Name of Unit	Gastrointestinal System, Disease of bones and Joints & Principles of Cancer: Classification, etiology and Pathogenesis of cancer.
Subject /Course name	Pathophysiology
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Learning Outcome of Module 04

LO	Learning Outcome	Course Outcome Code
LO 1	To understand about the Gastrointestinal System: Inflammatory bowel diseases Jaundice.	BP204T.4
LO 2	To understand about the Gastrointestinal System: Hepatitis (A, B, C, D, E, F).	BP204T.4
LO 3	To understand about the Gastrointestinal System: Alcoholic Liver Disease	BP204T.4
LO 4	To understand about the Disease of bones and Joints: Osteoporosis and Gout.	BP204T.4
LO 5	To understand about the Disease of bones and Joints: Rheumatoid Arthritis.	BP204T.4
LO 6	To understand about the Principles of Cancer: Classification, etiology and Pathogenesis of cancer.	BP204T.4

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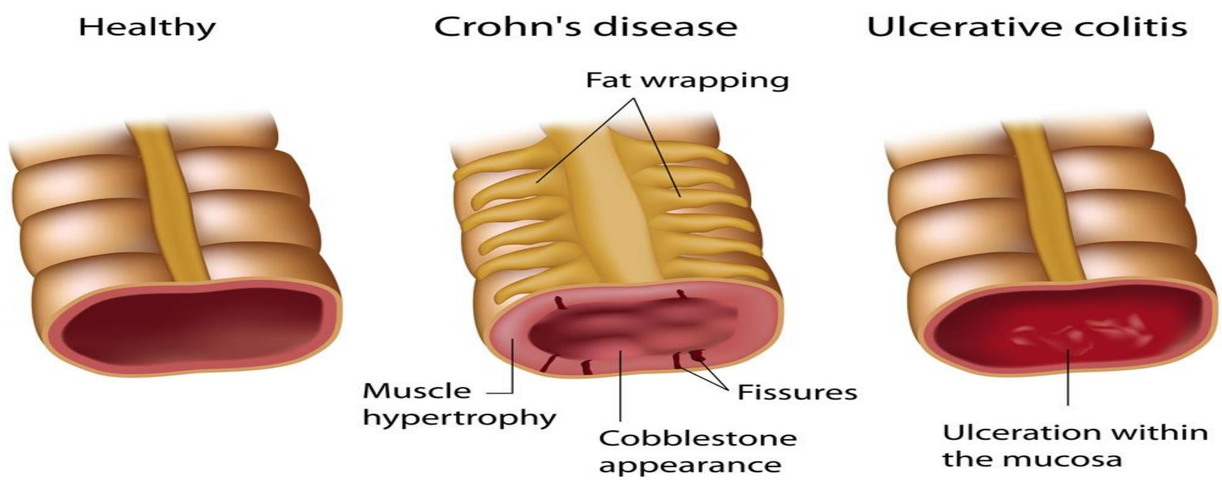
Topic
• Gastrointestinal System: Inflammatory bowel diseases, Jaundice • Gastrointestinal System: Hepatitis (A, B, C, D, E, F), Alcoholic Liver Disease • Disease of bones and Joints: Rheumatoid Arthritis, Osteoporosis and Gout • Principles of Cancer: Classification, etiology and Pathogenesis of cancer

INFLAMMATORY BOWEL DISEASES
(CROHN'S DISEASE AND ULCERATIVE COLITIS)



CROHN'S DISEASE

- Crohn's disease is a type of inflammatory bowel disease (IBD).
- It causes inflammation of your digestive tract, which can lead to abdominal pain, severe diarrhea, fatigue, weight loss and malnutrition.
- It is a chronic inflammation of the intestinal wall. The segment of terminal ileum and/or colon (large intestine) is most commonly affected and hence also known as regional enteritis, granulomatous ileitis, ileocolitis.
- Crohn's disease causes inflammation in part of your digestive system. Crohn's can affect any part of it, but it most often involves your small intestine and colon.
- Inflammation caused by Crohn's disease can involve different areas of the digestive tract in different people. This inflammation often spreads into the deeper layers of the bowel.
- Crohn's disease can be both painful and debilitating, and sometimes may lead to life-threatening complications

SIGNS AND SYMPTOMS

Diarrhea, Fever, Fatigue, Abdominal pain and cramping, Blood in your stool, Mouth sores

Reduced appetite and weight loss.

Pain or drainage near or around the anus due to inflammation from a tunnel into the skin (fistula)

ETIOLOGY

The cause of Crohn's disease is not known but the current research have proposed some possibilities mentioned below.

Genetics: Genetic factors have been implicated because approximately 20% of patients have a first degree relative with inflammatory bowel disease.

Infective agents: A variety of infective organisms including bacteria, virus, protozoa, fungi have been proposed but this theory lacks strong evidence.

Immunological mechanism: Immunological mechanisms proposed the role of humoral factors, cell mediated immunological factors and immunodeficiency but the exact role is not proven. These assumptions are based on certain changes like increased synthesis of IgG by lymphoid cells, IgE mediated hypersensitivity, immune deficiency of IgA, decreased number of T-cells, etc.

Psychology: Various psychological factors like emotions, extreme sensitivity, inability to express have long been thought to play an important role in exacerbation of condition. Investigations show that typical characters of a person have close relationship with the onset and progress of the disease.

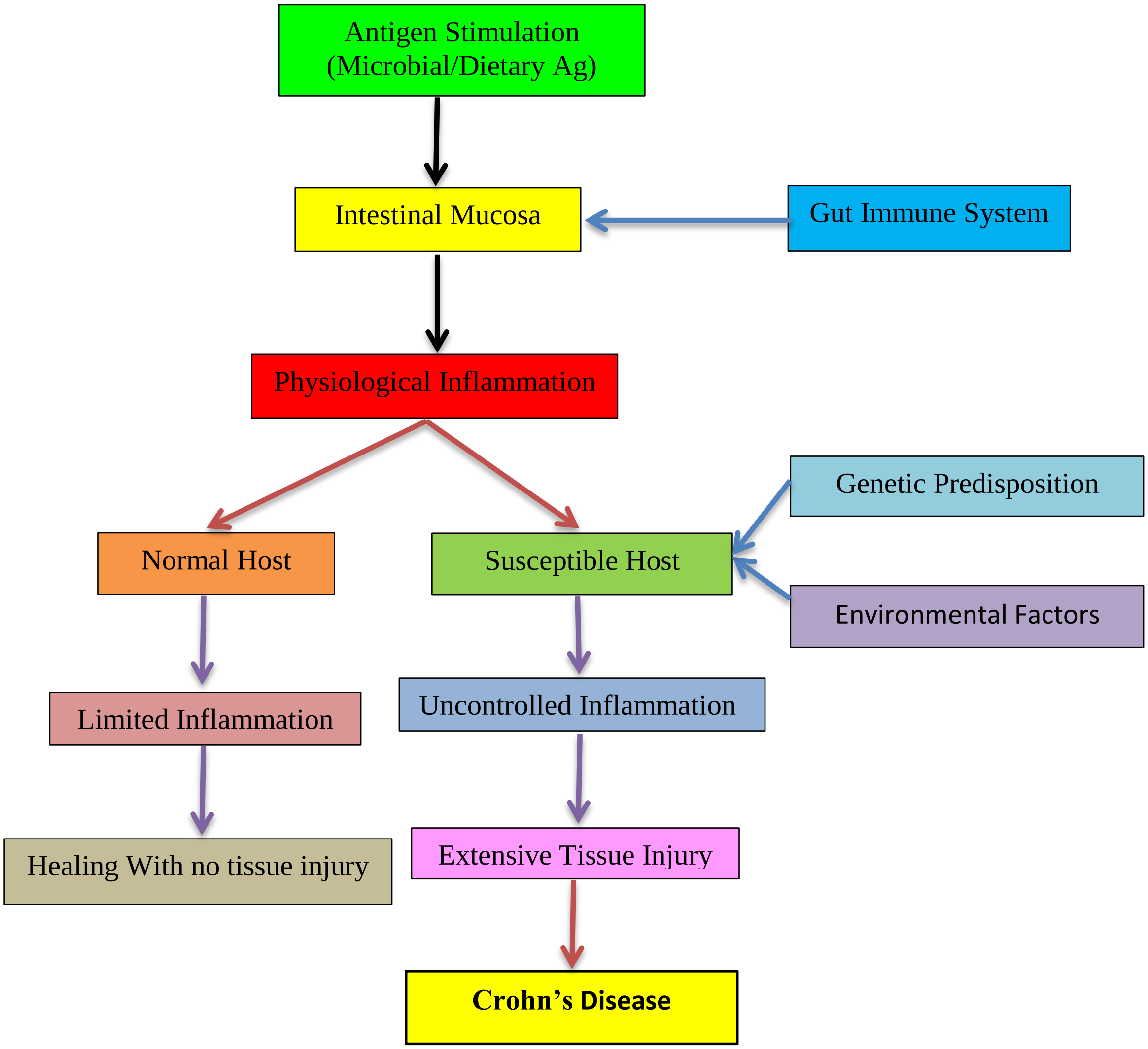
Miscellaneous:

Food allergy (Nutritional)

Trauma

PATHOPHYSIOLOGY

- Biopsies of the colon are taken to confirm the diagnosis.
- Crohns disease shows a transmural pattern of inflammation, showing entire depth of the intestinal wall.
- Ulceration is an outcome seen in highly active disease.
- Inflammation is characterized by focal infiltration of neutrophils, a type of inflammatory cell, into the epithelium.
- These neutrophils leading to inflammation or abscess.
- Granulomas known as giant cells, are found in 50% cases of Crohns disease.



DIAGNOSIS

Physical examination: A physician may suspect the disease with recurrent abdominal cramps followed by diarrhea. In addition, inflammation of joints and skin colouration give more clear indication.

General tests: These tests include blood tests and examination of stool's culture is useful to detect infection, if any. The above mentioned tests are unable to distinguish between Crohn's disease and other common diseases of ileocaecal region like appendicitis, appendix abscess, lymphoma of ileum, etc and need some special tests.

Special tests:

1. Radiology: A plain radiograph of the abdomen or barium enema X-ray recommended at the initial presentation. It can reveal abnormal mucosal pattern, extent of ulceration and any involvement small intestine.

2. Endoscopy: It is often used to assess the extent and severity of the disease and generally performed if the barium test indicates any abnormality, Endoscopy of the stomach and duodenum are usual.

3. Biopsy studies: Colonoscopic biopsies are often performed to confirm the diagnosis and even to distinguish the condition from other diseases causing colitis.

4. C.T. Scan: In selected case, it is employed to see the changes in the wall of intestine and identify abscesses.

ULCERATIVE COLITIS

Ulcerative colitis (UC) is an inflammatory destructive disease of the large intestine characterized by motility and secretion disorders. Inflammation usually occurs in the rectum and lower part of the colon, but it may affect the entire colon. UC is an inflammatory bowel disease (IBD) that causes inflammation in the small intestine and colon.

UC can be difficult to diagnose because its symptoms are similar to other intestinal disorders and another type of IBD called Crohn's disease (CD). UC may occur in people of any age, but most often it starts between ages 15 and 30, or less frequently between ages 50 and 70.

TYPES OF ULCERATIVE COLITIS: There are 4 types of ulcerative colitis (UC):

- **Ulcerative proctitis**
- **Proctosigmoiditis**
- **Left-sided colitis**
- **Pan-ulcerative colitis**

Ulcerative proctitis: It is a mild form of the disease and accounts for nearly 30% of all cases. Bowel inflammation is limited to the rectum, and because the affected area is so small, it is associated with fewer complications.

Proctosigmoiditis: Proctosigmoiditis Affects the rectum and the sigmoid colon (the lower segment of colon located right above the rectum). Symptoms include bloody diarrhea, cramps, and a constant feeling of the need to pass stool. Moderate pain on the lower left side of the abdomen may occur in active disease

Left-sided colitis: Left-sided colitis Begins at the rectum and extends up to a bend in the colon near the spleen called the splenic flexure. Symptoms include loss of appetite, weight loss, diarrhea, severe pain on the left side of the abdomen, and bleeding.

Pan-ulcerative colitis: Effects the entire colon. Symptoms include diarrhea, severe abdominal pain, cramps, and extensive weight loss. Potentially serious complications include massive bleeding and acute dilation of the colon (which may lead to an opening in the bowel wall) serious complications.

SYMPTOMS OF ULCERATIVE COLITIS

Ulcerative colitis symptoms can vary, depending on the severity Of inflammation .

You may have the following signs and symptoms, depending on which part of the colon is inflamed: Abdominal pain, Increased abdominal sounds, Bloody stools, Diarrhea, Fever Rectal, Pain and Weight loss.

CAUSES

Genes: Ulcerative colitis sometimes runs in families. Research suggests that certain genes increase the chance that a person will develop ulcerative colitis.

Abnormal immune reactions: Abnormal reactions of the immune system may play a role in causing ulcerative colitis. Abnormal immune reactions lead to inflammation in the large intestine.

Microbiome: The microbes in your digestive tract—including bacteria, viruses, and fungi—that help with digestion are called the microbiome.

Studies have found differences between the microbiomes of people who have IBD and those who don’t. Researchers are still studying the relationship between the microbiome and IBD.

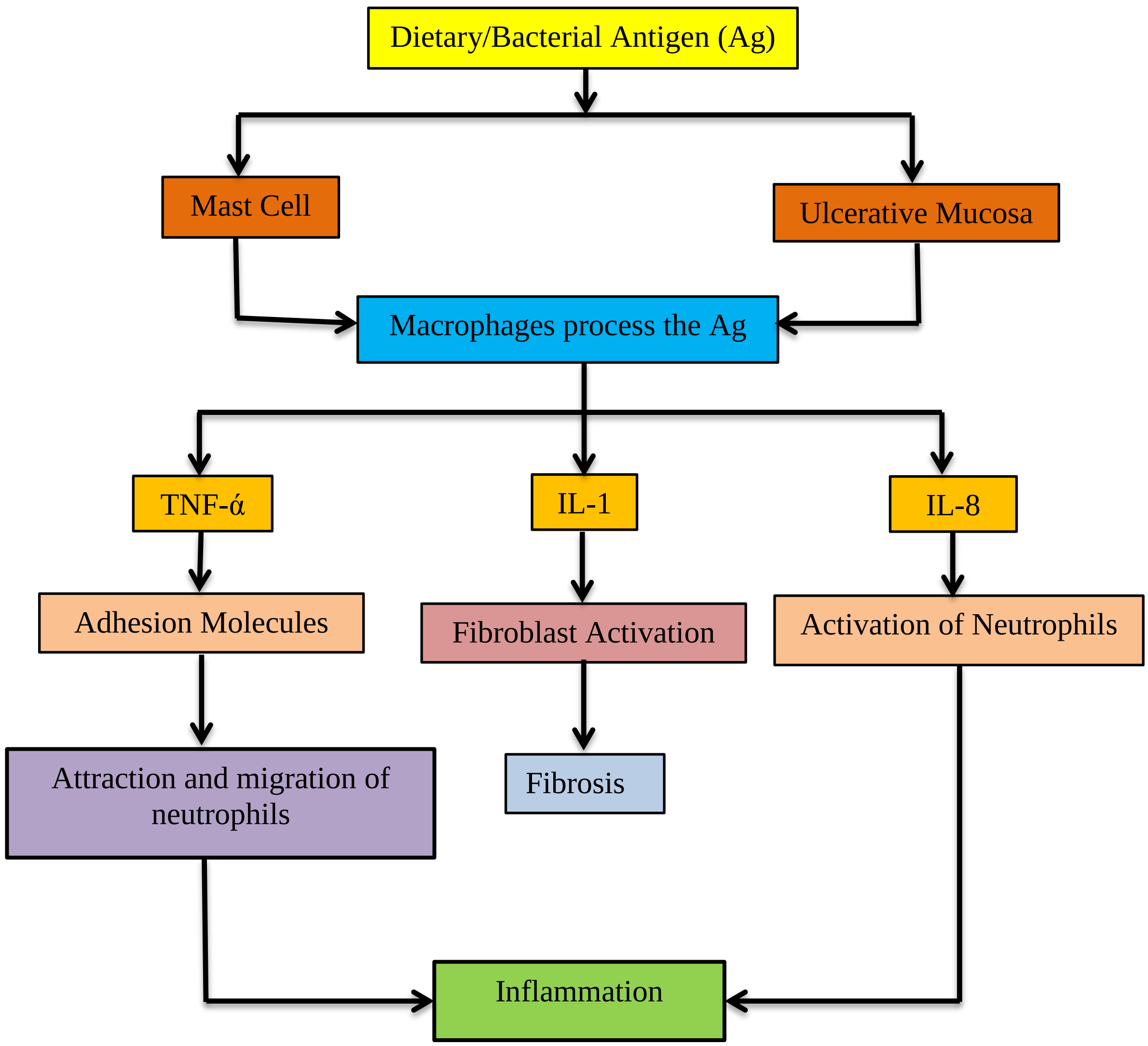
Environment: Experts think a person’s environment—one’s surroundings and factors outside the body—may play a role in causing ulcerative colitis.

Researchers are still studying how people’s environments interact with genes, the immune system and the microbiome to affect the chance of developing ulcerative colitis.

PATHOPHYSIOLOGY

- Dietary or bacterial antigens are either taken up by mast cells or pass between epithelial cells through ulcerated mucosa.

- Macrophages process the antigen and then secrete a series of cytokines, TNF-á.
- TNF-a is responsible for anorexia, malaise, fever and metabolic bone disease.
- IL-I activated CD4 lymphocytes, these secretes IL-3, IL-4 which activates mast cells and plasma cells.
- Mast cells secrete molecules like PAF, interleukins which are necessary for inflammation.
- Plasma cells secrete IgG and IgE.
- IL-8 activates and degranulates neutrophils,
- Toxic proteases and reactive oxygen species are released. These are cytotoxic and cause ulceration.



DIAGNOSIS:

The poor blood supply to the colon, bacterial or parasite infection, STD's etc. may lead to inflammation of colon which should not be mistaken as ulcerative colitis. The various investigations are carried out to confirm the ulcerative colitis followed by assessment of its severity

GENERAL INVESTIGATION:

Physical examination of patient: Recording of usual signs and symptoms

Blood test:

Anemia, elevated erythrocyte sedimentation rate (ESR), increased numbers of WBC, low levels of albumin are common indications.

Stool examination:

It is carried out to check for presence of pathogens, mucus, pus, etc.

SPECIAL INVESTIGATIONS:

Plain radiography:

Plain X-ray of abdomen may indicate the severity and extent of the disease. Barium enema X-ray studies can reveal the changes more accurately.

Sigmoidoscopy:

It gives confirmation of the disease and direct observation of the Severity of inflammation.

Colonoscopy:

Examination of complete colon to know extent of inflammation and associated changes. It is usually done, after initial therapy to avoid the risk of perforation during examination.

Biopsy study:

Microscopic examination of tissue sample taken from lining of rectum or sigmoidal colon is used to check the extent of severity. It gives reliable results even during symptoms-free periods, where other tests show normal results inspite of inflammation

JAUNDICE

- Jaundice (also called icterus) is when the skin and the whites of the eyes become a yellow color.
- People with jaundice have a problem with their liver, which stops it from removing heme properly. Heme (from hemoglobin) changes to a chemical called bilirubin after red blood cell death.
- Bilirubin causes the yellow coloring of the skin. Jaundice is common in newly born babies. It usually starts the second day after birth.
- Jaundice can also be caused by other diseases, like malaria, hepatitis, or gallstones.
- Jaundice is the most common of all liver problems. The yellow colour of the skin and mucous membranes happens because of an increase in the bile pigment, bilirubin, in the blood.
- The bile, made by the liver, is a vital digestive fluid needed for proper nutrition. It also stops decaying changes in food. If the bile is stopped from entering the intestines there is an increase in gases and other products. Normally, the production of bile and its flow is constant.

TYPES OF JAUNDICE

There are three types of jaundice:

***Haemolytic jaundice* -** Caused by destruction of red blood cells. This causes increased bilirubin formation and anaemia

***Obstructive jaundice* -** Caused by a blockage in the pathway where bilirubin is made in the liver cells and where bile goes into the duodenum

***Hepatocellular jaundice* -** Caused by damage to liver cells. The damage could be from a viral infection or toxic drugs.

Yellow discoloration of the skin and the whites of the eyes happens in all types of jaundice

CAUSES OF JAUNDICE

Jaundice occurs when there is:

1. Too much bilirubin being produced from the liver and unable to remove from the blood (for example, patients with Hemolytic Anemia have an abnormally rapid rate of destruction of their red blood cells that releases large amounts of bilirubin into the blood)

2. A defect in the liver that prevents bilirubin from being removed from the blood, converted tobilirubin/ glucuronic acid (conjugated) or secreted in bile.

3. Blockage of the bile ducts that decreases the flow of bile and bilirubin from the liver into the intestines. For example, the bile ducts can be blocked by Cancer, Gallstones, or inflammation of the bile ducts. The decreased conjugation, secretion, or flow of bile that can result in Jaundice is referred to as Cholestasis: however, Cholestasis does not always result in Jaundice.

Category	Definition
Prehepatic/hemolytic	The pathology occurs prior to the liver metabolism, due to either intrinsic causes to red blood cell rupture or extrinsic causes to red blood cell rupture.
Hepatic/hepatocellular	The pathology is due to damage of parenchymal liver cells.
Posthepatic/cholestatic	The pathology occurs after bilirubin conjugation in the liver, due to obstruction of the biliary tract and/or decreased bilirubin excretion

COMMON SIGNS AND SYMPTOMS

- Extreme weakness
- Headache
- Fever
- Loss of appetite
- Tiredness
- Severe constipation
- Nausea
- Yellow coloration of the eyes, tongue, skin and urine.
- Dull pain in the liver region.
- Obstructive jaundice may also cause intense itching.

BILIRUBIN METABOLISM

Bilirubin is a yellow bile pigment produced through the breakdown of red blood cells, which is known as haemolysis. Bilirubin is metabolised prior to excretion through the faeces and urine.

Forms of Bilirubin

Bilirubin exists in two forms; unconjugated and conjugated.

Unconjugated bilirubin is insoluble in water. This means it can only travel in the bloodstream if bound to albumin and it cannot be directly excreted from the body.

Conjugated bilirubin is water soluble. This allows it to travel through the bloodstream without requiring transport proteins like albumin, which means that it can also be excreted out of the body.

In the next section, we will explore the metabolic pathway of bilirubin in more detail.

1 Creation of Bilirubin

- Reticuloendothelial cells are macrophages which are responsible for the maintenance of the blood, through the destruction of old or abnormal cells.
- They take up red blood cells and metabolise the haemoglobin present into its individual components; haem and globin. Globin is further broken down into amino acids which are subsequently recycled.
- Meanwhile, haem is broken down into iron and biliverdin, a process which is catalysed by haem oxygenase. The iron gets recycled, while biliverdin is reduced to create unconjugated bilirubin.

2 Bilirubin Conjugation

- In the bloodstream, unconjugated bilirubin binds to albumin to facilitate its transport to the liver.
- Once in the liver, glucuronic acid is added to unconjugated bilirubin by the enzyme glucuronyl transferase.
- This forms conjugated bilirubin, which is soluble.
- This allows conjugated bilirubin to be excreted into the duodenum in bile.

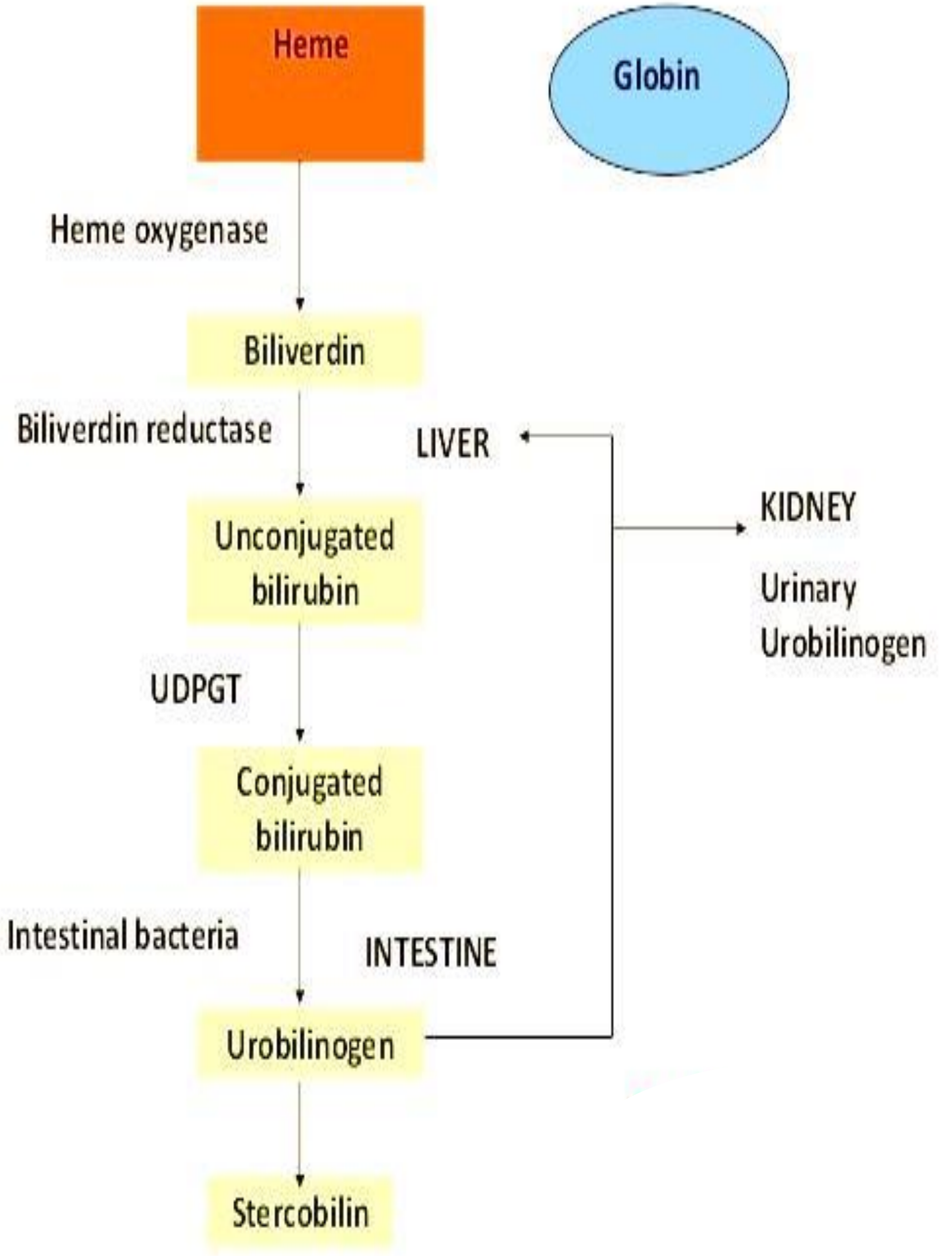
3 Bilirubin Excretion

Once in the colon, colonic bacteria deconjugate bilirubin and convert it into urobilinogen. Around 80% of this urobilinogen is further oxidised by intestinal bacteria and converted to stercobilin and then excreted through faeces.

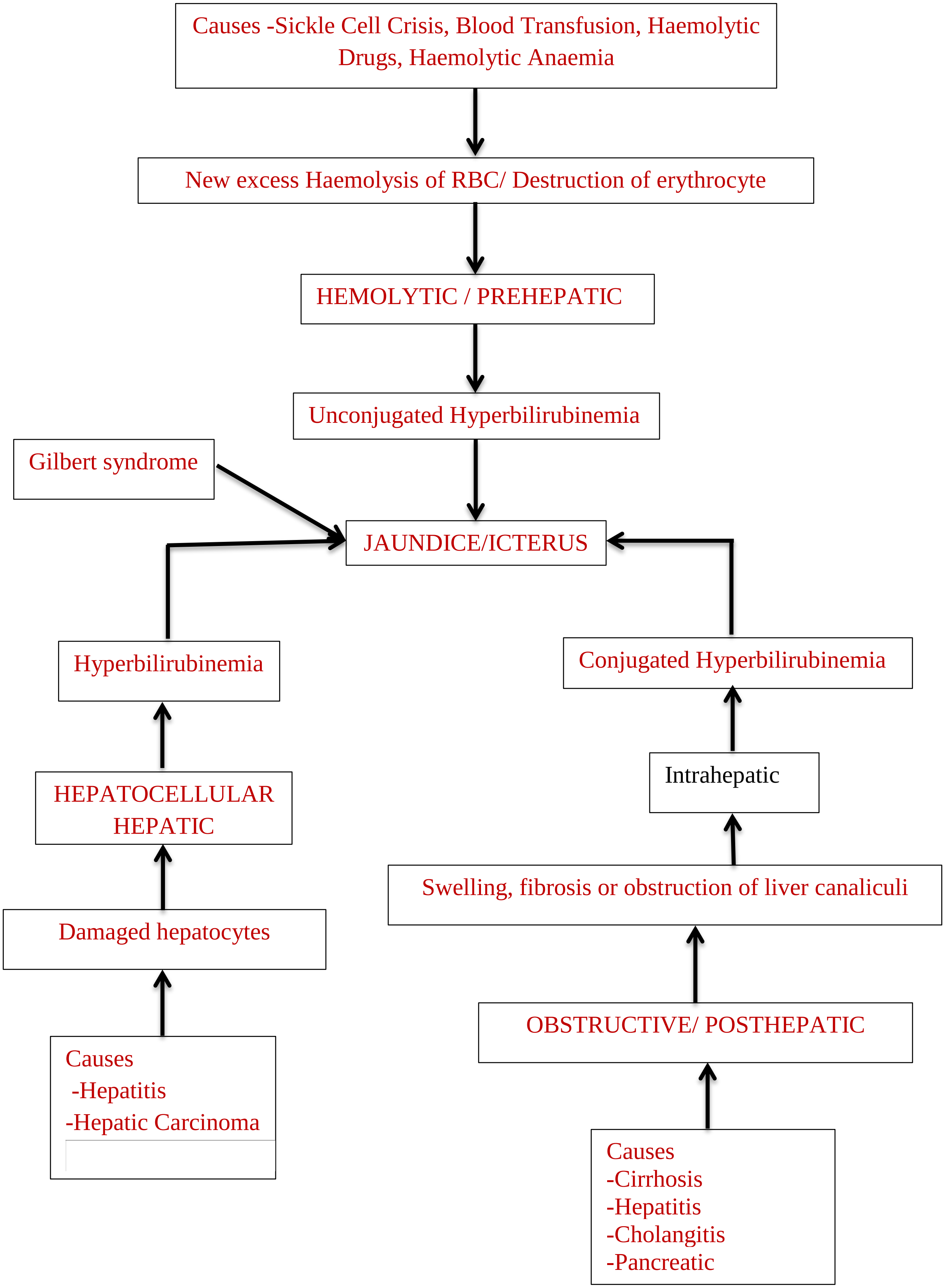
It is stercobilin which gives faeces their colour.

Around 20% of the urobilinogen is reabsorbed into the bloodstream as part of the enterohepatic circulation.

It is carried to the liver where some is recycled for bile production, while a small percentage reaches the kidneys. Here, it is oxidised further into urobilin and then excreted into the urine.



PATHOPHYSIOLOGY



DIAGNOSIS

The yellowing of skin and eyes are likely to be the main clues a doctor will use before confirming a Jaundice diagnosis.

A physical examination will be carried out to look for signs of swelling of the liver and legs, ankles or feet which might indicate Cirrhosis of the liver.

Hepatitis virus panel to look for infection of the liver

A diagnosis for jaundice in adults will be determined through tests. Recommended tests will relate to your overall symptoms. Common tests may involve:

Blood tests: The total amount of bilirubin in the body will be determined through a blood sample. Blood samples may also be used to diagnose various conditions causing jaundice, such as hepatitis. A doctor will also assess your CBC (complete blood count) and look for any signs of haemolytic anaemia (caused by abnormal degeneration of RBCs).

Liver function tests: Blood samples can also be used to measure levels of proteins and enzymes produced by the liver. The tests will show healthy function as well as damage caused by an impairment.

A liver biopsy: If any damage to the liver is suspected, small samples of liver tissue can be extracted for microscopic examination. This is done through the insertion of a needle between the lower ribs on the right-hand side to obtain a sample.

Imaging tests: Abdominal ultrasounds, MRI and CT scans can give your doctor detailed images of your internal organs – particularly the liver, pancreas and gallbladder. This will help to determine if there’s been any damage caused to your organs and also help to diagnose any underlying causes. If the liver is of concern, your doctor can determine its size and level of tenderness (which can indicate any abnormal function). In some cases, a HIDA scan (cholescintigraphy) may be recommended to check for any obstructions in the bile ducts (such as tumours and gallstones).

Urinalysis: The results of this test, which assesses the appearance, content and concentration of a sample of urine, is typically confirmed with a serum test (bilirubin levels and CBC).

Endoscopic retrograde cholangiopancreatography (ERCP): This invasive test will be used as necessary combining an endoscopy (a tube passed down the throat, into the stomach and duodenum, the first part of the small intestine) with a fluoroscopy (continuous X-ray image on a monitor) to determine abnormalities in the pancreatic or biliary ductal systems.

HEPATITIS

Hepatitis is a broad term that means inflammation of liver.

It is most commonly caused by viruses but also be caused by drugs(alcohol), chemicals, autoimmune diseases and metabolic abnormalities.

Viral hepatitis is a systemic disease with primary inflammation of the liver by any one of a heterogeneous group of hepatotropic viruses.

The most common causes of viral hepatitis are the five unrelated hepatotropic viruses Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E.

In addition to the nominal hepatitis viruses, other viruses that can also cause liver inflammation include Herpes simplex, Cytomegalovirus, Epstein–Barr virus, or Yellow fever.

Clinical Terms

Hepatitis: inflammation of liver;

Acute Viral Hepatitis: symptoms last less than 6 months

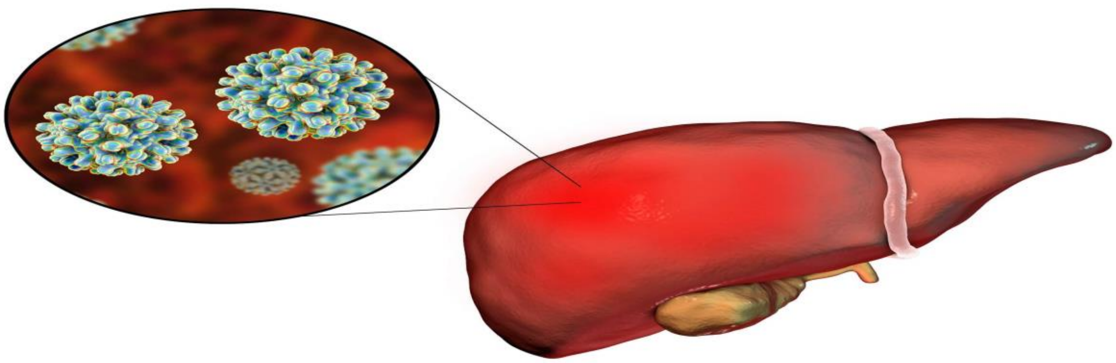
Acute Hepatic Failure: it is the appearance of severe complications rapidly after the first signs of liver disease (such as jaundice), and indicates that the liver has sustained severe damage (loss of function of 80-90% of liver cells).Massive hepatic necrosis with impaired consciousness within 8 weeks of onset of illness.

***Chronic Hepatitis*:** Inflammation of liver for at least 6 months

***Cirrhosis**:* Replacement of liver tissue

Fibrosis (Scar Tissue).These changes lead to loss of liver function.

Fulminant Hepatitis: severe impairment of hepatic functions or severe necrosis of hepatocytes in the absence of preexisting liver disease.



SYMPTOMS

Hepatitis A signs and symptoms typically don't appear until you've had the virus for a few weeks. But not everyone with hepatitis A develops them. If you do, hepatitis signs and symptoms can include:

- Fatigue
- Sudden nausea and vomiting
- Abdominal pain or discomfort, especially on the upper right side beneath your lower ribs (by your liver)
- Clay-colored bowel movements
- Loss of appetite
- Low-grade fever
- Dark urine
- Joint pain
- Yellowing of the skin and the whites of your eyes (jaundice)
- Intense itching

These symptoms may be relatively mild and go away in a few weeks. Sometimes, however, hepatitis A infection results in a severe illness that lasts several months.

TYPES OF HEPATITIS

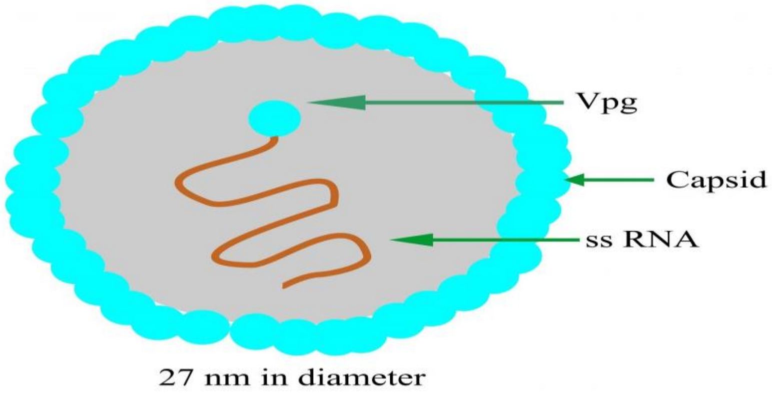
Five types of hepatitis have been identified:

- Hepatitis A, B, C, D, E.
- Hepatitis A is always an acute, short-term disease, while hepatitis B, C, and D are most likely to become ongoing and chronic.
- Hepatitis E is usually acute but can be particularly dangerous in pregnant women.
- The hepatitis A and E viruses typically cause only acute, or short-term, infections.
- Other less common viruses can also cause liver disease. These include Cytomegalovirus (CMV), Herpes virus, Rubella virus, Epstein-barr virus(EBV).

HEPATITIS A (Hep A)

A highly contagious liver infection caused by the hepatitis A virus (HAV). Hepatitis A virus is a ribonucleic acid (RNA) virus of the enterovirus family. It can cause acute hepatitis with jaundice.

Also cause acute liver failure. It does not cause long term infection. Incubation period is 3-5 weeks with an average of 28 days



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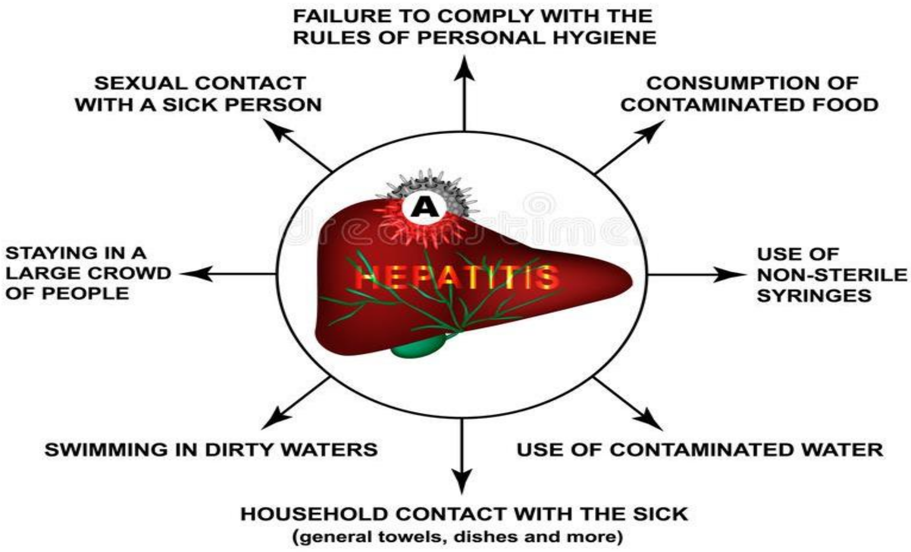
Structure of HAV

It is transmitted primarily through the fecal-oral route. Source of infection is Crowded conditions, poor personal hygiene, Poor sanitation, Contaminated food, water, shellfish, person with subclinical infections, infected food handlers. More prevalent in underdeveloped countries. People who travel to developing countries more likely to get Hep A.

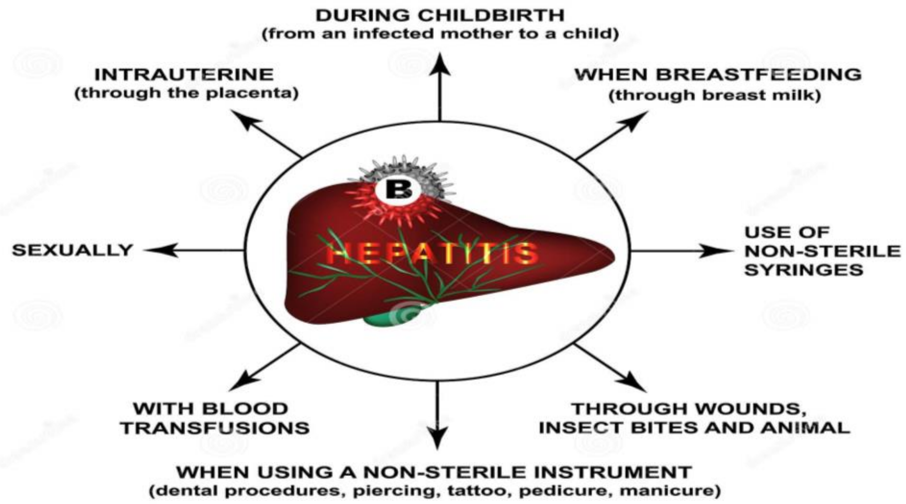
CAUSE



HEPATITIS B (Hep B) Hepatitis B virus can cause acute and chronic infection. Acute hepatitis B infection may last up to 6 months (with or without symptom) and infected persons are able to pass these virus during these time. Chronic hepatitis B is defined as persistence of HBsAg for 6 months or more after acute infection with HBV.

Incubation period is 2-5 months.

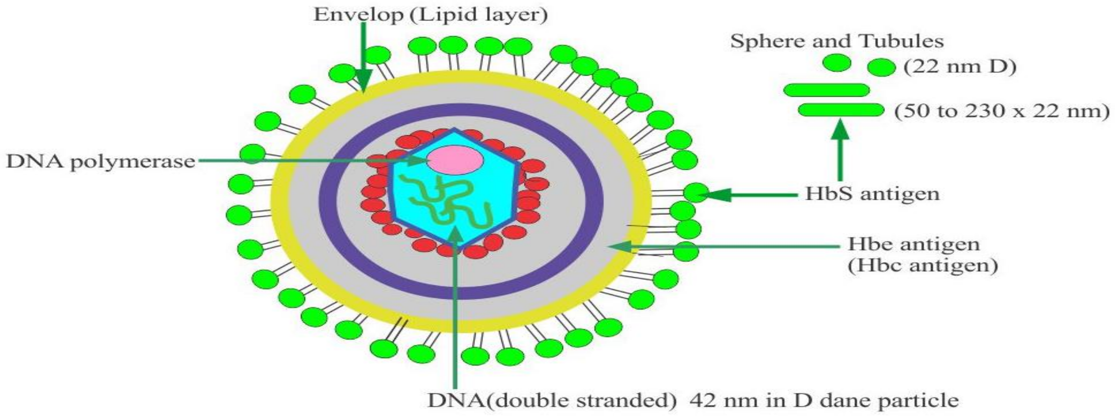
CAUSE



Hepatitis B virus is a complex structure with 3 distinct antigens:

1. HBcAg- Hepatitis B core antigen.
2. HBsAg- Hepatitis B surface antigen.
3. HBeAg- An independent protein circulating in the blood.

Mode of transmission is mainly sexual contact. Recognized as STD. It is much more infectious than HIV.



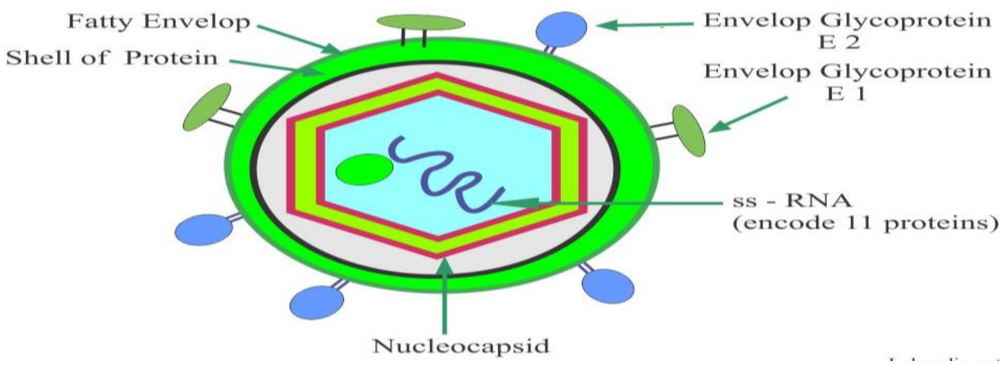
Structure of HBV

Further mode of transmission is Parenteral or permuscosal exposure to blood or blood products, perinatal transmission. Sources of infection are Contaminated needles, syringes, blood products. Homosexual men, Tattoo or body piercing with contaminated needles. Occurrence is for all ages, but mostly affects young adults worldwide. It is the main cause of cirrhosis and hepatocellular carcinoma worldwide.

HEPATITIS C (Hep C)

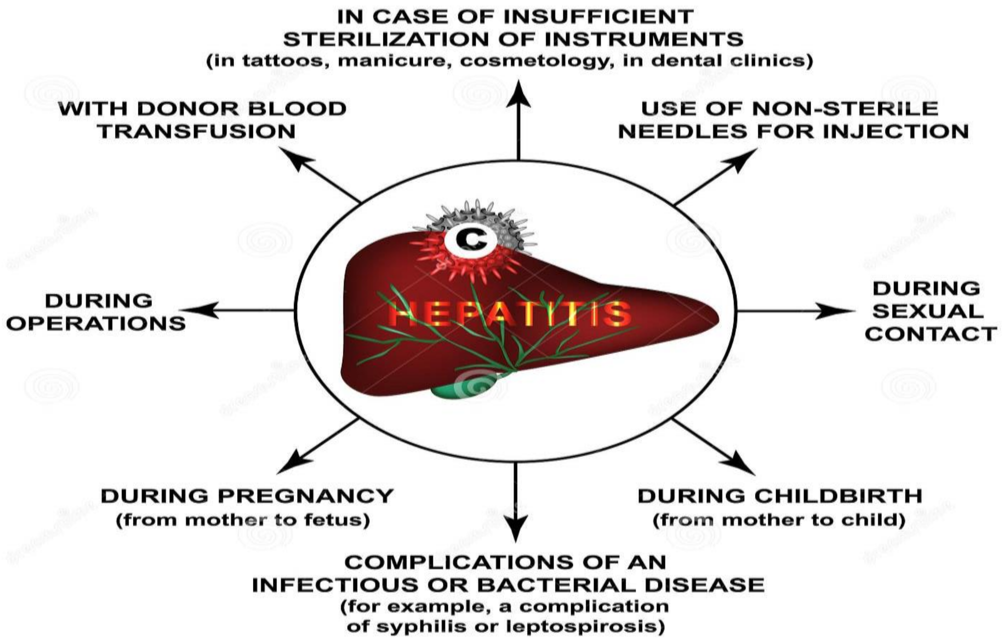
Hepatitis c virus is an RNA virus. Incubation period is 14-180 days (average 56). In most cases it is transmitted through blood or blood products, prior to 1992. It is also transmitted through unprotected sex, and contaminated or unsterile needles. It is found in I.V. drug users and renal dialysis patients. It can result in both acute and chronic illness.

Chronic HCV infection results in liver cirrhosis. There is no Vaccine for HCV.

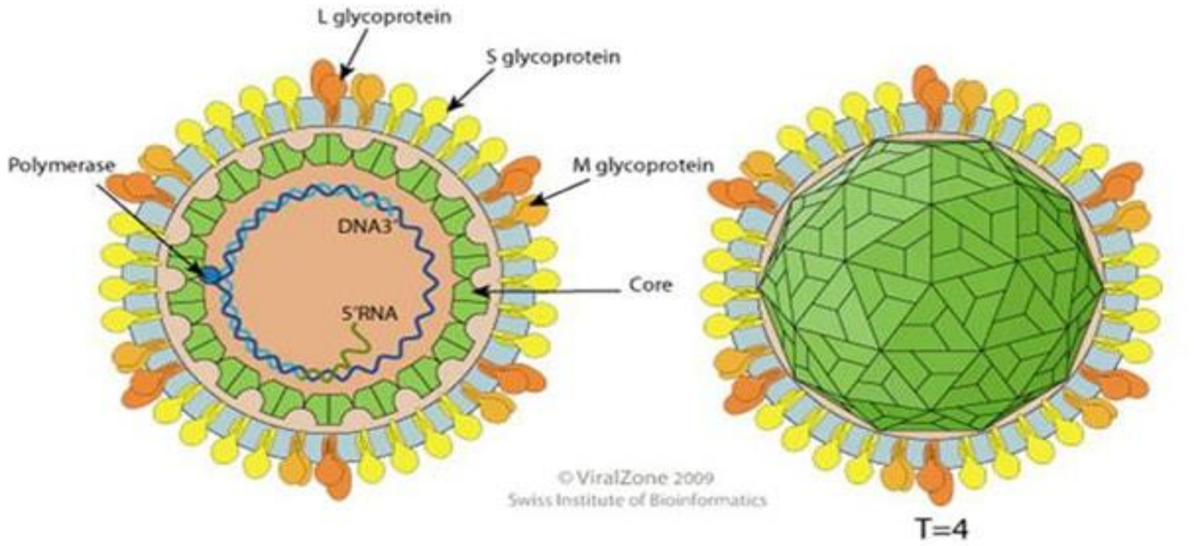


Structure of HCV

CAUSE

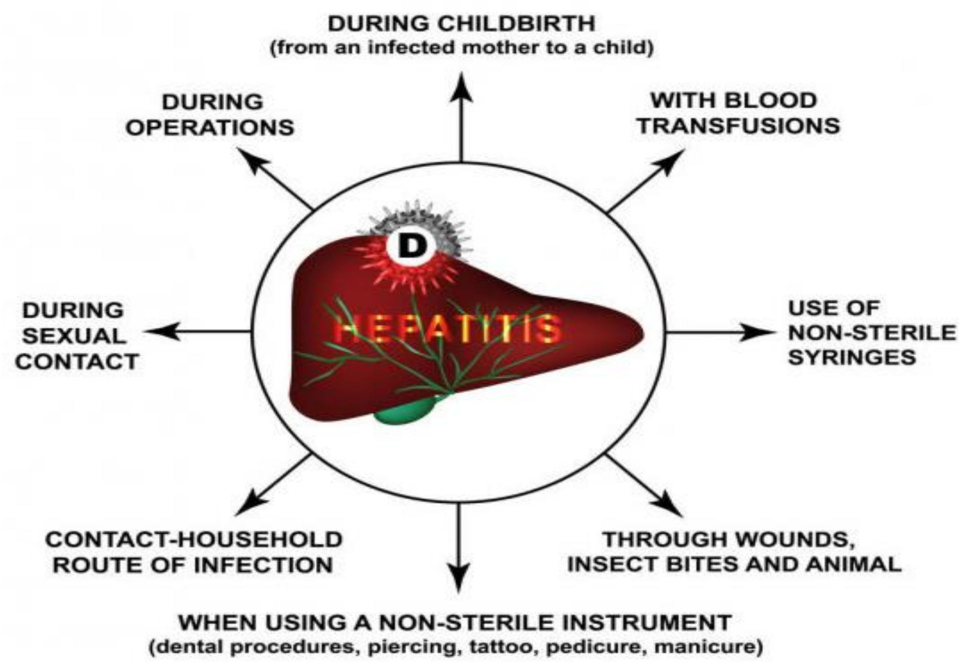


HEPATITIS D OR DELTA HEPATITIS HDV is a defective single – stranded RNA virus that cannot survive on its own. It requires hepatitis B to replicate. Incubation period is 2-26 weeks. Chronic carriers of HBV always at risk for transmission. Source of infection are same as HBV. HDV infection is only possible if a person is already infected with hepatitis B or a person can be infected with both viruses at the same time.

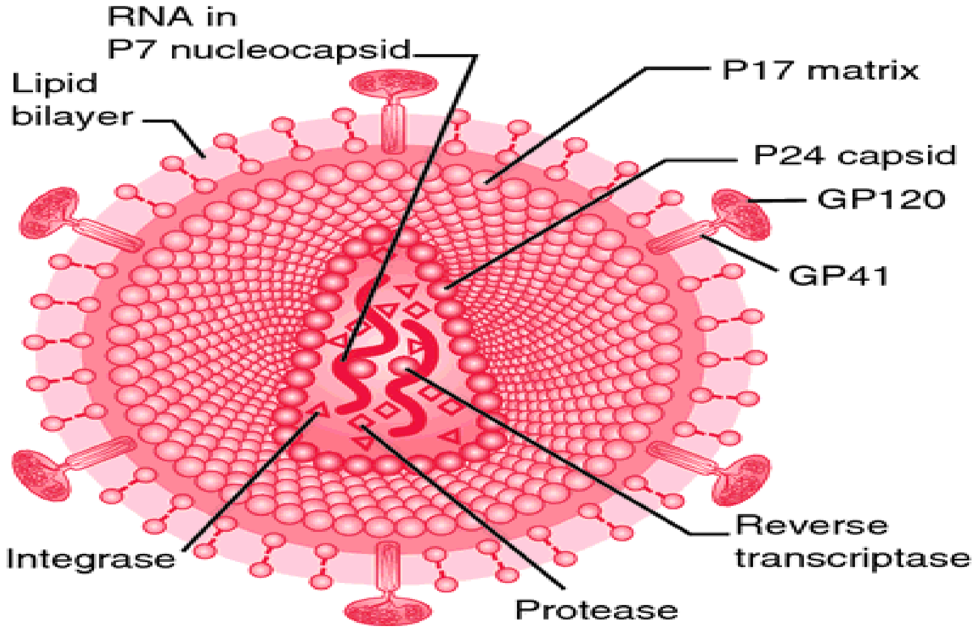


Structure of HDV

CAUSE

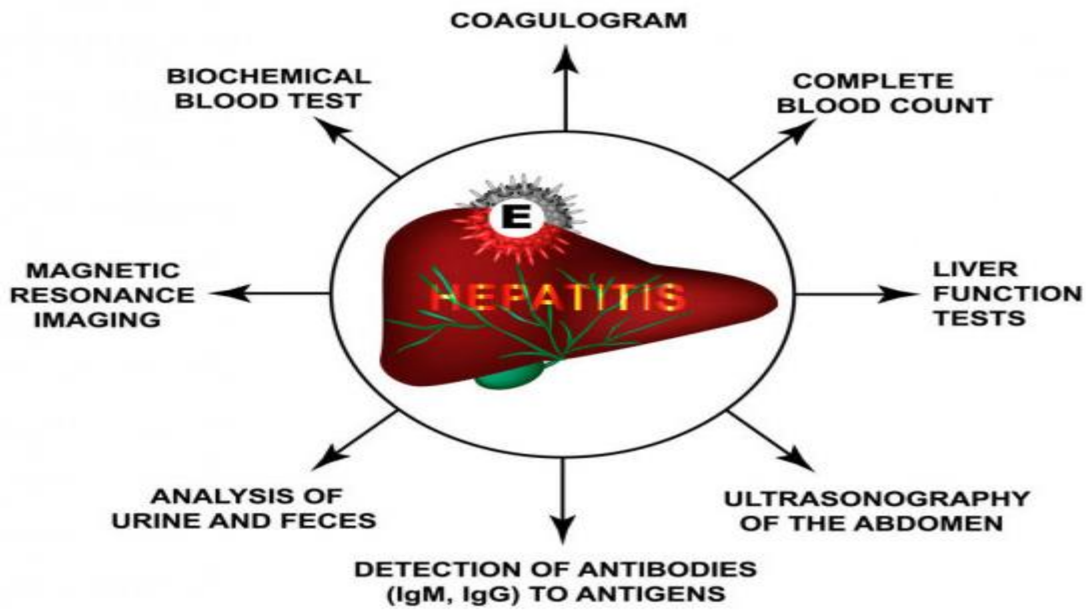


HEPATITIS E Hepatitis E virus (HEV) is an RNA virus and incubation period is 15-64 days. HEV has a fecal-oral transmission route. Source of infection is contaminated water, poor sanitation. Found in Asia, Africa and Mexico. More common in adults and severe in pregnant women. Hepatitis E usually resolves on its own within four to six weeks. Treatment focuses on supportive care, rehydration and rest.

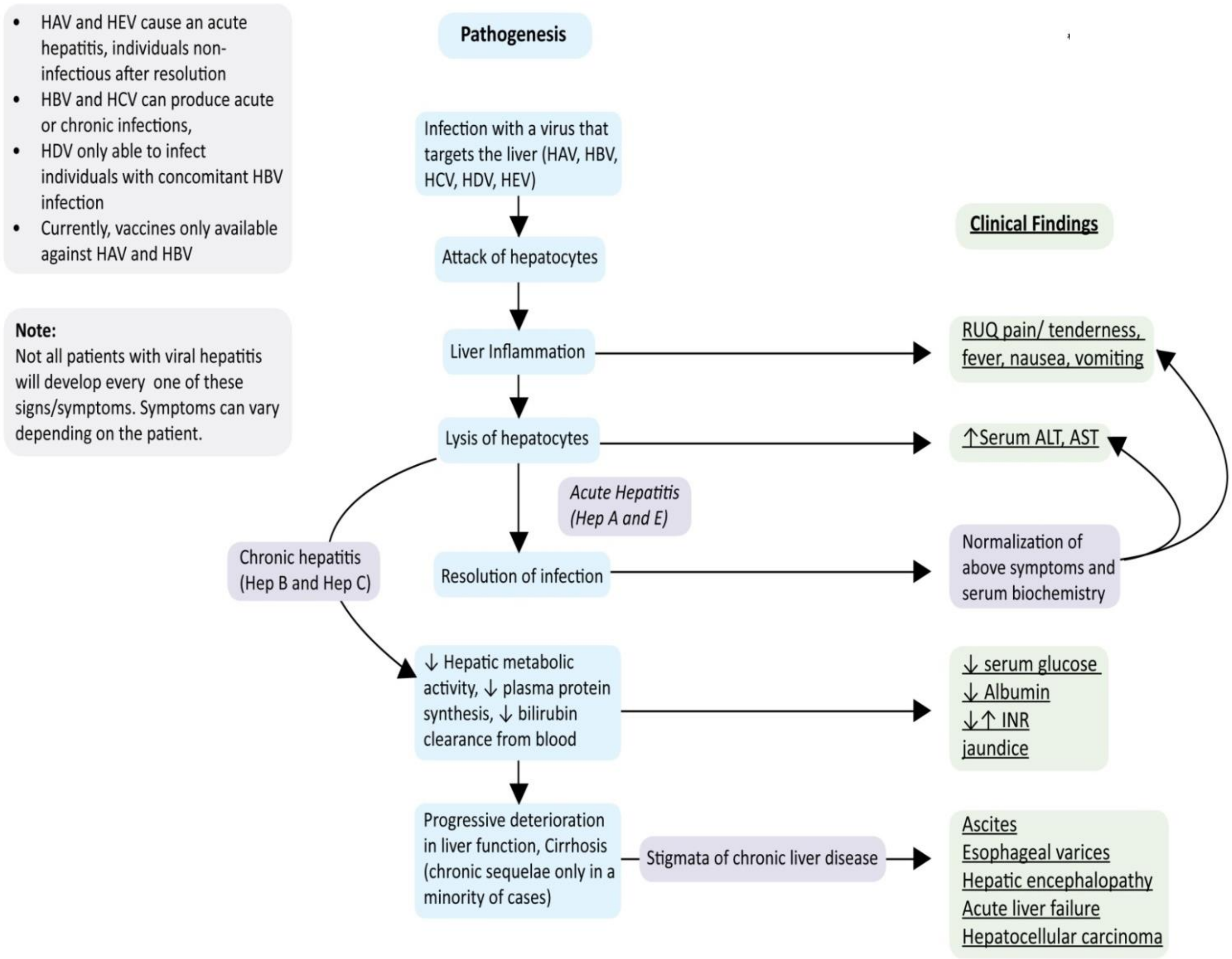


Structure of HEV

CAUSE



PATHOPHYSIOLOGY



DIAGNOSIS:

History and physical exam

To diagnose hepatitis, first your doctor will take your history to determine any risk factors you may have for infectious or noninfectious hepatitis.

During a physical examination:- your doctor may press down gently on your abdomen to see if there's pain or tenderness. Your doctor may also feel to see if your liver is enlarged. If your skin or eyes are yellow, your doctor will note this during the exam.

Liver function tests

Liver function tests use blood samples to determine how efficiently your liver works. Abnormal results of these tests may be the first indication that there is a problem, especially if you don't show any signs on a physical exam of liver disease. High liver enzyme levels may indicate that your liver is stressed, damaged, or not functioning properly.

Blood Tests

If your liver function tests are abnormal, your doctor will likely order other blood tests to detect the source of the problem. These tests can check for the viruses that cause hepatitis. They can also be used to check for antibodies that are common in conditions like autoimmune hepatitis.

Ultrasound

An abdominal ultrasound uses ultrasound waves to create an image of the organs within your abdomen. This test allows your doctor to take a close at your liver and nearby organs. It can reveal:

- Fluid in your abdomen & Liver damage or enlargement
- Liver tumors & Abnormalities of your gallbladder

Sometimes the pancreas shows up on ultrasound images as well. This can be a useful test in determining the cause of your abnormal liver function.

Liver Biopsy

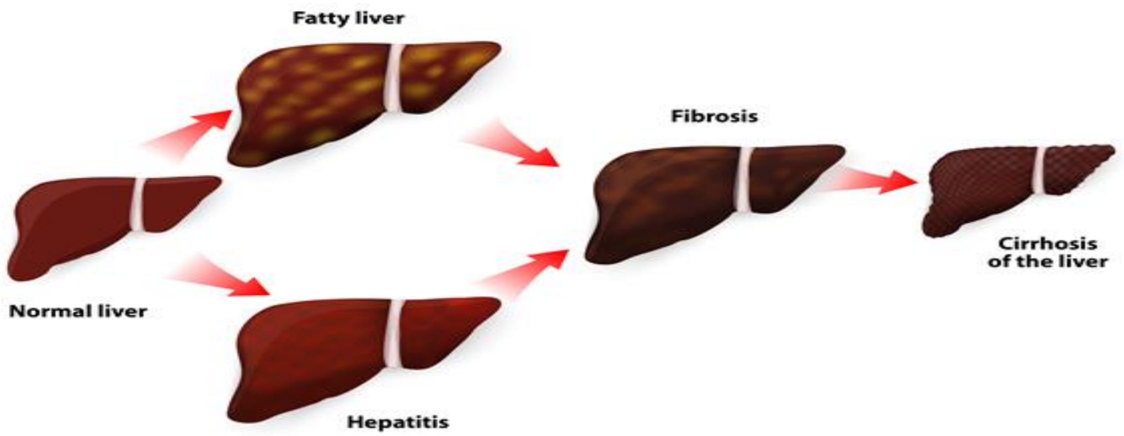
A liver biopsy is an invasive procedure that involves your doctor taking a sample of tissue from your liver. It can be done through your skin with a needle and doesn't require surgery. Typically, an ultrasound is used to guide your doctor when taking the biopsy sample.

This test allows your doctor to determine how infection or inflammation has affected your liver. It can also be used to sample any areas in your liver that appear abnormal.

ALCOHOLIC LIVER DISEASE

- Alcoholic liver disease is a result of over consuming alcohol that damages the liver, leading to a buildup of fats, inflammation, and scarring. It can be fatal.
- ALD, the term that encompasses the liver manifestations of alcohol overconsumption, including fatty liver, alcoholic hepatitis, and chronic hepatitis with liver fibrosis or cirrhosis.
- It may well represent the oldest form of liver injury known to humankind.
- Many people with alcoholic liver disease experience no symptoms in the early stage of the disease.

- Consumption of 60–80g per day (about 75–100 ml/day) for 20 years or more in men. Consumption of 20g/day (about 25 ml/day) for women significantly increases the risk of liver damage.
- Women have double the risk of getting ALD when compared to men
- 80% of alcohol passes through the liver to be detoxified. Chronic consumption of alcohol results in the secretion of pro- inflammatory cytokines (TNF-alpha, Interleukin 6 [IL6] and Interleukin 8 [IL8]), oxidative stress, lipid peroxidation, and acetaldehyde toxicity



STAGES

Alcoholic liver disease has four main stages:-

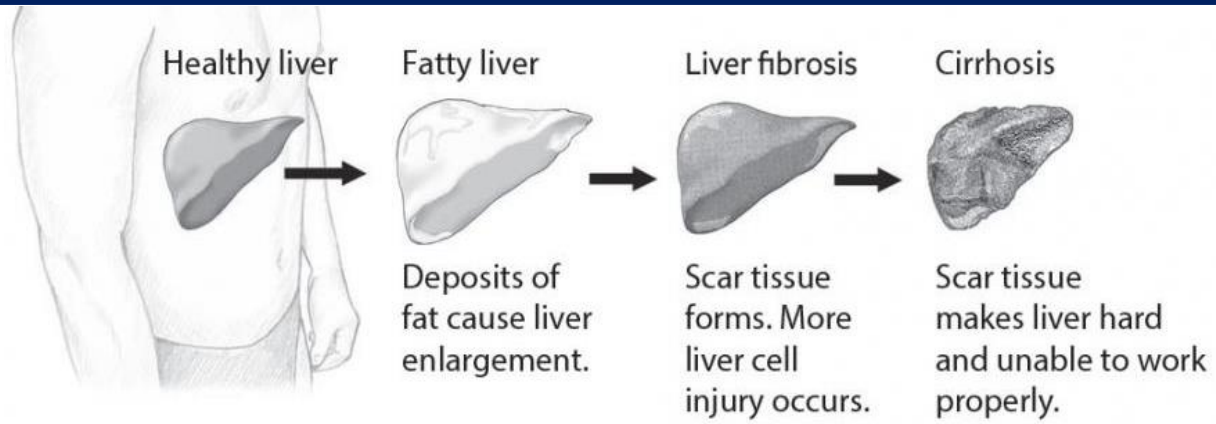
ALCOHOLIC FATTY LIVER DISEASE

Drinking a large volume of alcohol can cause fatty acids to collect in the liver. Sometimes, heavy drinking over a short period, even less than a week, can cause this. There are normally no symptoms, and this stage of the disease is often reversible if the individual abstains from alcohol from this point onward.

ALCOHOLIC HEPATITIS

Continued alcohol use will lead to ongoing liver inflammation. This can occur after many years of heavy drinking. It can also occur acutely during periods of binge drinking. Hepatitis is a general term swelling and inflammation of the liver from any cause.

If the individual abstains from alcohol on a long-term basis, alcoholic hepatitis is usually reversible.



FIBROSIS

Fibrosis is a buildup of certain types of protein in the liver, including collagen. It features in most types of chronic liver disease. Mild-to-moderate forms of fibrosis may be reversible Trusted Source. Continuous fibrosis and inflammation can lead to liver cancer.

CIRRHOSIS

Cirrhosis occurs when the liver has been inflamed for a long time, leading to scarring and loss of function. This can be a life-threatening condition. Cirrhosis damage is irreversible, but the patient can prevent further damage by continuing to avoid alcohol.

Life-long abstinence can improve liver function, but the permanent and severe damage from cirrhosis might mean that the patient needs a liver transplant to survive.

As the liver no longer processes toxins properly, it will be more sensitive to medications and alcohol. Alcohol use speeds up the destruction of the liver, along with reducing the liver's ability to compensate for the current damage.

CAUSES ALCOHOLIC LIVER DISEASE

Alcoholic liver disease is caused by long-term, extensive alcohol use. Not everyone who consumes a lot of alcohol gets alcoholic liver disease, but the more alcohol consumed on a regular basis, and the longer the alcohol use lasts, the greater your risk of developing alcoholic liver disease.

A number of factors may increase the risk of developing alcoholic liver disease. Not all people with risk factors will get alcoholic liver disease.

Risk factors for alcoholic liver disease include:

- Binge drinking
- Chronic alcohol use
- Cigarette smoking
- Coexistent liver disease (Hepatitis B or Hepatitic C infection)
- Female gender
- Obesity
- Ongoing alcohol consumption
- Poor nutrition

SYMPTOMS

Once alcoholic liver disease progresses, its symptoms become easier to recognize.

The more distinctive signs of later-stage liver disease include the following:

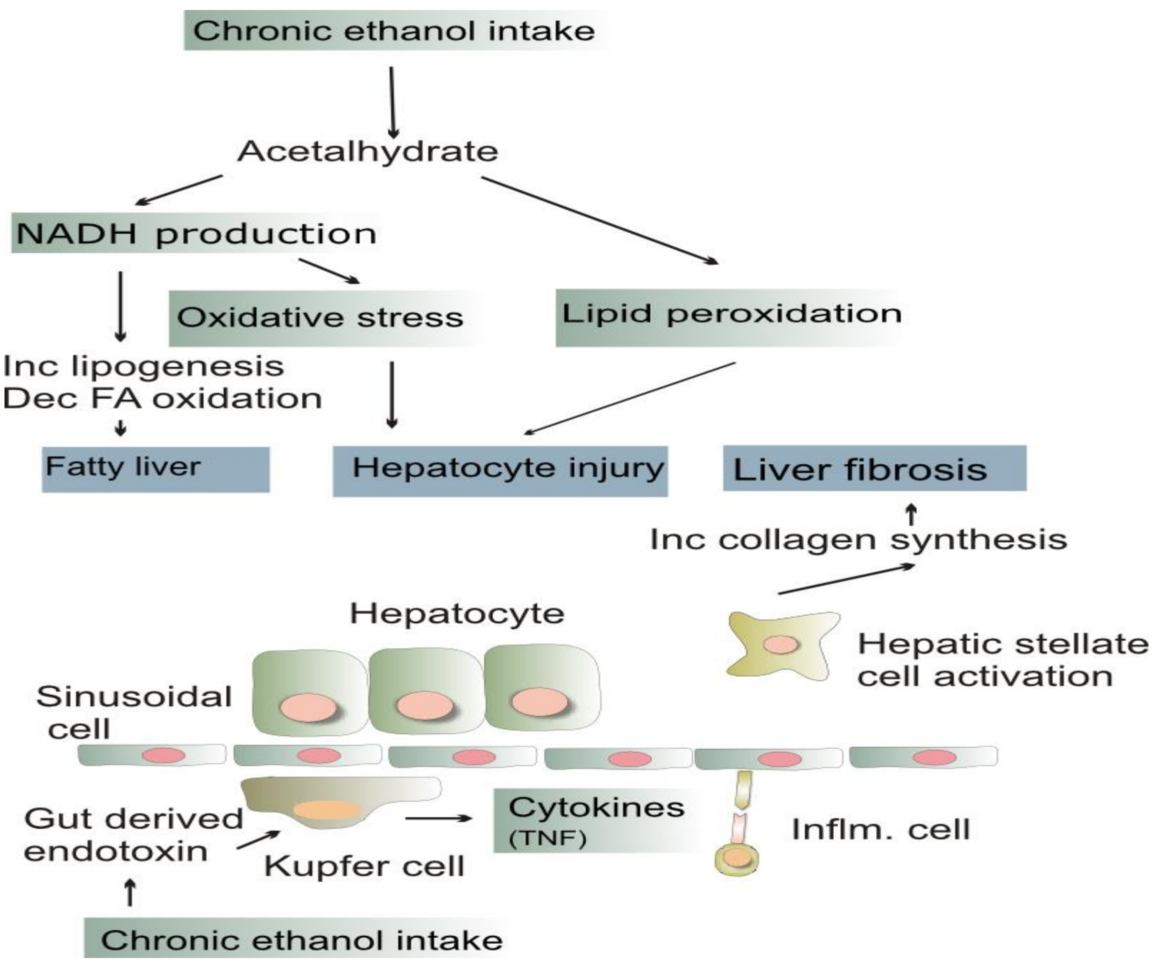
- jaundice, or a yellow tint of the whites of the eyes and the skin
- edema, or swelling of the lower limbs
- a buildup of fluid in the abdomen, known as ascites
- fever and shivering
- extremely itchy skin
- fingernails that curve excessively, known as clubbing
- losing a significant amount of weight
- general weakness and wasting muscles
- blood in vomit and stools
- bleeding and bruising more easily
- more sensitive reactions to alcohol and drugs

PATHOPHYSIOLOGY

- Alcohol consumption results in translocation of gut bacteria into the portal system along with lipopolysaccharides that interact with toll-like receptors and results in production of inflammatory and immunogenic mediators such as tumor necrosis factor α and interferons.
- Alcohol consumption causes shunting of normal substrates away from catabolism and toward lipid biosynthesis due to:
    - Excess NADH generation from alcohol dehydrogenase and acetaldehyde dehydrogenase

- Impaired assembly / secretion of lipoproteins and
- Increased peripheral fat catabolism

- P450 induction causes other drugs to be transformed to toxic metabolites; free radicals, from microsomal oxidation of alcohol, damage proteins and membranes
- Alcohol directly affects microtubular and mitochondrial function, also induces immunologic attack on hepatic neoantigens
- Acetaldehyde (alcohol metabolite) causes lipid peroxidation and acetaldehyde protein adduct formation
- Collagen deposition by perisinusoidal hepatic stellate (Ito) cells is due to Kupffer cell activation (release of TNF alpha, IL1 / 6, TGF-beta), platelet activating factor, influx of neutrophils into parenchyma
- Alcohol also causes derangements of vascular perfusion



DIAGNOSIS

LIVER FUNCTION TESTS

These are simple, inexpensive and easy to perform but cannot be used in alone to make diagnosis which include;

- Serum albumin levels and prothrombin time indicates hepatic protein synthesis,
- Bilirubin is a marker of whole liver function, transaminase levels indicate hepatocellular injury and death.
- Alkaline phosphatase levels estimate the impedance of bile flow.

IMAGING TESTS

An ultrasound scan, CT scan or a MRI scan also be carried. These scans produce detailed images of liver. Imaging studies do not confirm the presence of alcoholic liver disease . Can be used to assess for hepatic parenchymal changes. Ultrasound, CT scan, and MRI can be used to diagnose fatty change, cirrhosis, or neoplastic diseases of the liver.

LIVER BIOPSY

A fine needle is inserted into body and a small sample of liver cell is taken under local anaesthesia and is examined under microscope. Biopsy may be indicated in: Any patient with serum aminotransferases elevations that persist for >6 months, even if the patient is asymptomatic. Patients who have evidence of liver failure (eg, abnormal prothrombin time, hypoalbuminemia) in addition to elevated aminotransferases. If a coagulopathy is present, transjugular biopsy is usually safer than percutaneous biopsy. Patients in whom the diagnosis of alcoholic hepatitis.

DISEASE OF BONES AND JOINTS
(Rheumatoid Arthritis, Osteoporosis, Gout)

RHEUMATOID ARTHRITIS

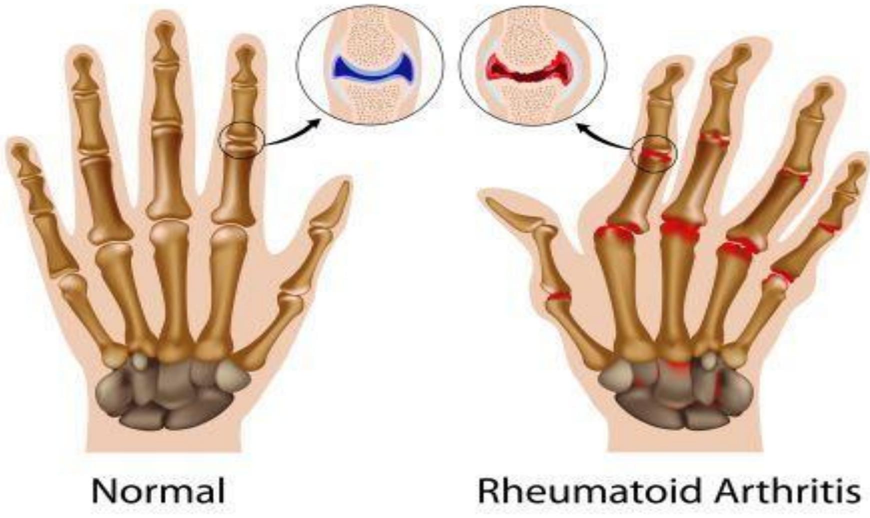
Rheumatoid arthritis (RA) causes joint inflammation and pain. It happens when the immune system doesn't work properly and attacks the lining of the joints (called the synovium). The disease commonly affects the hands, knees or ankles, and usually the same joint on both sides of the body. But sometimes, RA causes problems in other parts of the body as well, such as the eyes, heart and circulatory system and/or lungs. For unknown reasons, more women than men get RA, and it usually develops in middle age. Having a family member with RA increases the odds of developing RA.

Rheumatoid arthritis is a chronic inflammatory disorder that can affect more than just your joints. In some people, the condition can damage a wide variety of body systems, including the skin, eyes, lungs, heart and blood vessels.

An autoimmune disorder, rheumatoid arthritis occurs when your immune system mistakenly attacks your own body's tissues.

Unlike the wear-and-tear damage of osteoarthritis, rheumatoid arthritis affects the lining of your joints, causing a painful swelling that can eventually result in bone erosion and joint deformity.

The inflammation associated with rheumatoid arthritis is what can damage other parts of the body as well. While new types of medications have improved treatment options dramatically, severe rheumatoid arthritis can still cause physical disabilities



STAGES

RA is a systemic disease but the most characteristic lesions are seen in the synovium or within rheumatoid nodules. The synovium is engorged with new blood vessels and packed full of inflammatory cells

***STAGE 1 Pre-clinical*:** Before RA becomes clinically apparent the immune pathology is already beginning. Raised ESR, C-reactive protein (CRP), and RF may be detectable years before the first diagnosis.

STAGE 2 Synovial Early changes are: a. Vascular congestion with new blood vessel formation b. Proliferation of synoviocytes c. Infiltration of the sub synovial layers by polymorphs, lymphocytes and plasma cells. There is thickening of the capsular structures, villous formation of the synovium and a cell-rich effusion into the joints and tendon sheath.

STAGE 3 Destruction Persistent inflammation causes joint and tendon destruction. Articular cartilage is eroded. At the margins of the joint, bone is also eroded by granulation tissue invasion and osteoclastic resorption. Similar changes occur in tendon sheaths, caus in tenosynovitis. Partial or complete rupture of tendons. Swelling of the joints and tendons.

STAGE 4 Deformity Combination of articular destruction, capsular stretching and tendon rupture leads to progressive instability and deformity of the joints. The inflammatory process usually continues but the mechanical and functional effects of joint and tendon disruption now become vital.

SYMPTOMS

In the early stages, people with RA may not see redness or swelling in the joints, but they may experience tenderness and pain.

These symptoms are clues to RA:

- Joint pain, tenderness, swelling or stiffness that lasts for six weeks or longer.
- Morning stiffness that lasts for 30 minutes or longer.
- More than one joint is affected.
- Small joints (wrists, certain joints in the hands and feet) are typically affected first.
- The same joints on both sides of the body are affected.

Many people with RA get very tired (fatigue) and some may have a low-grade fever. RA symptoms may come and go. Having a lot of inflammation and other symptoms is called a flare. A flare can last for days or months.

CAUSES

Important factors in the evolution of RA are:

- Genetic susceptibility
- An immunological reaction; possible involving a foreign antigen, preferentially focused on synovial tissue
- An inflammatory reaction in joints and tendon sheaths
- The appearance of rheumatoid factors in the blood and synovium
- Perpetuation of the inflammatory process
- Articular cartilage destruction

Risk factors

Factors that may increase your risk of rheumatoid arthritis include:

Sex Women are more likely than men to develop rheumatoid arthritis.

Age Rheumatoid arthritis can occur at any age, but it most commonly begins in middle age.

Family history If a member of your family has rheumatoid arthritis, you may have an increased risk of the disease.

Smoking Cigarette smoking increases your risk of developing rheumatoid arthritis, particularly if you have a genetic predisposition for developing the disease. Smoking also appears to be associated with greater disease severity.

Excess weight People who are overweight appear to be at a somewhat higher risk of developing rheumatoid arthritis.

COMPLICATIONS

Rheumatoid arthritis increases your risk of developing:

Osteoporosis. Rheumatoid arthritis itself, along with some medications used for treating rheumatoid arthritis, can increase your risk of osteoporosis — a condition that weakens your bones and makes them more prone to fracture.

Rheumatoid nodules. These firm bumps of tissue most commonly form around pressure points, such as the elbows. However, these nodules can form anywhere in the body, including the heart and lungs.

Dry eyes and mouth. People who have rheumatoid arthritis are much more likely to develop jogren's syndrome, a disorder that decreases the amount of moisture in the eyes and mouth.

Infections. Rheumatoid arthritis itself and many of the medications used to combat it can impair the immune system, leading to increased infections. Protect yourself with vaccinations to prevent diseases such as influenza, pneumonia, shingles and COVID-19.

Abnormal body composition. The proportion of fat to lean mass is often higher in people who have rheumatoid arthritis, even in those who have a normal body mass index (BMI).

Carpal tunnel syndrome. If rheumatoid arthritis affects your wrists, the inflammation can compress the nerve that serves most of your hand and fingers.

Heart problems. Rheumatoid arthritis can increase your risk of hardened and blocked arteries, as well as inflammation of the sac that encloses your heart.

Lung disease. People with rheumatoid arthritis have an increased risk of inflammation and scarring of the lung tissues, which can lead to progressive shortness of breath.

Lymphoma. Rheumatoid arthritis increases the risk of lymphoma, a group of blood cancers that develop in the lymph system.

PATHOPHYSIOLOGY

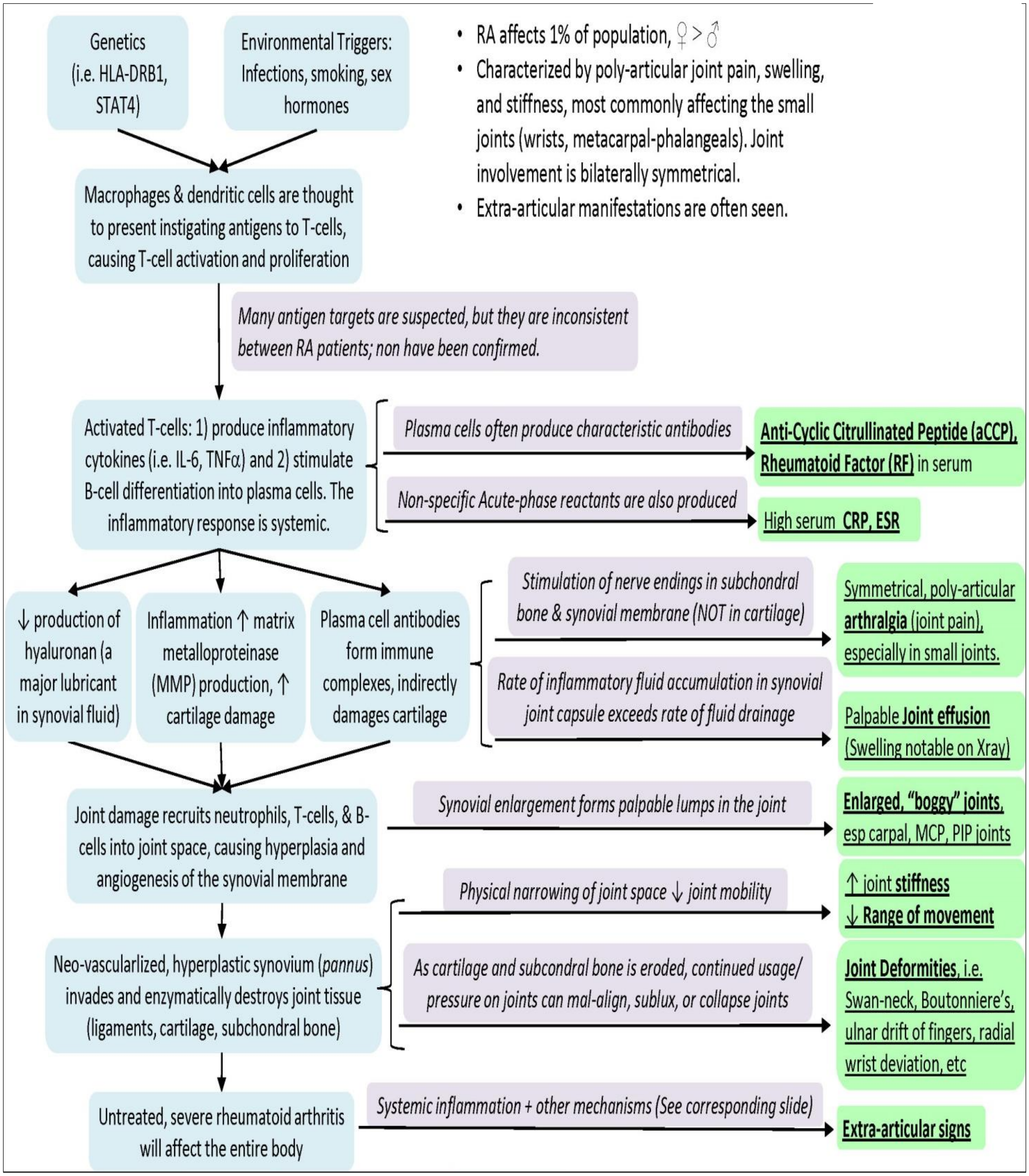
Genetic, epigenetic and environmental factors • The MHC class II gene, HLA-DR4, is the major susceptibility haplotype in 50–75% of Caucasian patients with RA • DR1 is more important in Indians and Israelis, and DW15 in Japanese • Porphyromonas gingivalis, present in the mouths of people with periodontal disease, appears to stimulate the production of ACPA linked to rheumatoid arthritis7

The clinical onset – infiltration of the synovial membrane with – Lymphocytes – Plasma cells – Dendritic cells – Macrophages. • CD4+ T lymphocytes, including Th1 cells and Th17 cells play a central role by interacting with other cells in the synovium.

Lymphoid follicles form within the synovial membrane in which T cell–B cell interactions lead B cells to produce cytokines and autoantibodies, including RF and ACPA.

- Synovial macrophages - activated by immune complexes - produce proinfla cytokines, including TNF, IL-1, IL-6 and IL-15.
- Proinflammatory cytokines act on synovial fibroblasts, to promote swelling of the membrane and damage to soft tissues and cartilage.
- Activation of osteoclasts and chondrocytes drives destruction of bone and cartilage
- The RA joint is hypoxic and this promotes new blood vessel formation (neoangiogenesis).

- The inflammatory granulation tissue (pannus) formed by the above sequence of events spreads over and under the articular cartilage, which is progressively eroded and destroyed.
- Later, fibrous or bony ankylosis may occur.
- Muscles adjacent to inflamed joints atrophy and may be infiltrated with lymphocytes



DIAGNOSIS

Getting an accurate diagnosis as soon as possible is the first step to treating RA effectively. A doctor with specialized training in treating arthritis (called a rheumatologist) is the best person to make a correct diagnosis, using medical history, a physical examination and lab tests.

Medical history

The doctor will ask about joint symptoms (pain, tenderness, stiffness, difficulty moving), when they started, if they come and go, how severe they are, what actions make them better or worse and whether family members have RA or another autoimmune disease.

Physical examination

The doctor will look for joint tenderness, swelling, warmth and painful or limited movement, bumps under the skin or a low-grade fever.

Blood tests

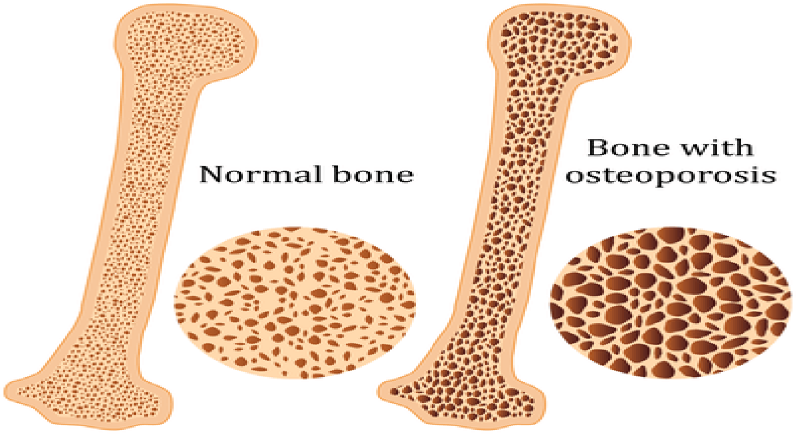
People with rheumatoid arthritis often have an elevated erythrocyte sedimentation rate (ESR, also known as sed rate) or C-reactive protein (CRP) level, which may indicate the presence of an inflammatory process in the body. Other common blood tests look for rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP) antibodies.

Imaging tests

Your doctor may recommend X-rays to help track the progression of rheumatoid arthritis in your joints over time. MRI and ultrasound tests can help your doctor judge the severity of the disease in your body.

OSTEOPOROSIS

Definitions Osteoporosis is defined as low bone mass and microarchitecture deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk. World Health organization (WHO) defines Osteoporosis as a bone density that falls 2.5 standard deviations (SD) below the mean for young healthy adults of the same race and gender— also referred to as a T-score of –2.5. 4

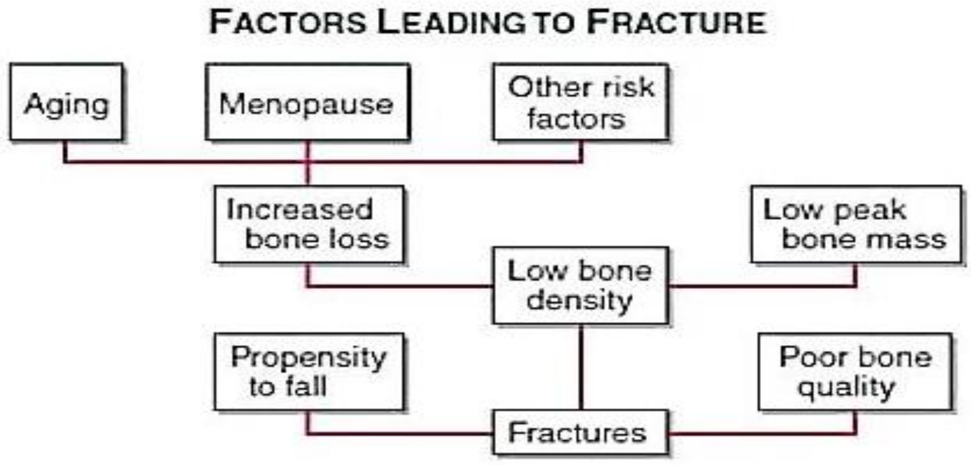


SYMPTOMS

There will be no symptoms in the early stage and most often remain unnoticed for decades. Bone fracture can be first sign or symptom. Both men and women show similar symptoms.

- Stooped posture
- Pain is associated with the fracture
- Location of pain depends on the Location of the fracture
- Repeated spine fracture can lead to lower back Pain
- Hip fracture can occur as slip and fall accidents
- Hip fracture may heal slowly

Osteoporosis, the "silent disease," has bone loss without symptoms. Onset only occurs with sudden strains, or fall causes a fracture or a vertebra to collapse. Collapsed vertebrae may initially be felt or seen in the form of severe back pain, loss of height, or spinal deformities such as kyphosis or stooped posture. Dowager’s hump (kyphosis + loss of height + cervical lordosis) present in severe cases. Peripheral fractures are more common in osteoporosis than hip and spine.

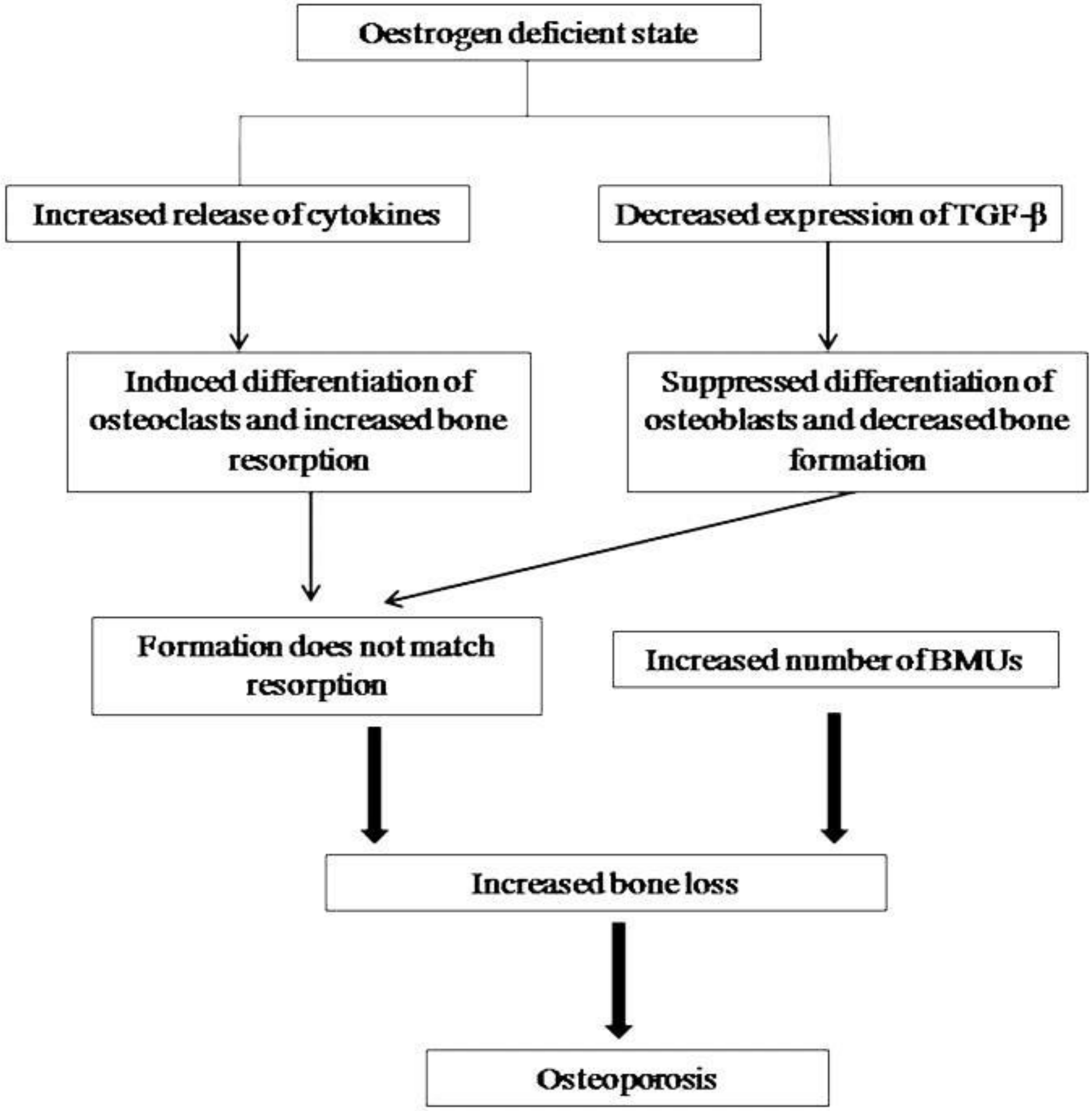


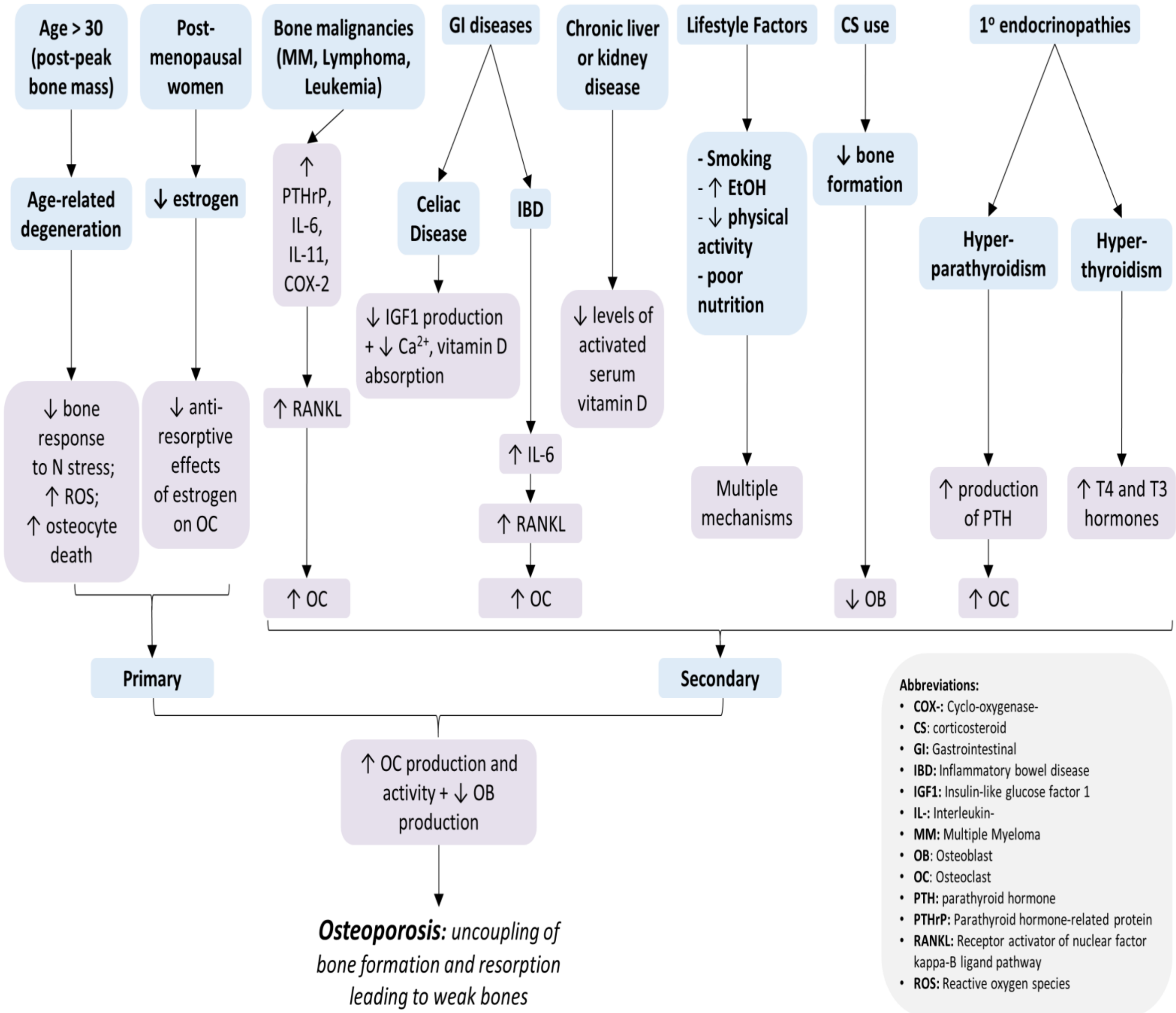
CAUSES

Caused due to multiple reasons. The most common causes may include:

- Lack of exercise
- Malnutrition – poor nutrition and good health due to inflammation or other disease condition
- Chemotherapy drugs – chemical drugs used to treat various types of cancer
- Low calcium diet
- Excessive alcohol consumption
- Chronic inflammation due to rheumatoid arthritis
- Hyperthyroidism – a condition in which too much thyroid hormone is produced by thyroid gland
- Low testosterone (sex hormone) levels in men
- Genetic disorders inherited from family
- The risk factors include:
- Age: 50 years or older are more prone to have osteoporosis
- Sex: women are more prone to osteoporosis
- Family history
- Menopause
- Low body weight
- Smoking
- Poor nutrition

PATHOPHYSIOLOGY Bone loss due to normal age related changes in bone remodelling as well as extrinsic and intrinsic factors that exaggerate this process. Bone remodelling has two primary functions: To repair micro damage within the skeleton to maintain skeletal strength. To supply calcium supply from the skeleton to maintain serum calcium. After age 30 to 45,the resorption and formation processes become imbalanced, and resorption exceeds formation. Excessive bone loss can be loss due to an increase in osteoclastic activity and/or osteoblastic activity.





DIAGNOSIS

Diagnosing osteoporosis typically requires several steps. A doctor will thoroughly evaluate your risk for osteoporosis as well as fracture risk. Steps for diagnosing osteoporosis include the following:

Taking a medical history

A doctor will ask questions related to osteoporosis risk factors. A family history of osteoporosis increases your risk. Lifestyle factors, including diet, physical activity, drinking habits, and smoking habits can also impact your risk. A doctor will also review medical conditions you have and medications you may have taken. Symptoms of osteoporosis that your doctor will likely ask you about include any bone fractures that occurred, a personal history of back pain, a loss of height over time, or a stooped posture.

Performing a physical exam

A doctor will measure a person's height and compare this to previous measurements. Height loss can indicate osteoporosis. Your doctor may ask if you have difficulty rising from a sitting position without using your arms to push yourself up. They may also perform blood tests to evaluate your levels of vitamin D, as well as some other blood tests to determine the overall metabolic activity of your bones. Metabolic activity may be increased in the case of osteoporosis.

Undergoing a bone density test

If a doctor determines that you are at risk for osteoporosis, you may undergo a bone density test. A common example is a dual energy X-ray absorptiometry (DEXA) scan. This painless, rapid test uses X-ray images to measure bone density and fracture risk.

Performing blood and urine testing

Medical conditions can cause bone loss. These include parathyroid and thyroid malfunctioning. A doctor may perform blood and urine testing to rule this out. Testing may cover calcium levels, thyroid function and testosterone levels in men.

GOUT

Gout is a common and complex form of arthritis that can affect anyone. It's characterized by sudden, severe attacks of pain, swelling, redness and tenderness in one or more joints, most often in the big toe.

Gout is a metabolic disorder of purine metabolism, characterized by intermittent attacks of acute pain, swelling and inflammation.

It always preceded by hyperuricaemia (6.0mg/dl) Hyperuricaemia due to excessive amount of uric acid production or decreased excretion

Hyperuricaemia - primary or secondary.

Primary hyperuricaemia classified as "Overproducers" or "under execrators"

Primary Hyperuricemia and Gout with No Associated Condition • Uric acid undersecretion(80%– 90%) • Idiopathic • Some drug therapy (Thiazide diuretics, furosamide, ethacrynic acid) • Urate overproduction (10%– 20%) • HGPRT deficiency • • PRPP synthetase overactivity (Phosphoribosyl pyrophosphate)

Secondary Hyperuricemia and Gout with Identifiable Associated Condition • develop during course of other diseases (Leukaemias, lymphomas, chemotherapy) • Some disorders Diabeticketoacidosis, lead poison, Lymphoproliferative diseases, Hemolytic anemias, psoriasis • Dual mechanism Obesity, Hypoxemia and hypoperfusion

Acute gout Painful arthritic attack of sudden onset. • Usually occurring at night or in early morning • Arthritic pain worsen progressively • Generally involves one or few joints • Most common site of initial attack metatarsophalangeal joint. • Other sites ankle, heel, knee, wrist, elbow and fingers.

Chronic gout • Frequency of attacks increases, continuous deposit leads to damage joints and chronic pain • Patients may develop large subacutenous tophi (Stones) in pinna of external ear, eyelids, nose and around joints • The ureate crystals in kidney leads renal disease. • Articular cartilage may be destroyed result in joint deformities

SYMPTOMS

The signs and symptoms of gout almost always occur suddenly, and often at night. They include:

Intense joint pain Gout usually affects the big toe, but it can occur in any joint. Other commonly affected joints include the ankles, knees, elbows, wrists and fingers. The pain is likely to be most severe within the first four to 12 hours after it begins

Lingering discomfort After the most severe pain subsides, some joint discomfort may last from a few days to a few weeks. Later attacks are likely to last longer and affect more joints.

Inflammation and redness The affected joint or joints become swollen, tender, warm and red.

Limited range of motion As gout progresses, you may not be able to move your joints normally.

CAUSES

Gout occurs when urate crystals accumulate in your joint, causing the inflammation and intense pain of a gout attack. Urate crystals can form when you have high levels of uric acid in your blood. Your body produces uric acid when it breaks down purines — substances that are found naturally in your body.

Purines are also found in certain foods, including red meat and organ meats, such as liver. Purine-rich seafood includes anchovies, sardines, mussels, scallops, trout and tuna. Alcoholic beverages, especially beer, and drinks sweetened with fruit sugar (fructose) promote higher levels of uric acid.

Normally, uric acid dissolves in your blood and passes through your kidneys into your urine. But sometimes either your body produces too much uric acid or your kidneys excrete too little uric acid. When this happens, uric acid can build up, forming sharp, needlelike urate crystals in a joint or surrounding tissue that cause pain, inflammation and swelling.

RISK FACTORS

You're more likely to develop gout if you have high levels of uric acid in your body. Factors that increase the uric acid level in your body include:

Diet Eating a diet rich in red meat and shellfish and drinking beverages sweetened with fruit sugar (fructose) increase levels of uric acid, which increase your risk of gout. Alcohol consumption, especially of beer, also increases the risk of gout.

Weight If you're overweight, your body produces more uric acid and your kidneys have a more difficult time eliminating uric acid.

Medical conditions Certain diseases and conditions increase your risk of gout. These include untreated high blood pressure and chronic conditions such as diabetes, obesity, metabolic syndrome, and heart and kidney diseases.

Certain medications Low-dose aspirin and some medications used to control hypertension — including thiazide diuretics, angiotensin-converting enzyme (ACE) inhibitors and beta blockers — also can increase uric acid levels. So can the use of anti-rejection drugs prescribed for people who have undergone an organ transplant.

Family history of gout. If other members of your family have had gout, you're more likely to develop the disease.

Age and sex. Gout occurs more often in men, primarily because women tend to have lower uric acid levels. After menopause, however, women's uric acid levels approach those of men. Men are also more likely to develop gout earlier — usually between the ages of 30 and 50 — whereas women generally develop signs and symptoms after menopause.

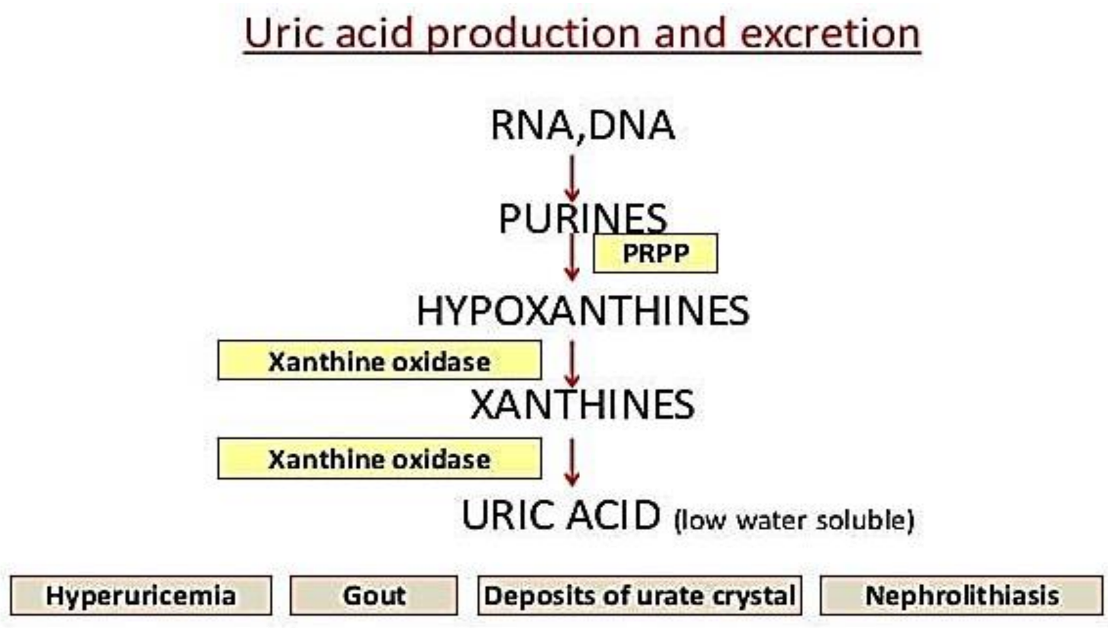
Recent surgery or trauma. Experiencing recent surgery or trauma can sometimes trigger a gout attack. In some people, receiving a vaccination can trigger a gout flare.

COMPLICATIONS

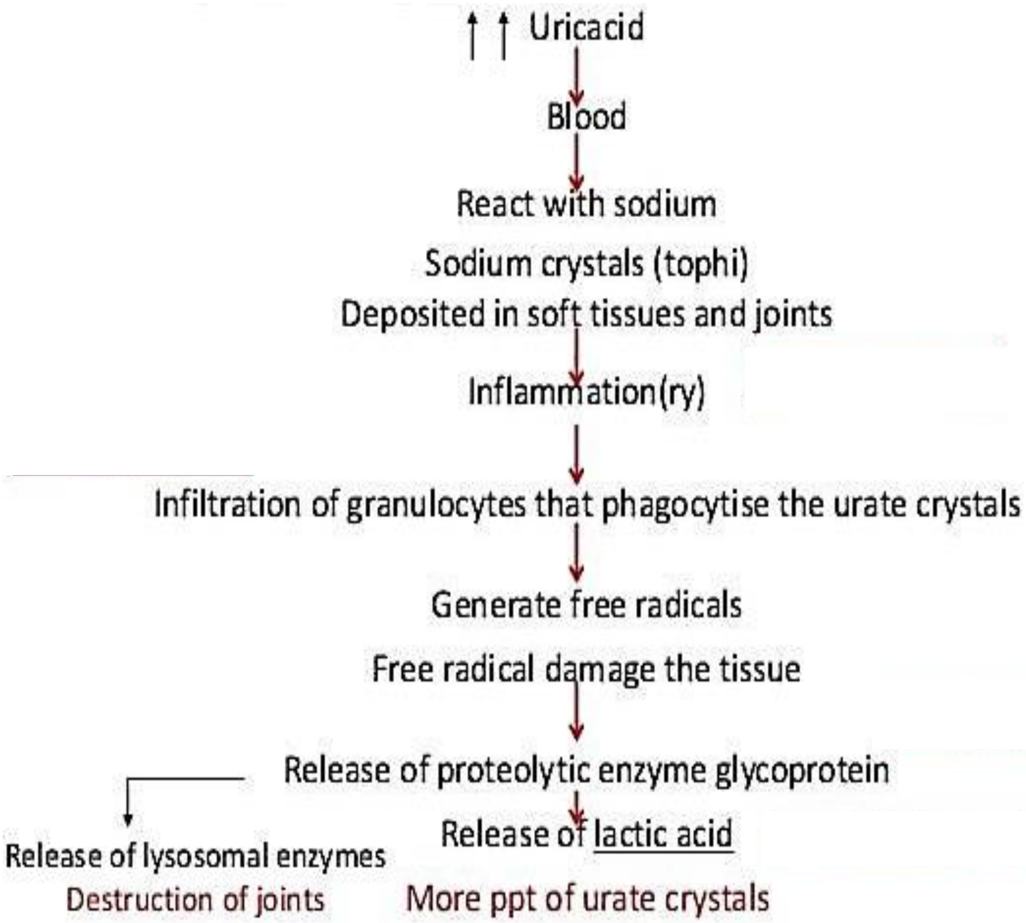
Recurrent gout Some people may never experience gout signs and symptoms again. Others may experience gout several times each year. Medications may help prevent gout attacks in people with recurrent gout. If left untreated, gout can cause erosion and destruction of a joint.

Advanced gout Untreated gout may cause deposits of urate crystals to form under the skin in nodules called tophi (TOE-fie). Tophi can develop in several areas, such as your fingers, hands, feet, elbows or Achilles tendons along the backs of your ankles. Tophi usually aren't painful, but they can become swollen and tender during gout attacks.

Kidney stones Urate crystals may collect in the urinary tracts of people with gout, causing kidney stones. Medications can help reduce the risk of kidney stones.



PATHOPHYSIOLOGY



DIAGNOSIS

Joint fluid test Your doctor may use a needle to draw fluid from your affected joint. crystals may be visible when the fluid is examined under a microscope.

Blood test Your doctor may recommend a blood test to measure the levels of uric acid in your blood. Blood test results can be misleading, though. Some people have high uric acid levels, but never experience gout. And some people have signs and symptoms of gout, but don't have unusual levels of uric acid in their blood.

X-ray imaging Joint X-rays can be helpful to rule out other causes of joint inflammation.

Ultrasound This test uses sound waves to detect urate crystals in joints or in tophi.

PRINCIPLES OF CANCER

- Cancer is defined as uncontrolled growth of a group of cells disregarding the normal rule of cell division. Such cells are known as cancer cells.
- Normal cells are under direct supervision and their growth, proliferation and cell division are supervised through signal transduction. However cancer cells develop autonomous mechanism for its growth and proliferation.
- Cancer is diseases which turns the normal cell into cancer cell by the process called carcinogenesis.
- Clinically, there are many types of cancer, but biologically, the origin of cancer is similar, which is due to defect in gene expression.
- There are some factors which are responsible for change of normal cell into cancer cell. Those factors or agents are known as carcinogens.
- It is believed that all cells carry certain cancer producing oncogenes.
- Oncogenes are the genes that are responsible for induction of tumors. Under certain conditions these genes are triggered to multiply rapidly into malignant neoplasm

How Cancer Develops

Cancer arises from a loss of normal growth control. In normal tissues, the rates of new cell growth and old cell death are kept in balance. In cancer, this balance is disrupted This disruption can result from uncontrolled cell growth or loss of a cell’s ability to undergo cell suicide by a process called “apoptosis”

Apoptosis, or “cell suicide,” is the mechanism by which old or damaged cells normally self-destruct

Cancer cells do not respond normally to body’s control mechanisms: • Ignore density dependent inhibition, cells continue to multiply until nutrients are exhausted • Divide excessively and invade other tissues.

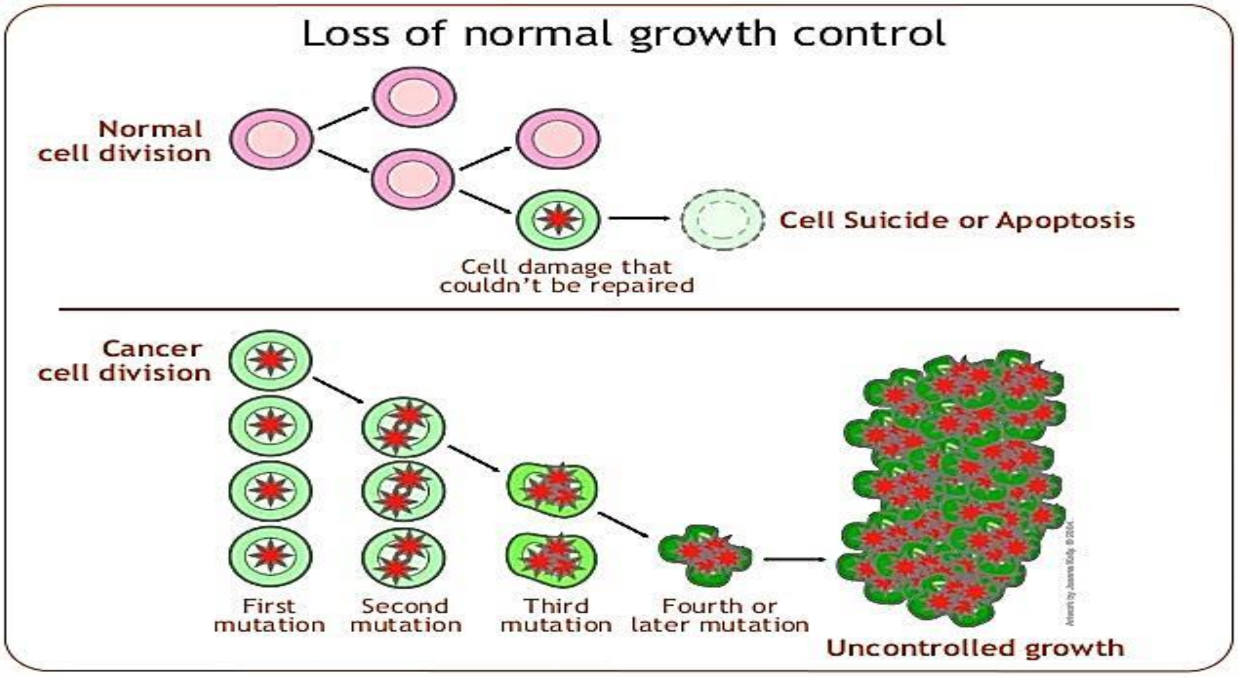
TYPES OF CANCER

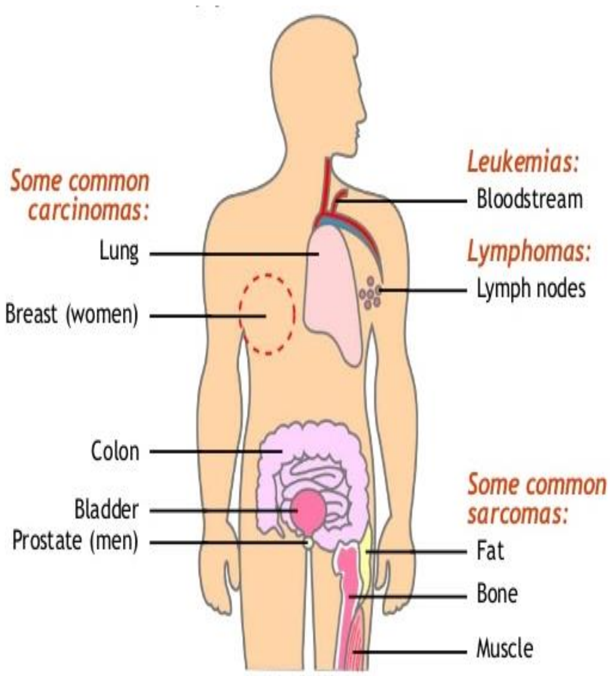
Carcinomas: - the most common types of cancer, arise from the cells that cover external and internal body surfaces. Lung, breast, and colon are the most frequent cancers of this type

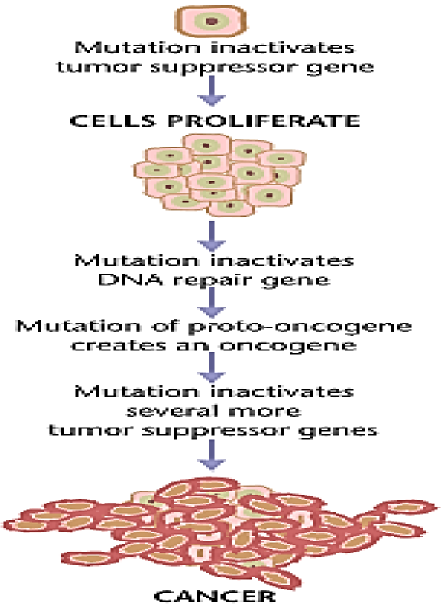
Sarcomas: - are cancers arising from cells found in the supporting tissues of the body such as bone, cartilage, fat, connective tissue, and muscle

Lymphomas: - are cancers that arise in the lymph nodes and tissues of the body's immune system

Leukemia's:- are cancers of the immature blood cells that grow in the bone marrow and tend to accumulate in large numbers in the bloodstream.







CAUSE

1. Environmental factors:

- Tobacco, smokes, diets, environmental pollutants etc
- Heavy smoking cause lung, oral cavity and oesophagus cancer.
- Excessive intake of alcohol cause liver cancer.

2. Chemical carcinogen:

Nickel compounds, cadmium, arsenic, nitrosamines, trichloroethylene, arylamines, benzopyrene, aflatoxins, reactive oxygen radicals etc

3. Physical carcinogen:

UV rays (ultraviolet), ionizing radiation (x-rays and gamma rays)

4. Biological carcinogen:

Virus: Virus has also been associated with various types of cancers. These viruses are called oncoviruses .

Rous sarcoma virus (RSV) is the first discovered retro-virus causing cancer.

Human papilloma virus (HPV), Epstein-BarrVirus, (EBV), Hepatitis B virus, Herpes virus, Hepatitis B and C virus is casually related with hepato-cellular carcinoma. Cytomegalovirus (CMV) is associated with kaposi's sarcoma. Human papilloma virus (HPV) is a chief suspect of cervix cancer.

Bacteria; Helicobacter pylori,

5. Endogenous factors:

Mutations, change in DNA replication, metabolic reactions generating, reactive oxygen radicals, Immune system defects, Ageing.

SYMPTOMS

Signs and symptoms caused by cancer will vary depending on what part of the body is affected.

Some general signs and symptoms associated with, but not specific to, cancer, include:

- Fatigue
- Lump or area of thickening that can be felt under the skin
- Weight changes, including unintended loss or gain
- Skin changes, such as yellowing, darkening or redness of the skin, sores that won't heal or changes to existing moles

- Changes in bowel or bladder habits
- Persistent cough or trouble breathing
- Difficulty swallowing
- Hoarseness
- Persistent indigestion or discomfort after eating
- Persistent, unexplained muscle or joint pain
- Persistent, unexplained fevers or night sweats
- Unexplained bleeding or bruising

PATHOPHYSIOLOGY

Regardless of difference in types of cancer histologically and physiologically, there is existence of a common pathophysiological process of malignant tumors or cancer development in the organism.

The commonly accepted basis of the pathogenesis of cancer is the damage to the genetic apparatus of cells (such as mutation, disturbance of gene expression, activation of tumor promoter gene, inactivation of tumor suppressor genes, etc.)

It is believed that damage to the genetic apparatus of the cell along with inactivation of anti-tumor genes takes place and is essential for the development of malignant tumors. But it should be noted that the inactivation of tumor suppressor gene is one of the natural physiological reactions of the organism, and when this reaction becomes pathophysiological condition of an organism it results in cancer development.

At the cellular level, the development of cancer is viewed as a multi-step process involving mutation and selection for cells with progressively increasing capacity for proliferation, survival, invasion, and metastasis.

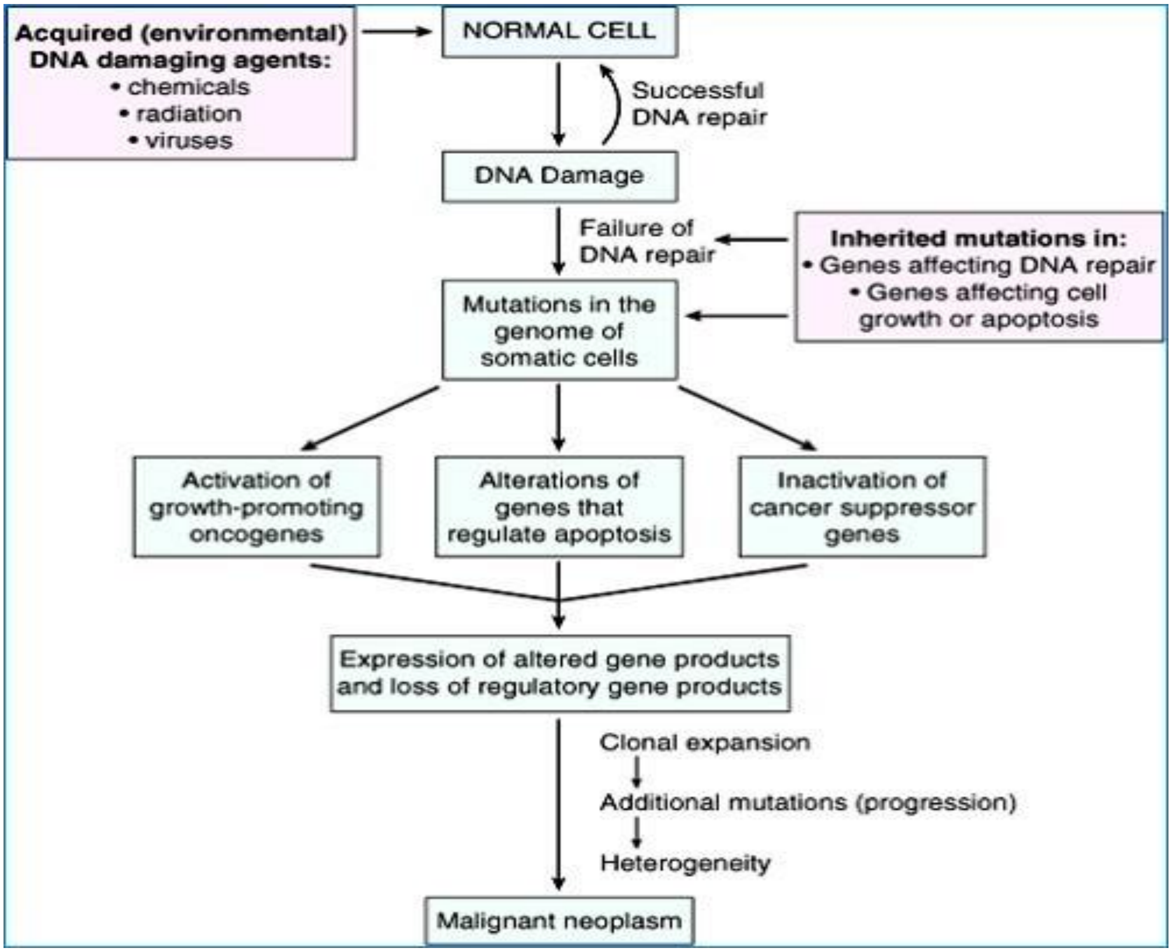
First Step: Mutation and Tumor Initiation

Genetic alteration leads to mutation in a single cell which results into abnormal proliferation of that cell known as tumor cell.

Second Step: Cell proliferation and Tumor Progression

Tumor progression continues as additional mutations occur within cells of the tumor population.

The mutated cells have some selective advantage over normal cell as such cells shows rapid growth and division. The descendants of a cell bearing such additional mutation will consequently become dominant within the tumor population



Third Step: Clonal Selection and Malignancy

Cell proliferation of tumor then leads to new clone of tumor cells with increased growth rate or other properties (such as survival, invasion, or metastasis) that confer a selective advantage. The process is called clonal selection.

Clonal selection continues throughout tumor development, so tumors continuously become more rapid-growing and increasingly malignant.

Fourth Step: Metastasis

Metastasis is a complex process in which cancer cells break away from the primary tumor and circulate through the bloodstream or lymphatic system to other sites in the body.

At new sites, the cells continue to multiply and eventually form additional tumors comprised of cells that reflect the tissue of origin.

The ability of tumors, such as pancreatic cancer and uveal (iris, ciliary body, or choroid of eye) cancers, to metastasize contributes greatly to their lethality.

Many fundamental questions remain about the clonal structures of metastatic tumors, phylogenetic relationships among metastases, the scale of ongoing parallel evolution in metastatic and primary sites, how the tumor disseminates, and the role that the tumor micro-environment plays in the determination of the metastatic site.

DIAGNOSIS

Physical exam: - Your doctor may feel areas of your body for lumps that may indicate cancer. During a physical exam, your doctor may look for abnormalities, such as changes in skin color or enlargement of an organ that may indicate the presence of cancer.

Laboratory tests: - Laboratory tests, such as urine and blood tests, may help your doctor identify abnormalities that can be caused by cancer. For instance, in people with leukemia, a common blood test called complete blood count may reveal an unusual number or type of white blood cells.

Imaging tests: - Imaging tests allow your doctor to examine your bones and internal organs in a noninvasive way. Imaging tests used in diagnosing cancer may include a computerized tomography (CT) scan, bone scan, magnetic resonance imaging (MRI), positron emission tomography (PET) scan, ultrasound and X-ray, among others.

Biopsy: - During a biopsy, your doctor collects a sample of cells for testing in the laboratory. There are several ways of collecting a sample. Which biopsy procedure is right for you depend on your type of cancer and its location. In most situations, a biopsy is the only way to definitively diagnose cancer.

Long answer questions (10 marks)

1. Write a detail note on Principles of cancer
2. Explain in details about Hepatitis.
3. Discuss about signs and symptoms, etiology, pathophysiology and diagnosis of Gout and RA
4. Write a detail note on Alcoholic Liver disease

Short answer questions (05 marks)

1. Explain the etiology, pathogenesis, diagnosis of Inflammatory bowel diseases
2. Explain the etiology, pathogenesis, signs, and symptoms of Gout
3. Describe the pathology of Rheumatoid Arthritis.
4. Write a short note on Jaundice.
5. Discuss the pathogenesis of cancer.

Very short answer questions (02 marks)

1. List any two inflammatory bowel diseases and their etiology.
2. Diagnostic test of Jaundice.
3. What is Rheumatoid arthritis?
4. Diagnostic test of Gout.
5. Etiology of Osteoporosis.
6. Signs and symptoms of Hepatitis A, B and D.
7. Enlist stages of Liver disease.
8. Define ulcerative Colitis & give its types.
9. Types of Jaundice.
10. Diagnostic Test for RA
11. Write down symptoms of hepatitis.