Liver

Liver diseases has many other manifestations, not only the liver

* Clinical manifestations from liver diseases are a reflection of most of its functions

* You should be familiar with the normal morphology to understand the disease, examine liver tissue to get the correct dx (clinical+histological)

* Liver diseases → primary: involving liver
  → secondary: // other organs

Liver

many functions → many manifestations (involving other systems)

- **Function:**

1-Metabolic : Glucose
2-Synthetic : Albumin, clotting factors …..
3-Detoxification : Drugs, hormones , NH3
4-Storage : Glycogen, TG, Fe, Cu, vit
5-Excretory : Bile

chemicals that can affect hepatocytes on long term or even short term

deals with all toxic substances that might enter the body detoxification to avoid injury & changes

triglycerides

any excess (even if it's normal) → ↓↓ & loss of function

synthesized in liver

- **Net wt. 1400 – 1600gm (2.5% of body wt)**
- **Blood supply:**

Portal v : 60 – 70%

Hepatic a : 30 0 40%

recieve substances → absorb → release

- **Microstructure**
- **Hexagonal lobules →6 acini**
- **Acinus is divided into 3 zones:**

+ detecting early dx diseases are more likely to start in one zone than the other

1-Zone 1 parynchema, hepatocytes surrounding the area closest to portal vein

Periportal areas – closet to the vascular supply

2-Zone 3 parynchema surrounding central vein

Pericentral area

3-Zone 2

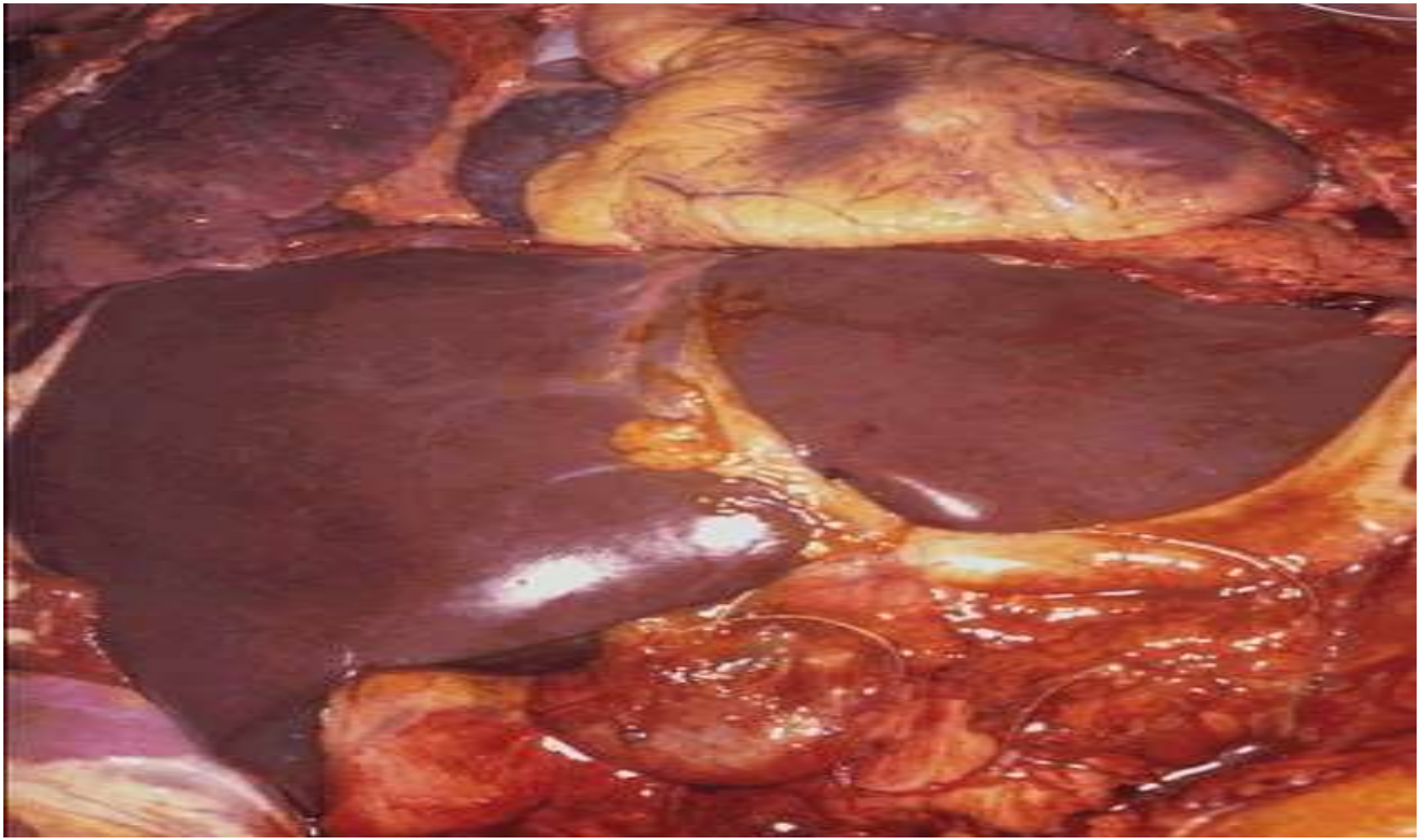
Inrermediate bet. Zone 1&2

?overlap in many diseases producing changes that might be similar and that's why we need to have a clue to reach the correct dx.

Normal Liver

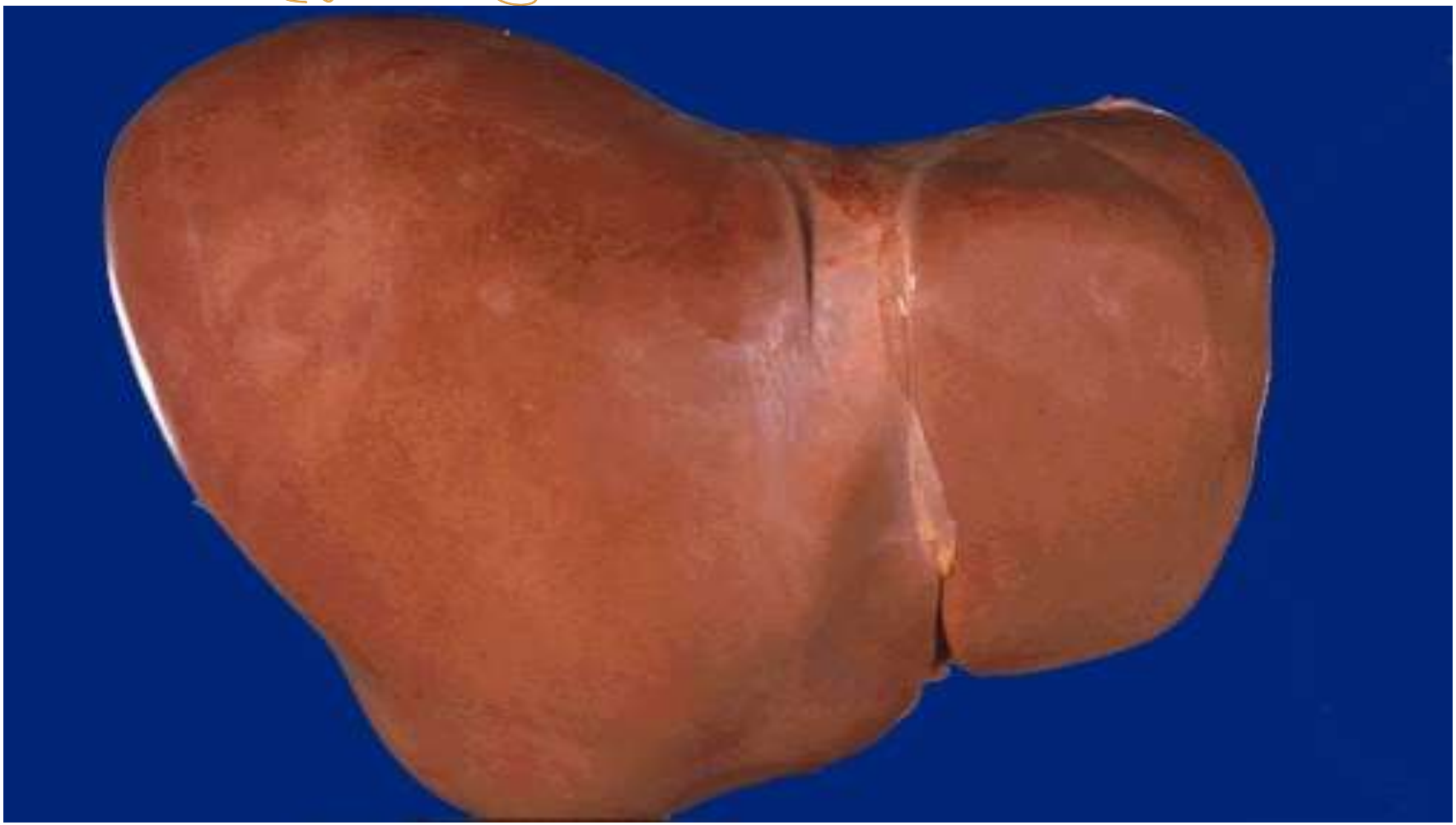
lobes: small shiny dark brown

yellow tissue surrounding // → fat



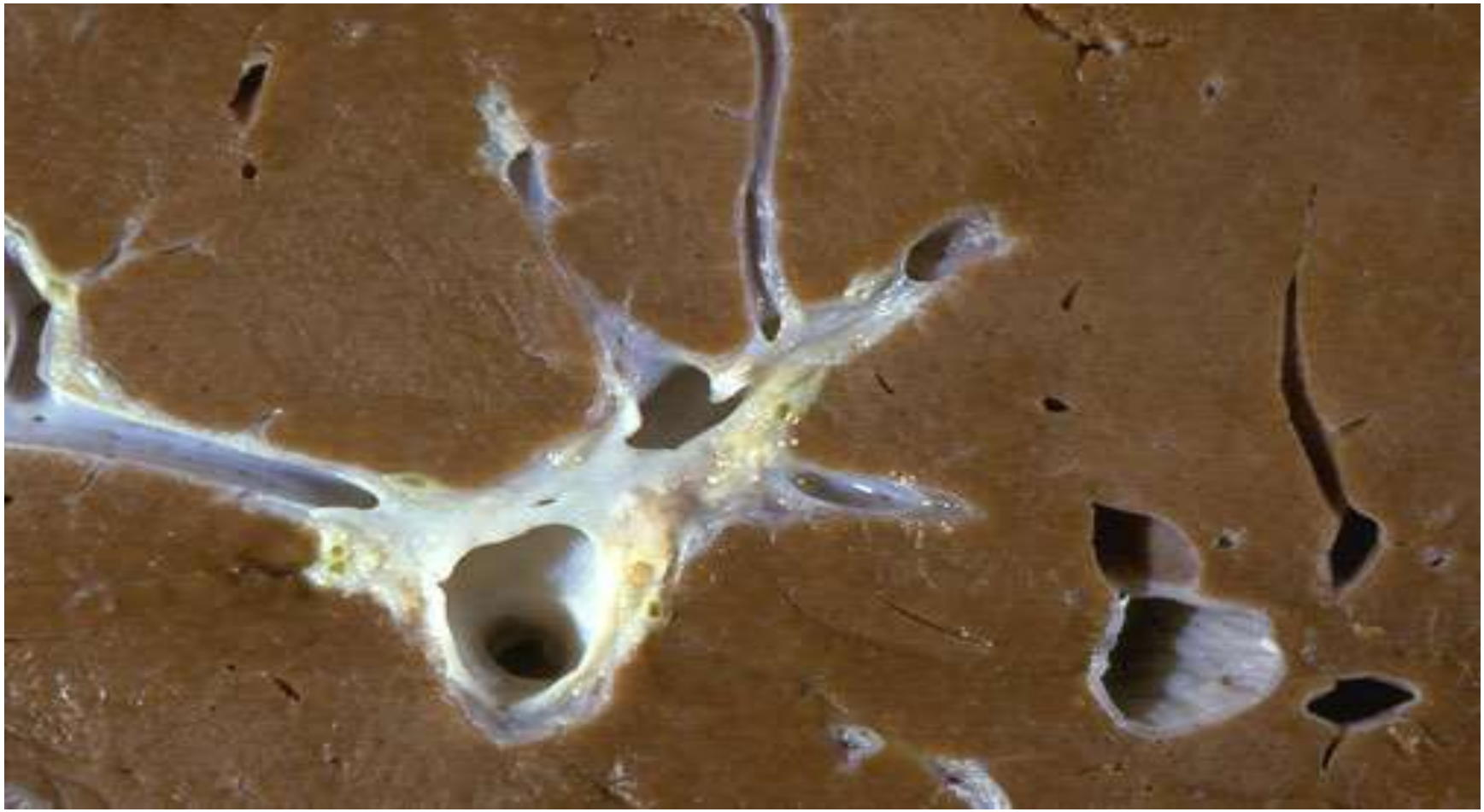
normal liver without fat

clean cut organ

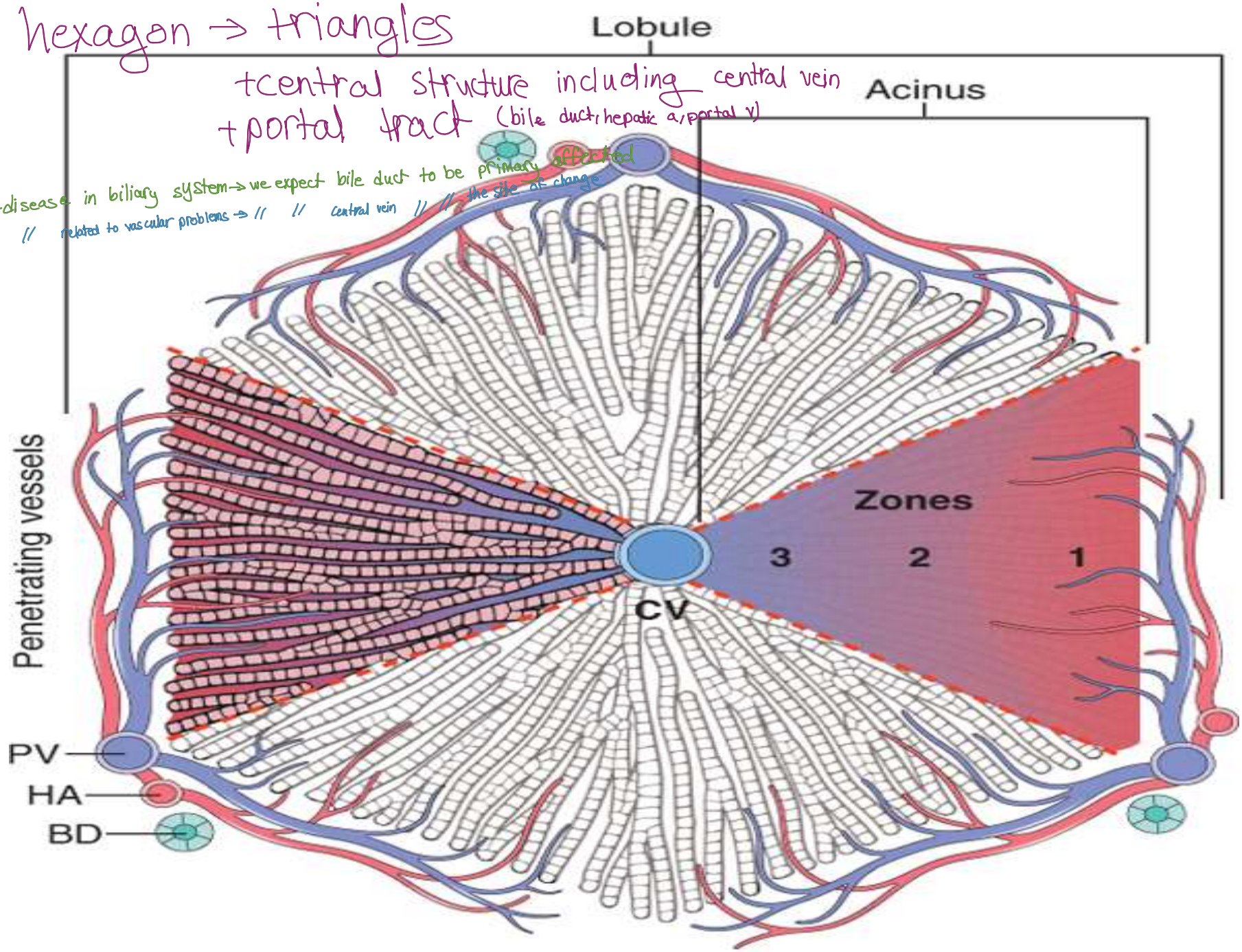


cross-sectional cut

depending on the cut, the sites might be variable.



hexagon → triangles

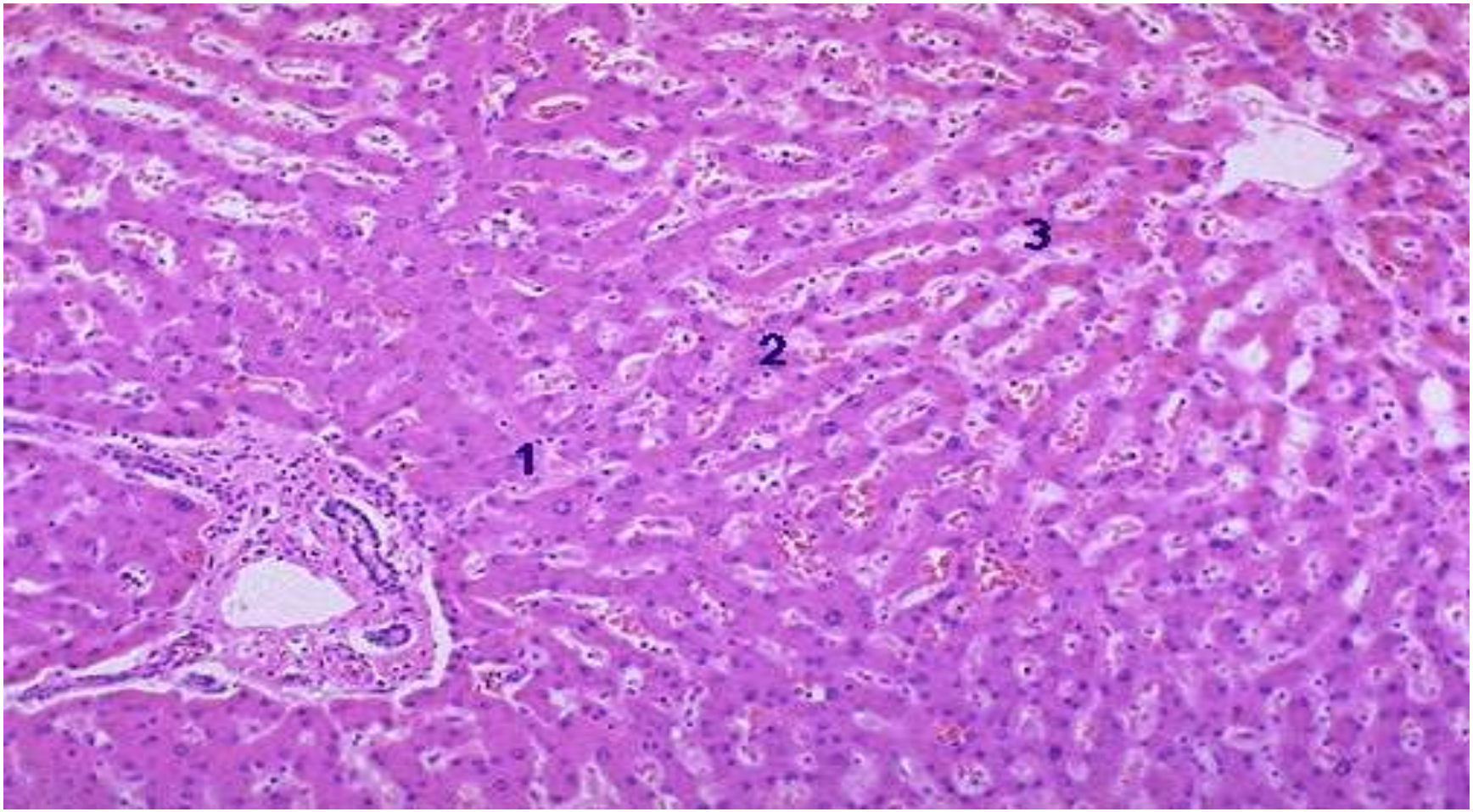


+central structure including central vein
+portal tract (bile duct, hepatic a, portal v)

*disease in biliary system → we expect bile duct to be primary affected
* // related to vascular problems → // // central vein // // the site of change

2 main structures → left: portal v
→ right: central v (pink)

cells in between
↳ liver parenchyma under microscope



Background of fibrous tissue (normal)

cells are arranged in lines
↳ 1 cell thick
?? sometimes separated by sinusoid

hepatocytes are close to those of blood (v. imp for function? hepatocytes should act directly close to blood in sinusoid
↳ has cells that act as Ⓜ 'Kupffer')

The parenbchyma is organized into plates of hepatocytes

Hepatocytes are radially oriented around terminal hepatic vein (central v.)

-Hepatocytes show only minimal variation in the overall size but nuclei may vary in size , number & ploidy esp. with advancing age

-Vascular sinusoids present bet. cords of hepatocytes

lab tests , special stains, serology

Hepatic injury

1-Inflammation (Hepatitis)

infectious or non-infectious organism
infiltration of liver by inflammatory cells
↳ (+) or others depending on the underlying disease
injury → mild / simple
→ severe / associated with more injuries
+cellular changes / degeneration of cells

2-Ballooning degeneration :

- simplest form of injury to cells? accumulation of water within the cells
- ↑size of cells - might not be associated with other features

-irregularly clumped cytoplasm showing large, clear spaces.

-Substances may accumulate in viable hepatocytes, including fat, iron, copper, minerals and retained biliary material

when cells are injured → subnormal function, starts to get rid of these toxic material(s), if it can't deal with them → accumulate → more injury
can be seen in different disease, cholestasis (deposition) in some diseases might be more prominant

3-Steatosis (fatty change)

-not diagnosis by itself, we need to find underlying cause
- depending on the fat deposits in cytoplasm of hepatocytes:

-classically a manifestation of alcoholic liver disease

viral infx, drugs (hepatitis C)

microvesicular:ALD,Reye syndrome,acute fatty change of pregnancy

macrovesicular:DM,obese

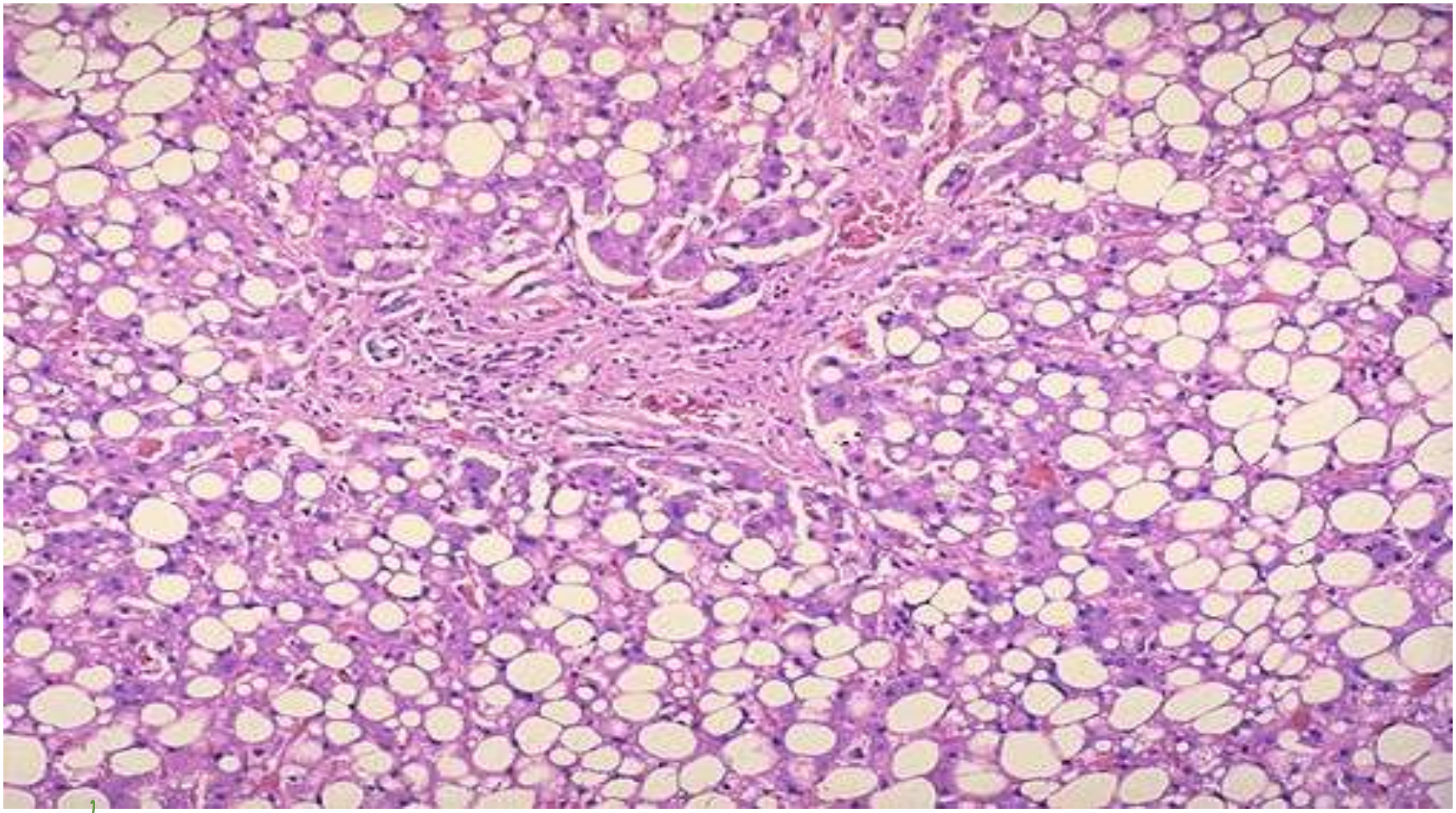
(metabolic)

reversible but also induce injury

fatty change

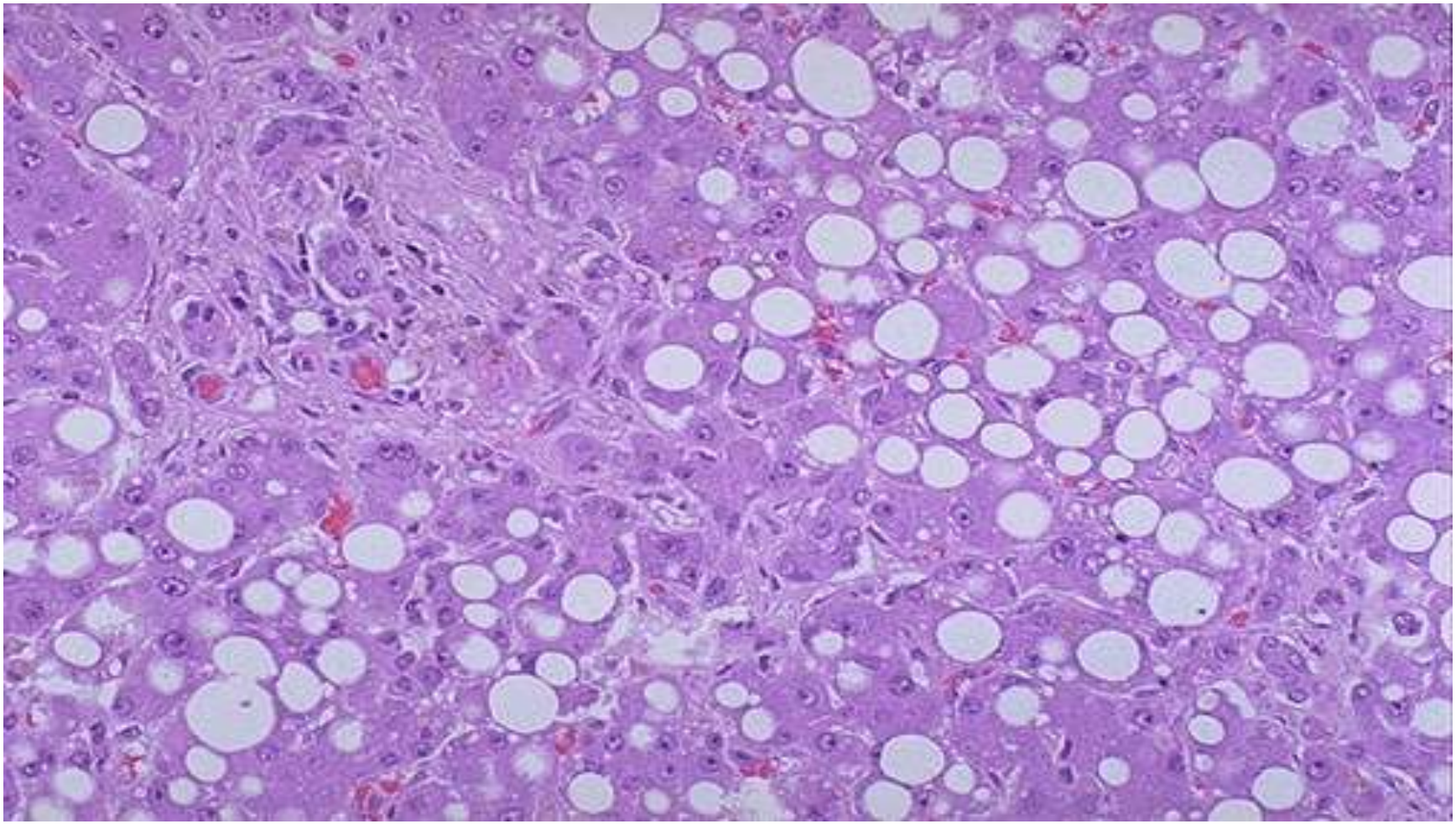
softer

severe? involves most of the hepatocytes



↳ empty spaces

during processing
the substance we use dissolves fat
irl it's filled with fat, not empty



depending on severity, the loss of function will be variable

clue about
different forms → outcome/progression
examine tissue whether there's necrosis or not

imp? indicates severity of disease

4-Necrosis

severe involves different cells
different types

- Depending on the type:

related to ischemia
Coagulative necrosis :around central v.

Councilman bodies

individual dead cells scattered between viable cells, can be seen in different types of diseases, such as: alcoholic liver disease, v. imp in diagnosis, liver can look smaller indicate previous exposure of liver to sth, mostly drug? uptake occurs along a long period of time, induce drug-based injury to the hepatocytes.

Lytic necrosis

abscess
infectious, viral

Depending on the cause

Ischemic

Toxic

common

each zone tells us about the severity of the disease & possible necrosis

-depending on location

Centrilobular necrosis: surrounding central vein, usually related to a vascular problem

Mid zonal :

peripheral Periportal : interface hepatitis (infectious necrosis)

Focal:

not commonly used

Piece meal necrosis

IMP TO KNOW + FOLLOW UP

bridging necrosis

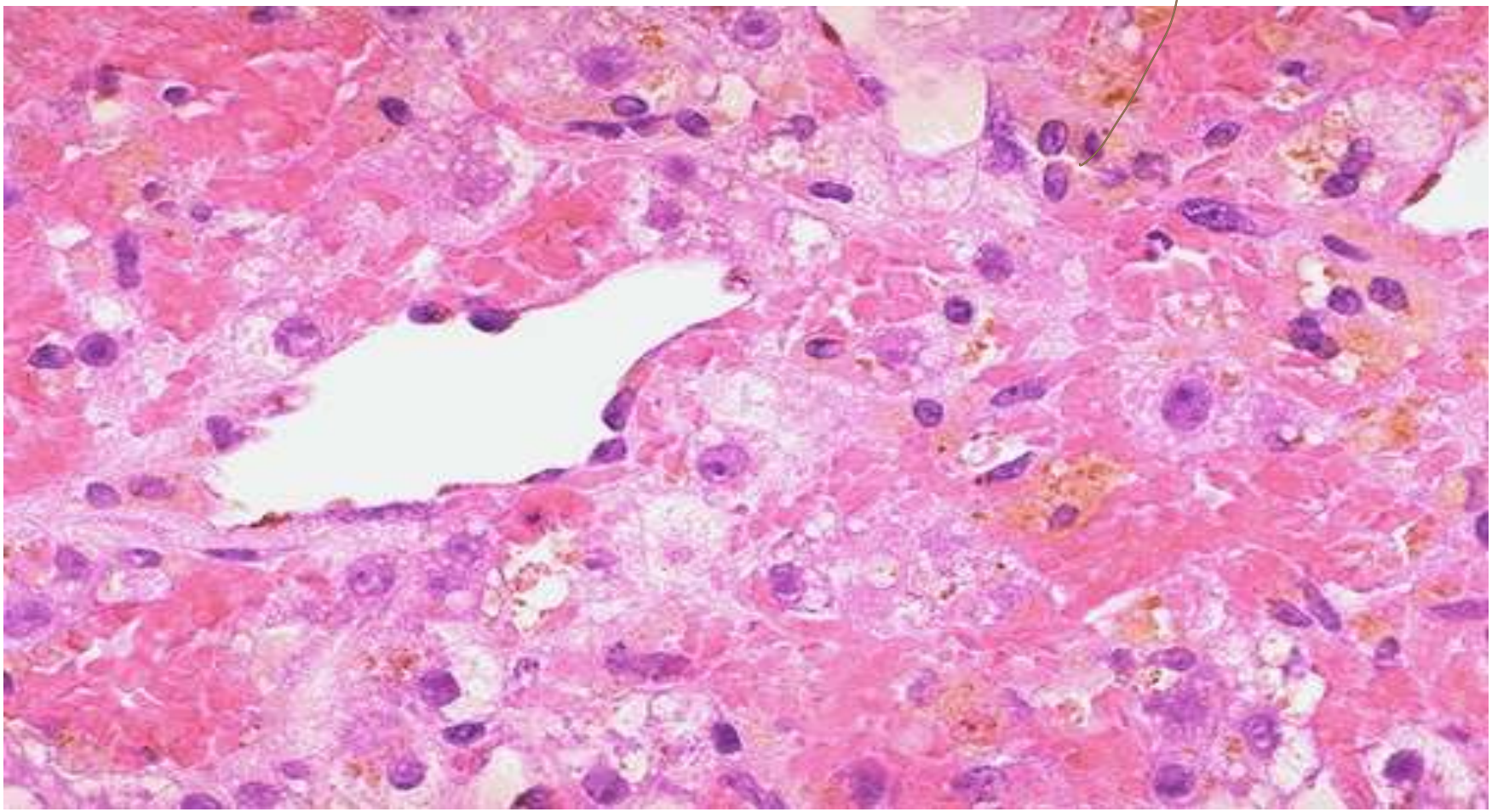
- V. imp aspect regarding necrosis? possibility to develop fibrosis or cirrhosis
- cirrhosis is a terminal irreversible complication of liver disease
- connects between 2 structures, either central v. to central w/portal area or portal area to portal area
- progressive, leads to involvement of cirrhosis.

Diffuse:

massive & submassive necrosis

- evaluation of the extent of necrosis is very important? extensive loss of hepatocytes → loss of hepatic function or hepatic failure
- liver has ↑ regenerative capacity, but liver with extensive loss of hepatocytes can fail, otherwise a small amount can carry minimal function to prevent hepatic failure, even though having a massive or submassive indicates severity

NOT all cells are viable, some are lost ? depositions of different materials



↑ capacity

5-Regeneration

-evidenced by increased mitosis or cell cycle markers.

lost cells should be compensated by regeneration in typical cases

→ stains that show activity of cell

-the cells of the canal of Hering are the progenitor for hepatocytes & bile duct cells (oval cells).

+ epithelial cells

6-Fibrosis

- normally very minimal, any increase of fibrous tissue # or appearance indicates abnormality.
- imp. in evaluation of disease process if the patient can be cured or at risk of chronicity
- trx should target this possibility in order to decrease the progression.
- fibrous tissue can appear anywhere in liver

-*portal or periportal fibrosis*

-pericentral- around the central vein.

-*pericellular fibrosis* or fibrous tissue may be deposited directly within the sinusoids around single or multiple hepatocytes

-*bridging fibrosis* possibility of developing cirrhosis

bridging fibrosis

can lead to development of

7-Cirrhosis formation of nodules that change the whole architecture of liver; irreversible, permanent

micronodular

Macronodular

8-Ductular proliferation ★diseases affecting biliary system, ↑#bile ducts in portal area, normally it's 1-2 per portal tract
↳associated with obstruction to overcome

ALL OF THESE FEATURES SHOULD BE EVALUATED FOR DIAGNOSIS

DDX !!
to interfere and help the patient

severe

Hepatic Failure

-It results when the hepatic functional capacity is almost totally lost (80 – 90%) even small #hepatocytes can carry out normal functions

-**Causes** many

1.Massive hepatic necrosis of liver parenchyma in fulminant hepatitis

-Fulminant viral hepatitis Hepatitis B, C, D, E *pregnant , we have to exclude it in endemic areas.

-Drugs & chemicals We should take drugs history since they can induce injury especially when used for a long period of time.

acetominophen (paracetamol) ↑ overdose usually associated with suicidal uptake

halothane anesthetic ,sudden onset of massive hepatic failure &complications just from the 1st time suddenly

anti TB drugs

CCL4 poisoning (toxins)

Mushroom poisoning

acute

2-Chronic liver disease more common, after years of having chronic disease

commonly caused by cirrhosis → end-stage hepatic failure

due to loss of function, liver might look normal

3-Hepatic dysfunction without overt cirrhosis

- -Reye's syndrome
- -Tetracyline toxicity
- -Acute fatty liver of pregnancy

-sudden liver failure in young children after viral infx.
-normal architecture & cells
-missed if not suspected

Clinical features

- reflection of function loss, and severity depends on loss of function
- We have to examine

1-Jaundice — Not all patients; Yellow coloration of skin & sclera, clear & obvious

2-Hypoalbuminemia → edema — since hepatocytes are injured and can NOT function

3-Hyperammonemia — urea cycle occurs in liver & ammonia (product of metabolism) can NOT be drained
↳ toxic, can injure other parts such as brain, special odor

4-Fetor hepaticus (musty or sweet & sour)

5-Palmar erythema — discoloration of palm (pink) ? ↑ estrogen levels, in males have different effects? deviation of metabolic towards hormones' surfaces

hyperestrogenemia

6-Spider angiomas — pulsating small arteries with radiating thin tortuous capillaries; also related to estrogen

7-Hypogonadism & gynecomastia — males
atrophy of testicles
enlargement of breast

v. serious complications

Consequences:

1-Multiple organ failure (gives a clue about the severity of the condition) kidneys & lung ? accumulation of different toxic substances (such as ammonia) (injury in alveolar cells → lung failure)

2-Coagulopathy → bleeding ? loss of clotting factors that are synthesized in liver (*cirrhosis)

def. factors II, VII, IX, X

3-Hepatic encephalopathy ? neurological manifestations due to liver failure → accumulation of ammonia (toxic, crosses BBB)

(abnormal movement, sensory loss) ↓level of conseiousness

Rigidity

Hyperreflexia

EEG changes

Seizures

Asterixis

4-Hepatorenal syndrome

Renal failure in patients with severe liver disease with no morpholagic or functional causes for renal failure

- kidneys are known to be normal, function normally, not affected by the initial process that caused liver failure
- We expect recovery of renal & restore post-function if the hepatic failure is corrected