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Rethinking Gallbladder Health:

Superfluous Organ or Vital Structure in Human Health?

Presenter: Amie Skilton
Naturopath, Nuritionist and Educator
Host: Linda Dal Molin

Presenter | Amie Skilton

Amie Skilton's professional journey spans nearly two decades as a functional medicine practitioner and educator in naturopathic medicine. Her expertise has brought her to conference stages, television, and digital platforms, where she has addressed a broad audience that includes functional medicine practitioners and the general public. Amie's approach deeply integrates environmental factors with traditional health practices, emphasising the significance of a harmonious relationship between individuals and their surroundings for optimal health.

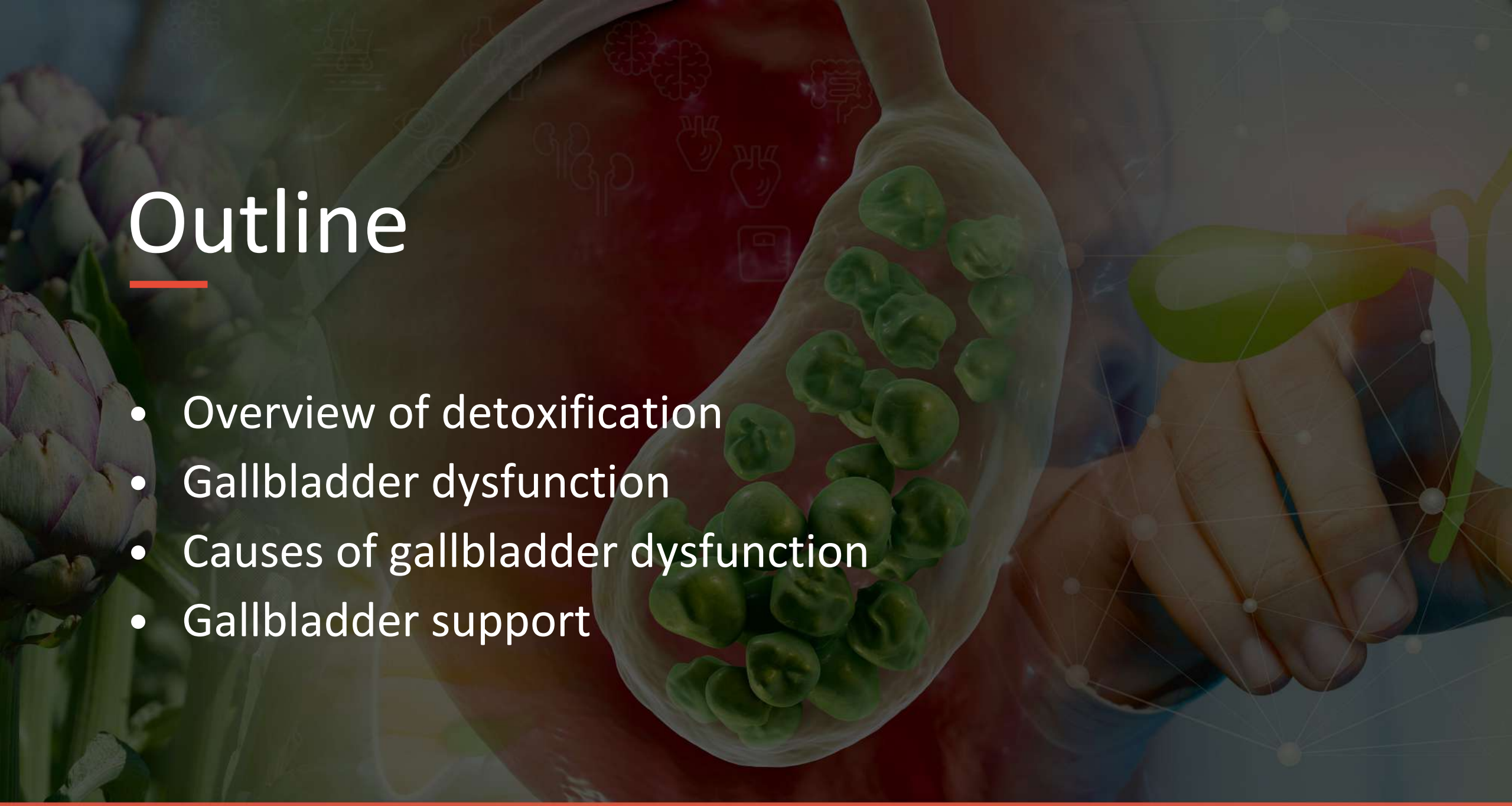
In 2017, Amie's personal health journey took a significant turn when she was diagnosed with Chronic Inflammatory Response Syndrome (CIRS), a condition often associated with mould exposure. This diagnosis transformed her health perspective and led her to become a certified Mould Testing Technician. Amie's experience with CIRS has greatly influenced her practice, emphasising the built environment's impact on health. Thus, she has expanded her clinical focus to include environmental health hazards alongside conventional naturopathic treatments.

Our Host | Linda Dal Molin

Linda Dal Molin is the Director of Sales and Education for Designs for Health Australia.

Linda has a Masters in Human Nutrition, Bachelor of Health Science (Complementary Medicine), Advanced Diploma Naturopathy. She has been a practitioner for 25 years and worked in the natural health space for 27 years.

Linda has developed a strong relationship with the Designs for Health practitioner community. She will moderate the Q&A discussion with Steven in this webinar and engage our live Designs for Health practitioner community to bring insight and practical clinical pearls for all.



Outline

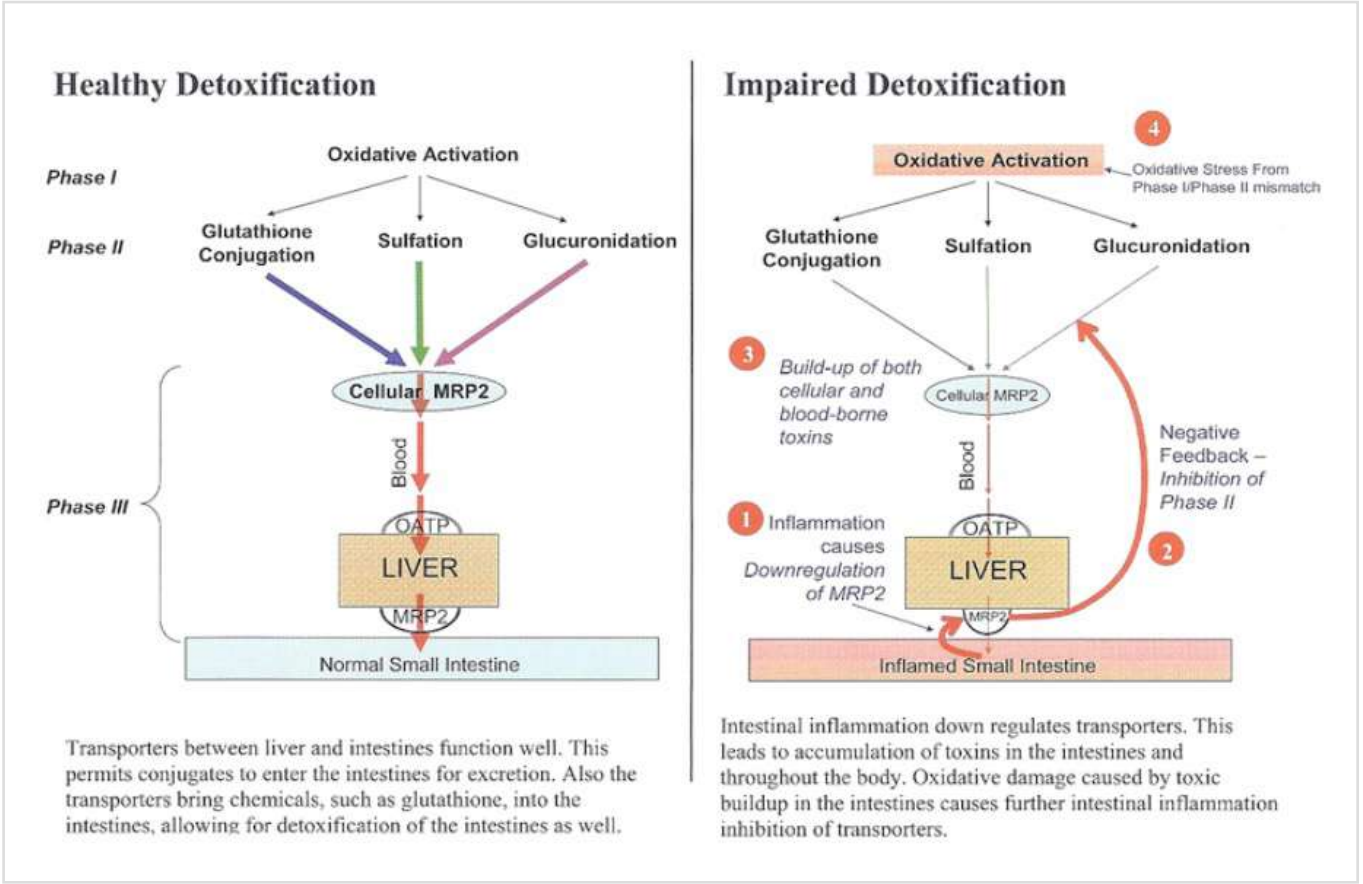
- Overview of detoxification
- Gallbladder dysfunction
- Causes of gallbladder dysfunction
- Gallbladder support

Outline

- **Overview of detoxification**
  - The gastrointestinal tract
  - Phases of liver detoxification (plus the gallbladder)
  - Bowels
  - Kidneys
  - Breath
  - Sweat

GI tract and detoxification

- 20-25% of the detoxification activities actually takes place in the gut mucosa – the microvilli themselves carry out a significant amount of detoxification through the production of CYP450 enzymes.
  - CYP3A and CYP2C represent the major intestinal CYPs, accounting for approximately 80% and 18%, respectively.[1]
- GI inflammation downregulates phase 2 activity in the liver.[2]



GI tract and gallbladder health

- Gut microbiota causally influences cholelithiasis and may be related to bile salt hydrolases[3]:
  - *Clostridium senegalense, Coprococcus*, and *Lentisphaerae* increased the risk of cholelithiasis and expressed more bile salt hydrolases
  - *Holdemania, Lachnospiraceae* UCG010, and *Ruminococcaceae* NK4A214 weakly expressed bile salt hydrolases and were implied to have a protective effect against cholelithiasis
- A large number of studies showed that the diversity of intestinal flora in patients with gallstones especially *Firmicutes* is reduced[4]
- *Desulfovibrionales* considered gallstone-promoting microbiota[5]

GI tract and gallbladder health

"Pathogenic microflora of the oral cavity (through mechanisms of immunomodulation) can affect the motility of the gallbladder and the expression of mucin genes (MUC1, Muc3, MUC4), and represent one of the promoters of stone formation in the gallbladder"[6]

GI tract and gallbladder health

There appears to be a significant alteration of the GI microbiome in cholelithiasis patients, and the GI microbiome is involved in the pathogenesis of cholelithiasis through several pathways[7]:

- Biliary microbiome induces gallstone formation by regulating bile acid metabolism;
- *Helicobacter* species induce gallstone formation by precipitating calcium;
- LPS upregulates mucins via the tumor necrosis factor-α converting enzyme/transforming growth factor-α/epidermal growth factor receptor pathway and the EP4/p38MAPK pathway; GUS and PL accelerate precipitation of calcium bilirubinate.

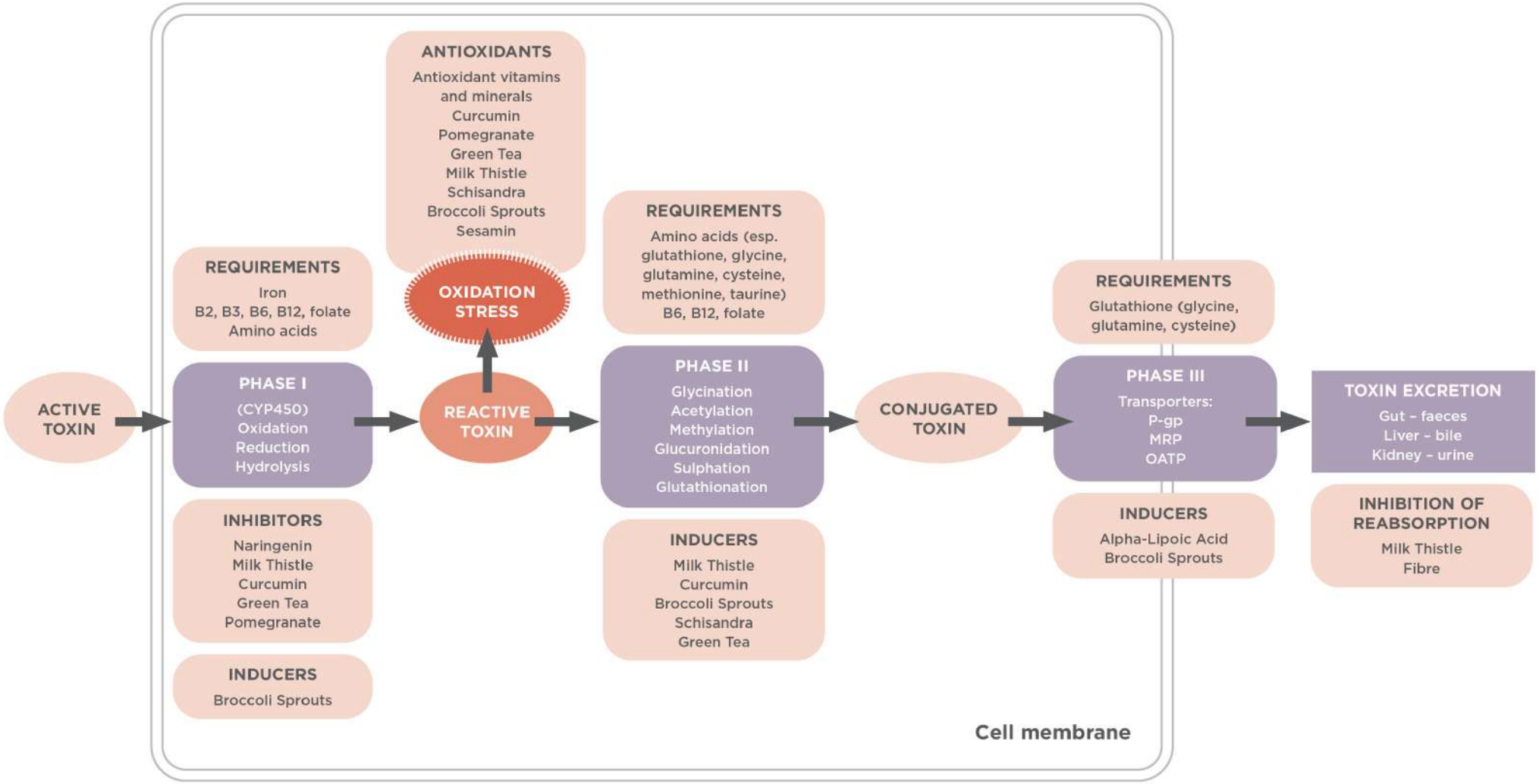
GI tract

Post cholecystectomy:

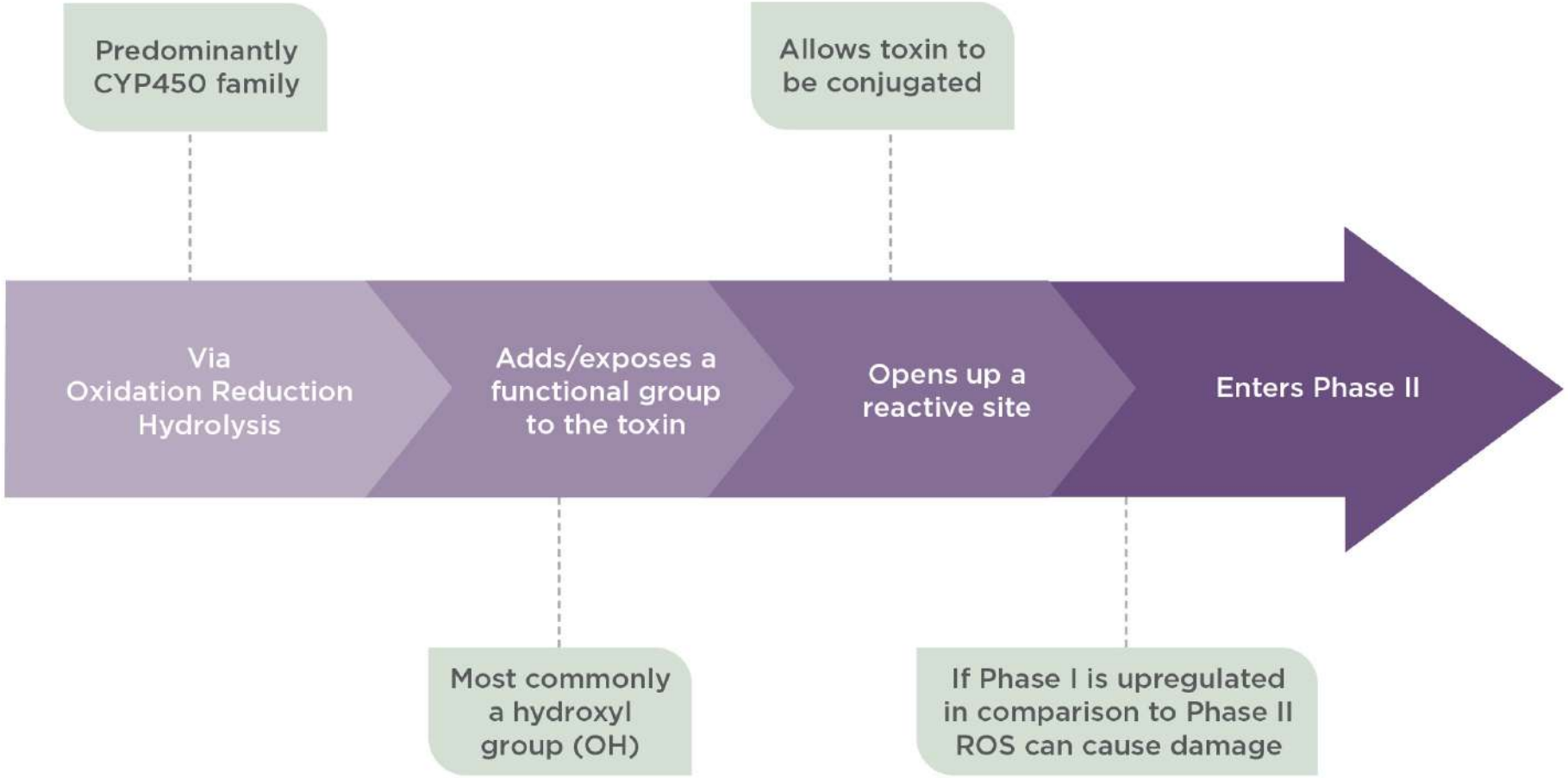
- Reduced microbiota diversity, a decrease in the potentially beneficial genus Faecalibacterium , and an increase in the opportunistic pathogen Escherichia/Shigella;[8]
  - post-cholecystectomy diarrhoea (PCD) is highly prevalent among outpatients with cholecystectomy, and gut microbiota alteration is correlated with it due to bile acids in the colon - stimulates colonic 5-HT and increases colon motility;[9,10]
- Cholecystectomy eliminated ageing-associated faecal commensal microbiota;[11]
- Absent intestinal bacteria, such as Bacteroides, were negatively related to secondary bile acids and may be a leading cause of colorectal cancer incidence in cholecystectomy patient.[11]

Bile acids are also well known to modulate intestinal and colonic motility, but until recently the underlying mechanisms were poorly understood. Bile acids inhibit gastric emptying and reduce small intestinal transit time but stimulate colonic peristalsis and increase colonic transit time.[12]

Liver detoxification – overview

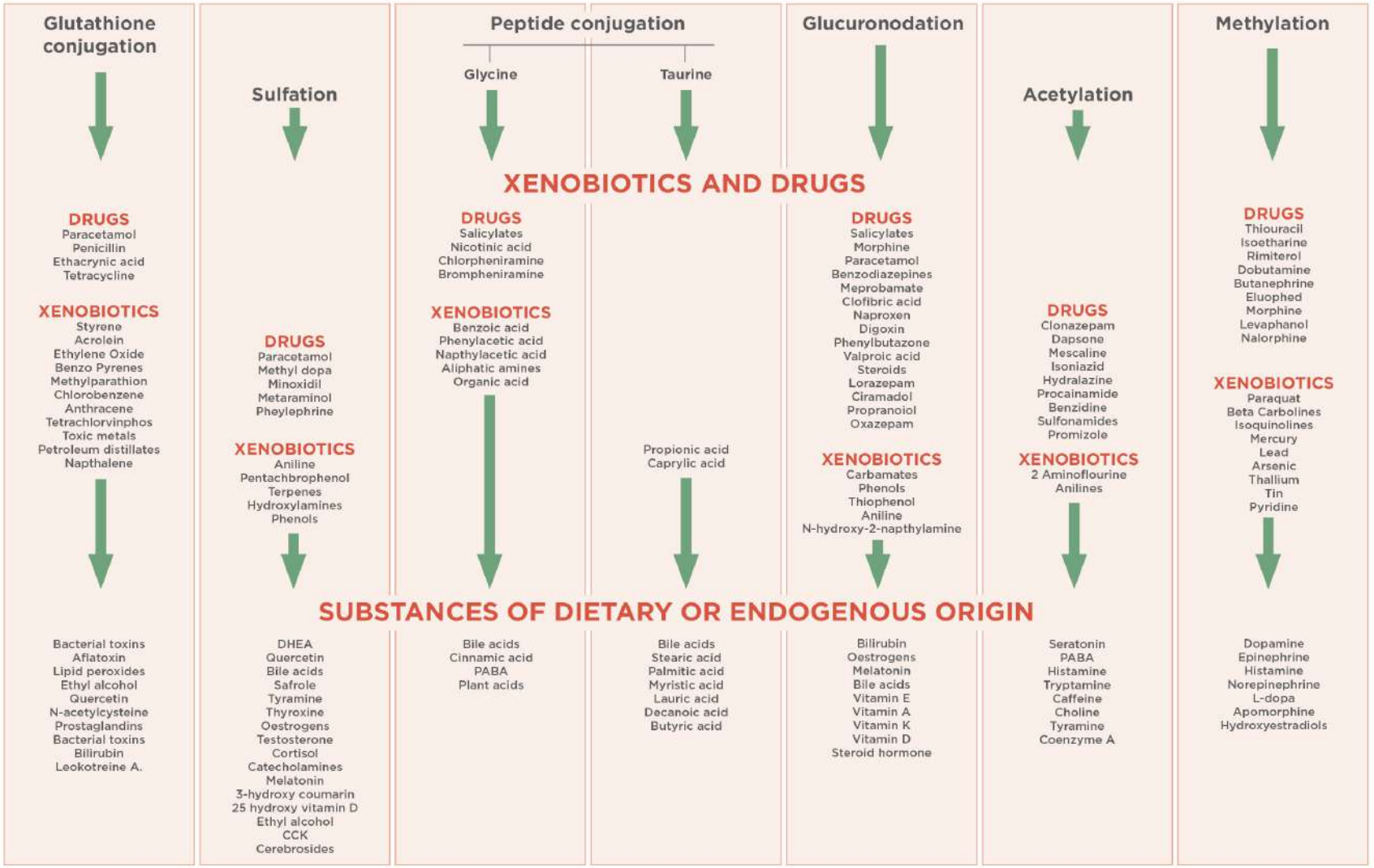


Liver detoxification – Phase I

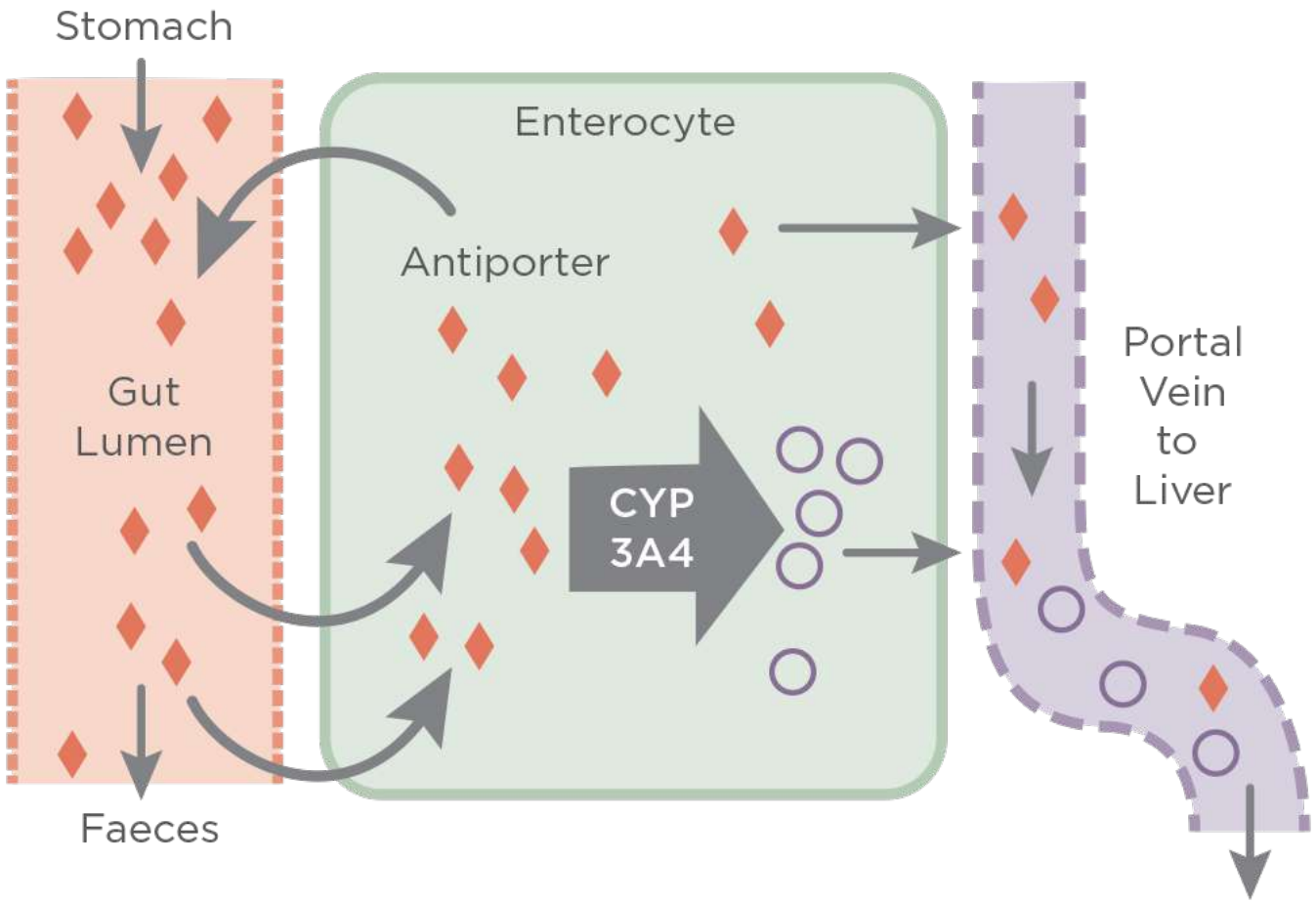


Liver detoxification – Phase II

Phase II Pathways



Liver detoxification – Phase III



Gallbladder

Bile[13]

- Bile is involved in the digestion of complex foods, in particular those containing high amounts of fat; it acts as a surfactant, helping fat emulsion by forming micelles, due to the amphipathic nature of the bile salts, thus making it easier for pancreatic lipases to hydrolyse triglycerides; micelles are also water soluble, thus facilitating absorption by the small intestine.
- It's the primary secretion of the liver – producing up to 800 mL per day.
- It is mainly composed of water (97–98%), but also contains bile salts (0.7%), bilirubin (0.2%), fats (0.51%; predominantly cholesterol, but also fatty acids and lecithin), and 200 meq/L of inorganic salts.
- Bile pigments are waste products generated by the degradation of old red blood cells; they include bilirubin, a yellow dye, and biliverdin, an oxidised form of bilirubin with a green colour.

Gallbladder

- Bile sludge is when bile becomes thick and viscous and congests inside the gallbladder. The sludge is a collection of mucus and particulate solids—usually cholesterol crystals, calcium bilirubinate, and calcium salts.[14]
- When bile becomes too thick, it can alter gallbladder contractibility. While bile sludge often clears up on its own, in many cases, it can linger for some time, resulting in digestive-related concerns.[14,15]
- In one study following more than 100 patients with bile sludge for 21 months, almost 25% developed more significant liver/gallbladder concerns.[15]

Gallbladder

Galbladder microflora[16]:

- in the biliary microecosystem, the main bacterial phyla were represented by *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, and *Proteobacteria* and significant differences in the relative abundance of different taxa were found in the control group (no record of hepatobiliary disorder) vs individuals suffering from lithiasis.
- *Propionibacteriaceae* were more abundant in bile samples from control subjects.
- in patients with cholelithiasis members of the families *Bacteroidaceae*, *Prevotellaceae*, *Porphyromonadaceae*, and *Veillonellaceae* were more frequently detected.

Kidneys

- CYP 450 enzyme activity occurs here also.
- Phase III detox occurs here – pH dependant (alkalise urine for max results).
- In a single pass 20% of renal blood flow is filtered by the glomeruli of the nephrons.
- The risk of kidney cancer is particularly high in the first 6 months after cholecystectomy and in patients who underwent a cholecystectomy before the age of 40 years (Kharazmi, 2023).

Breath

- Our lungs move up to 10,000 litres of air per day and robust CYP450 enzyme activity occurs here also:
  - CYP2A13 is mainly expressed in the respiratory tract and plays an important role in metabolic activation of tobacco-derived nitrosamines.[17]
- Laparoscopic cholecystectomy (vs open cholecystectomy) seems to be associated with small but sustained alterations in the control of breathing and mechanics, which might have an unfavourable clinical impact on patients with compromised lung function.[18]
- Ethanol and methanol are eliminated via the breath.[19]

Breath

Detection of poisoning by substances other than drugs: a neglected art.[20]

Breath odour	Likely poisons
Bitter almonds	Cyanide
Garlic	Malathion, parathion, arsenic, phosphorus, tellurium
Alcohol	Phenols, alcohols
Ethereal (sweet)	Ether
Stale tobacco	Nicotine
Acetone / penetrating	Lacquer
Coal gas	Carbon monoxide
Acrid	Paraldehyde
Phenolic (disinfectants)	Creosotes, phenols
Shoe polish	Nitrobenzene
Pears	Chloral

Skin and sweat

The skin also acts as an excretory organ; it's estimated that 3-4 million eccrine sweat glands (collectively weighing about the same as one kidney – 100g) are distributed over almost the entire human body surface, and:

- An individual can perspire as much as several litres per hour and approximately 10 litres per day.[21]
- Water-soluble exogenous and endogenous toxic/bioactive substances, such as metals[21] including arsenic/cadmium/lead/mercury/nickel/copper[22,23], pharmaceutical drugs[24], cocaine and heroin[25], BPA[26], cytokines[27], and steroids[28] can be eliminated in the sweat.
- Sweat has been analysed for approximately 120 various compounds, including toxic elements, and found that many toxic elements appeared to be preferentially excreted through sweat.[29]
  - Some xenobiotics that are rarely excreted in the urine without being metabolised, but can be excreted in the sweat e.g. excess nicotinamide cannot be eliminated through urine because of its reabsorption by the renal tubules, but it can be effectively excreted by the sweat gland.[30]

Outline

- **Gallbladder dysfunction**
  - Signs of dysfunction
  - Symptoms of dysfunction
  - Pathology markers of dysfunction – blood test
  - Pathology markers of dysfunction – stool analysis

GB dysfunction – symptoms

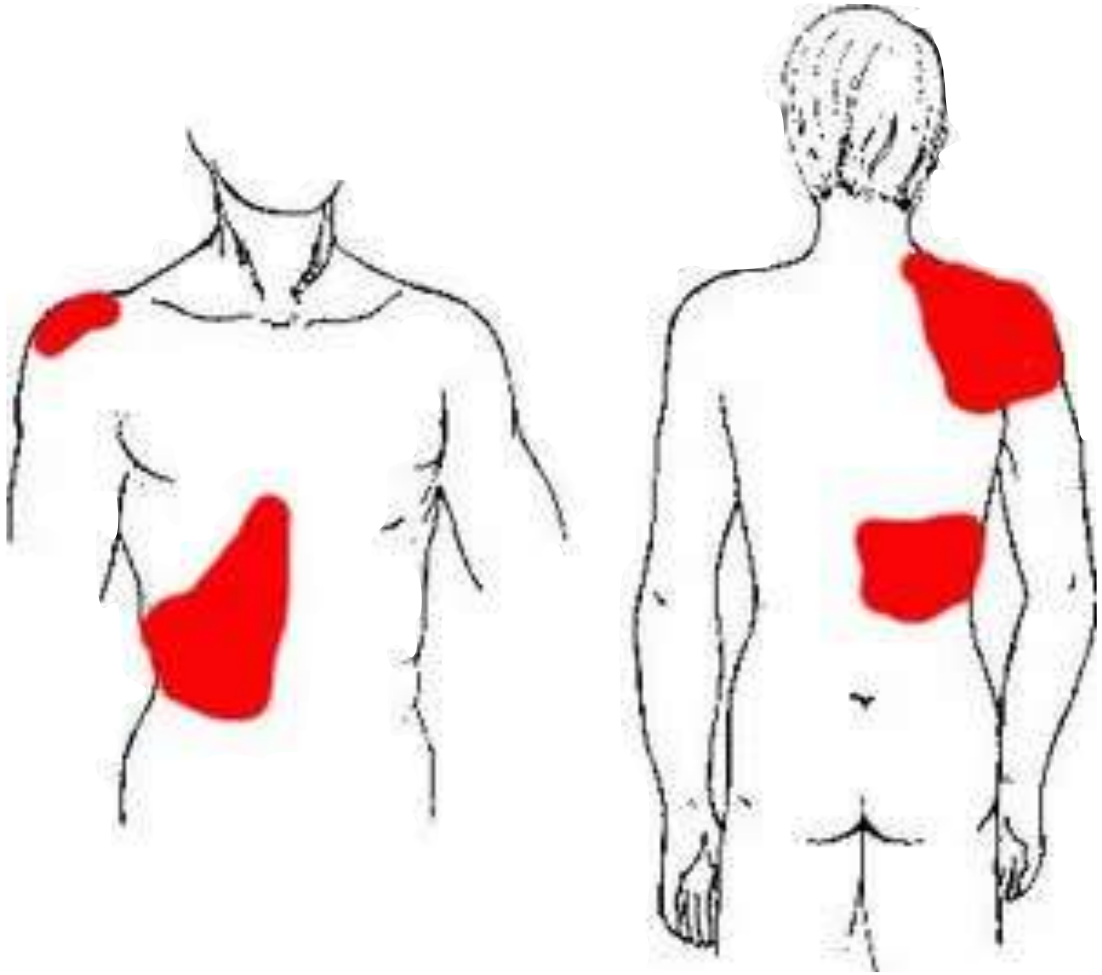
Clinical symptoms of cholestasis include jaundice, dark urine, and pruritis, as well as steatorrhea and fat and micronutrient malabsorption.

- Intolerance to fatty foods i.e. nausea.
- Light or clay coloured stools.
- Stools that float, appear frothy or foamy, and are foul smelling.
- An oily sheen on surface of toilet bowl.
- Symptoms of essential fatty acid deficiency.

GB dysfunction – symptoms

Pain[31]:

- RUQ or epigastric tenderness;
  - may be nocturnal or post-prandial;
- Typically episodic, can be mild to severe;
- Referred pain to top of right shoulder;
- May also experience posterior pain just below the right should blade.



GB dysfunction – signs

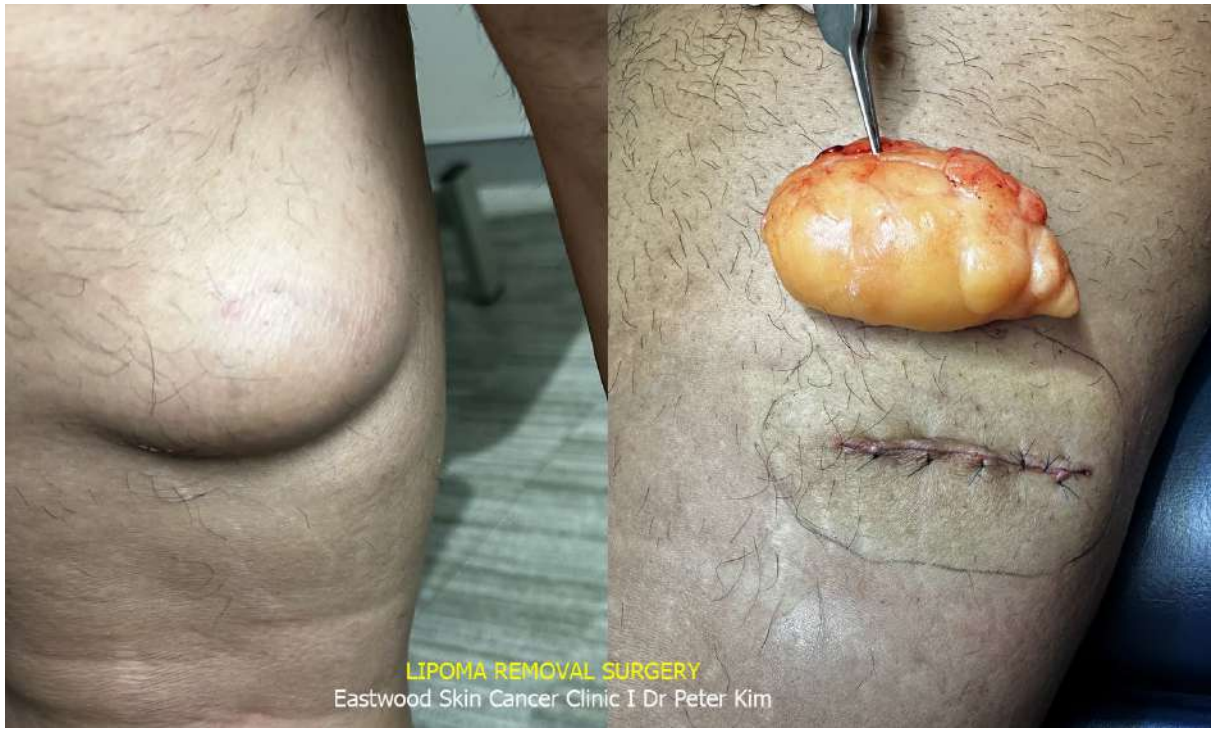
Jaundice:

- If a gallstone passes out of the gallbladder into the bile duct and blocks the flow of bile.
- Symptoms of jaundice include yellowing of the skin and whites of the eyes.

GB dysfunction – signs

Lipoma:

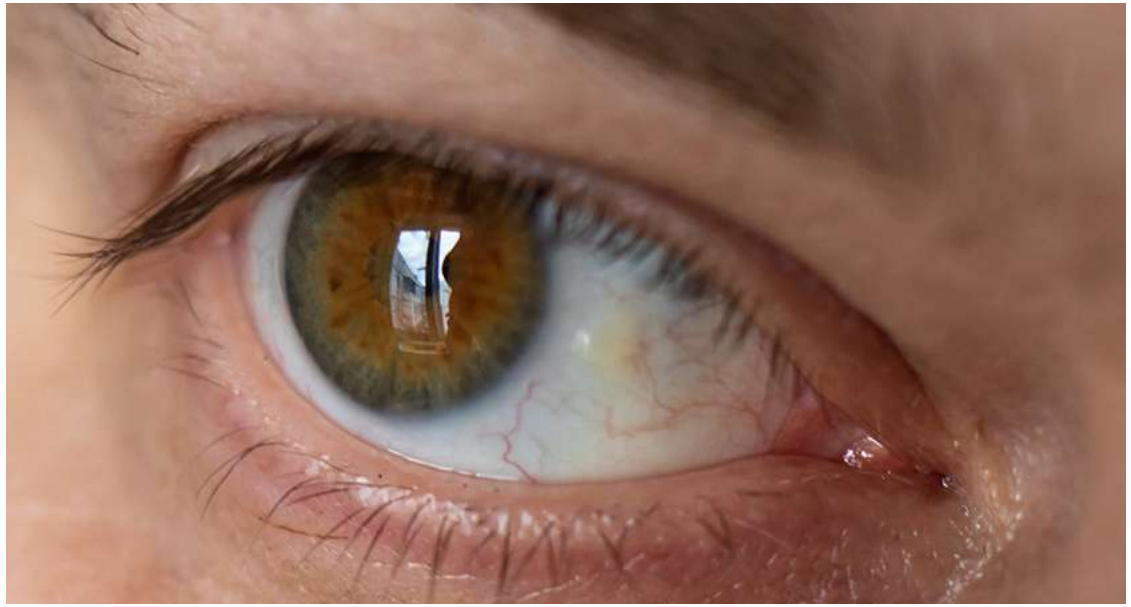
- These can be a result of trauma or genetic abnormalities but may also be related to obesity, alcohol abuse, **liver disease**, as well as glucose intolerance[32];
- The prevalence of hepatic lipoma is closely related to lipid metabolism disorders, such as dyslipidemia and nonalcoholic fatty liver disease (NAFLD).[33]



GB dysfunction – signs

Pinguecula:[34]

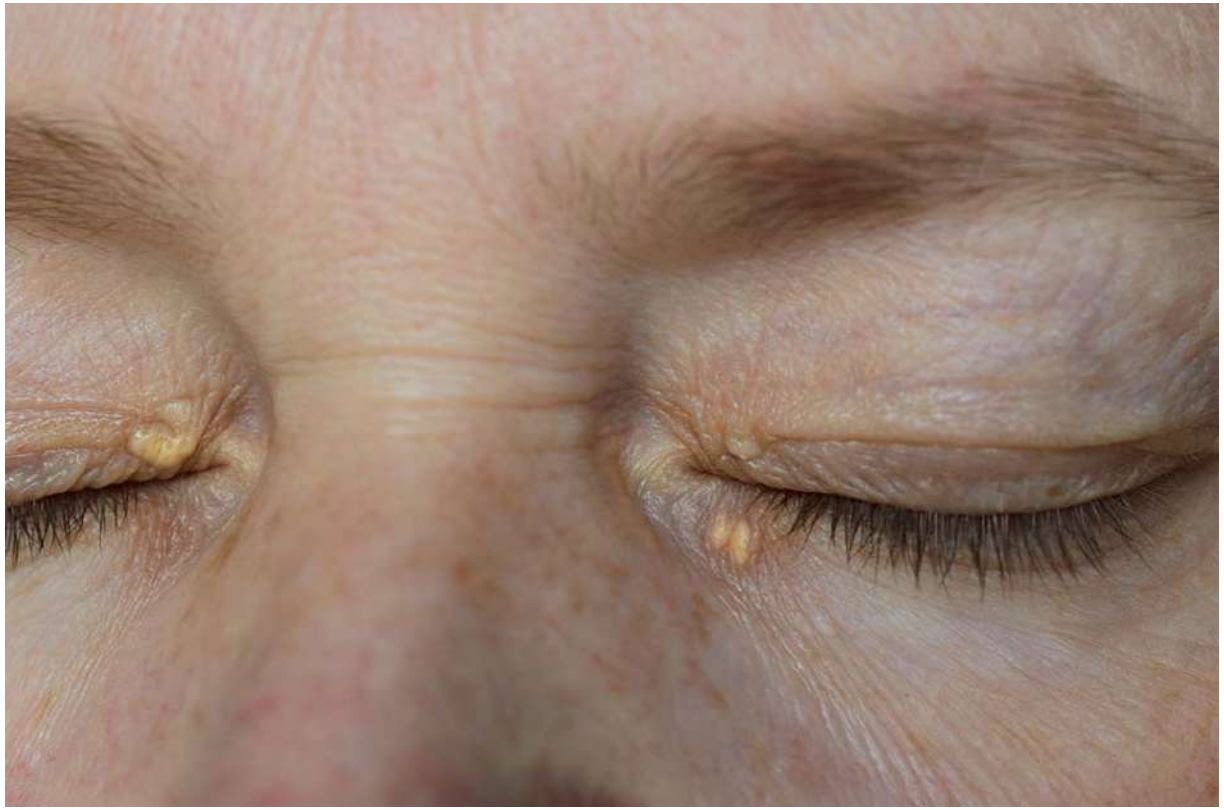
- A yellowish to brown (sometimes white) protruding lesion in the conjunctiva that is easily seen on the nasal and temporal sides of the cornea;
- Development is affected by a number of intrinsic and extrinsic factors including patient's age and levels of sun, wind, and dust exposure however are associated with p53 mutation and **increased cholesterol metabolism.**



GB dysfunction – signs

Xanthelasma:

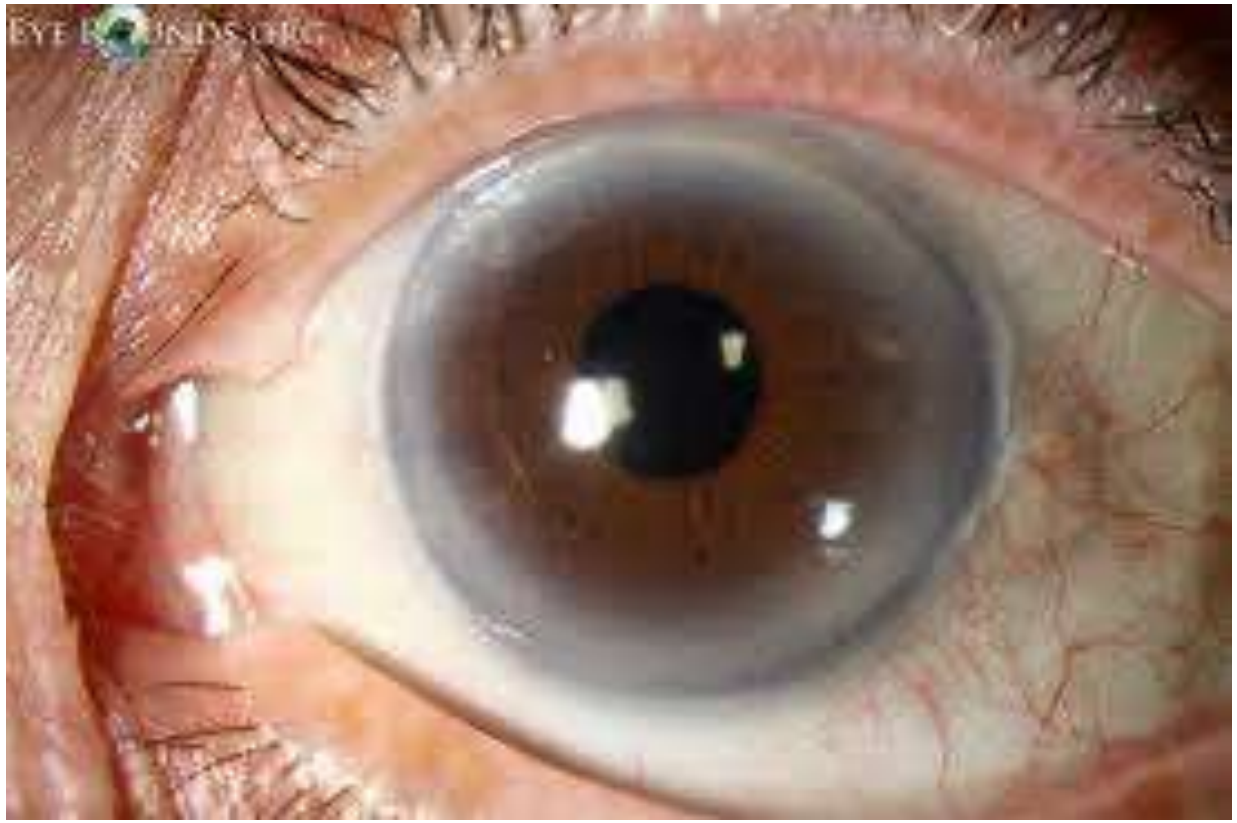
- Fatty yellowish bumps of cholesterol deposits around eyes* and often represents an underlying disorder of lipid metabolism;[35]
- Is a sign of hyperlipidemia and is closely linked to atherosclerosis;[36]
- Primary biliary cirrhosis (PBC) is associated with xanthelasma and xanthomata.[37]



GB dysfunction – signs

Arcus senilis[38,39]:

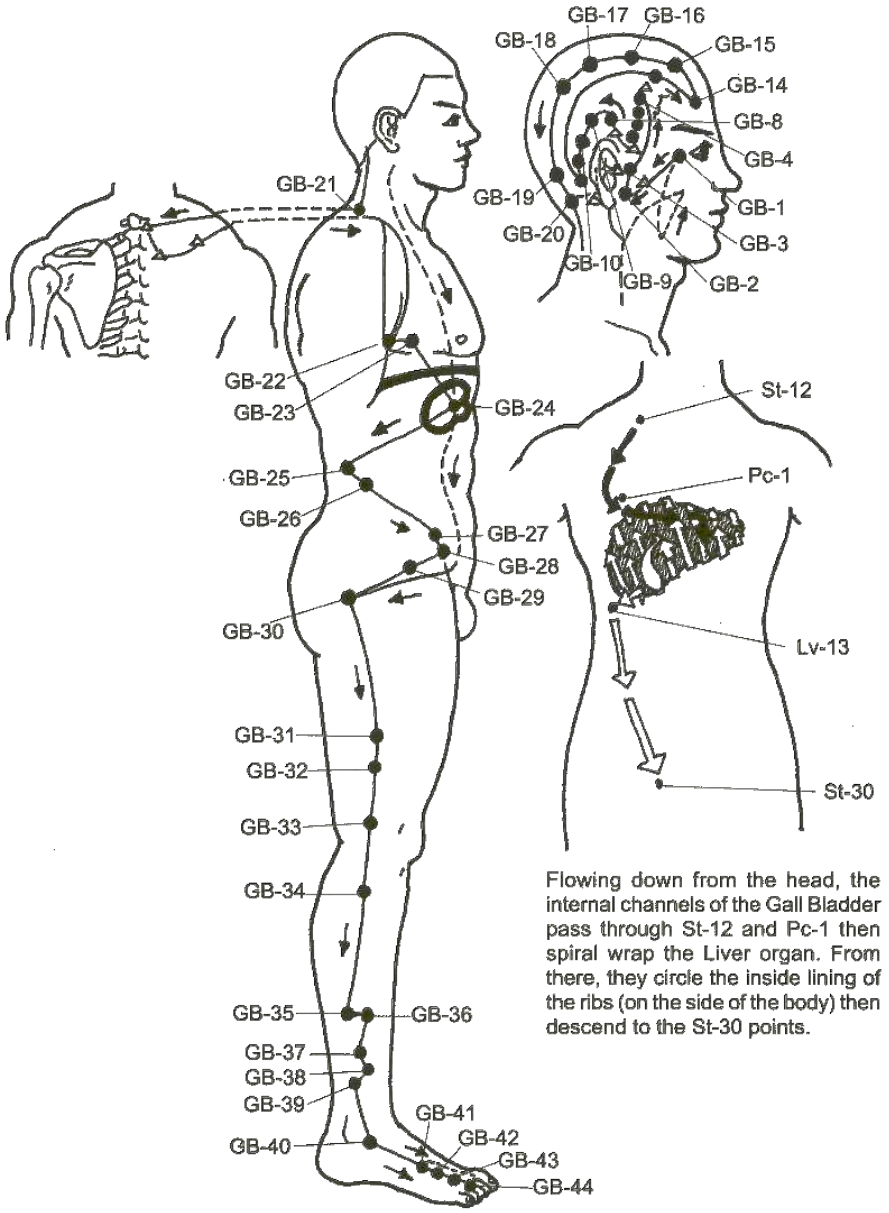
- Develops as a white-grey ring from deposits of lipids near the sclero-corneal margin;
- Commonly found in the elderly but associated with hypercholesterolemia in <40-45 years.



GB dysfunction – signs

TCM gallbladder (GB) meridian channels[40]:

- Skin eruptions, rashes, or irritation along these meridians may indicated GB issues;
- Headaches on any of the GB points may indicate liver/GB origin.



The Internal and External Qi Flow of the Gall Bladder (GB) Channels

GB dysfunction – signs

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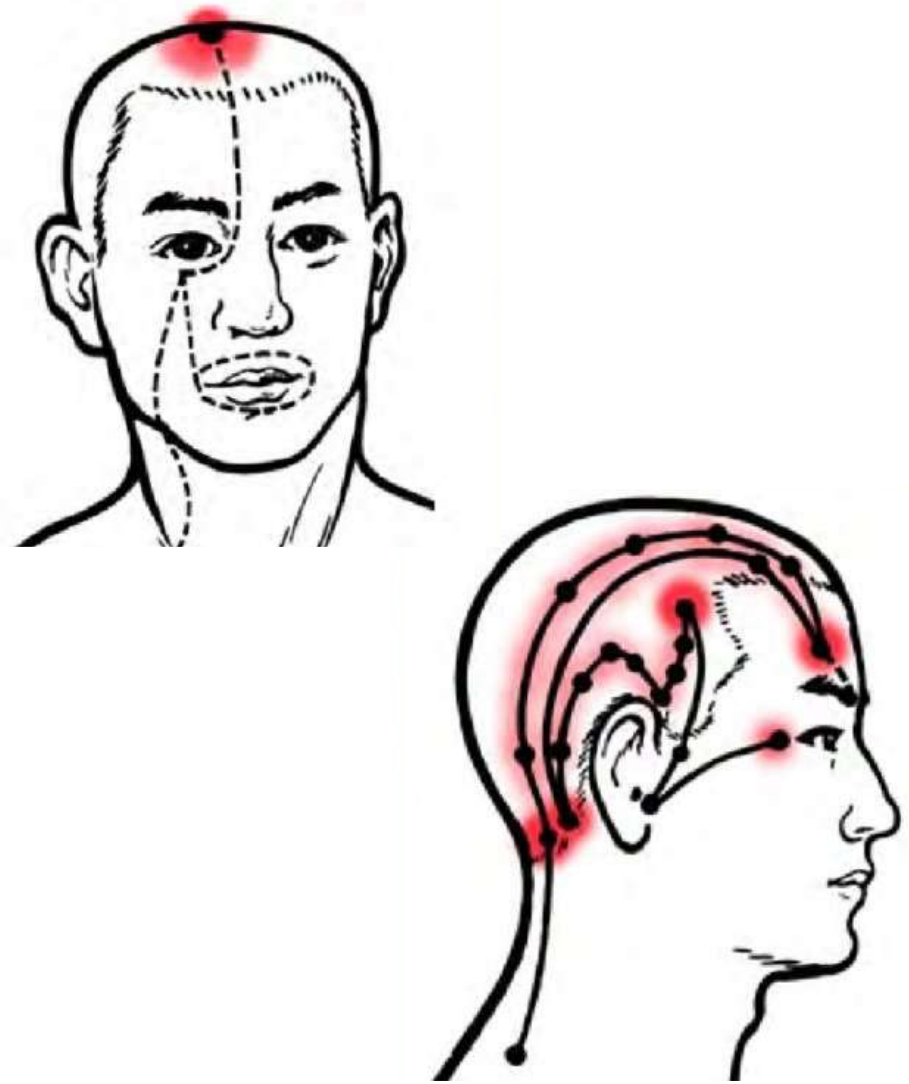


GB dysfunction – blood markers

Clinical Features of Gallstone-Related Diseases [41]

Biliary Colic	H&P: Severe, episodic, epigastric or RUQ pain; may be nocturnal, occasionally postprandial. +/- RUQ tenderness. Labs: No leukocytosis; normal total bilirubin and amylase/lipase. Imaging: RUQ ultrasound indicating cholelithiasis *without* findings of cholecystitis (Table 3).
Acute Cholecystitis	H&P: +/- fever; symptoms persist or worsening; positive for RUQ tenderness. Labs: Leukocytosis is common. Total bilirubin is usually normal to mildly elevated (<2.0 mg/dL), unless there is concomitant choledocholithiasis. Amylase and lipase are usually normal unless there is concomitant pancreatitis. Imaging: • RUQ ultrasound, see Table 3. The diagnosis of cholecystitis is NOT made based on ultrasound findings alone. Diagnosis is determined based on the clinical findings above, in combination with consistent ultrasound findings. • HIDA (only indicated if RUQ ultrasound is inconclusive, or contradicts the clinical impression) demonstrates lack of gallbladder filling.

GB dysfunction – blood markers

Clinical Features of Gallstone-Related Diseases[41]

Choledocholithiasis	H&P: Biliary pain, jaundice, no fever. Labs: Elevated bilirubin (total bilirubin often >2.0 mg/dL). Amylase/lipase are usually normal, unless there is concomitant pancreatitis. Imaging: RUQ ultrasound shows CBD dilation (>7 mm).**
Cholangitis	H&P: Jaundice, often febrile, RUQ tenderness. Labs: Elevated bilirubin (total bilirubin >2.0 mg/dL), leukocytosis. Amylase/lipase are usually normal to mildly elevated, unless there is concomitant pancreatitis. Imaging: RUQ ultrasound: CBD dilation (>7 mm).**
Gallstone Pancreatitis	H&P: +/- jaundice, +/- fever, epigastric tenderness. Labs: Normal or elevated bilirubin, elevated amylase and/or lipase to typically 3× upper limit of normal. Elevated ALT >150 suggests a biliary cause of pancreatitis, based on meta-analysis[1] Imaging: RUQ ultrasound: Cholelithiasis and biliary dilation variably present. Note: RUQ ultrasound is often limited for the evaluation of the pancreatic parenchyma. Absence of other common causes of pancreatitis: Ethanol abuse, hyperglycemia, hypertriglyceridemia, hypercalcemia, or medications known to cause pancreatitis.

GB dysfunction – blood markers

Cholesterol[42]:

- Thickened bile is the hallmark of biliary stasis and may occur if total cholesterol is increased >5.69 mmol/L – it may be the only finding on the them screen so watch for other signs/symptoms.
- If total cholesterol is increased >5.69 mmol/L, LDL is >3.1 mmol/L, triglyceride levels are increased >1.24 mmol/L, and HLD levels are decreased < 1.42 mmol/L then early development of fatty liver is possible.
- Liver congestion might also be indicated is ALT is below 10 as well.

GB dysfunction – blood markers

Bilirubin[42]:

- Increased total bilirubin levels are associated with a dysfunction or blockage of the liver, gallbladder, or biliary tree, or red blood cell hemolysis.
- Total bilirubin is composed of two forms of bilirubin:
  - Indirect (unconjugated) bilirubin, which circulates in the blood on its way to the liver bound to albumin – elevated levels are usually associated with increased RBC destruction; and
  - Direct (conjugated) bilirubin, which is the form of bilirubin made water-soluble before it is excreted in the bile – an increase associated with dysfunction in liver/gallbladder/biliary tree.
  - Fasting can cause false elevation.

GB dysfunction – blood markers

- Elevated SGOT/AST[42]: optimal 10-30 U/L, >30 is an issue associated with liver dysfunction (p130), >100 is alarming – indicates dysfunction outside liver and biliary tree.
- Elevated ALP[42,43]: ALP is an important indicator of cholestasis and hepatobiliary diseases in humans. Serum ALP levels can be elevated by cholestatic or infiltrative diseases of the liver and by diseases causing obstruction to the biliary system.

GB dysfunction – blood markers

Elevated gamma glutamic transferase (GGTP)[42]:

- Present in highest amounts in liver cells, to a lesser extent kidney, prose and pancreas – also found in biliary tract epithelial cells;
- Liberated following cell damage and/or biliary obstruction:
  - If GGTP is increased above ALT and AST issue is likely outside of liver but inside biliary tree (gall bladder, common bile duct and pancreas);
  - Increased GGTP (often 5 times higher than normal) PLUS increased ALP indicates biliary tree obstruction.

GB dysfunction – blood markers

Elevated gamma glutamic transferase (GGTP)[42]:

- If GGTP >30 and ALP >100 with normal or increased AST (>30) and ALT (>30) biliary obstruction is probable;
- Biliary obstruction with possible caclui becomes more likely with increased total bilirubin (>20.5 umol/dL) and direct bilirubin (>3.4 umol/dL).

GB dysfunction – stool markers

Steatocrit:

- Elevated steatocrit indicates an increased amount of fat in the faeces, suggesting that the body is not properly absorbing fats from the diet resulting in steatorrhea;
- Stools may be light-coloured, greasy, smelly, frothy/foamy, floating, hard to flush;
- This generally results from pancreatic exocrine insufficiency but can also occur as a symptom of various underlying gastrointestinal disorders, such celiac disease, Crohn's disease, or **issues affecting the liver, gallbladder or bile ducts (i.e. primary biliary cirrhosis)**, or medications that inhibit fat absorption such as orlistat.

GB dysfunction – stool markers

Elastase-1[44]:

- Pancreatic elastase 1 (PE1) is a proteolytic enzyme secreted exclusively by the human pancreas, and as such, it reflects overall pancreatic exocrine functionLowered elasase-1;
- The pancreatic elastase 1 faecal test is used to diagnose insufficiencies of the pancreas that may be a result of cystic fibrosis, chronic pancreatitis, pancreatic cancer, inflammatory bowel disease, **gallstones**, T1D, or Shwachman-Diamond syndrome.

Normal: >200 ug elastase/gram faecal matter

Moderate pancreatic insufficiency: 100-200 ug elastase/gram faecal matter

Severe pancreatic insufficiency: <100 ug elastase/gram faecal matter

GB dysfunction – stool markers

Betaglucaronidase (b-glucaronidase):

- High fat, high protein and low fibre diets are associated with higher b-glucuronidase activity compared to vegetarian or high soluble fibre diets;
- Higher b-glucuronidase may be associated with an imbalanced intestinal microbiota profile;
- Bacterial b-glucuronidase (bBG) appears to be an etiologic factor in pigment gallstone disease as it deconjugates conjugated bilirubin to form calcium bilirubinate gallstone[45];
  - Increase in the activity of human biliary beta-glucuronidase (hBG) may be a secondary response, developed after bile duct inflammation because it was elevated only when the bile duct obstruction was associated with infection[46];
- A study on the microbiome of gallstones and bile in patients with cholelithiasis found that 30% of cultured strains from cholesterol gallstones secrete β-glucuronidase (and phospholipase A2)[47];
  - *Pseudomonas spp.* were the dominant bacteria in the gallstones of cholesterol and bile and had the highest β-glucuronidase activity.

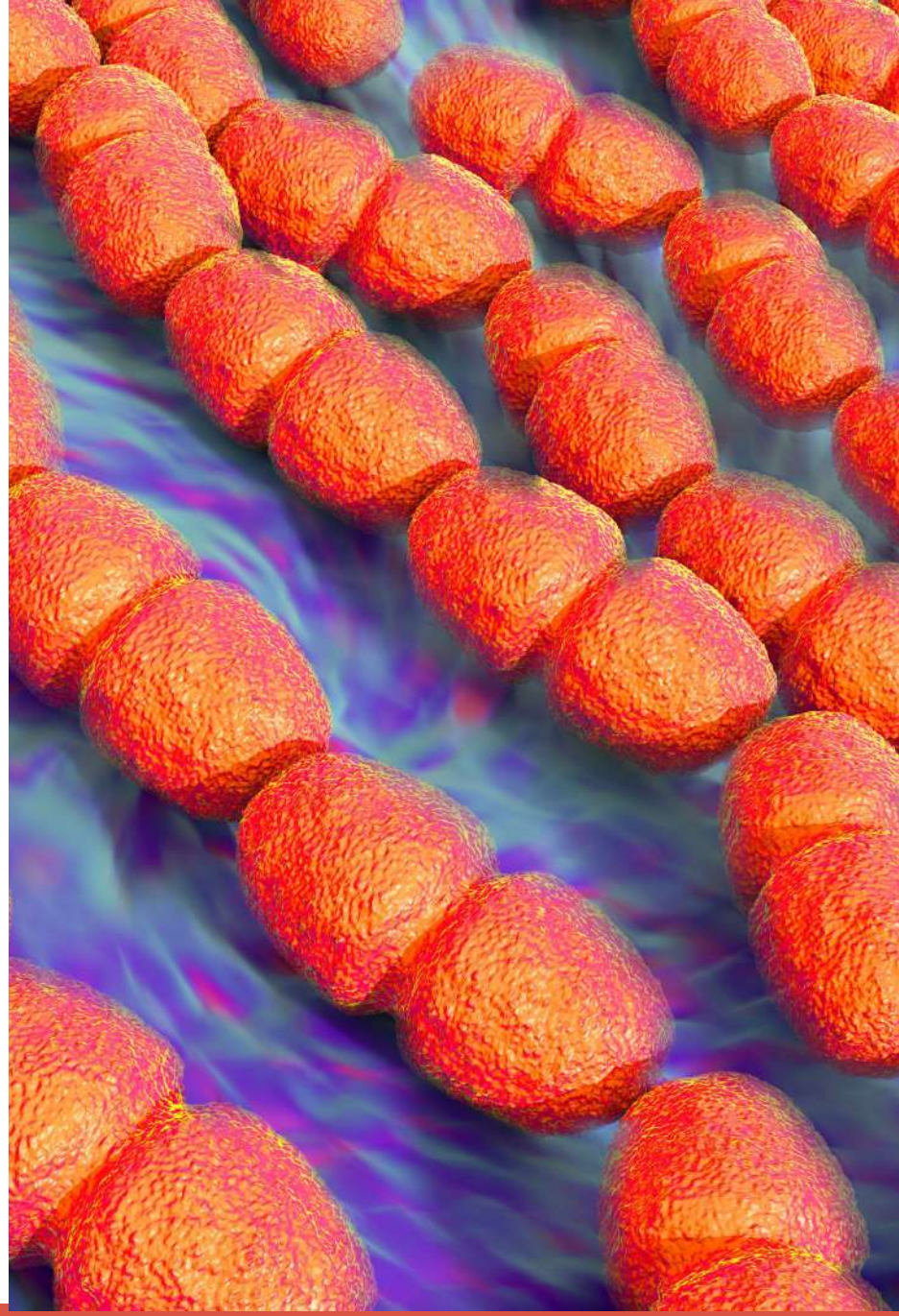
Outline

- **Causes of gallbladder dysfunction**
  - Infections
  - Mycotoxins
  - Vitamin D deficiency
  - Dietary influences
  - Hormones
  - Circadian rhythm
  - ANS

GB dysfunction – infections

Bacterial infections[48]:

- Gastrointestinal tract flora, such as *E. coli, Klebsiella* spp., *Enterococci* spp., *Bacteroides* spp;
- Also *Serratia marcescens*.



GB dysfunction – mycotoxins

Mycotoxins:

- According to animal studies, mycotoxin poisoning can lead to multifocal hepatocyte necrosis in the liver, the gallbladder mucosa becomes inflamed due to hyperplasia and necrosis of the bile duct, which further cause the gallbladder to become brittle;
  - Chronic aflatoxin exposure leads to biliary retention, biliary ductular hyperplasia, fibrosis (aflatoxin is produced by Aspergillus flavus found in WDBs)[49];
  - *Pithomyces chartarum* (also found in WDBs) causes damage to biliary tract, leads to obliterating cholangitis, and distorted fibrotic liver[50];
- CIRS-WDB patients often present with low VIP (vasoactive intestinal polypeptide)
  - VIP is a potent stimulant of fluid and bicarbonate secretion from cholangiocytes via cAMP-independent pathways, suggesting that this neuropeptide plays a major regulatory role in biliary transport and secretion[51].

GB dysfunction – deficiencies

Vitamin D deficiency:

- Vitamin D deficiency is suggested to be associated with gallbladder stasis[52]:
  - Low serum vitamin D level is associated with intrahepatic cholestasis of pregnancy[53];
  - A role for vitamin D supplementation is thought to have potential to prevent gallstones in this special population;
    - Gallstones to be associated to low vitamin D exposure in utero and to renal failure suggesting that vitamin D might have an impact on gallstone disease[54].

GB dysfunction – dietary

Dietary influences:

- Dietary fat has the strongest effect on emptying the gallbladder, which correlated with plasma CCK levels[55] – a low fat diet may result in reduced gallbladder emptying;
- A sedentary lifestyle and a diet rich in animal fats and refined sugars and poor in vegetable fats and fibres are significant risk factors for gallstone formation[56];
- Rapid weight loss i.e. HCG diet, VLCD:
  - risk of symptomatic gallstones requiring hospitalisation or cholecystectomy, was 3-fold greater with VLCD than LCD[57];
  - during active weight loss suggest that newly formed gallstones occur within 4 weeks and with incidence rates 15 to 25-fold higher than in the general obese population[58].

GB dysfunction – dietary

Gluten consumption in those with celiac gene and/or celiac disease[59,60,61]:

- Prevalence of biliary stones in celiac patients may be higher compared to the normal population;
- Enteropathy in the proximal part of the small intestine reduces the release of cholecystokinin (CCK) from the duodenal enteroendocrine cells (is synthesised and secreted by I-cells from the proximal small intestine mucosal epithelium in response to a meal with fat and protein):
  - It also appears that an abnormality in the gall bladder response to endogenous cholecystokinetic hormones (cholecystokinin and motilin) might also be a factor [brown 1987);
- Perturbation of bile composition occurs; hepatic production of bile cholesterol, phospholipids, and bile salts, as well as bile flow, increased almost double in patients with CD compared with healthy individuals' bile cholesterol levels, and their bile is supersaturated accordingly;
- Gallbladder dysmotility develops, which mainly expresses with an impaired emptying during the digestive phase:
  - Reversible with a gluten-free diet in most cases.

GB dysfunction – hormones

- Oestrogen increases the amount of cholesterol relative to bile salts and lecithin in bile, increasing the saturation of bile with cholesterol, which leads to cholesterol crystal formation[62]:
  - Excess of oestrogens can lead to decreased bile flow, toxic bile acid (BA) accumulation, subsequently causing intrahepatic cholestasis;
  - Oestrogen-induced cholestasis (EIC) may have increased incidence during pregnancy, and within women taking oral contraception and postmenopausal hormone replacement therapy, and result in liver injury, preterm birth, meconium-stained amniotic fluid, and intrauterine fetal death in pregnant women;
  - Impaired cell membrane fluidity, inflammatory responses and change of hepatocyte tight junctions are also involved in the pathogenesis of EIC;
- Oestrogens and oral contraceptives are both associated with several liver related complications including intrahepatic cholestasis, sinusoidal dilatation, peliosis hepatis, hepatic adenomas, hepatocellular carcinoma, hepatic venous thrombosis and an increased risk of gallstones.[63]

GB dysfunction – circadian

Melatonin:

- Plays a role in the modulation of biliary functions and liver damage in response to a number of insults - it inhibits cholangiocyte hyperplasia (it also appears to have hepatoprotective properties, may reduce fibrosis)[64];
- Improves cholestatic liver disease via the gut-liver axis;
- Melatonin Prevents Pigment Gallstone Formation Induced by Bile Duct Ligation[65];
- Melatonin helps in the recovery of gallbladder neuromuscular function during acute cholecystitis[66];
- Due to its antioxidant activity, along with its effect on the aging gall bladder myocytes, inhibits gallstone formation[67];

A clinical trial has validated the amelioration effects of bright-light therapy (BLT) on hepatogenic pruritus, potentially via restoring circadian rhythms through retino-thalamic pathway.[68,69]

GB dysfunction – circadian

Circadian rhythm:

- Plasma bile acids and key genes in bile acid biosynthesis are driven, in part, by hepatic molecular clock[70];
  - Bile acid concentration (and corresponding genes) exhibit significant circadian rhythms and circadian oscillations are flattened and altered following by cholecystectomy[71];
  - Eating outside of ideal feeding window associated with high biliary cholesterol content (and subsequent gallstone formation)[72];
- Sun exposure and UVR load were associated with a decreased risk of primary biliary cholangitis.[73]

Outline

- **Gallbladder support**
  - Manual therapies
  - Bitters and other herbs
  - Nutrients
  - Other interventions

Manual therapies

Coffee enema:

- Administration of coffee enemas stimulate bile excretion[74];
- Doctors at the University of Minnesota showed that coffee enemas stimulate an enzyme system in the liver called glutathione S-transferase by 600-700% above normal activity levels.

Manual therapies

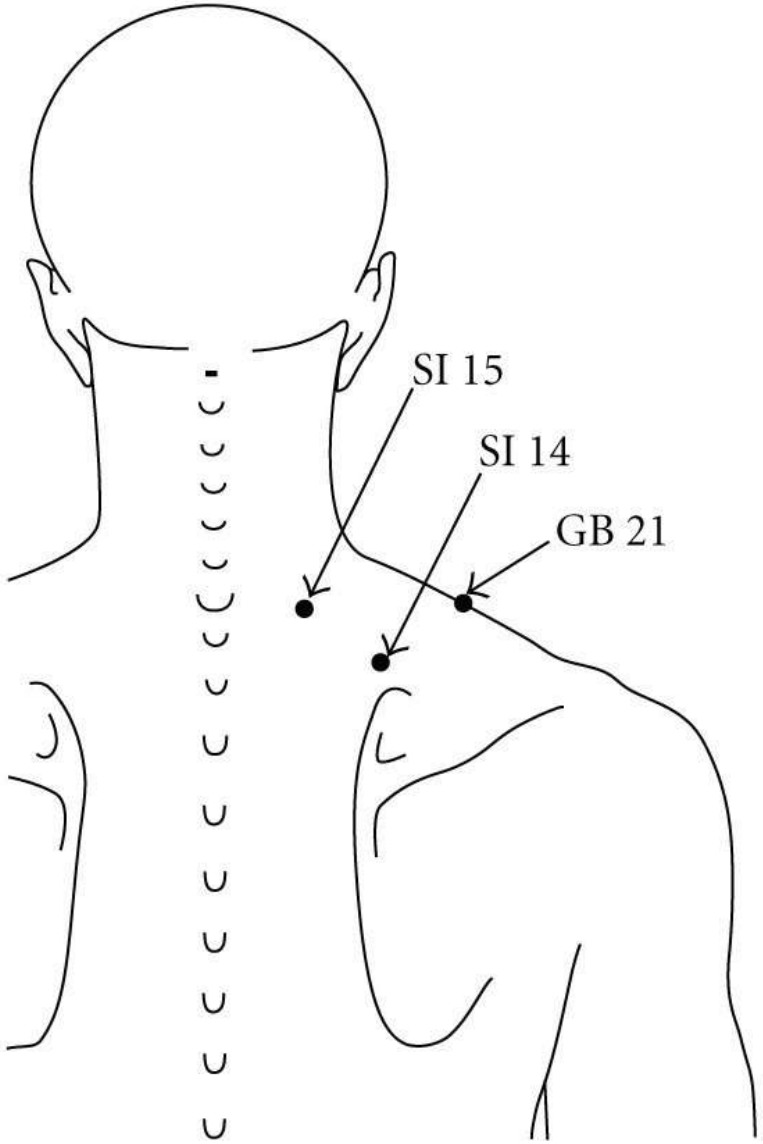
Castor oil packs:

- Preliminary evidence that castor oil packs may have a positive effect on normalising liver enzymes and cholesterol levels. and improving symptoms of constipation.[75,76]

Manual therapies

Acupuncture:

- Stimulation of Jianjing (GB 21) can effectively relieve shoulder-back pain and stomachache, and regulate the volume of the deflated and expanded gallbladder in cholecystitis patients.[77]



Bitters foods and herbs

- Lemon juice – accelerates hepatobiliary excretion[78];
- ACV – significantly decreases serum total cholesterol (along with fasting plasma glucose and HbA1C concentrations)[79];
- Gentian – has been used in Chinese herbalism for over 2000 years as an excellent tonic for digestive system, work on stomach, liver and gall bladder[80,81];
- Fruit and vegetables:
  - An inverse association between FV consumption and risk cholecystectomy in women (aged 48-60)[82,83];
  - High intake of broccoli and cabbage was associated with a decreased risk of gallbladder cancer.[84]

Bitters and other herbs

Globe Artichoke

- The chlorogenic acids (cynarin and caffeoylquinic acid) support the healthy functioning of both phase one and two detoxification pathways in the liver;
- Considered a most potent choleretic and cholagogue herbs available to practitioners. Effects on bile secretion occurs an hour after the administration of a single dose[85]:
  - the excretion of cholesterol and other solids, as well as increases in faecal bile salts have been shown in both pre- clinical and clinical studies – indicated for choleresis[86];
- Increases glutathione peroxidase activity – hepatoprotective and hepatorestorative:
  - A trophorestorative herb that can protect the integrity of bile canalicular membrane from chemically induced distortions.

Bitters and other herbs

St. Mary's Thistle or Milk Thistle:

- Traditionally used in Western Herbal Medicine as a hepatoprotective:
  - Properties can be attributed to the flavonolignan compound silymarin. Research has suggested that standardisation to between 70-80% of this component is best to achieve therapeutic effects;
  - The term "silymarin" actually refers to 7 flavonolignan compounds: silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, and silydianin. Some extracts may also contain the flavonoid taxifolin.
- Induces both phase one and two detoxification pathways – recoupling these phases.

Bitters and other herbs

St. Mary's Thistle or Milk Thistle

- The following functions that contribute to its activity in supporting liver health:[85-89]
  - Prevents uptake of toxins and pathogens by stabilisation of cell membranes. Silybinin and silymarin are incorporated into the outer cell membrane thereby altering its structure. In doing so, these compounds stabilise the membranes and regulate their permeability and subsequent intracellular contents. They prevent the penetration of toxins into the hepatocytes, providing a "toxin blockade";
  - Aids hepatic repair and regeneration by enhancing ribosomal RNA synthesis (via stimulating nucleolar polymerase A) and cellular proliferation;
  - Improves intracellular glutathione concentration;
  - Increases the proliferation of Kupffer cells.

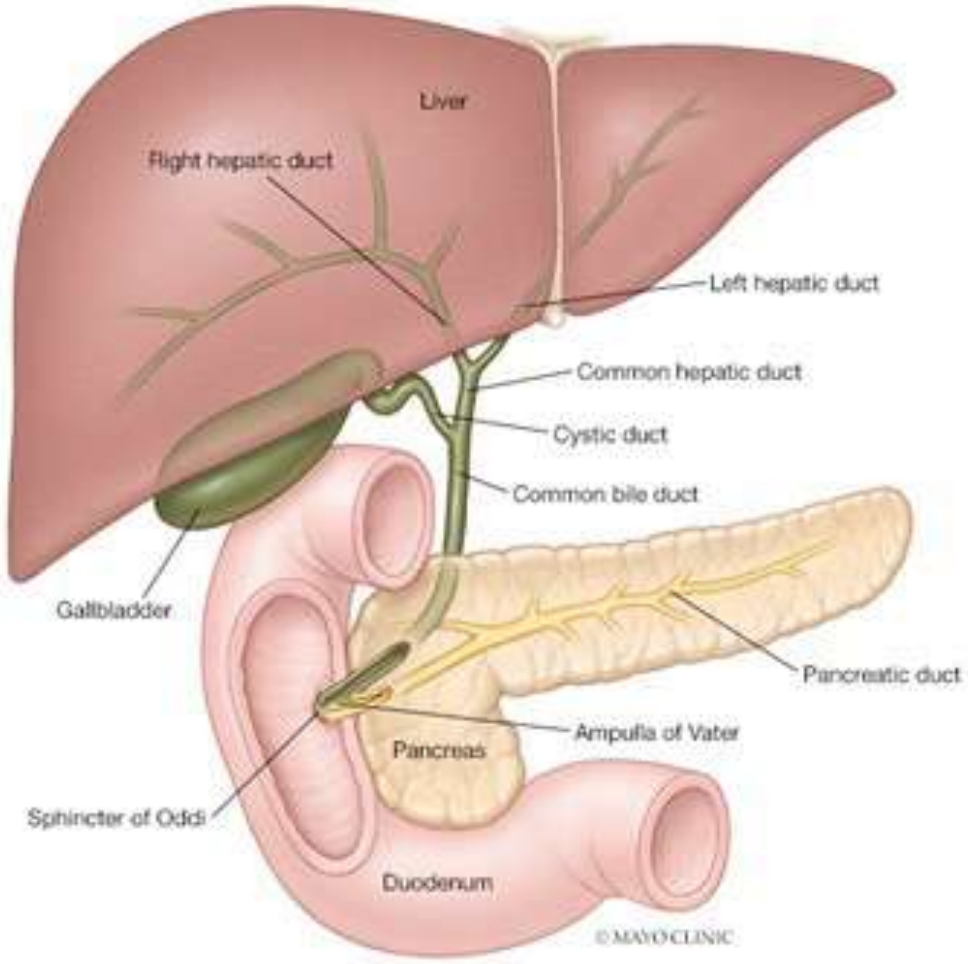
Bitters and other herbs

- Schisandra: a warming TCM herb that supports and protects many aspects of liver function. Lignan components are considered a primary therapeutic compound and have been shown to support hepatic functions such as glycogen and protein synthesis, and enzymatic activity during both phase one and two detox pathways. They also support liver health by assisting the regeneration of hepatocytes and inhibiting lipid peroxidation in liver tissues.[87,90]
- Rosemary: a potent antioxidant that induces several enzymes involved in phase two pathways, helping to keep balance between the two detox systems.[87]
- Beetroot: contains betaine and betanin which impart supportive effects on both liver health and function (reducing fatty infiltration of hepatocytes, improving glutathione status, supporting phase one and two detox pathways, thinning the bile and supporting gall bladder function).[91-94]

Nutrients

Lipotropic nutrients are useful to promote the flow of bile from the liver:

- Choline
- Taurine
- Methionine
- B6, B9, B12



Nutrients

- Magnesium sulphate (MgSO4):
  - oral administration of MgSO4 has a significant effect on Gallbladder volume with maximum effect at 1 and 2 hours after medication.[95]
- Calcium saccharate (calcium d-glucarate):
  - Enhances liver function through phase 2 glucuronidation pathways - downregulates hepatocyte apoptosis and reduces ROS production; [96]
  - Inhibits b-glucoronidase.[97]

Other interventions

Fibre:

- Decreases stool transit time;
- Acts to sequester conjugated xenobiotics and endobiotics located in the bile;
- Reduces the level of bacterial deconjugating enzymes in the stool;
  - Slippery elm: soluble fibre, contains mucilage, forms a gel-like layer, demulcent effect;
  - Inulin: prebiotic fibre, fermented by colonic bacteria for fuel, enhances bioavailability of minerals.

Other interventions

Essential oils:

- Peppermint oil and caraway oil show a relaxing effect on the gall-bladder.[98]
- In the 70's an approach to dissolving gallstones using natural medicines called terpenes was reported in several journals.[99] Such an approach has not gained wide acceptance, however, probably because the formula is not readily available. The predominant terpene in this formula is menthol, so essential oil of peppermint in capsule form may have a comparable effect. This use of peppermint is theoretical; no studies using peppermint oil to dissolve gallstones have been performed.

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