Alcoholic liver disease

Learning objectives

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Alcoholic liver disease:

Epidemiology:

1- The risk of alcoholic liver disease is variable (not every one who drink heavily will develop liver disease).

2-Only 10% of alcoholics have evidence of cirrhosis at postmortem.

3- Alcoholic liver disease does not occur below a threshold of 21 units/ week in women and 28 unit/week for men.

4- Most individuals with liver disease will have drunk heavily for >5 years.

5-The average of alcohol consumption of an individual with cirrhosis is 160 g/d for 8 years.

6-There is no clear linear relationship between dose and liver damage.

Risk factors for alcoholic liver disease:

1- Drinking patterns: type of beverage drunk does not affect risk, but liver damage is more likely to occur in continuous rather than binge drink.

2-Gender: the incidence of alcoholic liver disease increase in women. (Low body mass).

3- Genetic: alcoholism is more common in monozygotic than dizygotics. However, polymorphisms in the gene-coding enzymes involved in alcohol metabolism, TNF-α, aldehyde dehydrogenase(ALD), have yet to be linked to alcoholic liver disease.

4- Nutrition: study in animals given a choline-deficient diet are more likely to develop alcoholic liver disease , vitamin A and E deficiency.

Alcohol type	%	amount	units
Beer	3.5% 9%	440ml (1 pint) =	2 4
Wine	10%	125ml	1

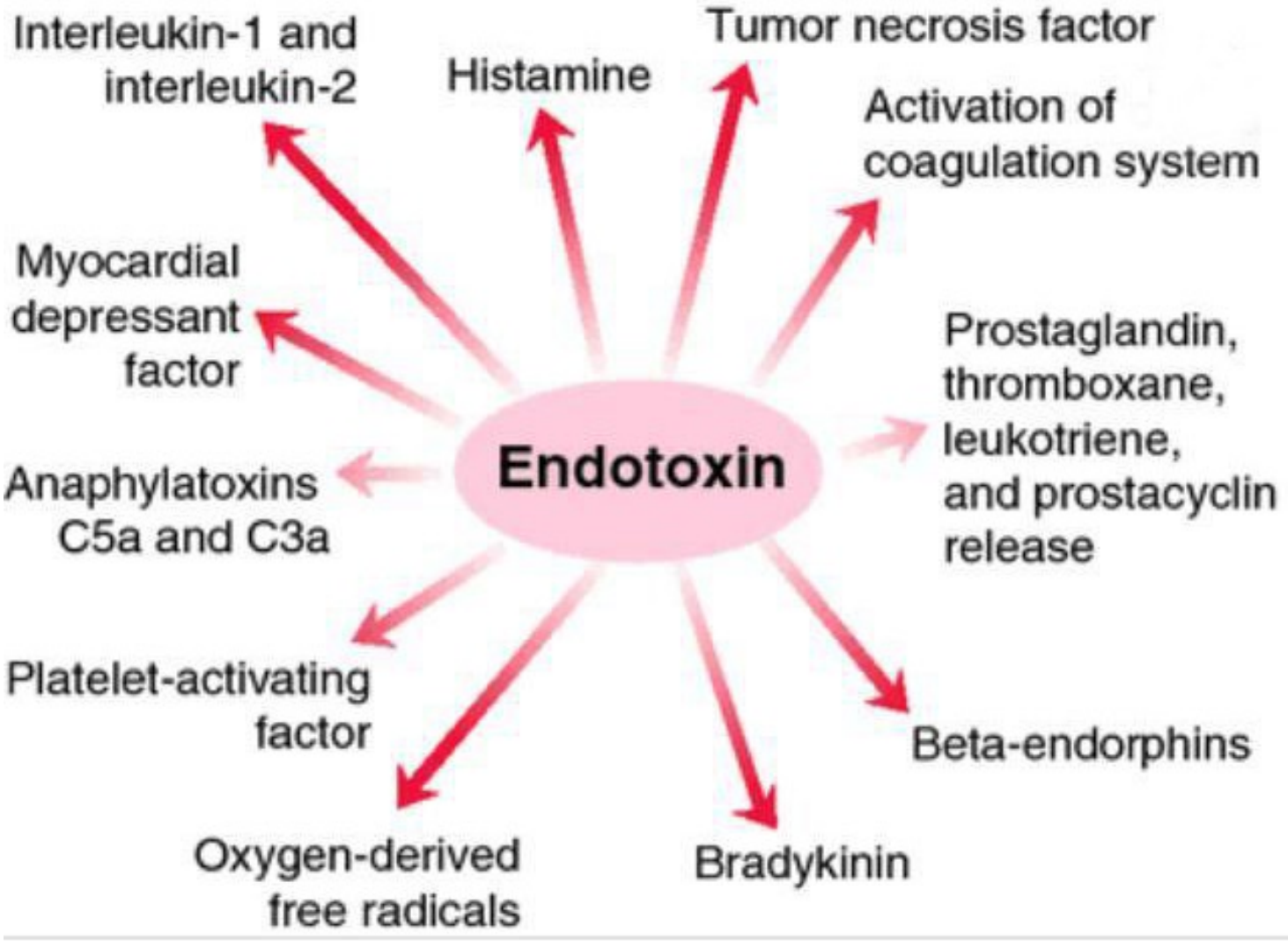
1 unit = 8gm

Aetiology: alcohol metabolized exclusively by liver

1- 80% of alcohol is metabolized by mitochondrial enzyme, Alcohol dehydrogenase (ADH) to acetaldehyde which produce cell injury by activation of the immune systems.

2- 20% metabolized in smooth endoplasmic reticulum by oxidase enzymes.

3- Cytokinase: increase endotoxin via increase gut permeability, increase TNF-α from monocytes, increase IL1, 2,6 and 8. Cytokines are also involved in fibrogenesis.


Interleukin-1 and interleukin-2
Histamine
Tumor necrosis factor
Activation of coagulation system
Myocardial depressant factor
Endotoxin
Prostaglandin, thromboxane, leukotriene, and prostacyclin release
Anaphylatoxins C5a and C3a
Platelet-activating factor
Beta-endorphins
Oxygen-derived free radicals
Bradykinin

Pathology:

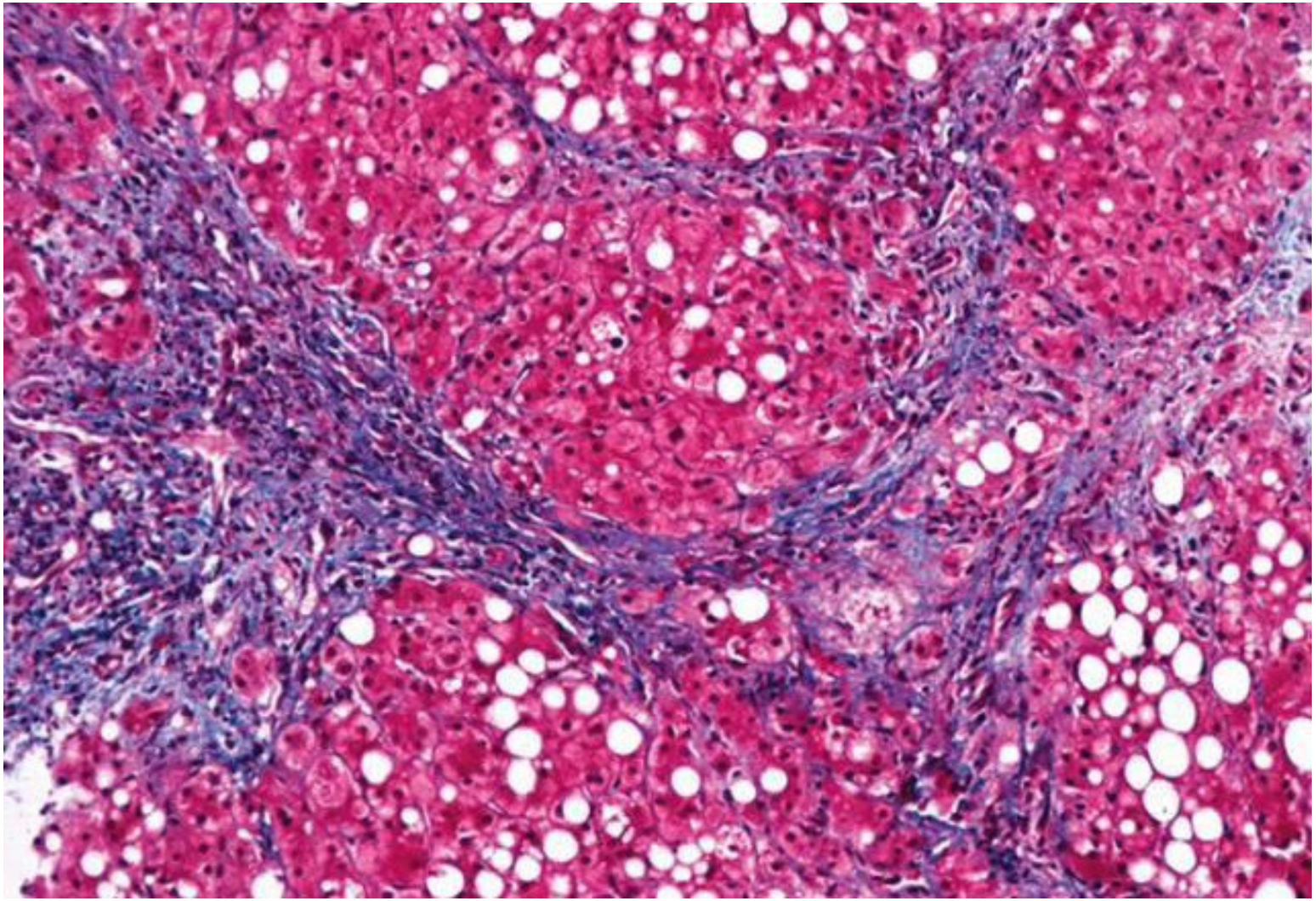
1- Alcoholic hepatitis (Lipogranuloma, neutrophil infiltration, Mallory's hyaline, pericellular fibrosis).

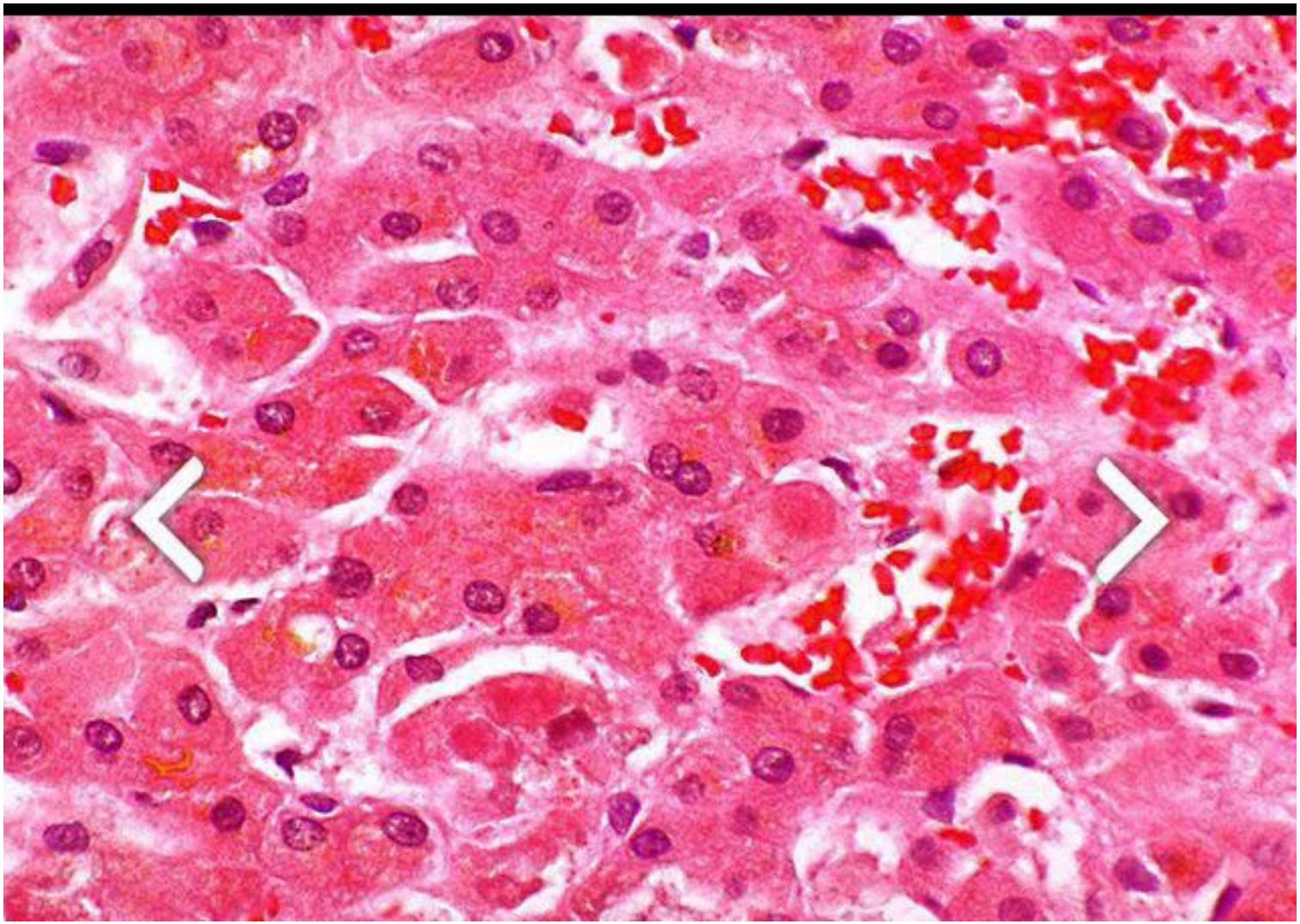
2- Macrovesicular steatosis.

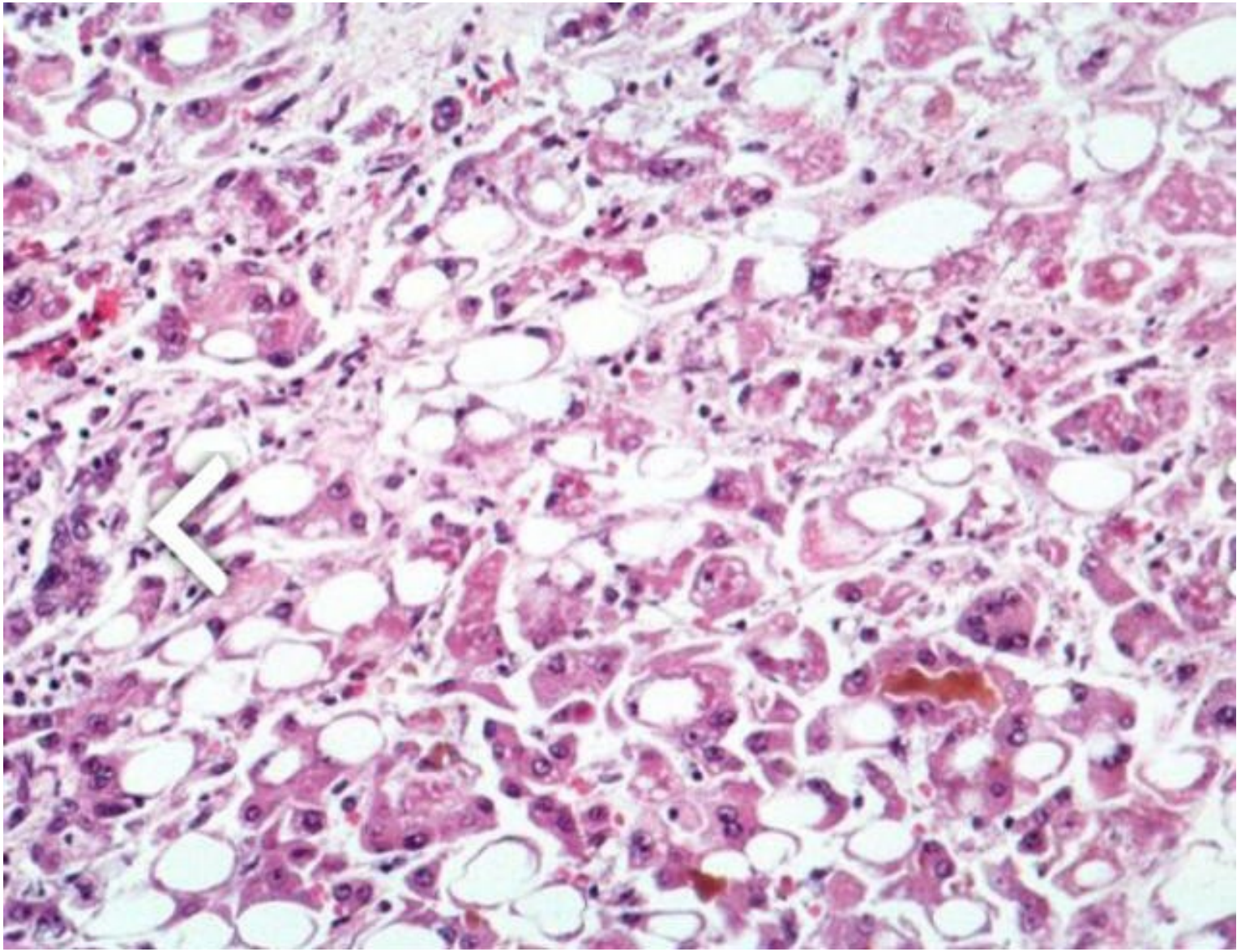
3- Fibrosis and cirrhosis.

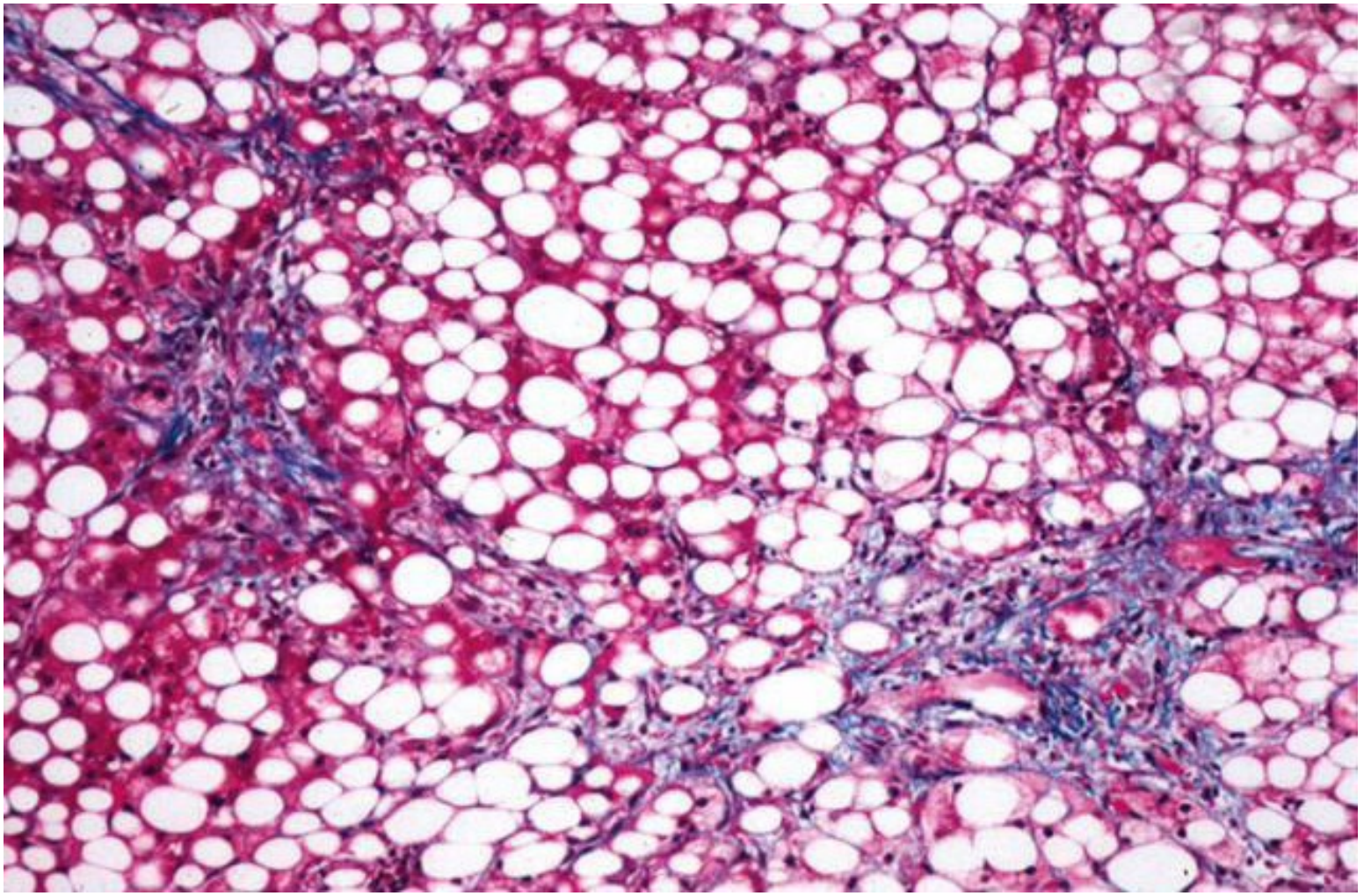
4- Central hyaline sclerosis.

Iron deposition is common and does not necessarily indicate haemochromatosis.









C/F:

1- Incidental abnormal LFT with normal or large liver (In fatty liver).

2- Alcoholic hepatitis: with jaundice, malnutrition, hepatomegaly, features of portal hypertension.

3- Cirrhosis: stigmata of chronic liver disease, large, normal or small liver, portal hypertension, hepato cellular carcinoma.

- In reality these syndromes overlap with each other.

*Peripheral stigmata of chronic liver disease, including dupytren's contractures and palmar erythema are more common in cirrhosis due to alcoholism.

Investigation:

1- Clinical history of alcohol misuse.

2- Macrocytosis with no anaemia.

3- Increase GGT which is not specific (steatosis and fibrosis).

4- Rib fractures (unexplained).

5- Jaundice (indicate alcoholic hepatitis).

6- Liver biopsy (extent of liver damage).

Management:

1- Cessation of alcohol. (most important treatment).

2- Treatment of complication (varices, encephalopathy and ascitis).

3- Good nutrition. (N.G)

4- Corticosteroids. (in sever alcoholic hepatitis). Contraindicated in variceal haemorrhage and sepsis.

5- Pentoxifylline: has weak anti. TNF action, beneficial in sever alcoholic hepatitis and reduce hepato renal failure.

6- Liver transplantation.

Liver tumors

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- Types and etiology-1
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Tumours of liver:

Hepatocellular carcinoma:

* Most common primary liver tumour.

*10-28/ 100.000.

*Increase in hepatitis C cirrhosis. (Europe and north America).

Aetiology:

*Chronic hepatitis B infections (in HBeAg +ve).

*Cirrhosis. (Hep. B, C, haemochromatosis, alcohol, NASH “non alcoholic steatohepatitis”, α_1 antitrypsin deficiency).

*Male gender and increase age (female with primary biliary cirrhosis do not require screening).

C/F:

1- Asymptomatic

2- Weight loss, anorexia, abdominal pain.

3- Features of underlying cirrhosis. (ascitis, jaundice, abnormal LFT and variceal hemorrhage.)

O/E:

1- Hepatomegaly or mass.

2- Bruit.

3- Intra abdominal bleeding.

Screening: ult at 3-6 months interval in high risk patients such as those with cirrhosis due to hep. B, C, haemochromatosis, alcohol, and α_1 - antitrypsin deficiency.

Investigations:

1- Serum markers (AFP 60%).

2- ult(2-3 cm).

3- CT(2 cm).

4- MRI.

5- Angiography.

6- Liver biopsy (for large tumour with no cirrhosis or Hept. B).

Management:

1- Hepatic resection. (for non-cirrhotic patients).

2- Liver transplantation.(5year survival 75% for single lesion <5cm or 3tumors <3cm)

3- Percutanouse ablation.(ethanol injection)cure rate 80% or radiotherapy

4-Chemoembolization.(the tumour is not radio or chemo sensitive) but hepatic artery embolisation with gelfoam and doxorubicin have 60% survival

5-chemotherapy.sorafenib (1st systemic therapy prolong survival)

2) Fibro lamellar hepatocellular carcinoma.

3) Other primary malignant tumours = rare. (haemangio – endothelial sarcomas)

4) Secondary malignant tumours. (lung, breast, abdomen and pelvis).

5) Benign tumours (haemangioma in 5/100 of population, adenoma (rare vascular tumours, more common in women and may be caused by oral contraceptive pills, androgens and anabolic steroids) , focal nodular hyperplasia (common in women<40years).