General Pathology Assignment - H12/02061/20

1. **Discuss inborn errors of metabolism**
   - Inborn errors of metabolism are genetic disorders that give rise to defects in metabolism
   - Most inborn errors are diseases that are generally inherited as autosomal recessive or X-linked traits.
   - The clinical manifestations are generally as a result of abnormal metabolite accumulations or deficiency of the desired product.
   - Some of inborn errors of metabolism include: phenylketonuria, galactosemia, cystic fibrosis, homocystinuria, glycogen storage diseases and Wilson disease. Some of these are discussed in detail below

   a) Phenylketonuria

   - Phenylketonuria is an autosomal recessive disorder caused by a severe deficiency of the enzyme phenylalanine hydroxylase leading to hyperphenylalaninemia.
   - Affected infants are normal at birth but within a few weeks develop an elevated plasma phenylalanine level, which impairs brain development.
   - About one third of these children are never be able to walk and two thirds cannot talk.

   i) Pathogenesis

   - The biochemical abnormality is the inability to convert phenylalanine into tyrosine
   - In normal children less than 50% of the dietary intake of phenylalanine is necessary for protein synthesis, the remainder is converted to tyrosine by phenylalanine hydroxylase system.
   - It is believed that excess phenylalanine or its metabolites contribute to the brain damage in Phenylketonuria.
   - The lack of tyrosine in phenylketonuria, a precursor of melanin, is responsible for the light color of hair and skin.
   - Mutations in both PAH alleles are required to develop the disease. Infants with mutations resulting in severely reduced PAH activity present with markedly elevated blood phenylalanine levels and the classic features of PKU, and those with up to 6% residual PAH activity present with milder disease.

   ii) Clinical features

   - Seizures
   - Other neurological abnormalities
   - Decreased pigmentation of hair and skin
   - A characteristic musty odor
   - Eczema
   - Hyperphenylalaninemia and the accompanying defects can be avoided by restricting phenylalanine intake early in life
   - Although 98% of PKU is attributable to mutations in PAH, approximately 2% occur due to abnormalities in synthesis or recycling of the cofactor tetrahydrobiopterin. It is important to recognize these variants of PKU because they cannot be treated by dietary restriction of PKU.

b) Galactosemia

- This is an autosomal recessive disorder of galactose metabolism resulting from accumulation of galactose-1 phosphate in tissues.
- There are two variants of galactosemia which include: total lack of galactose-1-phosphate uridyl transferase (GALT)which is the most common variant, deficiency of galactokinase.

i) **Pathogenesis**

- As a result of GALT deficiency, galactose-1-phosphate accumulates in many locations, including the liver, spleen, lens of the eye, kidneys, heart muscle, cerebral cortex, and erythrocytes.
- Alternative metabolic pathways are activated, leading to the production of galactitol (a polyol metabolite of galactose) and galactonate, an oxidized by-product of excess galactose, both of which also accumulate in the tissues.
- Long-term toxicity in galactosemia has been linked to these metabolic intermediates

ii) **Clinical features**

- There is hepatomegaly which develops early due to largely fatty change, but in time widespread scarring that closely resembles the cirrhosis of alcohol abuse may supervene.
- Opacification of the lens (cataract) develops, probably because the lens absorbs water and swells as galactitol, produced by alternative metabolic pathways, accumulates and increases osmotic pressure
- CNS alterations are observed though not as severe as in PKU.
- These infants fail to thrive almost from birth. Vomiting and diarrhea appear within a few days of milk ingestion.
- Accumulation of galactose and galactose 1-phosphate in the kidney impairs amino acid transport, resulting in aminoaciduria.
- Many of the clinical and morphologic changes of galactosemia can be prevented or ameliorated by early removal of galactose from the diet for at least the first 2 years of life

c) Cystic Fibrosis

- Cystic fibrosis is an inherited disorder of ion transport that affects fluid secretion in exocrine glands and in the epithelial lining of the respiratory, gastrointestinal, and reproductive ducts.
- This disease leads to abnormally viscous secretions that obstruct organ passages, resulting in most of the clinical manifestations such as pancreatic insufficiency, steatorrhea, malnutrition, hepatic cirrhosis, intestinal obstruction, and male infertility.

i) Pathogenesis

- Cystic fibrosis is the most common lethal genetic disease that affects Caucasian populations.
- The primary defect in cystic fibrosis is the abnormal transport of chloride and bicarbonate ions mediated by an anion channel encoded by the cystic fibrosis transmembrane conductance regulator (CFTR) gene
- CFTR regulates multiple ion channels and cellular processes. One of the ion channels that is of most pathophysiologic significance is the Epithelial sodium channel(ENaC).
- The ENaC is situated on the apical surface of epithelial cells and is responsible for sodium uptake from the luminal fluid, rendering the luminal fluid hypotonic. ENaC is inhibited by

normally functioning CFTR; hence, in cystic fibrosis, ENaC activity increases, markedly augmenting sodium uptake across the apical membrane

- The functions of CFTR are tissue specific. The function of CFTR in sweat glands is to reabsorb luminal chloride ions and augment sodium reabsorption via the ENaC.
- Therefore, in the sweat ducts, loss of CFTR function leads to decreased reabsorption of sodium chloride and the production of hypertonic sweat.
- In the respiratory and gastrointestinal systems, CFTR mutations result in loss or reduction of chloride secretion into the lumen, and active luminal sodium absorption is increased due to loss of inhibition of ENaC activity. These changes result in increased luminal reabsorption of water.
- The pathogenesis of respiratory and intestinal complications in cystic fibrosis seems to stem from an isotonic but low-volume surface fluid layer.
- In the lungs, this dehydration leads to defective mucociliary action and the accumulation of hyper concentrated, viscid secretions that obstruct the air passages and predispose to recurrent pulmonary.
- CFTR regulates transport of bicarbonate ions. In some CFTR mutants, chloride transport is completely or substantially preserved, and bicarbonate transport is markedly abnormal. Normal cells secrete alkaline fluids, in contrast, acidic fluids are secreted by mutant epithelial cells, because of lack of bicarbonate ions. The acidic environment results in decreased luminal pH that can lead to a variety of adverse effects such as increased mucin precipitation and plugging of ducts and increased binding of bacteria to plugged mucins. There is virtually always pancreatic insufficiency in patients who have issues with bicarbonate transport.

ii) Clinical features

- Chronic sinopulmonary disease manifested by: a) Persistent colonization/infection with typical cystic fibrosis pathogens, including Staphylococcus aureus, nontypeable Haemophilus influenzae, mucoid and nonmucoid Pseudomonas aeruginosa. b) Chronic cough and sputum production c) Airway obstruction manifested by wheezing and air trapping d) Digital clubbing
- Gastrointestinal and nutritional abnormalities, including: a) Intestinal: meconium ileus, distal intestinal obstruction syndrome, rectal prolapse b) Pancreatic: pancreatic insufficiency, recurrent acute pancreatitis, chronic pancreatitis c) Nutritional: failure to thrive (severe acute malnutrition), hypoproteinemia, edema, complications secondary to fat-soluble vitamin deficiency
- Salt-loss syndromes: acute salt depletion, chronic metabolic alkalosis

d) Homocystinuria

- Homocystinuria is a rare autosomal recessive metabolic disorder characterized by the abnormal accumulation of homocysteine in urine and blood

i) Pathogenesis

- It is primarily caused by a deficiency of the enzyme cystathionine beta-synthase (CBS), which is crucial in the methionine metabolism pathway.

- Methionine is metabolized to form homocysteine. Normally, homocysteine is either remethylated to methionine (via methionine synthase and betaine-homocysteine methyltransferase) or converted to cystathionine by CBS, which further leads to the production of cysteine.
- In homocystinuria, the lack of CBS activity prevents the conversion of homocysteine to cystathionine, leading to elevated levels of homocysteine and methionine in the blood and tissues. The accumulation of homocysteine leads to its spontaneous oxidation, forming homocysteine thiolactone and other reactive species, which can damage various tissues and organs.

Clinical Features

- Skeletal Abnormalities such as Marfanoid Habitus, Osteoporosis and Pectus Deformities
- Ocular Manifestations such as Ectopia Lentis and myopia
- Neurological Symptoms such as Developmental Delay, Seizures and Psychiatric Disorders

e) Glycogen storage diseases

- These are a group of inherited metabolic disorders caused by enzyme deficiencies that impair the synthesis or breakdown of glycogen.
- These deficiencies lead to the accumulation or defective release of glycogen in various tissues, particularly the liver, muscles, and kidneys.
- The clinical presentation varies depending on the specific enzyme affected, with symptoms ranging from mild to life-threatening.

Examples of glycogen storage diseases and the primary defective enzyme:

1. **GSD Type I (Von Gierke Disease):**

- **Enzyme Deficiency:** Glucose-6-phosphatase.
- **Affected Organs:** Liver, kidneys
- **Clinical Features:** Severe fasting hypoglycemia, hyperuricemia and hyperlipidemia, Lactic acidosis and growth retardation, Hepatomegaly

2. GSD Type II (Pompe Disease)

- **Enzyme Deficiency:** Acid alpha-glucosidase (acid maltase)
- **Affected Organs:** Muscle, heart
- **Clinical Features:** Infantile form presents with severe muscle weakness, hypotonia (reduced muscle tone), cardiomegaly (enlarged heart), and respiratory difficulties. Adult form has milder symptoms, mainly affecting skeletal muscles, leading to progressive muscle weakness.

3. GSD Type III (Cori Disease or Forbes Disease)

- **Enzyme Deficiency:** Debranching enzyme (amylo-1,6-glucosidase)
- **Affected organs**: Liver, Muscle
- **Clinical Features:** Hepatomegaly, mild hypoglycemia, and muscle weakness, cardiomegaly.

2. Write an essay on pathology of infections

Introduction

- Infection refers to the invasion of the body by harmful microorganisms and parasites
- The microorganisms include: bacteria, viruses and fungi
- Parasites include protozoa and helminths
- The pathology of infections refers to study of these infectious agents on how they cause disease, body's response to invasion and the resulting tissue and organ damage.
- Understanding the pathology of infections is crucial for diagnosing, managing and preventing infectious diseases.
- Infectious diseases remain one of the leading causes of death in both developed and developing countries.
- Infections cause significant morbidity and mortality, especially in individuals who are most vulnerable to illness: the very young, the elderly, the immune compromised, and the disenfranchised
- Infectious diseases elaborate the relationship between the host, infectious agents and the external environment.
- Infection results when an exogenous agent is introduced into a host from the environment or when an endogenous agent overcomes innate host immunity to cause disease
- Infections follow a general sequence of events known as the infection chain. The chain of events includes the infectious agent, reservoir, entry into a susceptible host, exit, and transmission to new hosts.
- In the upcoming sections, we shall briefly talk on these topics: The route of pathogen entry and spread, how pathogens cause disease, host response to infections, tissue and organ damage and we sum up with a brief discussion on chronic and latent infections.

a) The route of pathogen entry and spread.

Pathogens can enter the body through various routes, including the respiratory tract, gastrointestinal tract, skin, mucous membranes, and blood. Once inside the host, they may remain localized or spread to other parts of the body through the bloodstream (hematogenous spread), lymphatic system, or along nerve pathways.

1. Skin

- Major Local Defense(s): **Epidermal barrier**
- Basis for Failure of Local Defense
  a) Mechanical defects (punctures, burns, ulcers): Pathogens involved include, Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa
  b) Needle sticks: Human immunodeficiency virus, hepatitis viruses
  c) Arthropod and animal bites: Yellow fever, plague, Lyme disease, malaria, rabies
  d) Direct penetration: Schistosoma spp.

2. Gastrointestinal tract

- **Major Local Defense(s):**

i) **Epidermal barrier**

- Basis for Failure of Local Defense
  a) Attachment and local proliferation of microbes: Vibrio cholerae, Giardia duodenalis
  b) Attachment and local invasion of microbes: Shigella spp., Salmonella spp., Campylobacter spp.
  c) Uptake through M cells: Poliovirus, Shigella spp., Salmonella spp.

ii) **Acidic secretions**

- Basis for Failure of Local Defense
  a) Acid-resistant cysts and eggs: Many protozoa and helminths

iii) **Peristalsis**

- Basis for Failure of Local Defense
  a) Obstruction, ileus, postsurgical adhesions: Mixed aerobic and anaerobic bacteria (Escherichia coli, Bacteroides spp.)

iv) **Bile and pancreatic enzymes**

- Basis for Failure of Local Defense
  a) Resistant microbial external coats: Hepatitis A, rotavirus, norovirus

v) **Normal protective microbiota**

- Basis for Failure of Local Defense
  a) Broad-spectrum antibiotic use: Clostridioides difficile

3. Respiratory tract

- **Major Local Defense(s):**

i) Mucociliary clearance

- Basis for failure of Local Defense
  a) Attachment and local proliferation of microbes: Influenza viruses
  b) Ciliary paralysis by toxins: Hemophilus influenzae, Mycoplasma pneumoniae, Bordetella pertussis

ii) Resident alveolar macrophages

- Basis for failure of Local Defense
  a) Resistance to killing by phagocytes: Mycobacterium tuberculosis

4. Urogenital tract

- **Major Local Defense(s):**

i) Urination

- Basis for failure of Local Defense
  a) Obstruction, microbial attachment, and local proliferation: Escherichia coli

ii) Antibiotic use

- Basis for failure of Local Defense

a) Antibiotic use: Candida albicans

iii) Intact epidermal/epithelial barrier

- Basis for failure of Local Defense

a) Microbial attachment and local proliferation: Neisseria gonorrhoeae
b) Direct infection/local invasion: Herpes viruses, syphilis
c) Local trauma: Various sexually transmitted infections (e.g., human papillomavirus)

b) How pathogens cause disease

- The ability of a pathogen to cause disease is determined by its virulence factors.
- Some microorganisms live on and within our body without causing any disease and are called commensal microbes. These microorganisms may however turn pathogenic when they acquire virulence factors or when the immune system is suppressed.
- These virulence factors include: Adhesion to host cell, invasion, evasion of the immune system, colonization and production of toxins.
- Each of these factors are discussed in detail below.

i) **Adhesion to host cells and Colonization**

- Many microbes posses surface molecules that allow them to attach, adhere and colonize host cells and tissues.
- Pili enable many organisms to adhere to host cells, examples of this is Neisseria gonorrhea, has pili that allow it to bind to cervical cells and buccal cells to cause gonorrhea. Bacteria that do not produce these pili cannot grab hold of their victim. They lose their virulence and thus cannot infect humans.

ii) **Invasion of cells and tissues**

- Pathogens can proliferate locally, at the site of initial infection, or spread to other sites by direct extension (invasion) or by transport in the lymphatics, the blood, or nerves.
- Some pathogens secrete enzymes that break down tissues, allowing the organisms to spread contiguously in tissue. For example, Streptococcus pyogenes secretes hyaluronidase, an enzyme that degrades the extracellular matrix, enabling the bacteria to spread through tissues.
- the most common and efficient mode of microbial dissemination is through the bloodstream, by which the organism can reach all organs

iii) **Evasion of immune system**

- Most pathogens have developed one or more ways of evading the immune system.
- Antigenic variation. Antibodies against microbial antigens block microbial adhesion and uptake into cells, act as opsonins to facilitate phagocytosis, and fix complement.
- Some bacteria, like Mycobacterium tuberculosis, survive within macrophages by inhibiting phagosome-lysosome fusion.
- Establishing latency, during which viruses survive in a silent state in infected cells. Herpesviridae family viruses use this.

iv) **Production of toxin**

- Some bacteria establish an infection and produce damaging toxins.
- Clostridium botulinum produces botulinum toxin, a neurotoxin that blocks neurotransmitter release, leading to paralysis
- Staphylococcus aureus and streptococcus pyogenes elaborate pyrogenic exotoxins that stimulate the release of cytokines that cause rash, fever and toxic shock syndrome

c) Host response to Infection

- The outcome of infection is determined by the virulence of the microbe and the nature of the host immune response, which may eliminate the infection or, in some cases, exacerbate or cause tissue damage
- The body has two immune system components that fight infections, that is, innate and adaptive immune systems

i) **Innate immune system**

- This is the first line of defense against infections.
- It includes the cellular and humoral arms.
- The cellular arms has phagocytic cells, epithelial and endothelial cells, natural killer cells, innate lymphoid cells, and platelets. The phagocytic cells like macrophages engulf organisms while natural killer cells kill microbes directly.
- The innate response is nonspecific but rapid, involving the recognition of pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) such as toll-like receptors (TLRs).
- The innate system also comprises of physical barriers like the skin and mucous membranes, complement and contact cascades which are its humoral arm

II) **Adaptive immune system**

- This is the second line of defense.
- It comes in when the innate system has failed to contain the microorganism
- Like the innate system, the adaptive system has cellular and adaptive arms
- Cellular arm comprise of T and B cells. These cells produce cytokines that mediate immune response

- The humoral arm has antibodies produced by plasma cells. These antibodies work through neutralization of pathogen, opsonization and antibody dependent cell-mediated cytotoxicity.

d) Tissue and organ damage

- Infectious agents establish infection and damage tissues by a few mechanisms
- They can contact or enter host cells and cause cell death directly, or cause changes in cellular metabolism and proliferation that can eventually lead to transformation that may precipitate to cancer.
- They may release toxins that kill cells at a distance, release enzymes that degrade tissue components, or damage blood vessels and cause ischemic necrosis.
- They can induce host immune responses that, though directed against the invader, cause additional tissue damage. This is particularly evident in mycobacterium infection where the organism leads to formation of granulomas in the lungs and in hepatitis B and C infection which leads to liver cirrhosis.

e) Chronic and Latent Infections

- Chronic infections occur when the immune system is unable to completely eliminate the pathogen, leading to ongoing inflammation and tissue damage. Chronic hepatitis B and C are examples where persistent viral infection leads to chronic liver inflammation, fibrosis, and an increased risk of hepatocellular carcinoma.
- Latent Infections is where pathogens can enter a dormant state where they remain in the body without causing active disease but can reactivate under certain conditions. Herpesviruses, such as herpes simplex virus and varicella-zoster virus, establish latency in nerve cells and can reactivate years later, causing recurrent infections like cold sores or shingles.

Conclusion

- In summary, pathology of infections is wide subject that entails the relationship between pathogens and hosts, the mechanism of disease occurrence including the virulence factors of organisms and the protective features of the body and the aftermath of these microorganism invasion which may include tissue and organ damage.

3. Give a detailed account of atherosclerosis.

- Atherosclerosis is a vascular disorder characterized by the formation of intimal fibrous plaques that often have a central core rich in lipid (fibrofatty plaques).

- These plagues lead to gradual narrowing and hardening of the arteries, restricting blood flow and potentially leading to severe cardiovascular complications such as heart attacks, strokes, and peripheral artery disease.
- Atherosclerosis underlies the pathogenesis of coronary, cerebral, and peripheral vascular disease and causes more morbidity and mortality (roughly half of all deaths) in the Western world than any other disorder.
- The disease often begins in childhood, but symptoms are not usually evident until middle age.

Epidemiology

- Atherosclerosis is virtually ubiquitous among the populations of North America, Europe, Australia, New Zealend, Russia.
- In contrast, it is much less prevalent in Central and South America, Africa, and Asia.
- There is evidence that development of atherosclerosis depends on the life style and dietary customs.

Risk Factors

a) Non-modifiable factors

- **Age** - The development of atherosclerotic plaque is a progressive process that usually becomes clinically manifest in middle age or later
- **Sex –** Male and postmenopausal women have at increased risk due to reduced protective effect of estrogen
- **Genetics** - genetic abberrations in lipoprotein metabolism resulting in excessively high blood lipid levels

b) Modifiable risk factors

- **Hyperlipidemia** - more specifically hypercholesterolemia— is a major risk factor for atherosclerosis; even in the absence of other risk factors, hypercholesterolemia is sufficient to initiate lesion development.
- **Hypertension** - can increase the risk of ischemic heart disease by approximately 60% versus normotensive populations. Men whose blood pressure exceeds 169/90 mm Hg have a more than 5-fold greater risk of ischemic heart disease than those with blood pressures of 140/90 mm Hg or lower.

- **Smoking** - prolonged use, doubles the death rate from ischemic heart disease. Smoking cessation reduces that risk substantially.
- **Diabetes mellitus** - induces hypercholesterolemia and markedly increases the risk of atherosclerosis

Pathogenesis

- Atherosclerosis is a chronic inflammatory and healing response of arterial wall initiated by some form of endothelial injury
- Sequence of atherosclerosis progression:

i) **Chronic endothelial injury**

- Endothelial injury is the cornerstone of the response to injury development of atherosclerosis
- The three most important causes of endothelial dysfunction are hemodynamic disturbances, hypercholesterolemia, and inflammation.

ii) insudation of lipoproteins (mainly LDL and VLDL) into the vessel wall

iii) Modification of such lipoproteins by oxidation.

- With chronic hyperlipidemia, lipoproteins accumulate within the intima, where they may aggregate or become oxidized by free radicals produced by inflammatory cells
- Because the modified lipoproteins cannot be completely degraded, chronic ingestion leads to the formation of lipid-filled macrophages called foam cells

iv) adhesion of blood monocytes to the endothelium

v) migration of monocytes into the intima and their transformation into macrophages and foam cells,

vi) adhesion of platelets to focal areas of denudation or to adherent leukocytes

vii) release of factors from activated platelets, macrophages or vascular cells

viii) migration of smooth muscle cells from media into intima

ix) proliferation of smooth muscle cells in the intima and elaboration of extracellular matrix

x) accumulation of collagen anf proteoglycans

xi) Enhanced accumulation of lipids within macrophages, smooth muscle cells and extracellularly.

PLAQUE PROGRESSION

A. Fatty streaks

- present nearly universally in children
- They do not cause any disturbance in blood flow, however, they may be precursors of Atheromatous plaques.
- FSs begin as multiple yellow flat spots – fatty dots (FD) which are less than 1 mm in diameter
- Subsequently they merge into elongated (1 cm long and longer) FSs

- They are composed of lipid-filled foam cells with T-lymphocytes and extracellular lipids

B. Atheromatous plaques

- are the basic lesions within the intima, having a core of lipid (mainly cholesterol and cholesterol esters) and a covering fibrous cap
- Atheromatous plaques are also called fibrous, fibrofatty, lipid, or fibrolipid plaques which have white to whitish yellow colour and rise intima slightly into the lumen of the artery
- The centers of larger plaques may contain a yellow debris, hence the term *atheroma*
- The abdominal aorta is usually much more involved than thoracic aorta, and aortic lesions tend to be much more prominent around the origins (ostia) of its major vessel branches.

C. Fibroatheroma

- Has lipid core and fibrotic layer or multiple lipid cores and fibrotic layer or mainly calcific or fibrotic

D. Complicated lesion

- Surface defect, hematoma, hemorrhage, thrombus.

Consequences of atherosclerotic plaque

- **Atherosclerotic Stenosis**. In small arteries, atherosclerotic plaques can gradually occlude vessel lumens, compromising blood flow and causing ischemic injury.
- **Acute Plaque Change**. Plaque erosion or rupture
- **Thrombosis**
- **Hemorrhage**
- **Wall weakening**
- **Calcification**

4. Outline Neoplasia

Definition

- Neoplasia is an abnormal mass of tissue, growth of which is uncoordinated with that of normal body tissues and that persists after the cessation of the stimulus that caused it.

Classification

- Neoplasms can be classified as either benign or malignant
- Benign tumors reman localized
- Generally benign tumors can be locally excised
- Malignant neoplasms can invade and destroy adjacent sites
- Can cause death.
- Tumors have two basic components: Parenchyma which consists of neoplastic cells and stroma which consists of non-neoplastic, host derived connective tissue and blood vessels

Characteristics of Cancer cells

- Large number of dividing cells
- Large variably shaped nuclei
- Variation in size and shape
- Loss of normal cell features
- Large nucleus to cytoplasm ration.

Causes of Cancer

- Chemical carcinogens ie, Mutagens, Chemical carcinogens and their metabolism
- Physical Carcinogens(radiation) i.e, UV radiation, Asbestos
- Infectious pathogens(viral)i.e, Human T-cell leukemia virus, DNA viruses, Epstein-Bar virus, Hepatitis B virus.

Molecular Basis of Cancer

- A tumor is formed by the clonal expansion of a single precursor cell that has incurred genetic damage
- Principle target of cancer causing mutations are: a) The growth promoting proto-oncogenes. b) The growth inhibiting tumor suppressor genes c) Genes that regulate apoptosis d) Genes involved in DNA repair.

i) **Hallmarks of Cancer**

- Self -sufficiency growth signals
- Insensitivity to growth inhibitory signals
- Altered cellular metabolism
- Evasion of apoptosis
- Limitless replicative potential(immortality)
- Sustained angiogenesis
- Ability to invade and metastasize
- Ability to evade the host immune response

Clinical Aspects of Neoplasia

- **Local Effects**: Compression of adjacent tissues, obstruction of organs or vessels.

- **Systemic Effects**: Weight loss, fever, anemia, paraneoplastic syndromes.
- **Metastasis**: Secondary symptoms depending on the site of metastasis (e.g., bone pain, neurological symptoms)

Diagnosis of Neoplasia

- **Histopathological Examination**: Biopsy and microscopic examination to determine cell type and degree of differentiation.
- **Imaging Studies**: X-rays, CT scans, MRI, and PET scans.
- **Molecular and Genetic Testing**: Identification of specific mutations or biomarkers.

Grading of Tumors

- Grading is based on: a) Degree of anaplasia b) The rate of growth
- Grade 1: Well-differentiated <25%
- Grade 2: Moderate (25-50%) of anaplastic cells
- Grade 3: Moderately differentiated 50-75%
- Grade 4: Poorly-differentiated or anaplastic(>75% of anaplastic cells)

Treatment of Neoplasms

- **Surgery**: Removal of the tumor
- **Radiation Therapy**: Targeted destruction of tumor cells using ionizing radiation.
- **Chemotherapy**: Use of drugs to kill or inhibit the growth of neoplastic cells.
- **Targeted Therapy**: Drugs that specifically target molecular pathways involved in tumor growth.
- **Immunotherapy**: Enhancing the body's immune response against tumor cells.