FOUR COMMERCIAL QUINIDINE SULFATE TABLETS, J.D. Strum; J.L. Colaizzi; J.M. Jaffe; P.C. Martineau; R.I. Poust, Journal of Pharmaceutical Sciences, v66 n4 p539-42 (Apr 1977)

A comparative bioavailability study was performed using four commercially available, chemically equivalent brands of quinidine sulfate tablets. Two 200 mg tablets were administered to eleven different male subjects aged 20 to 37 years following a completely randomized crossover design. Serum levels, urinary excretion data, and derived pharmacokinetic parameters were compared statistically.

There were no statistical differences in the extent of quinidine absorption from the four brands of tablets as evidenced by cumulative urinary excretion values and the areas under the serum level-time curves. Significant differences in the mean serum levels at 0.5 and 1 hour and differences in the peak times and absorption rate constants indicate that there was a difference in the absorption rate between treatments A and D, and C and D. A significant difference in the peak times also was noted for treatments B and C. When mean disintegration times for the four tablet formulations were compared with their values for absorption rate, calculated peak time, and mean serum levels at 0.5 and 1 hour, rank-order correlations were observed. A considerable degree of variability in quinidine elimination was noted, with half-life values ranging from 2.71 to 8.12 hours (mean half-life of 5.36 hours). (JAM)

39 refs

KEYWORDS: Anti-Arrhythmia Agents: quinidine sulfate*. Pharmacokinetics: Acute Dose.

UM-77-P0061

INTRAINDIVIDUAL RELATIONSHIPS BETWEEN SERUM PROTEIN BINDING OF DRUGS IN NORMAL HUMAN SUBJECTS, PATIENTS WITH IMPAIRED RENAL FUNCTION, AND RATS, A. Yacobi; G. Levy, Journal of Pharmaceutical Sciences, v66 n9 p1285-6 (Sept 1977)

The serum protein binding of phenytoin, salicylic acid, sulfisoxazole, and warfarin was determined in normal human adults, in patients with impaired renal function (kidney donor and recipient), and in adult male Sprague-Dawley rats in order to investigate intrasubject serum protein binding patterns of several weakly acidic drugs. The results of the study showed that the free fraction values for salicylate and sulfisoxazole were significantly correlated in all three groups. The other correlations were statistically significant in only one or two of these groups. There was statistically significant negative correlation between albumin concentration and the free fraction values of salicylic acid and sulfisoxazole (but not of phenytoin and only under special circumstances with warfarin) in normal human subjects, and of phenytoin, salicylic acid, and sulfisoxazole (but not warfarin) in rats. No such correlation was observed for any of the drugs in patients with impaired renal function.

These observations show that no single weakly acidic drug can serve as an index for quantitatively determining the effect of disease or species differences on the serum protein binding of other weakly acidic drugs. (JA)

16 refs

KEYWORDS: Anti-Coagulants: warfarin. Anticonvulsants (Anti-Epileptics): phenytoin. Skin and Mucous Membrane Preparations: salicylic acid. Sulfonamides: sulfisoxazole. Variables Influencing Drug Concentration Data.

UM-79-P0062

PHARMACOKINETICS OF MORPHINE AND ITS SURROGATES II: METHODS OF SEPARATION OF STABILIZED HEROIN AND ITS METABOLITES FROM HYDROLYZING BIOLOGICAL FLUIDS AND APPLICATIONS TO PROTEIN BINDING AND RED BLOOD CELL PARTITION STUDIES, E.R. Garrett; T. Gurkan, Journal of Pharmaceutical Sciences, v68 n1 p26-32 (Jan 1979)

The inhibition of the spontaneous hydrolysis of heroin in fresh dog plasma and blood (half life = 8 min) is effected by 10 mg sodium fluoride/ml (half life = 40 min) and 35 micrograms tetraethyl pyrophosphate/ml (half life = 415 min). Tetraethyl pyrophosphate is the inhibitor of choice and gives the same stability for heroin as in phosphate buffer. Aged plasma loses its enzymatic efficiency. Heroin in cerebrospinal fluid hydrolyzes at rates similar to those in buffer. Modified extraction procedures developed for enzyme-inhibited plasma at pH 4.5 have high extraction efficiencies (86-100%) and permit isolation of undergraded heroin from its metabolites.

Separations of heroin and metabolites from enzyme-inhibited plasma were effected by high-pressure liquid chromatographic systems and from TLC with elution of pertinent developed spots. Efficiencies of these TLC recoveries were 81 $\pm$ 1% for heroin and 82 $\pm$ 1% for morphine. Contrary to the literature, heroin has significant protein binding where 40% of that not bound to an ultrafiltration membrane is bound to dog plasma proteins. The apparent partition coefficient is 1.4 $\pm$ 0.2 between red blood cells and plasma water, and it is 0.8 $\pm$ 0.1 between red blood cells and dog plasma. (JAM)

20 refs

KEYWORDS: Metabolites of Drugs and Other Agents: normorphine. 6-O-acetylmorphine. Opiates and Related Agents: heroin. morphine, normorphine. Pharmacokinetic Factors: Drug Absorption and Distribution. Specific Drug Screening: Other Techniques. Specific Drug Screening: Thin-Layer and Paper Chromatography.

UM-77-P0063

DIFFERENCES IN THE BINDING OF DRUGS TO PLASMA PROTEINS FROM NEWBORN AND ADULT MAN. II, H. Kurz; H. Michels; H.H. Stickel, European Journal of Clinical Pharmacology, v11 n6 p469-72 (1977)

The binding of certain drugs to isolated fractions of plasma proteins obtained from newborn and adult man was studied by equilibrium dialysis. For thiopental, desipramine, nitrofurantoin, sulfamethoxydiazine, metricillin, and salicyclic acid no difference was found between bindings to the albumin fraction from newborns and adults. However, for thiopental, desipramine, and promethazine, binding to the globulin fraction was smaller in the newborns than in adults. Addition of bilirubin to the albumin fraction decreased the binding of nitrofurantoin, sulfamethoxydiazine, and metricillin. No difference in the binding of metricillin to the albumin or globulin fractions from newborns and adults was found. The binding decreased, however, if both fractions were combined. Four mechanisms to explain the difference in binding between newborns and adults are discussed: (1) displacement of drugs by bilirubin, (2) different binding properties of cord and adult albumin, (3) different properties of the globulins, and (4) interaction of albumin with globulins in the newborn. (JA)

9 refs

KEYWORDS: Anti-Emetics: promethazine. Antidepressants: desipramine. General Anesthetics: thiopental. Major Tranquilizers (Antipsychotics and Neuroleptics): promethazine. Other Anti-Infective Agents: nitrofurantoin. Penicillins: methicillin. Skin and Mucous Membrane Preparations: salicylic acid. Sulfonamides: sulfameter. Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-79-P0064

DISTRIBUTION OF ETHANOL BETWEEN SALIVA AND BLOOD IN MAN, A.W. Jones, Clinical and Experimental Pharmacology and Physiology, v6 n1 p53-9 (1979)

Forty-eight male subjects aged 20 to 59 drank ethanol (0.72 g/kg) on a fasting stomach over a period of twenty minutes. Ethanol concentrations in saliva and capillary blood were determined at thirty- to sixty-minute intervals for the next seven hours.

The concentration of ethanol in saliva was generally slightly higher than in capillary blood, as expected from their relative water contents. The mean saliva/blood ethanol ratio between 60 and 360 minutes from the start of drinking was 1.082 (s.e.m.= 0.0059, n=336). Moreover, the saliva/blood ethanol ratio was remarkably constant throughout the absorption, distribution, and elimination phases of ethanol metabolism.

The saliva (y) and blood ethanol (x) concentrations were highly correlated (r=0.976, standard error =0.011, P<0.001). The regression equation was y= 0.109 + 1.071x. The saliva and blood ethanol concentrations reached zero nearly simultaneously, there being no appreciable time lag in the saliva.

The results indicate that saliva is a practical medium for ethanol determinations and that blood ethanol can be reliably estimated from analysis of a saliva specimen. Saliva ethanol analysis could well serve as supporting evidence in clinical medicolegal diagnosis of ethanol intoxication. (JAM)

6 refs

KEYWORDS: Nonbarbiturates: ethanol (ethyl alcohol)*. Drug Concentrations: Comparison of Body Fluids. Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-77-P0065

VERBESSERTE DOSIERUNG VON MEDIKAMENTEN DURCH MESSUNG IHRER PLASMA KONZENTRATION [IMPROVED DOSAGE OF DRUGS BY MEASURING PLASMA LEVELS], J. Bircher, Therapeutische Umschau/Revue Therapeutique, v34 n11 p830-4 (1977)

Recent research revealed that the therapeutic effect of several drugs is better correlated with plasma concentration than with dose. As a result, measurements of plasma concentrations have become clinical tools for determining the optimal dosage of such compounds. However, it is necessary to satisfy a number of conditions before the measurement of plasma levels of drugs can become clinically useful. For instance, the plasma concentrations should be relatively stable and representative for drug concentrations occurring at the site of action. For this reason, laboratory methods have been developed for only a relatively small number of drugs. The main purposes of measurement of plasma concentrations are to distinguish between symptoms due to disease and overdosage, to evaluate the causes of insufficient therapeutic effects, and to optimize dosage of drugs with a small therapeutic index. Drugs for which plasma concentrations are commonly measured include cardiac glycosides, antiepileptic agents, gentamycine, sulfonamides, quinidine, salicylates, and lithium. Like other diagnostic procedures, measurements of drug concentrations in plasma require appropriate clinical testing and critical evaluation of results. (JA)

14 refs German

KEYWORDS: Review: Drug Concentration-Effect Relationships.

UM-78-P0066

PHENYTOININTOXIKATION UND SERUMSPIEGEL [PHENYTOIN INTOXICATION AND SERUM LEVEL], R. Beier; M. Zschiesche; R. Cammann, Psychiatrie, Neurologie und Medizinische Psychologie, v30 n7 p414-23 (7 Jul 1978)

The symptomatology of phenytoin intoxication was observed in 189 adult patients and in seven children. Symptoms of cerebellar impairment were noted in the majority of cases. Phenytoin concentrations were found to lie between 14.4 and 77.7 mg/ml. Interindividual differences as to the toxic limit were quite considerable: one-third of the patients showing values higher than 20 mg/ml were free of obvious clinical symptoms, and one patient tolerated a serum concentration in excess of 30 mg/ml. On the other hand, the intraindividual toxic limit did not show any major variations: the clinical symptomatology of a patient correlated with his phenytoin serum concentration. After

phenytoin withdrawal, the serum concentration dropped exponentially. The half-life periods of elimination were found to be between 72 and 122 hours. (JAM)

19 refs

KEYWORDS: Anticonvulsants (Anti-Epileptics): phenytoin*. Epidemiologic Research: Drug Concentrations in Body Fluids.

UM-78-P0067

THE PHARMACOKINETIC ASPECTS OF THERAPY WITH PSYCHOTROPIC AGENTS, S. Kaumeier, International Journal of Clinical Pharmacology, v16 n1 p27-31 (1978)

This article reviews the major pharmacokinetic aspects of psychotropic agents, especially as these aspects influence the relationship between plasma level and therapeutic effect. Before the relationship between the blood level of a drug and the resulting effect can be determined, three problems must be solved: 1) identification of the chemical course of reaction between the drug administered and its resultant metabolites in reference to the totality of the organism and its biochemical reaction pattern; 2) the course of this reaction relative to intra- and interindividual differences; and 3) the protein binding properties of the drug in question, since protein binding affects drug distribution. Other decisive factors influencing drug plasma levels are mode of drug administration, blood distribution volume, reaction rate, elimination rate, and interaction of combined drugs. These problems must be dealt with before individualized drug therapy can be achieved. (HSRI)

24 refs

KEYWORDS: Central Nervous System (CNS) Agents. Review: Drug Concentration-Effect Relationships.

UM-77-P0068

PHARMAKOPSYCHOLOGISCHE UNTERSUCHUNGEN UBER KOMBINATIONSWIRKUNGEN VON ALKOHOL UND OXAZEPAM AUF DAS REAKTIONSVERHALTEN. II. MITTEILUNG: SUBJEKTIVE BEFINDLICHKEIT UND REAKTIONSVERHALTEN, M. Staak; K. Gottwald; H.J. Mallach; G. Schubring, International Journal of Clinical Pharmacology, V15 n5 p234-44 (1977)

Presented here is a psychopharmacological investigation of the subjective state of being and drug levels in a group of fourteen subjects who took alcohol, oxazepam, or a combination of the two. The study was done to determine whether there was a correlation between mood effects, performance, impairment, and blood levels.

In addition to a sedative effect, the interaction of alcohol and oxazepam resulted in changes of mood and related significant alterations of polarity profiles. A correlation of the changes of performance and the alterations of the polarity profiles with the respective blood levels of alcohol and oxazepam is demonstrated. (JAM)

13 refs German

KEYWORDS: Metabolites of Drugs and Other Agents: oxazepam*. Minor Tranquilizers (Anti-Anxiety and Ataractics): oxazepam*. Nonbarbiturates: ethanol (ethyl alcohol)*. Drug Concentration-Effect Study: Clinical Research. Drug Concentrations in Body Fluids: Acute Dose Study.

UM-77-P0069

PHARMACOKINETIC COMPARISON OF THE ONE-POINT METHOD WITH OTHER METHODS IN PREDICTING STEADY STATE DRUG CONCENTRATIONS IN MULTIPLE DOSING, W.A. Ritschel; W. Erni, International Journal of Clinical Pharmacology, v15 n6 p279-87 (1977)

The purpose of this study was to compare the one-point determination of a known drug's pharmacokinetics in a particular person with conventional methods for predicting steady state concentrations of drugs and to determine its degree of accuracy. In this method a test dose is given, a single blood sample is drawn toward the end of the first dosing, and the drug concentration determined. With knowledge of the drug concentration at a given time, the patient's serum creatinine, the biological half-life of the drug, and the approximate time required to reach the peak blood level, an approximation of the expected steady state can be calculated and adjustment of the dosage regimen can be made before the second dose is given. Using blood-level time profiles of five different

drugs, the maximum and minimum drug concentrations are determined according to four different methods.

It was demonstrated that the one-point method results in an acceptable estimate allowing prediction of steady state concentrations and adjustment of dose regimen based on one single blood level concentration determined during the later part of the first dosing interval, and utilizing literature on the biological half-life and the time to reach the peak. In case of renal impairment, a correction can be made after determination of serum creatinine in the one blood sample taken.

This study demonstrates that the one-point method may be a very useful and quick clinical tool to predict steady state concentrations and adjust dose regimens. Obviously, the one-point method will result in a useful estimate only if the blood sample is taken late enough, i.e., when the drug concentration is in the monoexponential elimination phase. Since only one blood sample is taken, exact measurement of the sample and reliable analytical methodology are indispensable prerequisites. (JAM)

13 refs

KEYWORDS: Adrenals: methylprednisolone sodium succinate. Anti-Asthmatics: proxyphylline*. Minor Tranquilizers (Anti-Anxiety and Ataractics): meprobamate*. Penicillins: penicillin V potassium*. Sulfonamides: sulfisoxazole. Pharmacokinetics: Acute Dose.

UM-77-P0070

PLASMA PROTEIN BINDING OF DRUGS IN THYROID DYSFUNCTION, J.G. Kelly; D.G. McDevitt, British Journal of Clinical Pharmacology, v4 n5 p626 (1977)

Described here is an investigation of plasma binding of isoprenaline and propranolol in patients with thyroid dysfunction. The investigation intended to determine whether or not the metabolism of these drugs is altered in these patients.

For each drug a small increase in protein binding was observed when both the hyperthyroid and hypothyroid patients became euthyroid. However, these small changes are unlikely to result in significant alterations in free drug concentrations, and probably do not account for the clinical manifestations of hyperthyroidism. (HSRI)

5 refs

KEYWORDS: Anti-Anginal Agents: propranolol. Anti-Arrhythmia Agents: propranolol. Hypotensive (Antihypertensive) Agents: propranolol. Sympathomimetic (Adrenergic) Agents: isoproterenol. Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-77-P0071

PLASMA-PROTEIN BINDING AS A DETERMINANT OF ADVERSE DRUG REACTIONS, G. Levy, Drug Design and Adverse Reactions, H. Bundgaard, et al., eds., p331-45, Alfred Benzon Symposium X, Copenhagen:Munksgaard (1977)

This review focuses largely on the effect of plasma protein binding on the time course of free drug concentrations in plasma. The discussion begins with a description of a theoretical model of the effect of plasma protein binding. Three drugs--warfarin, phenytoin, and bilirubin--are discussed in terms of protein binding and adverse reactions. These drugs were selected because they represent different orders of magnitude of plasma protein binding.

It is concluded that from a clinical pharmacokinetic point of view, the adverse reaction problems associated with variable plasma protein binding of drugs can be minimized by establishing the therapeutic concentration range of these drugs in terms of free rather than total drug, by monitoring free drug concentration in patients, and by reducing the dosing interval when protein binding is impaired in order to maintain the maximum concentration of free drug in the therapeutic range. (HSRI)

19 refs

KEYWORDS: Anti-Coagulants: warfarin. Anticonvulsants (Anti-Epileptics): phenytoin*. Blood Derivatives: bilirubin. Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-78-P0072

CORRELATION BETWEEN PLASMA DIPHENHYDRAMINE LEVEL AND SEDATIVE AND ANTIHISTAMINE EFFECTS. S.G. Carruthers; D.W. Shoeman; C.H. Hignite; D.L. Azarnoff, Clinical Pharmacology and Therapeutics, v23 n4 p375-82 (1978)

The sedative and antihistamine effects of diphenhydramine were assessed in relation to plasma concentration after placebo, diphenhydramine (50 mg) intravenously, and diphenhydramine (50 mg) orally to each of six healthy volunteers on three separate occasions. The following psychomotor tests were performed just before and at 1, 2, 3, 4, 5, 6, 7, 8, 24, and 30 hours after administration of each treatment: subjective sleep scale, reaction time, tapping test, and two sorting tasks.

Diphenhydramine plasma elimination half-life ranged from 3.0 to 4.3 hours; volume of distribution was 188 to 336 liters, and clearance was 637 to 1,014 ml/min. Systemic bioavailability of the oral preparation ranged from 0.26 to 0.60.

The sedative effect of intravenous diphenhydramine differed from that of placebo only during the first three hours. Antihistamine effect, as measured by reduction of histamine provoked skin wheal diameter, was significantly different from that of placebo for at least eight hours.

There was a positive correlation between plasma diphenhydramine level and sedative and antihistamine effects, but wide variation in the extent and rate of change of these effects was observed between the subjects. There appears to be a concentration range of 25 to 50 ng/ml, within which there is significant antihistamine effect without significant sedation. (JA)

18 refs

KEYWORDS: Antihistamine Agents: diphenhydramine*. Nonbarbiturates: diphenhydramine*. Antihistamine Agents. Drug Concentration-Effect Study: Clinical Research. Pharmacokinetics: Acute Dose.

UM-78-P0073

EFFECT OF A COCKTAIL ON DIAZEPAM ABSORPTION. D.J. Greenblatt; R.I. Shader; D.R. Weinberger; M.D. Allen; D.S. MacLaughlin, Psychopharmacology, v57 p199-203 (1978)

This study assessed the influence of ethanol on the rate and extent of diazepam absorption under controlled conditions that attempted to mimic actual circumstances. Four healthy male and two healthy female volunteers aged twenty-five to forty-two years ingested a single 5 mg tablet of diazepam with a typical ethanol-containing cocktail (1.5 ounces of 80 proof vodka plus 4 ounces of orange juice plus ice) or with a similar ethanol-free mixture (4 ounces of orange juice plus ice) in the fasting state on two occasions separated by at least one week. Diazepam concentrations in multiple plasma samples drawn from fifteen minutes to twenty-four hours after each dose were determined by electron-capture gas-liquid chromatography. Mean values of pharmacokinetic variables for diazepam taken without and with ethanol, respectively, were: peak plasma diazepam concentration, 221 vs 208 ng/ml; time of peak concentration, 0.79 vs 1.79 hours after dosing ($P<0.1$); apparent lag time prior to start of absorption, 16.5 vs 26.2 minutes; apparent first-order absorption half-life, 19.3 vs 34.6 minutes.

The completeness of diazepam absorption, judged by the area under the twenty-four hour plasma concentration curve, was nearly identical for the two conditions. Thus, coadministration of diazepam with the ethanol cocktail tended to slow the rate of diazepam absorption, but did not influence the completeness of absorption. Pharmacodynamic synergism of ethanol and diazepam, if it exists, cannot be attributed to enhancement of the rate or completeness of diazepam absorption. (JAM)

21 refs

KEYWORDS: Minor Tranquilizers (Anti-Anxiety and Ataractics): diazepam*. Muscle Relaxants (Central): diazepam*. Nonbarbiturates: ethanol (ethyl alcohol)*. Pharmacokinetic Factors: Drug Absorption and Distribution. Variables Influencing Drug Concentration Data.

UM-78-P0074

ETUDE HEMODYNAMIQUE DE L'ASSOCIATION BETA-BLOQUANTS ANALGESIQUES CENTRAUX: CONSEQUENCES PRATIQUES EN CHIRURGIE, A. Delhumeau; J.F. Cavellat; S. Albaret; J.L. Chassevent; M. Cavellat. Anesthie, Analgesic, Reanimation. v36 n3 p435-44 (1978)

The hemodynamic modifications registered after the experimental intravenous injection of fentanyl (0.005 mg/kg) and of propanolol (0.1 mg/kg) are modest. However, it must be remembered that experimental conditions differ from clinical treatment where the treatment is administered chronically.

Drug plasma levels are discussed, especially as they relate to effects on heart rate, systolic and diastolic pressure, and other physiologic variables. Adverse effects and therapeutic uses of fentanyl and propanolol are also discussed. (HSRI)

32 refs French

KEYWORDS: Anti-Anginal Agents: propranolol*. Anti-Arrhythmia Agents: propranolol*. Hypotensive (Antihypertensive) Agents: propranolol*. Opiates and Related Agents: fentanyl*. Drug Concentration-Effect Study: Clinical Research. Drug Concentrations in Body Fluids: Acute Dose Study.

UM-77-P0075

EFFECT OF ACTIVE DRUG METABOLITES ON PLASMA LEVEL-RESPONSE CORRELATIONS, A.J. Atkinson; J.M. Strong, Journal of Pharmacokinetics and Biopharmaceutics, v5 n2 p95-109 (1977)

Application of pharmacokinetic principles to patient therapy requires an understanding of the relationship between the plasma concentration of a drug and its pharmacological effects. However, this relationship is often complicated by the fact that many drugs are converted to active metabolites so that observed effects represent a composite of the pharmacological activity of a drug and its metabolites. This article discusses this problem, citing examples where an awareness of the activity of drug metabolites is essential for the proper interpretation of plasma level data and for the rational design of drug dosing regimens. In addition, methods are illustrated for assessing drug and drug metabolite potency based on a correlation of plasma levels with pharmacological response.

Discrepancies between the observed duration of drug action and the biological half-life of a given drug should suggest that an active drug metabolite may have been formed. As is illustrated by the anticonvulsant drug methsuximide, drug metabolite levels may be so much higher than those of the parent drug that only the metabolite levels are of routine clinical significance. In other cases, levels of both the parent drug and one or more metabolites must be considered together and combined according to their relative potency to give an index of total pharmacological activity. This situation poses obvious difficulties with respect to the ease and safety of drug therapy with these agents. It generally would seem preferable to treat patients with drugs that are converted to inactive metabolites or are excreted largely unchanged. (JAM)

33 refs

KEYWORDS: Anti-Arrhythmia Agents: lidocaine*. procainamide*. Anticonvulsants (Anti-Epileptics): methsuximide. Hallucinogens and Related Agents: lysergic acid diethylamide (LSD)*. Local Anesthetics: lidocaine*. Nonbarbiturates: glutethimide*. Anticonvulsants (Anti-Epileptics). Pharmacokinetic Factors: Drug Metabolism.

UM-77-P0076

EFFECT OF URINARY pH ON RENAL EXCRETION OF DRUGS [letter], P.L. Madan, Journal of the American Medical Association, v238 n3 p210 (18 Jul 1977)

Discussed in this letter-to-the-editor is the effect of urinary pH on renal excretion of drugs. In general, a substantial change in the urinary excretion of the unchanged form of a drug can be expected if the acidic drug has a pKa of 3.0 to 7.5 and if the basic drug has a pKa of 7.0 to 11.0. Some examples of drugs whose urinary excretion is pH-dependent include the following basic drugs showing greater clearance in acidic urine: amphetamine, chloroquine, codeine, imipramine, quinacrine, meperidine, morphine, nicotine, and procaine. Examples also include acidic drugs showing greater clearance in alkaline urine: acetazolamide, barbiturates, nitrofurantoin, phenylbutazone, probenecid, salicylic acid, and sulfonamides. (HSRI)

1 ref

KEYWORDS: Pharmacokinetics: Chronic Dose.

UM-77-P0077

THE EFFECTS OF CHRONIC ALCOHOL INGESTION AND ALCOHOLIC LIVER DISEASE ON DRUG-PROTEIN BINDING, S. Boobis; M.J. Brodie; A. Goldberg, Proceedings of the British Pharmaceutical Society, v4 n5 p4 (Jul 1977)

This paper reports the effects of chronic alcohol ingestion and alconolic liver disease on drug binding in eleven patients with cirrhosis and in twelve patients with alcoholic hepatitis. Binding of salicylate and phenylbutazone was reduced in the cirrhotics and binding of sulphadiazine and phenylbutazone was reduced in the patients with alcoholic hepatitis. In this latter group, also, significant correlations were obtained between drug binding and plasma bilirubin and albumin levels. These results suggest that while chronic alcohol ingestion in itself has no effect on drug binding to serum proteins, patients with alcoholic liver disease show reduced binding, a factor which should be taken into account when calculating the distribution of drugs in the patient with alcoholic liver disease. (HSRI)

3 refs

KEYWORDS: Analgesics and Antipyretics: phenylbutazone. Blood Derivatives: albumin. bilirubin. Skin and Mucous Membrane Preparations: salicylic acid. Sulfonamides: sulfadiazine. Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-77-P0078

ESTIMATION OF PHARMACOKINETIC PARAMETERS FROM POSTINFUSION BLOOD LEVEL DATA OBTAINED AFTER SIMULTANEOUS ADMINISTRATION OF INTRAVENOUS PRIMING AND INFUSION DOSES, S.M. Singhvi, Journal of Pharmaceutical Sciences, v66 n10 p1499-1501 (Oct 1977)

Occasionally, it is desirable to attain steady-state blood drug levels rapidly in pharmacokinetic studies as well as in the treatment of certain diseases. In these cases, it is useful to administer an intravenous priming dose in combination with continuous drug infusion. This paper presents mathematical relationships for the determination of pharmacokinetic parameters in those situations using postinfusion blood drug level data. The parameters obtained by this method are identical to the parameters obtained after a rapid intravenous injection of a drug. (JA)

4 refs

KEYWORDS: Variables Influencing Drug Concentration Data.

UM-77-P0079

[STUDIES ON DRUG INTERACTION OF COMBINED DRUG. II. INTERACTION AMONG ISOPROPYLANTIPYRINE, PHENACETIN, ALLYLISOPROPYLACETYLUREA AND CAFFEINE ON THE PLASMA LEVEL OF ISOPROPYLANTIPYRINE AND PHENACETIN IN DOGS], T. Nakajima; T. Okada; S. Takeuchi; M. Shimokawa; I. Kuruma; H. Kitagawa, Yakugaku Zasshi, V97 n6 p607-12 (1977)

This paper discusses interactions of isopropylantipyrine, phenacetin, allylisopropylacetylurea, and caffeine--all ingredients of a commercial analgesic preparation--on the plasma level and metabolism of isopropylantipyrine in dogs and rats. In the first series of experiments, the plasma level profiles of isopropylantipyrine and phenacetin in beagle dogs were investigated after oral administration of each drug administered alone and in combination with each other and in various combinations with caffeine or allylisopropylacetylurea.

Results of the study showed that the individual plasma levels of isopropylantipyrine and phenacetin were both elevated when combined with each other. The areas under the plasma level curves for isopropylantipyrine and phenacetin were increased by the combination with allylisopropylacetylurea.

In the second series of studies, distribution of isopropylantipyrine in several organs and tissues in rats was compared after administration alone and in combination with the other drugs. The concentration of isopropylantipyrine in all organs tested was found to be twice as high in rats receiving the analgesic combination drug than those treated with isopropylantipyrine alone. Metabolism of isopropylantipyrine by hepatic microsomal enzymes in the rats was inhibited noncompetitively by the addition of phenacetin or allylisopropylaceturea.

The paper concludes with a discussion, based on the results of this study, of the advantages of combining these ingredients to produce an effective analgesic preparation. (JAM)

12 refs Japanese

KEYWORDS: Analgesics and Antipyretics: phenacetin*, propyphenazone*. Sedatives and Hypnotic Agents: apronalide*. Stimulants: caffeine*. Pharmacokinetic Factors: Drug Absorption and Distribution. Pharmacokinetic Factors: Drug Metabolism. Pharmacokinetics: Acute Dose.

UM-77-P0080

PHARMACOKINETICS OF PAPAVERINE IN MAN, W.A. Ritschel; G.V. Hammer, International Journal of Clinical Pharmacology, v15 n5 p227-9 (1977)

This paper reviews literature concerning the pharmacokinetics of papaverine, an opium constituent which relaxes the smooth muscle of the larger blood vessels and decreases total peripheral resistance in man. A retrospective pharmacokinetic analysis was done of papaverine plasma levels based on published studies. Results of the literature survey indicate that for intravenous administration of papaverine the plasma level versus time curve can best be described by an open two-compartment model; for oral administration it is best described by an open one-compartment model.

The biological half-life of papaverine varies between 1.5 and 2.2 hours, and has a volume of distribution of approximately 15% of the body weight. Papaverine is practically completely metabolized and underlies the first-pass effect upon oral administration. (JAM)

15 refs

KEYWORDS: Vasodilating Agents: papaverine*. Pharmacokinetics: Acute Dose. Pharmacokinetics: Chronic Dose.

UM-77-P0081

RELATIONSHIP BETWEEN AGE AND TRICYCLIC ANTIDEPRESSANT PLASMA LEVELS, A. Nies; D.S. Robinson; M.J. Friedman; R. Green; T.B. Cooper; C.L. Ravaris; J.O. Ives, American Journal of Psychiatry, V134 n7 p790-3 (July 1977)

Reported here is a study investigating the relationship of age to tricyclic antidepressant plasma levels and metabolism, specifically for imipramine, desipramine, and amitriptyline. Plasma levels were determined in patient samples from two separate studies. The thirty-five amitriptyline patients ranged in age from 21 to 68 years, and were administered 25 mg amitriptyline three times daily for the first five days for four to six weeks. The twenty-three imipramine patients, aged 27 to 78, were treated daily with 150 mg of imipramine for a minimum of three weeks.

Plasma levels of the drugs were determined by gas chromatography using a nitrogen detector. Steady-state plasma levels of the two parent compounds, imipramine and amitriptyline, both showed significant positive correlations with age. In imipramine-treated patients this finding was associated with a decreased rate of drug elimination from plasma. In the case of the demethylated metabolites only the desipramine steady-state plasma levels showed a positive correlation with age; the nortriptyline steady-state levels did not.

These findings provide a partial explanation for the increased susceptibility of the older patient to tricylic antidepressant side effects and also provide a pharmacological rationale for use of lower dosages in this age group. The results of this study have the following implications for dosage strategies in older patients: (1) Doses of tricyclic antidepressants in the elderly should be reduced from the recommended dose by a third to a half. Thus, imipramine and amitriptyline dosage should have a maximum limit of 100 mg a day for most patients 65 years or older. (2) More frequent and more intensive monitoring of the elderly patient is indicated during initial treatment because due to the longer mean half-life in the elderly patient, steady-state levels may not be achieved for up to three weeks. (3) Because the lag period before onset of clinical antidepressant effects may include the time to reach steady-state, the standard three-week period for completion of an adequate therapeutic trial must be extended and sometimes doubled in some depressed geriatric patients. (HSRI)

19 refs

KEYWORDS: Antidepressants: amitriptyline*, imipramine*, Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-79-P0082

EFFECT OF ALTERED PLASMA PROTEIN BINDING ON APPARENT VOLUME OF DISTRIBUTION [letter], S. Oie; T.N. Tozer, Journal of Pharmaceutical Sciences, v68 n9 p1203-05 (Sep 1979)

This paper describes how altered plasma protein binding causes the changes in the apparent volume of distribution that commonly occur with age, disease, and drug interaction. Equations are provided for calculating various pharmacokinetic relationships between the drug, the plasma, and extracellular fluids. These equations are useful for analyzing and predicting alterations in the apparent volume of distribution of any drug when there is an alteration in the unbound fraction in plasma, in the unbound fraction outside of the extracellular fluids, in the volumes of the extracellular fluids, or in the extravascular to intravascular plasma protein ratio that occurs, for example, in prolonged bed rest and in severe burns. The equations are also useful in identifying where the alteration occurs. (HSRI)

9 refs

KEYWORDS: Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-79-P0083

FORECASTING INDIVIDUAL PHARMACOKINETICS, L.B. Sheiner; S. Beal; B. Rosenberg; V.V. Marathe, Clinical Pharmacology and Therapeutics, v26 n3 p294-305 (Sep 1979)

The ability to accurately forecast individual plasma concentrations resulting from a dosage regimen is central to making optimal dosage decisions. Traditionally, forecasting has relied on known factors influencing pharmacokinetics such as age, sex, and renal disease. This paper provides a more complete approach which relies on previously observed plasma concentrations. This framework for forecasting plasma concentrations (1) formulates a general model for patients that links dosage, time, and observable patient features (such as disease state) to plasma concentrations; (2) applies this model to the individual patient; and (3) subsequently adjusts the model taking into account observed patient responses. This model revision consists of applying Bayes' formula to adjust the prior probability distribution of the individual's kinetic parameters based on observed plasma concentrations and thus arrive at a revised distribution.

This forecasting approach is retrospectively applied to data resulting from administration of digoxin. The steps necessary to forecast optimal dosage of digoxin include the following: (1) collection of data from patients concerning digoxin dosage, values of observable features, and values of measured plasma concentrations; (2) creation of a kinetic model to deal with the realities of digoxin administration including irregular dosage schedules, varying dosage routes, and irregular times of sampling plasma for plasma concentrations; (3) establishment of a set of population parameter values, including values for the variance terms; and (4) determination of measures of the accuracy and precision of both plasma concentration prediction and the adjustment of the model to the individual.

The data used in the study were from 141 adult patients receiving digoxin and included dosage history, measured plasma concentrations, and routinely reported physical characteristics. All digoxin plasma concentrations were assayed by radioimmunoassay using identical equipment, materials, and procedures.

Results of the study indicate that for digoxin, use of one measured plasma concentration, as opposed to none, improves forecast precision for future plasma concentrations by a 40% decrement in variance of forecast error. Two plasma concentration measurements improve it by 67%. There is also an increase in forecast accuracy (decrement in mean of forecast error) as the number of plasma concentration determinations used increases. After only two, forecast accuracy and precision are as good as theoretically possible. Moreover, information from plasma concentrations is far more valuable for forecasting than that from observable patient features such as sex and age; use of this information does not improve accuracy and precision even as much as one plasma concentration measurement. (HSRI)

18 refs

KEYWORDS: Cardiac Glycosides: digoxin*. Drug Concentrations in Body Fluids: Chronic Dose Study. Epidemiologic Research: Drug Concentrations in Body Fluids. Pharmacokinetics: Chronic Dose.

UM-79-P0084

WHEN SHOULD PLASMA DRUG LEVELS BE MONITORED? A. Richens; S. Warrington, Drugs, v17 n6 p488-500 (June 1979)

Provided here is an overview of pharmacokinetic and pharmacodynamic principles and the interrelationships between drug dose, plasma level, and drug effects. The first part of the paper defines and discusses such concepts as dosage, compliance, bioavailability, plasma protein binding, plasma half-life and metabolism. Interpretation of plasma drug levels, therapeutic ranges, quality control of drug determinations, and uses and abuses of drug monitoring are also discussed.

The second part of the paper discusses drugs for which the monitoring of plasma level is justified. The antiepileptic drugs phenytoin, phenobarbitone, primidone, carbamazepine, ethosuximide, and sodium valproate are evaluated in terms of their metabolism, absorption, half-lives, and therapeutic plasma levels. Routine monitoring of plasma levels is particularly valuable for phenytoin, carbamazepine, and ethosuximide. Safe use of digoxin requires drug level monitoring, due to its low therapeutic ratio, especially in patients with renal impairment. Monitoring has proven most beneficial in the regulation of therapy with antidysrhythmic drugs such as lignocaine, procainamide, quinidine, phenytoin, mexiletine, and disopyramide.

The pharmacological effects of oral anticoagulants are easily monitored by measurement of the prothrombin time, therefore it is rarely necessary to measure the plasma concentration of these drugs. Monitoring of tricyclic antidepressants is a controversial subject; however, it appears to to be justified in a selected proportion of patients in whom a definite diagnosis of endogenous depression has been made. Routine monitoring is also essential for lithium and aminoglycoside antibiotics. (HSRI)

0 refs

KEYWORDS: Analgesics and Antipyretics: carbamazepine. Anti-Arrhythmia Agents: disopyramide. lidocaine. mexiletine. procainamide. quinidine sulfate. Anticonvulsants (Anti-Epileptics): carbamazepine. ethosuximide. phenobarbital. phenytoin. primidone. valproate sodium. Antidepressants: lithium. Barbiturates: phenobarbital. Cardiac Glycosides: digoxin. Local Anesthetics: lidocaine. Other CNS Agents: lithium. Variables Influencing Drug Concentration Data.

UM-79-P0085

DRUG BINDING IN HUMAN SERUM ALBUMIN AS ASSAYED BY DIAFILTRATION AND FLUORIMETRY, R. Geddes; P.M. White, Biochemical Pharmacology, v28 n15 p2285-88 (1 Aug 1979)

The binding of salicylate has been investigated by equilibrium ultrafiltration at various concentrations of human serum albumin up to 50 mg/ml. Very pronounced differences in the binding of the ligand at the different protein concentrations were observed; notably, the amount bound per protein molecule decreased at constant levels of free (not total) salicylate as the protein concentration was increased. A detailed investigation of the effect of the binding of the first molecules of salicylate to the protein by fluorescence indicated that the initial binding of salicylate was very tight indeed and induced a minor conformational change in the albumin allowing further molecules to be bound. This initial binding was also dependent on the protein concentration.

In summary, it may be concluded that the binding of salicylate to human serum albumin is a complex process even in the clinical setting. The initial binding of salicylate causes a distinct conformational change in the protein molecule which affects the binding of further molecules. Furthermore, both the initial and subsequent binding is grossly affected by the actual protein concentration in a complex manner. (JAM)

23 refs

KEYWORDS: Analgesics and Antipyretics: salicylate. Pharmacokinetic Factors: Drug Absorption and Distribution.

UM-79-P0086

PREDICTING STEADY STATE SERUM CONCENTRATIONS OF DRUGS, D.J. Greenblatt, Annual Review of Pharmacology and Toxicology, v19 p347-56 (1979)

This paper reviews and evaluates mathematical models for the prediction of steady state serum concentrations of drugs. In order to predict steady state serum concentrations for a given individual, a kinetic profile of the drug in question is needed. However, even the availability of such a profile does not assure accurate prediction of steady state concentrations during multiple-dose therapy due to several common misuses and abuses of the profile. Some of these are the following: (1) application of population-based parameters to individual patients; (2) incorrect evaluation of model parameters; (3) incorrect choice of model to explain the drug's kinetic behavior; (4) shift in the kinetic profile due to changes in patient characteristics, the nature of the disease, or coadministration of other drugs; and (5) the failure of the patient to take medications as described.

In spite of these potential difficulties, the use of mathematical models to predict steady state concentrations can be of great value in the clinical setting. The mathematical complexity of approaches to predicting steady state serum concentrations increases with the sophistication of the model. Complex computerized systems can involve considerable cost, but the cost is justified if the predictive system leads to more rational and systematic drug use, with accompanying increases in therapeutic success and reduction in episodes of toxicity. However, there is a need for periodic cost-effectiveness evaluation of these methodologies in comparison with more traditional and less expensive therapeutic approaches involving clinician implementation of kinetically based therapeutic guidelines together with monitoring and adjustment of therapy using actual serum concentration determinations. (AAM)

52 refs

KEYWORDS: Variables Influencing Drug Concentration Data.

UM-79-P0087

ERRORS IN INTERPRETATION OF DATA FROM EQUILIBRIUM DIALYSIS PROTEIN BINDING EXPERIMENTS, H.L. Behm; J.G. Wagner, Research Communications in Chemical Pathology and Pharmacology, v26 n1 p145-60 (Oct 1979)

This paper discusses common errors in interpretation of data from equilibrium dialysis protein binding experiments. The study illustrates the fact that incorrect calculation of the free or bound fraction using the initial drug concentration results in nonconstant errors in free fraction which increase in magnitude as drug concentration increases. Methods for estimating equilibrium drug concentration, the binding parameters corresponding to equilibrium conditions, and the free drug concentration in the initial plasma sample are presented.

In equilibrium dialysis protein binding experiments, the fraction of free or bound drug determined at equilibrium by dialysis of a patient plasma sample does not correspond to the drug concentration in the initial plasma sample, but to the drug concentration inside the plasma compartment of the dialysis apparatus at equilibrium. That fraction of free or bound drug corresponds to a lower total drug concentration than that in the initial plasma sample because of loss of drug due to passage of free drug into the buffer compartment in the equilibrium dialysis experiment. The magnitude of the difference between the initial drug concentration and the equilibrium drug concentration depends on the extent of drug binding and experimental conditions. If the initial total drug concentration in the plasma or serum sample as well as the fraction of drug bound at equilibrium as determined by radiotracer methods is known, then, using methods given in the text, the equilibrium drug concentration, the binding parameters corresponding to equilibrium conditions, and the free drug concentration in the initial plasma sample may be estimated. (JAM)

25 refs

KEYWORDS: Variables Influencing Drug Concentration Data.

UM-79-P0088

MULTICOMPARTMENT PHARMACOKINETIC ANALYSIS AND SIMULATIONS USING A PROGRAMMABLE CALCULATOR, S. Niazi, International Journal of Bio-Medical Computing, v10 n3 p245-55 (May 1979)

Due to interindividual variability or because of actual alterations to drug metabolism or excretory function arising from the disease state, it is desirable to determine the optimal therapeutic dose in each patient individually. This paper describes the application of an inexpensive programmable calculator (HP-97) to assist in prescribing an appropriate dosage schedule using a simplified method which is sufficiently accurate for general clinical use. Use of this calculator permits the fitting of plasma concentration profiles to one and two compartment open models. It also permits the calculation of fitted and derived parameters together with estimates of steady state plasma drug levels following various dosage regimens in clinical settings. (HSRI)

3 refs

KEYWORDS: Variables Influencing Drug Concentration Data.

UM-70-P0089

PHARMACOKINETIC ASPECTS OF ETHANOL-DRUG-INTERACTION, R. Schuppel, Alkohol und Verkehrssicherheit Konferenzbericht der 5., pI.17-I.19, Frieburg in Breisgau: Hans Ferdinand Schulz Verlag (1970)

Studies have shown that alteration of drug metabolism often results in changes in the pharmacokinetic behavior of drugs, which in turn has pharmacological and toxicological effects. This paper reviews studies which illustrate the effects of ethanol on the pharmacokinetics of various drugs including pentobarbital, aminopyrine, phenazon, barbital, and thiopental.

In vivo experiments have shown that ethanol acts as a potent inhibitor of certain reactions in the biotransformation of drugs. It diminishes hydroxylation of pentobarbital and phenazon resulting in a prolonged decrease of blood levels of these drugs and a derangement of the elimination pattern of typical metabolites in the urine compared to normal.

In vitro studies indicate that microsmal n-demethylation activity is materially inhibited by ethanol due to its binding to the microsomal hydroxylation enzyme system.

Studies have shown considerable variations in the responses of various hypnotics to additional ethanol dosage. Some drugs were potentiated by the doses of ethanol used, but others failed to show any effect. There seems to exist a strong correlation between the individual pattern of inactivation and the increase of the duration of action due to ethanol.

It is concluded that pharmacokinetic factors act in certain types of drug-ethanol interactions not fully recognized at the present time.

English translation of source title: Alcohol and Traffic Safety. Proceedings of the 5th International Conference on Alcohol and Traffic Safety. 22-27 September 1969 (HSRI)

4 refs

KEYWORDS: Analgesics and Antipyretics: aminopyrine, antipyrine. Barbiturates: barbital, pentobarbital. General Anesthetics: thiopental. Nonbarbiturates: ethanol (ethyl alcohol). Pharmacokinetic Factors: Drug Metabolism. Variables Influencing Drug Concentration Data.

UM-76-P0090

PHARMACOLOGICALLY ACTIVE DRUG METABOLITES: THERAPEUTIC AND TOXIC ACTIVITIES, PLASMA AND URINE DATA IN MAN, ACCUMULATION IN RENAL FAILURE, D.E. Drayer, Clinical Pharmacokinetics, v1 p426-43 (1976)

Drugs that are administered to man may be biotransformed to yield metabolites that are pharmacologically active. The therapeutic and toxic activities of drug metabolites and the species in which this activity was demonstrated are compiled for the metabolites of fifty-six drugs. The metabolite-to-parent drug ratio in the plasma of nonuraemic man and the percentage of urinary excretion of the metabolite in nonuraemic man are also tabulated. Those active metabolites with significant pharmacological activity and high plasma levels, both relative to that of the parent drug, will probably contribute substantially to the pharmacologic effect ascribed to the parent drug. Active metabolites may accumulate in patients with end stage renal disease if renal excretion is a major elimination pathway for the metabolite. This is true even if the active metabolite is a minor metabolite of the parent drug as long as the minor metabolite is

not further biotransformed and is mainly excreted in the urine. Minor metabolite accumulation may also occur if it is further biotransformed by a pathway inhibited in uraemia. Some clinical examples involving procainamide, pethidine (meperidine), clofibrate, and other drugs are presented. The high incidence of adverse drug reactions seen in patients with renal failure, therefore, may for some drugs be explained in part by the accumulation of active metabolites.

Monitoring plasma levels of drugs can be an important guide to therapy. Nevertheless, if a drug has an active metabolite, determination of the parent drug alone may cause misleading interpretations of blood level measurements. The plasma level of the active metabolite should also be determined and its time-action characteristics taken into account in any clinical decisions based on drug level monitoring. (JAM)

148 refs

KEYWORDS: Ganglionic Blocking and Stimulating Agents: 2,5-dimethoxy-4-methylamphetamine (DOM) (STP). Hallucinogens and Related Agents: lysergic acid diethylamide (LSD). mescaline. methylenedioxyamphetamine (MDA). phenethylamine (PEA). psilocin. N,N-dimethyltryptamine (DMT). 2,5-dimethoxy-4-bromoamphetamine (DOB). 2,5-dimethoxy-4-methylamphetamine (DOM) (STP). 3,4,5-trimethoxyamphetamine. 4-methoxyamphetamine (PMA). 5-methoxy-3,4-methylenedioxyamphetamine (MMDA). Stimulants: amphetamine. Unclassified Agents: tryptamine. Animal Research. Drug Concentrations in Body Fluids: Tabulated Data. Experimentation: Comparison of Different Drugs. Physiological Testing.

UM-72-P0091

DRUG INPUT OPTIMIZATION: BIOAVAILABILITY-EFFECTED TIME-OPTIMAL CONTROL OF MULTIPLE, SIMULTANEOUS, PHARMACOLOGICAL EFFECTS AND THEIR INTERRELATIONSHIPS, V.F. Smolen; B.D. Turrie; W.A. Weigand, Journal of Pharmaceutical Sciences, v61 n12 p1941-52 (Dec 1972)

Engineering control systems analysis and optimization techniques are developed, applied, and described with respect to their potential for providing rational approaches and quantitative criteria for such centrally important pharmaceutical problems as (a) the evaluation and time-optional, dynamic control of the therapeutic performance of drugs, drug products, and interacting drug combinations; (b) the optional design of the dynamic drug release behavior of drug dosage forms; and (c) patient-individualized determination of optimal drug dosage regimens. A functional analysis approach is exemplified by the computation of a time-optimal drug input, which could be achieved by an appropriate mode of drug administration which elicits optimally controlled time variations of drug-induced multiple, simultaneously occurring pharmacological effects. A computer simulation is performed to exemplify the manner in which an ideally sought level of therapeutic response intensity may be achieved as rapidly as possible without exceeding predetermined safe and tolerable levels of adverse drug effects. The significance and manner of determination of "single-dose" dose-effect relationships are exemplified, and their significance with respect to patient-individualized drug dosage regimens is discussed. The manner in which variations of drug effects can be interrelated with themselves and plasma drug levels is elucidated. (JA)

33 refs

KEYWORDS: Anorectic (Appetite Control) Agents: dextroamphetamine. Stimulants: dextroamphetamine. Sympathomimetic (Adrenergic) Agents: dextroamphetamine. Experimentation: Acute Dosage Study. Experimentation: Dose-Effect Study. Psychological Testing. Self-Evaluation of Drug Effects by Subjects. Variables Influencing Drug Concentration Data.