Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF HYPERTENSION

Hypertension (HTN) or high blood pressure, sometimes called arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is elevated. High blood pressure is said to be present if it is persistently at or above 140/90 mmHg.

Classification: Hypertension is classified as either primary (essential) hypertension or secondary hypertension.

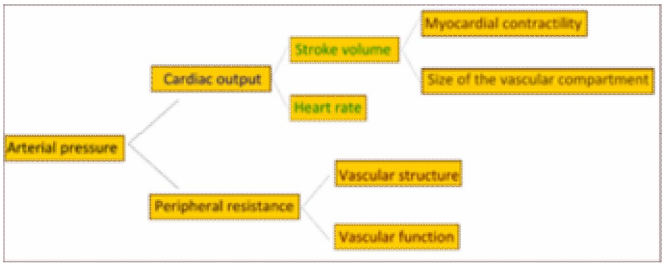
Signs and symptoms: Headaches, as well as light headedness, vertigo, tinnitus, altered vision or fainting episodes.

Causes:

Blood pressure rises with aging. Hypertension results from a complex interaction of genes and environmental factors.

Secondary hypertension results from an identifiable cause. Renal disease is the most common secondary cause of hypertension. Hypertension can also be caused by endocrine conditions, such as Cushing's syndrome, hyperthyroidism, hypothyroidism, acromegaly, Conn's syndrome or hyperaldosteronism, hyperparathyroidism and pheochromocytoma. Other causes of secondary hypertension include obesity, sleep apnea, pregnancy, coarctation of the aorta, excessive liquorice consumption and certain prescription medicines, herbal remedies and illegal drugs.

Pathophysiology



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1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**
3. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs.**
4. **Davidsons: Textbook of Medicine.**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF MYOCARDIAL INFARCTION

Myocardial infarction occurs when myocardial cells have reached the threshold of ischemia; which in turn cause the body's myocardial cell repair mechanism to first become overwhelmed and second to completely fail. When this mechanism fails, myocardial tissue necrosis causing irreparable tissue/cell death occurs.

Causes:

- Increased myocardial metabolic demand which include:
  - Extremes in physical exertion
  - Severe hypertension
  - Obstructive Cardiomyopathy
  - Severe aortic stenosis
  - Other cardiac valvular disorders
  - Low cardiac output states associated with a decrease in aortic diastolic pressure
- Decreased delivery of oxygen and nutrients to the myocardium (via the coronary circulation).
- An interruption in the delivery of oxygen and nutrients to the myocardium from a thrombus (that usually attaches itself to plaque).
- A high grade (usually > 75%) fixed coronary artery stenosis do to atherosclerosis.

Pathophysiology:

The most frequent cause of an acute MI is a disruption in the vascular endothelium that is associated with myocardial plaque. This combination causes the development of an intra-coronary thrombus, which causes the coronary artery affected to occlude. Within 20 to 40 minutes of an occlusion; irreversible myocardial cell damage/death occurs.

The severity of an acute MI depends on the level of occlusion in the coronary artery, the length of time of the occlusion and the patients own collateral circulation. Myocardial cell death first occurs in the portion of the artery that is most distal to arterial blood flow and as the occlusion increases the damage spreads from the myocardium to the endocardium and eventually to the epicardium. After cell death has reached the epicardium, the tissue/cell death then moves laterally to the areas of collateral perfusion.

References:

1. **Robins: Textbook of Pathology.**
2. **Lipincott, William & Wilkins. Applied Therapeutics- The clinical use of drugs.**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF CONGESTIVE CARDIAC FAILURE

Heart failure (HF), often called congestive heart failure (CHF) or congestive cardiac failure (CCF), occurs when the heart is unable to provide sufficient pump action to maintain blood flow to meet the needs of the body.

Common causes of heart failure: include myocardial infarction and other forms of ischemic heart disease, hypertension, valvular heart disease, and cardiomyopathy. The term *heart failure* is sometimes incorrectly used for other cardiac-related illnesses, such as myocardial infarction (heart attack) or cardiac arrest, which can cause heart failure but are not equivalent to heart failure.

Heart failure is a common, costly, disabling, and potentially deadly condition. In developed countries, around 2% of adults suffer from heart failure, but in those over the age of 65, this increases to 6–10%.

Pathophysiology

Heart failure is caused by any condition which reduces the efficiency of the myocardium, or heart muscle, through damage or overloading. As such, it can be caused by a wide number of conditions, including myocardial infarction (in which the heart muscle is starved of oxygen and dies), hypertension (which increases the force of contraction needed to pump blood) and amyloidosis (in which protein is deposited in the heart muscle, causing it to stiffen). Over time these increases in workload will produce changes to the heart itself:

The general effect is one of reduced cardiac output and increased strain on the heart. This increases the risk of cardiac arrest (specifically due to ventricular dysrhythmias), and reduces blood supply to the rest of the body. In chronic disease the reduced cardiac output causes a number of changes in the rest of the body, some of which are physiological compensations, some of which are part of the disease process:

In severe cardiomyopathy, the effects of decreased cardiac output and poor perfusion become more apparent, and patients will manifest with cold and clammy extremities, cyanosis, claudication, generalized weakness, dizziness, and syncope.

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF CARDIAC ARRHYTHMIAS

Cardiac dysrhythmia (also known as arrhythmia or irregular heartbeat) is any of a group of conditions in which the electrical activity of the heart is irregular or is faster or slower than normal. The heartbeat may be too fast (over 100 beats per minute) or too slow (less than 60 beats per minute), and may be regular or irregular.

Classification

Arrhythmia may be classified by rate (normal sinus rhythm, tachycardia, bradycardia) or mechanism (automaticity, reentry, junctional, fibrillation).
auses of SADS in young people include viral myocarditis, long QT syndrome, Brugada syndrome, Catecholaminergic polymorphic ventricular tachycardia, hypertrophic cardiomyopathy and arrhythmogenic right ventricular dysplasia.

Signs and symptoms

The most common symptom of arrhythmia is an abnormal awareness of heartbeat, called palpitations. These may be infrequent, frequent, or continuous. Some of these arrhythmias are harmless (though distracting for patients) but many of them predispose to adverse outcomes.
If an arrhythmia results in a heartbeat that is too fast, too slow or too weak to supply the body's needs, this manifests as a lower blood pressure and may cause lightheadedness or dizziness, or syncope (fainting). Some types of arrhythmia result in cardiac arrest, or sudden death.

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**
3. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs.**
4. **Davidsons: Textbook of Medicine.**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF SHOCK

Shock is a state in which there is failure of the circulatory system to maintain adequate cellular perfusion resulting in widespread reduction in delivery of oxygen & other nutrients to tissues.

Classification of shock

Shock can be divided into:

A. Hypovolemic shock

B. Cardiogenic shock

C. Distributive shock

Pathophysiology of shock:

In shock, the mean arterial pressure is less than 60 mmHg or the systolic blood pressure is less than 90 mmHg.

Regardless of the underlying pathology, shock constitutes systemic hypoperfusion due to reduction either in cardiac out put or in the effective circulating blood volume. The end results are hypotension followed by impaired tissue perfusion and cellular hypoxia.

Adequate organ perfusion depends on arterial blood pressure (BP) which, depends on:

1. Cardiac output (CO)
2. Peripheral vascular resistance (PVR)
   - CO = stroke volume X heart rate

In turn, stroke volume depends on:

- Preload i.e. blood volume,
- Afterload i.e. arterial resistance, &
- Myocardial contractility.

Therefore, shock (i.e. widespread decreased perfusion of tissues) occurs when the preload (i.e. the blood volume) is decreased, or when the afterload (the peripheral vascular resistance) is decreased, or when the myocardium fails to contract.

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**
3. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs.**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF BRONCHIAL ASTHMA

Asthma is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction and bronchospasm.

Signs and symptoms: Common symptoms include wheezing, coughing, chest tightness, and shortness of breath. Sputum may be produced from the lung by coughing but is often hard to bring up.

Causes

Asthma is caused by a combination of complex and incompletely understood environmental and genetic interactions. These factors influence both its severity and its responsiveness to treatment. It is believed that the recent increased rates of asthma are due to changing epigenetics (heritable factors other than those related to the DNA sequence) and a changing living environment.

Pathophysiology:

Asthma is the result of chronic inflammation of the airways which subsequently results in increased contractability of the surrounding smooth muscles. This among other factors leads to bouts of narrowing of the airway and the classic symptoms of wheezing. The narrowing is typically reversible with or without treatment. Occasionally the airways themselves change. Typical changes in the airways include an increase in eosinophils and thickening of the lamina reticularis. Chronically the airways' smooth muscle may increase in size along with an increase in the numbers of mucous glands. Other cell types involved include: T lymphocytes, macrophages, and neutrophils. There may also be involvement of other components of the immune system including: cytokines, chemokines, histamine, and leukotrienes among others.

References:

1. **Robins: Textbook of Pathology.**
2. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs.**
3. **Davidsons Text book of Medicine**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF PNEUMONIA

Definition:

Pneumonia is an inflammatory condition of the lung—affecting primarily the microscopic air sacs known as alveoli. It is usually caused by infection with viruses or bacteria and less commonly other microorganisms, certain drugs and other conditions such as autoimmune diseases.

Classification:

- Dependant on location (alveolar/interstitial)
- Dependant on extent (lobar/bronchopneumonia)
- Dependant on aetiology (bacterial/fungal/viral)
- Dependant on duration (acute/chronic)
- Dependant on clinical (community acquired/hospital acquired/special environment/immunosuppressed/aspiration)

Signs and symtoms:

People with infectious pneumonia often have a productive cough, fever accompanied by shaking chills, shortness of breath, sharp or stabbing chest pain during deep breaths, and an increased respiratory rate. In the elderly, confusion may be the most prominent sign. The typical signs and symptoms in children under five are fever, cough, and fast or difficult breathing.

Pathophysiology:

Transmission

- aspiration from oropharynx
- inhalation of infectious aerosols
- haematogenous dissemination
- direct inoculation + contiguous spread

Lost Defence Mechanisms

- loss or suppression of cough reflex
- injury to mucociliary system (e.g. cilia damage)
- interference of alveolar macrophage bactericidal and phagocytic ability
- pulmonary congestion + oedema
- accumulation of secretions

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF TUBERCULOSIS

Tuberculosis, MTB, or TB (short for *tubercle bacillus*) is a common, and in many cases lethal, infectious disease caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis*.

Signs and symptoms: General signs and symptoms include fever, chills, night sweats, loss of appetite, weight loss, and fatigue. Significant finger clubbing may also occur.

Causes: Mycobacteria, *M. tuberculosis* complex (MTBC) includes four other TB-causing mycobacteria: *M. bovis*, *M. africanum*, *M. canetti*, and *M. microti*. Other known pathogenic mycobacteria include *M. leprae*, *M. avium*, and *M. kansasii*. The latter two species are classified as "nontuberculous mycobacteria" (NTM). NTM cause neither TB nor leprosy, but they do cause pulmonary diseases that resemble TB.

Pathogenesis: TB infection begins when the mycobacteria reach the pulmonary alveoli, where they invade and replicate within endosomes of alveolar macrophages. The primary site of infection in the lungs, known as the "Ghon focus", is generally located in either the upper part of the lower lobe, or the lower part of the upper lobe. Tuberculosis of the lungs may also occur via infection from the blood stream. This is known as a Simon focus and is typically found in the top of the lung. This hematogenous transmission can also spread infection to more distant sites, such as peripheral lymph nodes, the kidneys, the brain, and the bones. All parts of the body can be affected by the disease, though for unknown reasons it rarely affects the heart, skeletal muscles, pancreas, or thyroid.

If TB bacteria gain entry to the bloodstream from an area of damaged tissue, they can spread throughout the body and set up many foci of infection, all appearing as tiny, white tubercles in the tissues. This severe form of TB disease, most common in young children and those with HIV, is called miliary tuberculosis. People with this disseminated TB have a high fatality rate even with treatment (about 30%).

References:

1. **Robins: Textbook of Pathology.**
2. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs.**
3. **Davidsons: Textbook of Medicine**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

CHRONIC OBSTRUCTIVE AIRWAY DISEASE INTRODUCTION AND CLASSIFICATION

Chronic obstructive pulmonary disease (COPD), also known as chronic obstructive lung disease (COLD), and chronic obstructive airway disease (COAD) among others is a type of obstructive lung disease characterized by chronically poor airflow.

Signs and symptoms: shortness of breath, cough, and sputum production.

Causes: The primary cause of COPD is tobacco smoke; with occupational exposures and pollution from indoor fires being a significant cause in some countries. Typically these exposures must occur over several decades before symptoms develop. A person's genetics also affects the risk.

Classification:

- asthma
- chronic bronchitis
- emphysema
- bronchiectasis

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**
3. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs.**
4. **Davidsons: Textbook of Medicine.**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF CHRONIC OBSTRUCTIVE AIRWAY DISEASE

Pathophysiology:

- COPD develops in response to a significant and chronic inflammatory response to inhaled irritants.
- The inflammatory cells involved include neutrophil granulocytes and macrophages, two types of white blood cell. Those who smoke additionally have Tc1 lymphocyte involvement and some people with COPD have eosinophil involvement similar to that in asthma. Part of this cell response is brought on by inflammatory mediators such as chemotactic factors.
- Other processes involved with lung damage include: oxidative stress produced by the high concentrations of free radicals in tobacco smoke and released by inflammatory cells, and breakdown of the connective tissue of the lungs by proteases that are insufficiently inhibited by protease inhibitors.
- The destruction of the connective tissue of the lung is what leads to emphysema, which then contributes to the poor airflow and finally poor absorption and release of respiratory gases. This poor gas exchange leads to low oxygen levels and eventually also high carbon dioxide levels in the blood.
- General muscle wasting that occurs in COPD may be partly due to inflammatory mediators release by the lungs into the blood. Emphysema is an enlargement of the air spaces after the terminal bronchioles, with destruction of their walls
-

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**
3. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs.**
4. **Davidsons: Textbook of Medicine.**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF PEPTIC ULCER

A peptic ulcer, also known as peptic ulcer disease (PUD), is a distinct breach in the mucosa of the stomach as a result of caustic effects of acid and pepsin in the lumen. Histologically, peptic ulcer is identified as necrosis of the mucosa which produces lesions equal to or greater than 0.5 cm (1/5").

Causes: Helicobacter pylori is one of the most common causes of peptic ulcer. Ulcers can also be caused or worsened by drugs such as aspirin, ibuprofen, and other NSAIDs.

Modified Johnson Classification of peptic ulcers:

Type I: Ulcer along the body of the stomach, most often along the lesser curve at incisura angularis along the locus minoris resistantiae.

Type II: Ulcer in the body in combination with duodenal ulcers. Associated with acid oversecretion.

Type III: In the pyloric channel within 3 cm of pylorus. Associated with acid oversecretion.

Type IV: Proximal gastroesophageal ulcer

Type V: Can occur throughout the stomach. Associated with chronic NSAID use

Signs and symptoms:

Abdominal Pain, classically epigastric strongly correlated to mealtimes. In case of duodenal ulcers the pain appears about three hours after taking a meal; bloating and abdominal fullness; waterbrash, nausea, and copious vomiting; loss of appetite and weight loss; hematemesis (vomiting of blood); this can occur due to bleeding directly from a gastric ulcer, or from damage to the esophagus from severe/continuing vomiting. melena,

Pathophysiology: A major causative factor (60% of gastric and up to 90% of duodenal ulcers) is chronic inflammation due to *Helicobacter pylori* that colonizes the antral mucosa. The immune system is unable to clear the infection, despite the appearance of antibodies.

Another major cause is the use of NSAIDs. NSAIDs block the function of cyclooxygenase 1 (*cox-1*), which is essential for the production of these prostaglandins responsible for mucosal protection.

References:

1. **Robins: Textbook of Pathology.**
2. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF AMOEBIC DYSENTERY

Amoebiasis, or Amebiasis, refers to infection caused by the amoeba *Entamoeba histolytica*]The term Entamoebiasis is occasionally seen but is no longer in use; it refers to the same infection.

Signs and symptoms: Symptoms can range from mild diarrhea to severe dysentery with blood and mucus. The blood comes from lesions formed by the amoebae invading the lining of the large intestine. In about 10% of invasive cases the amoebae enter the bloodstream and may travel to other organs in the body mainly liver.

Causes: Amoebiasis is an infection caused by the amoeba *Entamoeba histolytica* Likewise amoebiasis is sometimes incorrectly used to refer to infection with other amoebae, but strictly speaking it should be reserved for *Entamoeba histolytica* infection. Other amoebae infecting humans include

- Parasites
  - *Dientamoeba fragilis*, which causes Dientamoebiasis
  - *Entamoeba dispar*
  - *Entamoeba hartmanni*
  - *Entamoeba coli*
  - *Entamoeba moshkovskii*
  - *Endolimax nana* and
  - *Iodamoeba butschlii*.

Pathophysiology

Amoebiasis is usually transmitted by the fecal-oral route, but it can also be transmitted indirectly through contact with dirty hands or objects as well as by anal-oral contact. Infection is spread through ingestion of the cyst form of the parasite, a semi-dormant and hardy structure found in feces. Any non-encysted amoebae, or *trophozoites*, die quickly after leaving the body but may also be present in stool: these are rarely the source of new infections. Since amoebiasis is transmitted through contaminated food and water, it is often endemic in regions of the world with limited modern sanitation systems, including México, Central America, western South America, South Asia, and western and southern Africa.

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF BACILLARY DYSENTERY

Bacillary dysentery is associated with species of bacteria from the Enterobacteriaceae family. The term is usually restricted to Shigella infections.

Causes: Shigellosis is caused by one of several types of *Shigella* bacteria. Three species are associated with bacillary dysentery : *Shigella sonnei, Shigella flexneri* and *Shigella dysenteriae*. One study in China indicated that *Shigella flexneri* 2a was the most common serotype.

Salmonellosis caused by *Salmonella enterica* (serovar *Typhimurium*) has also been described as a cause of bacillary dysentery, though this definition is less common. It is sometimes listed as an explicit differential diagnosis of bacillary dysentery, as opposed to a cause.

Bacillary dysentery should not be confused with diarrhea caused by a bacterial infection. One characteristic of bacillary dysentery is blood in stool, which is the result of invasion of the mucosa by the pathogen.

Pathogenesis

Transmission is fecal-oral and is remarkable for the small number of organisms that may cause disease (10 ingested organisms cause illness in 10% of volunteers, and 500 organisms cause disease in 50% of volunteers). Shigella bacteria invade the intestinal mucosal cells but do not usually go beyond the lamina propria. Dysentery is caused when the bacteria escape the epithelial cell phagolysosome, multiply within the cytoplasm, and destroy host cells. Shiga toxin causes hemorrhagic colitis and hemolytic-uremic syndrome by damaging endothelial cells in the microvasculature of the colon and the glomeruli, respectively. In addition, chronic arthritis secondary to S. flexneri infection, called Reiter syndrome, may be caused by a bacterial antigen; the occurrence of this syndrome is strongly linked to HLA-B27 genotype, but the immunologic basis of this reaction is not understood.

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**
3. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF HEPATITIS

Definition: inflammation of hepatic parenchyma

Pathogenesis

- either infectious or non-infectious

Infectious

- liver almost always involved in all blood-born infections
- needle biopsy of used to diagnose occult infections, especially when military Tb suspected
- number of specifically hepatropic virus (hepetatis A, B, C, D, E, etc) which cause significant global mortality and morbidity
- all cause virtually same clinicomorphological pattern of acute hepatitis, but vary in ability to produce chronic, carrier state and fulminant hepatitis

	Clinical	Epidemiology
A	99% acute	3rd world, homosexuals, overseas travellers
B	60% subclinical, 30% acute, 10% chronic, 1% fulminant	3rd world, homosexuals, IDU, prostitutes
C	usually chronic (10^+ years)	Africa (10%)
D	usually coinfection with B frequently fulminant or chronic	rare in NZ, drug users, Mediterraneans
E	usually acute	Asia, overseas travellers

Non- Infectious

Agent	Notes
Alcohol	single largest cause of liver failure in US, degree of damage determined by duration, quantity and genetic makeup pathological liver show fatty change, portal and lobular PMN infiltrates, hepatocellular necrosis and eventual cirrhosis
Drugs/ toxins	toxic (dose-dependent) or idiosyncratic (unpredictable) can cause almost any type of hepatitis
Auto-immune	♀ > ♂, similar to viral but -ve serology and +ve autoantibodies often presents as acute hepatitis and characterised by ↑↑ plasma cellsresponds to steroids

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF TYPHOID FEVER

Typoid fever is an acute enteric disease caused by an obligate intracellular bacillus called Salmonella Typhi and this bacillus resides within mononuclear phagocytic cells of lymphoid tissues. The disease is unique humans and it is characterized by fever, splenomegaly and neutropenia.

T**ransmission:** Feco-oral routes through contaminated foods

Carriers:

- convalescent carrier – for up to 6 months of infection
- Chronic fecal and chronic urinary carriers are associated with chronic cholecystitis and pyelonephritis respectively.
- S. mansoni and S. hematobium co-infections protract the course of typhoid fever.

Pathogenesis:

- Infection is by ingestion of the organism, (>10 to the power of 7) in 50% of cases penetrate the small intestine mucosa and reach the circulation with transient bactremia
- The bacilli are taken by the lymphatic to lymph nodes and they are engulfed by mononuclear phagocytic cells.
- After a period of multiplication in these phagocytic cells, the organisms rupture the cells and invade blood stream via the thoracic duct. The liver, gallbladder, spleen, kidney and bone marrow become infected during this second bactermic phase.
- The main pathological changes are found in the gastrointestinal tract particularly The Payer's patches, which are the sub mucosal lymphoid follicles in this tract. This invasion arises from the gall bladder. Payer's patches may show Hyperplasia in first week, Necrosis in second week, Ulceration in third week, Healing in fourth week, Typhoid ulcers are oval and are situated longitudinally along the long axis of colon, which are in contradistinction of tuberculous ulcers set transversally.

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF EPILEPSY

Epilepsy is a common and diverse set of chronic neurological disorders characterized by seizures. Epileptic seizures result from abnormal, excessive or hypersynchronous neuronal activity in the brain.

Signs and symptoms: Epilepsy is characterized by a long term risk of recurrent seizures. These seizures may present in several ways.

Causes: Different causes of epilepsy are common in certain age groups.

- During the neonatal period and early infancy the most common causes include hypoxic ischemic encephalopathy, central nervous system (CNS) infections, trauma, congenital CNS abnormalities, and metabolic disorders.
- During late infancy and early childhood, febrile seizures are fairly common. These may be caused by many different things, some thought to be things such as CNS infections and trauma.
- During childhood, well-defined epilepsy syndromes are generally seen.
- During adolescence and adulthood, the causes are more likely to be secondary to any CNS lesion. Further, idiopathic epilepsy is less common. Other causes associated with these age groups are stress, trauma, CNS infections, brain tumors, illicit drug use and alcohol withdrawal.
- In older adults, cerebrovascular disease is a very common cause. Other causes are CNS tumors, head trauma, and other degenerative diseases that are common in the older age group, such as dementia.[29]

Pathophysiology:

One speculated mechanism for some forms of inherited epilepsy is mutations of the genes that code for sodium channel proteins; these defective sodium channels stay open for too long, thus making the neuron hyper-excitable. Glutamate, an excitatory neurotransmitter, may therefore be released from these neurons in large amounts, which — by binding with nearby glutamatergic neurons — triggers excessive calcium (Ca^{2+}) release in these post-synaptic cells. Such excessive calcium release can be neurotoxic to the affected cell. The hippocampus, which contains a large volume of just such glutamatergic neurons is especially vulnerable to epileptic seizure, subsequent spread of excitation, and possible neuronal death. Another possible mechanism involves mutations leading to ineffective GABA action. Epilepsy-related mutations in some non-ion channel genes have also been identified.

References:

1. **Robins: Textbook of Pathology.**
2. **Harsh Mohan: Textbook of Pathology**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF ACUTE RENAL FAILURE

Acute kidney failure is a rapid loss of kidney function.

Signs and symptoms

Accumulation of urea and other nitrogen-containing substances in the bloodstream lead to a number of symptoms, such as fatigue, loss of appetite, headache, nausea and vomiting. Marked increases in the potassium level can lead to irregularities in the heartbeat, which can be severe and life-threatening. Fluid balance is frequently affected, though hypertension is rare. Pain in the flanks may be encountered in some conditions this is the result of stretching of the fibrous tissue capsule surrounding the kidney.

Causes

The causes of acute kidney injury are commonly categorized into *prerenal*, *intrinsic*, and *postrenal*.

Diagnosis

Diagnosed on the basis of blood tests for substances normally eliminated by the kidney: urea and creatinine. Acute kidney injury is diagnosed on the basis of clinical history and laboratory data. A diagnosis is made when there is rapid reduction in kidney function, as measured by serum creatinine, or based on a rapid reduction in urine output, termed oliguria.

Treatment

The management of AKI hinges on identification and treatment of the underlying cause. In addition to treatment of the underlying disorder, management of AKI routinely includes the avoidance of substances that are toxic to the kidneys, called nephrotoxins. These include NSAIDs such as ibuprofen, iodinated contrasts such as those used for CT scans, many antibiotics such as gentamicin, and a range of other substances.[13]

Monitoring of renal function, by serial serum creatinine measurements and monitoring of urine output, is routinely performed. In the hospital, insertion of a urinary catheter helps monitor urine output and relieves possible bladder outlet obstruction, such as with an enlarged prostate.

References:

1. **Robins: Textbook of Pathology.**
2. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs.**

Malaria is caused by the intracellular protozoan parasite called Plasmodium species and plasomodium Falciprium is the worldwide infections that affect 100 million people and kill 1 to 1.5 million people yearly. P. Falciparium and P. Vivax, P. ovale, and P. malarie represent 60%, 49 %, <1.0% and reported cases respectively in Ethiopia. P. falciparum cause high parasitmias, severe anemia, cerebral symptoms, and pulmonary edma and death.

Pathogenesis (P. Falciparum):

- Infected humans produce gametocytes that mosquitoes acquire on feeding. Within these insects' body, the organism produces sporozites, which the mosquito transmits to human when it feeds
- Malarial sporozites after being released in the blood within minutes attach to a serum protein thrombosroridin and properidine located on the basolateral surface of hepatocytes. These sporozites multiply and release merozytes by rupturing liver cells.
- Once released, P. falciparum merozites bind by a parasite lactin like molecule to on the surface of red blood cell.
- Within 2 to3 weeks of hepatic infection, merozites rupture from their host hepatocytes and invade erythrocytes establishing erytrocytic phase of malarial infection.
- The merozites feed on hemoglobin grow and reproduce within erythrocytes. Repeated cycles of parasitemia occur with subsequent ruptures of these cells with resultant clinical manifestations such as chills, fever etc.
- P. Vivax merozites however, bind by homologous lectin to the Duffy antigen on RBC so many cases who are Duffy negative are resistant to this infection.
- HLA –B53 associated resistance in some Africans is related to the ability of HLA –B53 to present the liver stage specific malarial antigen to cytotoxic T-cells, which then kill malarial, infected hepatocytes.
- Individuals with sickle cell trait are resistant to malaria because the red cells that are parasitized in these individuals are removed by the spleen.
- Most malarial parasites infect new RBC & some develop to sexual form called gametocytes and the mosquito when it takes this blood meal the cycle continues.

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF LEPROSY

Leprosy or Hansen disease is a slowly progressive infection caused by *Mycobacterium leprae* affecting the skin and peripheral nerves and resulting mainly in deformity, paralysis and ulceration. Though *M. leprae* is in most part contained in the skin, the disease is believed to be transmitted from person to person through aerosols from lesions in upper respiratory tract.

Pathogenesis:

- The bacillus is acid fast, obligate intracellular organism that does not grow in culture and it grows best at 32-34 0C of the temperature of human skin.
- *M leprae* secrets no toxins but its virulence is based on properties of its cell wall. The bacilli thus produce either potentially destructive granulomas or by interference with the metabolism of cells. The bacilli are taken by alveolar macrophages; disseminate through the blood but grows only in relatively cool tissues of the skin and extremities.
- Leprosy is a bipolar disease. Two forms of the disease occur depending on whether the host mounts a T-cell mediated immune response (tuberculoid leprosy) or the host is anergic (lepromatous leprosy). The polar forms are relatively stable but the borderline forms (border line-tuberculoid, borderline-borderline, and borderline-lepromatous) are unstable without treatment. It may usually deteriorate to lepromatous leprosy. Patients with tuberculoid leprosy form granuloma with few surviving bacteria (paucibacillary disease). The 48 hour leporine skin test is strongly positive and this is effected largely by CD4 + type 1 helper T-cell that secretes IL-2 & interferon δ.
- In contrast, patients with lepromatous leprosy lack T-cell mediated immunity, and are allergic to lepromin and have diffuse lesions (globi) containing foamy macrophages, stuffed with large numbers of mycobacteria (multibacillary disease).
- Because of the diffuse parasite filled lesions lepromatous leprosy is more infectious than those with tuberculoid leprosy.

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

CANCER- INTRODUCTION AND CLASSIFICATION

Literally, neoplasia means new growth and technically, it is defined as abnormal mass of tissues the growth of which exceeds and persists in the same excessive manner after cessation of the stimulus, evoking the transformation.

Nomenclature: Neoplasms are named based upon two factors

- on the histologic types : mesenchymal and epithelial
- on behavioral patterns : benign and malignant neoplasms
- Nonneoplastic misnomers hematoma, granuloma, hamartoma
- Malignant misnomers melanoma, lymphoma, seminoma, glioma, hepatoma.

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

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PATHOPHYSIOLOGY OF HYPERSENSITIVITY

Hypersensitivity Reactions

The purpose of the immune response is to protect against invasion by foreign organisms, but they often lead to host tissue damage. An exaggerated immune response that results in tissue injury is broadly referred to as a hypersensitivity reaction.

Classification:

a. According to Gell and Comb's classification, hypersensitivity reactions can be divided into four types (type I, II, III, and IV) depending on the mechanism of immune recognition involved and on the inflammatory mediator system recruited.

b. Types – I II, and III reactions are dependent on the interaction of specific antibodies with the given antigen, whereas, in type IV reactions recognition is achieved by antigen receptors on T-cells.

1) Type I hypersensitivity (anaphylactic or immediate type) reaction

Type I hypersensitivity reaction may be defined as a rapidly developing Immunologic reaction occurring, within minutes after the combination of an antigen with antibody bound to mast cells or basophilic in individuals previously sensitized o the antigen. The reactions depend on the site of antigen exposure for example in skin – hive, upper respiratory tract – Hay fever, bronchial asthma and systemic reaction – anaphylactic syndrome.

2) Type II hypersensitivity reaction

Type II hypersensitivity is mediated by antibodies directed towards antigens present on the surface of exogenous antigens.

3) Type III hypersensetivity / immune complex-mediated

Type III hypersensitivity reaction is induced by antigen-antibody complex that produces tissue damage as a result of their capacity to activate the complement system. The antibodies involved in this reaction are IgG, IgM or IgA.

4) Type IV hypersensitivity (Cell-mediated) reaction

The cell-mediated type of hypersensitivity is initiated by specifically sensitized T lymphocytes.

References:

1. **Robins: Textbook of Pathology.**
2. **Davidsons: Textbook of Medicine.**

Class- *Second Year B. Pharm* ***Subject- Pathophysiology***

Subject Incharge- *Miss. Pujari R. R.* ***Lecture Synopsis No.***

PATHOPHYSIOLOGY OF INFLAMMATION

Definition: Inflammation is a local response (reaction) of living vasculaized tissues to endogenous and exogenous stimuli. The term is derived from the Latin "inflammare" to burn. Inflammation is fundamentally destined to localize and eliminate the causative agent and to limit tissue injury.

Thus, inflammation is a physiologic (protective) response to injury, an observation made by Sir John Hunter in 1794 concluded: "inflammation is itself not to be considered as a disease but as a salutary operation consequent either to some violence or to some diseases".

Causes:

Causes of inflammation are apparently causes of diseases such as

- **Physical agents** - mechanical injuries, alteration in temperatures and pressure, radiation injuries.
- **Chemical agents**- including the ever increasing lists of drugs and toxins.
- **Biologic agents (infectious)**- bacteria,viruses,fungi, parasites
- **Immunologic disorders**- hypersensitivity reactions, autoimmunity, immunodeficiency states etc
- **Genetic/metabolic disorders**- examples gout, diabetes mellitus etc…

Classification:

- Acute inflammation
- Chronic inflammation

Systemic effects of inflammation

The systemic effects of inflammation include:

a. Fever
b. Endocrine & metabolic responses
c. Autonomic responses
d. Behavioral responses
e. Leukocytosis
f. Leukopenia
g. Weight loss

References:

1. **Robins: Textbook of Pathology.**
2. **Lipincott, William & Wilkins.Applied Therapeutics The clinical use of drugs**