PANCREATIC AND BILIARY DISORDERS

(CHAPTER 43)

QUESTION 1

Describe the components of bile.

In its unconcentrated form, bile is **98% water**.

It also contains:

- 1% bile salts and bilirubin
- 0.5% lipids (cholesterol, fatty acids, lecithin, etc.)
- inorganic salts (electrolytes)

QUESTION 2

Where is bile produced?

Bile is produced by **hepatocytes**, the primary functional cells of the **liver**.

The hepatocytes dump bile into the intrahepatic bile ducts, which merge with ducts from the pancreas and gallbladder, and empty into the duodenum.

QUESTION 3

What are the functions of bile? Why are bile salts needed?

Bile has two primary purposes:

To aid in the **absorption of dietary fats** in the small intestine, and

To **transport waste products** from the liver (such as bilirubin) to be eliminated in the stool

The **bile salts** facilitate its primary purpose of bile, aiding in the absorption of dietary fats.

Bile salts are the conjugated forms of bile acids, having a hydrophilic end and a hydrophobic end.

These salts act as a surfactant, surrounding dietary fats in the intestinal lumen and forming **micelles** which are more easily absorbed.

QUESTION 4

Does the gallbladder add anything to bile?

The gallbladder doesn't really **add** anything, but does **concentrate** bile by removing the vast majority of its water content.

The lining of the gallbladder absorbs Na^+ and K^+ ions, causing water to follow by osmosis.

QUESTION 5

What are the functions of the gallbladder?

Two main purposes:

Concentrate bile by removing water content, and

Store bile until it is needed, then **eject** it into the duodenum in response to CCK

QUESTION 6

What happens to bile in the small intestine? In the large intestine?

The **ileum** of the small intestine **reabsorbs** 90-95% of the bile acids, which then return to the liver for reuse via the portal vein.

A small amount of bile continues on to the large intestine, where gut bacteria transform the bile acids into **secondary bile acids** through dehydroxylation.

These secondary bile acids are actually toxic, but are expelled in the stool fairly quickly.

QUESTION 7

How much pancreatic secretion is produced per day? What does it contain?

The pancreas produces over **one liter** of exocrine secretions per day.

It mainly contains various digestive enzymes (amylase, lipase, trypsinogen) for breaking down fats, starches, and proteins.

In addition, it also produces important **endocrine** secretions such as **insulin** and **glucagon**.

QUESTION 8

What substance is commonly found in gallstones? Describe the process of gallstone formation.

Gallstones are typically made mostly of **cholesterol**, hence why high cholesterol is a risk factor.

Process begins with excretion of **cholesterol-supersaturated** bile.

This enables the **nucleation** of cholesterol **crystals** to occur over time.

Combined with **hypomotility** (impaired bile flow,) crystals can coalesce to form gallstones.

QUESTION 9

What are the risk factors in gallstone formation?

- **Age over 40**, **female**
- High fat, high cholesterol, low fiber diet
- **Obesity** or **rapid weight loss**
- **Pregnancy** or **exogenous estrogen**, e.g. oral contraceptives
- **Native American** or **Hispanic**

QUESTION 10

What are black-pigmented stones associated with?

Pigment stones are different from normal cholesterol stones, and represent only about 20% of gallstones.

Their pigment comes from a high **bilirubin** content.

Black pigment stones are the more common type of pigment stone and are formed in the **gallbladder**.

They may be **idiopathic**, or associated with **cirrhosis** or excess **hemolysis**.

QUESTION 11

What about brown-pigmented stones?

Brown pigment stones are less common, and are formed in the **bile ducts** rather than the gallbladder.

They are seen more often in developing countries, and are associated with parasites (flatworm a.k.a. "liver flukes") or infection.

QUESTION 12

What is biliary colic? How is it elicited and what is it related to?

Biliary colic is a set of symptoms associated with **chronic cholelithiasis** (chronic gallstones,) caused by intermittent obstruction of the cystic duct.

Symptoms appear when cystic duct is obstructed by a stone, and can stop temporarily if the stone is passed into the CBD.

The symptoms typically onset or worsen **after eating** due to CCK secretion causing the gallbladder to contract.

QUESTION 13

Describe some symptoms of biliary colic.

Classic presentation: **epigastric/RUQ abdominal pain**, often radiating to the back

Symptoms also include nausea/vomiting, gas, bloating, and even diaphoresis (sweating.)

QUESTION 14

How is biliary colic diagnosed? What are the treatments?

Cholelithiasis is most often diagnosed by **ultrasound** of the abdomen, which is 90-95% sensitive for detecting gallstones.

Treatment depends on severity: mild cases can be treated by **chemical dissolution** or **lithotripsy**.

Severely acute cases may require **cholecystectomy** (complete removal of the gallbladder.)

QUESTION 15

During an inflammation of the gallbladder, what serious complications may occur?

Cholecystitis (gallbladder inflammation) can be acute or chronic, but is usually secondary to cholelithiasis.

Inflammation can cause bile stasis, which tends to facilitate **bacterial infection**.

Severe cases may progress to gallbladder rupture, gangrene, peritonitis, etc.

QUESTION 16

What is the treatment for acute cholecystitis?

Treatment for severe acute cholecystitis is typically **cholecystectomy**, or complete removal of the gallbladder.

In addition, **antibiotics** may be prescribed to manage any concurrent infection.

Ultrasound or **cholangiopancreatography** (MRCP/ERCP) may be performed if choledocholithiasis is suspected.

QUESTION 17

How common is biliary malignancy? What are the risk factors?

Cholangiocarcinoma (bile duct cancer) is aggressive and hard to catch early on, but **extremely** rare.

New diagnoses per year in the U.S.:

- Breast cancer – 275,000
- Lung cancer – 230,000
- Prostate – 175,000
- Bile duct – **8,000**

The "big bad" of cholangiocarcinoma risk factors:
primary sclerosing cholangitis (PSC)

PSC is an extremely rare, idiopathic disease marked by chronic **scarring** and **inflammation of the bile ducts**, leading to progressively worsening liver failure.

It is most commonly diagnosed in young, healthy, and **asymptomatic** white men in their 30s-40s. Most with PSC have some form of IBD, usually **ulcerative colitis**.

PSC is **very rare** itself (about 6 out of 100,000 people,) but there is **significant overlap** between PSC and CCA.

Those with PSC have an estimated **10-20%** lifetime risk of developing CCA.

PSC patients represent approximately **10%** of total cases of cholangiocarcinoma.

PSC-related CCA tends to develop in the first few years after initial diagnosis, and is one of the **most common reasons** why PSC patients don't make it to transplant.

Once diagnosed, PSC patients will typically undergo regular blood tests and MRCP/ERCP imaging for the rest of their lives to monitor for CCA.

Other risk factors include **hepatolithiasis** and parasitic **flatworm** infections ("liver flukes.")

QUESTION 18

What are the predisposing factors in acute pancreatitis?

2/3 of acute pancreatitis cases are secondary to **chronic alcohol abuse**.

Other factors include gallstones, biliary tract diseases, and hypertriglyceridemia.

QUESTION 19

Describe the three pathways that lead to pancreatitis.

All three pathways involve or result in injury to the **acinar cells**, which are responsible for producing the pancreas's exocrine secretions.

Acute pancreatitis can be caused by:

- **Direct injury** to the acinar cells, e.g. trauma, ischemia, infection
- Edematous ischemia caused by **obstruction** of the pancreatic duct or ampulla (most common)
- **Defective intracellular transport** causing intracellular activation of enzymes

QUESTION 20

Describe the clinical manifestations of acute pancreatitis.

Epigastric/LUQ pain, often radiating to the back

Severe **tenderness** on palpation

Nausea and **vomiting**

Abdominal distension and **hypoactive** bowel sounds

QUESTION 21

What is the preferred, "gold standard" diagnostic test for acute pancreatitis?

The #1 test for acute pancreatitis is a **CT of the abdomen**.

Patients with acute pancreatitis will often also have elevated LFTs and serum lipase, but **imaging** is first line for diagnosis.

QUESTION 22

How do acute and chronic pancreatitis differ?

Both are similar, but chronic pancreatitis is **irreversible** and often causes **less severe** pain.

The most common cause of both is **chronic alcohol abuse**.

QUESTION 23

What is the pathogenesis of (chronic) pancreatitis?

Inflammation leads to **necrosis** of the exocrine parenchyma, causing the acinar cells to be replaced with scar tissue (**fibrosis**.)

The pancreas can also harden due to deposition of **calcium deposits**, obstructing the flow of the already-reduced secretions.

QUESTION 24

Describe the clinical manifestations of chronic pancreatitis.

Progressive loss of both **endocrine** and **exocrine** pancreatic function (diabetes, fat malabsorption)

Epigastric/LUQ pain, just as in acute pancreatitis

Pain tends to **decrease** after several years of chronic inflammation

QUESTION 25

Describe the diagnostic process of chronic pancreatitis.

The process is similar to diagnosis of acute pancreatitis: **LFTs + imaging** (CT, MRCP/ERCP)

Calcifications can also be picked up via XR, and history of alcoholism may suggest the diagnosis

QUESTION 26

Describe the treatment options for chronic pancreatitis.

Lifestyle changes: stop drinking, low-fat diet

Pain management: medications or **celiac plexus block**

Dilatation and/or **stenting** of pancreatic duct or CBD

Enzyme replacement to aid with digestion

Drugs: H_2 receptor blockers or PPIs

QUESTION 27

How does pancreatic cancer rank as a cause of death?

Pancreatic cancer has the **fourth-highest** mortality rate among cancers.

Its median survival rate is **1 year**.

QUESTION 28

Describe treatment options for pancreatic cancer.

The best option is **pancreatectomy**, or surgical removal of the pancreas.

Downside: need **insulin** and **digestive enzyme** replacement

Chemotherapy can be used for follow-up or as an alternate treatment