put together by Alex Yartsev: Sorry if i used your images or data and forgot to reference you. Tell me who you are.
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Cholestasis and Biliary Colic

History of Presenting Illness: FAT, FEMALE, FERTILE, 40 y.o.

CHOLESTASIS → **Lasting Longer than 6 hours: PROBABLY CHOLECYSTITIS**

- **YELLOW EYES**
- **DARK URINE**
- **YELLOW SKIN**
- **ITCHY ALL OVER**
- **PALE STOOLS**
- **FAT MALABSORPTION**
- **High Cholesterol Xanthomae**

RULES OF THUMB:
- The eyes are the FIRST thing to go yellow.
- **Bilirubin over 30 = yellow eyes**
- **Bilirubin over 50 = yellow skin**
- The severity of itching does not correlate well with the bilirubin or bile salt levels.
- **The elderly will itch more.**

- **Nausea, Anorexia, Vomiting**

Cholangitis → **FEVER, perhaps even SEPSIS**

PAIN: ← Relieved by nitrates! Weird…

Mainly with the distension of the common bile duct;

- **Right Upper Quadrant**
- **Radiating to the back**
- **Severe + Constant**
- **Dull, "boring" pain**
- **Pleuritic-sounding**
- **Worst with fatty foods**
- **Onset in 1-2 hrs after meals**
- **Lasting 1 to 6 hours per episode:→**
- **Not relieved by any position**
- **not responding to antacids**

Pain should be poorly localised to T8 – T9 dermatomes. Localised Murphy's point pain = inflammation has reached the peritoneum, eg. cholecystitis.

If it lasts any longer, it may be an acute **cholecystitis.** Uncomplicated biliary colic leaves NO lasting symptoms after an acute attack.

(ED staff are prone to throwing a "pink lady" at any epigastric discomfort; a "pink lady" being 60ml milk of magnesia + 30ml of xylocaine viscous)

= so if that doesn't fix the epigastric pain, ITS NOT IN THE OESOPHAGUS OR STOMACH

The guy with cholestasis is otherwise asymptomatic and comes into hospital because his family made him. "Youre turning yellow, dad!"

The guy with biliary colic comes in to hospital because it hurts, though he can put up with it most days. He may not be yellow or particularly ill.

The guy with cholecystitis comes in to hospital because of constant unbearable localised RUQ pain, worse on inspiration. He's slightly febrile.

The guy with cholangitis is brought in by ambulance, is pale, febrile, and says he feels like he's about to die.

EXAMINATION

Try to find something to support a gallbladder source for this pain:

MURPHY'S SIGN: patient inspires while you have your hand deep in their RUQ. This causes the diseased gall bladder to ride into your fingers as the liver slips downwards. If there is any gall bladder inflammation, it will cause a sudden stop to the inspiration, due to extreme pain.

CORVOISIER'S LAW states that IF YOU CAN FEEL THEIR GALL BLADDER AND THERE IS JAUNDICE, then the patient is NOT JAUNDICED BECAUSE OF STONES. Basically this means they have a cancer in the biliary tree. Why? A fibrotic gall bladder, chronically ridden with stones, is not able to distend to a large enough size for you to feel it. If you can feel it, its probably a soft non-fibrosed gall bladder, dilated because a tumour is obstructing the outflow.

STIGMA OF CHRONIC LIVER DISEASE will probably be absent but if there is anything to suggest chronicity, ask yourself: is it due to the chronic bile outflow obstruction, or is there some other pathology which is causing it?

DIFFERENTIALS: why could they be yellow?…

- **Biliary colic (small stone)**
- **Choledocholithiasis (big stone)**
- **Cholecystitis**
- **Cholangitis**
  - ..and **Pancreatitis (?)**
  - **…and SEPSIS??**
- **Cancer of the Bile Duct, Gall Bladder or Head of Pancreas**
- **Recent transfusion** can make your eyes go yellow (blood in those bags is very old)
- **Chronic or acute liver disease** can cause this sort of presentation
- **Surgery** (prolonged bed rest, TPN, → gall bladder hypomotility, thus bile stasis, etc)
- **Are drugs responsible** (eg. asymptomatic anaesthesisa jaundice, flucloxicillin hepatitis)
- **"Gut claudication"** can cause transient pain right after meals (vascular disease in the gut results in exercise-induced lactic acidosis and thus PAIN)

INVESTIGATIONS

The USUALS:

These will be NORMAL in any uncomplicated biliary colic.

FBC – maybe leukocytosis, largely neutrophilic. Maybe nothing.

EUC – maybe hypokalemic, if patient has been vomiting. Probably nothing.

LFT – Alk Phos and GGT – will be elevated: it's the classical "obstructive pattern"
- Bilirubin will also be up if they are jaundiced

URINE DIPSTICK – will probably do nothing for you except exclude hematuria as the cause of the dark urine.

URINALYSIS bilirubin and urobilinogen will be present if the jaundice is due to poor bile flow (i.e conjugated bilirubin is in the blood stream)

The SPECIALS:

AMYLASE + LIPASE may be elevated if the pancreatic duct is also blocked (i.e the stone is at Ampulla of Vater level)
Also important because a head of pancreas cancer is one of the differentials for obstructive jaundice.

BLOOD CULTURES
Especially if the patient is febrile and acutely unwell; must rule out sepsis of an ascending biliary origin

Prothrombin Time (PT)
May be elevated, as you start losing your synthetic liver functions when there is a back-log of bile, and the fat-soluble vitamins aren't getting absorbed.

Fat-Soluble Vitamin Levels: if your bile is not making it out of the duct, you are malabsorbing fat and everything that comes along with fat. Can test for vitamins A, D, E, and K if the problem is long-standing

You need K to clot properly

IMAGING to CONFIRM your DIAGNOSIS

UPPER ABDO ULTRASOUND:

Ultrasonography provides greater than 95% sensitivity and specificity for the diagnosis of gallstones more than 2 mm in diameter. Ultrasonography is 90-95% sensitive for cholecystitis and is 78-80% specific. Studies indicate that emergency physicians require minimal training in order to use right upper quadrant ultrasonography in their practice.

Both have about the same sensitivity + specificity.

Endoscopic Retrograde Cholangio-Pancreatography (ERCP)
allows visualization of the anatomy and may be therapeutic by removing stones from the common bile duct. In a major teaching hospital, with two on-call gastroenterologists, this is the diagnostic and management measure of choice after a small stone has been visualised with ultrasound.

Magnetic Resonance Cholangio-Pancreatography
Non-invasive, but therefore also not a management option.

Findings suggestive of cholecystitis include:
- **wall thickening (>4 mm),**
- **pericholecystic fluid,**
- **subserosal edema (in the absence of ascites),**
- **intramural gas (gas gangrene of the gall bladder),**
- **sloughed mucosa.**

What if the imaging shows no stones?
About 5 to 10% of acute cholecystitis is acaclulous
The Gall Bladder is distended, theres fluid around and in its walls, the patient is febrile BUT NO STONE TO BE SEEN.
Whats happened? BILE STASIS due to some critical illness

- Prolonged TPN feeding
- Dehydration
- Heart failure

All these lead to hypomotility, increasing bile viscosity, microscopic stone formation and infiltration with gut flora, superimposed on a possibly ischaemic gall-bladder which makes an excellent host for bugs.
MORTALITY OF ACALCULOUS CHOLECYSTITIS IS FAR GREATER THAN OF THE CALCULOUS TYPE:
Already the patient is very ill, PLUS this is the sort of cholecystitis which can erode the wall quickly

Abdo X-ray will only pick up ~10% of the stones. Sometimes you may see
- **A calcified "porcelain" Gall Bladder**
- **An obvious huge radio-opaque stone**
- **Free air in the biliary tree and gall bladder wall: the "emphysematous" gall bladder, like gas gangrene: E.Coli and Clostridium. Commonly seen in acalculous cholecystitis.**
- **SINISTER SIGN: Free air under the diaphragm; means its perforated!!**
  Means that BILIOUS PERITONITIS IS ON ITS WAY!! >Unspeakable Nightmare<

Speaking of LFTs…

SOLITARY ELEVATION?
THINK EXTRAHEPATIC CAUSE !!… unless its AP

LIVER DEATH ENZYMES (transaminases)
Indicate liver parenchyma is involved.
LOOK AT WHICH IS THE HIGHEST!

AST = everywhere Aspartate aminotransferase
= when AST is the highest, its **ALCOHOLIC LIVER DISEASE**

Solitary AST: mild elevation normal,
→ **exercise, or acute skeletal or cardiac muscle injury**

ALT = LIVER ONLY Alanine aminotransferase
= when ALT is the highest, its **VIRAL HEPATITIS also glandular fever,**

MASSIVE ELEVATION OF ALT+AST = 15 times the norm =
ACUTE hepatitis, ischaemic hepatitis, Paracetamol overdose, drug reaction, hepatic vein thrombosis

CHOLESTASIS ENZYMES
Indicate that the bile duct cells are involved.
Will elevate to ~10x the normal in cholestasis.

AP = everywhere (bone, kidney, intestines)
Alkaline **P**hosphatase
THE MARKER OF POOR BILE FLOW
You may justifiably ask for AP fractionation (and this will tell you if it came from bone or liver).

Solitary AP = Bone disease, Pregnancy Chronic renal failure, Malignancies Congestive heart failure… **TAKES DAYS TO RISE**
Fungal infection of the liver, Amyloidosis, Lymphoma Metastasis, Hepatocellular carcinoma, Tuberculosis…

GGT = LIVER ONLY;
Gamma **G**lutamyl **T**ranspeptidase
Gets elevated in practically all types of liver disease

Solitary GGT is too sensitive: may be elevated in absence of liver disease. Usually indicates enzyme induction, eg.
→ **recent alcohol ingestion**

IN CIRRHOSIS:
The enzymes may NOT be elevated at all; Not enough liver cells to produce them!

LDH = in every tissue
Increased levels are found in myocardial infarction, liver disease, haemolysis, ineffective erythropoiesis, some malignancies (*esp* non-Hodgkin's lymphoma), muscle disease etc…

BILIRUBIN: is there too much of it or is it not being disposed of?
i.e → HAEMOLYSIS or LIVER DISEASE / CHOLESTASIS
→ bilirubin, GGT and AP = cholestasis
Levels greater than 3 mg/dL are usually noticeable as jaundice.
Because only conjugated bilirubin appears in urine,
the finding of bilirubinuria also implies liver disease.

Bilirubin SHOULD NOT be up in INFILTRATIVE liver disease

THUS:
→ **ELEVATED CONJUGATED = look for liver disorder**
in absence of liver disease, its got to be a weird congenital defect eg. Dubin-Johnson syndrome
→ **ELEVATED UNCONJUGATED = look at the blood smear**
Normal everything? Its probably ANOTHER weird syndrome, probably Gilbert's Syndrome which causes failure of hepatic bilirubin uptake

ALBUMIN:
A true indicator of liver function: a gauge of its failure, a herald of impending complications.
The half-life of serum albumin normally is 19–21 days,
Thus → **shows up CHRONIC PROBLEMS**
Albumin levels may be diminished due to poor nutritional status, severe illness with protein catabolism, nephrosis, and malabsorption

Prothrombin Time: vitamin K factors (2, 7, 9, 10)
May be diminished due to malabsorption
Half life of factors is 1-2 days ,
Thus → show up ACUTE PROBLEMS

WEIRDO TESTS
Ceruloplasmin for Wilson's disease (presents as psychiatric problem)
Blood Ammonia tests for hepatic encephalopathy (but EEG is diagnostic!)
Alpha-Fetoprotein is a sensitive marker for hepatocellular carcinoma
Alpha-1 Antytripsin deficiency of which causes hepatitis and cirrhosis
Anti-mitochondrial Antibody: if you suspect PRIMARY BILIARY CIRRHOSIS
(only other elevated enzyme = AP)

MANAGEMENT: SYMPTOMATIC (at the emergency department)

- Place patient on Nil-by-mouth (They may be having surgery soon)
- Rehydrate intravenously (patient may have been not eating and vomiting)
- Control itching with opiates! **They will also help the RUQ pain.**
  - Swine may tell you that morphine increases sphincter of Oddi spasm, and that therefore you should avoid it in this setting. Practically speaking, often the NSAIDs these swine would give do nothing for the patient's pain, and one may justifiably ignore their feeble complaints and opt in favour of more powerful and thus humanitarian opiate analgesia. Go Mighty Opium!
- **Control nausea + vomiting with metaclopromide or ondansetron**
- **IF FEBRILE, OR YOURE CERTAIN ITS CHOLECYSTITIS OR CHOLANGITIS:**
  Give Triple Antibiotic Therapy, favoured by the GI surgeons

Ampicillin, Gentamicin, Metronidazole

MANAGEMENT: DEFINITIVE; …meaning surgical.

ACUTE BILIARY COLIC:

Analgesia is all that is required in most cases.
Uncomplicated colic resolves by itself without surgical intervention.
Repeated rapidly recurring episodes herald the onset of complications (eg. cholecystitis). BOOK an OUT-PATIENT ELECTIVE ERCP for later…
→ ERCP: if there is a common bile duct stone, you should go after it.. Otherwise,

Wait 6 hours: let it develop into

CONTROVERSY: do you wait for complications?
Studies show that patients who have elective cholecystectomy after their episode of colic have shorter hospital stay and a less problematic recovery than those who patiently wait for a stone to obstruct their common bile duct.

ACUTE CHOLECYSTITIS:

Admit the pt.;

Now that your patient has a fever and physical signs, the surgeons will be much more interested. They may be persuaded to perform a

LAPAROSCOPIC CHOLECYSTECTOMY which may upgrade to
OPEN CHOLECYSTECTOMY if there is empyema, gangrene, abscess etc.

In elective laparoscopic cholecystectomy, the rate of conversion from a laparoscopic procedure to an open surgical procedure is approximately 5%. The conversion rate for emergency cholecystectomy where perforation or gangrene is present may be as high as 30%.

Either way: the gall bladder is now uselessly damaged and needs to come out.
If the patient is particularly elderly and feeble, you may want to merely decompress the gall bladder with a **percutaneous draining tube** which is less dangerous to install

ACUTE ACALCULOUS CHOLECYSTITIS

The patient is in great danger, MUST OPERATE:

This is an emergency open cholecystectomy, with drainage and debridement of any gangrenous tissue and debris.

CHOLANGITIS: obstruction of the common bile duct has favoured its colonisation with gut organisms, and now they creep up the hepatic biliary tree, soon to break into the hepatic parenchyma and subsequently into your bloodstream.

INFECTION LOCALISED TO BILIARY TREE:

- **Endoscopic Decompression + Drainage of bile duct**
- **Broad-spectrum Antibiotics, INTRAVENOUSLY**

INFECTION SPREAD : SEPTIC, LIVER ABSCESSES, etc

- **Open Cholecystectomy + Debridement**
- **Broad-spectrum Antibiotics, INTRAVENOUSLY**

Most common organisms are
- *Escherichia coli* (39%)
- *Klebsiella* (54%)
- *Enterobacter* (34%)
- enterococci (34%)

and most infections are polymicrobial

PROGNOSIS

Asymptomatic individuals with gallstones develop pain at a rate of 1% per year (i.e 10% chance in 10 years)
The frequency of progression to acute cholecystitis is 10-30%.
Most patients with acute cholecystitis have a complete remission within 1-4 days. However, 25-30% of patients either require surgery or develop some complication
Cholangitis mortality ranges from 7-40%.

EPIDEMIOLOGY

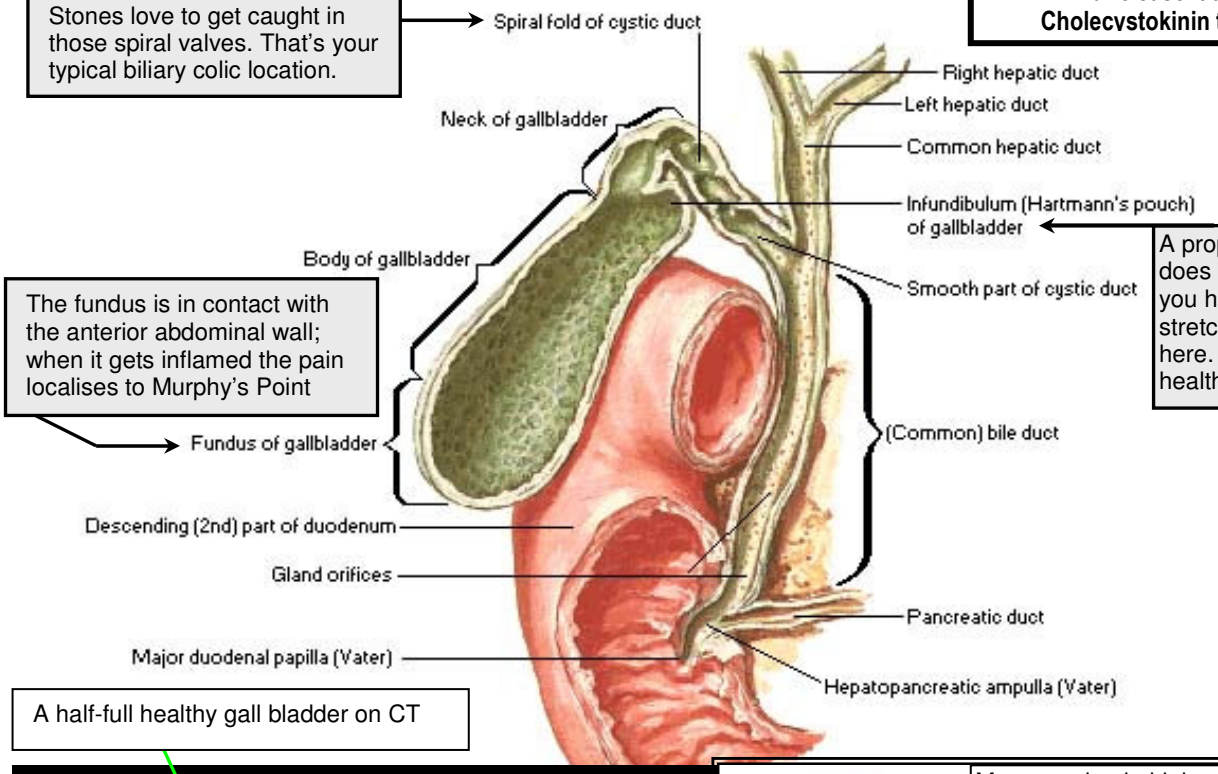
Rare in the under-20s
Prevalence increases with age
Women more than men
More common with obesogenic Western McDiet
Acalculous cholecystitis is more common in elderly men.

BASIC SCIENCES: ANATOMY + HISTOLOGY OF THE GALL BLADDER

- **50-100ml capacity; attached to posterior surface of Rt Lobe of Liver**
- **total daily flow about 500 to 600 ml of bile**
- **the FUNDUS touches the abdominal wall and causes localisation of pain**
- **the VEINS draining from the gall bladder pass directly into the liver.**

Major Function:
STORE and CONCENTRATE the BILE
And release it at the behest of Cholecystokinin the Gut Hormone

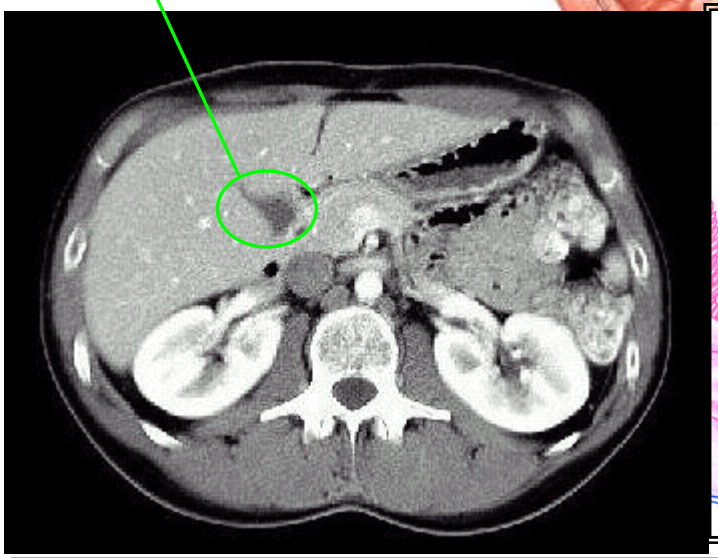
Stones love to get caught in those spiral valves. That's your typical biliary colic location.

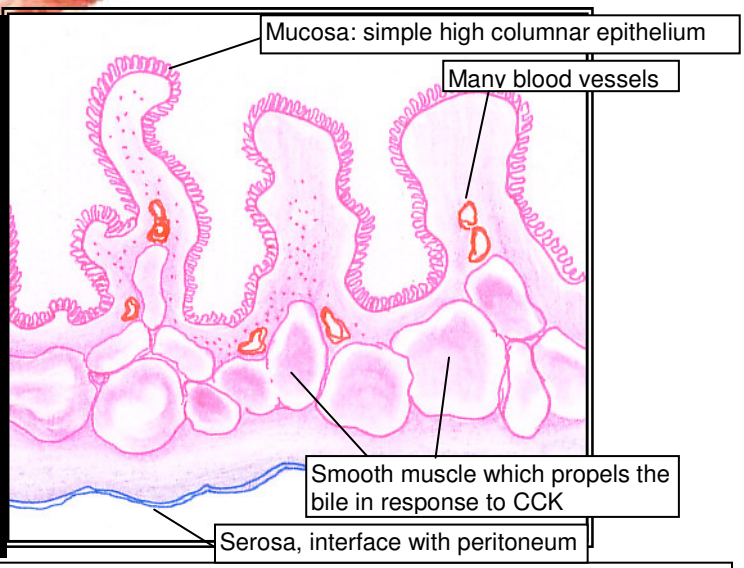


A proper Hartmann's pouch does not really form until you have had a gallstone to stretch out the GB wall here. Its just not visible in healthy gall bladders.

The fundus is in contact with the anterior abdominal wall; when it gets inflamed the pain localises to Murphy's Point

A half-full healthy gall bladder on CT





The gallbladder is a distensible sac and, when not distended, its mucosa is thrown into many folds. The lumen of the gallbladder is lined with a high columnar epithelium. The connective tissue wall contains abundant elastic fibers and layers of smooth muscle which predominantly run obliquely. The whole columnar lining is very uniform and rests on a highly vascular basement membrane. Its duty is to absorb inorganic salts and water, and these get carried off by the veins in the gall bladder wall → they go back to the liver.

Arterial Supply: Cystic Artery (branch of the Right Hepatic Artery)
Venous Drainage: Cystic Veins (go directly from GB wall to hepatic sinusoids
Sensory innervation: Right Phrenic Nerve

BASIC SCIENCES: CHOLESTEROL & BILE

That's supposed to be a sinusoid vein

80% of cholesterol is returned to the liver in the blood, in lipoprotein-bound form

← The HEPATOCYTE →

25% of cholesterol comes from **DE-NOVO BIOSYNTHESIS:**
10% in the hepatocytes, 15% in the small intestine.

mitochondrion

Acetyl CoA x 3 molecules → HMG-CoA

HMG-CoA Synthase

HMG-CoA Reductase

NUMEROUS INTERMEDIATE STEPS:
Mevalonate → isopentinyl pyrophosphate→ geranyl pyrophosphate → farnesyl pyrophosphate →squalene → lanosterol → and finally…

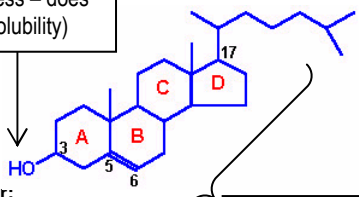
CHOLESTEROL

RATE LIMITING STEP!!
HMG-CoA reductase inhibitors halt this de - novo synthesis. THEY ARE KNOWN AS THE
! STATINS !

The by-products of this synthesis have their own weird little usefulness. They form coenzyme Q of the electron transport chain in the mitochondrion; they form the side chain of the Heme Alpha subunit; and some others.
STATINS WILL INHIBIT THIS AS WELL.

Cholesterol molecule

Hydrophilic polar group (internalised, useless – does not confer water solubility)



Solubility in water:
VERY POOR
10^{-8} mmol/l will dissolve

Non-polar sterol ABCD group and fatty side chain = EXTERNAL

BILE ACID SYNTHESIS:
this is how you rid yourself of excess cholesterol

CHOLESTEROL

7-alpha-hydroxylase ← **RATE LIMITING STEP!!**

7-hydroxycholesterol

Numerous complicated steps which we don't need to know about

Most bile acids don't get synthesised. They are reabsorbed from the distal ileum and recirculated.

Cholic Acid ← PRIMARY → Bile Acids **Chenodeoxycholic Acid**

← CONJUGATED →
with TAURINE or GLYCINE
by Acyltransferase

Glycocholic acid
Taurocholic Acid

Glycochenodeoxycholic Acid
Taurochenodeoxycholic Acid

TRANSPORT from the sinusoid to the liver happens via the Na^+/taurocholate cotransporter **(NTCP)** and the organic anion transporting proteins **(OATPs),** which also transport a large variety of non-bile salt organic anions.

PHOSPHOLIPIDS
= another bile component; the commonest one is Lecithin (phosphatidyl-choline). These are only slightly more water soluble than cholesterol.
EXIT via phospholipid export pump (MDR3)

Un-esterified raw CHOLESTEROL: Exit via two hemitransporters ABCG5 and ABCG8

SECRETION OF BILE ACIDS: (very soluble, up to 10^{-3} mmol/L)- **via**
the bile salt export pump (BSEP)
the conjugate export pump (MRP2) - also exports conjugated Bilirubin
the multidrug export pump (MDR1) - for hydrophobic cationic compounds

95% of the bile acids are reabsorbed by active transport in the distal ileum; they cycle about 10 times every day

Biliary Canaliculus:
Where the organic components of the bile will meet and mingle.
bile acids (80%) phospholipids (16%), unesterified cholesterol (4.0%).

Cl^- HCO_3

Canalicular cell:
Concentrates the bile using the Cl^-/HCO_3^- anion exchanger)

GALL BLADDER:
Bile maturation

So how do these three behave in aqueous solution?
- Cholesterol forms cholesterol monohydrate crystals in water.
- Lecithin forms bi-layered micelles, like oil droplets
- Bile salts will form micro-micelles (only a few molecules)

BUT: together they will form small micelles half-lecithin, half-bile salt; and within these the cholesterol can be dissolved as if in fat (though in reality the bile here is very watery). **!! IMPORTANT !!**

Gut bacteria convert the **primary bile acids** into the **secondary bile acids, DEOXYCHOLATE and LITHOCHOLATE**

The Gall Bladder epithelium actively pumps out much of the Na+, K+, Cl-, HCO3- and therefore also WATER. BILE CONCENTRATED 10 to 15 times RELEASE STIMULATED by cholecystokinin (when fat hits the gastric mucosa) and by secretin (when the duodenum becomes acidic)

Bile is released into the duodenum, where it does the needful (i.e neutralises stomach acid and emulsifies the dietary fats like a detergent so that the lipases have more surface area to work on.)

BASIC SCIENCES: PATHOLOGY OF STONE FORMATION

80% are cholesterol stones;
20% are bile pigment stones
composed of calcium bilirubinate …pigment stones only form when there is too much bilirubin being formed. Eg. when there is excess erythrocyte destruction. Plus normally bilirubin is conjugated and soluble.
THUS: pigment stones will only form when:

1. There is too much bilirubin
2. Some bacterium crawls up the common duct and deconjugates it, causing it to precipitate from the solution.

CHOLESTEROL in bile will be dissolved UP TO A POINT:
It requires the presence of much bile acid and phospholipid to form those mixed micelles it loves so well.
The Cholesterol Saturation Index (CSI) is a measure of whether there is enough micelles to dissolve it all.
Normally bile is UNDERSATURATED, i.e. CSI less than 1.0 – meaning that there's more than enough bile acids and phospholipids to dissolve the cholesterol.
A CSI greater than 1.0 means that the bile is supersaturated with cholesterol.
THUS: seeing as it cant very well dissolve in water, the cholesterol will **PRECIPITATE INTO CHOLESTEROL MONOHYDRATE CRYSTALS**

SUPER-SATURATED BILE: why??

- **Increased biliary cholesterol secretion**
  - As you **AGE** you lose some of your 7-alpha-hydroxylase, the rate-limiting step in making bile acids out of cholesterol. **THUS** you excrete more cholesterol and less bile acids, and the CSI rises to over 1.0
  - **OBESITY :** there is a linear relationship between weight and biliary cholesterol secretion. This may be due to increased de-novo synthesis.
  - **FEMALENESS** = estrogen causes more cholesterol to be excreted into bile, partly by increasing hepatic lipoprotein uptake. It's the downside of estrogen's lipid-lowering cardiovascular protection.
  - **McDiet :** vegetarians don't get gall stones. Fat carnivores always do.
  - **GENETICS:** stupidly, the liver of individuals so predisposed does not divert more cholesterol into bile acid synthesis. Instead it allows it all to just leak out into the biliary canaliculus. Seems to be some sort of negative feedback loop dysfunction, dominant trait involving at least 2 genes.

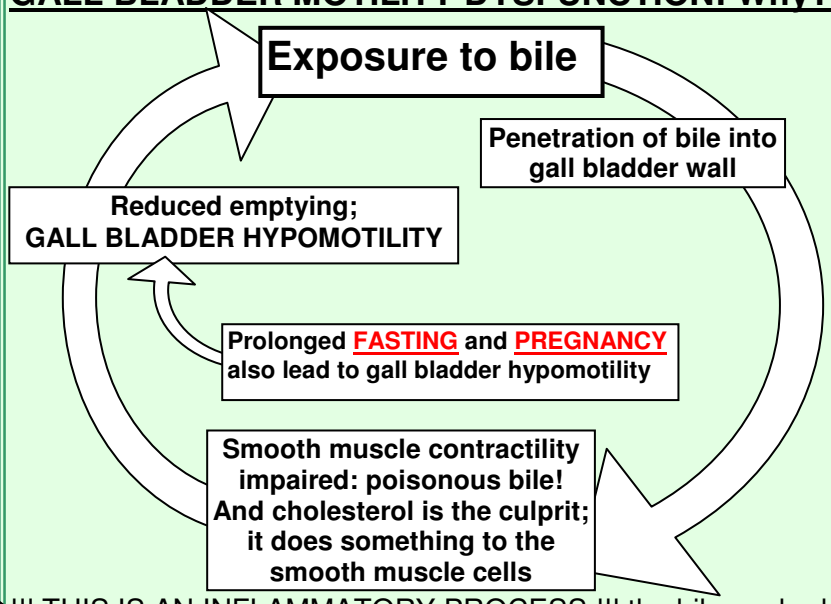
SUPERSATURATED BILE

But… healthy people often have supersaturated bile.

GALL BLADDER MOTILITY DYSFUNCTION

Immobile bile forms many tiny cholesterol monohydrate crystals, which form a sludge.

GALL BLADDER MOTILITY DYSFUNCTION: Why??



!!! THIS IS AN INFLAMMATORY PROCESS !!! the bile-soaked epithelium goes overboard with the production of mucous proteins.
THUS → MORE PROTEIN IN THE BILE
Plus, IgG secreted from the biliary canaliculi epithelium also contributes.

ALTERED KINETICS: too much protein in the bile

Protein in the bile causes NUCLEATION, where all the tiny crystals congregate into larger ones, and thus the stone is formed

A STONE SITS IN THE GALL BLADDER

Contractions push it into the bile duct

Obstruction of bilirubin secretion

JAUNDICE

Distension + inflammation of gall bladder

PAIN referring to back + shoulder blades

PAIN localising to Murphy's point

INFECTION ascending the stagnant bile duct

FEVER

Penetration of liver → SEPSIS

ACUTE ABDOMEN : PANCREATITIS

SYMPTOMS:

- Pain which is eventually VERY SEVERE
- Epigastric or LUQ
- MUCH WORSE AFTER EATING!!
- Better by leaning forward
- May be nauseous, light-headed, anaemic

SIGNS:

- EXQUISITE EPIGASTRIC TENDERNESS
- Possibly positive rebound
- **Signs of SHOCK !!**

90% caused by alcohol and gallstones

the other 10% :

- Hypercalcemia
- Drugs:
  - Sodium valproate
  - Salicylates
  - ACE inhibitors
  - Azathioprine
- Tumour
- Mumps or coxsackie virus
- Vascular anomaly
- ERCP complication
- Scorpion bite

PROGNOSTIC FACTORS

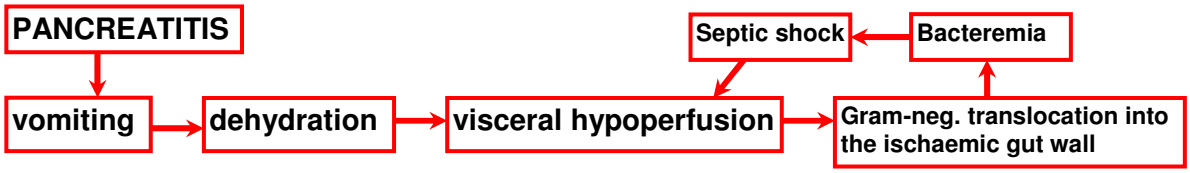
Early multiorgan failure from shock = 50% mortality

Mild disease = <5% mortality

Late infected necrosis = WILL KILL YOU

If youre over 55, with WCC over 16 and rising LFTs, youre prognosis is very poor

PATHOPHYSIOLOGY OF SHOCK FROM PANCREATITIS



IMMEDIATE MANAGEMENT:

Goal is to arrest progression before the development of systemic symptoms:

- Na+, Cl-, K+ and H+ are lost through vomiting: NEED TO REPLACE
  - Thus give oxygen, normal saline, analgesia,
  - Put in a central line
  - Urinary catheter to watch output: if acutely dropping, WORRY!
  - Replace fluids

RUN TESTS:

- FBC
- LFTs
- EUC + CMP(watch potassium and calcium)
- AMYLASE / LIPASE
  : not specific or sensitive; 20% of cases have normal results
  UNLESS: good pancreatitis history and levels elevated to over 1000 !!
  LIPASE MAY BE MORE SENSITIVE...

GALLSTONE PANCREATITIS

Have to do ERCP within 48 hrs;

STILL PROGRESSING? → do a **contrast CT**; may have become necrotic

SURGICAL MANAGEMENT:

NECROSECTOMY: scoop out the abscess, if...

- Clinical deterioration, AND
- Bacteriological proof of infection

High intraoperative mortality (~40%), due to Hemorrhage of splenic artery

(the one that runs almost through the pancreas)

= caused by inflammation, which weakens the vessel wall and produces a PSEUDOANEURYSM which often bursts in the surgeons hands.

COMPLICATIONS:

- Necrosis and infection in the remains of the pancreas
- Fluid at the operating site → increased intrabdominal pressure →
  → abdo compartment syndrome
- Colonic necrosis, inflammation and subsequent colonic artery thrombosis
- GI haemorrhage
- Respiratory failure
- Renal failure:
  - PRE due to hypovolemia
  - INTRA due to ischaemic tubular necrosis
  - POST due to pressure obstruction by abdominal compartment syndrome
- Hyperglycaemia (effectively, diabettis mellitus type 1)
- Hypocalcemia

PSEUDOCYST: (fake cyst - wall is not lined with epithelium)

Not cyst- instead a pocket formed by fibrin sheaths and adjacent organ walls; filled with necrotic filth.

- 35% of cases will go on to develop pseudocysts after pancreatitis
- Takes about a month to develop.
- 50% resolve in 3 months

SYMPTOMS:

pain (radiates to back) + gastric outlet obstruction

SIGNS: epigastric tenderness

Investigate with ultrasound and CT scan.

Management: drain it before it becomes infected!

- Endoscopy or US-guided

Cancers of the Bile Duct, Gall Bladder and Liver Tissue

- **Most will be secondaries. Even if you cant find the primary, its probably still secondaries.**

Commonest mets are from colo-rectal, lung, breast, pancreas , and stomach.

IN ABSENCE OF CIRRHOSIS, HEPATITIS or HAEMOCHROMATOSIS, PRIMARY LIVER CANCER IS ALMOST UNHEARD OF. Likewise cancer of the gallbladder, biliary tree and common bile duct. Rare as hens teeth, they are. But…

You have to start thinking along the CANCER lines if your patient has

- **PAINLESS INSIDIOUS JAUNDICE**
- **ACALCULOUS CHOLECYSTITIS**
- **WEIGHT LOSS**
- **FAT MALABSORPTION**
- **Employ Courvoisier's Law: if the gall bladder is distended in painless jaundice, there must be a tumour constricting the common bile duct**
- **These people will have a raised PT due to Vit. K malabsorption**
- **Bilirubin, Alk Phos and GGT will be elevated.**

Gall Bladder Cancer:

associated with gallstone disease, estrogens, cigarette smoking, alcohol consumption, obesity, and female sex. The epicenter of the tumor usually is the fundus, or neck, of the gallbladder. Local spread through the organ wall leads to direct liver invasion, or, if in the opposite direction, leads to transperitoneal spread (20% of patients at presentation).

Cholangiocarcinoma: More than 90% are adenocarcinomas, and the remainder are squamous cell tumors. Arise from the intrahepatic or extrahepatic biliary epithelium
Complete surgical resection is the only therapy to afford a chance of cure. Unfortunately, only 10% of patients present with early stage disease and are considered for curative resection.

Barrier Key-word for Hepatocellular carcinoma: Alpha-Foeto-Protein

The Acutely Painful Abdomen: Where does it hurt?…

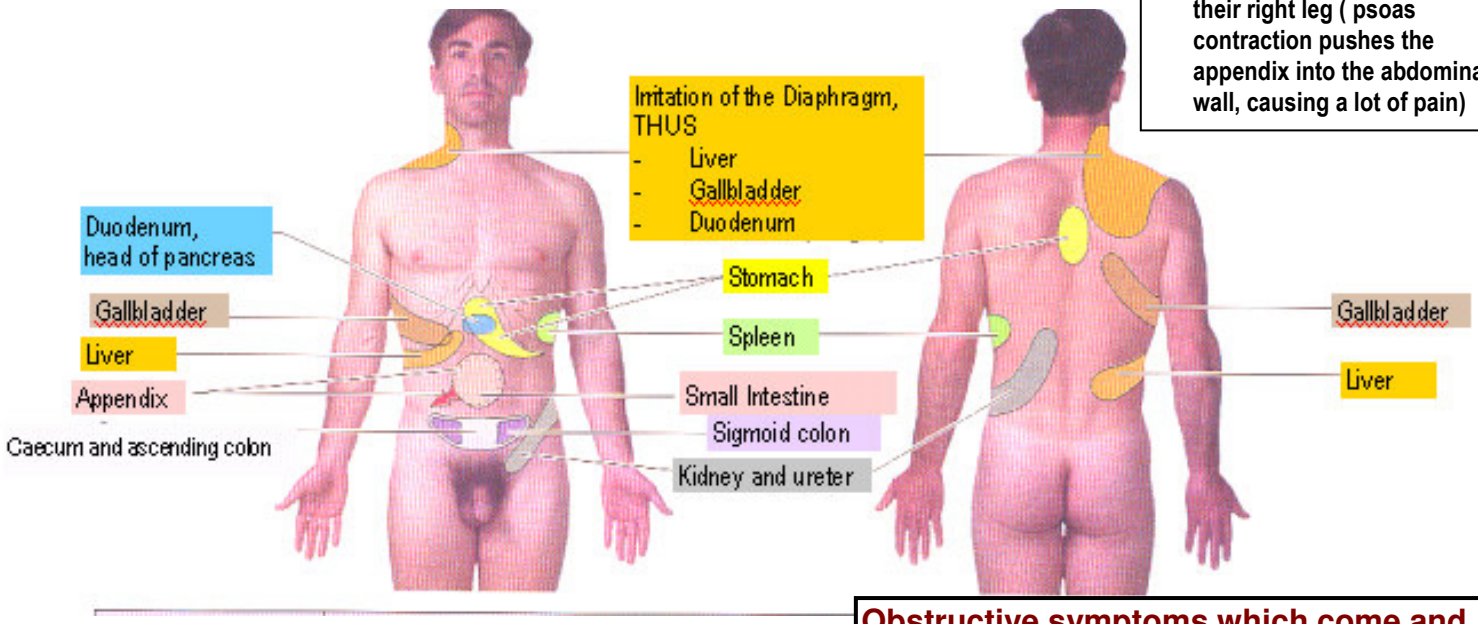
Rules of thumb:

- **Midline structure pain will radiate to the back**
- **If the viscera are inflamed, pain is diffuse**
- **If the abdominal wall is inflamed, the pain is localised to a discrete area**

Colic is distension of a hollow viscus.

APPENDIX PAIN:
Embarrassing to miss this diagnosis, its bread-and-butter stuff.
- Diffuse and Periumbilical pain at first;
- Moved to Right Iliac Fossa
- Now sharper
- The patient can not hop on their right leg (psoas contraction pushes the appendix into the abdominal wall, causing a lot of pain)

Characteristic locations:



Obstructive symptoms which come and go suddenly for several days in an elderly patient (over 65) should make you suspicious of a GALLSTONE ILEUS

* **oesophagus pain mimics cardiac pain – same referral**

Obstruction

Most often caused by post-operative adhesion (may take years)

- **Acute constipation, distension, nausea + vomiting, pain**
- **If constipation + distension is long-standing and progressive, consider partial narrowing or chronic process**
- **ASK how often the pain pulses are felt** →

Proximal obstruction = pain pulses every 3-4 minutes;

Distal obstruction = Pain pulses every 10-15 minutes

ASK ABOUT:
- **Previous episodes of obstruction**
- **Previous abdo / pelvic operations**
- **History of abdo cancer**
- **History of abdominal inflammatory disease: Eg.**
  - **Inflammatory bowel disease**
  - **Cholecystitis**
  - **Pancreatitis**
  - **Pelvic inflammatory disease**
  - **Abdominal trauma**

EXAMINATION:
- **How does the patient look?**
  - **If they are lying quite still, it looks like peritonism (bad sign !)**
- **What was aspirated through the NG tube?**
  - **CLEAR +/- food = gastric outlet obstruction**
  - **FECULENT = distal small bowel …or colonic obstruction with incomptetent iliocaecal valve**
  - **BILIOUS but NON-FECULENT = either**
    - **A medial or proximal small bowel obstruction, OR**
    - **a colonic obstruction with a competent ileocaecal valve**
      (or else the faeces would be regurgitating into the stomach out of the incompetent iliocaecal valve)
- **PUT YOUR FINGER IN IT!! → hematomae / abscesses get forgotten**
- **ABSENT BOWEL SOUNDS? – sinister; maybe ileus**
- **PICTURE OF ILEUS: mild diffuse pain, not the severe increasing localised pain of obstruction**

INVESTIGATIONS for bowel obstruction:

Bloods:

EUC **(Hypokalemic? Hyponatremic? Hypochloremic?)**
FBC **for Hb and white cells**
LFT **for cholestatic issues or portal HT**
Amylase + Lipase **for pancreatitis**

Abdo Xray

May see characteristic water vs. gas levels in distended loops of small or large bowel.

- ? is there gas distal to the obstruction **(if yes, then it is only a partial obstruction)**
- So theres no gas BELOW the obstructed section of colon;

BUT: is there gas in the small bowel?
Is it regurgitating into the small bowel from the blocked colon?
IF NOT = the iliocaecal valve is still competent

- are there haustra still visible **(if not, its REALLY distended!)**
- are there visible calculi**, or air in the biliary tree?**
- Is there air under the diaphragm**? = perforated viscus**

Barium enema

For bird-beak sign**: demonstrates sigmoid volvulus**
For apple-core sign: **demonstrates colonic carcinoma**

CT with oral / rectal contrast

MANAGEMENT

Resuscitation

- **IV fluids** (crystalloids, NS with K+ is good)
- **Urine output should be at least 0.5 ml/hr (i.e halve the patients weight and expect it in mls of urine per hour)**
- **Monitor fluid response**: **within 10-15minutes the urine output should change**
- **The need for surgery must be assessed**: **most of these things resolve on their own, but if the bowel wall is so distended that its ischaemic, then there is risk of fecal peritonitis from which theres a 50% chance of death – so don't let it get that far.**
- **!! NEVER LET THE SUN GO DOWN TWICE ON A BOWEL OBSTRUCTION!!**

Anaesthesiology 1.01

INDUCED, MAINTAINED, REVERSIBLE UNCONSCIOUSNESS with PARALYSIS

Induced how: WITH INTRAVENOUS DRUGS;

WHICH ARE RAPIDLY ACTING AND WILL PUT YOU OUT VERY QUICKLY.

BUT the IV drugs will only last a short while, as their circulating volume will decrease (with them being taken up into the tissue and metabolised)

PROPOFOL, the Milky Intravenous Beverage of Blissful Absence
Its lipid soluble, so it comes in an opaque white emulsion. Nobody knows exactly what it does, but it does it within 30 seconds; and within 5 minutes you're awake again.

MAINTAINED HOW?

WITH GAS.

The gas acts slowly (and smells bad) and therefore is useless for inducing the unconsciousness.
However, it works well as maintenance. Mix with O2 for maximum effect. Serve chilled.

ANAESTHETIC GASES: isofluorane, sevofluorane, enfluorane, desfluorane.
Once again, noby knows how they do what they do. Strangely, the noble gas **Xenon** has excellent anaesthetic properties, but its shamelessly expensive and the only people to use it routinely are Russians (who have cubic miles of it left over after their Cold-war uranium enrichment program.) Of course, there is the much maligned 'Critical Volume Hypothesis'. It states that the absorption of anaesthetic molecules could expand the volume of a hydrophobic region within the cell membrane and subsequently distort channels necessary for sodium ion flux and the development of action potentials necessary for synaptic transmission. There is limited support for this theory.

REVERSIBLE BY WHAT MEANS?

when the gas is turned off, it will diffuse out of the patient along a concentration gradient, just the way it entered. This means the patient will wake up (the initial IV drugs having worn off hours ago)

UNCONSCIOUSNESS is useful.

It dissociates the higher processing centres from the physical sensation of injury, which is pain.
HOWEVER because there are lower and more primitive processing bodies, pain stimulus will still provoke a response: a totally autonomic and animal response, namely-
- the **signs of shock** (peripheral vasoconstriction, tachycardia, increased BP, RAAS activation)
and also the **WITHDRAWAL REFLEX:** the spinal cord will command the limbs to jerk away from the injury.

THAT'S WHY WE SOMETIMES NEED PARALYSIS

This must be controlled with MUSCULAR RELAXANTS (paralysis toxins, eg. curare)

There are short acting ones eg. **suxamethonium = acteylcholine receptor agonist**

- causes prolonged depolarisation of skeletal muscles to a membrane potential above which an action potential can be triggered. The onset of muscle relaxation will be rapid after intravenous injection (30-60 seconds), and lasts 5-10 minutes. The muscle paralysis can be continued with intermittent intravenous boluses, using about 25% of the initial dose. The total dose should not exceed 6-8 mg/kg.)

There are long acting ones eg. **rocuronium = competitive acetylcholine receptor blocker**

These work when they outnumber the concentration of acetycholine at the neuromuscular junction.

TO COMBAT AND REVERSE THIS you need to **give an acetylcholinesterase inhibitor** eg. sarin gas (too permanent for clinical use but the concept is the same)- which will restore the balance in favour of acetylcholine (by inhibiting its breakdown).

BUT!! Its fine at the NICOTINIC neuromuscular junction receptors, but it will also happen at the MUSCARINIC receptors eg. the parasympathetic M3 receptors at the end of the avgus nerve, in the heart.

THIS CAUSES A PROFOUND BRADYCARDIA. To protect against this one must also give some atropine (or equivalent anticholinergic) to restore the heart rate.

Anaesthesiology 1.02

What you will see on an anaesthetic monitor:

ECG lead II (the one in the direction of heart propagation)
SaO2 saturation
Capnograph (measuring expired CO2)
(this means during expiration the trace falls to zero)
NEED TO KEEP THIS NUMBER ABOVE 30
- or else respiratory drive fails
Over 40 will probably trigger hyperventilation
Opiated patient breathing on their own can have a CO2 of 50 and still breathe: opiate drugs increase the respiratory drive threshold

ANAESTHETIC ASSESSMENT: pre-operative evaluation of fitness

Question One: can this patient get better before surgery?
Can we optimise their chances of surviving surgery by waiting for any other problems to be fixed first?

AIRWAY: can this patient be intubated?

Need to check **thyro-mental distance** (from tip of thyroid cartilage to chin)
Should be at least 3 fingers of t-m distance
How much of the UVULA can you see?
Mallampati score of laryngoscopability:
Grade 1: whole uvula can be seen
Grade 2: partially blocked
Grade 3: no uvula but soft palate
Grade 4: cant see anything except tongue
Can you fit your finger into the open TMJ?
Can you fit 2 fingers into the mouth? (width of laryngoscope blade)
Can you hyper-extend their neck?…

Then ask about medical background, eg.
- previous anaesthetic reactions
- exercise tolerance **(2 flights of stairs MINIMUM!!)**
- functional impairment due to respiratory or CVS disease
- can they lie down in the way which their procedure requires?
- Then, talk about liver + kidney disease