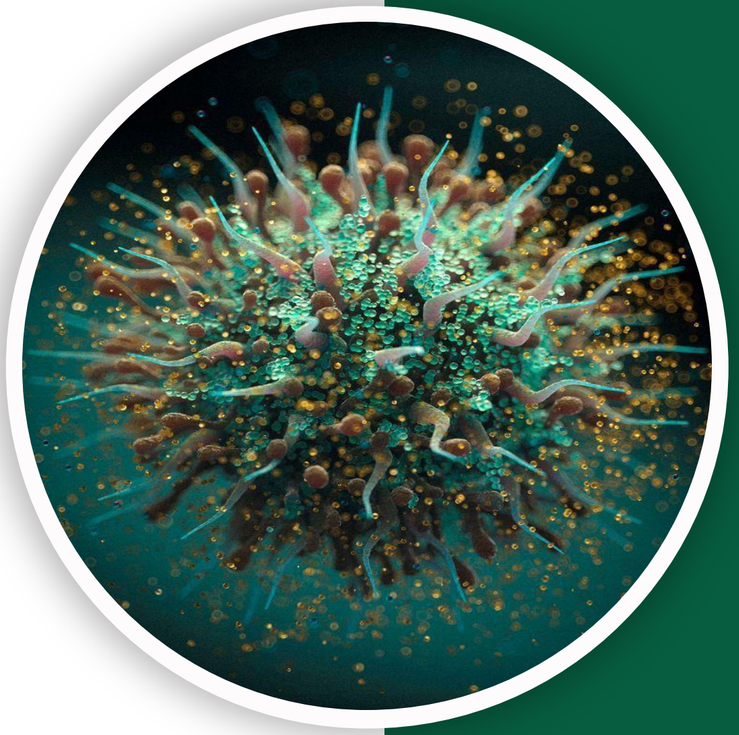
بسم الله الرحمٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Pathology | Lecture 4

Cases Discussion
Repair: 4&5



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CASE DISCUSSIONS REPAIR 2025 Al-Abbadi

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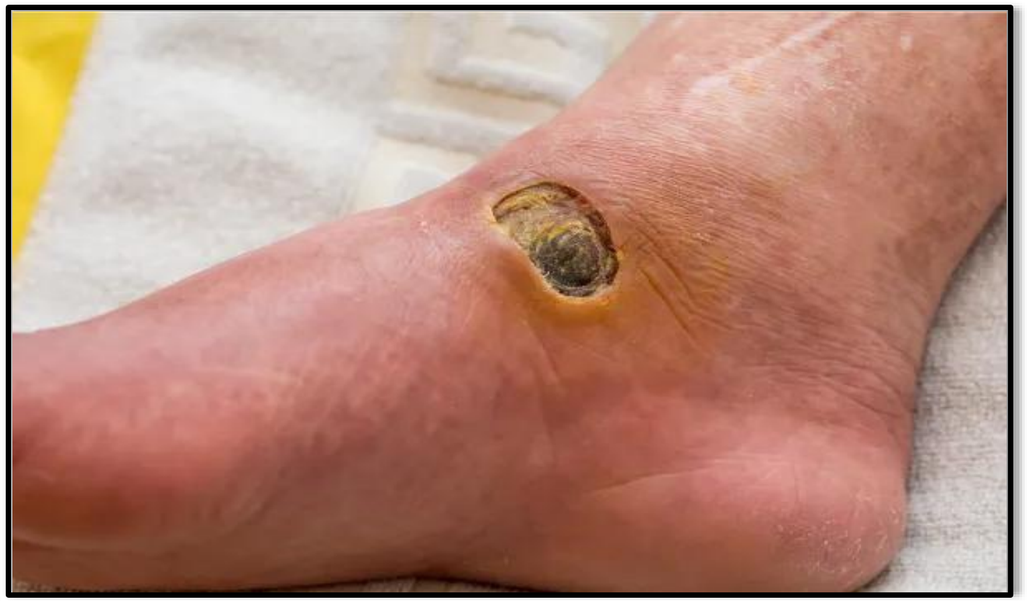
CASE 4:

A 60-year-old diabetic patient presents with a non-healing foot ulcers. The wound is 5 cm in diameter, with a foul odor and purulent discharge. The patient has a history of peripheral vascular disease. Gross pictures shown.

“Gross” in medicine means what you can see with the naked eye.

GROSS APPEARANCE ON PHYSICAL EXAMINATION:

Deep foot ulcer in diabetic patient

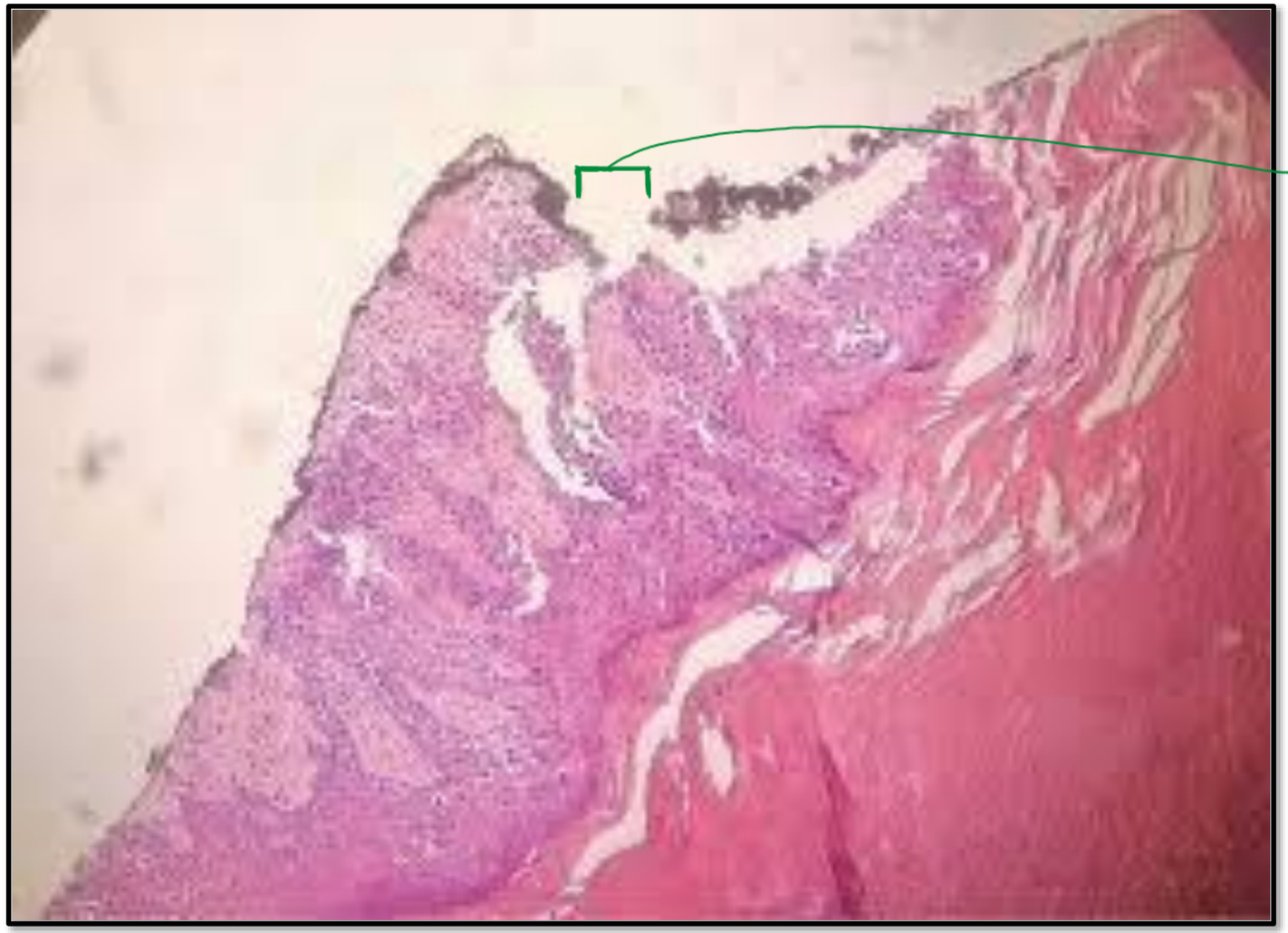


Gross pathology: These images represent a **deep ulcer** with associated **tissue loss.**

The **black coloration** represents **dead tissue**, which requires immediate **removal (debridement)**.

Note: The difference between ulcers and gangrene is that **ulcers** are specific to a localized area, while **gangrene** typically affects the entire region (a whole foot or toe).

MICROSCOPIC EXAMINATION AFTER DEBRIDEMENT:



In this section of squamous epithelium, we can identify the **ulcer** by observing the "loss of continuity in the mucosal surface."

This is a Skin ulcer but the same occur when having ulcer in the stomach or the small bowel or large bowel

DISCUSSION POINTS:

1. What are the factors that impair wound healing in this patient?

2. How does diabetes affect the inflammatory response and wound healing?

3. What are the potential treatment options for this patient?

1- What are the factors that impair wound healing in this patient?

For diabetic patients, **immune function is compromised**, making them susceptible to a **wide variety of infections**—not just chronic, but also acute ones. This is because diabetes, negatively affects **every cell and organ**, significantly reducing the body's ability to fight off disease. NEXT SLIDE TO UNDERSTAND MORE HOW IT AFFECT

- **Diabetes, which affects blood flow, neuropathy, and cellular function:**

Neuropathy: Loss of protective sensation means that the patient can't feel foot trauma, leading to unnoticed and untreated injuries.

Blood flow: Chronic hyperglycemia causes glycosylation (where sugar binds to vessel proteins). This process thickens the blood vessel walls and narrows the opening (lumen), which severely restricts blood flow.

- **Peripheral vascular disease, which reduces blood supply to the wound.**
- **Infection** super added infection will interfere with proper healing (The enemy to all physicians) **(indicated by purulent discharge and foul odor)**
- **Possibly poor nutrition or inadequate wound care.**

2- How does diabetes affect the inflammatory response and wound healing?

Diabetes impairs wound healing by:

- **Reducing blood flow and oxygen delivery** to tissues **(impaired angiogenesis (which is an important initial step in repair)).**
- **Impairing neutrophil and macrophage** function, leading to persistent infection, **which compromises the immune response to bacterial and fungal pathogens.**
- **Altering the balance (decreasing) of cytokines and growth factors** necessary for healing.
- **Increasing the risk of neuropathy**, which **reduces sensation** and increases the risk of further injury.

Student's question on the second point

WBCs travel through the blood and we don’t have enough blood reaching tissues so how do we have persistent infection ?

Everything is affected , it's not just the volume and flow of the blood will be decreased because the BV diameter is decreased in diabetes . So, when you have smaller lumen, the perfusion is less the number of cellular response is also less. So, it's like a cascade not just the blood flow is reduced also the cellular response is also imparted , not only that the hyperglycemia itself will also embark on specific functions of macrophages and neutrophils which are the initial important cells in inflammation

3- What are the potential treatment options for this patient?

Potential treatment options include:

- **Debridement** to remove dead tissues and promote healing (granulation tissue formation).
- **Antibiotics** to treat infections. (better to give oral or systemic antibiotics than typical because you're worried from spreading to the blood stream)
- **Offloading pressure** from the affected area (bed sore).
- Improving **glycemic control** to decrease complications.
- Advanced **wound care therapies** (e.g., negative pressure wound therapy, growth factors) "diabetic foot clinics" by adding nutrients to promote healing.
- **Revascularization** procedures to improve blood flow. (It can be achieved **surgically**, such as **arterial bypass surgery**, where a blood vessel (graft) is taken from another part of the body (or a synthetic graft) to bypass a blocked artery, **or** by **endovascular procedures** like angioplasty and stenting. These procedures are typically performed by **vascular surgeons** (and sometimes interventional cardiologists or radiologists) in hospitals.
- Last resort (if all the treatment options above failed): **Amputation** بَتْر

CASE 5:

A 55-year-old male with a history of chronic hepatitis C infection presents with abdominal distension, peripheral edema, and jaundice. Laboratory tests reveal elevated liver enzymes, low albumin levels, and a prolonged INR. Imaging studies show a nodular liver with signs of portal hypertension (CT and biopsies shown).

Diagnosis:

Abdominal Distension: This is identified as ascites. The patient's abdomen looks swollen (distension) because it is filed up with fluid (ascites).

Jaundice: This presents as discoloration of skin caused by the inability of the liver to conjugate bilirubin to make it more water-soluble for excretion.

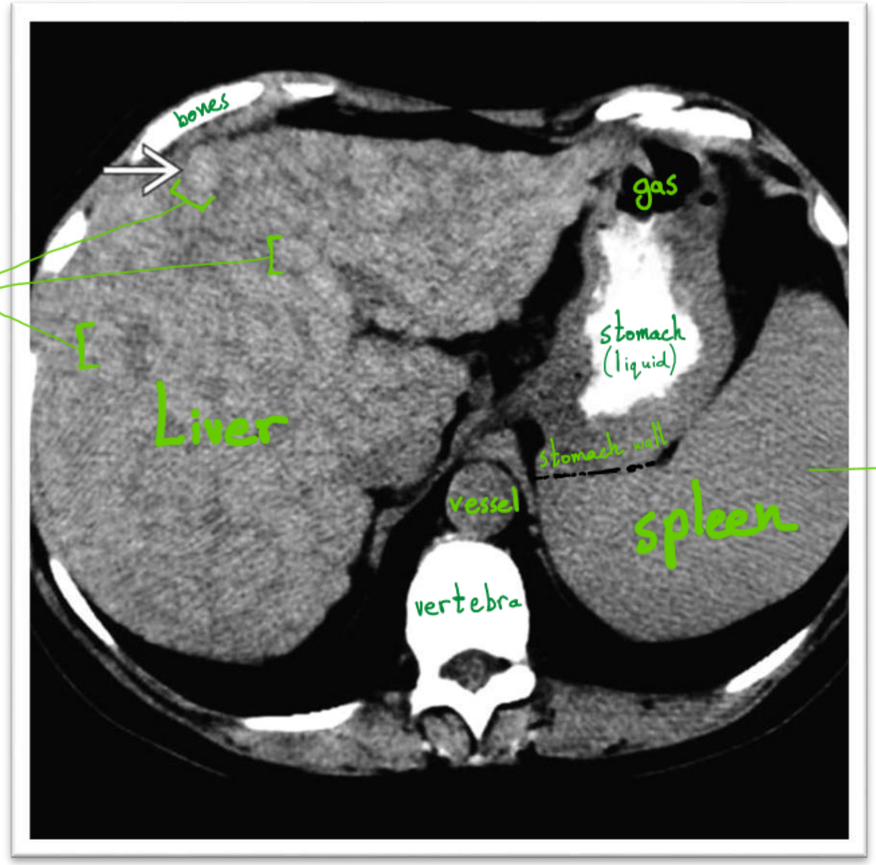
Elevated Liver Enzymes: This indicates injury in hepatocytes (specifically necrotic or damaged cells), which leads to the release of transaminase liver enzymes into the serum.

Low Albumin Levels: This reflects a decrease in blood protein levels due to poor hepatic protein synthesis. This drop affects oncotic pressure, causing fluid to shift from the intravascular to the extravascular space, which will definitely cause peripheral edema.

Prolonged INR International Normalized Ratio**:** This reflects the coagulation profile, specifically caused by a decrease in clotting factors synthesized by the liver. The patient's blood takes longer than normal to clot.

CT scan:

The **nodular appearance** of the liver indicates structural abnormality, consistent with **cirrhosis** and **shrinkage.**



This might indicate **splenomegaly (enlarged spleen)**, a sign of portal hypertension resulting from liver cirrhosis.

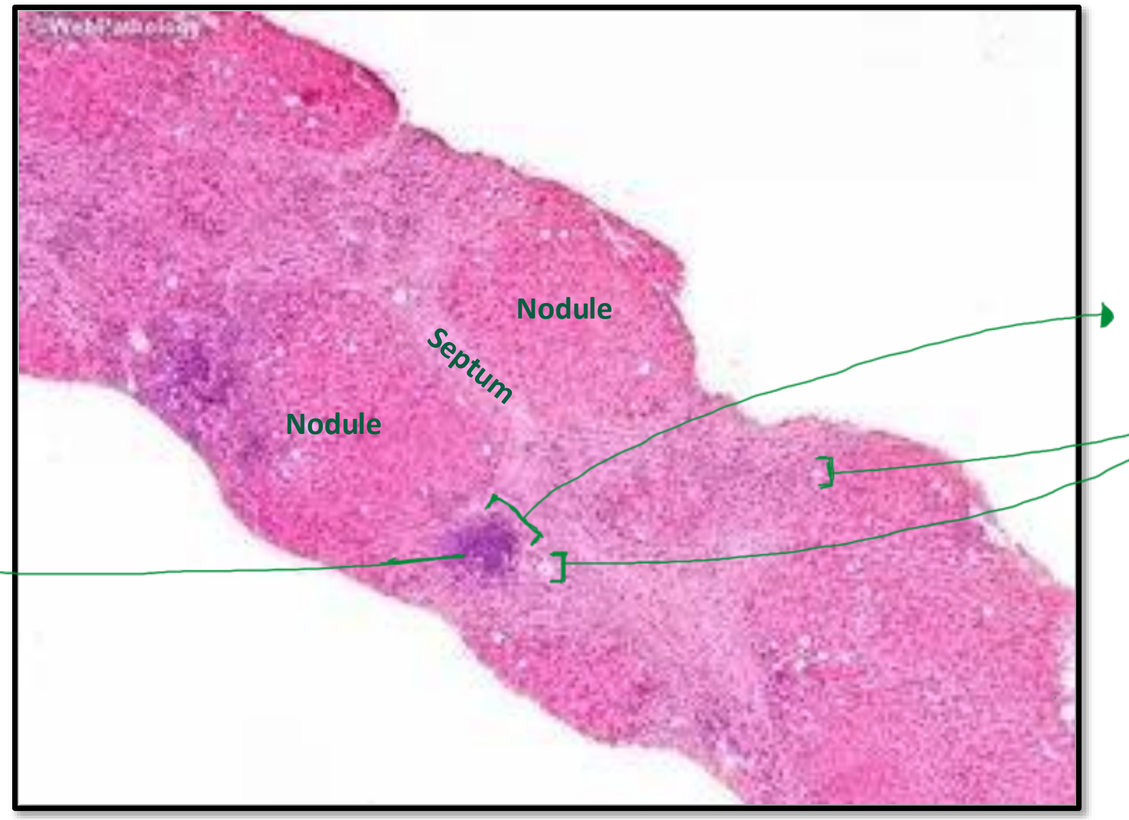
Explanation: Because the liver is scarred (cirrhosis), blood cannot flow through it easily. This causes pressure to build up in the portal vein, which backs up into the spleen, causing it to swell.

Needle biopsy:

Nodule: The large, round areas of regenerating liver tissue (dark pink) that are surrounded by fibrosis.

Septum: The lighter-colored band of scar tissue that forms a "bridge" between the nodules, indicating cirrhosis.

Lymphoid Follicle: The distinct dark purple areas of immune cells found within the scar tissue that represent active inflammation.



It is mentioned in the patient's history that he suffers from **Chronic Hepatitis C**, so some features known as **"Hepatitis C Triad"** will appear in this needle biopsy.

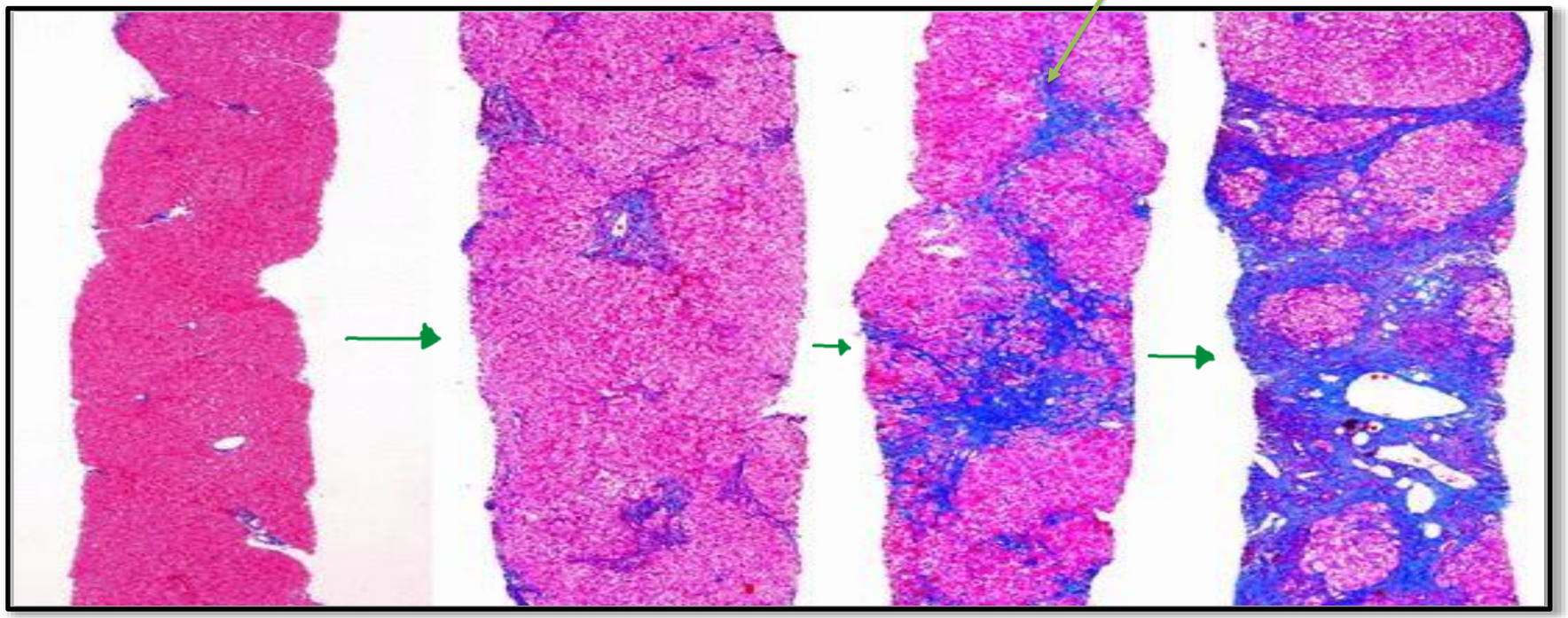
The "Hepatitis C Triad" (Diagnostic Features):

1- **Lymphoid Follicular Inflammation:** Aggregates of immune cells.
2- **Bile Duct Damage:** Injury to the bile ducts.
3- **Steatosis:** Presence of white fat deposits within the liver.

CIRRHOSIS (IMAGING AND TISSUE APPEARANCE):

Trichrome stain:

Once you start see, this collagen type 1 not 3



The difference between steatosis and steatohepatitis:

Steatosis: This is defined simply as fatty change within the liver.
Steatohepatitis: This is the most common chronic liver disease. It is characterized by an increase in glycogen and fats inside the liver cells (hepatocytes).

Grades here represent the timeline (about 15 years) of liver damage. It measures how far the scarring has spread, ranging from **Grade 0** (normal) to **Grade 4** (Cirrhosis).

Grade 0: Represents a normal liver with a completely intact architecture, showing no signs of nodules or cirrhosis. → **Grade 1** → **Grade 2-3** → **Grade 4:** This stage represents Cirrhosis. It is characterized by extensive fibrosis (scarring) that is primarily composed of Collagen Type I fibers.

1- What is the pathogenesis of cirrhosis (Fibrosis) in this patient?

- **Cirrhosis in this patient is caused by chronic hepatitis C infection, leading to:**
  - **Persistent inflammation and hepatocyte injury.**
  - **Activation of hepatic stellate cells (Kupffer cells: the tissue macrophages of the liver originally, they come from blood stream and monocytes), which produce excess extracellular matrix proteins (e.g., collagen).**
  - **Fibrosis and scarring, leading to distortion of the liver architecture and impaired liver function.**

Note: Transforming Growth Factor-beta (TGF-β) is the strongest fibrogenic growth factor, but it doesn't mean the other factors don't play role .

2- How does cirrhosis (Fibrosis) lead to the patient's symptoms?

Cirrhosis leads to:

- **Portal hypertension** (the portal BP very high), causing splenomegaly, varices, and ascites (abdominal distension). Varices are dilated blood vessels, especially around the esophagus. These varices can lead to bleeding sometimes it's difficult to control , and one of the major causes of death in patients with liver failure (life-threatening) .
- Decreased albumin production leading to decreased oncotic pressure , leading to **hypoalbuminemia and peripheral edema.**
- Impaired bilirubin metabolism, causing **jaundice.**
- **Coagulopathy** due to decreased production of clotting factors, leading to a prolonged INR.

All these act all together to cause fatality to patients with liver cirrhosis

3- What are the potential complications of cirrhosis?

Potential complications include: (All can be fatal)

- **Variceal bleeding (Esophageal varices).**
- **Hepatic encephalopathy due to the accumulation of toxic materials, affect your brain leading to a lot of problems in your capacity to stay awake**
- **Ascites and spontaneous bacterial peritonitis. (the presence of ascites alone will increase the risk of having inflammation of the fluid in the abdomen causing peritoneal inflammation peritonitis)**

Note: Hepatitis C is classified as an **oncovirus**. This simply means that it is a virus that has the ability to cause cancer.

- **Hepatocellular carcinoma(incurable cancer) . Higher risk**
- **Liver failure.**

Additional Resources:

رسالة من الفريق العلمي:

قالَ الحبيبُ -صلَّى الله عليه وسَلَّم-:
"ما لي وما للدُّنيا، ما أنا في الدُّنيا إلَّا كراكبٍ استَظلَّ تحتَ شجرةٍ، ثمَّ راحَ وترَكَها."

ربَّنا لا تجعلِ الدُّنيا أكبرَ همِّنا، ولا مبلغَ عِلمِنا، ولا إلى النّارِ مصيرَنا، ولا تسلِّط علينا من لا يرحَمُنا.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			