GIS

Pathology

|Modified slides

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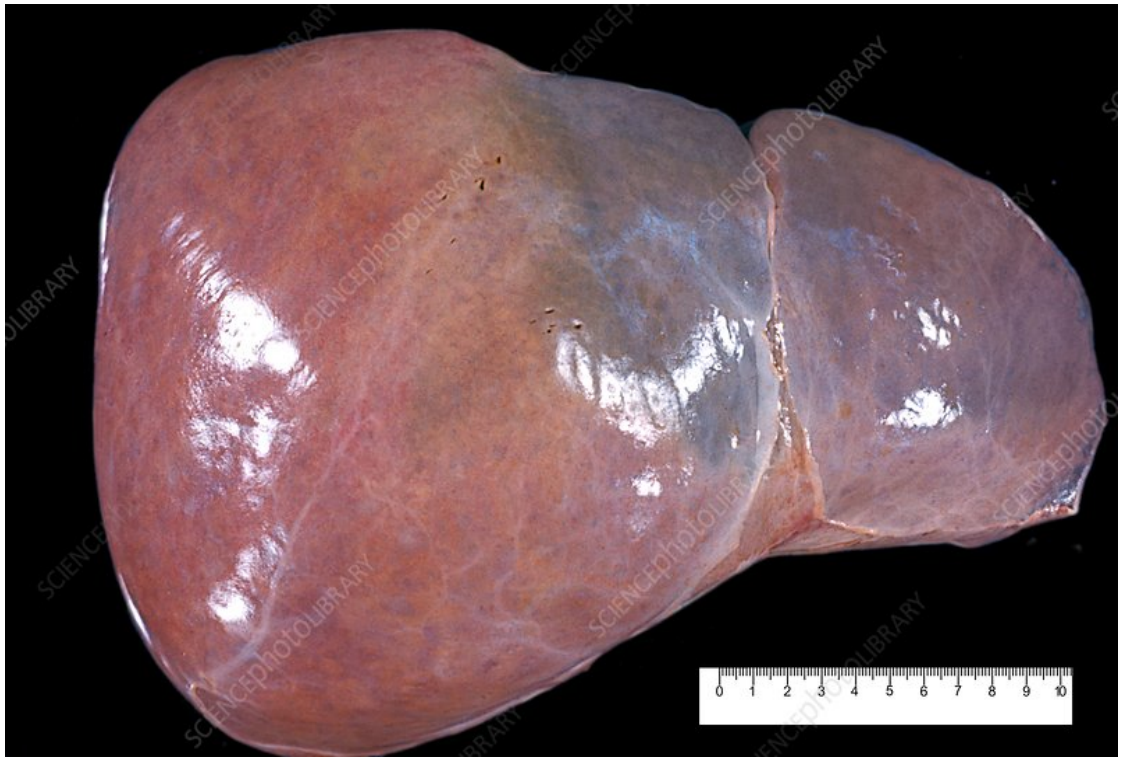
والاضافة مننا باللون الاحمر
لتعميق الفهم

LECTURE 1

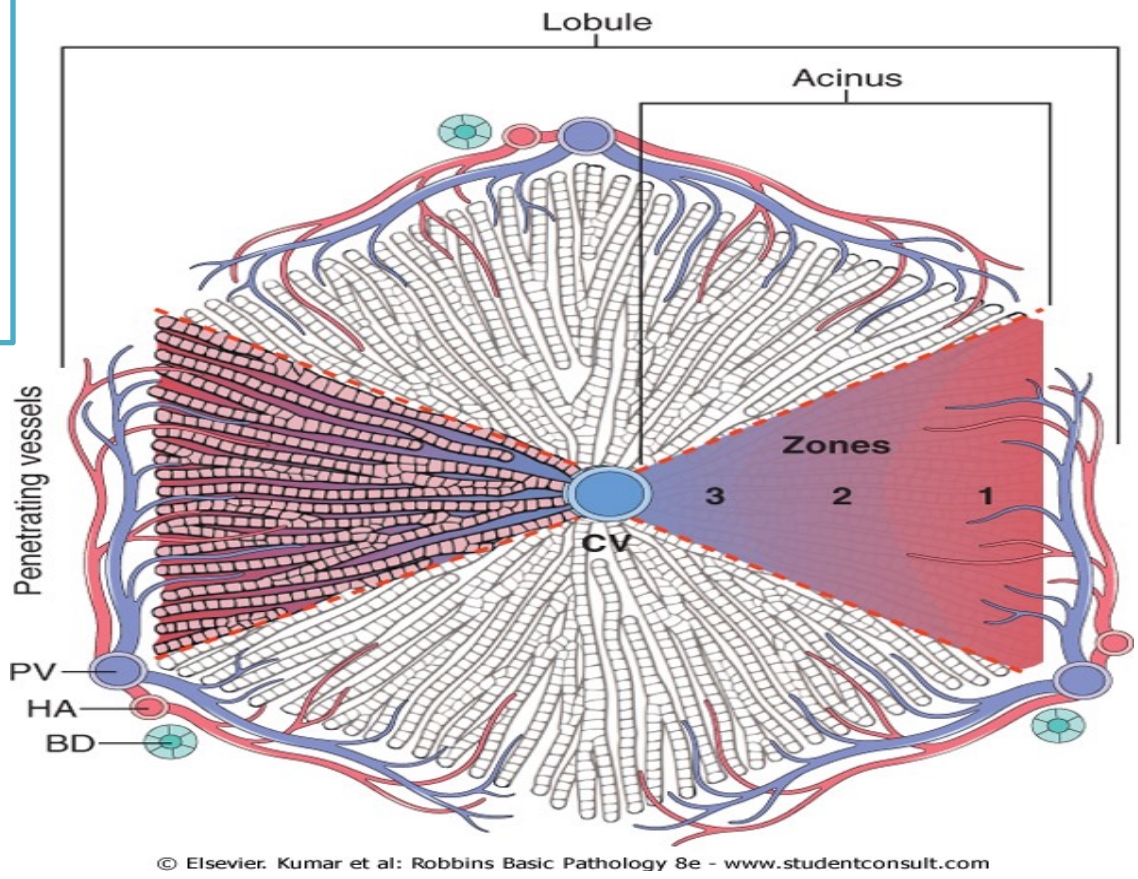
Liver is one of the most important organs in the body as it has many functions (metabolism ,detoxification,…) so any injury to it may lead to general diseases in the body (down in the picture you can see a gross image of the liver : a brown smooth structure)

Let's start with the definition of parenchyma: which is the functional tissue of a certain organ and in our case it is mainly built of hepatocytes



The functional unit of the liver is a hexagons structure (The lobule) which is composed of 6 acini that represents the liver parenchyma. Each acinus is composed of plates of hepatocytes radiating to the portal triad (PV: portal vein ,HA: hepatic artery branch (arteriole) ,BD: bile duct) surrounding a CV: central vein. Sinusoids are vascular layers separating cords of hepatocytes .

Each acinus is subdivided into:-
zone 1 (periportal):the usual entry of inflammations.
Zone 2(midzone)
Zone 3 (pericentral): most liver diseases occur here.



Note :-
all the previous structures represent the parenchyma of the liver

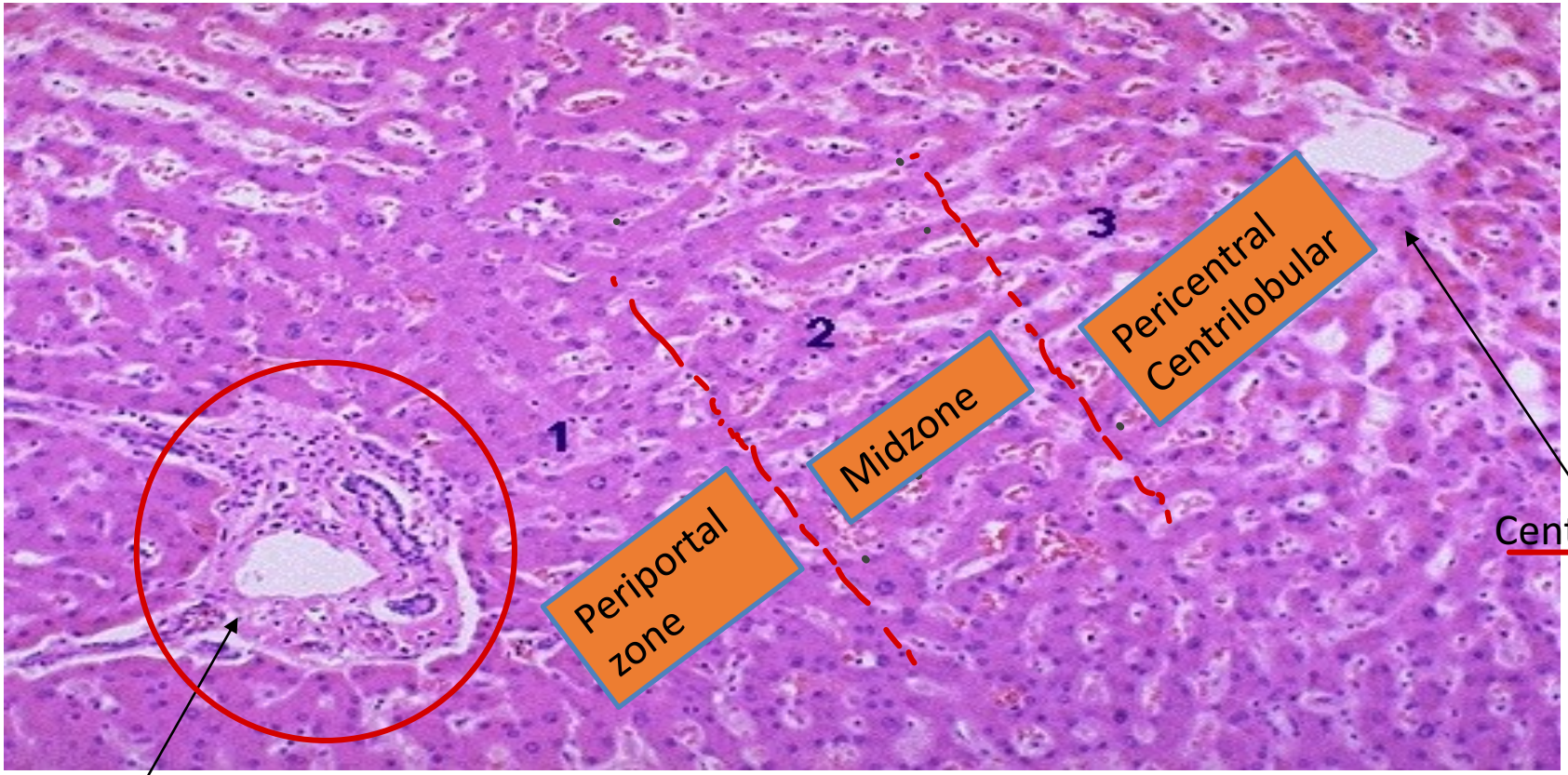
The parenchyma is organized into plates of hepatocytes.

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

This is a microscopic image of an acinus :-



(It is important to look at each zone as certain diseases occur in particular zones rather than the other. However, aggressive diseases affect all three zones)

Hepatic Injury

1 Inflammation (Hepatitis)

(which is manifested by the infiltration of the inflammatory cells)

2 Ballooning degeneration :

(Enlargement and death of hepatocytes)

-It describes irregularly clumped cytoplasm showing large, clear spaces(within the hepatocytes).

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

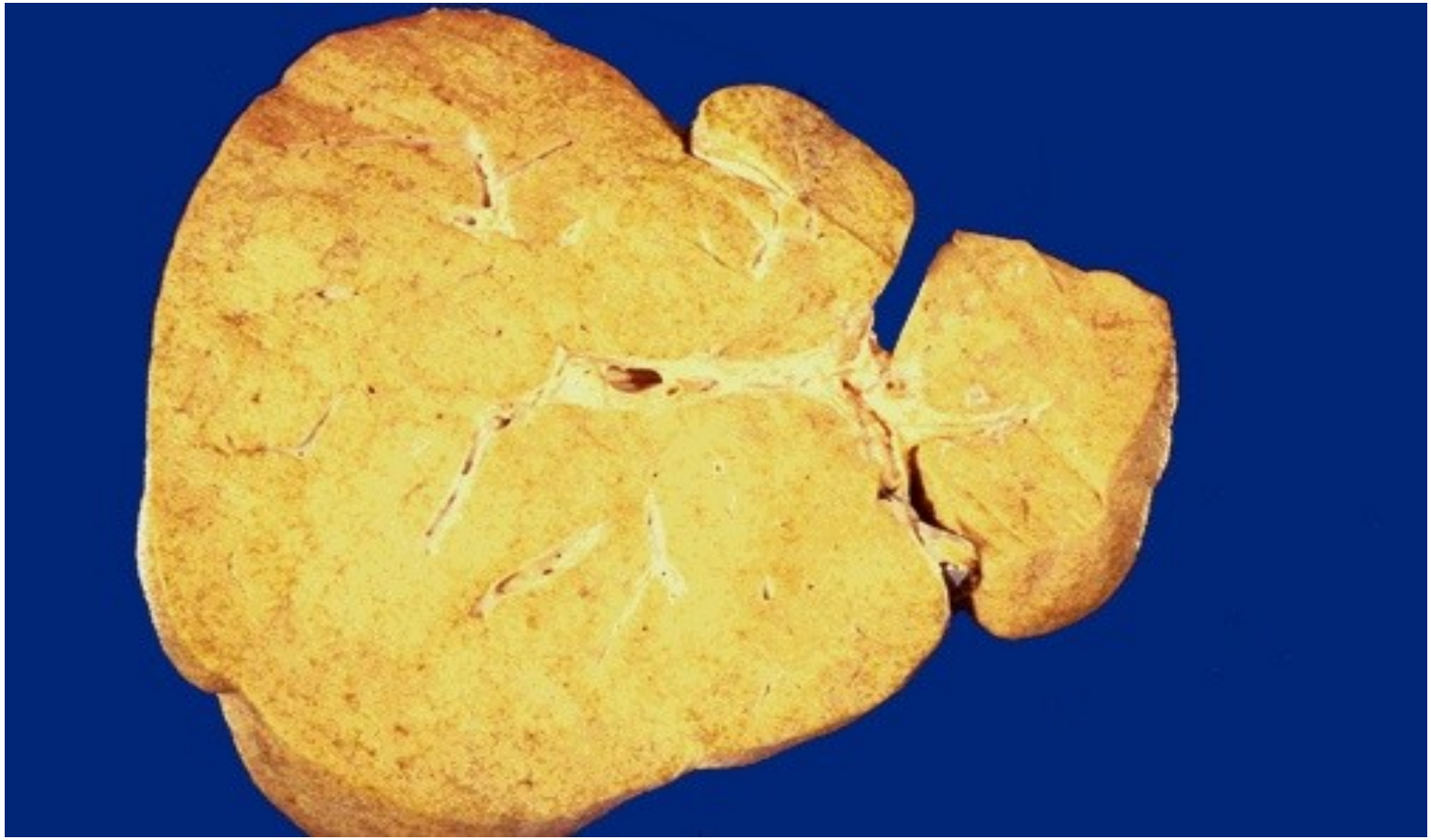
3-Steatosis (fatty change):

(Accumulation by infiltration of fat droplets in the parenchyma),it is divided into two types that may help us to know the specific disease that took place:

- Microvascular (presence of numerous small vesicles of fat):ALD (Alcoholic Liver Disease),Reye syndrome(using of aspirin with viral infection in children), acute fatty change of pregnancy .
- Macrovasicular (large globules of fat) :DM, obesity .

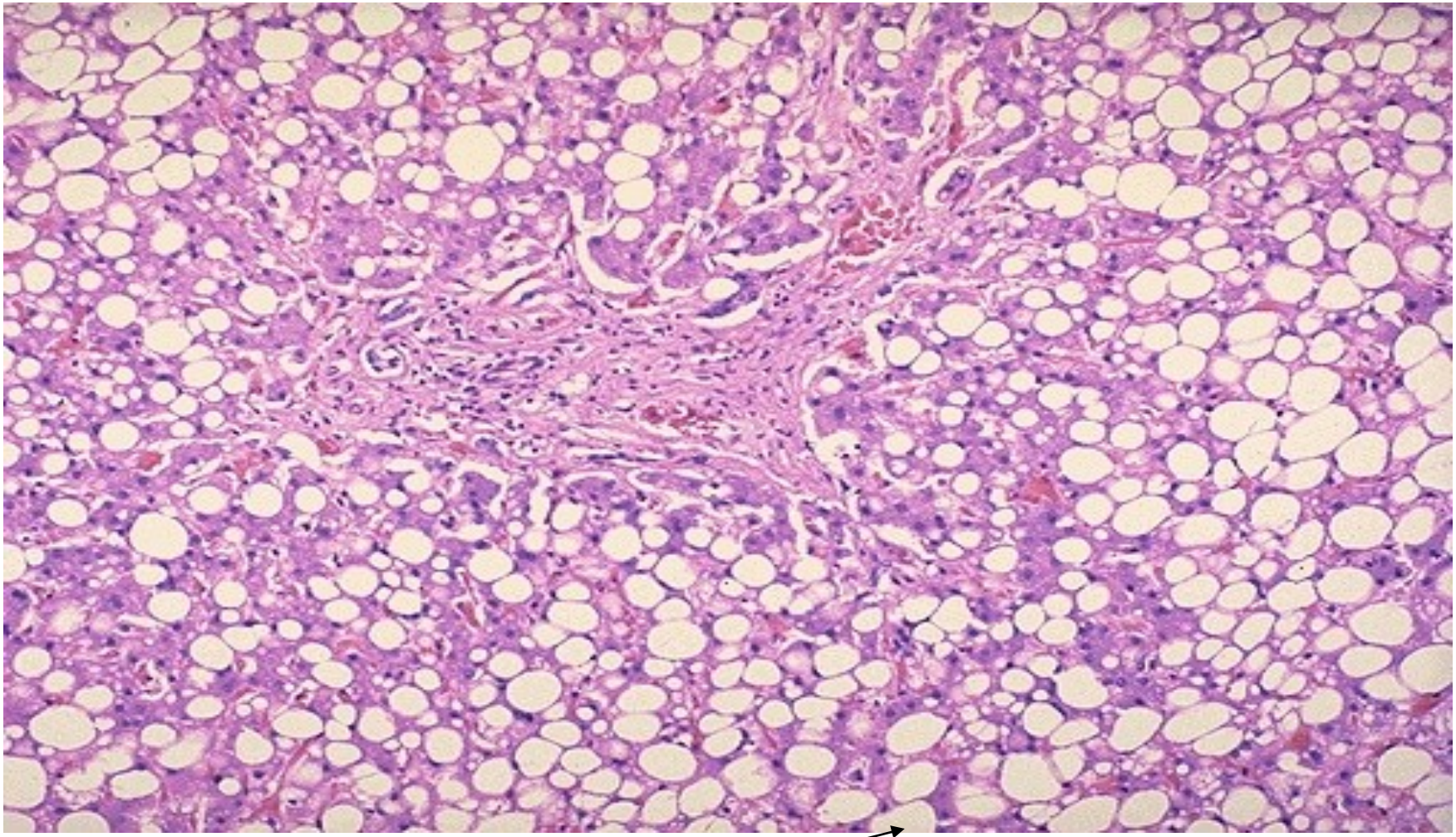
Fat accumulation begins in zone 3

Fatty change



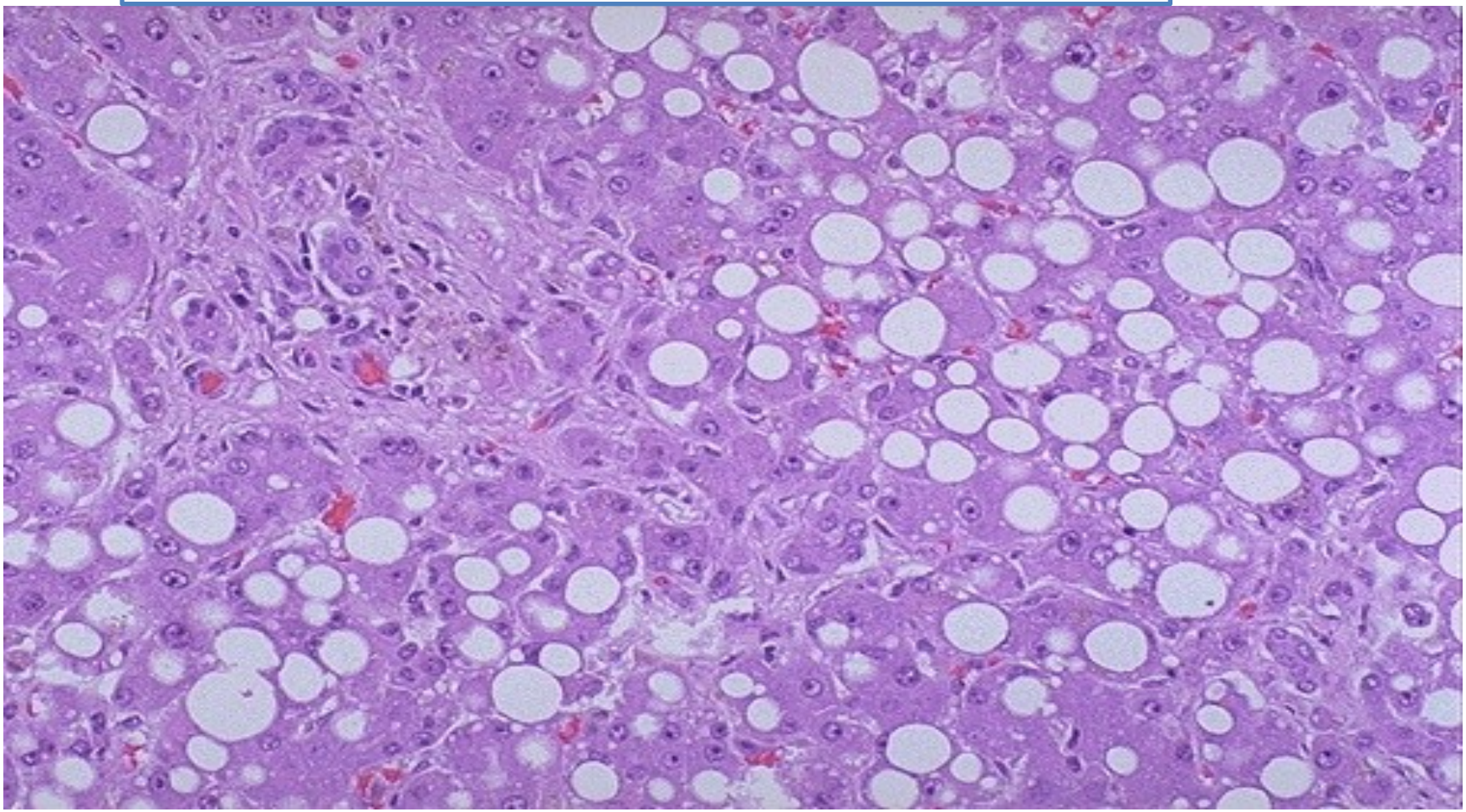
Note the change in color to yellow , and the structure to soft greasy consistency

-Microscopic image of fatty liver:-
-this is a severe form (you can see that almost all hepatocytes has fat accumulation).



8 Look at the fat infiltration within the cytoplasm of the hepatocytes

This is a higher magnification of the last slide :
it represents a macrovascular fatty change



Note:-
Microvascular fatty change may lead to macrovascular with more accumulation of fats

4-Necrosis

-We must be very curious and specific in evaluating necrosis ,cause and extensity , as it is an indication of the severity of the disease (very hard disease-->necrosis) and it is a very important step in transforming a disease into chronic one

Divided to many categories:-

- **Depending on the type:**

*Coagulative necrosis (caused by vascular problem): around central vein

*Councilman bodies (Severe acute or Chronic Injury may produce individual apoptotic hepatocytes scattered among the viable cells with prominent eosinophilic appearance. They Are important because they may occur without any other features or diseases ,so if we can see them that is a high index of previous injury)

*lytic necrosis (infectious agent usually and associated with liquefactive necrosis)

-Depending on the cause

* Ischemic
* Toxic : (Because liver is the place of metabolism ,so it's exposed to toxic metabolites)

-Depending on location

*Centrilobular necrosis (zone 3):(ischemic cause)

*Mid zonal

*Periportal (zone 1) : (occur during an inflammatory process (refer to slide 2) which may extent to other zones in parenchyma in a situation called **Interface hepatits**)

*Focal:

-Piece meal: (An old name of **Interface hepatits**)

-Bridging necrosis :necrosis that connect between two structures (I.e:CV&CV) ,and is important to evaluate because it increases the incidence of developing fibrosis (to be explained)

*Diffuse:

-Massive:(most hepatocytes involved)

-Submassive necrosis: (viable cells are still present)

5-Regeneration:

-evidenced by increased mitosis or cell cycle markers.

-(Important to know that the liver has a very high capacity for regeneration even with big injuries, so if there is still 10% viable cells in the parenchyma it can do its work as it can increase its capacity of function dramatically)

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

Extra information (black from doctor):-

Biliary tree

This is a system consisting of channels that carries bile from the source, this being the hepatocytes, all the way to the gallbladder and intestines. The epithelial cells lining this system are called cholangiocytes.The hepatocytes secrete bile into the bile canaliculi...These canals are lined by both hepatocytes and cuboidal cholangiocytes. The flow of bile is opposite to that of the blood and the canals of Hering are capable of contracting and assisting this flow towards the portal canal. The canals of Hering also posses hepatic stem cells(oval cells), which represent the source of hepatocytes and cholangiocytes.Oval cells only appears in case of injured liver when hepatocyte proliferation is inhibited by toxins or genetic changes

6-Fibrosis

(High index of chronicity (must preserved carefully) caused by severe injury to liver parenchyma and is irreversible) divided into:-

-portal or periportal fibrosis

-pericentral- around the central vein.

-bridging fibrosis

7-Cirrhosis (chronic irreversible case):-

*Micronodular&*macronodular

8-Ductular proliferation:-

(Is a case where biliary ducts largely proliferate to overcome some cases (mostly obstruction of certain ducts))

Hepatic Failure

-It results when the hepatic functional capacity is almost totally lost (80 - 90%) (as less than that can be compensated)

-**Causes**

1.Massive (acute) hepatic necrosis:-

-Fulminant viral hepatitis

-Drugs & chemicals:-

(liver injury is most common with drug toxicity, so keep in mind once you see any case of liver disease think firstly about drugs the patient is taking).Examples:-

1- Acetaminophen
2- Halothane (anesthetic agent)
3- Anti-TB drugs
4- CCL4 poisoning
5- Mushroom poisoning

2-Chronic liver disease:-

(more common than acute)

Note:-
First two can be manifestoed under the microscope

3-Hepatic dysfunction without overt (apparent) cirrhosis:-

(These disease has almost no microscopic manifestation. So, it might look normal under the microscope , and the failure is only functional)

-Reye's syndrome

-Tetracycline toxicity

-Acute fatty liver of pregnancy

4-Hepatorenal syndrome:-

(A failure in the kidney only because of a liver disease ,so if the drug is both toxic for liver and kidney it isn't considered Hepatorenal syndrome)

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

Massive hepatic necrosis

-Fulminant hepatic failure from the onset of symptoms to hepatic encephalopathy (within 2 -3 wks).

-Subfulminant (within 3 months).

Causes:

1-Viral hepatitis 50 - 65% (B, B-D, A,C hepatitis)

2-Drugs & chemicals 20 - 30% → Most important

3-Heat stroke

4-Hepatic vein obstruction

5-Wilson disease (excessive deposition of copper)

6-Acute fatty liver of pregnancy

7-Massive malignant infiltration

8-Reactivation of chronic HBV hepatitis on HDV superimposed infectio

9-Autoimmune hepatitis(rare)

وَاصْبِرْ لِحُكْمِ رَبِّكَ فَإِنَّكَ بِأَعْيُنِنَا
وَسَبِّحْ بِحَمْدِ رَبِّكَ حِينَ تَقُومُ