LIVER

Chapter 15

Normal Anatomy

- Averages **1400-1600** gm in adult.
- Covered by Glisson's capsule.
- Receives **70%** blood flow **from portal vein**, 30% hepatic artery.
- Architecture of liver lobule **(Fig 15.1)**.

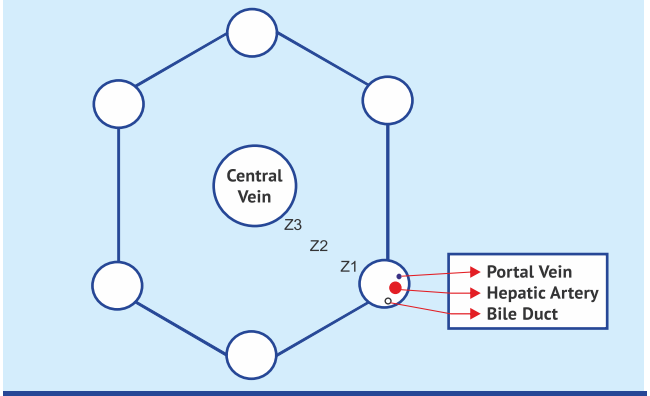


Fig 15.1: Liver Anatomy

- **Hexagonal lobule with terminal hepatic vein in the centre (central vein) divided into three zones :-**

Zone-1

- Periphery of lobules having portal tract containing **portal vein, bile ducts and hepatic artery**.

Zone-2

- Area between two areas are **midzonal area**.

Zone-3

- Area around terminal hepatic vein is known as **centrilobular zone**.

High Yield Info.....

1) **Most** susceptible to ischemic damage is **zone-3**^{Q} (less blood supply at this area).
2) **Most susceptible to toxin-inducedd** damage is **zone-1**^{Q} (richly blood supply).

- **Limiting plate :**
  - It is line up of hepatocytes surrounding portal tract cords.
  - They are **one cell thick** in adult; two in newborns (and in regenerating liver).

Liver Parenchyma (Image : 15.1)

- Hepatocytes are arranged in plates, lining the **blood-filled sinusoids**.
- Sinusoidal **endothelial cells are fenestrated**, allowing direct access of hepatocytes to constituents of the blood.
- On the **sinusoidal endothelial wall** lie phagocytic **Kupffer cells** and within the **Perisinusoidal space of Disse** are the hepatic **stellate cells or Ito cells.**
- **Stellate cells (=Ito cells)** are myofibroblast precursors important in **liver fibrosis.**

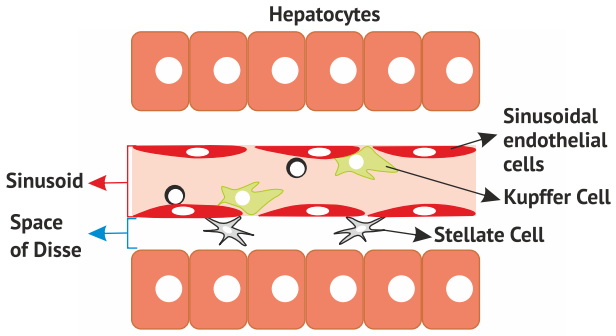


Image 15.1 Liver Parenchyma

High Yield Info.....

❖ **Hepatic fibrosis/cirrhosis**^{Q} is due to **collagen type-1**^{Q} and **type-3 both**^{Q}, produced by **Ito cells (stellate cells**^{Q}**)**.

Patterns of Liver Necrosis

A) Focal necrosis

- Focal areas of necorsis involving single cells or small group of cells.
- Involves any area of lobules and all lobules are not affected.
- **Biopsy shows :**
  - **Councilman bodies**^{Q} (apoptotic bodies) seen in **viral hepatitis**^{Q}.
  - **Kupffer cells hyperplasia** around necrotic liver cells.
- **Causes :**
  - Viral hepatitis; toxic damage and bacterial infections.

B) Zonal necrosis

- Identical region all liver lobules are affected **three types -**

1) Centrilobular^{Q} **(centrizonal) necrosis**

- It is seen in **cardiac failure**^{Q} or shock; **chloroform toxicity; viral hepatitis**^{Q}**; carbon tetrachloride** toxicity.

2) **Periportal[Q] necrosis**
   - It is seen in **eclampsia; phosphorus[Q] poisoning**.
3) **Midzonal[Q] necrosis**
   - It is seen in **yellow fever[Q]**.

High Yield Info.....

❖ **Piecemeal necrosis[Q]:**
- It is also known as **Troxic Hepatitis** (necrosis) or **Nibbling necrosis, Interface necrosis**.
- It refers to loss and **degeneration of (limiting plate) hepatocytes[Q]** at the lobularportal-interface, producing a moth-eaten irregular appearance.
- It is associated with a lymphocytic infiltrate into the adjacent parenchyma with destruction of individual hepatocytes along the edges of the portal tract.
- It is **seen in[Q]** following conditions -
  a) **Viral hepatitis[Q]** (especially **chronic hepatitis[Q]**)
  b) **Autoimmune hepatitis[Q]**
  c) **Steatohepatitis[Q]**

Hepatic - Infarcts

- It is very rare due to **dual blood supply**.
- It is seen in embolism; sepsis; eclampsia; PAN (polyarteritis nodosa); DIC (disseminated intravascular coagulation); portal vein obstruction, eg., Budd-chiari syndrome; chronic passive venous congestion **(nutmeg liver)[Q]** **(Image15.2)**.

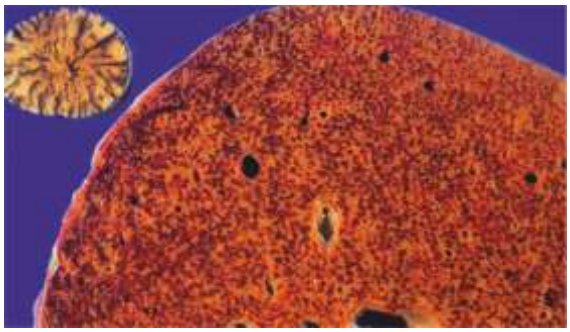


Image 15.2 Nutmeg liver: Seen in **Chronic passive congestion** due to right heart failure. Characteristic **"nutmeg liver" appearance** is due to:
a) **Congested red-brown pericentral zones** - Combination of hypoperfusion and retrograde congestion acts synergistically to cause centrilobular hemorrhagic necrosis.
b) **Normal-yellow or tan** colored **periportal regions**.

High Yield Info.....

Liver infarction:

❖ It can have both **"Red"[Q]** and **"White"[Q]** infarcts. **(Overall RED infarct> white infarct")[Q]**

- Chronic inflammation **damaging limiting plate[Q]** and extending into liver lobules.

Hepatitis (Table 15.1)

Classification of hepatitis

- Earlier classification was on the basis of histopathology:
  1) **Chronic persistent hepatitis[Q]**
     - Chronic inflammation is restricted to portal tract only and **limiting plate** is not damaged. **(Image : 15.3)**

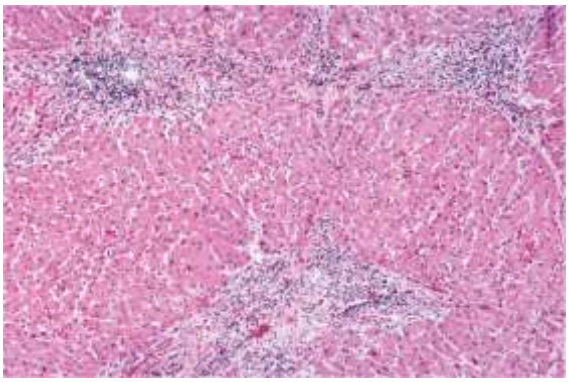


Image 15.3 Chronic persistent hepatitis Liver biopsy showing **mononuclear inflammation** restricted to **portal tract without damaging limiting plate** of portal tract.

  2) **Chronic active hepatitis[Q]**
     - Chronic inflammation **damaging limiting plate[Q]** and extending into liver lobules.

High Yield Info.....

❖ **Types of liver failure :**
1. **Fulminant**
   - Encephalopathy develops **within 2 weeks[Q]** of jaundice onset.
2. **Subfulminant**
   - Encephalopathy develops **within 3 months[Q]** of jaundice onset.
3. **Acute**
   - Encephalopathy develops **within 6 months[Q]** of jaundice onset

Latest classification of hepatitis is based on :

- Cause
- Histologic activity **(= grade)**.
- Degree of progression **(= stage)**.

1) **Classification by cause :**
   - Based on cause, e.g., viral hepatitis; autoimmune hepatitis; drug induced hepatitis, etc.
2) **Classification by grade (= histologic activity) :**
   - **Histologic activity[Q]** or **grade[Q]** is measured by

necrosis and inflammationϱseen on biopsy.

- Following features are considered.
  - Portal inflammation
  - Periportal necrosis
  - Piecemeal necrosis
  - Bridging necrosis

3) Classification by stage (= degree of fibrosis)

- Stage is correlated by degree of **fibrosis**.
- **It reflects progresion of disease as given below :**
  - 0- No fibrosis
  - 1- Mild fibrosis (within portal tract)
  - 2- Moderate fibrosis (portal and periportal)
  - 3- Severe fibrosis (bridging fibrosis)
  - 4- Cirrhosis

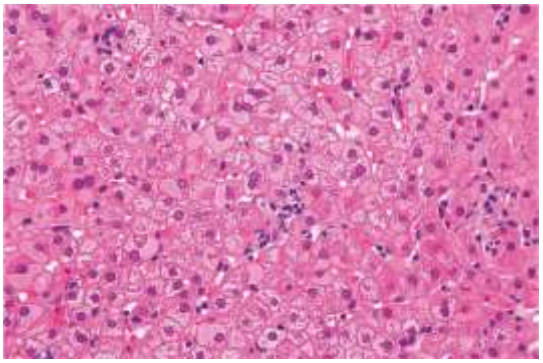


Image15.6 Ground glass hepatocytes Hepatocytes with **hazy and uniformly pale cytoplasm**. The **cytoplasm's granular** homogeneous eosinophilic staining is caused by the **presence of HBsAg**. They are seen in **chronic hepatitis.**

Table 15.1: Differences between Acute and Chronic Hepatitis

Acute Hepatitis	Chronic Hepatitis
1) **Ballooning degeneration**ϱ (swelling of hepatocytes) **(Image : 15.4)**	1) **Ground glass hepatocytes**ϱ due to HBsAg antigen into cytoplasm (also known as **Hadziyannis cells**ϱ or **Shikata cells**ϱ) **(Image : 15.6)**
2) Councilman bodies **(Apoptotic bodies)**ϱ **(Image : 15.5)**	2) **Piecemeal necrosis** ϱ (=**interface hepatitis)** in addition to **lobular hepatitis**. **(Image : 15.7)**
3) **Lobular Hepatitis**ϱ (Lobular architecture disruption).	3) **Bridging necrosis** and **fibrosis**ϱ**.**
4) **Bridging necrosis**ϱ **(central-portal bridging necrosis)** may occur in more **severe**ϱ **acute hepatitis**	4) Cirrhosis
5) **Spotty necrosis"**	5) Ductular reactions and **Fatty change** ϱ

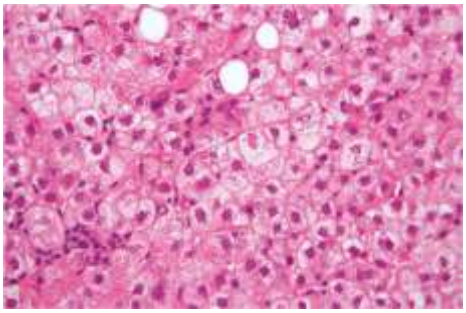


Image 15.4 Ballooning degeneration of hepatocytes Ballooned cells are typically **two to three times** the size of adjacent hepatocytes and are characterized by a **wispy cleared cytoplasm**. They are seen in acute hepatitis.

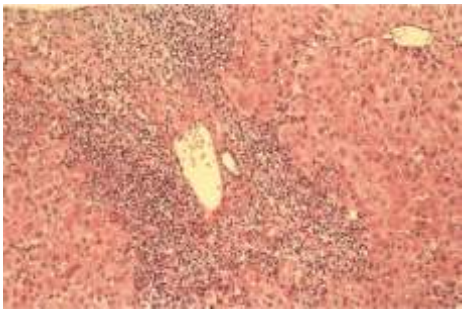


Image15.7 Interface hepatitis. Interface hepatitis is **penetration and disruption of limiting plate** of portal tract **by mononuclear inflammation** and inflammation extending into the surrounding hepatic lobule.

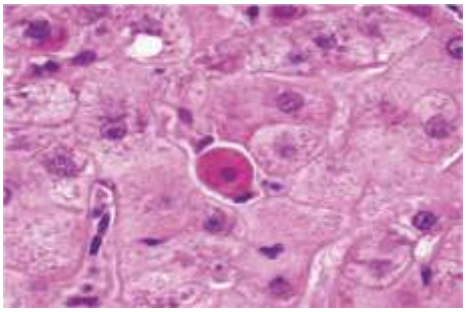


Image15.5 Councilman bodies Apoptotic hepatocyte or "dead red" is a cell with brightly eosinophilic cytoplasm.

High Yield Info.....

- **Chronic viral hepatitis** due to **HCV**ϱ will show characteristic **portal tract expansion**ϱ by a **lymphoid follicle**ϱ**.**

Jaundice

- Yellowish discoloration of skin and sclera due to high level of bilirubin.
- Clinical jaundice is categorized when **total bilirubin is > 2·5 mg/dl.**

- **Normally :**
  1) Total bilirubin - **0·3 to 1·0 mg/dl**
  2) **Direct (= conjugated) bilirubin**
     - Normal level is up to **0·3 mg/dl**
     - **Water soluble**
     - Easy glomerular filtration and excreted in urine.
  3) **Indiret (= unconjugated bilirubin) :**
     - Normal level is **0·3 to 0·7 mg/dl**
     - Lipophilic and **water insoluble**[Q]
     - **Tightly bound to albumin**
     - It cannot be excreted into urine
     - Can cross blood-brain barrier and damage brain of newborn **(kernicterus)** with erythroblastosis fetalis.

Types of Hyperbilirubinemia

1) Conjugated (= direct) type :
- When **direct bilirubin is more than 50%** of total bilirubin.
- **2 possibilities :**
  - If **alkaline phosphatase >AST/ALT** —Obstructive jaundice, e.g., gallstones; carcinoma of common bile duct and pancrease.
  - If **ALP < AST/ALT** —Hepatocellular damage e.g.,viral hepatitis.
- Causes-biliary tract obstruction and diseases (e.g., primary biliary cirrhosis and primary sclerosing cholangitis); Dubin-Johnson syndrome; Rotor syndrome.

2) Unconjugated (= indirect) type :
- When direct **bilirubin is less than 20%** of total bilirubin.
- Causes - hemolytic anemias; physiological jaundice of newborn; breast milk jaundice (due to betaglucoronidase in milk); diffuse hepatocellular damage (due to viruses, drugs and cirrhosis); Gilbert syndrome; **Crigler-Najjar syndrome type 1 and type 2.**

Hereditary Hyperbilirubinemia (Table 15.2)

1) Conjugated hyperbilirubinemia :

a) Dubin-Johnson syndrome :
- Autosomal recessive
- Mutation of canalicular **multi-drug resistant protein 2 (MRP2)**[Q]
- Dark **(black) pigmented liver**[Q] due to **epinephrine**[Q] metabolite
- Innocuous clinical course

b) Rotor syndrome
- Autosomal recessive
- **Normal**[Q] **liver histology**
- Innocuous clinical course

2) Unconjugated hyperbilirubinemia:

a) Crigler-Najjar syndrome type 1
- Autosomal recessive
- **Normal liver histology**[Q]
- Fatal in neonatal period

Table : 15.2 Hereditary Hyperbilirubinemia

Disorder	Inheritance	Defect	Liver Pathology	Clinical Course
A) **Unconjugated hyperbilirubinemia**				
1) Crigler-Najjar syndrome type-1	AR	Absent UGT 1 A1 activity	None	Fatal in neonatal period
2) Crigler-Najjar syndrome Type 2	AR	Decreased UGT1A1 activity	None	• Mild • Occasional kernicterus
3) Gilbert syndrome	AD > AR	Decreased UGT1 A1 activity	None	Innocuous
B) **Conjugated hyperbilirubinemia**				
1) Dubin-Johnson syndrome	AR	• Impaired biliary excreton of bilirubin glucuronides due to mutation in **canalicular Multidrug Resistance Protein-2 (MRP-2)**[Q]	**Black pigmented**[Q] cytoplasmic globules (due to) **epinephrine**[Q]	Innocuous
2) Rotor-syndrome	AR	• Decreased hepatic uptake and storage • Decreased biliary excretion	None	Innocuous

b) Crigler-Najjar syndrome type 2
- **Autosomal recessive >** autosomal dominant
- **Normal liver histology**
- Genetically mild with occasional kernicterus

c) Gilbert syndrome[Q]
- **Autosomal dominant >** autosomal recessive
- **Normal**[Q] **liver histology**
- Liver biochemical tests are normal except for **elevated bilirubin level (bilirubin usually < 3 mg/dl)**.
- **Not**[Q] **associated with cirrhosis**[Q]
- Precipitated by-stress; fatigue; alcohol use; reduced calorie intake.

Liver Function Tests

- Normal liver function tests (LFT's) do not exclude the possibility of chronic liver disease.
- LFTs will include analysis of liver synthetic function, liver cell integrity, and biliary excretion function. **(Table : 15.3 & Flow Chart : 15.1)**

Table : 15.3 Liver Function Tests

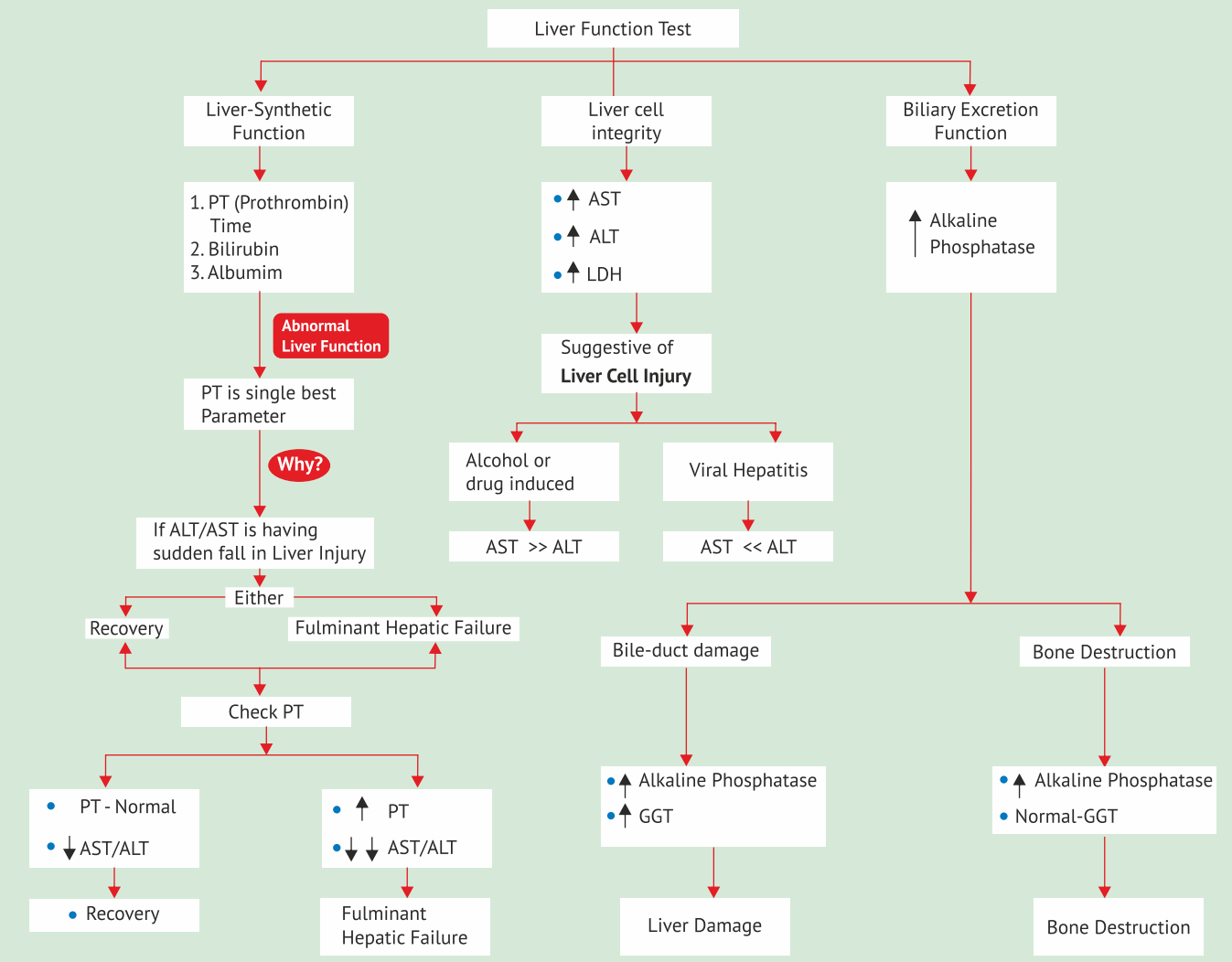
A) Liver cell integrity (It includes Cytosolic hepatocellular enzymes)	
1. Serum aspartate aminotransferase (AST) or serum glutamic oxaloacetic transaminase **(SGOT)**	• **Normal level** is **5-45 U/L.** • **Surrogate marker** of liver cell necrosis. • Raised in viral hepatitis, severe skeletal muscle trauma, extensive surgery, drug induced hepatic trauma. • Levels from **10-20 times higher** than normal may suggest **Myocardial infarction** and **alcoholic cirrhosis**. • These enzymes are found in the liver, RBCs cardiac and skeletal muscle, kidney and brain tissue. As a result, damage to any of these areas can result in an increased level on test result. • **High levels** are likely to be **liver or heart problems** or **muscle damage**.
2. Serum alanine aminotransferase (ALT or SGPT)	• **Normal level** is **5-45 U/L.** • **Surrogate marker of liver cell necrosis.** • High level suggests **viral or drug induced hepatitis**, or extensive hepatitis with necrosis or another source. • Found mainly in **liver.** • **More specific for liver damage** than AST. • Levels of **ALT and AST** both **raised above 2 times** of normal, then this is **significant.** • If transferases are **very high (greater than 1000 U/L),** then the diagnosis is **almost certainly hepatitis.** • **Alcoholic liver disease** will **never cause an AST of > 1000 U/L.**
3. Serum lactate dehydrogenase (LDH)	• Increased in **tumors** involving the liver.
B) Biliary excretory function (Substances normally secreted in bile)	
1) Serum bilirubin **a) Total:** unconjugated plus conjugated. **b) Direct:** conjugated only	• Serum levels increased in all forms of jaundice. • May be conjugated, unconjugated or mixed. • **Conjugated Bilirubin <20%** is seen in **Unconjugated hyperbilirubinemia**: e.g., extravascular hemolytic anemias (e.g. hereditary spherocytosis). • **Conjugated bilirubin 20%–50%** is seen in **Mixed hyperbilirubinemia** (e.g., viral hepatitis). • **Conjugated bilirubin >50%** is seen in **Conjugated hyperbilirubinemia** (e.g., liver cholestasis)
2. Urine bilirubin	• **Bilirubinuria** is seen in **viral hepatitis**, intrahepatic or extrahepatic obstruction of bile ducts.

C) Biliary excretory function (damage to bile canaliculus)	
1. Serum alkaline phosphatase (ALP)	• Normal (25-110 U/L). • Found in **cells lining of bile duct** and in **bone.** • **Physiologically** elevated level in **high bone turnover** (=adolescence) and in third trimester of pregnancy. • **Largely elevated** in **bile duct blockage,** and slightly raised in liver disease (e.g., hepatitis or liver cancer).
2. Serum gamma-glutamyl transpeptidase (GGT)	• Normal (< 65 U/L). • This enzyme is **induced by alcohol.** • **Surrogate marker** of **alcohol misuse.** • More sensitive marker for **cholestatic damage** than ALP. • Raised level is seen in **bile duct obstruction**. • GGT is often used to confirm that AST readings are due to liver damage. • Used to **monitor cirrhosis caused by alcoholism.**
3. 5' Nucleotidase	• Specific for **cholestasis** or damage to the intra- or extrahepatic biliary system. • Used as a **substitute for GGT** for ascertaining whether an **elevated ALP is of biliary or extra-biliary origin.**
D) Hepatocyte synthetic function (Proteins secreted into the blood)	
1. Serum albumin	• **Normal (3·5 to 5·3 g/dl).** • Major protein constituent of plasma and accounts for over 50% of all plasma proteins. • It is manufactured in the liver from ingested amino acids. • It helps to regulate osmotic pressure as well as transport nutrients and waste products. • **Half-life** of **Albumin is 3 weeks** (**Half-life** of **Pre-albumin is 2 days)**
2. Prothrombin time (PT)	• Reflects changes in levels of **coagulation factors**. • Prolonged in **liver failure** due to decreased synthesis of several clotting factors including those that are **vitamin K dependent.** • Increased PT is suggestive of **severe liver disease.**
3. Factor V	• Decreased in severe liver disease
4. Blood urea nitrogen (BUN)	• Urea cycle is present in the liver. • Decreased serum BUN is seen in **cirrhosis, fulminant hepatitis**
5. Serum ammonia	• **Ammonia** is metabolized in the **urea cycle** in the liver. • Derives from large bowel and amino acid degradation. • Increased serum ammonia is seen in **cirrhosis, Reye syndrome.**

High Yield Info.....

Ratio of "AST" and "ALT " can be useful in differential:

- **ALT is more specific for liver damage** than AST.
  1) **AST : ALT = 1**
     - Associated with **ischemia**[Q] (CCF and ischemic necrosis and hepatitis).
  2) **AST : ALT > 2**
     - Associated with **alcoholic hepatitis**[Q]
  3) **AST : ALT < 1**
     - High rise in ALT specific for hepatocellular damage.
     - Paracetamol toxicity with hepatocellular necrosis.
     - **Viral hepatitis, ischemic necrosis**[Q], toxic hepatitis.



Flow chart 15.1 : Liver Function Test Interpretation

Viral Hepatitis (Table 14.4)

Hepatitis A

- Non-enveloped **single stranded RNA**, icosahedral, 27 nm **(Picornavirus)**.
- **No direct cytopathic** effect.
- Incubation period is **2-6 weeks**.
- Most infections are **anicteric**.
- Self-limited illness (**no carrier state** or chronic state).
- Spread by feco-oral route.
- **Histology**
  - Inflammation restricted to portal and periportal areas (in contrast to hepatitis B, C which is panlobular).
- **Serology**
  - **IgM** is marker for **acute infection**; IgM may persist for 1 year.
  - IgG indicates lifelong immunity.
- Mortality is less than 0·5%

Hepatitis B

- Enveloped (42 nm) **Dane particle (Australia antigen)**; 27 nm hexagonal inner core with circular **double stranded DNA genome**.
- Incubation period is **2-26 weeks (8 weeks)**[o].
- Transmitted by blood products; needle stick injury; sexual transmission.
- Most cases subclinical
- 10% symptomatic cases develop **acute fulminant hepatitis** or chronic disease.
- Virus is **not cytopathic**[o] (integrates into **host DNA**) and injury is due to inflammation.
- May cause **"ground glass" cytoplasm** due to distention of smooth endoplasmic reticulum with virions. It is indication of **chronic carrier state**.
- **HBsAg** appears first-followed by **HBeAg**-disappears with **IgM anti-HBc** and **anti-HBe-HBsAg** drops after ~2 months-1-4 months **"window period"** (before anti-Hbs appears).

Table 15.3 : Hepatitis					
Virus	**Hepatitis A**	**Hepatitis B**	**Hepatitis C**	**Hepatitis D**	**Hepatitis E**
1. Type	Single stranded	Partially **dsDNA**ϱ	ssRNA	Circular defective ssRNA	ssRNA
2. Family	• Hepatovirus (= Picorna-virus)	Hepadnavirus	Flaviridae	Subviral particle in deltavirdae family	Hepevirus
3. Transm-ission	Feco-oral	Perinatal, parenteral and sexual contact	• Parenteral • **Intranasal cocaine**ϱ	Parenteral	**Feco-oral**ϱ
4. Incubation period	2-6 weeks	2-26 weeks (mean 8 weeks)	4-26 weeks (9 weeks)	Same as HBV	4-5 weeks
5. Chronicity	Never	**5-10%**ϱ	**> 80%**ϱ	-10% Coinfection -90-100% for superinfection	In Immunocom-promised hosts only
6. Diagnosis	Detection of serum IgM antibodies	Detection of HBsAg HBsAg or antibody to HBcAg PCR for HBV-DNA	• 3rd generation ELISA for anti-body detection • PCR for HCV-RNA	• Detection of IgM of IgG antibodies • HDV-RNA serum • HDAg in liver	• Detection of serum IgM and IgG antibodies • PCR for HEV-RNA

Serology of Hepatitis B:

- Sequence in which the various antigens or antibodies appears are i.e. **HbsAg-HbeAg-anti HbcAg-HBV-DNA).** **(Table : 15.5 and 15.6)**

Table 15.5 : Serology of Hepatitis B	
Serological Markers	**Interpretation**
1.) HBsAg	• **Earliest marker** of Hepatitis B infections. • Infected (can be **acute/chronic** or **carriers)**. • Persistence of HBsAg is used to differentiate acute from chronic infection. • Presence **longer than 6 months** after initial exposure indicates **chronic infection**. • HBsAg is known as **epidemiological marker of hepatitis B.**
2.) Anti-HBs	• Implies **either active or passive immunization** that usually persists for life. • Protected.
3.) Anti-HBc	• **HbcAg** is **not detectable in serum**. • **First** detectable antibody. • **IgM anti-HBc** indicates **acute infection**. • **Most reliable marker** of acute infection. • Only serologic marker detectable during the **"window period".** • **IgG anti-HBc** indicates **previous or ongoing infection**.
4.) HBeAg	• **High infectivity** and **active disease**. • Higher rates of viral transmission. • **Marker of viral replication** and **infectivity.** (**HBeAg** is produced only during **replication of the virus).**

5.) Anti-HBe	• **Low infectivity**. • **Loss of HBeAg** and **appearance of anti-HBe** in serum is called "**seroconversion**".
6.) HBV-DNA	• It measures **quantitative viral load.** • Indicates **viral burden** and **viral replication.** • **Assess recovery from infection** and candidacy for antiviral therapy. • To **differentiate** between **inactive carrier state and chronic active hepatitis** in chronic HBV infection.

High Yield Info.....

- **Qualitative marker** of HBV-replication is **HbeAg**.
- **Quantitative marker** (definitive) of HBV-replication is **HBV-DNA > HBV-DNA polymerase**.

Inactive carriers

- Refers to HbeAg-negative with normal serum ALT levels and low (< 2000 IU/mL) or undetectable HBV DNA.

Precore or basic core mutant HBV

- Also referred to as **HBeAg-negative** or **anti-HBe-positive** HBV infection.
- **They have :**
  - **HBeAg-negative**
  - **Anti-HBe-positive patients**
  - High serum **HBV-DNA** levels **(> 10000 copies/ml)** and
  - **Persistent or intermittent elevation** in alanine aminotransferase **(ALT) activity**.
- It presents **severe and progressive form** of liver disease.
- Associated with frequent development of **cirrhosis and HCC**.

High Yield Info.....

A) "Hepatitis B "Super carrier" :-
- **High titers** of HBsAg and HBV-DNA in blood along with HBeAg.
- It indicates early stage of carrier and "highly infectious".

B) "Hepatitis B "Simple carrier" :-
- **Low titers** of HBsAg, anti HBe positive, and HBV-DNA negative.
- It indicates late stage of carrier and they will transmit infection when large quantities of blood are transferred.

Hepatitis C

- Enveloped **single stranded RNA flavivirus**.
- Spread by **transfusion related hepatitis** also common in **IV drug users**; less commonly through **sexual transmission** and **vertical transmission**.
- Directly cytopathic
- **Histology**
  - Focal **macrovesicular fatty change**.
  - **Bile duct damage** and **lymphoid agregates** within portal tract is characteristic. **(Image : 15.8)**

Table 15.6 : Serology of Hepatitis B Infection

HBsAg	IgM anti-HBc	IgG anti-HBC	IgG anti-HBS	Inference
1.	+	+	-	- **Acute** hepatitis B-virus (HBV) infection
2.	-	+	-	- **Window period**
3.	-	-	+	+ Previous infection
4.	+	+/-	+	- Chronic infection
5.	-	-	-	+ Immunisation

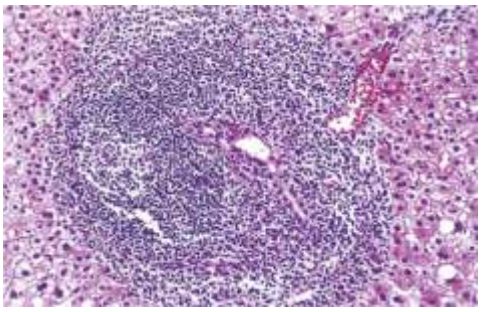


Image 15.8 Hepatitis C Virus Chronic viral hepatitis showing **mononuclear inflammation within portal tract** forming **lymphoid aggregates** (sometimes with germinal centers) are **characteristic of hepatitis C.**

- **Serology**
  - Initially **IgM anti-HCV** followed by **IgG anti-HCV antibodies**.
  - **Chronic infection** will show episodic elevations in serum transaminases with persistent HCV-RNA in blood.

High Yield Info.....

❖ **IgG anti-HCV antibodies** does **not provide effective immunity** due to **genomic instability** and **antigenic variability** seen in HCV.

Hepatitis D

- **Single stranded RNA virus**.
- Infective only when encapsulated by HBsAg.
- Can be directly cytopathic.
- More severe than other hepatitis infections.
- **Microvesicular**♀ **fatty liver** and **many acidophil bodies (= Councilman bodies**♀**)** are seen.
- **Igm anti-D** is most reliable marker of acute infection.

Hepatitis E

- **Single stranded RNA** viruses.
- Enterically transmitted.
- Incubation period is **4-5 weeks**.
- Self limiting (No chronic state).
- Associated with **high mortality during pregnancy**♀.

High Yield Info.....

Viral hepatitis

- Most Common **acute**♀ viral hepatitis (world/India) – **Hepatitis A**♀.
- Most Common **acute viral hepatitis**♀ in **children**♀ (World/India) – Hepatitis A
- Most Common **acute viral hepatitis (epidemic/sporadic)**♀ in adults (India /world) – **Hepatitis E**♀
- Most Common cause of **chronic Viral Hepatitis**♀ (world/India) – **Hepatitis C**♀
- Most Common Viral Hepatitis causing **HCC**♀ (world /India) – **Hepatitis B**♀
- Most Common cause of **carriers**♀ (world / India) – **Hepatitis B**♀
- Most common cause of **cirrhosis** – **Hepatitis C**♀.
- Most common type of **hepatitis associated with transfusion** – **Hepatitis B**♀
- Most common cause for **fulminant hepatitis** – **Hepatitis D**♀
- **Fulminant hepatitis**♀ is a **co-infection**♀ of hepatitis **B and D**♀
- **Chronicity**♀ is **superinfection**♀ of hepatitis **B and D**♀

Steatosis (Table 15.7)

Accumulations of **triglyceride**♀ **fat droplets** within hepatocytes is known as **fatty liver or steatosis**♀.

Table 15. 7: Steatosis (fatty liver)

Microvesicular (Image : 15.9) (multiple tiny droplets not displacing nucleus)	**Macrovesicular (Image : 15.10)** (single large droplet displacing nucleus to periphery)
1. **Reye syndrome**♀	1. Late alcoholic liver disease
2. **Acute fatty liver of pregnancy**♀	2. **Diabetes mellitus**♀-insulin resistance
3. Jamaican vomiting sickness	3. **Lipodystrophy**♀
4. Drugs-**valproic acid; tetracycline**♀	4. Protein energy malnutrition; starvation
5. Wolman disease	5. Dysbetalipoproteinemia
6. **Lysosomal acid lipase deficiency**♀	6. **TPN; jejunoileal bypass**♀
7. Early alcoholic liver disease	7. Inflammatory bowel disease
8. Chronic **viral hepatitis**♀	8. Syndrome X (obesity; DM; hypertriglyceridemia)
	9. Drugs-estrogens; calcium channel blockers
	10. **Phosphorus intoxication**♀

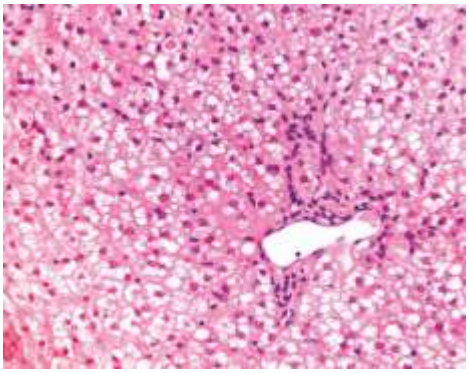


Image 15.9 Microvesicular steatosis, in which fat droplets are finely distributed in the hepatocyte cytoplasm with **central nucleus.**

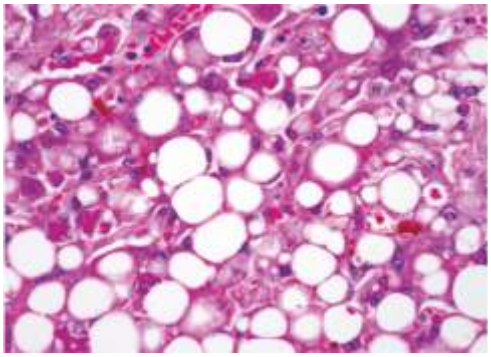


Image 15.10 Macrovesicular steatosis, showing **hepatocyte nuclei are displaced to periphery** by one or more fat vacuoles.

Reye Syndrome or Reye's Syndrome

- Also known as **Jamshedpur fever**
- Fatal syndrome that has detrimental effects to organs, especially be **brain**ǫ and **liver**ǫ.
- Lower level of blood sugar (hypoglycemia).
- Classic features are a **rash, vomiting and liver damage**ǫ.
- **Unknown etiology** but associated with **aspirin consumption**ǫ by children with **viral illness**ǫ, it also occurs in the absence of aspirin use.
- **Laboratory tests :**
  - Elevated liver enzymes, elevated ammonia levels, and low serum glucose levels.
- **Histologic changes**
- All cells have **pleomorphic, swollen mitochondira**ǫ that are reduced in number **(diagnostic finding)**ǫ.
- Liver shows fatty liver with **minimal inflammation (microvesicular steatosis**ǫ**)** and glycogen depletion.
- **Hepatic mitochondrial dysfunction** results in **hyperammonemia**ǫ, which is thought to induce **astrocyte edema**, resulting in cerebral edema and increased intracranial pressure (ICP).

Cirrhosis

- **End stage of chronic liver disease with following three characteristics:**
  - Entire liver architecture damage
  - Bridging fibrous septae
  - Regenerating parenchymal nodules
- **Two types of cirrhosis (Table 15.8)**

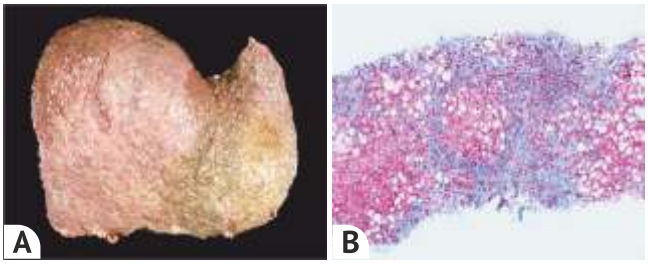


Image 15.11 : Micronodular cirrhosis.
a) Gross specimen showing small sized nodules throghout the liver surface without any normal smooth liver areas **(Blind man's diagnosis)**
b) Cirrhotic liver from a chronic alcoholic with small, regenerative nodules of parenchyma and fatty change.

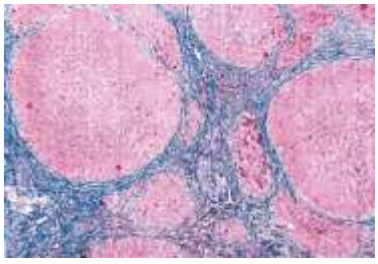


Image 15.12 Macronodular cirrhosis. Liver biopsy showing irregular nodules of varying size and irregular fibrous septa.

Table 15.8 : Cirrhosis

Micronodular (Image : 15.11 a & b) *(Nodule size < 3 mm*ǫ *in diameter)*	Macronodular (Image : 15.12) *(Nodule size > 3 mm*ǫ *in diameter)*
1. **Indian childhood cirrhosis**ǫ	1. Late stage alcoholic cirrhosis
2. Early stage of alcholic cirrhosis	2. Post-necrotic cirrhosis **(viral hepatitis)**ǫ
3. **Hemochromatosis**ǫ	3. **Wilson's disease**ǫ
4. Primary biliary cirrhosis	
5. Jejunoileal bypass	
6. Venous outflow obstruction **(Budd-chiari syndrome)**ǫ	

Autoimmune Hepatitis

- **Most common** autoimmune disease of liver in adults.
- Chronic progressive liver disease.
- Common on **females.**
- **Etiology:**
  - It is caused by viruses; drugs; autoimmune disorders (e.g., rheumatoid arthritis; Sjogren syndrome or ulcerative colitis).
- Classically females with **elevated serum IgG levels**[Q] but **no serum makers of viral hepatitis**[Q].
- **Classification (on the basis of antibodies) -**

1) Type-1 AIH

- It is a classic syndrome occurring in **young women**[Q].
- It is associated with marked hyperglobulinemia, lupoid features, circulating ANAs, and **HLA-DR3** or **HLA-Dr4**.
- **Auto-antibodies are:**
  a) **ANA**[Q] (antinuclear - **most common**[Q]);
  b) **SMA**[Q] (smooth muscle actin-**most specific**[Q]).
  c) **SLA /LPA**[Q] (soluble liver antigen/liver pancreas antigen)
- It shows autoantibodies against **atypical perinuclear antineutrophilic cytoplasmic antibodies (p-ANCA)**[Q].

2) Type-2AIH

- It is often seen in **children**[Q], more common in Mediterranean populations.
- It is associated to **HLA - DRB l**[Q] and **HLA - DQB l haplotypes**[Q].
- It is associated with **anti-LKM**[Q] and **anti-liver cytosol -1 antibodies**[Q].
  (NOTE: - It has no association[Q] **with ANA).**
- Anti-LKM represent heterogenous group of antibodies.
  1) **Anti-LKM 1 antibodies**[Q] are directed against cytochrome P450 2D6, which is also seen in **chronic hepatitis C**[Q].
  2) **Anti-LKM2**[Q] is seen in **drug-induced hepatitis**[Q].
  3) **Anti-LKM3**[Q] is seen in patients with **chronic hepatitis D**[Q].

3) Type III autoimmune hepatitis

- These patients **lack ANA and anti-LKM-1**[Q].
- They have circulating **antibodies to soluble liver antigen (SLA)**[Q].
- **Mostly female**[Q] with clinical features more severe than with type 1 autoimmune hepatitis.
- Type III autoimmune hepatitis is not a distinct category but considered as **spectrum of type I autoimmune hepatitis.**
- **Histology:**
  - **Typical histological finding**[Q] of AIH are
    1) **Interface hepatitis**[Q], lymphocytic or lymphoplasmacytic infiltrates in portal tracts and extending in the lobule. **(Image : 15.13)**

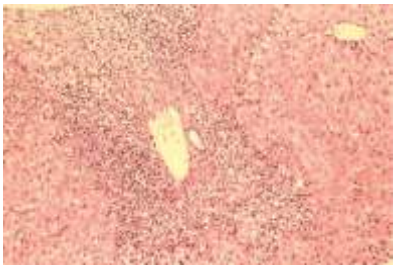


Image 15.13 Autoimmune hepatitis Liver biopsy showing characteristic **Lymphoplasmacytic interface hepatitis** containing plasma cells and lymphocytes at the interface between the portal tract and liver lobule.

2) **Emperipolesis**[Q] (active penetration by one cell into and through larger cell).
(Image : 15.14)

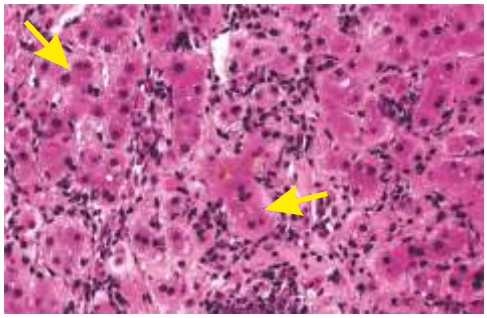


Image 15.14: Autoimmune hepatitis: (**Emperipolesis**) Active penetration by one cell into and through larger cell.

3) **Hepatic rosette**[Q] formation.
(Image : 15.15)

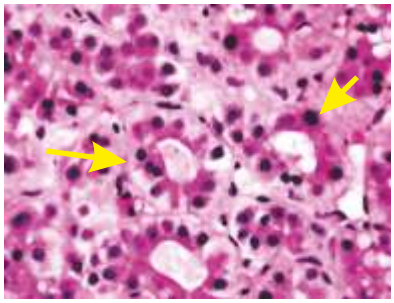


Image 15.15:Autoimmune hepatitis: (**Hepatic rosette formation**) hepatocytes form gland-like clusters.

- **Immunosuppression** is mainstay of therapy.
- **Transplantation** for end stage diseasee with recurrence.
- **Risk:** Liver cell failure and cirrhosis.

High Yield Info.....

❖ **Hepatitis C virus** (viral antigens **NS3 and NS5A**) is associated with autoimmune hepatitis subset with antibodies to **Liver-Kidney-Microsomal (LKM) antigen (anti-LKM)**. *(Harrison 19/e pg 2011)*

Alcoholic Liver Disease

- **Consists of three distinct forms:**

1) Steatosis (= fatty liver)

- **Initially microvesicular** type and **later macrovesicular** type. **(Image : 15.16)**
- It **starts at centrilobular** area and then becomes panlobular.

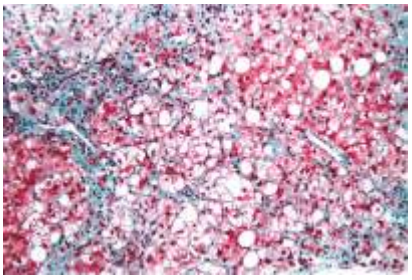


Image 15.16 : Alcoholic steatohepatitis : Liver biopsy showing both **microvesicular and macrovesicular steatosis** (seen as clear vacuoles), most **prominent around the central vein**. **Perisinusoidal Fine chicken-wire fibrosis** (fine thin green strands within the liver lobule) is **characteristic.**

2) Hepatitis

- **Ballooning degeneration** (hepatocyte swelling).
- Neutrophilic infiltrations
- Spotty necrosis
- **Mallory denk bodies** (intracytoplasmic **cytokeratin 8 and 18** intermediate filament) **(Image 15.17)**.

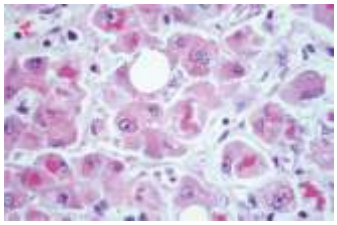


Image 15.17: Mallory Denk bodies. These are **globular eosinophilic hyaline material** within hepatocytes. It is **most often** seen in conjunction with **chronic alcoholism**. The **globules are aggregates of Cytokeratin intermediate filaments** in the cytoplasm resulting from hepatocyte injury.

- **Perivenular** and **perisinusoidal fibrosis** causing **central hyaline sclerosis**.
- **Giant mitochondria (megamitochondria)** is ultrastructural feature of alcoholic liver disease hepatocytes.

3) Cirrhosis

- Irreversible stage-initially micronodular and later macronodular.
- **Laennec-cirrhosis** shows **entire liver lobe** is replaced by **tough pale scar** tissue.

High Yield Info.....

❖ **Mallory-Denk bodies :**
- Intracytoplasmic **intermediate filament** made up of **cytokeratin 8 and 18**.
- **Seen in :**
  1) **Alcoholic liver disease**
  2) Non-alcoholic fatty liver disease (NAFLD)
  3) **Wilson's disease**
  4) Indian childhood cirrhosis
  5) Alpha-1 antitrypsin deficiency
  6) Chronic cholestatic disease
  7) **Primary biliary cirrhosis**
  8) Focal nodular hyperplasia
  9) **Hepatocellular carcinoma**
- **Mallory denk bodies are not seen in:**
  1) **Hemochromatosis**
  2) **Secondary biliary cirrhosis**

Non- Cirrhotic Portal Fibrosis (NCPF)

- High incidence in India (10-15%)
- **Etiology**
  - Associated with **HLA-DR-3**.
  - **E.coli** infections; **arsenic poisoning**; vinyl chloride todicity; **hypervitaminosis A**; drugs like steroids.
- **Male > female** affected.
- Age group affected are **30-40 years**.
- **Most common** presentation is **gastrointestinal bleeding** in 60-70% (due to rupture of **esophageal varices**).
- Massive **splenomegaly**.
- **Jaundice and ascites** is very **rare** (**liver** is of **normal** size).
- **Massive splenomegaly** and **variceal bleeding** without hepatomegaly is suggestive of **NCPF**.
- **Histology:**
  - **Hallmark** is **thrombosis** and **sclerosis** of portal vein and its branches.

- **Megasinusoids**[Q] **(periportal angiomatosis):** Aberrant blood vessels in **periportal areas** corresponding to dilated terminal portal vein branches.
- Portal and periportal inflammation and fibrosis.
- **Bridging fibrosis** is **not seen**[Q] in NCPF.

NAFLD (Non-Alcoholic Fatty Liver Disease)

- Chronic metabolic fatty liver disease
- **Males** and **females** are **equally**[Q] affected.
- No history of alcohol or intake of **very small quantities**[Q] **(less than 20g of ethanol/week)**.
- Associated with **obesity**[Q]**; dyslipidemia**[Q]; **hyperinsulinemia**[Q] and **insulin resistance**[Q].
- Mostly **asymptomatic**.
- **Spectrum of disorder will have the following phases**
  - **Steatosis**-microvesicular and macrovesicular both type containing **triglycerides**[Q].
  - **NASH (non-alcoholic steato-hepatitis)** fatty liver with mild nonspecific inflammation and centrilobular and periportal fibrosis. **(Image : 15.18)**

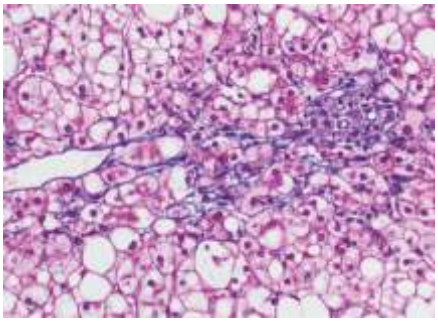


Image 15.18 Non-Alcoholic Steatohepatitis (NASH). Liver biopsy showing **pericellular fibrosis** around the **central venule (blue)** and **macrovesicular steatosis (Masson trichrome stain).**

  - **Cirrhosis** (cryptogenic cirrhosis) and **hepatocellular carcinoma**[Q].
- **NAFLD contributes** to the **progression of other liver diseases**[Q] such as **HCV infection and HCC**.
- **AST/ALT ratio is < 1**[Q] (in alcoholic liver **disorders > 2).**
- **Cardiovascular disease** is a frequent cause of **death**.

Wilson's Disease

- **Autosomal Recessive Disorder.**
- Mutation of **ATP7B gene**[Q] on **chromosome 13q**[Q], causing :-
  a) **Impaired copper excretion**[Q] into bile.
  b) **Failure to incorporate copper into ceruloplasmin**[Q].
  c) **Inhibits ceruloplasmin**[Q] secretion into the blood.
- Estimated total body copper is only **50 to 150 mg**.
- Toxic level of accumulation principally involves liver, brain, and eye.
- Symptoms usually appear between the ages of **6 and 20 years**.
- Hemolytic anemia and liver disease is suggestive of Wilson's disease.
- **Clinical features :**

1) Liver

- Most common presentation is acute or chronic liver disease (it **shows all spectrum ranging from fatty change; acute hepatitis; chronic hepatitis; cirrhosis; and massive liver necrosis**[Q]).

2) CNS

- Toxic injury affect the **basal ganglia (Putamen)**[Q] which shows **atrophy and cavitation**[Q] **(hepatolenticular degeneration)**.
- **Neuropsychiatric manifestations**, including mild behavioral changes, Frank psychosis, or a Parkinson disease-like syndrome (such as tremor), are the initial features.
- **Sensory abnormalities**[Q] and muscular weakness are **absent**[Q].

3) Ocular

- Nearly all patients with neurologic involvement develop eye lesions called **Kayser-Fleischer rings**[Q] **(green to brown deposits of** copper in **Descement's membrane**[Q] in cornea). **(Image : 15.19)**
- **Sunflower cataract**[Q]**.**

Image 15.19 Kayser-Fleischer ring. Copper deposition in the **Descemet membrane of the cornea** is visible as a **peripheral brown color**, which obstructs the view of the underlying iris.

- **Biochemical diagnosis -**
  - Decrease in **serum ceruloplasmin**.
  - An **increase** in hepatic copper content **(250 µg of copper per gram of dried liver tissues confirms wilson's disease)** (the **most sensitive and accurate test**[Q]).

- Increased **urinary excretion of copper** (the **most specific screening**[Q] test).

- **Serum copper**[Q] levels are of **no diagnositc value**[Q], since they may be low, normal, or elevated.
- Demonstration of **Kayser-Fleischer rings** favors the diagnosis.
- **Excess copper deposition demonstrated by special stains :**
  - **Rhodamine stain** - for **copper**[Q]. **(Image : 15.20)**
  - **Orcein stain** - for **copper-associated protein**[Q].

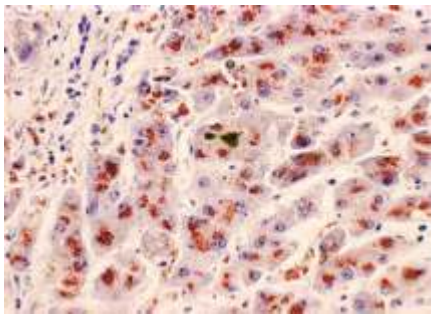


Image15.20 Rhodamine stain for copper Copper is seen as **red-brown cytoplasmic granules** within the liver tissue of a patient with Wilsons disease.

Hemochromatosis

- **Autosomal recessive disorder.**
- Most common metabolic cause of liver cirrhosis is **hemochromatosis**.
- Excessive accumulation of body iron mostly in liver and pancreas.
- **Hemochromatosis** for hereditary disease.
- **Hemosiderosis** for acquired deposition of iron in tissues.
- Total body iron pool ranges from **2 to 6 gm** in normal adults; about **0·5 gm** is stored in the liver.
- Iron accumulation is life long and rate of net iron accumulation is **0·5 to 1·0 gm/year**.
- **Disease** manifests after **20 gm** of stored iron have accumulated.
- Excess iron is directly toxic to host tissues.
- Main regulator of iron absorption protein **Hepcidin**[Q] (also known as liver expressed antimicrobial peptide or **LEAP1**), encoded by the **HAMP gene**[Q].
- **Adult hemochromatosis** is almost always caused by mutations of **HFE gene**[Q] at **chromosome 6p21·3**[Q]

Classification of Iron overload

A) Hereditary hemochromatosis:
- Mutations of genes encoding HFE, transferrin receptor 2 (TfR2), or hepcidin.
- Mutations of genes encoding **HJV (hemojuvelin**[Q]: juvenile hemochromatosis)

B) Hemosiderosis (secondary hemochromatosis) :
- Parenteral iron overload-transfusion; long term hemodialysis;
- Increased oral intake of iron seen in African iron overload **(Bantu siderosis)**.

- **Hemochromatosis is characterized by triad of :**
  1) **Micronodular**[Q] **cirrhosis** (liver)
  2) Diabetes mellitus (pancreas)
  3) **Skin pigmentation** (mainly due to **melanin** and **partially hemosiderin**).
- **Clinical features -**
  1) **Liver (Image : 15.21 & 15.22)**
     - **First and most commonly**[Q] affected organ
     - Micronodular cirrhosis
     - Hepatocellular carcinoma **(30%)**.

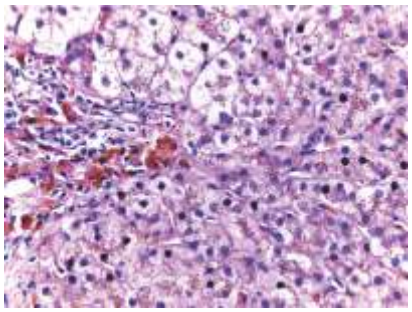


Image 15.21 Hemochromatosis. Liver biopsy showing hepatocytes with **coarse golden yellow granules** of hemosiderin within the cytoplasm.

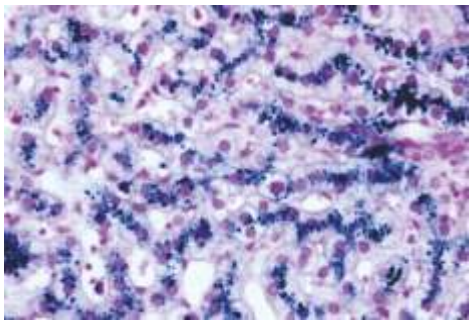


Image 15.22 Prussian blue stain (Hemochromatosis) Hemosiderin granules will stain **blue in color** with Prussian blue stain.

  2) **Pancreas**
     - Diabetes mellitus
  3) **Skin**
     - **Increased pigmentation**[Q] on face; neck and extensor aspects of forearm (bronzing of skin-**bronze diabetes**[Q]).
     - Pigmentation is **mainly due to melanin**[Q] and **partially due to hemosiderin**[Q].
  4) **Cardiac**
     - Restrictive cardiomyopathy; arrhythmia; congestive heart failure.

5) **Hypogonadism**
   - Due to **impairment of hypothalamopituitary function**[Q] by iron deposition and **not due to deposition**[Q] of iron in the testis.

6) **Joint**
   - Hemosiderin deposition in joint causing acute synovitis and **Pseudogout.**

High Yield Info.....

❖ **Best method to screen hemochromatosis**[Q] is **transferrin saturation**[Q].
Transferrin saturation is a first blood test to be elevated in hemochromatosis (sensitivity-94-98%). (Wintrobe 13/e p.678).

- **Treatment:**
  1) **Phlebotomy** (1-2 times/week) for removal of excess iron.
  2) **Chelating agent (desferrioxamine)** used only when anemia and hypoproterinemia is severe.

- Most common cause of death is cirrhosis > hepatocellular carcinomas.

Alpha-1 Antitrypsin Deficiency

- **Autosomal recessive**[Q] disorder.
- Abnormally low level of protease inhibitor (alpha-1 antitrypsin deficiency) causes **pulmonary emphysema** (panacinar type) and liver disorders **(cholestasis or cirrhosis)**.
- Also **associated with bronchiectasis; arterial aneurysm; cutaneous panniculitis**[Q] and **Wegener's granulomatosis**[Q].
- Presents with **neonatal hepatitis with cholestasis**.
- **Pathogenesis** is **protein misfolding**[Q] and accumulation of this protein within endoplasmic reticulum.
- **Histology** will show **PAS-positive and diastase resistant cytoplasmic globules**[Q] in **periportal hepatocytes**; fatty change, **Mallory-Denk-bodies**[Q]; and fibrosis of portal tract. **(Image : 15.23)**
- Risk-**cirrhosis and hepatocellular carcinomas** (2-3%).

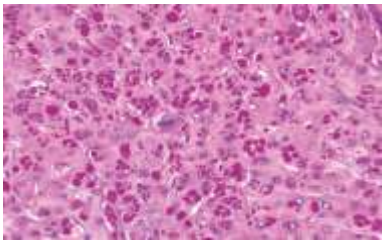


Image 15.23 Alpha1-Antitrypsin deficiency. A cirrhotic liver stained by the **periodic acid–Schiff (PAS) reaction** with diastase digestion to remove glycogen reveals numerous **magenta colored cytoplasmic globules within the hepatocytes.**

Major intrahepatic bile duct disorders

1) Primary biliary cirrhosis

- Inflammatory **autoimmune disease**[Q].
- Characterized by nonsuppurative, inflammatory destruction of medium-sized intrahepatic bile ducts.
- Mostly middle-aged women **(40-50 years of age group)**.
- Gender predilection-**female** to male; 6:1.
- Symptoms and sign-pruritus, jaundice, malaise, dark urine, light stools, and hepatosplenomegaly.
- Associated conditions are :
  - **Sjögren syndrome (70%)**[Q]; Scleroderma (5%); and Thyroid disease (20%).
- **Laboratory findings :**
  - **Conjugated hyperbilirubinemia**.
  - Increased serum alkaline phosphatase, bile acids and cholesterol.
- **Serology**
  a) **AMA-positive (95%)**[Q]
     - **M2 form of Anti-Mitochondrial Antibody**[Q] target the E2 component of the pyrurate dehydrogenase complex (PDC-E2).
     - **Most commonly**[Q] AMA is of **IgG1 and IgG3 classes**[Q].
  b) **ANA**[Q]-positive (50%)
  c) **ANCA**[Q]-positive (40%)
- **Histology** shows **dense lymphocytic infiltrate** in portal tracts with granulomatous destruction of bile ducts. **(Image : 15.24)**

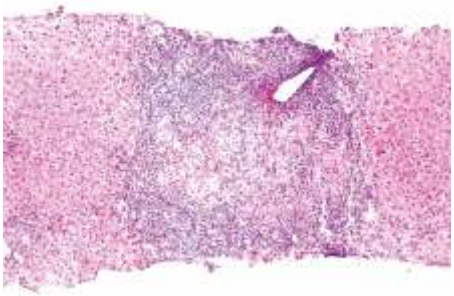


Image 15.24: Primary biliary cirrhosis. A portal tract is having **lymphocytes and plasma cells infiltrate** surrounding a destructive **granulomatous reaction** centered on a bile duct (the "**florid duct lesion**"). Florid duct lesion represents a damaged bile duct by the inflammation.

- Risk **micronodular cirrhosis; hepatocellular carcinoma**.
- Most common cause of death **liver cell failure** > variceal bleeding.

2) Secondary biliary cirrhosis

- Etiology is **extrahepatic bile duct obstruction**

(most common cause of obstruction in adults is extrahepatic cholelithiasis or **gallstones**) biliary atresia, gallstone, stricture, carcinoma of pancreatic head.

- Male and female equally affected.
- Symptoms and signs are pruritus, jaundice, malaise,dark urine,light stools, hepatosplenomegaly.
- **Laboratory findings**-Conjugated hyperbilirubinemia, increased serum alkaline phosphatase, bile acids, cholesterol.
- **Histology :**
  - Prominent bile stasis in bile ducts, bile ductular proliferation with surrounding neutrophils, portal tract edema.

3) Primary sclerosing cholangitis

- Its fibrosing cholangitis of bile ducts leading to inflammatory strictures and obliteration of **both intrahepatic and extrahepatic ducts**Q.
- **Etiology-**
  - Unkown etiology and associated with **HLA-B8, DR-3, DQ-2**.
  - Most probably **autoimmune**.
  - **50 to 70%**Q associated **with inflammatory bowel disease**Q **(ulcerative colitis > Crohn's disease)**; Riedel's thyroiditis.
- Male to female (2:1; 30-45 years age group).
- Symptoms and signs-pruritus, jaundice, malaise, dark urine, light stools, hepatosplenomegaly.
- **Laboratory findings :**
  - Conjugated hyperbilirubinemia
  - Increased serum alkaline phosphatase, Bile acids, and cholesterol.
  - **Elevated**Q serum **IgM**Q
  - Hypergammaglobulinemia
- **Antibodies seen are :**
  - **Anti-smooth muscle antibodies**.
  - Anti-nuclear antibodies (ANAs).
  - Rheumatoid factor.
  - **Atypical p-ANCA**Q (shows a perinuclear staining pattern but is directed aganist a nuclear envelope protein, instead of myeloperoxidase as is typical of p-ANCA antibodies).
- **Histology**
  - Concentric periductal fibrosis around affected ducts **("onion-skin fibrosis")**Q, segmental stenosis of extrahepatic and intrahepatic bile ducts.

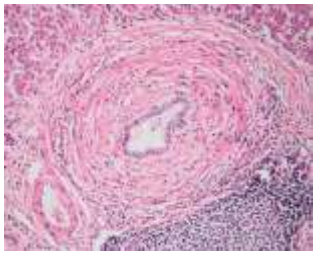


Image 15.25 Primary Sclerosing Cholangitis (PSC).
Liver biopsy showing **inflamed portal tract** with a dilated bile duct and **"onion skin" periductal fibrosis.**

- **Risk** is for biliary cirrhosis; chronic pancreatitis; hepatocellular carcinomas and cholangiocarcinoma.

Miscellaneous Important Liver And Biliary Disorders

1) Peliosis hepatisQ:

- Reversible **sinusoidal dilatation**
- Liver contains cystic spaces filled with blood which may or may not be lined by endothelial cells. **(Image : 15.26)**

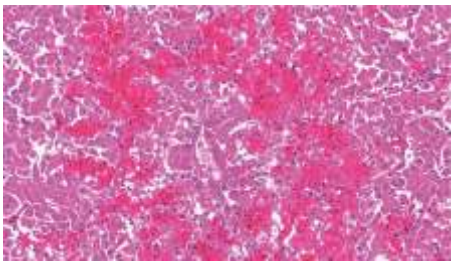


Image 15.26 Peliosis hepatis : It is a **vascular condition** of the liver characterized by a **proliferation of the sinusoidal hepatic capillaries** that results in **cystic blood-filled cavities** distributed randomly throughout the liver. **("Pelios"** means **blue/black or discolored extravasated blood).**

- **Associated with:**
  - **Cancer**Q
  - **Tuberculosis**
  - **AIDS**Q or **post-transplantation immunodeficiency**
  - **Anabolic steroids**Q
  - **Oral contraceptive pills**Q and **danazol**Q.

High Yield Info.....

FIBRIN RING GRANULOMAQ

- It consists of a **central lipid vacuole**Q (usually washed-out during fixing and staining, leaving only an empty hole) surrounded by a **dense red Fibrin ring**Q and epitheloid granuloma.
- It is seen in :
  a) **Q fever**Q
  b) **Hodgkin's disease**Q and
  c) **Infectious mononucleosis**Q

2) **Hepatic venous outflow obstruction**
   - They are two types:
     - Hepatic vein and IVC thrombosis-Budd-Chiari syndrome
     - **Veno-occlusive disease** (sinusoidal obstruction syndrome)-condition associated with small vein obstruction seen in high dose chemotherapy complication.
3) **Budd-Chiari Syndrome**
   - Due to **obstruction of hepatic vein**[Q] or inferior vena cava.
   - **Classical triad of :**
     - Hepatomegaly
     - Abdominal pain
     - Ascites
   - **Causes are :**
     - **Hepatic vein thrombosis**-CMPD (chronic myeloproliferative disorders-**polycythemia**[Q] is **most common**[Q] cause); inherited deficiency of anticoagulants protein C, S and antithrombin III; antiphospholipid syndrome; PNH; hepatocellular carcinoma; pregnancy and OCP.
     - Inferior vena cava membranous web.

Clinical features

Acute

- Abdominal pain; jaundice; hepatomegaly, ascites; raised liver enzymes and encephalopathy.

Fulminant

- Ealy presentation with encephalopathy and ascites. Liver cells necrosis; lactic acidosis; caudate lobe hypertrophy; **"SPIDER-WEB"**[Q] on imaging due to venous collaterals around obstruction.

Biliary Tree Anomalies

1) **Von meyenburg complexes :**
   - **"Bile duct microhamartomas"**[Q] consisting of dilated bile ducts within fibrous tissue in portal tract.
   - Origin is residual **embryonic bile duct remnants**[Q].
   - Associated with polycystic kidney disease **PKD1 gene mutations**[Q].
   - Clinically **insignificant**.
2) **Caroli disease :**
   - **Segmental dilatation** of larger ducts of **intrahepatic biliary tree**[Q] with associated bile inspissation.
   - Frequently complicated by cholelithiasis and hepatic abscess.
   - Increased risk of **cholangiocarcinoma**[Q].
3) **Alagille syndrome :**
   - **Autosomal dominant**.
   - Absent-intrahepatic bile duct along with peculiar facies; vertebral and cardiovascular defects.
   - Due to **mutation in Jagged-1 Notch signaling pathway** involved in development of many organ system.

Nodular Hyperplasias

- Solitary or multiple benign hepatocellular nodules in the **absence of cirrhosis**[Q].
- **Two types :**

a) **Focal nodular hyperplasia**
   - Mostly young to **middle aged** females.
   - Associated with use of **anabolic steroids**[Q] **or contraceptives**[Q].
   - **Central stellate fibrous scar**[Q] containing arterial blood vessels.
   - Hepatic1 functions and **AFP levels are normal**[Q].
   - Rarely grow or bleed.
   - **No malignant potential**[Q].

b) **Nodular regenerative hyperplasia:**
   - Diffuse nodular transformation of liver without fibrosis.
   - **Causes-condition affecting intrahepatic blood flow -**
     1) **Rheumatoid arthritis (most common**[Q]**)**
     2) Myeloproliferative disorders
     3) Hyperviscosity syndromes
     4) Solid organ transplantation (liver, kidney)
     5) HIV infection
     6) Vasculitis
     7) Drugs-anabolic steroids and cytotoxic drugs

Hepatic Tumours

- Most common hepatic neoplasm is **metastasis**[Q] (most common primary is from **colorectal carcinoma**[Q]) **(Image : 15.27 a and b)**
- Most common **benign neoplasm**[Q] of liver is **cavernous hemangioma**[Q].
- Most common **primary malignant tumor**[Q] of liver is **hepatocellular carcioma (Hepatoma)**[Q].
- Most common **primary malignant tumor**[Q] of liver in **childhood-hepatoblastoma**[Q].

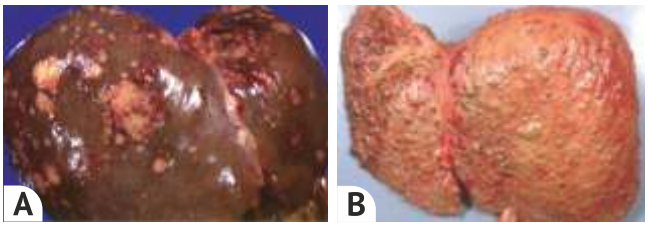


Image 15.27 Liver Metastasis versus cirrhosis (Blind Man's Diagnosis).

a) In metastases Liver will be showing **variable size of nodules** and **smooth areas between nodules**.

b) In cirrhosis Liver shows small regenerative nodules (less than 3 mm in size). It is considered as **Blind Man's Diagnosis** because blind man **differentiates cirrhosis from metastatic disease** by feeling **no "SMOOTH" areas between nodules of cirrhotic liver** (In metastases there will be smooth areas between nodules).

Benign Neoplasm

1) Hepatic adenoma (=liver cell adenoma) -

- Usually **female**[Q] (M:F = 1:9)
- **20-40 years** age group;
- Definite relationship to **oral contraceptives**[Q] **(80-90%)**, often **regress when discontinue**[Q].
- Most are solitary, right lobe, usually **> 10 cm** at presentation.
- More often symptomatic; hemorrhages are common and 25% present with hemoperitoneum.
- Well-defined capsule, well-differentiated hepatocytes with abundant cytoplasm, 2 cell layers thick, but **no portal triads, central veins, or fibrosis, and no bile ducts or connection with the biliary system**.
- Largest vessels are at the periphery and show intimal thickening and smooth muscle proliferation.
- **Absence**[Q] of **vascular invasion**[Q] differentiates from carcinoma.
- Often shows **"nodule within nodule"**[Q], infiltrative growth pattern, thick cords to sheets of cells.

2) Multiple hepatocellular adenomatosis

- Male and female are equally affected
- **No association**[Q] with **contraceptives**[Q]
- Patients are **older**
- Usually **> 10 nodules** of varying size.
- May be a very well-differentiated hepatocellular carcinoma.

Malignant Neoplasm

1) Angiosarcoma (=malignant hemangioendothelioma) -

- Freely **anastomosing vascular channels**; varying degrees of differentiation.
- Usually **factor VIII immunoreactive**[Q].
- Increased risk factors : Cirrhosis, **vinyl chloride**[Q] exposure, **thorium dioxide**[Q] exposure, **arsenic**[Q] exposure.
- Most patients die within 6 months of liver failure or abdominal hemorrhage.

2) Hepatoblastoma -

- **Most common primary malignant tumor**[Q] of **childhood**[Q], usually **in first 3 years**.
- Single, usually encapsulated; originate most commonly from **right lobe**[Q].
- Associated with **Wilms' tumor**[Q], glycogen storage disease, hemihypertrophy, virilization (ectopic steroid production), **Beckwith-Wiedemann syndrome, familial polyposis coli**.
- Tumor cells reactive for EMA, keratin, vimentin, AFP, CEA.
- Prognosis better than hepatocellular carcinoma

3) Hepatocellular carcinoma (=hepatoma) -

- Most common primary malignant tumor of adults.
- **Males** are commonly affected (M > F; 3:1; 20-40 yrs age group).
- Prevalent more in **Asia and Africa**.
- **Risk factors :**
  - Chronic hepatitis **(hepatitis B**[Q] **> C)**
  - Chronic alcoholism
  - **Tyrosinemia**[Q]
  - Hereditary hemochromatosis
  - **Aflatoxin**[Q] (toxin produced by fungus *Aspergillus flavus* contaminating peanuts).
  - NAFLD (non-alcoholic fatty liver disease).

Pathogenesis

- Chronic inflammation associated with genotoxic products, cytokine production and hepatocyte regeneration along with genetic susceptibility is basic mechanism.

- **HBV related HCC :**
  - Due to integration of **HBV-DNA** into host genome and proto-oncogene activation.
  - **X protein**[Q] of HBV transcriptionally activates viral gene and host gene.

Clinical features

- Commonly presents with ill-defined upper abdominal pain; malaise fatigue and weakness.
- Elevated serum **alpha-fetoprotein (50-70% cases)**[Q].

Morphology

- Unifocal, multifocal or diffuse infiltrative mass with **angioinvasive**[Q] (strong propensity to involve blood vessels) properties.
- **Mallory-Denk bodies**[Q] may be seen in cytoplasm
- **Tumor-markers of hepatocellular carcinoma -**
  - AFP
  - Hep-Par-1 (hepatocyte paraffin-1)
  - Des-gamma carboxy prothrombin (DCP), a protien induced by vitamin K abnormality (PIVKA-2).
  - **Neurotensin**[Q] (in case of **fibrolamellar variant**[Q] of hepatocellular carcinoma).
  - Vit B12 binding globulin
  - Glypican-3
  - Human hepatocyte growth factor
  - Insulin-like growth factor

Fibrolamellar carcinoma (variant of HCC)

- Young adults **(20-40 years)**
- **Equal gender** incidence **(India-females > males)**[Q]
- **Not associated** with **cirrhosis**[Q] or **HBV**[Q] infections.
- **Left lobe** is more commonly affected.
- **AFP - level is normal**[Q]; **neurotensin** is a tumor marker.
- **Histology** shows well-differentiated tumor cells which are separated by dense lamellar collagen bundles.
- Lymphatic spread
- **Better prognosis**[Q]

Gall Bladder and Pancreas

Gallstones (Cholelithiasis)

- It has a higher incidence in **women** and is often associated with obesity and multiple pregnancies.
- Risk factors (4 F's):
  a) Female
  b) Fat (Obesity)
  c) Fertile (multiple pregnancies)
  d) Forty (More than 40 years of age)
- Gallstones are formed due to increased cholesterol or bilirubin, decreased bile salts, and gallbladder stasis.
- **Types of gallstones:** They are of following two types: **(Table No.)**

Clinical features:

- Gallstones are frequently asymptomatic but can cause biliary colic (right upper quadrant pain due to impacted stones).
- **Diagnosis** is by **ultrasound**.

Complications:

- **Most common** complication is **cholecystitis.**
- Other complications are choledocholithiasis (calculi within the biliary tract), biliary tract obstruction, pancreatitis, cholangitis, and gallbladder cancer.

TYPES OF GALLSTONES

Cholesterol stones	Pigmented stones or Bilirubin stones
• It is composed of mostly **cholesterol monohydrate.**	• They are composed of **calcium salts** and **unconjugated bilirubin.**
• The incidence increases with age.	• Risk factors for developing pigmented bilirubinate stones are chronic hemolytic anemias, cirrhosis, bacterial infection, and parasites **(Ascaris or Clonorchis [Opisthorchis] sinensis).**
• Risk factors include female gender, obesity, pregnancy, oral contraceptives, and hormone replacement therapy (HRT).	
• **Most common** type of gallstones **(80%).**	

INFLAMMATORY CONDITIONS

Acute cholecystitis :

- It is an acute inflammation of the gallbladder usually caused by cystic duct obstruction by gallstones.
  a) Calculous cholecystitis:
  - It is **most common** type.

- It occurs due to **gallstone impaction** in the cystic duct resulting in inflammation and gallbladder wall thickening.
- It can produce secondary infections.

b) Acalculous cholecystitis:

- It occurs due to gallbladder stasis, hypoperfusion, or infection (CMV).
- It is seen in critically ill patients.

- Acute cholecystitis can present with biliary colic, right upper quadrant (RUQ) tenderness on palpation, nausea and vomiting, low-grade fever, and leucocytosis.
- Complications include gangrene of the gallbladder, perforation and peritonitis, fistula formation and gallstone ileus (small bowel obstruction by a large gallstone).

Chronic Cholecystitis:

- It is chronic inflammation of the gallbladder , usually caused by **gallstones.**
- It occurs due to chemical irritation from longstanding cholelithiasis, with or without superimposed bouts of acute cholecystitis.
- Clinically presents with vague right upper quadrant pain, especially after eating.
- It is characterized by herniation of gallbladder mucosa into the muscular wall (**Rokitansky-Aschoff sinuses**).
- **Porcelain gallbladder** is a late complication which shows **shrunken, hard gallbladder** due to chronic inflammation, fibrosis, and dystrophic calcification. It has high association with **gallbladder cancer (mostly adenocarcinoma).**

Disorders of the Extrahepatic Bile Ducts

Choledocholithiasis

- It refers to stones within the biliary tree.
- It occurs in 10% of patients with cholelithiasis.
  a) In **western countries**, almost all stones are gallbladder derived and are **cholesterol.**
  b) In **Asia**, they usually arise in the biliary tree and are **pigmented**.
- Symptoms are due to obstruction, pancreatitis, cholangitis, hepatic abscess, secondary biliary cirrhosis, and acute calculous cholecystitis.

Ascending Cholangitis

- It is bacterial infection of the bile ducts.
- Usually it occurs due to ascending infection with enteric gram-negative bacteria.
- Presents as sepsis (high fever and chills), jaundice, and abdominal pain
- **Charcot triad** of cholangitis includes **jaundice, fever, RUQ pain**.
- **Reynolds pentad** is **Charcot triad** plus **altered mental status** and **shock** (hypotension).
- Increased incidence with **choledocholithiasis** (stone in biliary ducts).

MISCELLANEOUS CONDITIONS

Cholesterolosis (Strawberry Gallbladder):

- It refers to an accumulation of **cholesterol-laden macrophages** within the mucosa of the gallbladder wall.
- **Gross examination** shows yellow speckling of the red-tan mucosa **("strawberry gallbladder").**
- **Microscopic examination** shows lipid-laden macrophages within the lamina propria.
- It has **no association** with inflammatory changes and no special association with cholelithiasis.

Mucocele (Hydrops of the Gallbladder)

- It occurs when **chronic obstruction of the cystic duct** leads to the resorption of the normal gallbladder contents and enlargement of the gallbladder by the production of large amounts of clear fluid (hydrops) or mucous secretions (mucocele).

Carcinoma of the Gallbladder

- Gall bladder carcinoma is more common in **females** older than 70 years. Tumors of the **gallbladder (gallbladder carcinoma)** are much more common than tumors arising from within the **bile ducts (cholangiocarcinoma).**
- Histologically they are **adenocarcinoma** arising from the glandular epithelium that lines the gallbladder wall.
- **Gallstones** are a **major risk factor**, especially when complicated by **porcelain gallbladder**.
- Classically presentation is with **cholecystitis** in an elderly female.
- They have **Poor prognosis.**

Cholangiocarcinoma

- Biliary tree malignancy arising from **bile ducts** (within liver or outside liver).
- **Classification (**on the basis of location):
  1) **Extrahepatic (most common type,** firm nodular mass; **90%).**
     a) **Perihilar-most common type (60%)** and known as **klatskins tumor** (located at the

junction of right and left hepatic ducts).
b) Distal bile duct (20-30%)
2) **Intrahepatic (10%)**

Risk factors :

a) Primary sclerosing cholangitis
b) Fibroploycystic disease of biliary system (Caroli's disease; choledochal cyst).
c) **Liver flukes-Clonorchis sinensis**; **Opisthorchis sinensis.**
d) Thorotrast contrast material.
e) Choledocholithiasis (Chronic Biliary inflammation and injury).
f) Chronic alcoholic liver disorders.
g) HCV infection.

Genetic alterations

- Overexpression of IL-6 → AKT activation →**overproduction of MCL-1** (anti-apoptotic protein).
- Decreased p53 expression.
- **K-RAS** overexpression.

Clinical features-

- Painless jaundice; pruritus; weight loss and alcoholic stools.

Histology

- **Adenocarcinoma** (well to moderately differentiated) with dense collagenous stroma (**Desmoplastic reactions).**
- Tumor cells are not bile stained (**bile staining** is seen with **hepatocellular carcinoma** since bile is synthesized by hepatocytes).

Pancreas embryology:

- Pancreas are derived from **foregut.**
- **Ventral pancreatic buds** contribute to uncinate process and main pancreatic duct.
- **Dorsal pancreatic bud** alone becomes the body, tail, isthmus, and accessory pancreatic duct.
- **Both** the ventral and dorsal buds contribute to **pancreatic head.**

a) Annular pancreas

- It is an abnormal rotation of ventral pancreatic bud forms a ring of pancreatic tissue which encircles 2nd part of duodenum.
- It may cause duodenal narrowing and vomiting.

b) Pancreas divisum:

- It's a common anomaly which occurs when ventral and dorsal parts fail to fuse at 8 weeks of intrauterine life.
- Mostly asymptomatic, but it may lead to chronic abdominal pain and pancreatitis.

Inflammation

A) **Acute pancreatitis**

- It is an **autodigestion of pancreatic parenchyma** due to premature activation of **trypsin** leading to activation of other pancreatic enzymes.
- This will result in **liquefactive haemorrhagic necrosis** of the pancreas and **fat necrosis** of the peripancreatic fat.

Etiology:

- Most commonly due to **alcohol** and **gallstones.**
- Other causes are idiopathic, trauma, steroids, mumps, autoimmune disease, Scorpion sting, Hypercalcemia, Hypertriglyceridemia (> 1000 mg/dL), ERCP, Drugs (e.g. sulpha drug and protease inhibitors).
- Mutations in the **cationic trypsinogen (PRSS1)** and **trypsin inhibitor (SPINK1) genes.**

Clinical features

- Nausea, vomiting, and acute epigastric abdominal pain radiating to the back.
- Periumbilical and flank hemorrhage due to spread of necrosis into the periumbilical soft tissue and retroperitoneum.
- Elevated serum **lipase** and **amylase** level (**lipase is more specific** for pancreatic damage).
- **Hypocalcemia** due to consumption of calcium during saponification during fat necrosis.

Gross examination

It will show focal hemorrhage and liquefication accompanied by chalky, white yellow fat necrosis of adjacent adipose tissue.

Microscopy:

Pancreatic tissue will show liquefactive necrosis of the pancreatic parenchyma with acute inflammation and enzymatic fat necrosis. Necrosis of blood vessels causes hemorrhage.

Diagnosis:

Diagnosis is done by **2 of 3 criteria:**

a) Acute epigastric pain often radiating to the back,
b) Serum amylase or lipase (**Lipase is more specific**) to **3× upper limit** of normal
c) Characteristic imaging findings.

Complications:

- **Shock** due to peripancreatic hemorrhage and fluid sequestration.
- **Pancreatic pseudocyst**:
  - It is formed by fibrous tissue surrounding liquefactive necrosis and pancreatic enzymes.
  - It will present as an abdominal mass with persistently elevated serum amylase.
  - Their rupture will be associated with release of enzymes into the abdominal cavity and hemorrhage.
- **Pancreatic abscess**
  - It is formed due to E. coli.
  - It will present with abdominal pain, high fever, and persistently elevated amylase.
- **Organ failure** (ARDS, shock, renal failure).
- **Hypocalcemia** due to precipitation of Ca2+ soaps.

B) Chronic Pancreatitis:

- It is chronic inflammation, atrophy, and fibrosis of the pancreas secondary to repeated episodes of acute pancreatitis.
- Most common cause of chronic pancreatitis is:
  a) Alcohol in **adults**.
  b) Cystic fibrosis in **children.**
- **Hereditary pancreatitis** due to mutations in the **pancreatic trypsinogen gene (PRRS1),** or the **SPINK1 gene** encoding a trypsin inhibitor

Clinical features

- Epigastric abdominal pain radiating to the back.
- **Pancreatic insufficiency**—results in malabsorption with steatorrhea and fat-soluble vitamin deficiencies.
- Dystrophic calcification of pancreatic parenchyma on imaging; contrast studies reveal a 'chain of lakes' pattern due to dilatation of pancreatic ducts.
- Secondary diabetes mellitus—late complication due to destruction of islets.
- Increased risk for pancreatic carcinoma.

Gross features:

Pancreas will be firm, white, and fibrotic.

Microscopy:

Pancreatic tissue will show extensive fibrosis with parenchymal atrophy and chronic inflammation.

- **Amylase** and **lipase** may or may not be elevated (**almost always elevated in acute pancreatitis).**

Pancreatic Neoplasms

- Pancreatic neoplasms are cystic or solid.

A) Cystic Neoplasms

- Cystic tumors constitute less than 5% of pancreatic neoplasms.
- They are painless and slow-growing masses.

1) Serous cystadenoma:

- Typically seen in women older than 60 years.
- Solitary, well-circumscribed nodules with a central stellate scar.
- They are composed of numerous 1- to 3-mm cysts lined by a glycogen-rich cuboidal epithelium and containing serous, watery fluid.
- Almost always benign and resection is curative.

2) Mucinous cystic neoplasm:

- Most commonly occur in **females,** and these are slow-growing painless masses in the **body or tail** of the gland.
- These are multiloculated cystic neoplasms filled with thick mucinous material.
- Cysts are lined by mucin-producing columnar cells within a dense stroma.
- **One third** of these lesions harbour an **invasive adenocarcinoma**.

3) Intraductal papillary mucinous neoplasm (IPMN):

- Most commonly **males** are affected.
- These are **intraductal mucin-producing neoplasms** arising in the **head** of the gland, and 10% to 20% are multifocal.
- They differ from mucinous cystic neoplasms by lacking a dense stroma and by involving a larger pancreatic duct.
- They have a similar malignant potential like mucinous cystic neoplasm.

4) Solid-pseudopapillary tumor:

- Mostly young females are affected and presents with abdominal discomfort due to their large size.
- These round and well-circumscribed neoplasms have solid and cystic regions.
- These tumors are associated with activating mutations of beta-catenin.
- Although some are locally aggressive, complete resection is usually curative.

B) Pancreatic Carcinoma

- Pancreatic carcinoma is most common between ages 60 and 80.
- Risk factors for pancreatic carcinoma are:
  a) Smoking
  b) Age > 50 years
  c) Diabetes mellitus
  d) Chronic pancreatitis (especially > 20 years)
  e) Family history of pancreatic cancer (e.g., **BRCA2 mutations** account for 10% of pancreatic cancer in Ashkenazi Jews).

Molecular cytogenetics:

- These are four genes are most commonly affected by somatic mutations in this neoplasm: **KRAS, CDKN2A/p16, SMAD4,** and **Tp53**.
  a) **KRAS** is the most common **oncogene mutation** in pancreatic cancers (**Overall most common gene mutation**).
  b) **p16 (CDKN2A) gene** is the most commonly inactivated **tumor suppressor gene** in pancreatic cancer.

Clinical Features:

- Abdominal pain radiating to back.
- Weight loss (due to malabsorption and anorexia).
- **Obstructive jaundice** with pale stools and palpable nontender gallbladder. It is associated with tumors that arise in the **head** of the pancreas (**most common site**). **Obstructive jaundice** with **palpable, nontender gallbladder** is known as **Courvoisier sign.**
- **Migratory thrombophlebitis (Trousseau syndrome):** It presents as swelling, erythema, and tenderness in the extremities (seen in 10% of patients).
- **Tumor markers** for pancreatic carcinoma include **CA19-9** and CEA (**CEA is less specific**).
- Very poor prognosis and 1-year survival is < 10%.

Microscopy

- Most common site of tumor origin is **pancreatic head (60%)**, followed by **body (15%)**, and **tail (5%).**
- Pancreatic adenocarcinoma arises from the duct epithelium.
- Tumor desmoplasia and perineural invasion are common.
- Most common site of metastases is **liver.**

1. **Nutmeg liver is seen in -** *(Recent Exam 2017,16,AI 13,14)*
   a) Right-sided heart failure
   b) Left-sided heart failure
   c) Increased pulmonary pressure
   d) Decreased pulmonary pressure
2. **In anoxia of liver, necrosis is seen in -** *(Recent Exam 2017,15)*
   a) Centrilobular region
   b) Around the periphery
   c) Around the central vein
   d) Around the bile duc
3. **Centrizonal necrosis of liver may be seen with -**
   a) Carbon tetrachloride (CCl_4) toxicity *(Recent exam 2017,13)*
   b) Congestive heart failure (CHF)
   c) Smoking (chronic)
   d) Chronic alcoholism
4. **Unconjugated hyperbilirubinemia is seen in -** *(AI 13,14)*
   a) Rotor's syndrome
   b) Dubin-Johnson syndrome
   c) Gilbert's syndrome
   d) Bile duct obstruction
5. **True regarding unconjugated bilirubin is -** *((Recent Exam 2015,13)*
   a) Not lipid soluble
   b) More water soluble
   c) Excreted by kidney easily
   d) Bound with serum albumin
6. **Liver biopsy is normal in -** *(PGI Nov 14, Recent exam 2016)*
   a) Dubin-Johnson syndrome
   b) Gilbert's syndrome
   c) Hemochromatosis
   d) Wilson's disease
   e) Rotor's syndrome
7. **Normal liver histology is seen in -** *(PGI nov 2016)*
   a) Gilbert's syndrome
   b) Rotor's syndrome
   c) Criggler-Najjar syndrome
   d) D-J syndrome
   e) Hemochromatosis
8. **In post-hepatic jaundice, the concentration of conjugated bilirubin in the blood is higher than that of unconjugated bilirubin because -** *(Recent Exam 2017,AIIMS Nov 02)*
   a) There is an increased rate of destruction of red blood cells
   b) The unconjugated bilirubin is trapped by the bile stone produced in the bile duct
   c) The conjugation process of bilirubin in liver remains operative without any interference
   d) The UDP-glulcuronoyl transferase activity is increased manifold in obstructive jaundice
9. **Gilbert's syndrome, true all except -** *(Recent Exam 2017,13,14)*
   a) Causes cirrhosis
   b) Autosomal dominant
   c) Normal liver function test
   d) Normal histology

HEPATITIS

10. **Councilman bodies are seen in -** *(Recent Exam 2017,16)*
    a) Alcoholic cirrhosis
    b) Wilson's disease
    c) Acute viral hepatitis
    d) Autoimmune hepatitis
11. **Histopathology of chronic hepatitis -** *(AI 13, 14)*
    a) Ballooning degeneration
    b) Councilman bodies
    c) Bridging fibrosis
    d) All of the above
12. **Piecemeal necrosis on liver biopsy is a feature of-** *(Recent Exam 2016)*
    a) Alcoholic hepatitis
    b) Indian childhood cirrhosis
    c) Chronic active hepatitis
    d) Primary alcoholic cirrhosis
13. **Chronic persistent hepatitis and chronic active hepatitis are differentiated by -** *(Recent Exam 17,16)*
    a) Anti-SM (smooth muscle) antibody
    b) CRP (C-reactive proteins)
    c) Arthritis
    d) Liver biopsy
14. **The liver biopsy in acute hepatitis due to hepatitis B virus is likely to show all of the following except-** *(Recent Exam 2014,15,AIIMS May 04)*
    a) Ballooning change of hepatocytes
    b) Ground glass hepatocytes
    c) Focal or spotty necrosis
    d) Acidophil bodies
15. **Ground glass hepatocytes are seen in which of the viral hepatitis -**
    a) HAV *(DNB June 14; JIPMER 12)*
    b) HBV
    c) HCV
    d) HDV
16. **Histological features of chronic hepatitis -** *(PGI May 13, Nov 14)*
    a) Fibrosis of porta hepatitis
    b) Architechtural changes
    c) Bridging necrosis
    d) Ballooning degenerations

FATTY LIVER

17. **Periportal fatty infiltration of liver is seen with -**
    a) Alcoholism *(Recent exam 2017,DNB Dec 07)*
    b) Viral hepatitis
    c) Malnutrition
    d) Tetracycline
18. **A 40 yrs old obese lady with diabetes mellitus; hypertriglyceridemia; RUQ pain and recurrent jaundice.What will be seen in liver Pathology-** *(Recent Exam 2017,16, AIIMS May 14)*
    a) NASH
    b) Microvesicular hepatosis
    c) Peliosis hepatitis
    d) Autoimmune hepatitis
19. **Increased IgA level is seen in?** (Recent Exam 15, JIPMER 14)
    a) Alcoholic hepatitis
    b) Biliary cirrhosis
    c) Gilbert's syndrome
    d) Autoimmune hepatitis
20. **Which one of the following diseases characteristically causes fatty change in liver -** *(Recent Exam 2017)*
    a) Hepatitis B virus infection
    b) Wilson's disease
    c) hepatitis C virus infection
    d) Chronic alcoholism
21. **Mega-Mitochondria is a characteristic feature of-**
    a) Alcoholic liver injury *(Recent Exam 2016, JIPMER 14)*
    b) Viral hepatis
    c) Peliosis Hepatitis
    d) None
22. **Pathological manifestation of chronic alcoholism include all of the following except -** *(AI 13,14)*
    a) Piecemeal necrosis
    b) Balloning degeneration
    c) Microvesicular fatty changes
    d) Central hyaline sclerosis

23. A 49 yr old male presents with symptoms that developed following a long weekend of binge drinking. His serum reveals GGT level of 65 IU/L. A liver biopsy reveals fatty change (steatosis) of numerous hepatocytes. This patient's liverabnormality is most likely the result of - *(Recent Exam 2013,JIPMER 2015)*
a) Decreased free fatty acid delivery to liver
b) Decreased production of triglycerides
c) Increased mitochondrial oxidation of fatty acids
d) Increased NADH production

24. Macrovesicular fatty liver is seen in - *(AI 96)*
a) Protein-energy malnutrition
b) Viral hepatitis
c) Acute fatty liver of pregnancy
d) Reye's syndrome

25. Mallory bodies contain - *(AI 13, 14; Recent Exam 2016)*
a) Vimentin
b) Cytokeratins
c) Desmin
d) Collagen

26. Which does not cause microvesicular steatosis - *(AI 13, 14)*
a) Alcoholic fatty liver
b) Tetracycline toxicity
c) Acute fatty liver of pregnancy
d) Reye's syndrome

27. Mallory hyaline is characteristic feature of - *((Recent Exam 2017,15)*
a) Hepatocellular carcinoma
b) Primary biliary cirrhosis
c) Alcoholic liver disease
d) Wilson's disease

28. Microvesicular fatty liver is caused by - *(AI 97)*
a) DM
b) Valproate
c) Starvation
d) IBD

29. A 4 yr old girl presents with severe vomiting after viral fever of 6 days. She develops cerebral edema later on. What would be the liver biopsy findings? *(AIIMS May 2014)*
a) Centrizonal hemorrhagic necrosis
b) Marked microvesicular steatosis
c) Ring granuloma
d) NASH

30. Mallory hyaline bodies are present in all of the following except-
a) Primary biliary cirrhosis *(DNB Nov 14)*
b) Secondary biliary cirrhosis
c) Indian childhood cirrhosis
d) Alcoholic cirrhosis

31. Which one of the following is not a feature of liver histology in noncirrhotic portal fibrosis (NCPF)- *(AI 05)*
a) Fibrosis in and around the portal tracts
b) Thrombosis of the medium and small portal vein branches
c) Nonspecific inflammatory cell infiltratess in the portal tracts
d) Bridging fibrosis

32. A yound boy presened with severe hematemesis. On Examination there was no hepatomegaly, Mild splenomegaly is present. Endoscopy shows esophageal varices. The most probabe diagnosis-
a) Veno-occlusive disease *(AIIMS Nov 2000)*
b) Budd-chiary syndrome
c) Cirrhosis liver
d) Noncirrhotic portal fibrosis

CIRRHOSIS

33. Micronodular cirrhosis is found in- *(Recent Exam 2017,15)*
a) Chronic hepatitis B
b) Alcoholic cirrhosis
c) Hemochromatosis
d) Chronic cirrhosis secondary to biliary cirrhosis

34. Collagen accumulated in Space of Disse in case of liver cirrhosis are -
a) 1 and 4 *(Recent Exam 2017,16; WBPG 16)*
b) 2 and 4
c) 1 and 3
d) 2 and 3

35. Micronodular cirrhosis is found in - (PGI May 14)
a) Jejunoileal bypass
b) Wilson's disease
c) Hemochromatosis
d) Chronic hepatitis B infection
e) Chronic hepatitis C infection

METABOLIC DISORDER

36. Hemochromatosis is a defect in metabolism of -
a) Iron *(Recent Exam 2017, 14)*
b) Copper
c) Magnesium
d) Calcium

37. All are seen in hemochromatosis except - *(Recent exam 2016)*
a) Hypogonadism
b) Arthropathy
c) Bronze diabetes
d) Deferoxamine is the treatment of choice

38. Diabetic patient with liver cirrhosis and hyper-pigmentation, diagnosis is - *(Recent Exam 2013,14)*
a) Wilson's disease
b) Hemochromatosis
c) Primary sclerosing cholangitis
d) Hepatitis B

39. Wilson's disease is characterized by - *(Recent exam 2018, AI 13, 14)*
a) Increased serum ceruloplasmin
b) Decreased copper excretion in urine
c) Increased copper in liver
d) Autosomal dominant

40. Gene of Wilson's disease is- *(Recent Exam 2017,16)*
a) ATP 7A
b) ATP 7B
c) ADP 7A
d) ADP 7B

41. Raised iron content is not found in which organ in hemochromatosis
a) Heart *(Recent Exam 2016, AIIMS Nov 2009)*
b) Skin
c) Testis
d) Pituitary

42. Gene for Wilson's disease is located on chromosome - *(AI 13, 14)*
a) 7
b) 10
c) 13
d) 17

LIVER TUMORS

43. Which virus causes hepatocellular carcinoma -
a) Arbo *(Recent Exam 2017,14)*
b) Herpes
c) Hepatitis-A
d) Hepatitis-B

44. Most common benign tumour of liver is - *(Recent Exam 2016)*
a) Papilloma
b) Hepatic adenoma

c) Ameboma
d) Hemangioma

45. AFP is raised in - *(Recent exam 2017)*
a) Hepatic adenoma
b) Hepatocellular carcinoma
c) Focal nodular hyperplasia
d) None of the above

46. Best prognosis is seen in - *(Recent Exam 2015, AIIMS 98)*
a) Fibrolamellar hepatoma
b) Hepatoblastoma
c) Angiosarcoma
d) Cholangiosarcoma

47. Angiosarcoma of liver is associated with - *(Recent Exam 2016)*
a) Nickel
b) Chromium
c) Cadmium
d) Arsenic

48. True about fibrolamellar carcinoma of liver is all except - *(AIIMS Nov 01)*
a) Females do not have increased incidence than males
b) Has good prognosis
c) Not associated with liver cirrhosis
d) Serum AFP levels are usually > 1000 mg/litre

49. Thorium dioxide causes - *(AI 13, 14)*
a) Lymphoma
b) Lymphangiosarcoma
c) Angiosarcoma
d) Hemangioma

BILIARY TRACT

50. The following condition of GB is precancerous - *(AI 2013, 14)*
a) Cholesterosis
b) Porcelain gallbladder
c) Biliary atresia
d) Choledochal cyst

51. Canals of herring are present in - *(PGI 98)*
a) Spleen
b) Liver
c) Lymph node
d) Bone marrow

52. Adenocarcinoma of gallbladder are always located in - *(AIIMS 86)*
a) Fundus
b) Neck
c) Harman's pouch
d) Bile duct

53. Klatskin's tumor is - *(AI 13, 14)*
a) Nodular type of cholangiocarcinoma
b) Fibrolamellar hepatocellular carcinoma
c) Gallbladder carcinoma
d) Hepatocellular carcinoma

54. Primary biliary cirrhosis positive for- *(AI 13, 14)*
a) PANCA
b) Anti-mitochondrial antibody
c) Anti-nuclear antibody
d) Anti-microsomal antibody

55. Which is risk factor for cholangiocarcinoma - *(AI 13, 14)*
a) Obesity
b) Primary sclerosing cholangitis
c) Salmonella carcinoma
d) HBV infection

56. Sclerosing cholangitis is associated with - *(AI 13, 14)*
a) Ulcerative colitis
b) Celiac sprue
c) Wilson's disease
d) Whipple's disease

57. Focal diffuse gallbladder wall thickening with comet tail reverberation artifacts on USG is seen in - *(DNB Dec 08)*
a) Adenomyomatosis of gallbladder
b) Ca gallbladder
c) Adenomatous polyps
d) Xanthogranuloma

MISCELLANEOUS

58. Peliosis hepatis is caused by all except - *(Recent Exam 2016,15)*
a) Analgesics
b) Anabolic steroids
c) OC pills
d) Danazol

59. Child treated for viral fever with aspirin and now presenting with confusion, vomiting, cerebral edema and acute liver failure. Liver biopsy will show characteristic pathology of steatosis due to which of the following? *(Recent Exam 2017; Jipmer 14)*
a) Defect in urea cycle
b) Defect in beta oxidation
c) Defect in glycogen
d) Defect in protein metabolism

60. Von meyenburg complexes is seen in - *(PGI Nov 10)*
a) Brain
b) Liver
c) Kidney
d) Spleen
e) Pancreas

61. Intake of which of these cause vascular lesions in liver -
a) Halothanes *(AIIMS Dec 97)*
b) INH
c) Steroids
d) CPZ

62. Chronic active hepatitis seen in - *(CUPGEE 97)*
a) Methyldopa
b) Oestrogen
c) Erythromycin
d) Tetracycline

63. Nutmeg liver is gross appearacne of liver in one of the following-
a) Cirrhosis of liver *(Recent Exam 16, TNPSC 2K)*
b) Hepatoma
c) Secondary carcinomatous deposit in liver
d) Chronic passive congestion in liver

64. Major source of collagen in cirrhosis -
a) Kupffer cells *(Recent Exam Nov 16, Jipmer 02)*
b) Ito cell (hepatic stellate cell)
c) Hepatocyte
d) Canalicular cell

65. In chronic inflammation confined to portal tract with intact limiting membrane and normal lobular parenchyma, the histopathological diagnosis would be - *(Recent Exam 2015, ICS 98)*
a) Active hepatitis
b) Chronic active hepatitis
c) Chronic persistent hepatitis
d) Alcoholic hepatitis

66. Pathological change of liver cells in acute viral hepatitis is -
a) Ballooning degeneration *(Recent Exam 2016, AIIMS 87, AI 90)*
b) Ground glass hepatocytes
c) Piecemeal necrosis
d) Fatty change

67. Chronic active hepatitis is most reliably distinguished from chronic persistent hepatitis by the presence - *(UPSC 02)*

a) Extrahepatic manfestation
b) Significant titre of antismooth muscle antibody
c) Characteristic liver histology
d) Hepatitis B surface antigen

68. Which of the following is single most important indicator of likelihoodness of progression of hepatitis to liver crrhosis - *(MH 10)*
a) Etiology
b) Associated serological findings
c) Presence of bridging necrosis
d) Presence of mallory hyaline

69. In cirrhosis liver all are seen except - *(Kerala 96)*
a) Loss of normal architecture
b) Degeneration of hepatocytes
c) Fatty infiltration
d) Loss of intercellular connective tissue matrix

70. Midzonal necrosis is liver may occur in- (Bihar 91)
a) Enteric fever
b) Yellow fever
c) Scarlet fever
d) Rheumatic fever

71. Microvesicular type to fatty liver is seen in the following except-
a) Acute fatty liver of pregnancy *(Recent Exam 2014, UPSC I-08)*
b) Alcoholic liver disease
c) Reye's syndrome
d) Phosphorus intoxication

72. Macronodular cirrhosis is considered once nodule diameter is greater than - *(Recent Exam Aug 2013, Kerala 04)*
a) 1 mm
b) 2 mm
c) 3 mm
d) 4 mm

73. Fatty change in liver is seen with use of - *(PGI 79, Delhi 93)*
a) Tetracycline
b) Erythromycin
c) Chlorpromazine
d) Acetoaminophen

74. Alcoholic hyaline, in alcoholic liver disease is composed of -
a) Lipofuscin *(UP 07)*
b) Eosinophilic intracytoplasmic inclusionss
c) Basophilic intracytoplasmic inclusions
d) Hemozoin

75. In alcoholic liver disease, which of the following pigments deposited in the hepatocytes - *(Recent Exam 2015, UP 08)*
a) Hemosiderin
b) Hemoglobin
c) Lipofuscin
d) Melanin

76. Vinyl chloride has been implicated in - *(JIPMER 88)*
a) Angiosarcoma of liver
b) Angiofibroma of nose
c) Hepatomas
d) Bladder cancer

77. Mallory hyaline is seen in - *(Delhi PG Feb 09)*
a) Hepatitis C infection
b) Amebic liver abscess
c) Indian childhood cirrhosis
d) Autoimmune hepatitis

78. HBV is not associated with - *(Karnat 96)*
a) Chronic active hepatitis
b) Chronic persistent hepatitis
c) Post necrotic cirrhosis
d) Cholangiocarcinoma

79. Patient had recurrent episodic jaundice, given steroids, improved. ANA positve (1;40) treated by immunosuppressive drugs-
a) Non-alcoholic steatohepatitis *(AIIMS May 2014)*
b) Peliosis hepatis
c) Autoimmune hepatitis
d) Primary biliary sclerosis

80. Which of the following is not correct about fibrolamellar variant of hepatocellular carcinoma- *(Recent Exam 2016)*
a) Occurs in young males and females
b) Hepatitis B virus is an important risk factor
c) Often has a better prognosis
d) Is a hard scirrhous tumour

81. Cholangiocarcinoma of liver caused by - *(UP 08)*
a) Hepatitis B infection
b) Cirrhosis of liver
c) Alpha-fetoprotein
d) Clonorchis sinensis infection

82. "Onion skin" fibrosis of bileduct is seen in - *(COMED 09)*
a) Primary biliary cirrhosis
b) Primary sclerosing cholangitis
c) Extrahepatic biliary fibrosis
d) Congenital hepatic fibrosis

83. Grossly pigmented liver is seen in --- syndrome - *(AI 96)*
a) Criggler-Najjar syndrome
b) Gilbert's syndrome
c) Dubin-Johnson syndrome
d) Rotor's syndrome

84. Which one of the following is not a feature of liver histology in non-cirrhotic portal fibrosis (NCPF) - *(DPG 10)*
a) Fibrosis in and around the portal tracts
b) Thrombsis of the medium and small portal vein branches
c) Non-specific inflammatory cell infiltrates in the portal tracts
d) Bridging fibrosis

85. The genetic defect in Dubin-Johnson syndrome is - *(Recent Exam 2017, 16)*
a) Mutation in gene for multiple drug resistance protein 2
b) Mutation in UDP-glucuronyl transferase
c) Mutation of chromosome 23
d) Flash mutations

86. Skin pigmentation to bronze diabetes is due to - *(JIPMER 90)*
a) Hemosiderin
b) Lipofuscin
c) Melanin
d) Both melanin and hemosiderin

87. Single most indicator of likelihoods of rapid progression of hepatitis to liver cirrhosis is - *(MH 11)*
a) Associated serological finding
b) Underlying etiology
c) Presence of bridging necrosis
d) Presence of Mallory hyaline

88. Primary sclerosing cholangitis is likely to be associated with -
a) Adenocarcinoma of pancreas *(JIPMER 11)*
b) Cholangiocarcinoma
c) Hepatocellular carcinoma
d) Adenocarcinoma of gallbladder

89. Increased vitamin B-12 level is seen in all except-
a) Cirrhosis *(Recent Exam 2013;16, AI 10)*
b) Primary hepatocellular carcinoma
c) Hepatitis
d) Cholestatic jaundice

EXTRA EDGE MCQS

1. Which of the following sentences about hepatitis E virus *(HEV)* is true?
a) HEV infections are always self-limiting.

b) Chronic HEV infection occurs exclusively in immunosuppressed patients.
c) HEV infection cannot be diagnosed biologically.
d) HEV RNA is never detected in blood.

2. A 26-year-old man comes to your office for an Examination because of tremors, spasticity, and drooling. He has headaches and fatigue. On physical Examination, he is very slightly icteric, the liver is not palpable, and no spider angiomata are present, but he has resting and intention tremors and spasticity. Laboratory tests show elevated AST and ALT and a ceruloplasmin level of 70 mg/L. The diagnosis is
a) Hemochromatosis
b) Gaucher's disease
c) Biliary cirrhosis
d) Wilson's disease

3. A 43-year-old woman comes to your office complaining of pruritus, mainly of the soles and palms, and fatigue. She has minimal jaundice and steatorrhea. Laboratory tests show a slightly elevated bilirubin, an elevated alkaline phosphatase, and a positive IgG antimitochondrial antibody test. The likely diagnosis is
a) Extrahepatic biliary tract obstruction
b) Alcoholic hepatitis
c) Viral hepatitis
d) Primary biliary cirrhosis

4. A 35-year-old woman comes to your office with complaints of fatigue, anorexia, nausea, and vomiting. She does not have fever. Her urine is dark and her stool is clay colored. On physical Examination, her liver is slightly enlarged and minimally tender. She does not have edema or spider angiomata. Laboratory tests show the following: negative HBsAg, positive IgM anti-HAV, positive IgM anti-HBc, and negative anti-HCV. The most likely diagnosis is
a) Acute hepatitis A
b) Acute hepatitis B
c) Acute hepatitis A and B
d) Chronic hepatitis B

5. A 51-year-old man health care worker whom you Examine for the first time feels well. You do a complete physical Examination, which is normal except for slight overweight and borderline hypertension. It is interesting that his laboratory studies show the following hepatitis B virus profile: positive HBsAg, negative anti-HBs, low levels of IgG anti-HBc, positive anti-HBeAg, and negative anti-HBe. The likely diagnosis is
a) Acute HBV infection, high infectivity
b) Late-acute HBV, low infectivity
c) Recovered from HBV infection
d) Chronic HBV infection, high infectivity

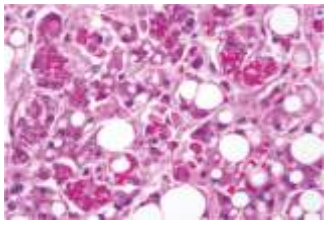
6. A mononuclear portal inflammatory infiltrate that disrupts the limiting plate and surrounds individual hepatocytes (piecemealnecrosis) is characteristic of
a) Ascending cholangitis
b) Chronic active hepatitis
c) Acute alcoholic hepatitis
d) Cholestatic jaundice

7. A 55-year-old woman manager of a regional long-distance telephone office whom you Examine for the first time feels well. You do a complete physical Examination, which is normal except for a few very small palpable and moveable, nontender nodes in both cervical chains and occasional wheezes in the lungs. However, her laboratory studies show the following hepatitis B virus profile: negative HBsAg, positive anti-HBs, low levels of IgG anti-HBc, negative anti-HBeAg, and positive anti-HBe. The likely diagnosis is
a) Acute HBV infection, high infectivity
b) Late-acute HBV, low infectivity
c) Recovered from HBV infection
d) Chronic HBV infection, high infectivity

8. Dilated sinusoids and irregular cystic spaces filled with blood within the liver, which may rupture, leading to massive intraabdominal hemorrhage, are most commonly associated with
a) Salicylates
b) Estrogens
c) Anabolic steroids
d) Acetaminophen

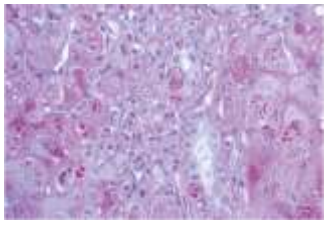
9. Male presents with symptoms that developed following a long weekend of binge drinking. His serum reveals a γ-glutamyl transferase (GGT) level of 65 IU/L. A liver biopsy reveals fatty change (steatosis) of numerous hepatocytes. This patient's liver abnormality is most likely the result of
a) Decreased free fatty acid delivery to the liver
b) Decreased production of triglycerides
c) Increased mitochondrial oxidation of fatty acids
d) Increased NADH production

10. A 38-year-old man presented with nausea, upper abdominal pain, and jaundice following a heavy bout of alcohol drinking. Serum bilirubin and liver Enzymes were elevated. Liver Biopsy was done and histopathology is shown in the image. Identify this accumulations seen in the biopsy?



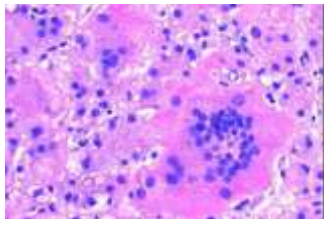
a) Alpha 1-Antitrypsin globules
b) Bile pigment
c) Mallory-Denk bodies
d) Viral inclusions (HBsAg)

11. A 28-year-old man has had increasing shortness of breath and Breath sounds are decreased in all lung fields. He has family history of liver disease and he had developed marked icterus as a neonate. His liver biopsy stained with PAS shows histopathology given in image. This patient is having high risk for development of which of the following conditions?



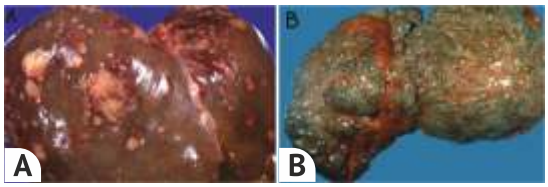
a) Acute fulminant hepatitis
b) Bronchiectasis
c) Pulmonary emphysema
d) Systemic lupus erythematosus

12. LIVER biopsy showing characteristic cells shown in image. Most likely diagnosis will be:



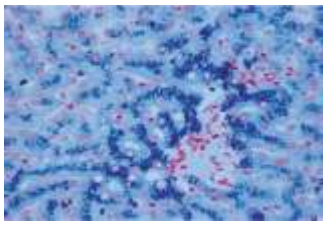
a) Liver cirrhosis
b) Ground glass hepatocytes of hepatitis-B virus
c) Neonatal hepatitis
d) Hepatocellular carcinoma

13. There are two gross specimens of liver are given below and labelled as "A" and "B". Which of the following is true statement?



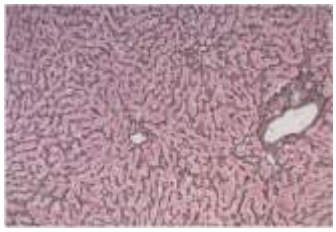
a) A is Cirrhosis; B is Metastatic liver
b) A is Metastatic liver; B is Cirrhosis
c) A is Metastatic liver; B is Liver Abscess
d) Both are metastatic liver.

14. A 34-year-old Infertile male was diagnosed to have liver cirrhosis and liver biopsy with special stain was seen as shown in image. True statement regarding this clinicopathological condition is :



a) Biopsy is showing Oil red o stain and direct damage of testis is the reason for infertility
b) Biopsy is showing Perl's prussian blue stain and direct damage of testis is the reason for infertility
c) Biopsy is showing Perl's prussian blue stain and hemosiderin deposition is the most common cause of bronze diabetes in this disorder.
d) Biopsy is showing Perl's prussian blue stain and Melanin deposition is the most common cause of bronze diabetes in this disorder.

15. Identify this special stain performed on liver biopsy:



a) Warthin starry silver stain.
b) Grimelius silver stain
c) Steiner silver stain
d) Sweets reticulin stain

LATEST QUESTIONS

1. Specific enzyme increased in alcoholic liver disease *(AIIMS Nov 2018)*

a) ALT b) LDH
c) GGT d) ALP

2. A 30-year-old male patient presented to AIIMS OPD with complaints of fever, abdominal pain and loss of appetite, dark yellow colored urine and pale stools. He had one-week history of jaundice and laboratory reports were showing total bilirubin -18.5mg/dL, direct bilirubin - 9.6mg/dL, SGOT-896U/L, and SGPT-995U/L. A clinical diagnosis of acute hepatitis was made. which of the following investigations will you do for confirmation of diagnosis? *(AIIMS May 2018)*

a) HBs Ag, HBe Ag, anti - HAV, Anti - HCV
b) HBs Ag, Anti - HBc IgM, anti - HAV, anti - HCV
c) Anti HBc IgG, HBE Ag, Anti HBe, anti - HAV, Anti - HCV
d) HBs Ag, Anti HBs IgM, HBe Ag, anti - HAV, Anti - HCV

3. MRP 2 associated with which of the following? *(Recent exam 2019)*

a) Rotor syndrome
b) Dubin-Johnson syndrome
c) Crigler-Najjar syndrome
d) Gilbert syndrome

4. Space of disse is in: *(Recent exam 2019)*

a) Spleen
b) Lymph node
c) Liver
d) Bone

5. Vitamin A is stored in *(Recent exam 2019)*

a) Ito Cell
b) Hepatocyte
c) Endothelial cell
d) Kupffer cell

AIIMS NEW PATTERN BASED QUESTIONS

Hepatic Pathology (EMQ)

For each of the following clinical histories, match the most characteristic, diagnostic hepatic morphologic finding:

1. A 48-year-old woman who has never smoked has experienced increasing dyspnea for several years. Spirometry reveals findings characteristic for an obstructive lung disease, and a pulmonary ventilation-perfusion scan reveals decreased areas of perfusion in all lung fields, while a chest radiograph reveals increased areas of lucency in all lung fields. Her cardiac function is still normal. She has a firm liver edge on physical examination:
2. A 45-year-old woman is obese and has a history of diabetes mellitus. She uses alcohol rarely. On abdominal CT scan, the liver is slightly enlarged and shows uniform decreased attenuation. Laboratory findings show: serum total protein 7.0 g/dL, albumin 3.8 g/dL, alkaline phosphatase 62 U/L, AST 87 U/L, ALT 84 U/L, total bilirubin 1.2 mg/dL, and direct bilirubin 0.8 mg/dL:
3. A 38-year-old woman has had nausea for the past week. On examination she has scleral icterus and a slightly increased liver span. Laboratory studies show total protein 5.5 g/dL, albumin 3.1 g/dL, total bilirubin 6 mg/dL, AST 109 U/L, ALT 122 U/L, and alkaline phosphatase 62 U/L. Serologic studies show HBsAg positive and HBeAg positive:
4. A 48-year-old man has sudden severe hematemesis. Upper GI endoscopy shows ruptured esophageal varices:
5. A 66-year-old man has weight loss of 4 kg and malaise for 4 months. One examination his liver span is increased. Laboratory studies show AST 30 U/L, ALT 25 U/L, total bilirubin 1 mg/dL, and alkaline phosphatase 199 U/L. CT imaging of his abdomen shows a solitary irregular 11 cm mass in the right lobe of his liver:

Options

A. Central venular sclerosis
B. Centrilobular congestion
C. Cholangiocarcinoma
D. Hemosiderin deposition
E. Macrovesicular steatosis
F. Periportal PAS-positive globules
G. Interface hepatitis
H. Portal fibrosis

1. **Ans. is 'a' i.e., Right-sided heart failure**
   [Ref: Robbin's 9th/e p. 865; 8th/e p. 872]
2. **Ans. is 'a' i.e., Centrilobular; 'c' i.e., Around the central vein**
   [Ref: Schiffs diseases of liver 8th/e p. 1221]
3. **Ans. is 'a' i.e., Carbon tetrachloride (CC l4) toxicity; 'b' i.e., Congestive heart failure (CHF)** *[Ref: Chandrasoms Taylor 3rd/e p.639]*
4. **Ans. is 'c' i.e., Gilbert's syndrome**
   [Ref: Robbin's 9th/e p. 854; 8th/e p. 841]
5. **Ans. is 'd' i.e., Bound with serum albumin**
   [Ref: Robbin's 9th/e p. 853; 8th/e p. 839-840]
   Direct (=conjugated bilirubin.
   - Normal level is up to 0.3 mg/dl
   - Water soluble
   - Loosely bound to albumi
   - Easy glomerular filtration and excreted in urine Indirect (= unconjugated) bilirubin:
   - Normal level is 0.3 to 0.7 mg/dl
   - Lipophilic and water insoluble
   - Tightly bound to albumin
   - Cannot excreted into urine
   - Can cross blood-brain barrier and damage brain of newborn *(kernicterus)* with erythroblastosis fetalis.
6. **Ans. is 'b' i.e., Gilbert's syndrome; 'e' i.e., Rotor's syndrome**
   [Ref: Robbin's 9th/e p. 854; 8th/e p. 841]
7. **Ans. is 'a' i.e., Gilbert's syndrome; 'b' i.e., Rotor's syndroe; 'c' i.e., Crigler-Najjar syndrome** *[Ref: Robbin's 9th/e p.865; 8th/e p.872]*
8. **Ans. is 'c' i.e., The conjugation process of bilirubin in liver remains operative wihout any interference**
   [Ref: Harrison 's 18th/e p. 324; Robbin's 9th/e p.852 and 8th/e p. 840-841]
9. **Ans. is 'a' i.e., Causes cirrhosis**
   [Ref: Harrison's 18th/e p.2534; Robbin's 9th/e p.854 and 8th/e p.841]
   Gilbert's syndrome
   - Autosomal dominat > autosomal recessive
   - Normal liver histology
   - Liver biochemical tests are normal except for elevated bilirubin level (bilirubin usually < 3 mg / dl)
   - Not associated with cirrhosis
   - Precipitated by – stress; fatigue; alcohol use; reduced calorie intake
10. **Ans. is 'c' i.e., Acute viral hepatitis** *[Ref: Robbin's 9th/e p.899]*
11. **Ans. is 'c' i.e., Bridging fibrosis**
    [Ref: Robbin's 9th/e p. 837; 8th/e p. 552-555]
12. **Ans. is 'c' i.e., Chronic active hepatitis**
    [Ref: Robbin's 9th/e p.837; 8th/e p.866; Chandrasoma 3rd/e p.645]
13. **Ans. is 'd' i.e., Liver biopsy**
    *[Ref: Harrison's 18th/e p.2567; Robbin's 8th/e p.*850,851,844]
    1. **Chronic Persistent Hepatitis:**
       - Chronic inflammation is restricted to portal tract only and limiting plate is not damage.
    2. **Chronic Active Hepatitis:**
       - Chronic inflammation damaging limiting plate and extending into liver lobules.
14. **Ans. is 'b' i.e., Ground glass hepatocytes**
    [Ref: Harrison 18th/e p. 837; 17th/e p. 1938, 1939; Robbin's Illustrated 9th/e p.837 and 8th/e p.851-853]
15. **Ans. is 'b' i.e., HBV** *[Ref: Robbin's 9th/e p. 838; 8th/e p. 850]*
16. **Ans. is 'a' i.e., Fibrosis of porta hepatitis; 'b' i.e., Architechtural changes; 'c' i.e., Bridging necrosis**
    [Ref: Robbin's 9th/e p.837; 8th/e p.852-853; Sheila Sherlock 11th/e p. 322]
17. **Ans. is 'c' i.e., Malnutrition**
    [Ref: Harsh Mohan p. 735; Robbin's 8th/e p. 36-37]
18. **Ans. is 'a' i.e., NASH**
19. **Ans. is 'a' i.e., Alcoholic hepatitis**
    - Alcoholic hepatitis - IgA (heavy drinkers with advanced liver disease often present with high IgA values).
    - Primary biliary cirrhosis- IgM
    - Autoimmune hepatitis – IgG
20. **Ans. is 'd' i.e., Chronic alcoholism**
21. **Ans. is 'a' i.e., Alcoholic liver injury**
    - Megamitochondria means mitochondrial size > nucleus of cells.
22. **Ans. is 'b' i.e., Balloning degeneration**
    [Ref: Robbin's 9th/e p. 843 and 8th/e p. 857-858]
23. **Ans. is 'd' i.e., Increased NADH production**
    - **Alcholic liver Steatosis results from** *(Robbin's 8/e p. 859)*:
    - Shunting of substrates away from catabolism and toward lipid biosynthesis a result of excess generation of reduced NADH by alcohol dehydrogenase and acetaldehyde dehydrogenase.
    - Impaired lipoprotein assembly and secretion.
    - Increased peripheral catabolism of fat.
24. **Ans. is 'a' i.e., Protein-energy malnutrition**
25. **Ans. is 'b' i.e., Cytokeratins**
    [Ref: Robbin's 9th/e p. 843; 8th/e p. 555]
    Mallory Denk bodies:
    - Intracytoplasmic intermediate filament made up of cytokeratin 8 and 18.
    - **Seen in:**
      1. Alcoholic liver disease
      2. Non-alcoholic fatty liver disease (NaFLD)
      3. Wilson's disease
      4. Indian childhood cirrhosis
      5. Alpha-1 antirypsin deficiency
      6. Chronic cholestatic disease
      7. Primary biliary cirrhosis
      8. Focal nodular hyperplasia
      9. Hepatocellular carcinoma
    - **Mallory Denk bodies are not seen in:**
      1. Hemochromatosis
      2. Secondary biliary cirrhosis
26. **Ans. is 'a' i.e., Alcoholic fatty liver**
    [Ref: Shiela Sherlock 11th/e p. 62,462]
27. **Ans. is 'c' i.e., Alcoholic liver disease**
    [Ref: Robbin's 9th/e p. 843; 8th/e p. 555]
28. **Ans. is 'b' i.e., Valproate** *[Ref: Shiela Sherlock 11th/e p. 62,462]*
29. **Ans. is 'b' i.e., Marked microvesicular steatosis**
    Reye syndrome or Reye's syndrome
    - Fatal syndrome that has detrimental effects to organs, especially the brain and liver.
    - Causing lower level of blood sugar *(hypoglycemia)*.
    - Classic features are a rash, vomiting, and liver damage.
    - Exact cause is unknown but associated with aspirin consumption by children with viral illness, it also occurs in the absence of aspirin use.
    - Liver - fatty liver with minimal inflammation (Microvesicular Steatosis).
30. **Ans. is 'b' i.e., Secondary biliary cirrhosis**
    [Ref: Robbin's 9th/e p. 843,859; 8th/e p. 555]
31. **Ans. is 'd' i.e., Bridging fibrosis**
    - **Histologyof NCPF:**
    - Hallmark is thrombosis and sclerosis of portal vein and its branches
      Megasinusoids *(periportal angiomatosis)*: Aberrant blood vessels in periportal areas corresponding to dilated terminal portal vein branches.
    - Portal and periportal inflammation and fibrosis.
    - Bridging fibrosis is not seen in NCPF.

32. **Ans. is 'd' i.e., Noncirrhotic portal fibrosis**
[Ref: API 6th/e p. 582; Ribbin's 9th/e p. 871]
33. **Ans. is 'a' i.e., Chronic hepatitis B**
34. **Ans. is 'c' i.e., 1 and 3**
35. **Ans. is 'a' i.e., Jejunoileal by pass; 'c' i.e., Hemochromatosis**
36. **Ans. is 'a' i.e., Iron** *[Ref: Robbin's 9th/e p. 847; 8th/e p. 1309]*
37. **Ans. is 'd' i.e., Desferrioxamine is the treatment of choice**
[Ref: Robbin's 9th/e p. 849; 8th/e p. 862-863]
38. **Ans. is 'b' i.e., Hemochromatosis** *[Ref: Robbin's 9th/e p. 849]*
39. **Ans. is 'c' i.e., Increased copper in liver**
[Ref: Harrison 18th/e p. 3188; Robbins 9th/e p. 849 and 8th/e p. 864]
    - **Biochemical diagnoisi of Wilson's disease**

    1. Dicrease in serum ceruloplasmin.
    2. An increase in heptic copper content (250 go of copper per gram of dried liver tissue confirms Wilson's disease - the most sensitive and accurate test)
    3. Increased urinary excretion of copper (the most specific screening test).

    - Serum copper levels are of no diagnostic value, since they may be low, normal, or elevated.
    - Demonstration of Kayser - Fleischer rings favors the stains.
    - Excess copper deposition demonstrated by special stains.
        a. Rhodamine-stain-for copper
        b. Orcein stain – for copper - associated protein
40. **Ans. is 'b' i.e., AT P 7B** *[Ref: Robbin's 9th/e p. 850; 8th/e p. 863-864]*
41. **Ans. is 'c' i.e., Testis** *[Ref: Robbin's 9th/e p. 850; 8th/e p. 862-863]*
    - Hypogonadism in hemochromatosis is due to impairment of hypothalamopituitary function by iron deposition and not due to deposition of iron in the testis.
42. **Ans. is 'c' i.e., 13** *[Ref: Robbin's 9th/e p. 850; 8th/e p. 864]*
43. **Ans. is 'd' i.e., Hepatitis-B**
[Ref: Robbin's 9th/e p. 870; 8th/e p. 878-879]
44. **Ans. is 'd' i.e., Hemangioma** *[Ref: Robbin's 9th/e p. 867; 8th/e p. 877]*
HEPATIC TUMORS:
    - Most common hepatic neoplasm is metastasis (most commonly from colorectal carcinoma).
    - Most coomon benign neoplasm of liver is liver is cavernous hemangioma.
    - Most common primary malignant tumour of liver is hepatocellular caricnoma (=hepatoma)
    - Most common primary malignant tumor of liver in childhood – Heptoblastoma
45. **Ans. is 'b' i.e., Hepatocellular carcinoma**
[Ref: Robbin's 9th/e p. 873; 8th/e p. 879]
46. **Ans. is 'a' i.e., Fibrolamellar hepatoma**
[Ref: Robbin's 9th/e p. 873; 8th/e p. 879]
47. **Ans. is 'd' i.e., Arsenic**
[Ref: Robbin's 9th/e p. 875; 8th/e p. 877]
48. **Ans. is 'd' i.e., Serum AFP levels are usually > 1000 mg/litre**
[Ref: Chandrasoma Taylor 3rd/e p. 660; Harrison 18th/e p. 784 and 17th/e p. 584; Robbin's 9th/e p. 873 and 8th/e p. 879]
Fibrolamellar carcinoma (variant of HCC):
    - Young adults *(20-40 years)*
    - Equal gender incidence *(India – Females > males)*
    - No associated with cirrhosis or HBV infections
    - Left lobe is more commonly affecte
    - AFP level is normal; neurotensin is a tumor marker.
    - AFP level is normal; neurotensin is a tumor marker.
    - Histology shows well-differentiated tumor cells are separated by dense lamellar collagen bundles.
    - Lymphatic spread
    - Better prognosis
49. **Ans. is 'c' i.e., Angiosarcoma**
[Ref: Robbin's 9th/e p. 875; 8th/e p. 524-525]
50. **Ans. is 'b' i.e., Porcelain gallbladder 'd' i.e., Choledochal cyst**
[Ref: Handbook of Liver diseases 2nd/e p. 402]
51. **Ans. is 'b' i.e., Liver** *[Ref: Robbin's 9th/e p. 822; 8th/e p.535]*
52. **Ans. is 'a' i.e., Fundus; 'b' i.e., Neck**
[Ref: Robbin's 9th/e p. 880; 8th/e p. 888]
53. **Ans. is 'a' i.e., Nodular type of cholangiocarcinoma**
[Ref: Robbin's 9th/e p. 874; 8th/e p. 880]
Cholangiocarcinoma
    - Biliary tree malignancy arising from bile ducts (within liver or outside liver)
    - **Classification (on the basis of location)**
        1. **Extrahepatic (most common type, firm nodular mass; 90%)**
    - Perihilar – most common type *(60%)* and known as klatskins tumour (located at the junction of right and left hepatic ducts)
54. **Ans. is 'b' i.e., Anti-mitochondrial antibody**
[Ref: Robbin's 9th/e p. 858; 8th/e p. 867-68]
55. **Ans. is 'b' i.e., Primary sclerosing cholangitis**
[Ref: Robbin's 9th/e p. 874; 8th/e p. 880]
56. **Ans. is 'a' i.e., Ulcerative colitis**
[Ref: Robbin's 9th/e p. 860; 8th/e p. 869]
57. **Ans. is 'a' i.e., Adenomyomatosis of gallbladder**
[Ref: Biliary lithiasis; Basic Science, Current Diagnosis and Management. p. 82]
58. **Ans. is 'a' i.e., Analgesics** *[Ref: Robbin's 9th/e p. 863; 8th/e p. 872]*
Peliosis hepatitis:
    - Reversible sinusoidal dilatation
    - Liver contains cystic spaces filled with blood which may or may not be lined by endothelial cells.
    - Associated with:
    - Cncer
    - Tuberculosis
    - AIDS or post-transplantation immunodeficiency
    - Anabolic steroids
    - Oral contraceptive pills and danazol.
59. **Ans. is 'b' i.e., Defect in beta oxidation**
    - Mitochondrial damage is the reason it's a case of Reye syndrome.
60. **Ans. is 'b' i.e., Liver** *[Ref: Robbin's 9th/e p. 867; 4th/e p. 869]*
61. **Ans. is 'c' i.e., Steroids** *[Ref: Robbin's 7th/e p. 918]*
62. **Ans. is 'a' i.e., Methyldopa**
[Ref: Harrison 18th/e p. 2563-2564; 17th/e p. 1951]
63. **Ans. is 'd' i.e., Chronic passive congestion in liver**
[Ref: Robbin's 9th/e p. 823; 8th/e p. 837]
64. **Ans. is 'b' i.e., Ito cell (hepatic stellate cell)**
[Ref: Robbin's 9th/e p. 823; 8th/e p. 837]
    - Hepatic fibrosis / cirrhosis is due to collagen type - 1 and type - 3 both, produced by Ito cells *(stellate cells)*
65. **Ans. is 'c' i.e., Chronic persistent hepatitis**
[Ref: Harrison 16th/e p. 1845]
66. **Ans. is 'a' i.e., Ballooning degeneration**
67. **Ans. is 'c' i.e., Characteristic liver histology**
[Ref: Robbin's 9th/e p. 837; 8th/e p. 899; Chandrasoma Taylor 3rd/e p. 645]
68. **Ans. is 'a' i.e., Etiology** *[Ref: Robbin's 7th/e p. 595]*
69. **Ans. is 'c' i.e., Fatty infiltration**
[Ref: Chandrasoma Taylor 3rd/e p. 653; Robbin's 9th/e p. 827 and 8th/e p. 837]
70. **Ans. is 'b' i.e., Yellow fever** *[Ref: Chandrasoma Taylor 3rd/e p. 639]*
71. **Ans. is 'd' i.e., Phosphorus intoxication causes Macrovesicular steatosis** *[Ref: Has been explained]*
72. **Ans. is 'c' i.e., 3 mm** *[Ref: Robbin's 7th/e p. 882; 6th/e p. 553]*
73. **Ans. is 'a' i.e., Tetracycline**
[Ref: Robbin's 9th/e p. 840 (Table 18.5); 8th/e p. 556]
74. **Ans. is 'b' i.e., Eosinophilic intracytoplasmic inclusionss**

[Ref: Robbin's 9th/e p. 843; 8th/e p. 555]

75. **Ans. is 'c' i.e., Lipofuschin (Due to free radical injury caused by alcohol)** *[Ref: Robbin's 8th/e p. 858; 7th/e p. 905]*
76. **Ans. is 'a' i.e., Angiosarcoma of liver**
[Ref: Robbin's 9th/e p. 875; 8th/e p. 877]
77. **Ans. is 'c' i.e., Indian childhood cirrhosis**
[Ref: Robbin's 9th/e p. 843; 8th/e p. 555]
78. **Ans. is 'd' i.e., Cholangiocarcinoma**
[Ref: Robbin's 9th/e p. 832-833; 8th/e p. 845]
79. **Ans. is 'c' i.e., Autoimmune hepatitis**
80. **Ans. is 'b' i.e., Hepatitis B virus is an important risk factor**
[Ref: Robbin's 9th/e p. 873; 8th/e p. 879 and Harrison 18th/e p. 784 and 11th/e p. 55]
81. **Ans. is 'd' i.e., Clonorchis sinensis infection**
[Ref: Robbin's 9th/e p. 874; 8th/e p. 880; Harsh Mohan 8th/e p. 657]
82. **Ans. is 'b' i.e., Primary sclerosing cholangitis**
[Ref: Robbin's 9th/e p. 860; 8th/e p. 669]
83. **Ans. is 'c' i.e., Dubin-Johnson syndrome**
[Ref: Robbin's 9th/e p. 854; 8th/e p. 841]
84. **Ans. is 'd' i.e., Bridging fibrosis** *[Ref: Ackerman 9th/e p. 959]*
85. **Ans. is 'a' i.e., Mutation in gene for multiple drug resistance protein 2**
[Ref: Robbin's 9th/e p. 854; 8th/e p. 841]
86. **Ans. is 'd' i.e., Both melanine and hemosiderin**
[Ref: Robbin's 9th/e p. 849; 8th/e p. 862]
Skin in hemochromatosis
    - Increased pigmentation on face; neck and extensor aspects of forearm *(bronzing of skin – bronze diabetes)*
    - Pigmentation is mainly due to melanin and partially due to hemosiderin.
87. **Ans. is 'b' i.e., Underlying etiology** *[Ref: Robbin's 7th/e p. 898]*
88. **Ans. is 'b' i.e., Cholangiocarcinoma**
[Ref: Robbin's 9th/e p. 860; 8th/e p. 868]
89. **Ans. is 'd' i.e., Cholestatic jaundice**
    - Increased vitamin B-12 in cirrhosis ,hepatitis and hepatocellular carcinoma is caused by cobalamin release during hepatic cytolysis and/or decreased cobalamin clearance by the affected liver.
    - Whereas in cholestatic jaundice due to bile cannot flow from the liver to the duodenum so level of vit b12 remains low in cholestatic jaundice.

EXTRA EDGE MCQS

1. **Ans. is 'b' i.e., Chronic HEV infection occurs exclusively in immunosuppressed patients.**
HEV infection is generally self-limiting but may become chronic in immunosuppressed patients. It is diagnosed by the presence of anti-HEV antibodies, in particular anti-HEV IgM at the acute stage, although HEV RNA can be detected in feces and blood.
2. **Ans' is 'd' i.e., Wilson's disease.**
This patient's clinical and laboratory findings suggest Wilson's disease. These patients manifest neurologic findings, including tremors, spasticity, drooling, and dysphagia. The Babinski response may be present. The eyes show deposits of copper in Descemet's membrane of the cornea; the lack of them excludes the diagnosis. Also, the ceruloplasmin level is less than 200 mg/L.
3. **Ans. is 'd' i.e., Primary biliary cirrhosis.**
The signs and symptoms in this patient suggest primary biliary cirrhosis (PBC), especially pruritus, a disease that occurs predominantly in women ages 35 to 60. The slightly elevated bilirubin and the elevated alkaline phosphatase are common in cirrhosis, and in particular, elevated alkaline phosphatase occurs in PBC. However, a positive IgG antimitochondrial antibody is detected in more than 90% of patients with PBC and provides an important diagnostic finding.
4. **Ans. is 'c' i.e., Acute hepatitis A and B.**
This patient has both hepatitis A and B virus infections. Both viruses can infect the same person. Clinical findings are consistent with anacute hepatitis; they are not specific for one virus. The positive IgM anti-HAV and the positive IgM anti-HBC are evidence of acute infection with both viruses. The negative HBsAg is consistent with this antigen being below the threshold of detection.
5. **Ans. is 'd' i.e., Chronic HBV infection, high infectivity.**
The positive HBsAg in hepatitis B virus infection, together with low levels of IgG anti-HBc, positive HBeAg, and negative anti-HBe, fit the picture of chronic HBV infection with high infectivity. In chronic or late-acute HBV of low infectivity, the HBeAg would be negative. Persons immunized with HBV vaccine show only anti-HBs. Persons who have recovered from HBV infection are negative for HBsAg.
6. **Ans. is 'b' i.e., Chronic active hepatitis**
    - In **chronic active hepatitis**, an intense inflammatory reaction with numerous plasma cells spreads from portal tracts into periportal areas. The reaction destroys the limiting plate and results in formation of periportal hepatocytic islets. Prognosis is poor, and the majority of patients develop cirrhosis.
    - **Chronic persistent hepatitis** is usually a sequela of acute viral hepatitis and has a benign course without progression to chronic active hepatitis or cirrhosis. The portal inflammation does not extend into the periportal areas, and this differentiates chronic persistent hepatitis from chronic active hepatitis.
7. **Ans. is 'c' i.e., Recovered from HBV infection.**
The serologic pattern in this case is a person who has recovered from HBV infection. They possess anti- HBs, the protective antibody in HBV infection, IgG anti-HBc, and anti-HBc. The anti-HBc may be positive or negative in persons who recover from HBV.
8. **Ans. is 'c' i.e., Anabolic steroids.**
    - **Peliosis hepatis** is an abnormality of the hepatic blood flow that results in sinusoidal dilation and the formation of irregular blood-filled lakes, which may rupture and produce massive intraabdominal hemorrhage or hepatic failure.
    - Peliosis hepatitis is most often associated with the use of\ **anabolic steroids**, but more rarely it may be associated with **oral contraceptives**. Reye's syndrome, characterized by microvesicular fatty change in the liver and encephalopathy, has been related to the use of salicylates in children with viral illnesses.
    - Acetaminophen toxicity results in centrilobular liver necrosis, while estrogens may be related to thrombosis of the hepatic or portal veins.
9. **Ans is d. Increased NADH production.**
    - Alcohol can produce hepatic steatosis via several mechanisms, such as increased fatty acid synthesis, decreased triglyceride utilization, decreased fatty acid oxidation, decreased lipoprotein excretion, and increased lipolysis. Ethanol is taken up by the liver and is converted into acetaldehyde by either alcohol dehydrogenase (the major pathway), microsomal P-450 oxidase, or peroxisomal catalase.
    - These pathways also convert nicotinamide adenine dinucleotide (NAD) to NADH. This excess production of NADH changes the normal hepatic metabolism away from catabolism of fats and toward anabolism of fats (lipid synthesis), resulting in decreased mitochondrial oxidation of fatty acids and increased hepatic production of triglyceride. Ethanol also increases lipolysis and inhibits the release of lipoproteins. Increased lipolysis increases the amount of free fatty acids that reach the liver.
10. **Ans is c) Mallory-Denk bodies.**
This image shows globular eosinophilic cytoplasmic inclusions

called Mallory-Denk bodies. These cytokeratin inclusions are characteristic of, but not specific for, alcoholic hepatitis.

11. **Ans is C) Pulmonary emphysema.**
PAS-positive globules in the liver seen here are **characteristic of α1-antitrypsin (AAT) deficiency**. Deficiency of AAT also allows unchecked action of **elastases in the lung,** which **destroys the elastic tissue** and **causes emphysema.** AAT can produce a picture of chronic hepatitis in adults; it can lead to neonatal hepatitis with acute but often transient liver injury.
12. **Ans is C) Neonatal Hepatitis .**
Neonatal hepatitis will be showing MULTINUCLEATED GIANT CELLS.
13. **Ans is b) A is Metastatic liver; B is Cirrhosis.**
In **metastatic (A) liver** there will be normal smooth surface in between tumor nodules, whereas, in **cirrhotic liver (B**) there will be diffuse nodules throughout liver surface without any normal smooth surface. **(BLINDMAN's Diagnosis)**
14. **Ans is d) Biopsy is showing Perl's prussian blue stain and Melanin deposition is the most common cause of bronze diabetes in this disorder.**
In this Hemochromatosis liver biopsy was stained for **iron (blue) with Perl's prussian blue stain**. Testicular failure is due to pituitary damage by iron (Not direct damage). **Skin pigmentation** is most commonly by **melanin >>>Hemosiderin.**
15. **Ans is d) Sweets reticulin stain.**
Reticulin stain is used to visualize reticular fiber and used extensively in liver histopathology.
Results:
a) Reticulin fibres----Black
b) Nuclei----Red

LATEST QUESTIONS

1. **Ans is c) GGT**
2. **Ans is b) HBs Ag, Anti - HBc IgM, anti - HAV, anti – HCV**
3. **Ans is b) Dubin-Johnson Syndrome**
4. **Ans is c) Liver**
5. **Ans is a) Ito Cell**

AIIMS NEW PATTERN BASED QUESTIONS

1. **Ans is f) Periportal PAS-positive globules** - The disease that relates panlobular emphysema with hepatic disease is alpha-1-antitrypsin (AAT) deficiency. AAT is a protease inhibitor that prevents ongoing pulmonary damage. AAT deficiency can lead to portal fibrosis and cirrhosis. Lung and liver disease may not be present together.
2) **Ans is e) Macrovesicular steatosis -** She has a fatty liver with non-alcoholic steatohepatitis (NASH). It has pathologic features similar to chronic alcoholism, but without a history of enough alcohol intake to account for the findings.
3) **Ans is g) Interface hepatitis**- This is an acute hepatitis B viral infection. The inflammation can be minimal when most patient clear the infection.
4) **Ans is h) Portal fibrosis** - The varices suggest portal hypertension, and that requires portal fibrosis to be present, typically advanced to cirrhosis.
5) **Ans is c) Cholangiocarcinoma -** The solitary mass suggests a primary cancer. Cholangiocarcinomas arise in conjunction with many of the same risk factors (viral hepatitis, alcoholic cirrhosis) as hepatocellular carcinoma, but less frequently.