Gastrointestinal System:

* **Peptic Ulcer:** It is a lesion in the lining (mucosa) of the digestive tract, typically in the stomach or duodenum, caused by the digestive action of pepsin and stomach acid or due to imbalance b/w the aggressive factor & defensive factor.

- Lesions may subsequently occur into the lamina propria and submucosa to cause bleeding. Ulcer may also occurs in the lower oesophagus due to refluxing of gastric content.
- Most of the peptic ulcer occur either in the duodenum, or in the stomach. Rarely in certain areas of the small intestine.

• **Pathophysiology of peptic ulcer:** Under normal conditions, a physiologic balance exists b/w gastric acid secretion and gastroduodenal mucosal defense. Mucosal injury and, thus, peptic ulcer occur when the balance b/w the aggressive factors and the defensive mechanisms is disrupted. Aggressive factors, such as NSAIDs, Helicobacter pylori infection, alcohol, bile salts, acids and pepsin, can alter the mucosal defense by allowing back diffusion of hydrogen ions and subsequent epithelial cell injury.

Defensive Factor (↓)	Aggressive Factors (↑)
- Bicarbonate	- HCl
- Mucus layer	- Pepsins
- Prostaglandins	- Helicobacter pylori
- Mucosal blood flow	- NSAIDs (non-steroidal anti-inflammatory drug e.g., aspirin).
- Epithelial renewal	- Nitric oxide
- Mucin	- Bile acids
- Glycoproteins.	- Smoking and alcohol.

• **Aetiology / risk factors:**

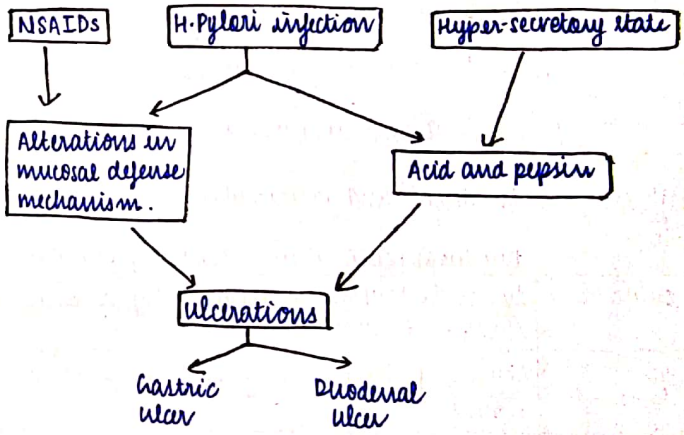
A) **Life style:** Smoking, acidic drinks, medications.

B) **H-Pylori infection:** 90% have this bacterium, passed from person to person (fecal-oral route or oral-oral route).

C) **Age:** Duodenal (30 to 40 years) and Gastric over 50 years.

D) **Gender:** Duodenal ulcer are 7 ing in older women

E) **Other factors:** Stress can worsen but not the cause.



• **Types of peptic ulcer:** Peptic ulcer is of 2 types:

A) Gastric peptic ulcer.

B) Duodenal peptic ulcer.

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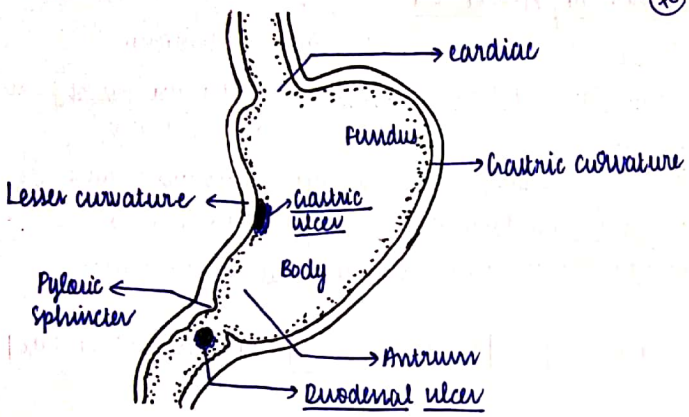

Fig; Gastric and duodenal ulcers

- **Difference b/w duodenal and gastric ulcers:**

	Duodenal peptic ulcer	Gastric peptic ulcer
Cause	due to distruption of mucus membrane.	due to hyper-secretion of pepsin.
Age	Any age specially 30 to 40 years.	Middle age 50 to 60 years.
Pain	Epigastric, discomfort	Epigastric can radiate to back.
Sex/aender	More in ♂	More in ♀.
Onset	2-3 hrs after eating and midnight.	Immediately after eating.
Aggressive by	Hunger	Eating
Relieved by	Eating	Lying down as vomiting
Duration	1 to 2 months	Few weeks
Vomiting	Uncommon	Common (to relieve the pain).
Appetite	Good	Patient afraid to eat.
Diet	Good, eat to relieve the pain.	Avoid fried food
Weight	No weight loss.	Weight loss.

- **Complications of peptic ulcers:**

1.) **Hemorrhage:** Blood vessels damaged as ulcer erodes into the muscles of stomach and duodenal wall. Coffee ground vomitus or occult blood in tarry stools.

2.) **Perforation:** An ulcer can erode through the entire wall. Bacteria and partially digested food spill into peritoneum = peritonitis.

3.) **Narrowing and obstruction (pyloric):** Swelling and scarring can cause obstruction of food leaving stomach = repeated vomiting.

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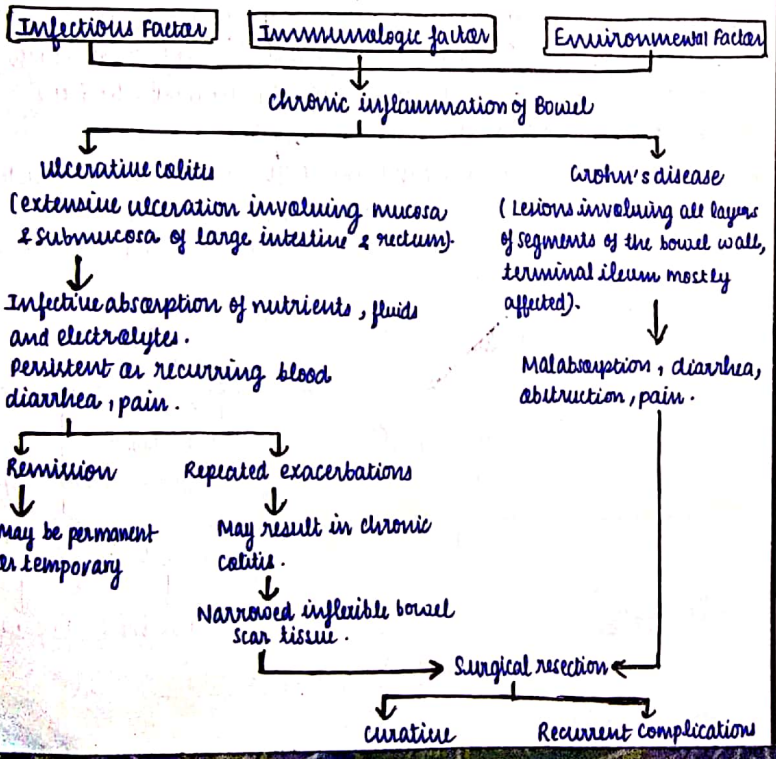
* **Inflammatory Bowel diseases (IBD):** It is a chronic relapsing inflammatory disease of ileum, colon or both.

- **Aetiology:** Idiopathic (i.e., Unknown cause); but may cause due to environmental or genetic factors.
- **Classification of IBD:** The 2 major types of IBD are:
  1) Ulcerative colitis
  2) Crohn's disease or Regional enteritis.



- **Comparison of the main features of ulcerative colitis and Crohn's disease:**

Features	Ulcerative colitis	Crohn's disease
1) Definition	-Chronic inflammatory disease of mucosa of the colon and rectum	-Chronic inflammatory condition of alimentary tract. -Regional ileitis.
2) Incidence	-Usually b/w 20 and 40 yrs of the age (mean value 34 years). -More womens are affected as compare to men. -Smoking is not a risk factor.	-Usually b/w 20 and 40 yrs of the age (mean value 26 years). -♂ & ♀ both are equally affected. -Smokers are at a higher risk.
3) Main site of lesion.	-Rectum is always involved with variable spread along colon	-Anywhere in digestive tract from mouth to anus commonly terminal ileum is affected.
4) Tissue involved.	-only mucosa is involved.	-Entire thickness of the wall inflammed and thickened tissue, ulcer and fistulae (an abnormal connection b/w organs) are common.
5) Nature of lesions	-Continuous lesion- Mucosa is red & inflammed	-Skip lesions (chronic patchy inflammation with oedema of the full thickness of intestinal wall results in partial or obstruction of the lumen)

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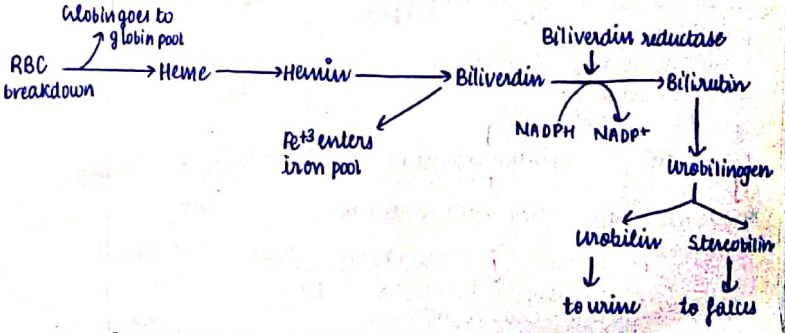
6.) Symptoms	Bloody diarrhoea.	Diarhoea, abdominal pain & weight loss.
7.) Complications	- Systems problems, ankylosing spondylitis (inflammation in joint) and cancer (in severe or chronic cases). - Toxic megacolon (colon looses its muscle and tone). - There is high risk of electrolyte imbalance, perforation and hypobolamic shock which may be fatal if untreated.	- Secondary infection occured when inflammed area ulcerate. - Fibrous addition and subsequent intestinal obstruction caused by healing process. - Peri-anal fistulae, fisure (a long, deep crack).
8.) Prognosis (opinion on the basis of medical condition).	- Surgical removal of entire colon cures the condition but significantly risk of cancer may be enhance.	- In severe cases, surgery may improve condition but relapse rate are very high. There is slightly red risk of cancer.

*Jaundice: (or Icterus)

- Jaundice is not a disease in itself but refers to the yellow pigmentation of the skin, mucous membrane and sclerae by the abnormal bilirubin metabolism and its excretion
- Bilirubin pigment has high affinity for elastic tissue and hence, jaundice is particularly noticeable in tissues rich in elastin content.
- Jaundice is the result of elevated levels of bilirubin in the the blood termed as hyperbilirubinaemia. Normal serum bilirubin concentration ranges from 0.3 to 1.3 mg/dL, about 80% of which is unconjugated. Jaundice become clinically evident when the total serum bilirubin level exceeds 2mg/dL.
- Bilirubin is formed by breakdown of Hb, is normally conjugated in and excreted in the bile. conjugation makes bilirubin water soluble & enhances its removal from the blood, an essential step in the excretion



Fig; Formation of bilirubin and its excretion

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- Unconjugated bilirubin which is fat soluble has a toxic effect on brain cells. It is unable to cross BBB (blood brain barrier) until the plasma level rises above 340 micro mole/L, but when it does, it may cause neurological damage such as seizure.

Signs: Itching, pruritis (due to unconjugated bile).

- **Classification of jaundice:** It is of 4 types:

A) Pre-hepatic or hemolytic jaundice.
B) Hepatic jaundice
C) Obstructive jaundice
D) Neonatal jaundice.

A) **Pre-hepatic or hemolytic jaundice:**
- Increased hemolysis of RBCs (i.e., malaria, sickle cell anaemia).
- Characteristics:
  a) Elevation in serum unconjugated bilirubin.
  b) Increased excretion of urobilinogen in urine.
  c) Dark brown faeces due to high content of stercobilinogen.

B) **Hepatic jaundice:**
- Due to dysfunction of liver.
- Characteristics:
  a) Red level of conjugated and unconjugated bilirubin serum.
  b) Dark colored urine due to excessive excretion of bilirubin or urobilinogen.
  c) Pale colour stool due to absence of stercobilin.

C) **Obstructive jaundice:**
- Due to obstruction in bile duct, the conjugated bilirubin from liver enters into circulation.
- Characteristics:
  a) Red level of conjugated bilirubin in serum.

b) Dark coloured urine due to bilirubin excretion
c) Clay coloured faeces due to absence of stercobilinogen

D) **Neonatal jaundice:** Jaundice appears in neonates when the total serum bilirubin is more than 3mg/dl. It may be results of unconjugated or conjugated hyperbilirubinaemia; the former being more common.

- **Inherited unconjugated bilirubinemia:** It leads to Crigler-Najjar syndrome, Gilbert's syndrome.
- **Inherited conjugated bilirubinemia:** It leads to Dubin-Johnson syndrome and Rotor syndrome.

- **Differences b/w unconjugated and conjugated bilirubin:**

Feature	Unconjugated bilirubin	Conjugated bilirubin
1) Normal serum level	More	Less (less than 0.25 mg/dl)
2) Water solubility	Absent	Present
3) Affinity to lipids (Alcohol solubility)	Present	Absent
4) Serum albumin binding	High	Low
5) Renal excretion	Absent	Present.
6) Bilirubin albumin covalent complex formation.	Absent	Present.
7) Affinity to brain tissue	Present (Kernicterus)	Absent.

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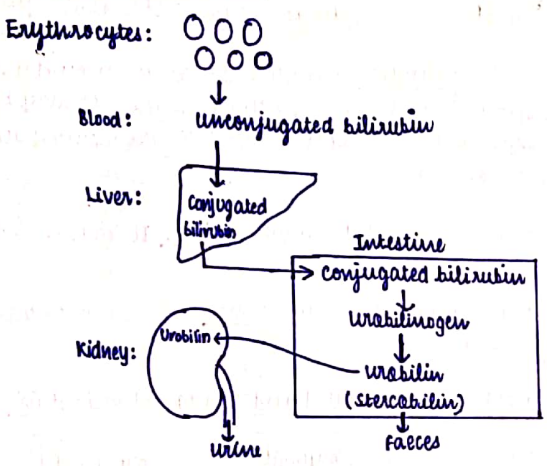
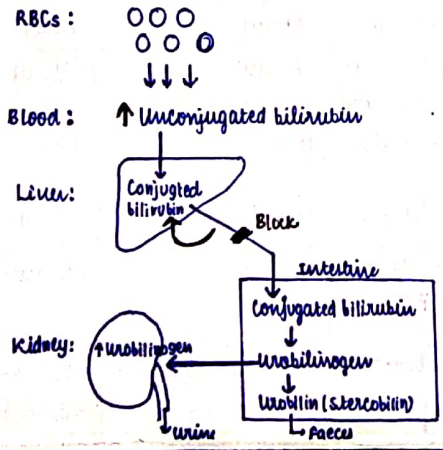
• **Normal bilirubin metabolism:**



• **Alteration in bilirubin metabolism:**



✳ Hepatitis (A, B, C, D, E, F):

• Inflammation of liver results from infectious and non-infectious causes.

- Infectious causes: viruses and parasites.
- Non-infectious causes: drug and toxic agents, auto-immunity.

• Sign and symptoms: Nausea, vomiting, abdominal pain, fever, fatigue, loss of appetite, rashes, joint pain, yellowing of skin and eye.

• Viral hepatitis: Infection of the liver caused by Hepatotropic viruses currently there are 5 main types of hepatotropic viruses causing distinct type of viral hepatitis:

a) Hepatitis A virus (HAV), causing a faecally-spread self-limiting disease.

b) Hepatitis B virus (HBV), causing a parenterally transmitted disease that may become chronic.

c) Hepatitis C virus (HCV), previously termed non-A, non-B (NANB) hepatitis virus involved chiefly in transfusion-related hepatitis.

d) Hepatitis delta virus (HDV) which is sometimes associated as super-infection with hepatitis B infection

e) Hepatitis E virus (HEV), causing water-borne infection.

• Aetiologic classification of hepatitis: Based on the etiologic agent, viral hepatitis is currently classified in 5 etiologic type - hepatitis A, hepatitis B, hepatitis C, hepatitis D, and hepatitis E. The contrasting features of major types of hepatitis are presented in table:

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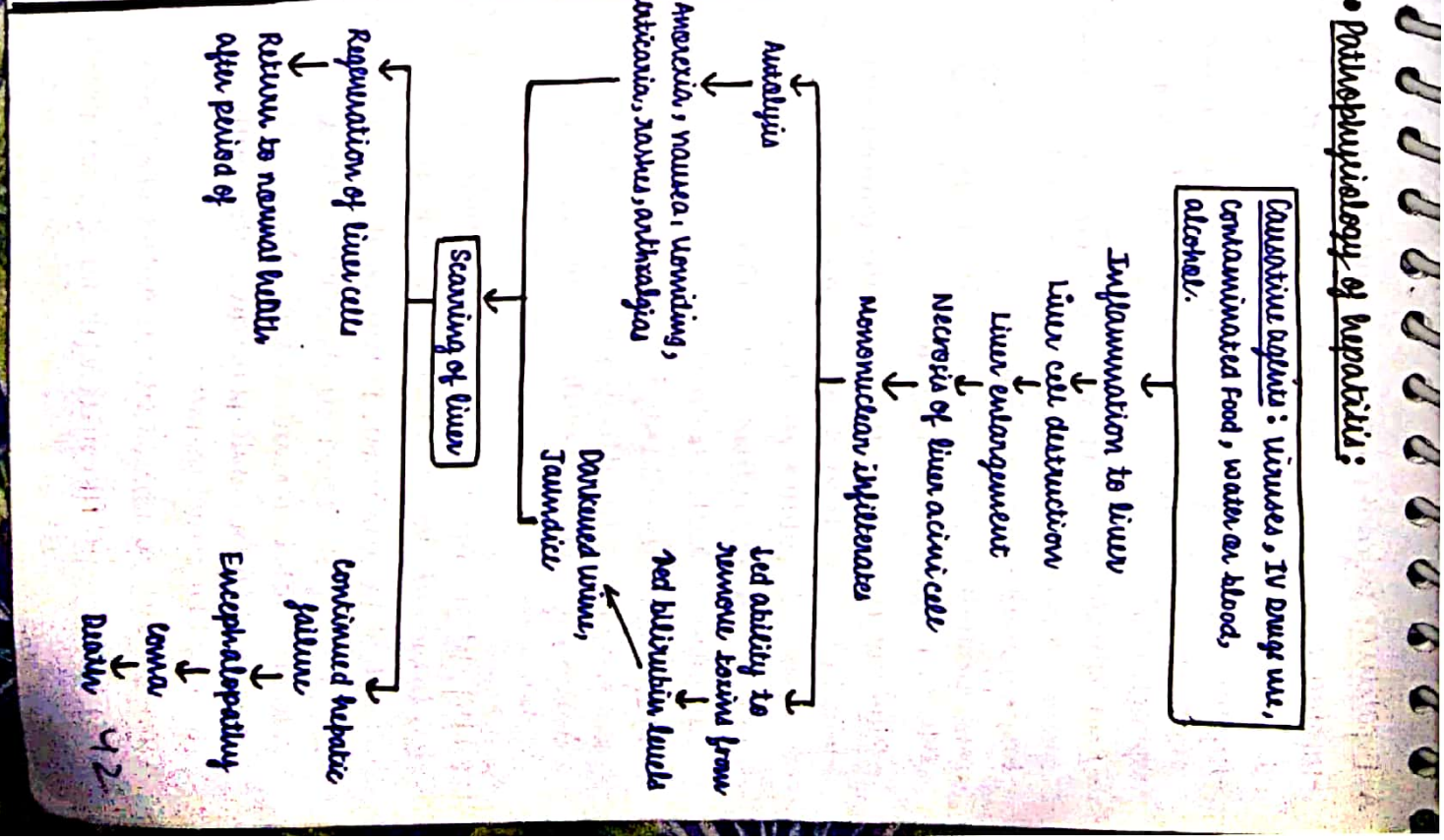
Table: Features of various type of hepatitis virus: (B1)

Feature	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
1) Agent	HAV	HBV	HCV	HDV	HEV
2) Year identified	1973	1965	1989	1977	1980
3) Viral particle	27 nm	42 nm	30-60 nm	35-37 nm	32-34 nm
4) Genome	RNA, ss, linear	DNA, ss/ds	RNA, ss, linear circular	RNA, ss, circular	RNA, ss, linear
5) Morphology	Icosahedral, non-enveloped	Double-shelled, enveloped.	Enveloped	Enveloped, replication defective	Icosahedral, non-enveloped.
6) Spread	Faeco-oral	Parenteral, Close contact	Parenteral, Close contact	Parenteral, close contact	water-borne
7) Incubation period	15-45 days	30-180 days	20-90 days	30-50 days	15-60 days
8) Antigens	HAV	HBsAg HBcAg HBeAg HBxAg	HCV RNA C 100-3 C 33c NS5	HBs Ag HDV	HEV
9) Antibodies	anti-HAV	anti-HBs anti-HBc anti-HBe	anti-HCV	anti-HBs anti-HDV	anti-HEV
10) Severity	Mild	occasionally severe	Moderate	occasionally severe	Mild
11) Chronic hepatitis	None	Occasional	Commmon	Common	None
12) Carrier Stage	None	< 1%.	< 1%.	1 to 10%.	Unknown
13) Hepato-cellular carcinoma	No	present	present	May be present or absent.	None
14) Prognosis	Excellent	Worse with age	Moderate	Acute good, chronic poor	Good

• Pathophysiology of hepatitis:



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A.) **Hepatitis A:** Infection with HAV causes Hepatitis A (infectious hepatitis).

- Hepatitis A is responsible for 20 to 25% of clinical hepatitis in the developing countries of the world.
- Hepatitis A is usually benign, self-limiting disease and has an incubation period of 15-45 days. The disease occurs in epidemic form as well as sporadically.
- **Route of transmission:** It exclusively spread by Faeco-oral route. The spread is related to close personal contact such in overcrowding, poor hygienic and sanitary conditions.
- Most frequently affected age group is 5 to 14 years; adults are often infected by spread from children.
- **Pathogenesis:** Evidence that hepatitis caused by HAV has an immunologic basis comes from demonstration of following antibodies acting as serum markers for hepatitis A infection:

1.) IgM anti-HAV antibody appears in the serum at the onset of symptoms of acute hepatitis A.

2.) IgG anti-HAV antibody is detected in the serum after acute illness and remains detectable indefinitely. It gives life-long protective immunity against reinfection with HAV.

B.) **Hepatitis B:** Hepatitis B (serum hepatitis) caused by HBV infection has longer incubation period (30-180 days).

- **Route of transmission:** It transmitted parenterally such as in recipients of blood and blood product, intravenous drug addicts, patients treated by renal dialysis and hospital workers exposed to blood, and by intimate physical contact such as from mother to child and by sexual contact.
- **Pathogenesis:** There are 3 antigen-antibody system:

a.) **HBsAg-anti HBs system:** HBsAg appears 1 to 2 weeks (late up to

11 to 12 weeks) after exposure, persists for 1 to 6 weeks (even for 5 months) in acute hepatitis B.

ii.) In chronic patients as carrier, HBsAg persists many years.

iii.) HBsAg is the marker of infectivity.

iv.) HBsAg can be found in blood and secretions: saliva, urine, semen, tears, sweat and breast milk.

v.) Anti-HBs appear after HBsAg disappear several weeks (or months) anti-HBs is protective antibody, can persist for many years.

b.) **HBcAg-anti-HBc system:** i.) HBcAg can be found in the nuclei of liver cells, no free HBcAg in serum.

ii.) HBcAg is the marker of replication of HBV.

iii.) The stage is c/a window phase.

iv.) Anti-HBc IgM is a marker of acute infection and accute attack of chronic infection of HBV. Anti-HBc IgG is the marker of past infection, high titer means low level replication of HBV.

c.) **HBeAg-anti HBe system:**

i.) HBeAg is a soluble antigen.

ii.) HBeAg is a reliable indicator of active replication of HBV.

iii.) Anti-HBe is a marker of reduced infectivity. It exist long may be a marker of integration of HBV into liver cell.

C.) **Hepatitis C:** The diagnosis of this major category of hepatitis was earlier made after exclusion of infection with other known hepatitis viruses in those times and was initially named non-A, non-B (NANB) hepatitis. However, after it was characterized, it was renamed as hepatitis C.

- **Route of transmission:** Hepatitis C infection is acquired by blood transfusions, blood products, haemodialysis, parenteral drug abuse and accidental cuts and needle-pricks in health workers.

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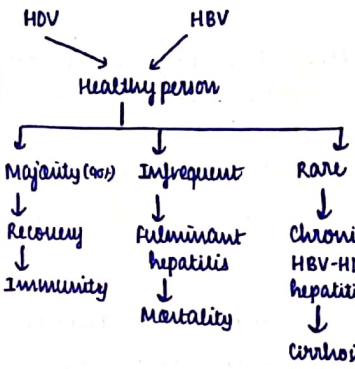
- About 90% of post-transfusion hepatitis is of hepatitis C type. About 1 to 2% of volunteer blood donors and up to 5% of professional blood donors are carriers of HCV.
- Hepatitis C has an incubation period of 20 to 90 days (mean 50 days).
- Clinically, acute HCV hepatitis is milder than HBV hepatitis but HCV has a higher rate of progression to chronic hepatitis than HBV.
- **Pathogenesis:** HCV induces hepatocellular injury by cell-mediated immune mechanism is supported by the following:
  a) It is possible that the host lymphoid cells are infected by HCV.
  b) HCV-activated CD_4+ helper T lymphocytes stimulates CD_8+ T lymphocytes via cytokines elaborated by CD_4+ helper T cells.
  c) The stimulated CD_8+ T lymphocytes, in turn, elaborate antiviral cytokines against various HCV antigens.
  d) Further support to this T-cell mediated mechanism comes from the observation that immune response is stronger in those HCV-infected persons who recover than those who harbour chronic HCV infection.
  e) There is some role of certain HLA alleles and innate immunity in rendering variable response by different hosts to HCV infection.
  f) Natural killer (NK) cells also seems to contribute to containment of HCV infection.
  g) In a subset of patients, there is cross reactivity b/w viral antigens of HCV and host autoantibodies to liver-kidney microsomal antigen (anti-LKM) which explains the association of autoimmune hepatitis and HCV hepatitis.

D) **Hepatitis D:** Infection with delta virus (HDV) in the hepatocyte nuclei of HBsAg-positive patient is termed hepatitis D. HDV is a defective virus for which HBV is the helper. Thus, hepatitis D develops when there is concomitant hepatitis B infection. HDV infection and hepatitis B may be simultaneous (Co-infection); or HDV may infect a chronic HBsAg carrier (super-infection) shown in fig;

(83)

A) **Co-infection**



B) **Super infection**

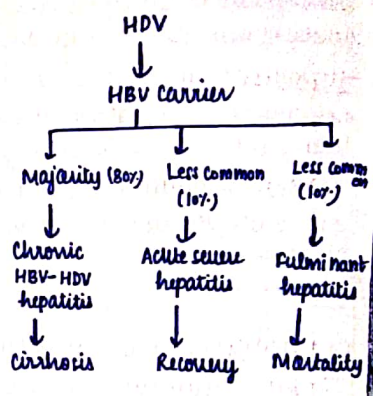


Fig: Consequences of Coinfection (A) V/S superinfection (B) in combined HDV-HBV infection.

- **Route of transmission:** Intravenous drug abusers, homosexuals, transfusion recipients, and healthcare workers.
- **Pathogenesis:** HDV, unlike HBV, is thought to cause direct cytopathic effect on hepatocytes. However, there are examples of transmission of HDV infection from individuals who themselves have not suffered from any attack of hepatitis, suggested that it may not be always cytopathic.

E) **Hepatitis E:** Hepatitis E is an enterically-transmitted virus, previously labelled as epidemic or enterically transmitted variant of non-A non-B hepatitis.
- **Route of transmission:** The infection is generally acquired by contamination of water supplies such as after monsoon flooding. However, compared with HAV, secondary person-to person infection does not occur with HEV. Thus, HEV has some common epidemiologic features with HAV.

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- HEV infection has ~~some~~ a particularly high mortality in pregnant women but is otherwise a self-limited disease and has not been associated with chronic liver disease.

- **Hepatitis E Virus (HEV):** HEV is a single stranded 32-34 nm, icosahedral non-enveloped virus. The virus has been isolated from stools, bile and liver of infected persons. Serologic markers for HEV include the following:

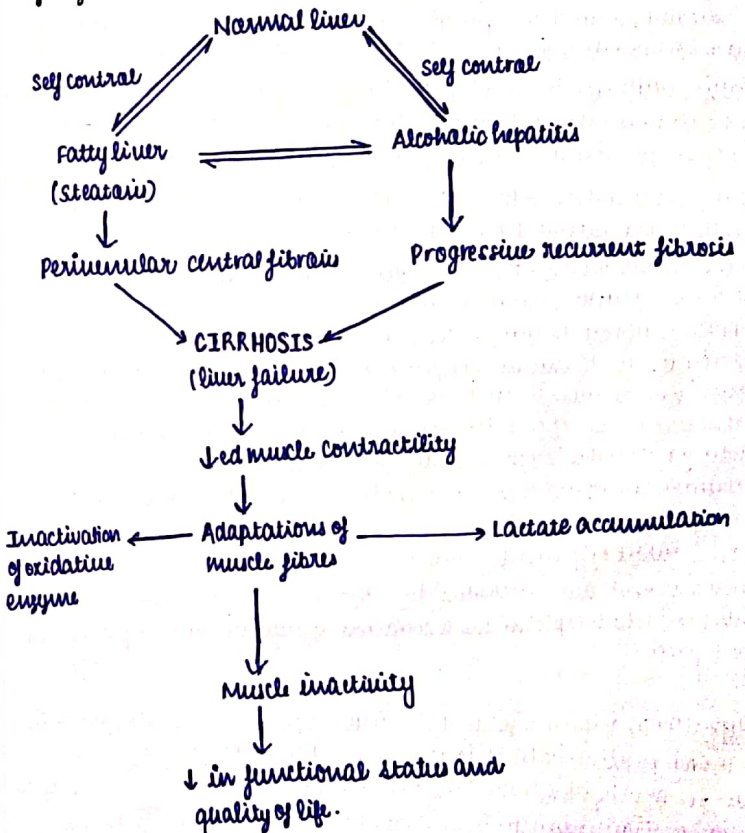
  A) Anti-HEV antibodies on both IgM and IgG class. Both fall rapidly after acute illness but routine serologic testing for HEV antibodies is not available.

  B) HEV-RNA.

F) **Hepatitis F:** It is caused by the Hepatitis F virus (HFV) a Toga virus.

- **Route of transmission:** HFV transmitted through the ingestion of contaminated food and water (called the faecal-oral route); the spread of these agents is aggravated by crowded condition and poor sanitation.

* **Alcoholic liver disease:** Alcoholic liver disease is the term used to describe the spectrum of liver disease: alcoholic steatosis (fatty liver), alcoholic hepatitis and alcoholic cirrhosis.



Fig; Progress of alcoholic liver disease

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- Alcohol is used as a medicine for antiseptic purpose.
- Alcoholic liver disease is term used to describe the spectrum of liver injury associated with acute (100 to 200 mg/dL) and chronic (400mg/dL) alcoholism.
- **Epidemiology:** (60 to 70%. population is affected by alcohol abuse & alcohol abuse is major cause of cirrhosis.
- **Cause:** Alcoholism blocks the normal metabolism of protein, fats and carbohydrates. Alcohol related injury to different organs is due to toxic effect of alcohol and accumulation of its main toxic metabolite acetaldehyde in the blood.

– Alcoholics commonly have induced microsomal P-450 oxidase (enzyme) system and are more susceptible to Acetaminophan drug toxicity.

– Alcohol is metabolized in liver via microsomal P-450 system when the blood alcohol level is high. Acetaldehyde so formed is toxic and may cause membrane damage and cell necrosis.

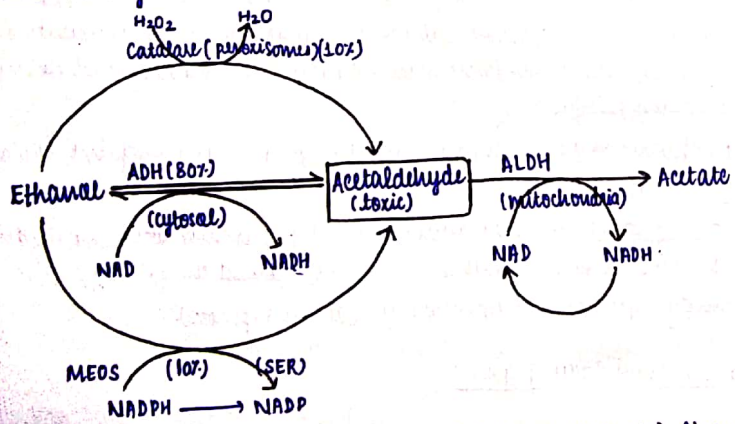

Fig: Metabolism of ethanol in liver

∵ ADH = Alcohol dehydrogenase
∵ ALDH or ACDH = Hepatic acetaldehyde dehydrogenase
∵ NAD = Nicotinamide adenine dinucleotide
∵ NADH = reduced NAD.
∵ MEOS = Microsomal ethanol oxidising system
∵ SER = smooth endoplasmic reticulum.

- **Effect of alcohol:**

Part	Level of alcohol	Effect
1.) CNS	⩾100mg/dL	CNS atrophy, Motor incoordination
	100 to 200mg/dL	Depression of cortical centre, impaired judgement and drowsiness.
	>300mg/dL	Stupor (Status peridion), coma
	>400mg/dL	Anaesthesis, depression of medullary centre and mortality due to respiratory attack.
2.) Stomach	–	Vomiting, acute gastritis, peptic ulcer.
3.) Liver	–	Cirrhosis (liver failure), fatty liver
4.) Pancreas	–	Necrosis (cell mortality), pancreatitis.
5.) Sex organs (testis)	–	Testicular atrophy, infection.

- **Risk factors of alcoholic liver disease:** A few risk factors have been implicated:

A.) Drinking patterns
B.) Gender
C.) Malnutrition
D.) Infections

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E) Genetic factors

F) Hepatitis B and C infection.

• **Pathogenesis:** It is known that ethanol and its metabolites are responsible for ill-effects on the liver in a susceptible chronic alcoholic having above-mentioned risk factors:

A) Direct hepatotoxicity by ethanol.

B) Hepatotoxicity by ethanol metabolites.

C) Oxidative stress.

D) Immunological mechanism

E) Inflammation

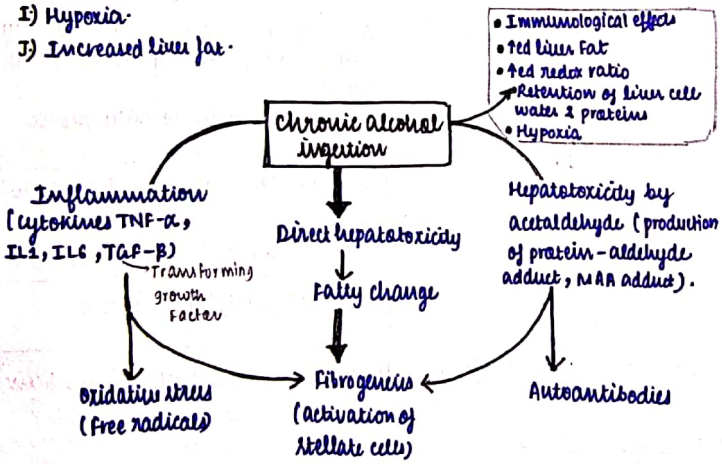
F) Fibrogenesis

G) Increased redox ratio: NADH : NAD ratio in hepatocytes.

H) Retention of liver cell water and proteins.

I) Hypoxia.

J) Increased liver fat.



Fig; Pathogenesis of alcoholic liver disease (TNF-α, Tumour necrosis factor-α ; MAA, malon-di-aldehyde acetaldehyde ; IL, interleukin)

DISEASE OF BONES and JOINTS:

* **Gout:** Gout is a disorder of purine metabolism manifested by the following features, occuring singly or in combination:

A) Increased serum uric acid concentration (hyperuricaemia).

B) Recurrent attacks of characteristic type of acute arthritis in which crystals of monosodium urate monohydrate may be demonstrable in the leucocytes present in the synovial fluid.

C) Aggregated deposits of monosodium urate monohydrate (tophi) in and around the joints of extremities.

D) Renal disease involving interstitial tissue and blood vessels.

E) uric acid nephrolithiasis.

• **Types of gout:** It can be classified into 2 types:

A) Acute gout

B) Chronic gout.

A) **Acute gout:** Sudden onset of severe inflammation in a single joints (metatarsophalangeal joints of great toe) due to precipitation of urate crystals in the joint space. The joint becomes red, swollen and extremely painful.

B) **Chronic gout:** when pain and stiffness persists in a joint b/w attack of gout. This stage is chronic.

- **Symptoms:** Hyperuricaemia, Tophi (It is chalk like stone under the skin in pinna, eyelids, nose and around the joints), Gouty nephropathy (deposition of urate in nephrons).

• **Pathophysiology of gout:**

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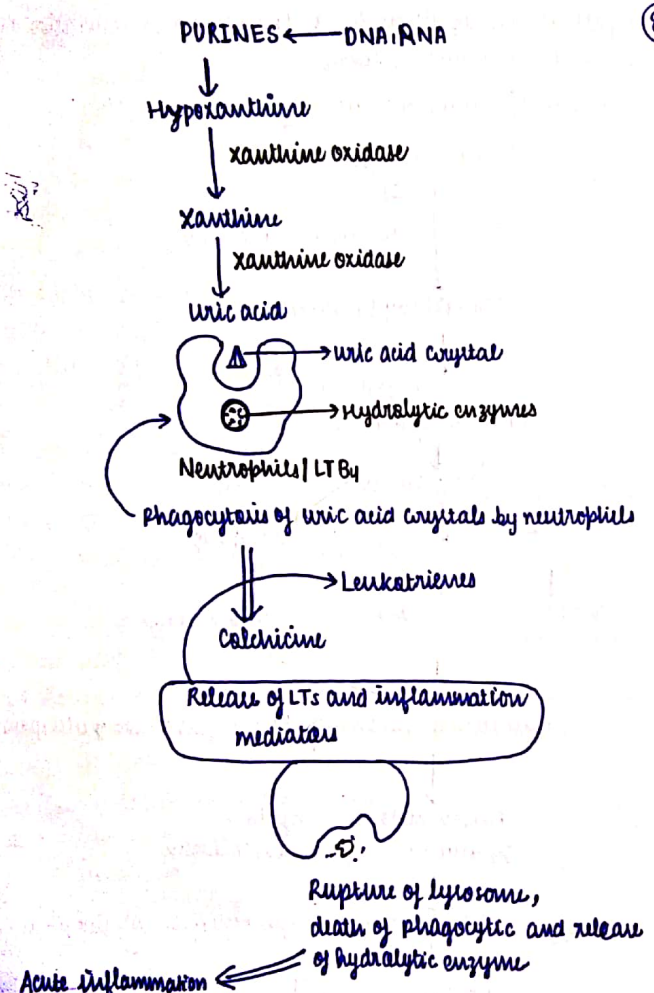

Fig: Pathophysiology of gout

- Gout is a metabolic disorder as a result of over production of purine metabolites (uric acid) characterized by hyperuricaemia in which sodium urate crystals deposit in Metalloris joint (finger joints and toe joints), kidney and subcutaneous tissue. When plasma urate level is higher than normal value (1 to 4 mg/dL).
- Sodium urate in human being is the end product of purine metabolism. The deposition of urate crystals initiate an inflammatory proces such as the infilteration of granulocytes that phagocyte the urate crystal. The proces generates the oxygen metabolites which damage the tissue resulting in release of lysosomal enzymes that promotes the inflammatory response. In addition, lactate production in the synovial fluid present in the joints ↑ces, the resulting local ↓ in the pH fasters further depoition of urate crystals.
- Uric acid, a product of purine metabolism has low water solubility especially at low pH. The cause of hyperuricaemia is over production of uric acid relative to patient's ability to excrete it.

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* **Rheumatoid arthritis:** Rheumatoid arthritis is an auto-immune disorder and chronic inflammation of peripheral synovial joints.

• **Symptoms:** Haematological, neurologic & cardiovascular abnormality, low grade fever, joint pain in hands and feet. Swelling and destruction of cartilage and bone, ultimately results in permanent disability. Formation of nodules of connective tissue c/a rheumatoid nodules.

• **Aetiology:** Auto-immunity and it is also mediated by the viral infection.

• **Pathological Changes:** In early rheumatoid arthritis, large amount of neutrophils are Ont in synovial joint which contains synovial fluid. chronically hypertrophy and hyperplasia forms projection into joint capsule.

-Rheumatoid arthritis is characterized by bone erosion caused by osteoclast and cartilage dissociation by proteolytic enzyme (Metalloproteinase enzyme).

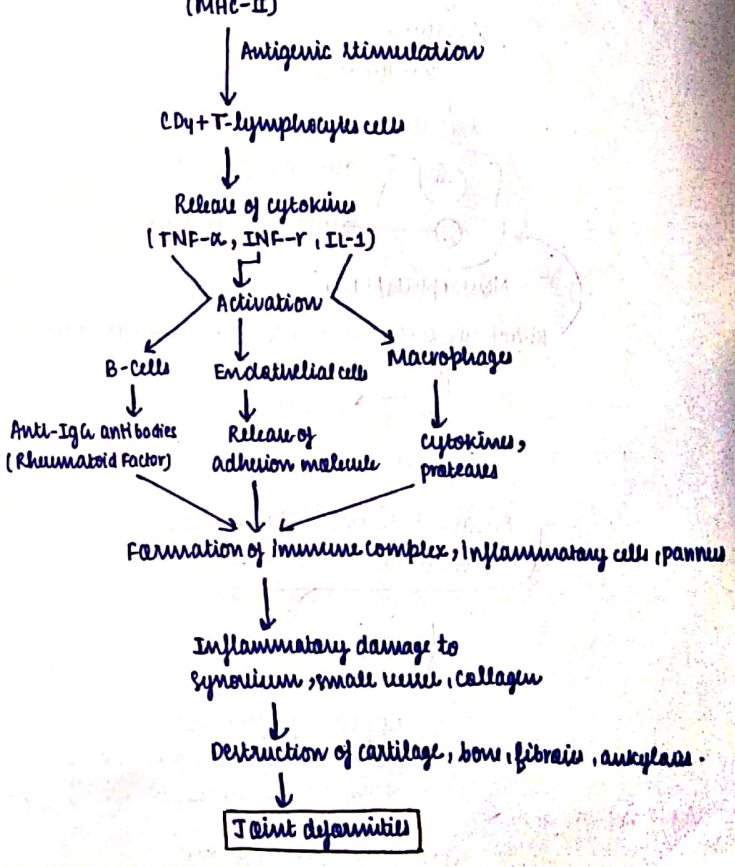
• **Types of arthritis:** There are variant forms of rheumatoid arthritis:

A.) **Juvenile rheumatoid arthritis:** Juvenile RA is found in adolescent patients under 16 years of age is characterized by acute onset of fever and predominant involvement of knees and ankles.

B.) **Fatty's syndrome:** It consists of polyarticular RA associated with splenomegaly and hypersplenism and consequent haematologic derangements.

C.) **Ankylosing spondylitis or rheumatoid spondylitis:** It is rheumatoid involvement of the spine, particularly sacroiliac joints, in young male patients. The condition has a strong HLA-B27 association and may be associated inflammatory disease

• **Pathogenesis of rheumatoid arthritis:**



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* Osteoporosis: or osteopenia

- It is a common clinical syndrome involving multiple bones in which there is quantitative reduction of bone tissue mass. This reduction in bone mass results in fragile skeleton associated with increased risk of fractures and consequent pain and deformity.
- This condition is particularly common in elderly people and more frequent in postmenopausal women.
- **Symptoms:** Immobility, skeletal deformity, gradual loss of height with age which is caused due to compression of vertebrae.
- **Pathogenesis of osteoporosis:** osteoporosis is conventionally classified into 2 major groups: Primary and secondary.

A.) **Primary osteoporosis:** It primarily results from osteopenia without an underlying disease or medication. Primary osteoporosis is subdivided into 2 types:

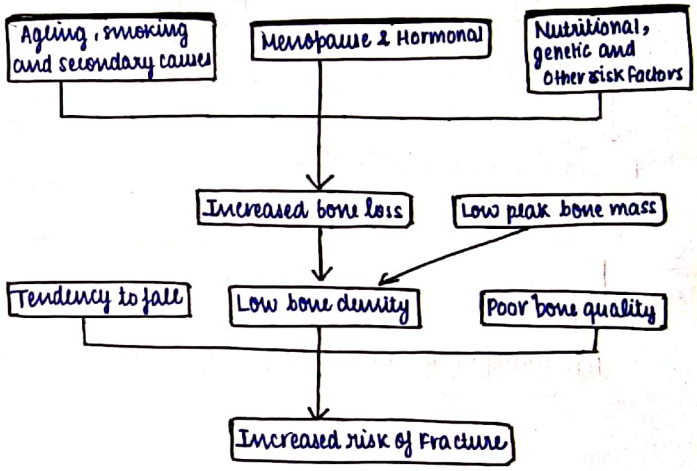
a.) **Idiopathic type** found in the young and juveniles and is less frequent.

b.) **Involutional type** seen in postmenopausal women and ageing individuals and is more common.

- It results from the excessive osteoclastic resorption and slow bone formation. The risk factors are:

I.) Genetic factors
II.) sex → More frequent in females.
III.) Reduced physical activity
IV.) Deficiency of sex hormones → (oestrogen deficiency in ♀ & androgen deficiency of ♂)
V.) Combined deficiency of calcitonin and oestrogen.
VI.) Hyperparathyroidism
VII.) Deficiency of vitamin-D
VIII.) Local factors that ↑ osteoclastic resorption & ↓ bone formation.

B.) **Secondary osteoporosis:** It is attributed to a number of factors and conditions (e.g immobilisation, chronic anaemia, acromegaly, hepatic disease, hyperparathyroidism, hypogonadism, thyrotoxicosis and starvation), or as an effect of medication (e.g., administration of glucocorticoids, anti-convulsant drugs and large dose of heparin).



- **Pathophysiology of osteoporosis:** (due to oestrogen deficiency) on next page:

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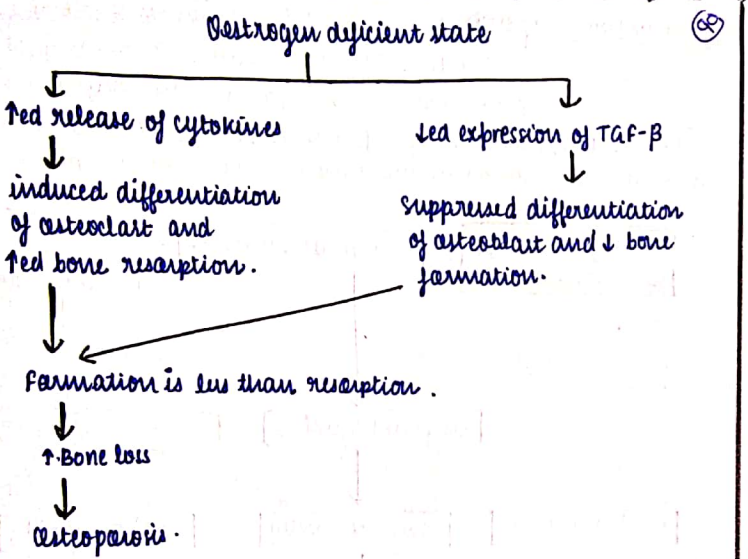

Fig; Pathophysiology of osteoporosis (due to oestrogen deficiency)

∵ Difference b/w osteoporosis and rheumatoid arthritis:

Rheumatoid arthritis	Osteoporosis
1.) Swelling and inflammation in synovial membrane and bone erosion.	1) The decrease in bone mass and density which enhances the susceptibility to fractures.
2.) Severe pain during movement of joint.	2) No pain occurs.
3.) Morning stiffness occurs in joints.	3.) No morning stiffness occurs.
4.) Fracture do not occurs.	4.) Very high chances of the fracture.
5.) It is an auto-immune disorder or sometimes may occurs due to viral infection	5.) It is not an auto-immune disorder but occurs due to low vitamin D, calcium, protein intake and estrogen deficiency in females.
6.) The main affected part is joints, that's why named arthritis ('arth' means 'joint' and 'itis' mean inflammation).	6.) The mass and density of the bone is decreased which ↑ses risk of fracture.
7.) Immobility due to inflammation in joint.	7.) Immobility due to ↓ed bone density.

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PRINCIPLES OF CANCER:

* **Cancer:** (Or Neoplasm/tumour)
  - It is defined as the mass of tissue formed as a result of abnormal, excessive, uncoordinated, autonomous and purposeless proliferation of cells, even after removal of growth stimulus which caused it.
  - Neoplastic cells loose control and regulation of replication and forms an abnormal mass of tissue.
  - **Characteristics of tumour cells:** The following are the characteristics of tumour cells:
    A.) Self-sufficiency in growth signals.
    B.) Insensitivity to anti-growth signals.
    C.) Resistance to apoptosis.
    D.) Limitless replicative potential (uncontrolled proliferation)
    E.) Tissue invasion and metastasis (distant spread)
  - **Components of tumour cells:** All tumours, benign as well as malignant, have 2 basic components:
    A.) **Parenchyma:** It comprised by proliferating tumour cells; parenchyma determines the nature and evolution of the tumour.
    B.) **Supportive stroma:** It is composed of fibrous connective tissue and blood vessels. It provides the framework on which the parenchymal tumour cells grow.
  - **Aetiology of cancer:** The cancer can be caused due to:
    1.) Viruses (papilloma, Epstein-Barr, hepatitis B, retrovirus).
    2.) Radiation exposure
    3.) Environmental/industrial carcinogens (i.e., Diet and nutrition, Drug induced cancer, Nickel, etc).
    4.) Tobacco and alcohol consumption.
    5.) Immunodeficiency syndromes; HIV is associated with the Kaposi's sarcoma, non-hodgkin's lymphoma
    6.) Genetic susceptibility syndromes.

  - **Classification of tumours:** It is of 2 types:
    A.) **Benign tumours** (They are generally slow growing and localised without causing much difficulty to the host).
    B.) **Malignant tumours** (They proliferate rapidly spread throughout the body and may eventually cause mortality of the host).
  - **Comparison b/w Benign and malignant tumours:**

Features	Benign	Malignant
I) Clinical and gross features		
a.) Boundaries	Encapsulated	Poorly-circumscribed and irregular
b.) Surrounding tissue	Often compressed	Usually invaded.
c.) Size	Usually small	Often larger
d.) Secondary changes	Occurs less often	Occur more often.
II.) Microscopic Features		
a.) Pattern	Usually resembles the tissue of origin closely.	Often poor resemblance to tissue of origin.
b.) Basal polarity	Retained	Often loss
c.) Pleomorphism	Usually not present	Often present.
d.) Nucleo-cytoplasmic ratio	Normal	Increased

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e.) Anisonucleosis	Absent	Generally present.
f.) Hyperchromatism	Absent	often present.
g.) Mitosis	May be present but are always typical mitoses.	Mitotic figures red and are generally atypical & abnormal.
h.) Tumour giant cells	May be present but without nuclear atypia.	present with nuclear atypia
i.) Chromosomal abnormalities	Infrequent	Invariably present.
j.) Function	Usually well maintained.	May be retained, lost or become abnormal.
III.) Growth rate	Usually slow	Usually rapid
IV.) Local invasion	Often compresses the surrounding tissues without invading or infiltrating them.	Usually infiltrates and invades the adjacent tissues.
V.) Metastasis	Absent	Frequently present.
VI.) Prognosis	Local complications	Death by local and metastatic complications

- **Pathogenesis of cancer:** Carcinogenesis or oncogenesis or tumorigenesis means mechanism of induction of tumours (pathogenesis of cancer.

Based on causative agents, etiology and pathogenesis of cancer are discussed under following 3 headings:

A.) Chemical carcinogens and chemical carcinogenesis.

B.) Physical carcinogens and radiation carcinogenesis

C.) Biological carcinogens and viral oncogenesis.

A.) **Chemical carcinogenesis:**

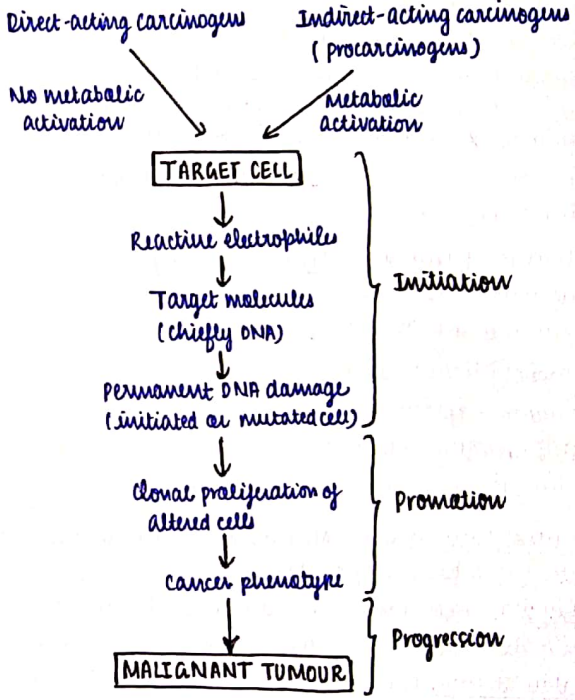

Fig: Sequential stages of chemical carcinogenesis in evolution of cancer

B.) **Physical carcinogenesis:** Physical agents in carcinogenesis are divided into 2 groups:

a) **Radiation**, both ultraviolet light and ionising radiation, is the most important physical agent

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b) Non-radiation physical agents are various forms of injury and are less important. Mechanical injury to the tissues as prolonged contact with certain physical agents has been observed to have higher incidence of certain cancers.

C) Biological carcinogenesis: Epidemiological studies on different types of cancer indicates the involvement of transmissible biologic agents in their development, chiefly viruses. Other microbial agents implicated in carcinogenesis are as follows:

a) Parasites: Schistosoma haematobium infection of the urinary bladder is associated with high incidence of squamous cell carcinoma of the urinary bladder.

b) Fungus: Aspergillus flavus grows in stored grains and liberates aflatoxin; its human consumption, especially by those with hepatitis B virus infection, is associated with development of hepatocellular carcinoma.

c) Bacteria: Helicobacter pylori, gram-positive spiral-shaped bacteria, colonises the gastric mucosa and has been found in cases of chronic gastritis and peptic ulcer. Its prolonged infection may lead to gastric lymphoma and gastric carcinoma.

d) Viral carcinogenesis: It has been estimated that about 20% of all cancers worldwide are due to persistence of virus infection.
- Most of the common viral infections (including oncogenic viruses) can be transmitted by one of the 3 routes:
  i) Horizontal transmission
  ii) Parenteral route
  iii) Vertical transmission.
- Based on their nucleic acid content, oncogenic viruses fall into 2 broad groups:

(93)

i) Those containing deoxyribonucleic acid are c/a DNA oncogenic viruses.

ii) Those containing ribonucleic acid are termed RNA oncogenic viruses or retroviruses.

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