



DVT Science \

Pseudoscience

Lies & Wives tales
(or the truth as we know it)

Bruce Mintz DO FSVM
Clinical Associate Professor Internal Medicine
Medical Director Vascular Technology Training Program
Rutgers New Jersey Medical School, Newark ,NJ
Attending Cardiovascular Medicine Gagnon Heart & Vascular Institute
Director Anticoagulation Services
Morristown, Medical Center Morristown , N.J



Remember when this was
funny?



I have no disclosures!

Venous Thromboembolism (VTE)

Incidence and Impact in the United States

- **Approximately 2 million VTEs occur every year¹**
- **Each year 1 person in 1000 will experience his/her first VTE in the US²**
 - **One third manifest pulmonary embolism ([PE], with or without deep vein thrombosis [DVT])**
- **Death within 1 month of diagnosis²:**
 - **~6% of DVT cases**
 - **~12% of PE cases**
- **Recurrent DVT:**
 - **~17% of DVT patients 2 years after initial treatment³**
 - **~30% of DVT patients 8 to 10 years after initial treatment^{*†3,4}**



1. Hirsh J, Hoak J. *Circulation*. 1996;93:2212-2245.
2. American Heart Association. *Heart Disease and Stroke Statistics – 2004 Update*.
3. Prandoni P et al. *Haematologica*. 1997;82:423-428.
4. Pengo V et al. *N Engl J Med*. 2004;350:2257-2264.



If you cannot get rid of the family skeleton, you may as well make it dance.

George Bernard Shaw

Always wear the white hat!!!



What are the questions Asked?

Science and pseudoscience

- **Is one drug like another?**
- **Should you cross your legs ?**
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Routine Duplex in THR
- Pregnancy
- Does size matter
- Screening for DVT
- Birth control with DVT
- ETOH
- You can genetically predict clots?
- Do I have to scan both legs

A question asked many a time before

March 26, 1949

March 26, 1949

CHICAGO MEDICAL SOCIETY BULLETIN

CAN WE LOOK FORWARD TO BETTER ANTICOAGULANTS THAN HEPARIN AND DICUMAROL?

KARL PAUL LINK,
University of Wisconsin,
Madison, Wis.

A long time coming...

New and Emerging Anticoagulants

■ Anti – Xa : direct

- Rivaroxaban (oral)
- Apixaban (oral)
- Edoxabam (oral)
- Betrixiban (oral)
- Otamixaban (parenteral)
- LY – 517717 (oral)
- DU – 176B (oral)
- DX – 9065a (parenteral)
- PRT054021 (oral)

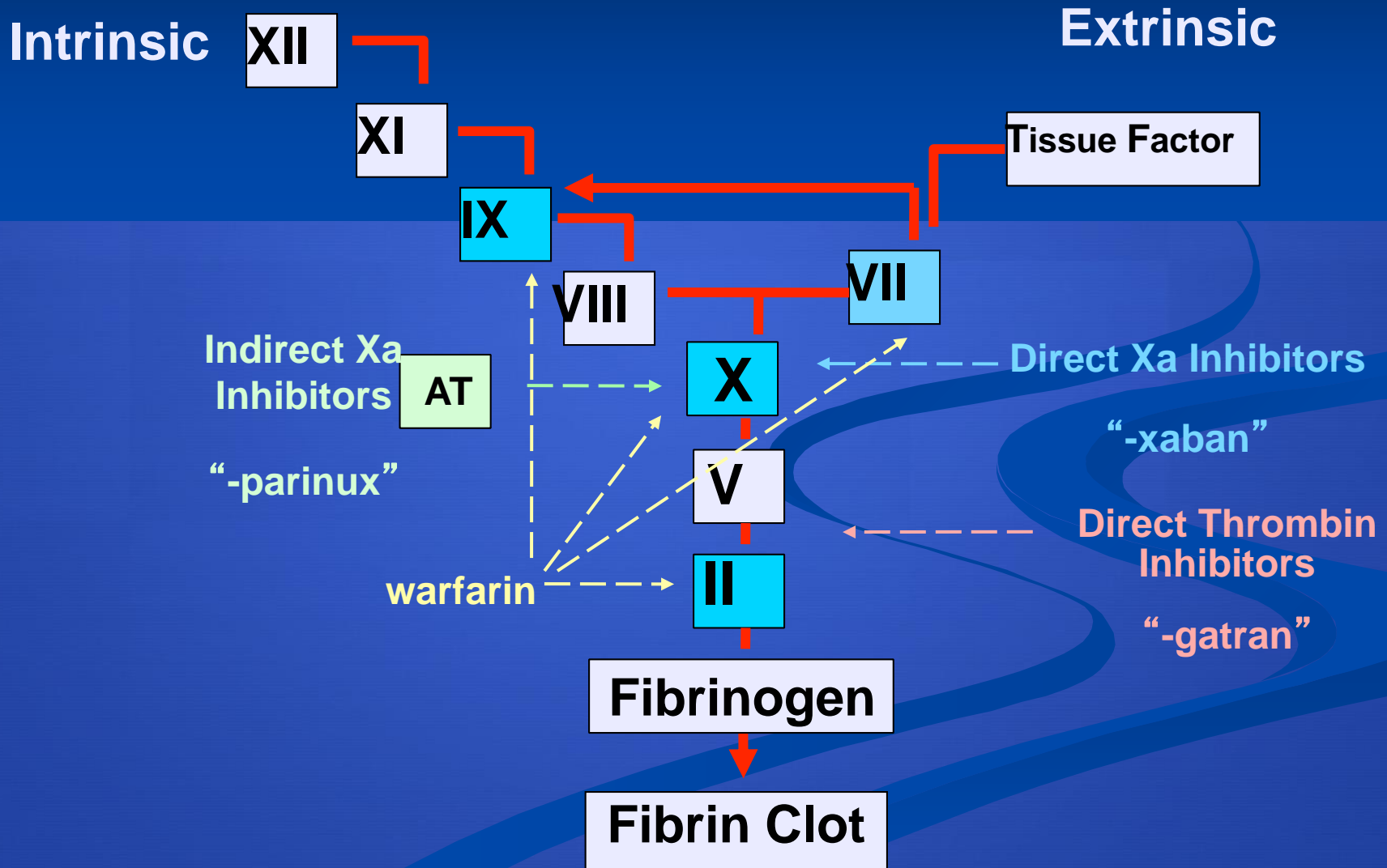
■ Anti – Xa : indirect

- Idraparinux biotinylated (parenteral)

■ Anti – IIa

- Dabigatran (oral)
- Odiparcil (oral)
- Flovagatran (parenteral)
- Pegmusirudin (parenteral)
- Peg Hirudin
- Desiruidin

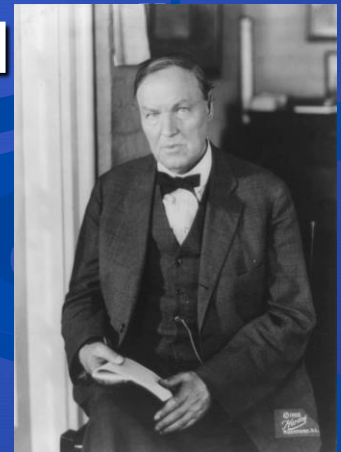
Site of Action for New Anti-thrombotic Agents



**" I never wanted to see anybody
die,
but there are a few obituary
notices**

I have read with Great pleasure

Clarence Darrow



**An anthropomorphic
perspective of Coumadin**

Be careful what you wish
for!!!



**Did you or a loved one suffer
serious **internal bleeding**
injury while taking a **blood thinner**?**

[click here to learn more](#)

YOU MAY BE ENTITLED TO COMPENSATION, PLEASE ACT NOW!

Advantages of 'Old' Anticoagulants

- Familiarity
- No unexpected side effects
- Demonstrated use in multiple clinical areas

Would Warfarin be approved if it was subjected to our current regulatory environments?

Problems with Warfarin

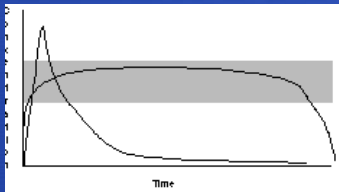


- **Food and drug interactions**



dosage adjustments &
freq. monitor with INR

- **Genetic variation in metabolism**



- **Narrow therapeutic window, slow onset of action**

overlap with
parenteral drugs



Anticoagulant Evolution

	1930s	1940s ...	1980s	1990s	2000s
Class	Heparin	VKA	LMWH	Direct Thromb. Inhibit.	Indirect Xa inhibitors Direct Inhibitors
Target	ATIII + Xa + IIa (1:1 ratio)	II, VII, IX, X (Protein C,S)	ATIII + Xa + IIa (Xa > IIa)	Thrombin	ATIII + Xa FXa; FIIa; others
Route	Parenteral	Oral	Parenteral	Parenteral	Parenteral Oral
	Monitored	Monitored	Non monitored	Monitored Non monitored	Non monitored

Now
Reversibility

DOAC Acute Treatment: Trial Designs

Study Drug	No. of Pts	PE or PE and DVT, n (%)	Isolated DVT, n (%)	Unprovoked, n (%)	Previous VTE, n (%)	TTR on VKA, %
Apixaban						
AMPLIFY	5395	1836 (34)	3532 (65)	4845 (90)	872 (16)	61
Dabigatran						
RE-COVER	2539	786 (31)	1749 (69)	Not reported	649 (26)	60
RE-COVER II	2568	815–819 (32)	1748–1750 (68)	Not reported	(17.5)	57
Edoxaban						
HOKUSAI-VTE	8240	3319 (40)	4921 (60)	5410 (66)	1520 (18)	64
Rivaroxaban						
EINSTEIN-DVT	3449	23 (1)	3405 (99)	2138 (62)	666 (19)	58
EINSTEIN-PE	4832	4832 (100)	0 (0)	3117 (65)	944 (20)	63

Pts, patients; TTR, time in therapeutic range; VKA, vitamin K antagonist
 van der Hulle T et al. *J Thromb Haemost.* 2014;12:320-328. Dobesh PP et al. *Drugs.* 2014;74:2015-2032.

The New Anti-Coagulants, Thromboembolism: It is a moving target !!

**When you understand the drug ,the Pharmaceutical
Companies rework the data and send it back in different
packaging**



CAPRIE trial/ CHARISMA trial

- Clopidogrel was shown to reduce risk in CVD in the PAD population of 24%



CHARISMA

3/12/2006 NEJM Clopidogrel and Aspirin versus Aspirin alone
for the prevention of Atherothrombotic Events.

- 15,603 patients double blinded and prospectively randomized with either evident CVD or multiple risk factors
- Treatment=Clopidogril 75mg plus ASA 75-162mg
- Control =Placebo Plus ASA 75-162mg
- Conclusion no difference in outcome!

DOAC Acute Treatment: Meta-analysis of Efficacy/Safety

DOACs decrease the risk for recurrent VTE and major bleeding compared with VKAs

Outcome	Pooled Abs Risk Difference, % (95% CI)	NNT With NOAC to Prevent 1 Event (95% CI)
Recurrent VTE	-0.24 (-0.60–0.11)	417 (167 to -909)
Fatal PE	0.01 (-0.06–0.08)	10 000 (1667 to -1250)
Overall mortality	-0.10 (-0.47–0.28)	1000 (213 to -357)
Major bleeding	-0.67 (-1.13 to -0.21)	149 (88–476)
Non-fatal bleeding, critical site	-0.38 (-0.65 to -0.10)	263 (153–1000)
CRNM bleeding	-1.77 (-3.40 to -0.15)	56 (29–667)
Non-fatal ICH	-0.14 (-0.31–0.03)	714 (323 to -3333)
Major GI bleeding	-0.16 (-0.42–0.11)	625 (238–909)
Fatal bleeding	-0.09 (-0.17–0.00)	1111 (588–0)

DOACs Compared With LMWH and Warfarin

But never with each other!!

● Efficacy

- All 4 DOACs are noninferior to LMWH/VKA for efficacy, regardless of weight, PE versus DVT, chronic kidney disease, and cancer¹

- Edoxaban: prespecified submassive PE subgroup showed superiority²

- Safety of DOACs combined (meta-analysis; N=27,023)¹

- 39% less major bleeding

- 64% less fatal bleeding

- 63% less ICH than LMWH/VKA

Cost of DOAC's

Table. Oral Anticoagulants for Treatment of Venous Thromboembolism

Drug	Mechanism of Action	Usual Dosage	Cost ^a \$
Warfarin generic (Coumadin)	Vitamin K antagonist	2-10 mg ^b once/d	6.00 43.00
Rivaroxaban (Xarelto)	Direct factor Xa inhibitor	15 mg bid for 3 wks, then 20 mg once/d ^c	265.00
Apixaban (Eliquis) ^d	Direct factor Xa inhibitor	10 mg bid for 7 d, then 5 mg bid ^e	265.00
Dabigatran etexilate (Pradaxa) ^d	Direct thrombin inhibitor	150 mg bid ^f	265.00

Emerging Antidotes for the DOACs

- **Idarucizumab¹ → Dabigatran**
 - Fully humanized antibody fragment that binds dabigatran with approximately 350x greater affinity than thrombin²
 - Phase 3 RE-VERSE AD trial underway in bleeding and surgical patients
 - **Granted Breakthrough Therapy designation by FDA in 2014**
- **Andexanet alfa³ → Factor Xa inhibitors**
 - Recombinant, modified factor Xa molecule that sequesters factor Xa
 - Initiated phase 3 trial with apixaban, rivaroxaban; ongoing phase 2 trial with edoxaban
 - **Granted Breakthrough Therapy designation by FDA in 2013**
- **Aripazine (PER977)⁴ → Universal**
 - Small molecule that purportedly reverses effect of dabigatran, rivaroxaban, apixaban, edoxaban, fondaparinux, and LMWH
 - Initiated phase 3 trial with edoxaban

FDA, US Food and Drug Administration

1. Schiele F et al. *Blood*. 2013;121:3554-3562. 2. Boehringer Ingelheim Pharmaceuticals, Inc. Press release. 2014. http://us.boehringer-ingelheim.com/news_events/press_releases/press_release_archive/2014/06-26-14-boehringer-ingelheim-investigational-antidote-pradaxa-dabigatran-etexilate-mesylate-fda-breakthrough-therapy-designation.html. Accessed September 13, 2014. 3. Crowther M. Presented at AHA Scientific Sessions, Chicago, IL; 2014. 4. BusinessWire. Press Release 2014. Available at: <http://www.businesswire.com/news/home/20141006006122/en/Perosphere-Daiichi-Sankyo-Enter-Clinical-Trial-Collaboration#.VLvbBSvF9Es>. Accessed Jan 18, 2015.

Reversal Strategies

- 4F-PCCs (Kcentra) should be considered for warfarin-associated bleeding, if available.
- **Time is your friend** with DOAC-treated patients—consider a conservative approach
- **Serious bleeds (especially ICH) less common** with **DOACs** than with warfarin
- Unlike warfarin-treated patients, normal levels of clotting factors are present
- **Emerging antidotes for the DOACs are either on the market or pending approval.**

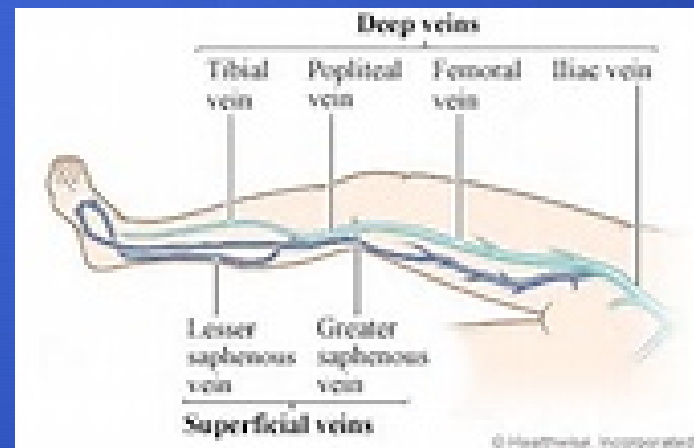
Things I am asked all the time ?

Science and pseudoscience

- Is one drug like another
- **Should you cross your legs**
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- SO I have to eat What
- Screening for DVT
- Birth control with DVT
- ETOH
- Travel
- NSAID

Is crossing your legs a risk?

No Greater Risk
Pseudo-Science



What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Throw in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- **Routine Duplex**
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Screening for DVT
- Birth control with DVT
- ETOH
- Is one agent like another
- Does compliance matter
- If I walk will I make it embolise

**Is screening high risk patients for
DVT before Discharge
reasonable?**

Is screening Screening for DVT Before Hospital Discharge reasonable?

- Some clinicians have advocated for high-risk orthopedic surgery groups the routine screening for and subsequent treatment of asymptomatic DVT before the thrombus could extend to produce symptomatic DVT or PE.⁴³²
- “We do not advocate this approach because it has not been shown to be effective in preventing clinically important VTE.” Chest Guidelines
- **Routine screening for asymptomatic DVT using DUS was not shown to be sensitive.**

What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH

Dehydration?

- American College of Chest Physicians (ACCP)
- **"No definitive evidence" that dehydration is linked with an increased risk of DVT.**

What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Airplane flight
- ETOH
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Will I bleed to death
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Screening for DVT
- Birth control with DVT

Air Travel?

Commercial Airline Pilots and VTE ?

- The symptomatic VTE rate within 30 days of a long-haul flight has been estimated to be approximately one in 2 million arriving passengers with a case fatality rate of only 2%.⁷²²
- In another study,⁷²³ the risk of fatal PE associated with air travel > 8 h was 1.3 per million people < 60 years old.
- **YOUR PILOT IS NOT AT HIGHER RISK!**

How about where you sit on the plane ?

- Do you automatically up your risk depending on which ticket you buy?



- Answer :Yes and no!

- First the 'yes'. Studies have shown that you're more likely to develop DVT if you sit in a window rather than the aisle seat.





Coach Class Syndrome

● Thromboembolic risk?



First Class Vs Coach Risk



BRITISH AIRWAYS 



AIRPLANE FLIGHT

Is there evidence that airplane flight is dangerous!!

- Drink Fluids
- Avoid Coffee and ETOH
- Don't wear short, tight socks, and try not to cross your legs a lot. You might want to wear compression stockings. They'll help your blood flow and keep swelling down..

Internet website

Recommendations

AIRPLANE FLIGHT

Is there evidence that airplane flight is dangerous!!

- Drink Fluids **NOPE**
- Avoid Coffee and ETOH **NOPE**
- Don't wear short, tight socks, and try not to cross your legs a lot. You might want to wear compression stockings. They'll help your blood flow and keep swelling down.. **NOPE**

Internet website

Recommendations

What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- **Early ambulation**
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH

Ambulation

An abundance of data!!

What are the questions Asked?

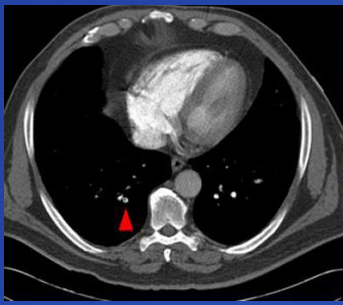
Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- **Provocation**
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH

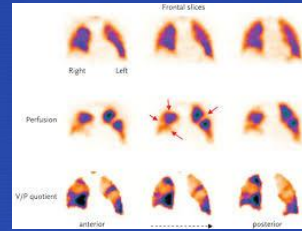
New recommendations How long to treat with Anticoagulants (D-Dimer and Duplex)

- *VTE (proximal DVT or PE) provoked by surgery: recommend 3 months.*
- *VTE (proximal DVT or PE) provoked by non-surgical transient risk factor (e.g. estrogens, pregnancy, leg injury, flight > 8 hrs): suggest 3 months.*
- *Unprovoked VTE (proximal DVT or PE): suggest long-term.*
- *Distal DVT:*
 - *if not severely symptomatic : suggest no anticoagulation, but f/u Doppler ultrasound;*
 - *If severely symptomatic: suggest 3 months.*

- What is the first line treatment for a Sub-segmental Pulmonary Embolism?
- Heparin?
- LMWH?
- IVC FILTER?
- 10-a Inhibitor (Epixaban or Riveraxiban)



Sub-segmental PE:



- Anticoagulation is suggested for patients at higher risk for recurrence, i.e. patients who are hospitalized, have reduced mobility, have cancer, had unprovoked sub-segmental PE, have low pulmonary reserve, or marked respiratory symptoms.

- In Patients with no involvement of more proximal pulmonary arteries) and no proximal DVT:

No anticoagulation is suggested but simply surveillance in patients who are at low risk of VTE recurrence (e.g. patients with recent surgery or other transient risk factor.

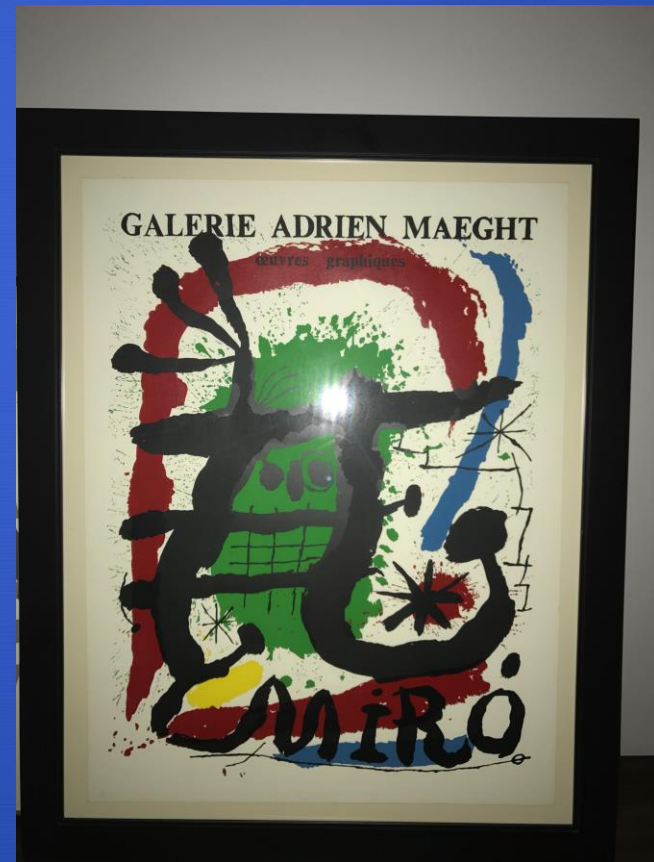
What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- **Location Location Location**
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- **Does size matter**
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH
- Choice of anticoagulants
- Timeframes of treatment

Location Location Location

- Upper Extremity
- Proximal
- Calf clot
- Mesenteric
- Mondor's



Burden of DVT and PE

Size does matter

DVT

- 25% of calf vein DVTs Propagate to involve proximal lower extremity veins (popliteal, femoral, or iliac veins)¹
- Up to 50% of patients develop long-term complications, such as post-thrombotic syndrome and chronic venous insufficiency²
 - *50% of proximal lower extremity DVTs result in PE¹*

PE

- Leading preventable cause of death in hospitalized patients³
- Up to 25% of cases present as sudden death²
- Without treatment, approximately 30% of patients die⁴
 - *Adequate treatment reduces mortality to 8%*

1. Revis T et al. Deep vein thrombosis & pulmonary embolism. In: CDC 2014 The Yellow Book. Available at: <http://www.cdc.gov/travel/yellowbook/2014/chapter-2-the-pre-travel-consultation/deep-vein-thrombosis-and-pulmonary-embolism>. Accessed January 27, 2015.
2. Beckman MG et al. *Am J Prev Med*. 2010;38:S495-S501 3. Walter RJ et al. *Curr Med Res Opin*. 2014;30:1975-1989. 4. Carson JL et al. *N Engl J Med* 1992;326:1240-1245.

- What is the most common cause of UEDVT?

- Paget Schroeder 1970 (Outpatient)
- Iatrogenic (Inpatient)

- Incidence of pulmonary embolism (PE) associated with isolated upper extremity deep venous thrombosis (UEDVT) is variable (1%-13%).
- *Chest* 2008 guidelines, treatment UEDVT with anticoagulation to ameliorate symptoms, and decrease the risk of subsequent PE

Internal Jugular, Subclavian, and Axillary Deep Venous Thrombosis and the Risk of Pulmonary Embolism

Kevin M. Major; Sebina Bulic; Vincent L. Rowe; Kevin Patel; Fred A. Weaver

DISCLOSURES *Vascular*. 2008;16(2):73-79.

Any time you see new Veins ?



What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- **Stockings**
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH

Compression stockings

Sox Trial

- Do they reduce your chance of DVT?
- “Compression stockings must be properly fitted to be effective, can't prevent all clots, and can have side-effects,”
- For instance, they can increase superficial phlebitis (inflammation of the surface veins), lead to blistering and local skin allergies.

Compression Stockings

Pseudo-Science we can live with!

- Clinicians need to realize that despite the ubiquity of compression stockings, the net benefits and risks of this seemingly innocuous intervention remain uncertain,” concludes an editorial that accompanies the study in the **Annals of Internal Medicine.**

What are the questions Asked?

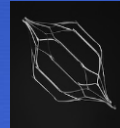
Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH

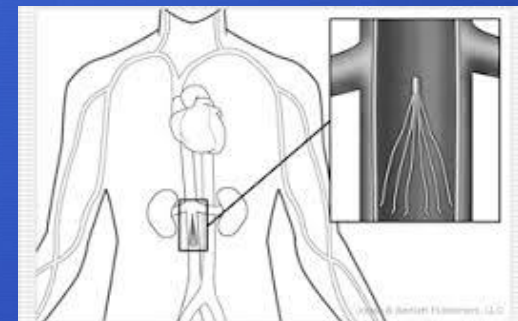
IVC Filters

- Easy to insert
- Very effective
- Low failure rate
- Don't Have to worry about anticoagulation
- Good for high fall risks
- We can take them out now
- MAY THROMBOSE
- MAY MIGRATE
- MAY EMBOLIZE
- MIGHT BLEED
- RARELY ARE TAKEN OUT
- ARE EXPENSIVE

Indication for Caval Interruption



- Failed anticoagulation
- Contraindication to anticoagulation
- Bleeding Diathesis
- Fall risk
- Non-compliance?
- Thrombus Load?



Consider Removable Filters When Appropriate

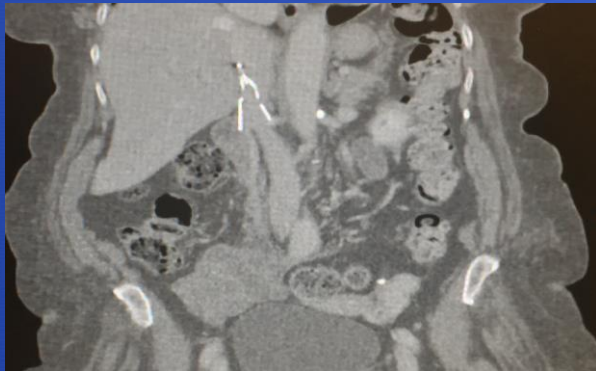
Complications with filters

- **IVC thrombosis 12% of the cases with retrievable filters, and 6% with permanent filters**
- **30%-35% clinical signs of venous insufficiency at 6 years even when treated with anticoagulation following filter placement**
- **(1%), filter migration.**
- **Fracture**
- **(3%-69%), and penetration of the IVC (9%-24%)**





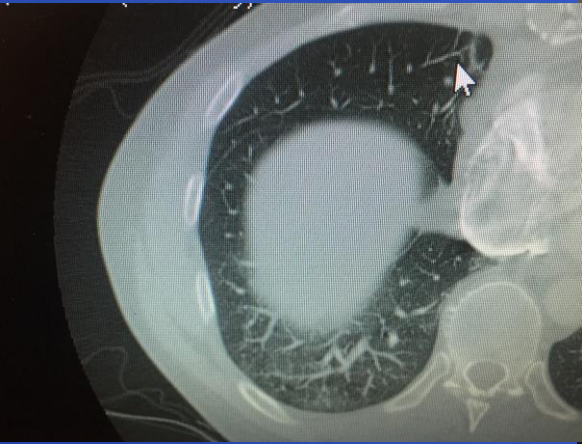
An advertisement for an IVC filter warning. The background is blue with a white grid pattern. At the top left, there is a diagram of a human torso with the inferior vena cava highlighted in blue. To the right of the diagram, the text "IVC FILTER WARNING" is written in large, bold, red letters. Below this, the text "CAUSING SERIOUS INJURIES!" is written in white. Underneath, a list of injuries is shown in yellow: "Heart Damage", "Lung Damage", "Internal Bleeding", and "Death". To the left of this list is a small image of a document titled "FDA WARNING". At the bottom of the advertisement, the text "You may be entitled to FINANCIAL COMPENSATION!" is written in white, with "FINANCIAL COMPENSATION!" in red. Below this, the phone number "1-800-522-9404" is displayed in large white letters, and the logo for "KNIGHTLINE LEGAL" is at the bottom.



*"Nothing you can't spell
will ever work."*

– Will Rogers

Why don't we just put in a filter ?



What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- **Homans sign**
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Screening for DVT
- Birth control with DVT
- ETOH

DVT ,Clinical Exam

- Normal 50% to 80% (Venogram proven DVT)



- Abnormal 30% (Normal Venogram)

What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Screening for DVT
- Birth control with DVT
- ETOH

Active Malignancy Requires Long-term Anticoagulation

- 20% of patients with VTE have active malignancy¹
- Anticoagulation decreases risk of recurrence by up to 50%¹
- **Current treatment of choice:**
 - **LMWH for ≥ 6 Months and while active (indefinite)^{1,2}**
- Is there a role of the DOACs in treating and preventing VTE in patients with cancer?

Cancer Workup after Unprovoked Clot ----Less is more NEJM

- The subsequent discovery of cancer 1%(In the following year)
- Two randomized or quasi-randomized studies involving a total of 396 patients.
- **There was insufficient evidence regarding the effectiveness of testing for undiagnosed cancer in reducing cancer-related and venous-thrombo- embolism–related morbidity and mortality and that the results could be consistent with either harm or benefit**



Screening for occult Cancer in Unprovoked VTE

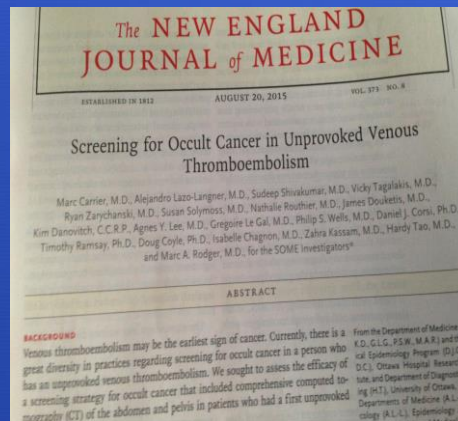
Mark Carrier, A Lazo-Langner, MD NJEM8/26/15

- **Unprovoked DVT may be the earliest sign of cancer!**
- Up to 10% of patients with unprovoked DVT are Dx with cancer within a year of VTE.
- 60% of cancer are Dx shortly after Dx of unprovoked VTE
- Thereafter the incidence of cancer diagnosis gradually returns to rate of general population in 1 year
- ***Screening should be undertaken in age appropriate fashion****



SCREENING FOR OCCULT CANCER IN UNPROVOKED VTE

- Screening CT of the abdomen and pelvis did not lead to fewer missed cancers than with a limited screening strategy.
- The screening that included CT did not appear to detect significantly more occult cancers (including early cancers), shorten the time to cancer diagnosis, or reduce cancer-related mortality.



NJEM Trial

Role of DOACs in Cancer Patients: Use Caution

- Patients with active cancer enrolled in pivotal trials; subgroup analyses performed
- **However, more studies are needed**
 - To date, low number of patients
 - Current studies not designed to distinguish between cancer types, cancer treatment, and duration of cancer treatment
- DOACs rely on absorption via GI tract
 - Chemotherapy and radiation can have negative affect on GI tract
 - **May alter the absorption of DOACs—increasing/decreasing anticoagulant effect**

Conclusions

- For VTE in patients with active malignancy, the current standard of care is **LMWH Indefinite while active**
- In subgroup analyses, all 4 DOACs reduce the risk of VTE recurrence in patients with active cancer compared with LMWH/VKA
 - Major bleeding is reduced by dabigatran, rivaroxaban, and apixaban
- **Safety and efficacy of DOACs not yet established**
 - More studies needed to define appropriate patient populations regarding thrombophilia ,cancer/treatment type and DOAC dosing

ORIGINAL ARTICLE

Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism

New England Journal of Medicine

CONCLUSIONS

- Oral edoxaban was noninferior to subcutaneous dalteparin with respect to the composite outcome of recurrent venous thromboembolism or major bleeding. The rate of recurrent venous thromboembolism was lower but the rate of major bleeding was higher with edoxaban than with dalteparin. (Funded by Daiichi Sankyo; Hokusai VTE Cancer ClinicalTrials.gov number, [NCT02073682](https://clinicaltrials.gov/ct2/show/study/NCT02073682).)

What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Screening for DVT
- Birth control with DVT
- ETOH

Dan L. Longo, M.D., *Editor*

Thrombophilia Testing and Venous Thrombosis

Jean M. Connors, M.D.

Recommendation

Explanation

Do not test at time of VTE event

Test at completion of anticoagulant therapy for provoked VTE; for unprovoked VTE, test after treatment for acute event if cessation of anticoagulant therapy is contemplated and test results might change management strategy

Do not test while patient is receiving anticoagulant therapy

Test when VKA has been stopped for at least 2 wk, DOAC has been stopped for at least 2 days (preferably longer), and UFH or LMWH for antithrombin levels has been stopped for more than 24 hr

Do not test if VTE is provoked by strong risk factors

Strong risk factors are major trauma, major surgery, immobility, major illness

Consider testing

Consider testing in patients in whom VTE occurs at a young age in association with weak provoking factors or a strong family history of VTE or in patients who have recurrent VTE

Identify goals of testing

Identify goals in order to aid decision making regarding future VTE prophylaxis, to guide testing of family members (especially regarding risk associated with COC or pregnancy in female family members), and to determine cause (especially for severe VTE, fatal VTE in family members, or VTE in an unusual location); test results alone should not be used for decision making regarding duration of anticoagulant therapy

* COC denotes combination oral contraceptives, DOAC direct oral anticoagulant, LMWH low-molecular-weight heparin, UFH unfractionated heparin, and VKA vitamin K antagonist.

Thrombophilia Work-up

- Acute MI
- Post Surgery
- Hip fracture
- >60
- Long Plane Ride

No Specific Tests

Thrombophilia Evaluation

- Pregnancy
- ERT
- Unusual location
- Recurrent DVT
- Unusual circumstances
- Known Family History

Thrombophilia

Predisposition to thrombosis.

- May be associated with disease, drug exposure or may be inherited
- Most patients with a a thrombophilia **do** **not** develop thrombosis DE novo
- Thrombophilia must be considered in context of other risk factors for thrombosis and predictors of recurrence



What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- **Obesity**
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Screening for DVT
- Birth control with DVT

Obesity



- 30 are more times likely than people of normal weight to get a blood clot deep in a DVT
- Extra fat around your belly will also stop blood from moving easily through the deep veins



What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- **Varicose veins**
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH

Varicose veins



- 132 out of 2,357 (5.6 %) DVT episodes among patients with VV compared to 728 out of 80,588 (0.9 %) in the patient cohort without VV ($p < 0.0001$).

Strong associations between VV and DVT in a general practice population with documented VV. Special medical attention is required for patients with VV, a history of previous venous thromboembolism, comorbid malignancy, and recent hospital discharge, particularly those with a combination of these factors.



What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- **Will I bleed to death**
- Smoking
- Pregnancy
- Routine Duplex in THR
- **Pregnancy**
- How long is recovery after DVT
- Does size matter
- Screening for DVT
- Birth control with DVT

Varicose Veins. Will I bleed to death?



What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH

Things I am asked all the time Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- **Smoking**
- Pregnancy increases
- Routine Duplex in THR
- Pregnancy
- How long is recovery after DVT
- Does size matter
- Legs
- Chest
- Screening for DVT
- Birth control with DVT
- ETOH

Smoking

large population-based case–control
studies

- Smoking is a moderate risk factor for venous thrombosis,
- Smoking acts synergistically with oral contraceptives.
- Joint effect of smoking with the factor V Leiden mutation or the prothrombin 20210A mutation was slightly higher than the sum of the separate effects

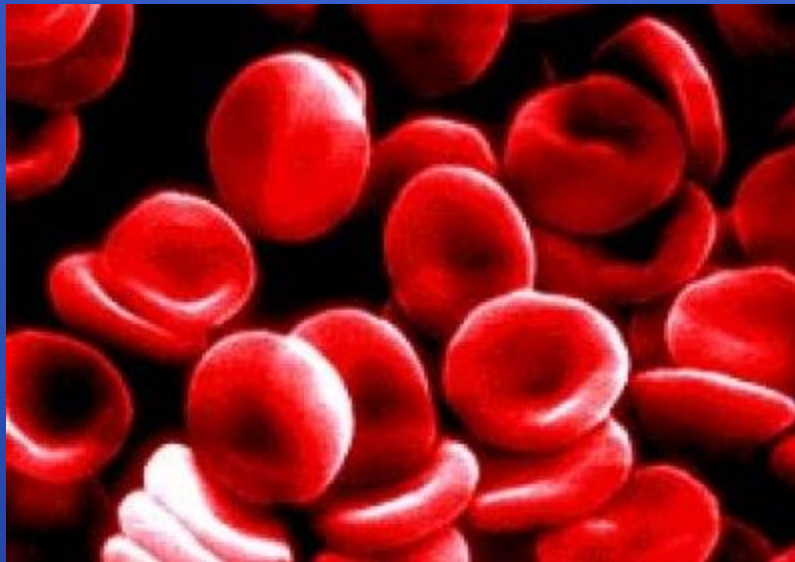
What are the questions Asked?

Science and pseudoscience

- Should you cross your legs
- Hydration
- Early ambulation
- Provocation
- Location Location Location
- Stockings
- Put in a filter
- Homans sign
- Clots = malignancy
- You can genetically predict clots
- Types of prophylaxis Aspirin???
- Long term illness
- Obesity
- Varicose veins
- Smoking
- **Pregnancy i**
- **Birth control with DVT**
- Routine Duplex in THR
- How long is recovery after DVT
- Does size matter
- Screening for DVT
- ETOH

Hematologic Changes during Pregnancy

- Maternal plasma volume increases 50%
- RBC increases yet there is a physiologic anemia due to dilution of 15%



OB-GYN/VTE Facts

- PE is the leading cause of maternal mortality
- 40% of all deaths following gynecologic surgery are directly attributable to PE
- Most patients who succumb to a post-operative PE do so within 2 hours of onset



Prevention is preferred
over treatment

Best Birth-control in Thromboembolic disease

- Skyla – A New IUD, Suitable for Women at Risk for DVT and PE
- (LARC) Copper-releasing IUD in thrombophilia
- Yasmin, Yaz and Other Drospirenone Contraceptives:
(+) Higher Risk for VTE



Birth Control

- Progestin-releasing IUDs (e.g. Mirena[®]) appear to not increase the risk for VTE.
- Oral progestin-only contraceptives (minipill) may lead to an increased risk of VTE, but this is not certain. ...
- Injectable progestins appear to lead to an increased risk of VTE.

Role of aspirin

- In patients with unprovoked venous thromboembolism (VTE) who stop anticoagulation, aspirin is suggested.

Rivaroxaban or Aspirin for

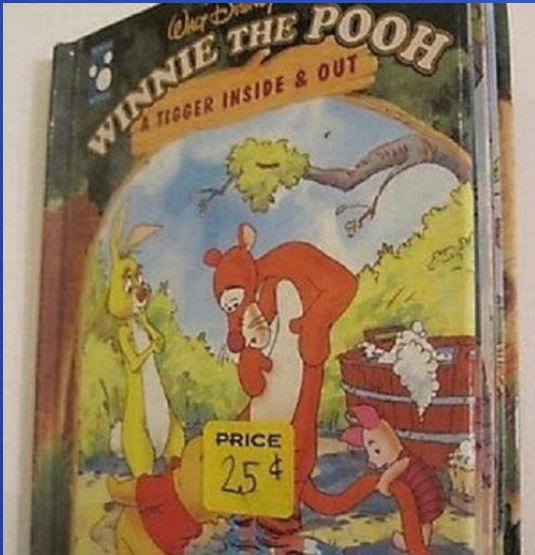
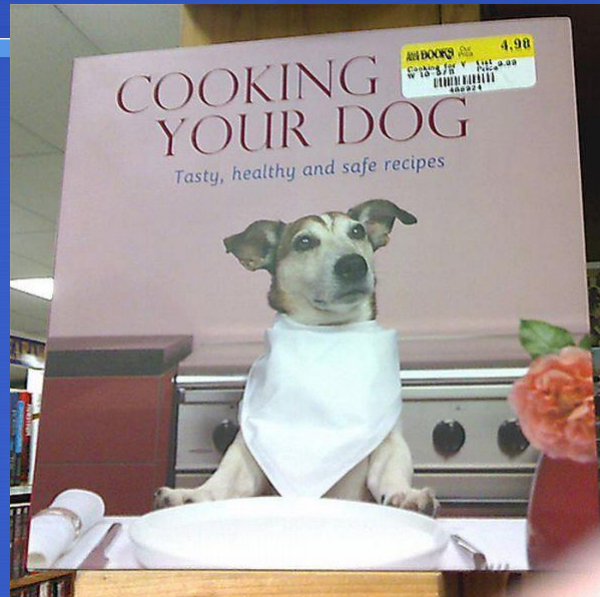
Extended Treatment of Venous Thromboembolism

J.I. Weitz, A.W.A. Lensing, M.H. Prins, R. Bauersachs, J. Beyer-Westendorf, H. Bounameaux, T.A. Brighton, A.T. Cohen, B.L. Davidson, H. Decousus, M.C.S. Freitas, G. Holberg, A.K. Kakkar, L. Haskell, B. van Bellen, A.F. Pap, S.D. Berkowitz, P. Verhamme, P.S. Wells, and P. Prandoni, for the EINSTEIN CHOICE Investigators*

The new england journal of medicine — March 30, 2017 —

- Patients with venous Thromboembolism with ongoing risk factors have an appreciable risk of recurrence because even with aspirin, with recurrent venous thromboembolism of 3.6%, as compared with a rate of recurrence of 5.6% (unprovoked)
- **Patients who required extended treatment with therapeutic doses of anticoagulant agents were excluded.

Sometimes medicine is confusing!



Conclusion
Always wear the white hat!!!

Thank You !!!

- “There is nothing either good or bad, but thinking makes it so.” ...



Hamlet



Goals

- Address some of the burning questions related to thromboembolic disease
- Attempt to bring evidence based recommendations to a confusing topic
- Look at some of the the current trials and how the clinician should apply information from pharma



Moribund foot



Lymphangiocarcinoma Carcinoma



Are stasis ulcers benign and what is the best antibiotic?



Squamous Cell Degenerative Carcinoma



Marjolin's
ulcer