LIVER DYSFUNCTION

(CHAPTER 44)

QUESTION 1

List the major functions of the liver.

The liver does a **lot**!

- produces **bile** to aid with fat absorption
- manufactures proteins, such as **albumin** and **clotting factors** II, V, VII, IX, X, XI, and XII
- stores and **recycles red blood cells**

- stores **iron** and **fat-soluble vitamins** (A, D, E, K)
- stores **triglycerides** and **cholesterol**, and exports them to the blood via lipoproteins
- breaks down **tons** of chemicals in the blood that are too big to be immediately filtered by the kidneys

QUESTION 2

What is bilirubin? What is the difference between conjugated and unconjugated bilirubin?

Bilirubin is produced as a byproduct of **hemolysis** (the breakdown of hemoglobin from old RBCs.)

It has two forms:

conjugated (direct) bilirubin

unconjugated (indirect) bilirubin

Unconjugated (indirect) bilirubin is the **direct product** of heme catalysis.

It is a "raw" form that needs to be processed (conjugated) before it can be used in bile.

Enzymes in the liver bind unconjugated bilirubin to glucuronic acid, making it **water-soluble**.

Conjugated (direct) bilirubin has been processed by the liver, making it available for use in the bile.

From here, it will pass into the small intestine through the bile ducts, along with bile acids.

Intestinal bacteria convert conjugated bilirubin to stercobilin, which is what gives feces its brown color.

QUESTION 3

How does jaundice develop?

The basic idea is that there is a **build-up of bilirubin** in the blood for some reason.

Normal total bilirubin level is below 1.2 mg/dl; values above 2-3 mg/dl can result in visible jaundice.

Hyperbilirubinemia causes yellow discoloration of skin, sclera, etc.

The causes of jaundice can be grouped into three categories...

Pre-hepatic, **hepatic**, and **post-hepatic**

Pre-hepatic jaundice is caused by **increased production** of **unconjugated** bilirubin (e.g. hemolytic anemia)

(↑ **unconjugated** bilirubin—produced faster than the liver can process it)

Hepatic jaundice is caused by **liver damage** slowing down the **conjugation** of bilirubin (e.g. hepatitis, cirrhosis)

(↑ **unconjugated** bilirubin—normal production but being conjugated too slowly)

Post-hepatic jaundice is caused by a **back-up** in the biliary system, blocking **conjugated** bilirubin from exiting the liver (cholestasis)

(↑ **conjugated** bilirubin—conjugated normally but not being cleared fast enough)

QUESTION 4

Why would ammonia rise in a patient with liver disease?

The liver is responsible for converting ammonia produced by amino acid catabolism to **urea**.

If liver function is impaired, ammonia conversion slows and it builds up in the blood.

QUESTION 5

When the liver is injured, which enzymes change? How and why does this change occur?

Liver function tests or **LFTs**:

- Aspartate aminotransferase (AST)
- Alanine amine transferase (ALT)
- Alkaline phosphatase (ALP)
- γ-glutamyltransferase (GGT)

AST, ALT, ALP, and bilirubin are included as part of the standard **comprehensive metabolic panel** (CMP,) a very common set of blood tests.

GGT usually isn't run unless there is suspicion of liver damage, to confirm source of enzyme elevation.

5'-nucleotidase is also sometimes used to identify liver problems.

These enzymes are typically found **inside** hepatocytes, but will leak into the blood when these cells die.

This makes them useful markers for identifying liver damage.

QUESTION 6

What is portal hypertension? Why do gastroesophageal varices develop?

Quick review of A&P:

The GI tract **absorbs nutrients** from the intestinal lumen and dumps them into the venous circulation

The veins coming from the **GI tract**, **pancreas**, and **spleen** all converge to the **hepatic portal vein**.

The HPV carries nutrients to the liver, where they are initially processed before passing on to the heart.

If bloodflow through the liver is impeded, blood will get backed up into the HPV and its internal pressure will increase.

Gastroesophageal varices are varicose veins **inside** the upper GI tract, caused by portal hypertension.

These varices can cause bleeding into the upper GI tract, presenting as **hematemesis**.

QUESTION 7

What are the other manifestations of portal hypertension?

caput medusae – distended, "snake-like" veins visible on surface of abdomen

ascites – remember the unit on fluid balance? Venous obstruction → increased CHP → edema.

splenomegaly – increased venous pressure causes swelling of the spleen

QUESTION 8

How are the kidney and the brain affected by liver disease?

hepatorenal syndrome – extremely dangerous complication of end-stage liver failure

Severe liver failure results in greatly diminished bloodflow to the kidneys.

Median time to mortality at this stage: **1 month**

hepatic encephalopathy – **excess ammonia** in blood results in diminished CNS function

Symptoms: **confusion**, **lethargy**, loss of fine motor control, LOC, seizures

QUESTION 9

Is all hepatitis caused by a virus?

Most forms of hepatitis are viral, but not all!

Hepatitis means liver inflammation—also includes:

- autoimmune hepatitis (AIH)
- non-alcoholic steatohepatitis (NASH)
- toxic hepatitis (including alcoholic hepatitis)

Note that all the "lettered" forms of hepatitis (A-E) are **viral**–but not all hepatitis is infectious!

QUESTION 10

Which forms of hepatitis can be prevented through vaccination?

There are two forms of hepatitis vaccine:

hepatitis A and **hepatitis B**

Caveat: You can't get **hepatitis D** unless you also have B, so the HBV vaccine works for both.

There is **no vaccine** for hepatitis C or E!

(You are safe from hepatitis F because it doesn't exist. 😛)

QUESTION 11

Which form of hepatitis has the highest risk of progressing to a chronic disease?

The most common form of chronic hepatitis is **hepatitis C**, occurring in an estimated 1% of the U.S. population.

Approximately **70%** of HCV cases progress to chronic disease.

Note that "hepatitis G," a subset of HCV, has an even higher rate of chronic **infection**, but is no longer believed to cause disease in humans and thus isn't a "true" hepatitis.

(HAE and HEE are **acute only** and don't cause chronic disease at all!)

QUESTION 12

Is there a risk of contracting hepatitis from an asymptomatic carrier?

Yes. Symptoms may not develop for the first 2-6 months of infection, and 10% of chronic HBV patients **never** develop symptoms despite being infected.

QUESTION 13

Compare the prodromal and icteric phases of acute hepatitis.

Rembember what **prodromal** means from the "Foundations" unit—**vague**, **non-specific** symptoms.

The **prodromal phase** of acute hepatitis infection is characterized by:

- Anorexia (loss of appetite) and weight loss
- Nausea, vomiting, and diarrhea
- Diffuse arthralgias (joint pain)

The **icteric phase** of acute hepatitis infection is characterized by:

- Jaundice ("icterus" means jaundice)
- More unconjugated bilirubin → darker urine
- Less conjugated bilirubin → lighter stool

QUESTION 14

How does cirrhosis develop?

Cirrhosis is the **gradual**, **chronic scarring** of the liver due to long-term hepatic injury.

Damage to hepatocytes results in the parenchyma (connective tissue) inside the liver being gradually replaced by scar tissue in a process known as **fibrosis**.

This scar tissue buildup is the reason for the decrease in bloodflow that causes **portal hypertension**.

QUESTION 15

What is non-alcoholic fatty liver disease (NAFLD?) What are the possible risks for those with this disorder, and who is most likely to develop it?

We've talked about FLD before in the "Causes of Disease" unit–decreased liver function leads to cellular inclusions of triglycerides.

As the name suggests, NAFLD is simply FLD that is not associated with chronic alcohol abuse.

Risk factors for NAFLD – obesity, diabetes mellitus, hypertriglyceridemia

Risk factors of NAFLD – non-alcoholic steatohepatitis (NASH,) cirrhosis, hepatocellular carcinoma (liver cancer)