CELLULAR ADAPTATION & CELL INJURY

(1) What is Cell injury?

- **When cells are exposed to injurious agent beyond limit is defined as Cell injury.**

(2) Mention different causes of Cell death.

- **Ischemia**
- **Infection**
- **Toxins**
- **Immune reaction**

(3) Mention two patterns of cell death.

1) **Necrosis**
2) **Apoptosis**

(4) What is necrosis?

- **It is a type of cell death occurring after abnormal stresses (eg. Ischemia, Chemical injury.**

(5) What is Apoptosis?

- **It is a process by which cell dies through activation of internally controlled suicide program.**

(6) What is Pathological Calcification?

- **Deposition of calcium at the site of cell death is known as pathological calcification.**

(7) What is hyperplasia?

- **Increase number of cells with cell division in an organ or tissue is known as hyperplasia.**

(8) What is hypertrophy?

- **Increase in the size of cells without cell division in an organ or tissue is known as hypertrophy.**

Dr. CHERRY SHAH

(9) Which are the types of Physiological hyperplasia?

- **Mainly two types 1) Hormonal**
  - **Female breast**
  - **Pregnant uterus**
- **2) Compensatory**
  - **Capacity of Liver to regenerate**
  - **Unilateral Kidney**

(10) Describe the mechanisms of hyperplasia

- **Increased local proliferation of growth factors.**
- **Hormones acting as growth factors.**
- **And role of stem cells.**

(11) Give examples of Hormone induced Pathological Hyperplasia.

- **Endometrial hyperplasia**
- **Benign prostatic hyperplasia**
- **Regress with elimination of hormones**

(12) What are the beneficial effects of hyperplasia?

- **It is an important response to wound healing by proliferation of fibroblasts and blood vessels that leads to healing of cells.**

(13) What is Growth factor induced hyperplasia?

- **Stimulation associated with viral infection e.g. Papilloma virus**
- **Skin warts**
- **Hyperplastic epithelium**

(14) Give example of hypertrophy.

- **Myocardial Fibers**

(15) Which type of muscles is capable of hypertrophy? Why?

- **Striated muscles of heart and skeletal muscle**
- **Because they cannot adopt to increased metabolic demands by mitotic division**

(16) Why muscles bulge in body builders? Give example

- **Increased demand leads to increase in size as work load is shared by all cellular components.**
- **For e.g. – Uterus hypertrophy due to estrogen.**
  – Breast hypertrophy in response to prolactin during lactation

(17) Give example of hypertrophy and hyperplasia occurring together.

- **Uterus during pregnancy**

(18) Which genes are induced in hypertrophy?

- **Growth Factor- TGF-B, Insulin like GF, FGF**
- **Vasoactive agents – Angiotensin II, Endothelin**

(19) What happens in cardiac hypertrophy?

- **Mechanical triggers e.g stretch**
- **Trophic trigger e.g Polypeptide GF like IGF I, Vasoactive agents like angiotensin II**

(20) What is Atrophy?

- **Shrinkage in size of cell by loss of cell substance is known as Atrophy.**

(21) Give example of physiological Atrophy

- **Embryonic structures like notochord, thyroglossal duct.**

(22) What are Autophagic vacuoles?

- **It is a membrane bound vacuoles within cells containing cell components.**
- **E.g. – Mitochondria, Endoplasmic Reticulum**

(23) What are Residual bodies?

- **Some cell debris in autophagic vacuoles that resist digestion and persists in the cell is known as Residual bodies.**
- **e.g. Lipofuschin granules.**

(24) What is brown atrophy?

- **Lipofuschin granule, when present in sufficient amount, gives brown color and is known as BROWN ATROPHY.**

(25) Most common metaplasia seen in cigarette smoker?

- **Ciliated columnar epithelium of trachea and bronchi are replaced by stratified squamous epithelium.**
- **Stones in excretory ducts of salivary glands, pancreas and bile ducts cause replacement of secretory columnar epithelium to stratified squamous epithelium.**

(26) What changes occur when there is squamous metaplasia in respiratory tract?

- **Important protective mechanism of mucus secretion is lost leading to undesirable effects.**

(27) Give an example where squamous to columnar cell metaplasia occurs & why?

- **Barret's esophagus. Squamous to intestinal type of columnar metaplasia occur under influence of refluxed gastric acid.**

(28) Which type of carcinoma occurs in Barret's esophagus?

- **Adenocarcinoma.**

(29) Give examples of connective tissue metaplasia.

- **Bone formation in muscle like Myositis Ossificans commonly seen after bone fracture**

(30) What are the hallmarks of reversible cell injury?

- **Reduced oxidative phosphorylation.**
- **ATP depletion.**
- **Cellular swelling caused by changes in ion concentration and water influx.**

(31) What are indications of irreversible cell injury?

- **Amorphous densities in mitochondria.**
- **Functional like loss of membrane permeability.**

(32)What is the cause of necrosis?

- **It is Damage to membrane causing lysosomal enzymes enters cytoplasm causing digestion of cell .Cellular content leaking out leading to necrosis.**

(33)What is mechanism of apoptosis?

- **It is a physiological mechanism by which stimuli that leads to damage to DNA causing nuclear dissolution without complete loss of membrane.**

(34)What % of ATP depletion is necessary to cause cell injury?

- **More than 5% to 10%**

(35)Which cellular organelle is most commonly injured in cell injury?

- **Mitochondria**

(36) What are mechanisms of mitochondrial injury?

- **Increase in cytosolic calcium**
- **Oxidative stress**
- **Breakdown of phospholipids through phospholipase A2 or sphingomyelin pathway**

(37) Which ions is most important mediator in cell injury?

- **Calcium**

(38) Which enzymes are activated by calcium?

- **ATPase – Causes ATP depletion**
- **Phospholipase – Cause membrane damage**
- **Protease endonuclease**

(39) What are O_2 derived free radicals?

- **Cells generate energy by reducing molecular O_2 from water. During this process small amount of partially reduced reactive oxygen forms are produced by mitochondrial respiration. They are called as O_2 derived free radicals. They can causes damage to the lipids, proteins and nucleic acids.**

(40) What is oxidative stress?

- **Imbalance between free radical generation and radical scavenging system can lead to oxidative stress and associated cell injury.**

(41) Which are toxic intermediates?

- **Superoxide (O_2^-)**
- **H_2O_2**
- **OH^-**

(42) What are the effects of O_2 derived free radicals?

- **Lipid peroxidation**
- **Oxidative modification of protein**
- **Lesions in DNA**

(43) Which vitamin causes termination of oxygen free radicals?

- **Vitamin E**

(44) Which are the mechanisms to remove free radicals?

- **Antioxidants like - Vitamin E**
  - Ascorbic acid
  - Glutathione
- **Binding of iron and copper to storage and transport proteins**
  e.g, - Transferrin
  - Ferritin
  - Lactoferrin
  - Ceruloplasmin
- **Enzymes –Catalase**
  - **Superoxide dismutase**
  - **Glutathione peroxidase**

(45) Which biochemical defects contribute to membrane damage in cell injury?

- **Mitochondrial dysfunction**
- **Loss of membrane phospholipids**
- **Cytoskeletal abnormalities**
- **Reactive O_2 species**
- **Lipid breakdown products**

(46) How cytoskeletal abnormalities affect membrane permeability?

- **Cytoskeleton is anchored between plasma membrane and cell interior. Increased in calcium leads to activation of proteases and leads to damage to cytoskeleton.**
- **It is most commonly seen in myocardial cells.**

(47) What happens when there is injury to lysosomal membrane?

- **Leakage of enzymes into cytoplasm like RNases, DNases, proteases, phosphatases and glucosidases that will lead to enzymatic digestion of cell components causing necrosis.**

(48) Which two phenomenon characterize irreversible cell injury?

- **Inability to reverse mitochondrial dysfunction**
- **Development of profound disturbances in membrane function**

(49) Give examples of tissue specific marker of cell injury and death using blood samples.

- **Cardiac muscle – Isoform of Creatine Kinase, Troponin**
- **Liver, Bile duct – Isoform of Alkaline phosphates, SGPT**

(50) What are microscopic changes occurring in cellular swelling?

- **Small clear vacuoles in cytoplasm, hydropic changes or vacuolar degeneration are microscopic changes occurring in cellular swelling.**

(51) What are the clear vacuoles in cytoplasm?

- **They are distended and pinched off segments of Endoplasmic Reticulum.**

(52) What is Autolysis?

- **Enzymes derived from lysosomes of dead cells causing digestion is known as Autolysis.**

(53) Why necrotic cells show increased eosinophillia?

- **Loss of normal basophilia imparted by RNA in cytoplasm and increased binding of eosin to denatured intracytoplasmic proteins leads to increased eosinophilia in necrotic cells.**

(54) Why necrotic cells have more glassy homogenous appearance?

- **Due to loss of glycogen particles**

(55) Why cytoplasm of cell in necrosis becomes moth eaten?

- **Because of digested organelles of cytoplasm by enzymes**

(56) What are myelin figures?

- **Dead cells replaced by large whorled phospholipid masses are called as myelin figures.**

(57) How does calcification occur in necrosed cell?

- **Phospholipid precipitates are phagocytosed or degraded in fatty acids which are then calcified.**

(58) What nuclear changes occur in necrosis?

- **It occurs due to nonspecific breakdown of DNA.**
- **Karyolysis – Basophilia of chromatin fade due to DNase activity**
- **Pyknosis - Nuclear shrinkage and increased basophilia (DNA condenses)**
- **Karyorrhexis - Pyknotic nucleus undergo fragmentation.**

(59)What is Coagulative necrosis?

- **Coagulative necrosis is preservation of basic outline of is coagulated cell for atleast some days.**

(60)Which type of necrosis occurs in myocardial infarction?

- **In myocardial infarction, coagulative necrosis occur in which acidophilic, coagulated, anucleate cells persist for weeks.**

(61) Example of coagulative necrosis.

- **Hypoxic death of cells in all organs except brain is example of coagulative necrosis.**

(62)What is liquifactive necrosis?

- **Liquifactive necrosis is characteristic of focal bacterial or fungal/microbial infection**
- **Completely digest the dead cells forming liquid viscous mass like pus.**

(63)Which type of necrosis occurs in hypoxic cell death in brain?

- **Liquifactive necrosis.**

(64)What is gangrenous necrosis and what is wet gangrene?

- **Gangrenous necrosis generally applied to necrosis in limb due to loss of blood supply causing coagulative type necrosis.**
- **If it is superimposed by microbial infection causes liquifactive type of necrosis, which is called as WET GANGRENE.**

(65)What is caseous necrosis?

- **Coagulative type of necrosis found in tuberculous infection due to cheesy white appearance.**
- **Inspite of coagulative necrosis, architecture is completely obliterated.**

(66)What is fat necrosis?

- **A focal area of fat destruction occurring as a result of release of activated pancreatic lipases is known as fat necrosis.**

(67) What is dystrophic calcification?

- **If necrotic cells are not promptly destroyed or reabsorbed calcium salts deposit on them causing dystrophic calcification.**

(68)What is ischemia –reperfusion injury?

- **Some times in ischemia, when blood flow is restored to cells which have not died in injury proceeds to accelerated phase.**

  E.g,: Myocardial infarction

  Cerebral infarction

(69)What happens in mercury poisoning?

- **Mercury binds with sulfahydryl group of cell membrane and protein**
- **It increases membrane permeability**
- **It Inhibits ATPase dependant transport**
- **GIT and Kidney maximum affected in mercury poisoning**

(70)What happens in cyanide poisoning?

- **Cyanide is poisonous to mitochondrial cytochrome oxidase**
- **It blocks oxidative phosphorylation.**

(71)What happen in carbon tetrachloride (CCl_4) poisoning?

- **CCl_4 used in dry clearing industry**

- **Converted to CCl_3 by P-450**
- **CCL_3 causes antioxidation of fatty acids of membrane phospholipids**
- **Lipid peroxidation occurs.**
- **Rapid breakdown of structure and function of Endoplasmic Reticulum.**
- **Mainly affects LIVER (fatty liver)**
- **It causes mitochondrial injury**

(72)What is happen in Acetaminophen toxicity?

- **It is analgesic**
- **Acetaminophen is detoxified in liver by GSH**
- **If large dose-GSH depleted , then accumulation of toxic metabolites in cell**
- **Massive necrosis occur**

(73)What is apoptosis?

- **Greek word Apoptosis meaning 'Falling off'**

(74)What is physiological Apoptosis? Give example.

- **Serves to eliminate cells that are no longer needed.**
- **Example**
  1. **Programmed destruction of cells**
     -Embryogenesis like implantation, involution
  2. **Hormone dependent involution**
     -Endometrial breakdown during menstruation
     -Ovarian follicular atresia in menopause
     -Regression of locality breast after weaning
     -Prostatic Atrophy after castration
  3. **Death of neutrophils in acute inflammation and lymphocyte in immune response**
  4. **Cell death due to cytotoxic T cells.**

(75)What is pathologic Apoptosis?

- **Due to injurious stimuli like –radiation**
  -Anticancer drugs damaging DNA
  -Repair not coping with injury-cell kills itself
  -Heat
  -Hypoxia
- **Viral Disease-Hepatitis**
- **Pathologic atrophy in parenchymal organs after duct obstruction like pancreas, parotid gland and kidney**

- **Cell death in tumors**

(76) What are the morphological features of Apoptosis?

- **Cell shrinkage.**
- **Chromatin Condensation.**
- **Cytoplasmic Blebs and apoptotic bodies**
- **Phagocytosis of Apoptotic cells.**

(77) What are Apoptotic bodies?

- **Apoptotic cells first shows extensive blebbing – then fragmentation into Membrane bound apoptotic bodies composed of cytoplasm and highly packed granules with or without nuclear fragments.**

(78) What are Biochemical features of Apoptosis?

- **Protein Cleavage.**
- **DNA Breakdown.**
- **Phagocytic Recognition.**

(79) What are Caspases ?

- **Cystine Proteases present in normal cell as inactive Proenzymes → Activated by Apoptosis → cause protein hydrolysis.**

(80) What is action of Caspase?

- **Cause protein hydrolysis.**
- **Cleave the vital cellular proteins like laminin.**
- **Breaks the nuclear scaffold and cytoskeleton.**
- **Activate DNAse → Degrade the DNA.**

(81) How an Apoptotic Cells recognized?

- **This cells express Phosphotidylserine in outer layer of plasma membrane which has flipped out.**
- **It is stained by special dye Annexin V.**

(82) Which death receptors initiates Extrinsic pathway of Apoptosis?

- **Death receptors – Members of TNF : TNF – 1 and Fas (CD 95)**

(83) What is initiation phase of Apoptosis?

- **When Caspases become catalytically active.**

(84) What is execution phase of Apoptosis?

- **When Caspases act to cause cell death.**

(85) What is Death Domain?

- **They are death receptors member of TNF Family containing cytoplasmaic domain involved in protein – protein interaction essential for delivering of apoptotic signals.**

(86) Examples of Death Receptors?

- **TNF 1.**
- **Fas (CD 95)**

(87) By which protein, execution phase of apoptosis is inhibited?

- **FLIP- binds to procaspase but cannot cleave and activate it as it lacks enzymatic activity.**

(88) Which are anti-apoptotic molecules?

- **Bcl-2 family of proteins**
- **Bcl-X**
- **They reside in mitochondrial membranes and cytoplasm**

(89) Which protein activate Caspase leak out in intrinsic pathway?

- **Cytochrome C**

(90)What does term "Caspase" means?

- **C- Cysteine protease**
- **Aspase- Unique ability of enzymes to cleave after aspartic acid residues.**
- **Approx- 10 members are there.**

(91) What are initiator Caspases?

- **Caspase 8 and Caspase 9**

(92) Which are executioner Caspases?

- **Caspase-3 and Caspase-6**

(93) Which signals induce apoptosis?

- **Lack of growth factor or hormone**
- **Injurious agents**

(94) Which are examples of apoptosis due to lack of growth factor?

- **Lymphocytes are not stimulated with antigens or cytokines**
- **Hormone deprived cells**
- **Neurons deprived of nerve growth factors**

(95) What is Dysregulated Apoptosis?

- **Too little or too much apoptosis is known as dysregulated Apoptosis.**

(96) Give examples of Dysregulated Apoptosis.

- **Defective apoptosis and increased red cell survival**
  - **Cancer**
  - **Autoimmune disorder**
- **Increased apoptosis and cell death**
  - **Neurodegeneration in Spinal muscular dystrophy**
  - **Ischemic injury in myocardiac infaction and stroke**

(97) In what ways lysosomes are involved in breakdown of phagocytosed material?

- **Heterophagy and Autophagy**

(98) What is Heterophagy?

- **It is the process in which lysosomal digestion of ingested material from extracellular environment occur.**

(99) What is Endocytosis?

- **Taking up of extracellular material by cells is known as Endocytosis.**

(100)What is Pinocytosis?

- **Uptake of soluble smaller macromolecules is known as Pinocytosis.**

(101) What is Autophagy?

- **It refers to the lysosomal digestion of cells own components.**

(102) What are residual bodies?

- **Enzymes in lysosomes are capable of degrading proteins and carbohydrates but some lipids remain undigested. These are Residual bodies.**

(103) What is lipofuscin pigment?

- **Lipofuscin pigments are granules representing undigested material derived from intracellular lipid peroxidation.**

(104) What are hereditary lysosomal storage disorders?

- **Hereditary lysosomal storage disorders are caused by deficiency of enzyme that degrade various macromolecules particularly neurons.**

(105) Which drug interferes with lysosomal function? How?

- **Chloroquine interferes with function of lysosome by raising its internal pH and hence inactivating enzymes within it.**
- **This mechanism is beneficial in case of Autoimmune diseases like Rheumatoid arthritis.**
- **It can also be harmful as abnormal accumulation of glycogen and phospholipids in lysosome can cause Toxic Myopathy.**

(106) Which drugs cause hypertrophy of smooth Endoplasmic Reticulum?

- **Barbiturates cause hypertrophy of Endoplasmic reticulum particularly of hepatocytes.**

(107) In which conditions there is mitochondrial alterations?

- **Mitochondrial alteration occurs in liver in case of alcoholic disease and in nutritional deficiencies.**

(108) In which conditions there is increase in number of mitochondria?

- **There is increase number of mitochondria in certain benign tumors of salivary gland, thyroid, parathyroid and kidney.**
- **Unusually large abnormal cristae are seen in inherited metabolic diseases of skeletal muscle.**

(109) What does cytoskeleton consists of?

- **Cytoskeleton consists of Microtubules, Actin filaments, Myosin filaments and Intermediate filaments.**

(110) What abnormalities are seen in Actin filaments?

- **Drugs like cytochalasin B prevents polymerization of Actin filaments.**
- **Toxin in mushrooms prevents movement of Actin filaments by binding to it.**

(111) What are intermediate filaments?

- **Intermediate filaments are filaments, that provide flexible intracellular scaffold that organizes cytoplasm and resists forces applied to cell.**

(112) What are different types of intermediate filaments?

Different types of intermediate filaments are as following:

- **Keratin in epithelial tissue.**
- **Neurofilament in neural tissue.**
- **Desmin in muscle cells.**
- **Vimentin in connective tissue.**
- **Glial tissue in Astrocytes.**

(113) What are Mallory bodies?

- **Mallory bodies are abnormality of keratin filaments that lead to accumulation of keratin in hepatocytes.**
- **These are eosinophilic in appearance seen in alcoholic liver disease.**

(114) What happens in Alzheimer's Disease?

- **In Alzheimer's disease; intermediate filaments, microtubules and neurofilament tangles are found in brain.**

(115) What is Wiskott- Aldrich Syndrome?

- **Wiskott- Aldrich syndrome is an inherited disease characterized by eczema, platelets abnormalities and immune deficiency.**

(116) What is meant by Steatosis?

- **Steatosis is defined by accumulation of triglyceride in parenchymal cells.**

(117) In which organs, fatty changes are seen?

- **Fatty changes are seen mainly in Liver.**
- **Other organs in which fatty changes can be seen are: Heart, muscle and kidney.**

(118) What are the causes of Steatosis?

- **Causes of Steatosis are as following:**
  - **Diabetes Mellitus**
  - **Obesity**
  - **Anorexia**
  - **Alcohol abuse**

(119) How will you differenting clear vacuoles in cell of fatty change with Water Or Polysaccharide accumulation (Glycogen)?

- **Lipid -> Avoidance of Fat solvent in Paraffin embedding.**
  -> Prepare frozen section of fresh or aqueous formalin fixed tissue.
  -> Staining by Sudan IV or Oil red O (Orange Red Color)
- **Glycogen -> PAS Positive**
- **Neither -> Water**

(120) What are Liposomes ?

- **In beginning stage of fatty change there is development of minute membrane bound inclusion closely applied to Endoplasmic Reticulum known as Liposomes.**

(121) What changes are seen in Heart in Fatty Change?

- **Due to hypoxia , two patterns are seen.**
  1. **Hypoxia -> Anemia -> Intracellular deposits of fat with bannds of yellowed myocardium with bands of red brown uninvolved myocardium. -> <u>TIGEROID EFFECT</u>**
  2. **More pronounced Hypoxia or Myocarditis (Diphtheria) -> more uniformly attached Myocytes.**
  3. **.**

(122) Where is most of the Cholesterol is used?

- **In the formation of Cell Membrane.**

(123) What happens in Atherosclerosis?

- **Atherosclerotic Plaques – smooth muscle cells and macrophages with in intimal layer are filled with lipid vacuoles made up with cholesterol and cholesterol esters. (Foamy Cells)**

(124) What is Xanthoma?

- **Clusters of lipid laden (cholesterol) macrophages seen in subepithelial connective tissue of skin and tendon in hyperlipidemic states.**

(125) What is Cholesterolsosis ?

- **Focal accumulation of cholesterol laden macrophages in lamina propia of Gall Bladder.**

(126) What is Nieman Pick Disease ?

- **Lysosomal storage disease in which enzyme involved in cholesterol trafficking is mutated and cholesterol accumulation occurs in multiple organs.**

(127) What are Rusell Bodies ?

- **Plasma cells synthesize excessive amounts of protein as in IgG immunoglobulins. This leads to distension of Endoplasmic Reticulum, which becomes distended, large homogeneous with eosinophilic inclusions -> Rusell Bodies.**

(128)Give the example of hyaline changes.

- **Intracellular hyaline changes- Rusell bodies**
  - Mallory bodies
- **Extracellular hyaline changes-Walls of arterioles in Hypertension and Diabetes**

(129)How glycogen is best preserved in cytoplasm?

- **Glycogen is best preserved in cytoplasm by nonaqueous fixatives, best is absolute alcohol.**

(130) Give the name of special stain for glycogen.

- **Special stain for glycogen : Best Carmine and PAS**

(131) In which condition glycogen deposition occurs?

- **Diabetes Mellitus- Found in distal portion of proximal convoluted tubules and descending loop of henle**
  - Liver cells
  - Beta cells of Islets Langerhans
  - Heart muscle cells
- **Glycogen storage diseases**

(132)Give the name of common exogenous pigments.

- **Carbon , Coal dust in lung ANTHRACOSIS can cause pneumoconiosis in coal workers**

(133) Which is wear and tear pigments?

- **Lipofuschin also known as lipochrome – composed of polymers of lipids and phospholipids with proteins.**

(134) What is Brown pigment and where it is seen?

- **Brown pigment is Lipofuschin in cells of liver and heart of aging patients and patients with cancer cachexia.**

(135) Give the name of Endogenous pigments.

- **Lipofuschin**
- **Melanin**
- **Hemosiderin**

(136) When is melanin formed?

- **Melanin is formed when enzyme tyrosinase catalyses oxidation of tyrosine to dihydroxyphenylalanine in melanocytes.**

(137) Which are endogenous brown and black pigments found in body?

- **Main is Melanin pigment found in body.**
- **Homogentisic acid in ALKAPTONURIA.**

(138) What is Alkaptonuria?

- **A pigment Homogentisic acid is deposited in skin, connective tissue and cartilage. This pigmentation is known as OCHRONOSIS.**

(139) What is Hemosiderin?

- **It is the hemoglobin derived golden-yellow to brown granular or crystalline pigment, in which form iron is stored in the cells.**

(140) How Hemosiderin granules are formed?

- **Iron is carried by specific proteins 'TRANSFERRIN', that is stored in association with protein APOFERRITIN to form ferritin micelles. When local or systemic excess of iron ferritin forms it will store as Hemosiderin granules.**

(141) What does Hemosiderin granules represents? Where are the commonly seen?

- **It represents the aggregates of ferritin micelles. They can be commonly seen in mononuclear phagocytes of bone marrow, spleen and liver.**

(142) What is the common example of local Hemosiderosis?

- **Common bruise.**
- **After hemorrhage –> Red blue**
- **With lysis of red blood cells-->hemoglobin to Hemosiderin**
- **Green blue – Biliverdin(green bile)->Billirubin(red bile) ->Golden yellow – Hemosiderin**

(143) What are causes of systemic Hemosiderosis?

- **Increased absorption of dietary iron**
- **Impaired use of iron**
- **Hemolytic anemias**
- **After transfusion because of transfused red cells**

(144) Microscopically, where the iron pigments are seen?

- **In mononuclear cells of Liver, Pancreas, Breast and Endocrine organs.**

(145) Which special stain is used for iron pigments?

- **Prussian blue stain. It contains potassium ferrocyanide which is converted by iron into blue black ferric ferrocyanide.**

(146) What is Hemochromatosis?

- **More extreme accumulation of iron is known as Hemochromatosis.**
- **It is associated with liver fibrosis, Heart failure and Diabetes mellitus**

(147) What is dystrophic calcification?

- **When deposition of calcium occurs locally in dying tissue with normal calcium levels and absence of calcium dearrangments.**

(148) What is metastatic calcification?

- **Deposition of calcium in normal tissue is known as metastatic calcification. It mainly results from hypercalcaemia secondary to disturbances in calcium metabolism.**

(149) In which type of necrosis, dystrophic calcification is seen?

- **Coagulative necrosis**
- **Caseous necrosis**
- **Liquifactive necrosis**
- **enzymatic necrosis of fat**

(150) What are common sites of dystrophic calcification?

- **Atheroma in advanced Atherosclerosis**
- **Develops in aging and damaged heart valves**
- **Tuberculous lymph node**

(151) What are Psammoma bodies?

- **Dystrophic calcification in which single necrotic cells became encrusted by mineral deposits. The progressive acquisition of outer layers cause lamellated configuration which is called Psammoma bodies.**

(152) What happens in Asbestosis of Lung?

- **Dystrophic calcification in which calcium salts gather about long slenders spicules in asbestosis in lung creating beaded dumbbell forms.**

(153) Where does initiation of dystrophic calcification start intracellularly?

- **In mitochondria of dead cells**

(154) Where does initiation of dystrophic calcification occurs extracellularly?

- **In phospholipid in membrane bound vesicle in cartilage and bone known as matrix vesicles.**

(155) Mention the causes of hypercalcemia.

- **Increased secretion of parathyroid hormones. E.g, Hyperparathyroides**
- **Destruction of bone tissue in primary bone tumors. E.g, Multiple myeloma**
- **Skeletal metastasis. E.g, Breast carcinoma**
- **Vitamin D related disorders e.g, vitamin D intoxication, sarcoidosis**
- **Renal failure**

(156) What is milk alkali syndrome?

- **Excessive ingestion of calcium and absorbable antacids like milk or calcium carbamate leads to milk alkali syndrome.**

(157) Which are the common sites of metastatic calcification?

- **Interstitial tissues of gastric veins.**

DISEASES OF INFANCY AND CHILDHOOD

(1)What are different periods of childhood?

- **Neonatal period- First 4 weeks of life**
- **Infancy- 1st yr of life**

(2) What is meant by Malformation?

- **A primary error of morphogenesis with intrinsically abnormal development process is known as malformation.**
- **E.g, Congenital heart disease, anencephaly**

(3) What is meant by Disruption?

- **Secondary destruction of organ that was previously normal in development.**

(4) What is meant by Deformation?

- **Extrinsic disturbance of development is known as deformation.**

(5) What is meant by Syndrome?

- **It is constellation of congenital anomalies.**

(6) What is Agenesis?

- **Complete absence of organ is known as Agenesis.**

(7) What is Aplasia?

- **Absence of organ due to failure of development is known as Aplasia.**

(8)What is Atresia?

- **Absence of opening of a hollow organ like trachea or intestine is known as Atresia.**

Dr. CHERRY SHAH

(9) What is Hypoplasia?

- **Incomplete development or decrease in size of organ is known as Hypoplasia.**

(10) What is Hyperplasia?

- **Enlargement of organ due to increase number of cells is known as Hyperplasia.**

(11) Which viruses are responsible for causing congenital anomalies?

- **Cytomegalovirus**
- **AIDS**
- **Herpes**

(12) Which infections occur transplacentally?

- **Parasitic infections - Toxoplasma, Malaria**
- **Viral & Bacterial infections – Listeria, Treponoma, HIV , HbsAg**

(13) What is hemolytic disease of New born?

- **Caused by blood group incompatibility between mother and fetus by certain Rh antigens**

(14) Why ABO incompatibility is less severe than Rh incompatibility in fetus?

- **Anti –A and Anti –B are of Ig M type and does not cross placenta.**
- **Neonatal red cells express blood group antigen A and B poorly.**
- **Many cells other than RBCs express A and B antigens and thus absorb some transferred antibody.**

(15) In which infants ABO incompatibility is common?

- **Infants of A and B blood group to blood group O mothers.**

(16) What are the consequences of excessive destruction of red cells in neonates?

- **Anemia**
- **Jaundice because of hemolysis produced by unconjugated bilirubin**

(17) What are other causes of Hydrops fetalis apart from blood group incompatibility?

- **Cardiovascular defects**
- **Chromosomal anomalies e.g,Turner syndrome**
- **Fetal anemia. e.g, Parvovirus B19**
- **Twin gestations**
- **Infection e.g, Cytomegalovirus, Syphilis, etc.**

(18) What is bone marrow picture in Hydrops fetalis?

- **Compensatory Erythroid hyperplasia to compensate anemia except for Parvovirus infections**
- **Extramedullary hematopoesis in liver, spleen and lymph nodes**

(19) What is peripheral blood smear picture in Hydrops fetalis?

- **Large number of immature red cells including reticulocytes, normoblasts and erythroblasts**

(20) What is Kernicterus?

- **Most serious damage in Hydrops fetalis**
- **Billirubin crosses blood brain barrier and all parts of brain affected**
- **Blood bilirubin more than 20 mg/dl**

(21) What are pathologic changes occuring during galactosemia?

- **Jaundice- hepatomegaly -> Fatty changes**
- **Cataract**
- **Septicemia**
- **Hemolysis and coagulopathy**

(22) What is cystic fibrosis?

- **Disorder of iron transport in epithelial cells affecting fluid secretion in exocrine glands and epithelial lining of Respiratory, GIT and Reproductive tract.**

(23) Which is most common abnormality in cystic fibrosis?

- **Pancreatic abnormalities with accumulation of mucus in small ducts.**

(24) Which lesions mimic tumors or act like tumor like lesions in children?

- **Heteropia (choristoma)**
- **Hamartoma**

(25) What is Choristoma?

- **Microscopically normal cells or tissues present in abnormal locations.**

(26) What is Hamartoma?

- **Excessive focal overgrowth of cells and tissues native to organ in which it occurs.**

(27) Which are most common benign tumors occurring in children?

- **Soft tissue tumors of mesenchymal derivation.**
- **Eg.,Hemangiomas, Lymphangiomas, Teratoma.**

(28) What are Portwine stains?

- **Hemangiomas in children where flat, large lesions are referred as Portwine stains.**

(29) Which teratoma are common in children?

- **Sacrococcygeal teratoma**

(30) Which malignancies are common in children?

- **Leukemia**
- **Retinoblastoma**
- **Neuroblastoma**
- **Wilm's tumor**
- **Hepatoblastoma**
- **Rhabdomyosarcoma**
- **Soft tissue sarcoma**
- **Osteogenic sarcoma**

(31) Which type of leukemia is common in children?

- **Acute Lymphoblastic Leukemia**

(32) Which posterior fossa neoplasms are common in children?

- **Juvenile Astrocytoma**
- **Medulloblastoma**
- **Ependymoma**

(33) Why most malignant tumors in children have suffix of 'Blastoma'?

- **As they tend to have more primitive rather than pleomorphic microscopic appearance showing features of organogenesis specific to the site of tumor origin.**
- **E.g. Neuroblastoma, Retinoblastoma**

(34) What are small round blue cell tumors?

- **Many childhood tumors are as small round cell tumors due to their primitive histologic appearance.**

(35) Which tumors are included in group of small round blue cell tumors?

- **Neuroblastoma**
- **Wilm's tumor**
- **Lymphoma**
- **Rhabdomyosarcoma**
- **Ewing's sarcoma**
- **PNET**
- **Medulloblastoma**
- **Retinoblastoma**

(36) How will you differentiate small round blue cell tumors?

- **A combination of chromosome analysis, immunoperoxidase staining and Electron microscopy.**

(37) What are neuroblastic tumors?

- **They demonstrate features like**
  - **Spontaneous differentiation of neuroblastic into mature elements.**
  - **Spontaneous tumor regression.**
  - **Wide range of clinical behavior and progression.**

(38) Give example of Neuroblastic tumor.

- **Neuroblastoma**

(39) Which gene mutation is responsible for Anaplastic lymphoma kinase?

- **ALK (Anaplastic lymphoma Kinase)**

(40) Which types of rosettes are seen in Neuroblastoma?

- **Homer Wright pseudorosettes in which tumor cells are concentrically arranged around central space filled with eosinophillic fibrillary material corresponding to neuritic processes of neuroblasts.**

(41)Which immunostain is used in neuroblastoma?

- **Neurospecific enolase**

(42)What is ganglioblastoma?

- **Larger cells representing ganglion cells found admixed with neuroblasts.**

(43)Which is important diagnostic test for neuroblastoma?

- **Increased catecholamines in blood.**
- **Increased VMA and HVA in urine.**

(44)Which are prognostic criteria for neuroblastoma?

Good prognostic criteria:

- **Younger than 18 months**
- **Morphology – gangliocyte differentiation**
- **N-myc if not amplified**
- **Telomerase expression –if absent**
- **Tyrokinase A expression present**
- **Tyrokinase B expression absent**

(45)At which age Wilm's tumor is at peak?

- **Between 2 to 5 years**

(46)What is synchronous Wilm's tumor?

- **When both kidneys are involved simultaneously.**

(47)What metachronous Wilm's tumor?

- **Metachronous Wilm's tumor is when both kidneys are involved one by one.**

(48)What are genetic risk factors of Wilm's tumor?

- **-WAGR syndrome-deletions 11p113**
  -PAX-6
- **Denys Drash Syndrome**
- **Beckwith Wiedeman Syndrome**

(49) What are nephrogenic rests?

- **Precursor lesion of Wilm's tumor seen adjacent to renal parenchyma.**

(50)Which molecular parameters correlate with bad prognosis of Wilm's tumor?

- **Loss of genetic material on chromosome 11q and 16q and gain of chromosome 1q.**

ENVIRONMENTAL AND NUTRITIONAL DISEASES

(1) Which metals can cause pathology in human beings?

- **Metals causing pathology in human beings are: Lead, Mercury, Arsenic and Cadmium**

(2) Which are main sources of lead exposure?

- **Main sources of lead exposure are: Air, food and water, paints, gasoline, toys,batteries etc.**

(3) Which system is disturbed maximum by lead poisoning?

- **System disturbed maximum by lead poisoning is: CNS and peripheral neuropathies.**

(4) Where is lead most commonly incorporated after absorption?

- **Lead is most commonly incorporated after absorption in bones and teeth competing with calcium.**

(5) What is maximum allowed level of lead absorption?

- **Maximum allowed level of lead absorption is: 10 µg/dl.**

(6) What are major effects of lead poisoning on brain?

- **As lead is blood brain barrier permeable, it inhibits neurotransmitters especially in children.**

(7) What is effect of lead poisoning on bone?

- **It inhibits normal remodelling of cartilage and primary bone trabeculae in epiphyses especially in children by increasing chondrogenesis and delaying cartilage mineralization.**

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(8) What is effect of lead poisoning on heme synthesis?

- **It inhibits activity of two enzymes: δ – aminolevulinic acid dehydratase and Ferrochelatase causing Microcytic hypochromic anemia.**

(9) How is lead poisoning diagnosed?

- **Unexplained anemia with basophilic stippling.**

(10) What blood and bone marrow changes are seen in lead poisoning?

- **Appearance of scattered ringed sideroblasts.**
- **Red cell precursors with iron stained by Prussian blue.**
- **Microcytic hypochromic anemia with mild hemolysis.**
- **Punctate basophilic stippling of red cells.**

(11) What is lead colic?

- **In lead poisoning, there is poor localized extremely severe pain in abdomen.**

(12) Which organic solvents increase risks of leukemia?

- **Rubber workers to benzene and 1,3-butadiene**

(13) Which chemicals are potent carcinogens in lung and bladder cancer?

- **Polycyclin hydrocarbons in steel foundries, tar and soot.**

(14) Which chemicals are endocrine disruptors with antiestrogenic and antiandrogenic activities?

- **Organochlorides especially pesticides like DDT and PCB.**

(15) Which chemicals cause Pneumoconiosis?

- **Inhalation of mineral dusts;**
- **Eg., Coaldust- mining of hard coal**
  Silica- stone cutting
  Asbestosis- mining, fabrication.

(16) Which chemical can cause Angiosarcoma of liver?

- **Vinyl Chloride**

(17) Which is the commonest cancer caused by Tobacco?

- **Lung cancer**

(18) Which is the addictive substance in Tobacco?

- **Nicotine**

(19) Which tumor suppressor oncogenes are mutated in Cigarette smoking?

- **K-RAS**
- **p53**

(20) What are effects of alcohol on liver?

- **Fatty change**
- **Cirrhosis**

(21) Which vitamin deficiency is common in chronic Alcoholism?

- **Thiamine (Vitamin B1)**

(22) What is Fetal Alcohol Syndrome?

- **Excess consumption of alcohol in first trimester of pregnancy leads to microcephaly, growth retardation and facial abnormalities on newborn.**

(23) Which cancers are commonly associated with alcohol consumption?

- **Oral cavity**
- **Oesophagus**
- **Liver**
- **Breast cancer in female**

(24) Which tumor is common due to oral contraceptives ?

- **Hepatic Adenoma**

(25) Which cancers are common due to radiation?

- **Leukemias (Acute Myeloid)**
- **Tumors of thyroid, breast and lungs**
- **Myelodysplastic syndrome**
- **Hodgkin's lymphoma**

(26) Which vitamin is lacking in polished rice?

- **Thiamine**

(27) What is artificially fed infants are lacking?

- **Iron**

(28) What is the normal range of vitamin- D?

- **20 to 100 ng/ml**

(29) Which are the diseases occurring due to Vitamin D deficiency?

- **Rickets**
- **Osteomalacia**
- **Hip fractures**

(30) What are causes of vitamin D deficiency?

- **Deficient diet**
- **Limited exposure to sun light**
- **Frequent pregnancies followed by lactation**

(31) What are consequences of Vitamin D deficiency?

- **In children: Metastatic calcification**
- **In adults: Bone pain and Hypercalcemia**

(32) Which exogenous substances are responsible for cancer?

- **Aflatoxin: Hepatocellular carcinoma**
  :Causing mutation in codon 249 of p53 gene
- **Artificial sweeteners: Bladder carcinoma**

(33) Which endogenous substances act as carcinogens?

- **Nitrosamines and Nitrosamides → Gastric cancer**

(34) Which cancer occurs in case of low fiber intake?

- **Colon Cancer**

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GENETICS

(1) What is human genome composed of?

- **2% protein, more than half of repetitive DNA sequencing**

(2) What is Genomics? Give example.

- **Study of all genes in genome and their interaction.**
  E.g, DNA microarray/ Analysis

(3) What are the most common DNA variants seen in human?

- **Single nucleotide polymorphism copy number variations**

(4) What is meant by single nucleotide Polymorphism (SNPS)?

- **It represent variation at single isolated nucleotide positions either within exon, intron or intergenic regions or coding region**

(5) What are copy number variations (CNVS)?

- **It consists of different numbers of large contagious stretches of DNA from 1000 base pairs to millions of base pairs.**

(6) What is Epigenetics?

- **Heritable changes in gene expression that are not caused by alteration in DNA sequence is known as Epigenetics.**

(7)What is proteomics?

- **Measurement of all proteins expressed in a cell or tissue is known as proteomics.**

(8) What are Micro RNAS?

- **They do not encodes the proteins but inhibit gene expression causing gene regulation**
- **Approx 1000 genes in human encoding micro RNAS.**

Dr. CHERRY SHAH

(9)What are small interfering RNAS?

- **Gene slicing RNAS**

(10)Give classification of Human genetic disorders.

1. **Disorder related to mutation in single gene**
   E.g, Sickle cell anemia
2. **Chromosomal disorders- arises from structural or numeric alterations in autosomes or sex chromosomes**
3. **Complex with multigenic disorders- Caused by interactions between multiple variant form of genes and environmental factors known as POLYMORPHISM'.**
   E.g, Atherosclerosis
   - Diabetes
   -Hypertension

(11)What is mutation?

- **Mutation is a permanent damage in DNA.**
- **Those affecting germ cells -> transmitted to progeny**
- **Affecting somatic cells -> do not cause Hereditary disease**

(12) What is point mutation?

- **A single nucleotide base is substituted by different base.**

(13)Why point mutations are known as Missense Mutation?

- **Point mutation alter code in a triplet of bases and lead to replacement of one amino acid by another; altering meaning of sequence of encoded protein. So it known as Missense Mutation.**

(14)What is conservative Missense Mutation?

- **Substituted amino acid causes little change in function of protein.**

(15)What is non conservative Missense mutation?

- **Normal amino acid replaced by very different amino acid.**
- **Example: Sickle cell mutation. Glutamic acid replaced by valine**

(16)What is Non sense mutation or Stop codon?

- **In point mutation, an amino acid codon can change to chain terminator Example: Beta^{0}Thalessamia**

(17) Give example of Mutation within noncoding sequence.

- **Hereditary anemia**
- **Abnormal mRNA resulting from mutation affecting introns or slice junction**

(18)What are frame shift mutations?

- **Small deletions or insertions involving coding sequence lead to alterations in reading frame of DNA strand –is FRAMESHIFT MUTATION.**

(19)What are trinucleotide repeat mutations?

- **Amplification of sequence of three nucleotides.**

(20)What is codominance?

- **Gene expression and mendelian points are dominant or recessive but in some cases both alleles of a gene pair contribute to phenotype ->CODOMINANCE. Example: Blood group antigen ,HLA antigens**

(21)What are Mendelian disorders?

- **Mostly are results of single gene mutation with large effects.**

(22)What is pleiotropism?

- **Single mutant gene lead to many end effects is pleiotropism.**
- **Example: Sickle cell anemia**

(23)What is incomplete penetrance?

- **In autosomal dominant disease, some individuals inherit mutant gene but are phenotypically normal is Incomplete penetrance.**

(24)What is variable expressivity?

- **In autosomal dominant trait is seen in all individuals carrying the mutant gene but is expressed differently – is VARIABLE EXPRESSIVITY.**
- **Example: Neurofibromatosis- Range from brownish spots on skin to multiple skin tumors**

(25) Environmental factors affecting e.g. Familial hypercholesterolemia.

- **Expression of disease informed of Atherosclerosis is conditioned by dietary intake of lipids.**

(26) Example of delayed age of onset disease.

- **Huntington disease- signs and symptoms do not appear till adulthood**

(27) What are the biochemical mechanisms of autosomal dominant diseases?

- **Most mutations lead to reduced product of a gene product and give rise to inactive protein → Loss of function mutation**
- **Up to 50% loss is compensated**

(28) Give example of biochemical mutations in Autosomal dominant diseases.

A) LDH receptor less than 50%

- **Familiar hypercholesterolemia**
- **Atherosclerosis**

B) Osteogenesis imperfecta →characterized by marked deficiency of collagen

(29)What is gain on function mutation?

- **The protein product of this mutation acquires new properties e.g., Huntington disease→ trinucleotide repeat mutation affecting Huntington gene give rise to abnormal protein called Huntington→ toxic to neurons**

(30)Give Examples of CNS autosomal dominant diseases.

- **Huntington disease**
- **Neurofibromatosis**
- **Myotonic dystrophy**
- **Tuberculous sclerosis**

(31) Give Example of Urinary autosomal dominant diseases.

- **Polycystic kidney disease**

(32) Give Example of GIT autosomal dominant diseases.

- **Familial Polyposis Coli**

(33) Give Examples of Hematopoietic autosomal diseases.

- **Hereditary Spherocytosis**
- **Von Willebrand disease**

(34) Give Examples of Skeletal muscle autosomal diseases.

- **Marfan syndrome**
- **Osteogenic imperfect**
- **Ehlerdanlos Achondroplasis**

(35) Give Examples of Metabolic autosomal dominant diseases.

- **Familiar hypercholesterolemia**
- **Acute Intermittent Porphyrias**

(36)What is mechanism of Autosomal Recessive disease?

- **Results only when both alleles at given locus are mutated.**

(37)Which are main characteristics of Autosomal Recessive diseases?

- **Trait mainly does not affect parents of affected individual but sibling show disease.**
- **Siblings have one in four chance of having trait (25%).**
- **Can be of consanguineous marriage.**

(38) Difference between Autosomal dominant and Autosomal Recessive.

Autosomal Recessive	Autosomal Dominant
Expression of defect is more uniform	Less uniform
Complete penetrance common	Uncommon
Onset early	Early or late onset
Most of mutated genes encode enzymes.	-

- **Most of metabolic diseases are Autosomal Recessive.**

(39)Give examples of Metabolic Autosomal Recessive disease.

- **Cystic fibrosis**
- **Phenyl ketonuria**
- **Galactosemia**
- **Hemocysteinuria**
- **Lysosomal storage disease**
- **α_1- Antitrypsin deficiency**
- **Wilsons disease**
- **Hemochromatosis**
- **Glycogen storage disease**

(40) Give examples of Hemopoetic Autosomal Recessive disease.

- **Sickle cell anemia**
- **Thalassemia**

(41) Give examples of Endocrine Autosomal Recessive disease.

- **Congenital Adrenal Hyperplasia**

(42) Give examples of Skeletal Autosomal Recessive disease.

- **Ehler Danlos syndrome**
- **Alkptonuria**

(43) Give examples of Neuronal Autosomal Recessive disease.

- **Neurogenic muscular atrophies**
- **Friedrich ataxia**
- **Spinal muscular atrophy**

(44)What are characteristics of X linked disorder?

- **Almost recessive**
- **Males with Y-mutations are infertile: No Y linked inheritance.**
- **Male is hemizygous for X-linked mutant genes, therefore disorders expressed in males.**
- **Male cannot transmit disorder to sons.**
- **Daughters are carriers.**
- **Females express partially.**

(45)Give example of X-linked disorder?

- **G_6PD Deficiency.**
- **Expressed mainly in males.**

(46) Give example of X-linked dominant disorder.

- **Vit-D resistant rickets**

(47) Give example of Musculoskeletal X-linked recessive disorder.

- **Duchenne muscular dystrophy**

(48) Give examples of Blood X-linked recessive disorder.

- **Hemophilia A and B**
- **G6PD deficiency**

(49) Give example of Immune X-linked recessive disorder.

- **Agammaglobinemia**
- **Wiskott Aldrich syndrome**

(50) Give example of metabolic X-linked recessive disorder.

- **Diabetes Insipidus**
- **Lesch Nyhan syndrome**

(51) Give example of Nervous X-linked recessive disorder.

- **Fragile X syndrome**

(52) Mandelian disorders.

- **(I) Enzyme related:**

1) Phenylalaninhydroxylase → Phenylketonuria (mutation)
2) Hexosaminidase → Taysach's (mutation)
3) Adenosine Deaminase → Severe combined Immunodeficiency (point mutation)

(II) Enzyme inhibitor mediated:

1) α1 antitrypsin → Emphysema , Liver disease (missence mutation)

(III) Receptor mediated:

1) Low density lipoprotein (LDL) → Familial hypercholesterolemia (deletion, point mutation)

2) Vitamin- D → Vit-D resistant rickets (point mutation)

(IV) Transport mediated:

1) O2 - Hemoglobin → α- thalassemia, β- thalassemia Sickle cell disease (deletion, defective mRNA process, point mutation)

2) Ions → Cystic fibrosis - Transmembrane conductase regulator (deletion)

(V) Structural:

1) Extracellular: a) collagen → Osteogenesis imperfecta, Ehler Danlos syndrome (deletion point mutation)

b) Fibrillin → Marfan's syndrome (Missense mutation)

(VI) Cell membrane:

1) Dystrophin → Duchenne Becker muscular dystrophy (deletion)

2) Spectrin, Ankyrin (heterogenous) → Hereditary Spherocytosis

(VII) Hemosiderin:

Factor VIII – Hemophilia A (deletion, insertion, mutation)

(VIII) Growth regulation:

1) Rb protein → Retinoblastoma (deletion)

2) Neurofibromin → Neurofibromatosis-1 (heterogenous)

(53) Give examples of Enzyme defects.

- **1) GALACTOSEMIA: Deficiency of Galactose-1 phosphate uridyltransferase → Accumulation of galactose → Tissue damage.**

2) Deficiency of degradative enzymes in lysosomes → accumulation → LYSOSOMAL STORAGE DISEASE

3) Tyrosinase deficiency → Deficiency of conversion of tyrosine to melanin → ALBINISM

4) α1-antitrypsin deficiency → unable to inactivate neutrophil elastase in lungs → destruction of walls of lungs alveoli → EMPHYSEMA

(54) Defects in receptors and transport system.

- **1) HYPERCHOLESTEROLEMIA → reduced synthesis of factors of LDL receptors → defective transport of LDL into cells → excessive cholesterol synthesis.**

2) CYSTIC FIBROSIS: Transport system for chloride ions in exocrine glands, sweat ducts, lungs and pancreas is defective.

(55) Alteration in structure, function or quantity of Nonenzyme protein.

- **1) Sickle cell disease → defects in structure of globin molecule.**
- **2) Thalassemia → mutation in globin genes.**
- **3) Osteogenesis Imperfecta → defect in structure of collagen**
- **4) Hereditary Spherocytosis → defect in structure of spectrin**
- **5) Muscular dystrophies → defect in structure of dystrophin.**

(56)Give examples of genetically determined adverse reaction to drugs.

- **G6PD Enzyme deficiency – enhanced by antimalaria drugs Primaquine→ hemolytic anemia**

(57) Which disorders are associated with defect in structural proteins?

- **1) Marfan syndrome**
- **2) Ehler Danlos syndrome**

(58) Marfan syndrome mainly affects

- **Autosomal dominant condition**
- **Skeleton**
- **Eyes**
- **Cardiovascular system**

(59) Causes of Marfan syndrome.

- **Inherited defect in extracellular glycoprotein called Fibrillin –I.**

(60) What is Ehler Danlos Syndrome?

- **Defect in the synthesis of structure of fibrillar collagen**

(61) Which are the disorders resulting from mutation affecting collagen synthesis?

- **1) Ehler Danlos Syndrome**
  2) Osteogenesis Imperfecta
  3) Alport Syndrome
  4) Epidermolysis Bullosa

(62) Which disorders are associated with defect in receptor proteins?

- **Familial hypercholesterolemia**
  (Mutation in gene encoding the receptor of LDL involved in the transport and metabolism of cholesterol)

(63) Which disorders are associated with defect in enzymes?

- **1) Lysosomal storage diseases**
  2) Glycogen storage diseases
  3) Alkaptonuria

(64) What is Tay-Sachs Disease?

- **Lysosomal storage disease caused by inability to catabolize GM2 gangliosides due to deficiency of enzyme Hexosaminidase- α subunit.**

(65) What is Niemann- Pick disease?

- **Lysosomal storage disease characterized by accumulation of Sphingomyelin due to inherited deficiency of Sphingomyelinase**

(66) What is Gaucher Disease?

- **Lysosomal storage disorder with deficiency of glucocerebrosidase enzyme deficiency accumulating glucocerebroside.**

(67) What are Gaucher cells?

- **Glucocerebrosides accumulating in massive amounts within phagocytic cells throughout body is known as Gaucher cells**
- **Seen in Liver, Bone marrow, Lymphnodes, etc.**

(68) In which type of Gaucher Disease, Splenomegaly is seen?

- **Gaucher disease Type- I**

(69) What are glycogenoses?

- **Glycogen storage disease resulting from hereditary deficiency of one of the enzyme involved in synthesis or degradation of glycogen**

(70) What are subgroup of Glycogen storage disease?

- **1) Hepatic form- Deficiency of enzyme Glucose 6 phosphatase**
  - **Deficiency of enzyme liver phosphorylase**
- **2) Myopathic form- Deficiency of muscle phosphorylase**
- **3) Associated with deficiency of α- glucosidase(Acid maltase)→ cardiomegaly**

(71) What are Alkaptonuria?

- **Lack of Homogentisic oxidase , an enzyme converting Homogentisic acid to methyacetoacetic acid.**
- **Black coloured urine.**

(72)What is karyotyping?

- **Karyotyping is study of chromosomes.**

(73)In which phase karyotyping is done?

- **Karyotyping is done in arrest dividing cells in metaphase with spindle inhibitors and stain.**

(74)Which stain is used in karyotyping?

- **Giemsa stain is used in karyotyping ,hence known as G- banding.**

(75) What is euploid?

- **Euploid is exact multiple of haploid chromosomes.**

(76) What is Aneuploidy?

- **Any error in meiosis or mitosis and cell acquires a chromosome component not an exact multiple of 23.**

(77)What is mosaicism?

- **Mitotic error in early development giving rise to two or more population of cells with different chromosomal component in same individual.**
- **More common in sex chromosomes. Example: Turner's syndrome, Down syndrome.**

(78)What is deletion?

- **Loss of portion of chromosome.**

(79)What in Inversion?

- **Rearrangement that involves two breaks within single chromosome with reincorporation of inverted intervening segment.**
  A) Paracentric- involving one arm
  B) Pericentric -involving both arms.

(80)What is isochromosome?

- **One arm of chromosome is lost and remaining arm is duplicated so either two short arms or two long arms.**

(81)What is translocation?

- **Segment of one chromosome transferred to another is translocation.**

(82) What is the most common cause of Down syndrome?

- **Meiotic nondisjunction**

(83) Examples of Trisomy.

- **Down syndrome (Chromosome 21)**
- **Edward syndrome (Chromosome 18)**
- **Patau syndrome (Chromosome 13)**

(84)What is Di-George syndrome?

- **22q11 deletion**
- **Thymic hypoplasia**
- **Parathyroid hypoplasia**
- **Cardiac malformation**

(85) What is Lyon hyposthesis?

- **1) Only one of X chromosome is genetically active**
  2) Other X undergoes heteropyknosis and is inactive (maternal or paternal)
  3) Inactivation on all cells of blastocyst
  4) Inactivation persists in all cells

(86) What is Barr Body (X- chromatin)?

- **Inactive X gene in females**
- **Seen in interphase nucleus as darkly staining small mass in contact with nuclear membrane**

(87)What is Klinefelter syndrome?

- **Male hypogonadism when there are two or more X chromosome and one or more Y chromosome 46XXY (90%)**

(88) What is Turner syndrome?

- **Complete or partial monosomy of X chromosome and characterized by hypogonadism in females**

(89) What is Hemaphrodite?

- **Presence of both ovarian and testicular tissue is known as Hemaphrodite.**

(90) What is Pseudohemaphroditic?

- **Disarrangement between phenotype and gonadal sex (ovaries with male external genitals)**

(91) What does PCR analysis do?

- **Amplification of DNA**

(92) What does FISH do?

- **Uses DNA probes that recognize sequences specific to particular chromosomal regions**

(93) What is Epigenetics?

- **Study of heritable chemical modification of DNA or chromatin that does not alter the DNA sequence itself.**

HEMODYNAMICS

(1) How much body weight is of water?

- **60% (2/3rd Intracellular & 1/3rd Extracellular).**

(2) How much body water is in plasma?

- **5%**

(3) What is Edema?

- **An abnormal increase in interstitial fluid within tissues.**

(4)What is Anasarca?

- **Severe, generalized edema with widespread subcutaneous swelling.**

(5) What is Transudate?

- **Protein poor fluid.**
- **Eg., Seen in Heart failure, Renal failure, Hepatic failure, Malnutrition.**

(6) What is Exudate?

- **Protein rich fluid—Inflammatory.**

(7) What are Pathophysiologic causes of edema?

- **Increased in Hydrostatic pressure.**
- **Decreased in Plasma osmotic pressure.**
- **Lymphatic obstruction**
- **Sodium retention**
- **Inflammation**

(8) What are causes of increased hydrostatic pressure?

- **Congestive cardiac failure**
- **Cirrhosis of liver**
- **Deep vein Thrombosis**

Dr. CHERRY SHAH

(9) What are causes of reduced plasma osmotic pressure?

- **Hypoproteinemia**
- **Nephrotic syndrome**
- **Cirrhosis of liver**
- **Malnutrition**

(10) What are causes of salt and water retention?

- **Excessive salt intake**
- **Increased Renin-angiotensin, Aldosterone secretion**
- **Primary disorders of kidney**
- **Congestive cardiac failure**
- **Malignancies**

(11) What are causes of lymphedema?

- **Filariasis**
- **Malignancy invasion**

(12) Which are most common organs to be affected by edema?

- **Brain**
- **Lung**
- **Subcutaneous tissue**

(13) What is dependant edema?

- **Distribution of fluid affected by gravity is dependant edema**
- **Eg. Edema of Legs when standing**

(14) What is pitting edema?

- **Finger pressure over tissue displaces interstitial fluid leaving depression.**

(15) What is cause of periorbital edema?

- **Severe renal disease**

(16) What is hyperemia?

- **It is active process in which arteriolar dilation leads to increased blood flow.**
- **Tissue turn red due to engorgement of vessels (erythema)**

(17) What is congestion?

- **It is a passive process resulting from reduced outflow of blood from tissue**
- **Dusky reddish blue color (cyanosis)**

(18) What is the consequence of chronic passive congestion?

- **Ischemic tissue injury and scarring**
- **Small hemorrhagic foci - Cluster of Hemosiderin laden macrophage**

(19)What are heart failure cells?

- **In chronic pulmonary congestion, septa gets thickened, fibrotic and alveoli contain numerous Hemosiderin laden macrophages that are known as heart failure cells.**

(20) What is nutmeg liver?

- **In chronic passive hepatic congestion, centrilobular region becomes red brown accentuated against surrounding zones of uncongested tan liver that gives appearance of nutmeg.**
- **There is centrilobular hemorrhage, hemosiderin laden macrophages and degeneration of hepatocytes.**

(21)What is Hemorrhage?

- **Extravasation of blood in extravascular space.**

(22)What is Hematoma?

- **Hemorrhage when contained within a tissue accumulation is called Hemorrhage.**

(23)What is Petechie?

- **Minute 1-2 mm hemorrhage in skin, mucus membrane or serosal surface is called Petechie.**
- **Reasons are Thrombocytopenia, Uremia.**

(24)What is Purpura?

- **Larger hemorrhages >3 mm are called Purpura.**
- **Vasculitis.**
- **Amyloidosis.**

(25)What is Echymoses?

- **Larger > 1 to 2 cm are Echymoses – leads to Bruise.**
- **Red cells degraded -> Phagocytosed by Macrophage -> Hemoglobin ->Convert to Bilirubin (blue-green) -> Hemosidrin (gold brown) -> Bruise.**

(26)What are consequences of Hemorrhage?

- **Hemorrhagic Shock.**
- **Iron Deficiency Anemia.**

(27)What is Thrombosis?

- **Blood clot formation within intact vessel.**

(28) Which are components of hemostasis & thrombosis?

- **Vascular wall**
- **Platelets**
- **Coagulation cascades**

(29) What is hemostasis?

- **Hemostasis is consequences of tightly regulated process maintaining blood in fluid state in normal vessels, but also permits rapid formation of hemostatic plugs at site of injury.**

(30) What is primary Hemostasis?

- **Endothelial injury >> which exposes thrombogenic subendothelial ECM>> causes platelets adherence and activation>> there is change in shape of platelets and release of secretory granules>> platelets aggregation>> Formation of hemostatic plugs.**

(31) What is Secondary hemostasis?

- **Injury>> Tissue factors exposed (Factor III & Thromboplastin) >> Acts with factor VII >> Thrombin formation>> Cleaves fibrinogen>> Fibrin>> Fibrin meshwork.**

(32) Which is counter regulatory mechanism for hemostatic plug?

- **Tissue Plasminogen activator**

(33) Which factors in endothelium exhibit Anti-platelet activity?

- **Prostacyclin & Nitric oxide**

(34) Which factors in endothelium exhibit Anti-coagulant effect?

- **Thrombomodulin**
- **Protein S, a cofactor of protein C.**
- **Tissue factor pathway inhibitor.**

(35) Which factor in endothelium exhibits Fibrinolytic effect?

- **Tissue type Plasminogen activators**

(36) How do endothelial cells show effect on platelets?

- **Endothelial injury>> Adhesion of platelets through interaction with Von Willebrand factor.**

(37) How does endothelial cell exhibit procoagulant effect?

- **In presence of cytokines, endothelial cells synthesize tissue factor which activates extrinsic coagulation pathway.**

(38) How does endothelial cells exhibit Anti-fibrinolytic effects?

- **Endothelial cells secrete inhibitors of plasminogen activator which limit fibrinolysis.**

(39) What is role of platelets in vascular injury?

- **Adhesion and shape change**
- **Secretion**
- **Aggregation**

(40) How is platelet adhesion mediated?

- **Via Interaction with vWF (Von Willebrand factor).**

(41)Which disease occurs if receptor of vWF (Von Willebrand factor) is absent?

- **Bernard Soulier.**

(42)Which types of granules are present in platelets?

- **Alpha (α) granules.**
- **Dense granules.**

(43)What does α granule contain?

- **Adhesion molecule of P- selectin.**
- **Fibrinogen.**
- **Fibronectin.**
- **Factor V, VIII and IV.**
- **Platelet derived Growth Factor (PDGF).**
- **Tumor Growth Factor-β (TGF-β).**

(44)What does Dense Granules of Platelets contain?

- **ADP.**
- **ATP.**
- **Calcium.**
- **Histamine.**
- **Serotonin.**

(45)How does Serotonin of Platelets help?

- **Secretion of Calcium from dense granules → activate coagulation cascade.**
- **ADP → potent platelet activator.**

(46)How does platelet aggregation occur?

- **Adhesion – Release of granules.**
- **ADP and TxA2 – Amplifies platelet aggregation → Hemostatic plug.**
- **Coagulation cascade – Thrombin → Platelet plug.**

(47)What is importance of GpIIb-IIIa receptor in platelet?

- **Induces binding of fibrinogen → Platelet aggregation.**
- **Absence results in bleeding disorder→ Glanzmann Thromboasthenia.**

(48)How do leucocytes adhere to platelets?

- **Through P-selectin.**

(49)What is Thromboplastin?

- **A membrane bound lipoprotein factor II also known as Tissue Factor which activates extrinsic pathway of Coagulation Cascade.**

(50)Which are standard assays to asses Coagulation Pathway?

- **PT & APTT.**

(51) What does ProthrombinTime assess?

- **Function of factors VII, X, II, V and fibrinogen (extrinsic pathway).**

(52) Why is citrate used in Prothrombin time?

- **It chelates Ca^{++} and presents spontaneous clotting.**

(53) Principle of PT?

- **Adding tissue factor and phospholipids to citrated plasma and add Ca^{++} externally.**

(54) What does aPTT assay?

- **Screens function of proteins of intrinsic pathway- XII, XI, IX, VIII, X, V, II and fibrinogen.**

(55) How intrinsic pathway is initiated?

- **Activates factor XII, phopholipids and Ca^{++}.**

(56) How does thrombin exhibit proinflammatory action?

- **Through activation of protease activated receptors on endothelial cells.**

(57) Which endogenous anticoagulant control clotting (Natural anticoagulants)?

- **1) Antithrombin- III --- Inhibits activity of thrombin and factors IX, X, XI, XII.**
  --- Acts by binding to heparin like molecules.
  2) Protein C & Protein S --- Vit K dependent.
  ---Acts in complex inactivating factor Va and VIIIa.
  3) TFPI--- Protein by endothelium
  ---Inactivates tissue factor-VIIa.

(58) Which enzyme activates fibrinolysis? How?

- **Enzyme <u>Plasmin</u>, by breaking down fibrin & interfering with its polymerization.**

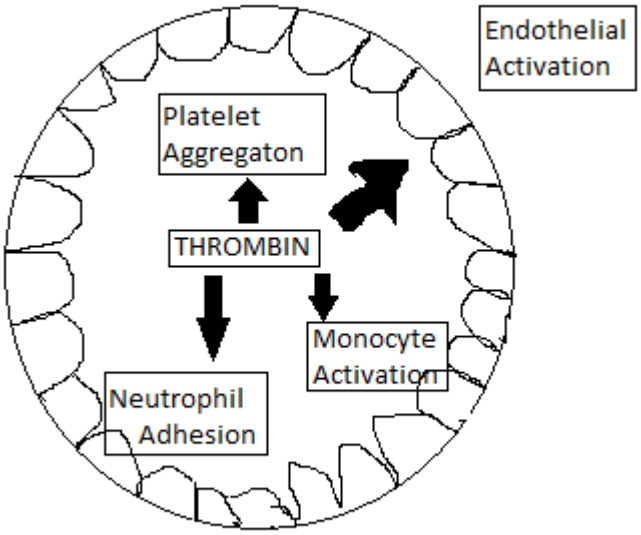
(59) How is D-Dimer useful for DIC, Deep vein thrombosis and Pulmonary embolism?

- **Because of fibrinolysis FSP are formed which act as weak anticoagulants.**

(60) Which is potent plasminogen activator?

- **t – PA from endothelium.**
- **Confirms fibrinolytic activity to sites of recent thrombosis.**
- **Urokinase like PA**
- **Bacterial enzyme streptokinase.**

(61)What is role of thrombin in hemostasis?



(62)What is Virchow's Triad?

- **Three primary abnormalities causing thrombus formation.**
- **A) Endothelial injury**
- **B) Stasis of turbulent blood flow.**
- **C) Hypercoagulability of blood.**

(63)What are consequences of endothelial injury?

- **Thrombus formation within cardiac chambers due to Myocardial infarction.**
- **Over ulcerated plaques in atherosclerotic arteries.**
- **Vasculitis.**

(64)Which procoagulant factors are produced by endothelium?

- **Platelet adhesion molecules.**
- **Tissue Factor.**
- **PAIS.**

(65) Which anticoagulant factors are produced by endothelium?

- **Thrombomodulin.**
- **PGI_2.**
- **t-PA.**

(66)What alteration occurs in blood flow leading to thrombus formation?

- **Turbulence.**
- **Stasis.**

(67)What can be cause of Turbulence?

- **Atherosclerotic plaque.**

(68) What can be cause of Stasis?

- **Aneurysm.**
- **Hyperviscocity like in Sickle cell Anemia.**

(69)What is Thrombophilia or Hypercoagubility?

- **Any alteration in coagulation pathway predisposing to thrombosis.**

(70)Causes of Thrombophilia?

- **Primary Genetic cause- V gene mutation (Leiden Mutation).**
  Prothrombin gene mutation.

  Antithrombin III deficiency
  Protein C deficiency
  Protein S deficiency

- **Secondary cause- Bed rest, MI, AF, Cancer, Injury, DIC etc.**

(71)Role of homocysteine in thrombosis .

- **Prothrombin**
- **Caused due to deficiency of cystathione beta-synthetase**

(72)What can reduce homocysteine levels?

- **Folic acid**
- **Pyridoxine**
- **Vitamin B_{12}**

(73)What is heparin induce thrombocytopenia?

- **Thrombocytopenia following administration of unfractioned heparin inducing antibodies causing consumption activation platelets causing thrombocytopenia.**

(74)What is anti phospholipids antibody syndrome?

- **Anti phospholipids antibody syndrome has clinical manifestation like recurrent thrombosis, recurrent miscarriage , cardiac valve vegetations, thrombocytopenia induce hypercoagulation.**

(75)What are lines of Zahn?

- **Thrombi having gross and microscopic laminations representing pale platelet and fibrin deposits alternating with dark red cell rich layers.**

(76)What is significance of lines of Zahn?

- **They signify that thrombus is antemortem in opposite to non laminate postmortem thrombi.**

(77)What are manual thrombi?

- **Thrombin occurring in heat chambers or in aortic lumen.**

(78)Which are common sites of arterial thrombi?

- **In descending order,**
  Coronary
  Cerebral
  Femoral

(79)What are arterial thrombi formed of?

- **Arterial thrombi formed of friable meshwork of platelets ..,fibrin, red cells and leucocytes.**

(80)What are red thrombi?

- **Venous thrombi as they contain more enmarked red cells and few platelets.**

(81) Give common sites of venous thrombi.

- **90% lower extremity, upper extremity, periprostatic plexus, ovarian /periuterine veins.**

(82) What are differences between postmortem and antemortem clots?

Gelatinous with dark red dependent portion where RBCs have settled by gravity and a yellow chicken fat.

- **Not attached to underlying wall.**

(83)What are vegetations?

- **Thrombi on heat valves are called vegetations. Example: infective endocarditis.**

(84)Which kind of endocarditis occurs in SLE?

- **Libman sacks**

(85)What are different fates of thrombus?

- **Propagation**
- **Embolization**
- **Dissolution**
- **Organization and recanalisation**

(86) Causes of venous thrombosis.

- **Superficial-> Sephanous-> Varicosity-> varicose ulcers**
- **DVT-> larger leg veins popliteal , femoral , iliac**

Lead to pulmonary infarction with hypercoagulable state, immobilization

(87)What is migratory thrombophlebitis or Trousseau syndrome?

- **Tumor is associated with inflammation and coagulation factors released from tumor cells contributing to increased risk of thromboembolism called as migratory thrombophlebitis or Trousseau syndrome.**

(88)What is DIC?

- **Sudden or insidious onset of widespread fibrin thrombi in microcirculation.**
- **Use of platelets and coagulation factors.**
- **Bleeding occur.**

(89)What is embolus?

- **Detached intravascular solid, liquid or gaseous mass carried by blood to a site distant from its point of origin.**

(90)Give types of embolus.

- **Fat droplets**
- **Nitrogen bubbles**
- **Cholesterol (Atherosclerotic)**
- **Foreign bodies**
- **Tumor**
- **Bone fragments**

(91) What is most common cause of pulmonary embolism?

- **DVT.**

(92) What is Saddle embolism?

- **Embolus occurring in main Pulmonary Artery at bifurcation.**

(93)What is Paradoxical embolism?

- **Pulmonary embolus passing through inter atrial or inter ventricular defect and gain access to systemic circulation.**

(94)Why pulmonary infarction doesn't occur?

- **As lung has dual blood supply.**

(95) Most common cause of Fat emboli?

- **Fracture of long bones having fatty marrow.**

(96)What is Fat embolism syndrome?

- **Pulmonary insufficiency + Neurological symptoms + Aneurysm + Thrombocytopenia.**

(97)What is Decompression sickness?

- **Individuals experience sudden decrease in atmospheric pressure e.g. scuba and sea divers.**

(98)What is Caisson's disease?

- **Chronic form of decompression sickness – where persistence of gas emboli in skeletal system leads to multiple foci of ischemia, necrosis in femoral heads, tibia, humerus.**

(99)What is an Infarct?

- **An area of ischemic necrosis caused by occlusion of either arterial supply or venous drainage.**

(100)What are causes of Infarction?

- **Thrombosis**
- **Embolism**
- **Local vasospasm**
- **Atherosclerotic plaque**
- **Vessel compression**
- **Torsion**
- **Traumatic rupture**

(101) Types of Infarction

- **Red infarction occur in:**
  - **(1) Venous occlusions (ovary)**
  - **(2) In loose tissue (lung)**
  - **(3) In dual circulation tissue (lung & Small intestine)**
  - **(4) Angioplasty**
- **White infarction occur in:**
  - **(1) Arterial occlusion in Heart, Spleen and Kidney.**

(102) Ischemic coagulative necrosis except BRAIN where there is liquefactive necrosis.

(103) Factors influencing infarct

- **Nature of vascular supply- alternative**
  - ✓ **Dual vascular supply in:**
    - **Lung – Pulmonary and Bronchi**
    - **Liver – Hepatic and Portal**
    - **Hand and forearm – Radial and Ulnar**
- **More prone to infarction are SPLEEN and KIDNEY due to end arteries.**
- **Rate of occlusion development.**
- **Valuability to Hypoxia:**
  - ✓ **Neurons irreversible damage—3-4 mins**
  - ✓ **Myocardium irreversible damage —20-30 mins**
- **O_2 content of blood.**

SHOCK

(104) What is Shock?

- **Shock is Systemic hypotension due to either reduced cardiac output or reduced effective circulatory blood volume leading to impaired tissue perfusion and cellular hypoxia.**

(105) Causes of shock

- **Cardiogenic:**
  - ✓ **Low cardiac output due to myocardial pump failure**
  - ✓ **Myocardial damage (infarction)**
  - ✓ **Ventricular arrhythmia**
  - ✓ **Cardiac temponade**
  - ✓ **Pulmonary embolism**
- **Hypovolemic:**
  - ✓ **Loss of blood or plasma volume**
  - ✓ **Low cardiac output**
- **Septic:**
  - ✓ **Infection- vasodilatation and peripheral pooling of blood.**
- **Neurogenic:**
  - ✓ **Less common- Anesthetic accided Spinal cord injury**
- **Anaphylactic**

(106) Commonest shock leading to death?

- **Septic – by gram positive bacteria.**

(107) Major factors contributing to septic shock?

- **Inflammatory mediators**
- **Complements**
- **Endothelial cell activation and injury**
- **Metabolic abnormalities**
- **Immature suppression**
- **Organ dysfunction**

(108) What is " Waterhouse Frideichsen Syndrome"?

- **In septic shock- Patients exhibit Insulin resistance—lead to Hyperglycemia – Decreases neutrophilic fuction—Deficit of Glucocorticoids—Depression of synthetic capacity of adrenal glands or frank adrenal necrosis due to DIC (Disseminated Intravascular Coagulation).**

(109) Stages of shock

- **Initial Nonprogressive: Reflux compensatory mechanisms activated and perfusion of organs maintained**
- **Progressive: Tissue hypoperfusion- Hypoxia- Acidosis.**
- **Irreversible: Severe cell and tissue injury.**

(110) Organ changes in shock

- **Adrenal: Cell lipid depletion**
- **Kidney: Acute tubular necrosis**
- **Lungs: Diffuse alveolar damage (SHOCK LUNG)**
- **In septic shock: DIC(Disseminated Intravascular Coagulation). Micro thrombi in brain, heart, lungs, kidney, adrenal glands.**
- **In GIT: Petechial hemorrhage.**

(111)Which tissues do not revert for ischemic shock?

- **Neuronal and myocytes**

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Immunity

(1) What is Innate immunity?

- **Defense mechanism present even before infection- first line defense**

(2)What is Adaptive immunity?

- **Mechanisms that are stimulated by microbes-more powerful than innate immunity.**

(3)What are components of innate immunity?

- **Epithelial barriers**
- **Dendritic cells (Produce Type I Interferon)**
- **Natural killer cells**
- **Plasma protein including proteins of complement system.**

(4)What are components of Adaptive immunity?

- **Lymphocytes and their products including antibodies.**

(5)What is humoral Immunity?

- **Adaptive type of immunity which protects against extracellular microbes and toxins-mediated by B lymphocytes, antibodies and immunoglobulins.**

(6)What is cellular immunity?

- **Defense against intracellular microbes mediated by T –lymphocytes.**

(7)What are naive cells?

- **Mature lymphocytes that have not encountered the antigen for which they are specific.**

(8)What are effecter cells?

- **Mature lymphocytes that are activated by recognition of antigens performing function of eliminating microbes.**

(9)What are memory cells?

- **Mature lymphocytes which live in state of heightened awareness and are able to combat microbes if it returns.**

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(10)Where does T –lymphocytes develop?

- **Thymus**

(11)What % of T lymphocytes are present in blood?

- **60-70%**

(12)What is TCR?

- **T-cell Receptor present on T cell which recognises a specific cell bound antigen.**

(13)Where does B –lymphocytes develop?

- **B-lymphocytes develop from precursors in bone marrow.**

(14)What % of B lymphocytes are present in blood?

- **10% to 20% are present in blood.**
- **Also present in lymph nodes, spleen and mucosa associated lymphoid tissues.**

(15)What are antigen binding components of B cell receptors?

- **IgM and IgG antibodies**

(16)What is origin of plasma cells?

- **After stimulation by antigen, B cells develop into PLASMA CELLS which secret antibodies.**

(17)What are Dendritic cells?

- **Antigen presenting cells for initiating primary T-cell responses against protein antigen.**

(18)Where are dendritic cells located?

- **Dendritic cells located under epithelium and in interstitium of all tissue.**

(19)What are Langerhans cells?

- **Langerhans cells are immature dendritic cells within epidermis.**

(20)What are follicular dendritic cells?

- **Follicular dendritic cells are present in germinal centers of lymphoid follicles playing role in humoral immunity.**

(21)What are functions of macrophages in Immunity?

- **Function as antigen presenting cells to T-cell activation**
- **Key effector cells in cell mediated immunity and humoral immunity.**

(22) What are natural killer cells?

- **Constitutes 10 to 15% of blood**
- **Larger than lymphocytes**
- **Kill variety of infections or tumor cells without prior exposure**
- **<u>CD16 and CD56</u> Identify NK cells**
- **Also secret cytokines**

(23) Which are the generative organs for T and B lymphocytes?

- **Thymus and bone marrow**

(24) Which are peripheral lymphoid organs?

- **Lymphnodes, Spleen, Mucosal and Cutaneous lymphoid tissue.**

(25) Give examples of mucosal lymphoid tissue.

- **Pharyngeal tonsils and Peyer's patches**

(26) What is germinal centre of lymphnode?

- **If B cells in follicle of lymphnode has recently responded, the follicle may contain a central region called as germinal centre.**

(27) What is Major Histocompatibity Complex (MHC) ?

- **They are responsible for tissue compatibility of individual.**
- **Physiologic function is to display peptide fragments of proteins for recognition by antigen specific T cells.**

(28) Where is MHC located?

- **On small segment of Chromosome 6.**

(29) Which cells are class I MHC restricted?

- **CD8+ T cells**

(30) Which cells are class II MHC restricted?

- **CD4+ T cells**

(31) Which inflammatory diseases are associated with HLA-B27?

- **Ankylosing Spondylitis**
- **Post infections Arthropathy**

(32) Which diseases are associated with DR locus?

- **Autoimmune diseases**

(33)Which diseases are associated with HLA –BW 47 and HLA-A?

- **21-hydroxylase deficiency**
- **Hemochromatosis**

(34)Which cytokines mediate innate immunity?

- **TNF,IL-F,IL-12**

(35)Which cytokines mediate Adaptive immunity?

- **IL-2,IL-4,IL-5**

(36)What is hypersensitivity?

- **An excessive response to antigen is called Hypersensitivity.**

(37)What is Immediate or Type I Hypersensitivity?

- **Rapid immunologic reaction occurring within minutes of antigen antibody reaction in individual previously sensitized. Mast cells play important role called ALLERGY.**

(38) What are mediators of Immediate Hypersensitivity reaction?

- **Ig E antibody- dependent on activation of mast cells and leucocytes.**

(39)What is the difference between mast cell and basophils?

- **Mast cells are present in tissue near blood vessels and nerves while basophils are circulating in blood.**

(40)What is type II or Antibody mediated Hypersensitivity?

- **Cased by antibodies that react with antigens present on cell surface or extracellular matrix.**

(41)Which are the examples of Type II Hypersensitivity reaction?

- **1)Transfusion Reactions**
- **2)Hemolytic Disease of Newborn**
- **3)Autoimmune Hemolytic Anemia**

(42) What is Type III Hypersensitivity reaction?

- **Type III Hypersensitivity is a Hypersensitivity in which antigen-antibody complexes produce tissue damage mainly by eliciting inflammation at sites of deposition.**

(43) Which are examples of Type III Hypersensitivity reaction?

- **Examples of Type III Hypersensitivity reactions are:**
    - **SLE, Poststreptococcal glomerulonephritis, polyarteritis nodosa.**

(44) What is Type IV Hypersensitivity reaction?

- **Type IV Hypersensitivity reactions is a cell-mediated hypersensitivity reaction.**
- **It's a hypersensitivity initiated by antigen-activated T lymphocytes including CD4+ T cells and CD8+ T cells.**

(45) What is fibrinoid necrosis?

- **The necrotic tissue deposits of immune complexes, complements and plasma proteins produce a smudgy eosinophilic deposit obscuring cellular details is known as fibrinoid necrosis.**

(46) What is Arthus reaction?

- **Arthus reaction is a localized area of tissue necrosis resulting from acute immune complex Vasculitis usually eliciated in skin.**

(47) Give examples of Type IV Hypersensitivity.

- **Examples of Type IV Hypersensitivity are:**
  - **Type 1 Diabetes mellitus**
  - **Multiple sclerosis**
  - **Rheumatoid arthritis**
  - **Crohn's disease**

(48) What is Autoimmunity?

- **Autoimmunity is an immune reaction against self-antigens.**

(49) Which are organ specific Autoimmune diseases?

- **Organ specific autoimmune diseases are mediated by T cells.**
- **Examples are: Type 1 Diabetes mellitus**
  Multiple sclerosis

(50) Which are T-cell mediated systemic Autoimmune diseases?

- **T-cell mediated systemic Autoimmune diseases are:**
  - **Rheumatoid arthritis**
  - **Systemic sclerosis**

(51) Which are organ specific Antibody mediated Autoimmune diseases?

- **Organ specific Antibody mediated Autoimmune diseases are:**
  - **Autoimmune hemolytic anaemia**
  - **Autoimmune thrombocytopenia**
  - **Grave's disease**

(52) Which is systemic Antibody mediated Autoimmune disease?

- **Systemic Antibody mediated Autoimmune disease is:**
  Systemic lupus erythematosis (SLE)

(53) What are mechanisms of autoimmunity?

- **Mechanisms of autoimmunity are as follows.**
  Combination of the inheritance of susceptibility genes contributing to breakdown of self-tolerance and environmental triggers such as infections and tissue damages promoting activation of self-reactive lymphocytes.

(54) What are Antinuclear Antibodies (ANA)?

- **Antinuclear Antibodies are Antibodies directed against nuclear antigens.**
- **Four groups are there:**
  - **Antibodies to DNA**
  - **Antibodies to Histones**
  - **Antibodies to Non-Histone proteins**
  - **Antibodies to Nucleolar antigens.**

(55) What is method of detecting ANA?

- **Method of detecting ANA is Indirect Immunoflorescence.**
- **Various staining properties of Indirect Immunoflorescence are:**
  - **Diffuse nuclear staining: Antibodies against Chromatin, Histones and double-stranded DNA**
  - **Peripheral or rim staining: Antibodies against double-stranded DNA**
  - **Speckeled pattern: Antibodies against Non-nuclear constituents.**
  - **Discrete spots: Antibodies against RNA.**

(56) Which cells allow viral transmission of HIV?

- **Cells allowing viral transmission of HIV are: Dendritic cells or CD4+ lymphocytes.**

(57) Does HIV spread through breast milk?

- **Yes, HIV spreads through breast milk.**

(58) Which antigen is first seen in HIV?

- **Antigen is first seen in HIV is: P24.**

(59) Which glycoprotein of HIV binds to CD4 cells?

- **Gp-120 binds to CD4 cells.**

(60) Which parasitic opportunistic infections occur in AIDS?

- **Parasitic opportunistic infections occuring in AIDS are:**
  - **Cryptosporidiosis**
  - **Toxoplasmosis**

(61) Which fungal opportunistic infections occur in AIDS?

- **Fungal opportunistic infections occuring in AIDS are:**
  - **Candidiasis**
  - **Histoplasmosis**
  - **Cryptococcus**

(62) Which bacterial opportunistic infections occur in AIDS?

- **Bacterial opportunistic infections occurring in AIDS are:**
  - **Atypical mycobacterial infections**
  - **Salmonella**
  - **Nocardiasis**

(63) Which viral opportunistic infections occur in AIDS?

- **Viral opportunistic infections occurring in AIDS are:**
  - **Cytomegalovirus**
  - **Herpes simplex**

(64) Which tumors occur in AIDS?

- **Tumors occurring in AIDS are:**
  - **Kaposi sarcoma**
  - **Lymphoma**
  - **Carcinoma cervix**
  - **Anal cancer**

(65) Which are common sites of lymphoma in AIDS?

- **Common sites of lymphoma in AIDS are:**
  - **CNS- Most common**
  - **GIT**
  - **Orbit**
  - **Salivary glands**

(66) What is Amyloid?

- **Amyloid is defined as a pathologic proteinaceous substance deposited in the extracellular space in various tissues and organs of the body.**

(67) What is the appearance of Amyloid on H & E stain?

- **Amyloid is amorphous, eosinophilic and hyaline in appearance on H & E stain.**

(68) Which is most widely used method to detect Amyloid?

- **CONGO RED STAIN- impending pink or red colour to Amyloid.**
- **Polarizing microscope- Apple green birefringence.**

(69) What is mechanism by which Congo red stains Amyloid?

- **Mechanism by which Congo red stains Amyloid is:**
  - **Cross ß- pleated sheet conformation of Amyloid**

(70) What is chemical composition of Amyloid?

- **Chemical composition of Amyloid is:**
  - **95 % - Fibril proteins**
  - **5 %- P-component and glycoproteins**

(71) Which are three distinct forms of Amyloid?

- **Three distinct forms of Amyloid are:**

  (1) AL- Amyloid Light chain- Derived from Ig light chains

  (2) AA- Amyloid Associated- Derived from unique non-Ig protein synthesized by liver
  - Associated with chronic inflammation (Secondary Amyloidosis)

  (3) Aß- Produced by ß Amyloid precursor protein- Found in Alzheimer's disease.

(72) Which other biochemically distinct proteins are found in Amyloid?

- **1)Transthyretic – binds and transports thyroxine and retinol**
- **2)β2 microglobulin – component of MHC class i molecules found in patients with long term hemodilysis**
- **3) Prion proteins**

(73) What is pathogenesis of Amylodosis?

- **It results from abundant folding of proteins which are deposited as fibrils in extracellular tissues disrupting normal function**

(74) What is primary Amyloidosis?

- **Associated with immunocyte disorder usually AL type**

(75) What is secondary Amyloidosis?

- **It occurs as the complication of underlying chronic inflammation**
- **Usually AA protein**

(76) What are Bence Jones proteins?

- **Light chain of either k or λ variety elaborated in serum**

(77)What are common inflammatory conditions responsible for secondary Amyloidosis?

- **Rheumatoid arthritis**
- **Amkylosis spondylitis**
- **Crohn's disease, ulcerative colitis**

(78) In which carcinomas secondary Amyloidosis is commonly seen?

- **Renal cell carcinoma**
- **Hodgkin's Lymphoma**

(79) Give examples of familial form of Amyloidosis

- **Familial Mediterranean Fever by gene called PYRIN**

(80) What are common sites of localized Amyloidosis?

- **Lung, larynx, skin, urinary bladder, tongue**
- **AL protein- represent primary amyloidosis**

(81) In which endocrine tumors Amyloid is found?

- **Medullary carcinoma of thyroid gland**
- **Islet tumor of Pancreas**
- **Pheochromocytoma**
- **Undifferentiated carcinoma of stomach**
- **In islets of Langerhans in individuals with type II diabetes mellitus**

(82) What is senile systemic Amyloidosis?

- **Seen in elderly patients generally in heart**
- **Composed of normal transthyretin**

(83) What is sago spleen?

- **Amyloid deposits in splenic follicles producing tapioca like granules called as SAGO SPLEEN**

(84) What is Lardaceous spleen?

- **Amyloid involves walls of splenic sinuses and connective tissue framework in red pulp giving rise to large map like area of amyloidosis known as Lardaceous spleen**

(85) Which organs are commonly involved in Amyloidosis?

- **Kidney, liver, spleen, heart**
- **Adrenal, thyroid gland, pituitary gland, GIT**

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INFECTIOUS DISEASES

(1)What are Prions?

- **Prions are composed of abnormal forms of host protein -Prion protein (Prp).**
- **Cause transmissible encephalopathies –Example: Kuru, CJD etc.**
- **They are found in neurons.**

(2)Which virus form inclusion bodies?

- **Cytomegalovirus**
- **Herpes**

(3)What are inclusion bodies?

- **Some viral particles aggregate within cells ,they infect and form inclusion bodies.**

(4)Give example of virus causing chronic infection.

- **Hepatitis B**

(5) Give example of virus causing benign or malignant tumor.

- **HPV**

(6) Give example of opportunistic fungi.

- **Candida**
- **Aspergillus**
- **Mucor**
- **Cryptococcus**

(7) Give example of blood borne parasites.

- **Plasmodium**
- **Trypanosoma**
- **Leishmania**

Dr. CHERRY SHAH

(8)Which parasitic infection is caused by sexual transmission?

- **Trichomonas vaginilis**

(9)Which are most common intestinal parasite?

- **E. Histolystica**
- **Giardia**

(10)Which organisms are transmitted by leucocytes?

- **HIV**
- **Mycobacteria**
- **Leishmania**

(11)Which infection occurs by placental fetal route?

- **Rubella**
- **Treponoma Pallidum**
- **CMV,HBV,HTLV-1,AIDS**

(12)Which viruses are transmitted through saliva?

- **Epstein barr virus**
- **Cytomegalovirus**
- **Mumps**

(13)To which cellular receptor HIV binds to enter cell?

- **HIV glycoprotein gp120 to CD_4 on T cell.**

(14) What is toxin? Give different types of toxin.

- **Any bacterial substance that contributes to illness is considered as toxin.**
- **Toxins are endotoxin compounds of bacterial cell. Example: lipopolysaccheridses**
- **Exotoxins- protein secreted by bacteria .Example: Enzymes and neurotoxin**

(15)Give examples of injurious effects of Host immunity.

- **Granulomatous inflammation in Tuberculosis produces tissue damage and fibrosis.**
- **Liver damage following HBV and HCV infection.**
- **Rheumatic Heart disease following streptococcal infection.**
- **Poststreptococcal glomerulonephritis.**

(16)Which sites are in accessible to host immune system?

- **Lumen of intestine**
- **Gallbladder**
- **Cysts caused by parasite having dense capsules.**

(17)Which antimicrobial peptides of cell help in immunity?

- **Defensin**
- **Cathecidins**
- **Thrombocidin**

(18)Which microorganisms grow inside phagocytes?

- **Mycobacteria**
- **Leishmania**
- **Toxoplasma**

(19)Which infections are cause of staphylococcus aureus?

- **Furuncle or Boil**
- **Carbuncle**
- **Paronychia**
- **Lung infections**
- **Ritter disease in children**

(20)Which infections are caused by streptococcus?

- **Suppurative infections of skin ,lungs, oropharynx and heart valves**
- **Post infectious syndrome like rheumatic fever glomerulonephritis, erythema nodosum**
- **Pharyngitis**

(21)What is significance of pseudomonas?

- **Most common cause of hospital acquired infections**
- **Corneal keratitis in users of contact lenses.**
- **Endocarditis, osteomyelitis**
- **External otitis in swimmers and diabetics**
- **Necrotizing pneumonia**

(22)Why does Mycobacteria retain stain even when treated with acid and alcohol?

- **They have unique waxy wall composed of mycolic acid which retains stain.**

(23)What does Mantoux test signify?

- **Delayed hypersensitivity in patient of tuberculosis after 2 to 4 weeks of infection.**
- **A positive result signifies T-cell mediated immunity to mycobacterial antigen.**

(24)In which conditions you see false negative results in Mantoux test?

- **Viral infections**
- **Sarcoidosis**
- **Malnutrition**
- **Hodgkin's lymphoma**
- **Immunosuppression**

(25) In which conditions you see false positive reactions in Mantoux test?

- **Atypical mycobacterial infection**
- **Prior BCG vaccination**

(26)What is the pathogenesis of caseating granuloma formation in tuberculosis?

- **It is result of hypersensitivity that develops in concert with protective host immune response.**

(27)Which cells are primarily affected in tuberculosis?

- **Macrophages**

(28)How macrophages are converted into epithelial cells and giant cells?

- **By IFN gamma**

(29)What is primary tuberculosis?

- **Form of tuberculosis that develops in previously unexposed , unsensitized person**
- **Source of organism are exogenous.**

(30)What are common lesions seen in progressive primary tuberculosis?

- **Lower and middle lobe consolidation**
- **Hilar lymphadenopathy**
- **Pleural effusion**
- **Cavitation rare**

(31)What is secondary tuberculosis?

- **Tuberculosis arising in previously sensitized host.**
- **Mostly by reactivation of latest infection.**

(32)What are common lesions seen in secondary tuberculosis?

- **Involving apex of upper of one of both lungs.**
- **Regional lymph nodes are less involved.**
- **Cavitations are common.**

(33)What are clinical manifestations of tuberculosis?

- **Low grade fever**
- **Weight loss**
- **Night sweats**
- **Anorexia**
- **Purulent sputum**

(34) How can tuberculosis be diagnosed?

- **History and physical examination**
- **Radiographic consolidation and cavitations**
- **Acid fast smears**
- **Culture- requires two weeks of infections**
  In liquid culture it may be diagnosed within 2 weeks
- **PCR amplification – can detect as low as 10 organisms**

(35) Which is gold standard test for diagnosis of Tuberculosis?

- **Culture as it also allow doing susceptibility**

(36) What atypical features are seen in AIDS associated Tuberculosis?

- **Increased frequency of false negative sputum smears and tuberculin test due to allergy**
- **Absence of characteristic granuloma**

(37)What is Ghon focus?

- **In primary tuberculosis distal airspace of lower part of upper lobe close to pleura is affected with development of inflammation and consolidation**

(38) What is Ghon focus complex?

- **The combination of infected tuberculosis, caseating parenchymal lung lesion with nodal involvement in primary tuberculosis.**

(39)What is Renke complex?

- **Ghon complex undergoing fibrosis due to development of cell mediated immunity undergoes fibrosis seen as calcification on radiology in primary tuberculosis.**

(40) What is progressive pulmonary tuberculosis?

- **May ensue in elderly and immunocompromised host**
- **Atypical lesion expand in lung, erodes the bronchi and vessels causing hemoptysis**

(41 What is Milliary pulmonary Tuberculosis?

- **Tuberculous organism drain through lymphatics, enter the venous blood and circulate back to lung**
- **Individual lesions are microscopic or small, visible foci of yellow white consolidation scattered through the lung parenchyma (like millets)**
- **Can lead to pleural effusion and empyema.**
-

(42)What is Systemic Milliary Tuberculosis?

- **It occurs when bacteria disseminated through systemic arterial system**
- **Seen mainly in liver, spleen and bone marrow, adrenal meninges, kidneys and fallopian tubes.**

43) What is isolated tuberculosis?

- **Tuberculosis appearing in any organs or tissue seeded hematogenously and presenting manifestation.**
  e.g, meninges, brain, kidneys, fallopian tubes, adrenal

(44) What is Pott disease?

- **When vertebrae are affected by tuberculosis it is known as Pott diseases.**

(45) What is Srofula?

- **Lymphadenitis mostly cervical occurring in patients with extra pulmonary tuberculosis.**

(46) In which type of leprosy neuronal involvement is seen?

- **Tuberculoid leprosy.**

(47)What are different types of leprosy?

- **Tuberculoid Leprosy – peripheral nerves most affected.**
- **Lepromatous Leprosy – earlobes and feet affected.**
- **Borderline Tuberculosis.**

(48) What is paucibacillary leprosy?

- **On microscopy leprosy shows granulomatous lesion but bacilli are almost never found – reflecting strong T-cell immunity.**
- **Generally seen in tuberculoid leprosy.**

(49) What are lepra cells?

- **In lepromatous leprosy microscopic picture shows large aggregate of lipid laden macrophages known as lepra cells, often filled with acid fast bacilli so also called multibacillary leprosy.**

(50) Which organism causes Syphilis?

- **Treponoma Palladium.**

(51) By which techniques Treponoma Palladium is visualized?

- **Silver stain.**
- **Dark field examination.**
- **Immunofloroscence.**

(52) What is Primary Syphilis?

- **Occurs approx. 3 weeks after contact with infected individual.**
- **Chancre at the site of invasion of penis, cervix, vagina or anus.**
- **Plenty of Spirochetes present.**
- **Can be stained by immunoflorescent stain.**

(53) What is chancre?

- **Single, firm, non-tender, raised, red lesion at site of treponemal invasion on penis, cervix, vagina or anus in primary syphilis is known chancre.**

(54) What is secondary syphilis?

- **It occurs 2 to 10 weeks after primary syphilis.**
- **There is proliferation of spirochetes within skin and mucocutaneous tissue.**

(55) What is condyloma lata?

- **Broad based, elevated plaque on moist areas of skin, anogenital region, inner thigh, axilla etc in secondary syphilis is known as condyloma lata.**

(56) What is tertiary syphilis?

- **Tertiary syphilis occurs after latent period of 5 years or more.**
- **Systemic manifestations like cardiovascular syphilis – aortitis syphilis, neurosyphilis – general paraesis, tabes dorsalis occurs in tertiary syphilis.**

(57) What is benign tertiary syphilis?

- **Benign tertiary syphilis is characterized by gummas at various sited like bone, skin etc. which occurs in tertiary syphilis.**

(58) What are gummas?

- **Nodular lesion in bone, skin, mucous membrane of mouth seen in benign tertiary syphilis is known as gumma.**
- **It is related to development of delayed hypersensitivity to bacteria.**

(59) What is congenital syphilis?

- **Congenital syphilis occurs when treponema pallidum crosses the placenta from an infected mother to fetus.**
- **It occurs while mother is in primary or secondary stage.**
- **It is manifested by nasal discharge.**
- **Hepatomegaly.**
- **Bullous or desquamated rash on hand, feet, mouth or anus is seen.**

(60) Which serological test are done for diagnosis of syphilis?

- **Nontreponemal antibody test measures antibody to cardiolipin and phospholipid measured by RPR and VDRL.**
- **Antitreponemal antibody test.**

(61) Which are screening test for syphilis?

- **RPR and VDRL are screening test for syphilis.**
- **It becomes positive after 4-6 weeks of infection.**
- **Always positive in secondary syphilis but negative in tertiary syphilis.**

(62) Which test is important for early diagnosis of syphilis?

- **Immnunofluoroscence test is important for early diagnosis.**

(63) In which conditions false positive VDRL results are seen?

- **Certain acute infection.**
- **Collagen vascular disease – Systemic Lupus Erythematosus.**
- **Pregnancy.**
- **Hypergammaglobulinemia.**
- **Lepromatous leprosy.**

(64) Which are specific test for diagnosing syphilis?

Following tests are specific for diagnosing syphilis:

- **Fluorescent treponemal antibody adsorption test.**
- **Microhemagglutination assay.**

(65) Which stain is used to demonstrate spirochetes?

- **Warthin starry stain is used to demonstrate spirochete.**

(66) What are fungi?

- **Fungi are eukaryotes with cell walls giving them their shape.**

(67) What is fungal hyphae?

- **Fungal cells grow on multicellular filaments called mosts which consist of thread like filaments known as hyphae.**

(68) What are psuedohyphae?

- **Most of yeast reproduce by budding but some of these buds fail to detach and become elongated to form pseudohyphae.**

(69) How will you diagnose fungus?

Fungus can be demonstrated by

- **Histologic examination.**
- **Species specific culture examination.**

(70) Which are common infection caused by candida?

- **It is most common in AIDS patient.**
- **Thrush – infection of mucosal membrane of oral cavity.**
- **Esophagitis.**
- **Vaginitis.**
- **Cutaneous infections.**

(71) Where does Aspergillosis occur?

Aspegillosis occurs as:

- **Allergic bronchopulmonary aspergillosis.**
- **Sinusitis.**
- **Pneumonia.**

(72) How Aspergillus is seen microscopically?

- **It is seen as proliferating masses of hyphae forming fungal balls lying freely in cavity with sparse inflammatory reaction.**
- **It forms septate filaments branching at acute angle.**

(73) How is fungi of Mucormycosis seen morphologically?

- **Fungi of Mucormycosis is seen as non-septate, irregularly wide with frequent right-angled branching filaments.**

(74) Which organs are commonly infected in Mucormycosis?

- **Organs commonly infected in Mucormycosis are:**
  - **Nasal sinuses**
  - **Lungs**
  - **Gastrointestinal tract**

(75) Which common parasites infect human being and how?

- **Common parasites infecting human being are:**
  - **E. Histolytica- Amoebic dysentery, Liver abscess**
  - **Giardia- Diarrhoea, Malabsorption**
  - **Trichomonas vaginalis- Urethritis, Vaginitis**
  - **Plasmodium- Malaria**
  - **Leishmania- Kala-azar**

(76) Which is the infectious state of Malaria?

- **The infectious state of Malaria is: Sphorozoites**

(77) Which is the first stage of malarial parasite in RBCs?

- **The first stage of malarial parasite in RBCs is: Trophozoite**
- **Trophozoite is defined by single chromatin mass**

(78) How is Schizont defined?

- **Schizont is defined by multiple chromatin masses.**

(79) What are merozoites?

- **Schizonts develop into merozoites which on lysis of red cells, infect other RBCs.**

(80) What are Gametocytes?

- **Gametocytes are defined as sexual forms of malarial parasites which infect the mosquito's during blood meal.**

(81) Which is the first organ to be affected in malaria?

- **The first organ to be affected in malaria is – Liver.**

(82) Why P. falciparum is more severe than any other plasmodial form?

- **P. falciparum is more severe than any other plasmodial form as**
  - **They infect RBCs at any age.**
  - **They cause infected RBCs to clump and stick to endothelial cells, blocking blood flow causing manifestations of cerebral malaria, leading to death of children.**
  - **Stimulates production of high levels of cytokines which suppress RBC production and initiates fever.**

(83) In which conditions, plasmodium infection cannot cause severe manifestations?

- **Plasmodium infection cannot cause severe manifestations in**
  - **HbS trait - because of low oxygen concentration as parasite dies in low oxygen concentration.**
  - **HbC – Because of reduced parasite proliferation**
  - **Absence of Duffy antigen as P.Vivax binds to it.**
  - **Endemic as immune mediated resistance.**

(84) Which pigment is seen in spleen and liver in plasmodium infection?

- **Pigment seen in spleen and liver in plasmodium infection is: Hemozoin**

(85) Which organism is responsible for cysticercosis?

- **Organism responsible for cysticercosis is: Taenia Solium**

(86) Which organism is responsible for Hydatid cyst?

- **Organism responsible for Hydatid cyst is: Echinococcus granulosis**

(87) Where are cysticercosis seen commonly?

- **Cysticercosis are seen commonly in: Brain, muscles, skin and heart**

(88) Where are Hydatid cyst commonly seen?

- **Hydatid cyst are commonly seen in: Liver, lung, bones and brain**

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INFLAMMATION

(1) What is unique feature of inflammation?

- **The unique feature of inflammation is accumulation of fluid and leucocytes in extravascular space due to reaction of blood vessels.**

(2) What are harmful consequences of inflammation?

- **Inflammation can underlie chronic disease like rheumatoid arthritis, atherosclerosis, lung fibrosis etc..**

(3) Which are structural fibrous proteins in Extracellular matrix?

- **Collagen and elastin are structural fibrous proteins in Extracellular matrix.**

(4) Which are adhesive glycoproteins in extracellular matrix?

- **Fibronectin, laminin, tenacin, nonfibrillar collagen are adhesive glycoproteins in extracellular matrix.**

(5) What is basement membrane made up of?

- **Basemembrane is made up of adhesive glycoproteins and proteoglycans.**

(6) What is acute inflammation?

The features of acute inflammation are:

- **Rapid in onset**
- **Relatively short duration**
- **Edema**
- **Predominantly neutrophils**

(7) What is chronic inflammation?

The features of chronic inflammation are:

- **It is longer in duration**
- **There is proliferation of blood vessels, fibrosis and tissue necrosis**
- **Predominant inflammatory cells are lymphocytes and macrophages**

(8) Which are cardinal signs of inflammation?

- **Cardinal signs of inflammation are:**
  - **Rubor.(Redness)**
  - **Tumor.(Swelling)**
  - **Calor.(Heat)**
  - **Dolar.(Pain)**

(9) Who added fifth cardinal sign of inflammation?

- **Virchow added fifth cardinal sign of inflammation and that sign is - LOSS OF FUNCTION.**

(10)Who described Triple response (Role of chemical mediators in inflammation)?

- **Sir Thomas Lewis(Flare and wheal Response)**

(11)Which are three main components of Acute inflammation?

- **Alterations in vascular caliber(Increased blood flow).**
- **Changes in vascular permeability**
- **Cellular events**

(12) What is exudation?

- **Exudation is defined as escape of fluid, proteins and blood cells from vascular system to interstitial tissue and body cavities.**

(13) What is exudate?

- **Exudate is an extravascular fluid with high protein cellular debris and specific gravity above 1.020.**
- **It implies alteration in normal permeability of small blood vessels in an area of injury.**

(14) What is transudate?

- **Transudate is fluid with low protein content and specific gravity less than 1.012**
- **It results from osmotic or hydrostatic imbalance across vessel wall without increase in vascular permeability.**

(15) What is edema?

- **Edema is defined as excess of fluid in interstitial or serous cavities.**
- **It may be either exudate or transudate.**

(16) What is pus?

- **Pus is a purulent exudate rich in leukocytes(mostly neutrophils), debris of dead cells and microbes.**

(17)Which chemical mediators cause vasodilatation?

- **Histamine and nitric oxide cause vasodilatation by acting on vascular smooth muscle.**

(18) Which chemical mediators cause vasodilatation gaps by causing in vascular permeability by causing gaps in endothelial cells?

- **Histamine**
- **Prostaglandin**
- **Leukotrienes**
- **Neuropeptide**
- **Cytokines- IL-1,TNF,INF-r**

These are responsible for IMMEDIATE TRANSIENT RESPONSE.

(19) Why change in vascular permeability by causing endothelial gaps is more prominent in venules?

- **May be there is greater density of receptors for mediators in veins.**

(20) How does chemical mediators change vascular permeability by causing endothelial cell gap ?

- **By causing phosphorylation of contractile and cytoskeletal proteins like myosin.**
- **This cause contraction of endothelial cells.**

(21)What is immediate sustained response?

- **Immediate sustained response occurs in severe burns or lytic bacterial injuries.**
- **It is caused due to direct endothelial injury due to endothelial cell necrosis and detachment.**
- **All levels of microcirculation are affected.**

(22)What is delayed prolonged response?

- **Increase vascular permeability**
- **After 2 to 12 hours**
- **Venules and capillaries**
- **Caused by mild to moderate thermal injury and sunburn**

(23)Give examples of delayed prolong response.

- **Sunburn**

(24)What is angiogenesis?

- **During repair, endothelial cells proliferate and form new blood vessels. This is angiogenesis.**

(25)What is extravagation?

- **Sequence of events in which leucocytes are transferred from vessel lumen to interstitial tissue.**

(26)What is diapedesis?

- **Diapedesis is transmigration of leucocytes across the endothelium.**

(27) What is Margination?

- **Blood flow slows down in early inflammation, hemodynamic changes occur and WBC around peripheral position along endothelial surface.**

(28) What is Rolling?

- **Individual and rows of leucocytes tumble slowly along endothelium and adhere to it transiently.This is known as Rolling.**

(29) What is Pavementing?

- **An event when leucocytes come to rest at appoint and adhere to endothelium is known as Pavementing.**

(30) What are four groups of Adhesion molecules?

- **Selectins**
- **Immunoglobulins**
- **Integrins**
- **Mucin like glycoprotein**

(31) What does Selection group of adhesion molecules consist of?

- **E- Selectin – Endothelium**
- **P- Selectin – Endothelium and platelets**
- **L – Selectin- Leucocytes**

(32) What does Immunoglobulin group of Adhesion molecules consist of?

- **ICAM-1 (Inter Cellular Adhesion Molecule)**
- **VCAM-1 (Vascular Cell Adhesion Molecule)**

(33) What does Integrins groups of Adhesion molecules consist of?

- **$ß_2$ integrins- LFA -1**
  - **Mac-1**
- **$ß_1$ integrins –VLA-4**

(34) Which glycoprotein act as Adhesion molecules?

- **Heparan Sulphate**

(35) What is a hemophilic adhesion molecule? Give examples.

- **Adhesion molecules binding to each other e.g, PECAM-1. Helps in leucocytes diapedesis, mainly in veins.**

(36) How does leucocytes transverse basement membrane?

- **By secreting collagenases which break the membrane.**

(37) How does leucocytes adhere to Extracellular matrix?

- **Leucocytes adhere to Extracellular matrix through $ß_1$-integrin and CD 44.**

(38) Which are genetic defeciences in leucocyte adhesion molecule?

Following are the genetic defeciencies in Lecocyte adhesion molecule:

- **Leucocyte Adhesion Deficiency – 1 : $ß_2$ integrin (LFA-1, MAC-1).**
- **Leucocyte Adhesion Deficiency – 2 : Sialyl Lewis X, E selectin.**

(39) Why are neutrophils predominant in inflammation in first 24 to 48 hours?

Neutrophils are predominant in inflammation in first 24 to 48 hours because,

- **They are more in number**
- **They respond more rapidly to chemokines**
- **Attach firmly to adhesion molecules like P-selectin and E-selectin**
- **Are short lived and undergo apoptosis while monocytes survive longer**

(40) What are exceptions to role of neutrophils in acute inflammation?

Following are the exceptions to rule of neutrophils in acute inflammation:

- **In Pseudomonas infection neutrophils remain for 2 to 4 days**
- **In case of viral infection lymphocytes predominate in early period**
- **In Hypersensitivity reaction eosinophils predominate.**

(41) What is chemotaxis?

- **Chemotaxis is emigration of leucocytes in tissues towards site of injury after extravasation from blood vessel.**

(42) Which are exogenous chemotactic agents?

- **Bacterial products are exogenous chemotactic agents.**

(43) Which are endogenous chemotactic agents?

- **C5a, LTB4 and IL-8 are endogenous chemotactic agents.**

(44) What occur in chemotaxis?

- **Polymerisation of actin occurs in chemotaxis.**

(45) Which are actin regulatory proteins in chemotaxis?

- **Filamin, gelsolin, profilin and calmodulin are actin regulatory proteins in chemotaxis.**

(46) What happens when leucocytes are activated?

- **Production of arachidonic acid metabolites**
- **Degranulation and secretion of lysosomal enzymes**
- **Secretion of cytokines**
- **Modulation of leucocyte adhesion molecule**

(47) Which surface receptors of leucocytes are responsible for their activation?

- **Toll like receptors**
- **Seven transmembrane G receptors**
- **Phagocytic receptors for cytokines**
- **Receptors for opsonin**

(48)Which cytokine act as phagocytic receptor?

- **IFN-1**

(49)What is opsonization?

- **Process of coating a particle. Example: microbe to target it for phagocytosis is opsonization.**

(50)What are opsonins?

- **The substances which process of coating particle like microbe to target it for phagocytosis are called opsonins.**

(51)Which substances act as opsonins?

- **Antibodies like Ig G, complements, lectins**
- **IgG antibodies recognized by Fcr receptor of phagocytes**
- **Mannose binding lectin, fibrinolectin, fibrinogen, C- Reactive protein**

(52)Which are steps of phagocytosis?

- **1)Recognition and attachment of particle to be ingested by leucocyte**
- **2) Its engulfment with formation of phagocytic vacuole.**
- **3) Killing and degradation of ingested material.**

(53)Which receptors are important to ingest and bind microbes in phagocytosis?

- **Mannose and Scavenger**

(54)How superoxide is formed in process of killing?

- **Due to rapid activation of NADPH oxidase which oxidases NADPH and reduce O_2 to superoxide.**

(55)Which products are formed from superoxide in process of killing?

- **H_2O_2 by dismutation**
- **Further reduced to OH**
- **By catalase to H_2O and O_2**

(56)Where are reactive O_2 intermediates formed in process of killing?

- **In lysosome**

(57) Which enzyme help H_2o_2 to kill microbes in process of killing?

- **Myeloperoxidase formed in azurophilic granules of neutrophils helps H_2o_2 to kill microbes in process of killing .**

(58) What is action of myeloperoxidase enzyme in process of killing?

- **Myeloperoxidase enzyme in presence of Cl^- converts H_2o_2 into $HOCl^-$ which is powerful microbial agent.**

(59) Which are oxygen independent mechanisms in process of killing?

- **Bactericidal permeability increasing proteins activates phospholipase which in turn causes degradation of phospholipid.**
- **Lysozyme hydrolyses glycopeptides coat (muramic acid) of bacteria.**
- **Lactoferrin which is iron binding protein present in secondary granules of neutrophils having antibacterial property.**
- **Major basic protein present in eosinophils is cytotoxic to parasites.**
- **Defensins is antimicrobial peptide which binds to microbial membrane and increase its permeability.**
- **Elastase enzyme breaks down peptide bond of bacterial membrane.**

(60) Which is optimal pH for action of lysosomal enzymes for killing?

- **pH – 4 to 5 is the is optimal pH for action of lysosomal enzymes for killing.**

(61) Which chemical mediators are responsible for release of leucocyte products?

- **Lysosomal enzymes, reactive oxygen metabolites, prostaglandins and leukotrienes are responsible for release of leucocyte products.**

(62) What are mechanisms of release of leucocyte products?

- **Regurgitation during feeding**
- **Frustrated phagocytosis**
- **Cytotoxic release**

(63) What is regurgitation during feeding?

- **Release of leucocyte products occur if phagocytic vacuole remains transiently open to outside. This is regurgitation during feeding.**

(64) What is frustrated phagocytosis?

- **When cells are exposed to potentially ingestible materials eg. Immune complexes which triggers leucocyte activation but these fixed immune complexes cannot be phagocytose.Instead lysosomal enzymes are released in it. This is known as frustrated phagocytosis.**

(65) What is meant by cytotoxic release?

- **After phagocytosis, potentially membranolytic substances eg. Urate crystals damage membrane of phagolysosome.**

(66) What happens when there is deficiency of leucocyte adhesion molecules 1 and 2?

- **Bacterial infection and impaired wound healing occurs in deficiency of leucocyte adhesion molecule.**

(67) What is Chediak Higashi (Defect in phagolysosome) Syndrome?

- **It is Autosomal Recessive disease.**
- **Abnormalities in melanocytes and nervous system**
- **Neutropenia**
- **Defective Granulation**
- **Giant granules**
- **Reduced lysosomal enzymes in phagocytic vacuoles**

(68) What happens in defects in microbicidal activity?

- **It occurs in chronic granulomatous disease.**
- **It is oxygen dependant pathway**
- **Defects in genes encoding several components of NADPH oxidase**
- **H_2o_2 is not generated**

(69) What is role of mast cell in inflammation?

- **Mast cell release histamine, Leukotrienes and cytokines which are useful in inflammation.**

(70) What is role of macrophage in inflammation?

- **Macrophage recognize microbial products and secret cytokines.**

(71) What is Chediak-Higashi Syndrome?

- **It is an autosomal recessive disease.**
- **Characterized by defect in phagolysosome.**
- **Features of the disease are as following:**
  - **Neutropenia.**
  - **Defective circulation.**
  - **Giant granules.**
  - **Reduced lysosomal enzymes in phagocytic vacuoles.**
  - **Abnormalities in melanocytes and nervous system.**

(72) What happens when there is a defect in microbicidal activity?

- **Defect in microbicidal activity occurs in chronic granulomatous disease.**
- **There is a defect in O_2 dependant pathway, H_2O_2 is not generated.**
- **There are defects in genes encoding several components of NADPH oxidase.**

(73) What is role of mast cells in inflammation?

- **Mast cells release histamine, leukotrienes and cytokines in the process of inflammation.**

(74) What is role of macrophage in inflammation?

- **Macrophage recognizes microbial products and secretes cytokines.**

(75) Which are plasma derived chemical mediators?

- **Complements are plasma derived chemical mediators and kinins to be activated.**

(76) Which are cell derived chemical mediators?

- **Cell derived chemical mediators are sequestrated in intracellular granules eg. Histamine or are synthesized in response to stimuli eg. Prostaglandins and cytokines.**

(77) Which cell is richest in histamine?

- **Mast cells are richest in histamine.**
- **Histamine is also present in basophils and platelets.**

(78) What is action of histamine on blood vessels?

- **Histamine causes:**
  - **Dilatation of arterioles.**
  - **Increased permeability of venules.**
  - **Immediate transient response.**

(79) Which systems form plasma proteases?

- **Complement, kinins and clotting systems form plasma proteases.**

(80) How many proteins are present in complement system?

- **About 20 components and their cleavage products are there in complement system.**

(81) What is action of complement system in Acute Inflammation?

- **Increased Vascular Permeability**
- **Chemotaxis**
- **Opsonisation**

(82)Which is critical step in biological function of complement?

- **Activation of C_3**

(83)Which are three pathways?

- **Classical**
- **Lectin**
- **Alternative**

(84)Which is Immunological Pathway in Complement System?

- **Classical Pathway.**

(85)Which microbial surface molecular activate alternative pathway in Complement System?

- **Complex Polysaccharides**
- **Cobra venom**

(86)How Lectin Pathway is activated?

- **When plasma mannose binding lectin binds to carbohydrates on microbes and activates C_1.**

(87)How is C_5 Convertase formed?

- **C_{3b} + fragment of complement.**

(88)What is Membrane Attack Complex?

- **C_{5b-9} combination causing cell lysis.**

(89)What are roles of C_{5a}, C_{3a} and C_{4a} in Acute Inflammation?

- **Cause histamine release -> Increase Vascular Permeability causing Vasodilatation.**
- **Activate lipoxygenase pathway of Arachidonic Acids.**

(90)What are Anaphylotoxins?

- **C_{3a},C_{5a},C_{4a} cause anaphylaxis.**

(91)What are action of C5a?

- **Leucocyte Adhesion**
- **Chemotaxis**
- **Leucocyte activation**
- **Activation of lipo-oxidase pathway**

(92)What is role of C3b?

- **Act as opsonin in phagocytosis**

(93)Which proteolytic enzymes activate C_3 and C_5 in inflammation?

- **Plasmin**
- **Lysosomal enzymes**

(94)What is role of bradykinin?

- **Increase vascular permeability**
- **Contraction of smooth muscle**
- **Dilatation of blood vessels**
- **Pain**

(95)Which protease generates various kininogens?

- **Kallikreins**

(96)Which coagulation factor triggers kinin system?

- **Hageman factor**

(97)How Hegman factor is activate?

- **Hageman factor is activate by negatively charged surfaces. Example- Collagen**

(98)Which clotting factor provide main link between coagulation system and inflammation?

- **Thrombin**

(99)What are actions of thrombin in inflammation?

- **It cleaves soluble fibrinogen in fibrin clot**
- **It mobilizes adhesion molecules**
- **It produce chemokines; prostaglandins, PAF, nitric oxide**
- **Induce CO_2**

(100)What are actions of plasmin in inflammation?

- **Plasmin lyses fibrin clots**
- **It cleaves C_3**
- **It degrades fibrin into fibrin splitting products.**
- **It activates Hageman factor**

(101) Which mediators increase vascular permeability?

- **Mediators increasing vascular permeability are: C_{3a}, C_{5a} and bradykinin**

(102) Which systems are initiated by Activated Hageman factor?

- **Systems, activated by Hageman factor are:**
  - **Kinin**
  - **Clotting**
  - **Fibrinolytic**
  - **Complement- Anaphylotoxins**

(103) What is arachidonic acid?

- **Arachidonic acid is a 20- carbon polyunsaturated fatty acid derived from dietary sources or conversion of fatty acid- linoleic acid.**

(104) How arachidonic acid is released?

- **Arachidonic acid is released from membrane phospholipid by action of enzyme phospholipase which is activated by physical or chemical injury.**

(105) Which biochemical signals activate phospholipase?

- **Increased cytosolic Ca^{++} activates phospholipase.**

(106) Which enzymes synthesize arachidonic acid metabolites?

- **Enzymes synthesizing arachidonic acid metabolites are:**
  - **Cyclooxygenase.**
  - **Lipoxygenase.**

(107) Which products are formed by cyclo-oxygenase pathway?

- **Products formed by cyclooxygenase pathway are:**
  - **Prostaglandins.**
  - **Thromboxanes.**

(108) Which products are formed by lipoxygenase pathway?

- **Products formed by lipoxygenase pathway are:**
  - **Leukotrienes.**
  - **Lipoxines.**

(109) Which agents suppress cyclooxygenase activity?

- **Agents suppressing cyclooxygenase activity are:**
  - **Aspirin.**
  - **NSAIDS.**

(110) Which prostaglandins are important in Acute Inflammation?

- **Prostagliandins important in Acute inflammation are: PGE_2, PGD_2, PGF_2, PGI_2 and TXA_2.**

(111) What is significance of thromboxane synthetase?

- **It is present in platelets**
  - **Potent platelet aggregator**
  - **Vasoconstrictor**
  - **Gets converted into inactive TXB_2**
- **It is absent in endothelium**
  - **Instead it possesses prostacyclin synthetase which forms prostacyclin**
  - **Inhibits platelet aggregation**
  - **Vasodilator**

Imbalance between these two cause thrombus formation in coronary and cerebral arteries.

(112) Which prostaglandin is responsible for pain and fever?

- **PGE_2 is responsible for pain and fever.**

(113) What is the action of PGD_2 , PGE_2 and PGF_2?

- **Vasodilation**
- **Increase vascular pressure**
- **Cause edema**

(114) What is importance of COX-2 enzyme?

- **It is absent in tissue in resting stage.**
- **Induced by variety of inflammatory stimuli**
- **It stimulates production of Prostaglandins that are involved in inflammatory reaction.**

(115) What is importance of COX-1?

- **It is produced in response to inflammation.**
- **It is involved in inflammation as well as in homeostatic function.**

(116) In which cell 5-lipooxygenase is predominantly found?

- **In neutrophils, 5-lipooxygenase is predominantly found.**

(117) From where Leukotrienes are formed?

- **From 5-HETE (Hydroxyeicosatetraenoic acid), Leukotrienes are formed.**

(118) What are the actions of LTB_4?

- **It is potent chemotactic agent of neutrophil**
- **Helps in aggregation and adhesion of WBCs to venular endothelium**
- **Helps in generation of oxygen free radicals**
- **Helps in release of Lysosomal enzymes**

(119) What are action of LTC_4, LTD_4, LTE_4?

- **Intense vasoconstriction**
- **Bronchospasm**
- **Increased vascular pressure**

(120) What are lipoxins and what is their function?

- **Lipoxin is the product of Arachidonic acid**
- **It is produced by interaction of platelets with leucocytes**
- **Function**
    - **Inhibits leucocyte recruitment**
    - **Adhesion to endothelium**
    - **Inhibit neutrophil Chemotaxis**

(121) Which are cyclooxygenase inhibitors and how do they act?

- **Cyclooxygenase inhibitors are:**
    - **Aspirin**
    - **Non-steroidal anti-inflammatory drugs.**
- **They act by inhibiting prostaglandin synthesis.**

(122) Which are broad spectrum inhibitors and what is their action?

- **Broad spectrum inhibitors are glucocorticoids.**
- **They act by inhibiting genes encoding COX-2, phospholipase A2, cytokines, IL-1, TNF and nitric oxide synthase.**

(123) From what platelet activating factor is derived?

- **Platelet activating factor is derived from antigen stimulated IgE and sensitized basophils.**

(124) What is platelet activating factor?

- **Platelet activating factor is an acetyl-glycerol ether phosphoryl choline, a phospholipid with glycerol backbone.**

(125How does platelet activating factor mediates its effect?

- **Platelet activating factor mediates its effect by acting as a single G-protein coupled receptor.**

(126) How action of platelet activating factor is regulated?

- **Platelet activating factor is inactivated by platelet activating factor acetohydrolases.**

(127) What are actions of platelet activating factor?

- **Actions of platelet activating factor are:**
  - **Platelet stimulation**
  - **Vasoconstriction**
  - **Bronchoconstriction**
  - **Increasing leukocyte adhesion**
  - **Boosting synthesis of other enzymes.**

(128) What are cytokines?

- **Cytokines are proteins produced by lymphocytes and macrophages.**

(129) Name two main cytokines mediating inflammation?

- **Two main cytokines mediating inflammation are: TNF and IL-1**

(130) From where cytokines are produced?

- **Cytokines are produced from activated macrophages.**

(131)How is production of cytokines stimulated?

- **Production of cytokines is stimulated by endotoxin and other microbial products, immune complex.**

(132)What are actions of cytokines?

- **Actions of cytokines are on endothelium leukocyte and fibroblast.**
- **Cytokines also cause induction of systemic acute phase reaction.**

(133) What are actions of cytokines on endothelium?

- **Synthesis of endothelial adhesion molecules and chemical mediators**
- **Also increase thrombogenicity**

(134)What are systemic acute phase reactions by cytokines?

- **Fever**
- **Loss of appetite**
- **Slow wave sleep**
- **Septic shock**
- **Hypotension**
- **Decrease VR**

(135)What is role of TNF in cachexia?

- **TNF regulates body mass by promoting lipid and protein mobilization and also by suppressing appetite. Sustained production of TNF causes cachexia.**

(136)What are chemokines?

- **Chemokines are family of small proteins acting primarily as chemo attractants for specific type of leucocytes.**

(137)Which are four major groups of chemokines?

- **1. Alfa C-X-C**
- **2.Beta C-C**
- **3.Gamma C**
- **4.CX_3C**

(138)What are alpha chemokines? Give example.

- **One amino acid separating cysteine residue.**
- **Act on neutrophils.**
- **Example:IL_8**
- **Secreted by macrophage endothelial cells.**

(139)What are beta chemokines?

- **Beta chemokines two conserved cysteine residue**
- **MCP-1,eotaxin ,M1p-1alfa,RANTES -**
  Attract monocytes, eosinophils , basophils and lymphocytes.
- **Eotaxin attract eosinophils.**

(140)What are gamma chemokines?

- **Gamma chemokines are lack of two of four conserved cysteins**
- **Specific for lymphocytes.**

(141)What are CX_3C?

- **CX_3C contains 3 amino acids beta two cysteine.**
- **Fractline**
- **Two forms: Bound and free**
  - **Bound form: Induced by endothelial cells. Promotes strong adhesion of monocytes and T cells.**
  - **Free form: Devided by proteolysisof membrane bound proteins acts on same cells.**

(142)What is action of NO (nitrous oxide)?

- **Paracrine action causing relaxation of vascular smooth muscle cells.**
- **Increase vasodilatation**
- **Decrease platelet aggregation and adhesion**

(143)From where NO is derived?

- **Endothelial cells**
- **Macrophages**
- **Neurons**

(144)How NO is synthesized?

- **From L-arginine by enzyme nitric oxide synthatase**

(145)What are different types of NO?

- **Endothelial**
- **Neuronal**
- **Inducible**

(146) How is Nitric Oxide activated?

- **Increased cytoplasmic Ca^{++} by activated cytokines activate endothelial as well as neuronal Nitric oxide.**

(147) What are action of Nitric Oxide?

- **Vasodilation**
- **Inhibits platelet aggregation and adhesion**
- **Microbicidal**

(148) When is Nitric Oxide production reduced?

- **In endothelial diseases like atherosclerosis, Diabetes, Hypertension there is reduced production of Nitric Oxide.**

(149) Which cells have Lysosomal granules?

- **Neutrophils**
- **Monocytes**

(150) Which enzymes are secreted by specific or secondary granules of neutrophils?

- **Lysozyme**
- **Collagenase**
- **Gelatinase**
- **Lactoferrin**
- **Plasminogen activator**
- **Histamine**

(151) Which enzymes are secreted by azurophilic or primary granules of neutrophils?

- **Myeloperoxidase**
- **Lysozyme**
- **Defensins**
- **Acid hydrolases**
- **Neutral proteases like elastase, cathepsin, collagenase**

(152) Name two antiproteases

- **α_1 – antitrypsin: inhibits neutrophils elastase**
- **α_2 – antitrypsin: macroglobulin**

(153) On what does production of O_2 derived free radicals are dependent?

- **Production of O_2 derived free radicals are dependent on activation of NADPH oxidase system.**

(154) Name O_2 derived free radicals

- **Superoxide (O_2^-)**
- **Hydrogen peroxide ($H_2 O_2$)**
- **OH^-**

(155) What is action of O_2 derived free radical?

- **It increases expression of chemokines and endothelial leucocytes and endothelial leucocyte adhesion molecules**
- **Destroys phagocytosed microbes**
- **Endothelial damage leads to increased vasoactive peptides**
- **Inactivation of anti-proteases**

(156)Name some antioxidants?

- **Copper containing serum protein-ceruloplasmin**
- **Iron free fraction of serum-Transferrin**
- **Enzyme-superoxide dismutase**
- **Enzyme- catalase that causes detoxification of H_2O2**
- **Enzyme- glutathione peroxidase that causes detoxification of H_2O_2**

(157) Name neuropeptides playing role in inflammation?

- **Substance P**
- **Neurokinin –A**

(158) Which mediator is activated by hypoxia?

- **Mediator activated by hypoxia: Hypoxia induced factor 1α**
- **It increases vascular permeability.**

(159) What is basis of gout?

- **Necrotic cells in inflammation causes breakdown of DNA that leads to release of uric acid which causes crystallization leading to gout.**

(160) What is resolution?

- **After inflammation, there is neutralization and elimination of injurious stimuli that causes restroration of site of inflammation leading to resolution.**

(161) What is fibrosis?

- **After acute inflammation when healing occurs by connective tissue replacement is known as fibrosis.**

(162) Give examples of serous inflammation?

- **Examples of serous inflammation are:**
  - **Pleural,pericardial,peritoneal effusion**
  - **Burns causing skin blister**

(163) Where does fibrinous inflammation occur?

- **Fibrinous inflammation occur in meninges,pericardium and pleura.**

(164) What is meant by organization?

- **Organization is meant by conversion of fibrinous exudates into scar tissue**

(165) What is pus?

- **Pus is a purulent exudate consisting of neutrophils, necrotic cells and edema fluid.**

(166) Give examples of suppurative inflammation.

- **Examples of suppurative inflammation are: Acute appendicitis, Abscesses.**

(167) What is abscess?

- **Abscess is a localized collection of purulent inflammatory tissue comprising of,**
  - **Central region: composed of mass of necrotic tissue and leukocytes.**
  - **Outer region: preserved neutrophils**
  - **Still outer region: Vascular dilatation and fibroblastic proliferation.**

(168) What is ulcer?

- **Ulcer is a local defect or excavation of surface of an organ or tissue produced by sloughing of inflammatory necrotic tissue.**
- **E.g. Peptic ulcer.**

(169) What is chronic inflammation?

- **Chronic inflammation is an inflammation of prolonged duration in which active inflammation, tissue destruction and attempts of repair are present.**

(170) What are causes of chronic inflammation?

- **Causes of chronic inflammation are:**
  - **Persistent infections by viruses, fungi, bacteria. E. g. Trepanoma Pallidium.**
  - **Prolonged exposure to exogenous or endogenous toxic agents. E.g. Silica, atherosclerosis.**
  - **Autoimmunity- Rheumatoid arthritis, Lupus erythmatosis.**

(171) What is MNS (Mononuclear phagocyte system) or RES (Reticuloendothelial system)?

- **It consists of closely related cells of bone marrow origin including monocytes and tissue macrophages.**

(172) Give examples of tissue macrophages?

- **Examples of tissue macrophages are:**
  - **Liver- Kupffer cells**
  - **Spleen and lymph nodes- Sinus histiocytes**
  - **Lungs- Alveolar macrophages.**

(173) What is role of lymphocytes and macrophages in chronic inflammation?

- **Role of macrophages:**
  - **Display antigens to T- cells**
  - **Produce cytokines**
  - **Activate T lymphocytes.**
- **B-lymphocytes:**
  - **Produce antibodies**
  - **Produce plasma cells.**

(174) What is lymphoid organogenesis? Give examples.

- **Lymphoid organogenesis: In strong chronic inflammation, there is accumulation of lymphocytes, antigen producing cells and plasma cells assuming morphologic features of lymphoid organs like lymph nodes with well formed germinal centers.**
- **E.g.: Synovium in patient of Rheumatoid arthritis.**
-

(175) What is role of eosinophils in chronic inflammation?

- **Eosinophils are recruited by eotaxin.**
- **Eosinophilic granules have Major Basic Protein.**
- **Eosinophils are toxic to parasites and cause lysis of mammalian epithelial cells thus controlling parasitic infections.**

(176)What is role of mast cells in inflammation?

- **In acute reactions, IgE antibody binds to cells Fc receptors.**
- **Cells release histamine and products of arachidonic acids.**
- **Occurs during anaphylactic reaction to foods, insect venom or drugs.**

(177)In which chronic conditions, neutrophils are seen?

- **Chronic osteomyelitis**
- **Chronic lung damage due to smoking**

(178)What is granulomatous inflammation?

- **Granulomatous inflammation is a distinctive pattern of chronic inflammatory reaction characterized by focal accumulation of activated macrophages of developing in epithelial like (epitheloid) appearance.**

(179)What is granuloma?

- **It is a focus of chronic inflammation consisting of a microscopic aggregation of macrophages that are transformed into epithelial like cells surrounded by mononuclear leucocytes principally lymphocytes and plasma cells.**

(180)What are different types of granuloma?

- **Foreign body granuloma – Formed due to foreign body**
- **Immune granuloma- Caused by microbes. Example : Tuberculosis**

(181)What is tubercle?

- **Granuloma in tuberculosis characterized by presence of central caseous necrosis.**

(182)What is acute phase response?

- **Acute phase response is systemic changes associated with inflammation.**

(183)Which mediator is responsible for acute phase response?

- **Cytokines are responsible for acute phase response.**

(184)What are systemic effects of inflammation?

- **Fever, leucocytosis, acute phase proteins.**
- **Sepsis.**

(185) What is mechanism of fever?

- **Exogenous pyrogens stimulate leucocytes.**
- **Release cytokines which increase cyclo oxygenase**
- **Convert Amino acids into prostaglandins(PGE_2)**
- **Produce neurotransmitters like cyclic AMP**
- **Hypothalamus set temperature at higher level**

(186) How does NSAIDS or aspirin act?

- **Reduce fever by inhibiting cyclooxygenase**

(187) Which acute phase proteins increase in inflammation?

- **Mostly synthesis by liver which include C-reactive protein,fibrinogen,serum amyloid.**

(188) How is formation of acute phase protein stimulated?

- **By cytokines e.g IL-6,CRP,fibrinogen, IL-1,TNF**

(189) Why is rouleax formation seen in inflammation?

- **It is seen due to rise in fibrinogen and also increased in ESR**

(190) Why is CRP increased in myocardial infarction?

- **Inflammation may predispose to atherosclerotic plaque which leads to thrombosis and infarction**

(191)Why does leucocytosis occur in inflammation?

- **It occur due to accelerated release of cells from bone marrow by cytokines.**

(192)Why there is shift to left in inflammation?

- **It occurs due to accelerated release of cells from bone marrow by cytokines.**

(193) Which chemical mediator can cause DIC?

- **High levels of TNF by inhibiting natural anticoagulant.**

(194) What is Septic shock?

- **It is clinical triad of DIC,hypoglycemia and cardiovascular failure.**

(195)What is cause of hypoglycemia?

- **Release of cytokines leads of liver injury causing failure to maintain blood glucose levels due to gluconeogenesis from stored glycogen.**

(196) What is the cause of cardiovascular failure?

- **Cytokines leads to overproduction of NO in cardiac Myocytes that causes loss of perfusion pressure and heart failure.**

(197) What lung damage occurs in systemic inflammatory response?

- **Adult Respiratory distress syndrome occurs due to neutrophil mediated endothelial injury allowing fluid to escape from blood into airspace.**

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NEOPLASIA

(1) What is Neoplasia?

- **Neoplasia means New growth.**

(2) What are two basic components of neoplasm?

- **Two basic components of neoplasm are:**
  - **Clonal neoplastic cells representing parenchyma**
  - **Reactive stroma of connective tissue, blood vessels, macrophages and lymphocytes.**

(3) What is desmoplasia? Give examples of desmoplastic tumors?

- **Tumor in which parenchymal cells stimulate formation of abundant collagenous stroma.**
- **E.g. Breast cancer.**

(4) What are adenomas?

- **Adenomas are benign epithelial neoplasms derived from glands.**

(5) What are papillomas?

- **Papillomas are benign epithelial neoplasm producing microscopically or macroscopically visible finger-like or warty projections from epithelial surfaces.**

(6) What are cystadenomas?

- **Cystadenomas are benign epithelial surfaces forming large cyst masses.**

(7) What is polyp?

- **Polyp is a neoplasm, benign or malignant producing macroscopically visible projection above a mucosal surface.**

(8) What are sarcomas?

- **Sarcomas are malignant tumors arising in mesenchymal tissue.**
- **E.g. Fibrosarcoma, Chondrosarcoma.**

(9) What are carcinomas?

- **Carcinomas are malignant tumors of epithelial origin, derived from any of three germ layers.**

(10) What are mixed tumors?

- **Mixed tumors are defined as divergent differentiation of single neoplastic clone along two lineages.**
- **E.g. Benign-Pleomorphic adenoma,**
  Malignant- Pleomorphic carcinoma, Wilm's tumor

(11)What is Teratoma?

- **Neoplasm which contains recognizable mature or immature cells or tissues representing of more than one germ cell layers.**

(12)Which benign sounding tumors are malignant?

- **Lymphoma**
- **Melanoma**
- **Seminoma**
- **Mesothelioma**

(13)What is Hamartoma?

- **Disorganized benign appearing masses composed of cells indigenous to the particular site.**

(14)What is Choristoma?

- **Congenital anamoly describes as heterotopic rest of cells.**

(15)What is Differentiation?

- **It refers to the extent to which neoplastic parenchymal cells resemble the corresponding normal parenchymal cells both morphologically and functionally.**

(16)What is Anaplasia?

- **Lack of differentiation (Reversal of differentiation to primitive level)**

(17)Which well differentiated tumors appear like normal?

- **Adenocarcinoma of Thyroid**
- **Squamous cell Carcinoma**

(18)What is pleomorphism?

- **Cells and Nuclei show variation in size and shape.**

(19)What is Hyperchromatic nuclei?

- **Nuclei contain abundant chromatin and are dark staining.**

(20)What is normal nuclear cytoplasmic ratio? What change occurs in this in malignancy?

- **Normal is 1:1 which changes to 1:4 to 1:6 in malignancy.**

(21)What does mitoses indicate?

- **High proliferative activity of parenchymal cells.**

(22)In which tissue numerous mitosis is not significant?

- **Bone Marrow as it exhibits rapid turnover.**

(23)What is loss of polarity?

- **Orientation of anaplastic tissues is markedly disturbed.**

(24)How will you differentiate between Tumor giant cells and inflammatory giant cell ?

- **Inflammatory giant cells contain small normal appearing nuclei, in contrast to Tumor giant cells containing huge polymorphic two or more nuclei.**

(25)What is Metaplasia?

- **Replacement of one type of cells with another type.**

(26)Give examples of Metaplasia.

- **Barrett's oesophagus**

(27)What is Dysplasia?

- **It is disordered growth in which there is loss in uniformity of individual cells as well as loss of architectural orientation.**

(28)What is Carcinoma in Situ?

- **When dysplastic changes are marked and involve the entire thickness of epithelium but the lesion remains confined to only basement membrane.**

(29)What is invasion?

- **When the tumor cells breach the basement membrane it is Invasion.**

(30)In well differentiated Squamous cell carcinoma what is elaborated?

- **Keratin**

(31)What is the size of smallest clinically detectable mass?

- **1 gm.**

(32)What is growth fraction?

- **The proportion of cells within tumor that are in proliferative pool.**

(33)Which tumors are with high growth fraction?

- **Leukemia**
- **Lymphoma**
- **Small cell carcinoma of Lung**

(34)Which tumors are with low growth fraction?

- **Cancers of Colon and Breast.**

(35)What is the capsule of benign tumor made up of?

- **Largely from extracellular matrix of the mature tissue due to atrophy of normal parenchymal cells under presence of expanding tumor.**

(36)Name benign tumor lacking capsule.

- **Hemangioma**

(37)What is Metastases?

- **Tumor implants which are discontinuous with the primary tumor.**

(38)Which malignant tumors don't metastasize?

- **Glioma**
- **Basal cell carcinoma of Skin**

(39)Which carcinomas generally metastasize by seeding in Body cavities and surfaces?

- **Carcinoma of Ovary**

(40)What is Sentinal lymphnode?

- **It is the first node in regional lymphatic basin receiving lymph flow from primary tumor.**

(41)What are common modes of spread in carcinoma and sarcoma?

- **Carcinoma: Lymphatic node**
- **Sarcoma: Hematogenous**

(42)Which organs are most frequently involved in hematogenous spread of metastasis?

- **Liver**
- **Lung**

(43)Which cancers have propensity to invade veins?

- **Renal cell carcinoma**
- **Hepatocellular carcinoma**

(44)Which are common sites of metastasis in?

- **Breast carcinoma: Bone**
- **Bronchogenic carcinoma: Adrenals and Brain**
- **Neuroblastoma: Liver, Bones**

(45)Which environmental factors are carcinogenic?

- **Ultra-violet rays, smog**
- **Medications eg. Methotrexate**
- **Asbestos, Vinyl chloride**
- **High fat diet**
- **Alcohol**

(46)Which neoplasms are commonly seen in infancy and childhood?

(Small round / blue cell tumors)

- **Neuroblastoma**
- **Wilm's tumor**
- **Retinoblastoma**
- **Leukemias**
- **Rhabdomyosarcoma**

(47)Give examples of Autosomal Dominant Inherited Cancers.

- **Retinoblastoma, Osteosarcoma: RB tumor suppressor gene**
- **MEN-I**
- **MEN-2**
- **Colon cancer: APC gene.**

(48)Give examples of Inherited Autosomal Recessive Syndromes with defective DNA repair.

- **Xeroderma Pigmentosum**
- **Fanconi Anemia**

(49)Give examples of Familial Cancers.

- **Breast cancer: BRCA-1 & BRCA-2**
- **Ovarian cancer**
- **Melanoma: mutation in P16 tumor suppressor gene**
- **Lymphoma**

(50)Give examples of cancers associated with Chronic Inflammation.

- **Helicobactor pylori gastritis**
- **Ulcerative colitis**
- **Chronic pancreatitis**
- **Viral hepatitis**
- **Cystitis**
- **Barett's oesophagus.**

(51)Give examples of Precancerous conditions.

- **Chronic atrophic gastritis of pernicious anemia**
- **Solar keratosis of Skin**
- **Chronic ulcerative colitis**
- **Leukoplakia of oral cavity, vulva and penis**
- **Villous Adenoma of colon**

(52)Give examples of cancer occurring from benign conditions.

- **Villous Adenoma of colon**
- **Leiomyoma**
- **Pleomorphic Adenoma**

(53)What are Oncogenes?

- **Genes promoting Autonomous cell growth in cancer cells are called Oncogenes.**

(54)What are Proto oncogenes?

- **Unmutated cellular counter parts of genes promoting autonomous cell growth in cancer cells are Proto oncogenes.**

(55)What are Oncoproteins?

- **Oncoproteins resemble normal products of proto oncogene except that they are devoid of important internal regulatory elements.**
- **Their production in transformed cells does not depend on growth factors or external signals.**

(56)Which Growth factors are associated with which tumors?

- **PDGF-β: Asrtocytoma, Osteosarcoma**
- **FGF: Carcinoma of Stomach, Carcinoma of Bladder, Carcinoma of Breast**
- **TGF-α: Astrocytoma, Hepatocellular carcinoma**
- **HGF: Thyroid carcinoma**

(57)Which proto Oncogenes are related to growth factors?

- **PDGF-β: SIS**
- **FGF: HST I**
- **TGF-α: TGF A**
- **HGF: HGF**

(58)Which Growth factor receptors with which proto oncogene are related to which tumors?

Growth factor receptor	Proto oncogene	Tumors
EGF-receptor	ERBB-1 ERBB-2	Squamous cell carcinoma of Lung Glioma
FMS like Tyrosine kinase receptor for neurotrophic factors	FLT3 RET	Breast Carcinoma Ovarian Carcinoma Leukemia Men-2A & B
PDGF	PDGFR-β	Glioma Leukemia
Receptor for Stem cell	KIT	GIST

Factor		**Seminoma**

(59)Which proteins involved in signal transduction are related to which proto-oncogenes and tumor?

Signal transduction	Proteins	Tumors
GTP Binding	KRAS	Colon, lung,pancreas tumors
	HRAS	Bladder, kidney tumors
	NRAS	Melanoma, Hematological malignancies
Non receptor tyrosine kinase	ABL	Chronic Myeloid Leukemia Acute Lymphoblastic Leukemia
RAS Signal transduction	BRAF	Melanoma
Wnt Signal transduction	B- Calenin	Hepatoblastoma Hepatocellular Carcinoma

(60)Which Nuclear Regulatoty Proteins related to which Proto oncogene causes which tumors?

Nuclear Regulatoty Proteins	Proto oncogene	Tumors
Transcriptional Activators	C-MYC	Burkitt's Lymphoma
	N-MYC	Neuroblastoma Small cell carcinoma of Lung
	L-MYC	Small cell carcinoma of Lung

(61) Which cell cycle regulators related to which protooncogenes

causes which tumor?

CELL CYCLE REGULATOR	PROTO-ONCOGENE	TUMOR
Cyclins	Cyclin D	Mantle cell lymphoma
	Cyclin E	Breast and Oesophageal Carcinoma
Cyclin dependant Kinase	CDK4	Glioblastoma, Melanoma, Sarcoma

(62) Which is the internal control or checkpoints of cell cycle? How does it function?

- **P53 gene – Tumor suppressor gene causes cell arrest and apoptosis at G_1/S phase of cell cycle if DNA damage is there.**
  - **Inhibits cell cycle**
- **E.g.: Ataxia Telegiectasia**

  Mutated – Activated when DNA breaks

  - Arrests cell cycle at G_2M phase

(63) Name some tumor suppressor genes at cell surface level related to tumor.

- **TGF-β : Carcinoma colon**
- **E-cadherin : Carcinoma stomach**

(64) Name some tumor suppressor genes in inner part of plasma membrane related to tumor.

- **NF_1 : Neuroblastoma, Neurofibromatosis-1**

(65) Name some tumor suppressor genes at cytoskeleton level related to tumor.

- **NF_2 : Schwannoma, Meningioma.**

(66) Name some tumor suppressor genes at cytosol level related to tumor.

- **APC/ β-catenin : Carcinoma of stomach, Colon**
- **PTEN: Endometrial, Prostate Carcinoma**
- **$SMAD_2$, $SMAD_4$: Colon, Pancreas tumor**

(67) Name some tumor suppressor genes at nucleus level related to tumor.

- **RB – Retinoblastoma, Osteosarcoma**
- **P53 – Most human carcinoma**
- **WT_1 – Wilm's Tumor**
- **P16/INK4a – Pancreatic, Breast, Malignant melanoma, Esophageal Carcinoma**
- **BRCA1, BRCA2 – Female breast carcinoma, Carcinoma Ovary**

(68) Which mutation occur in genes in retinoblastoma?

- **Mutation occur at Chromosome locus 13q14**

(69) Where is P53 gene located?

- **On chromosome 17p13.1 P53 gene is located.**

(70) Why is P53 gene called molecular policeman?

- **P53 prevents the propagation of genetically damaged cells. Hence, it is known as molecular policeman.**

(71)How does P_{53} gene act?

- **Activation of temporary cell cycle onset(quiescence)**
- **Induction of permanent cell cycle onset(senescence)**
- **Triggering programmed cell death(apoptosis)**

(72)Why P_{53} gene is called guardian of genome?

- **P_{53} senses the damage in DNA of cell and induce repair gene.**
- **A cell which cannot be repaired is directed by P_{53} to undergo Apoptosis.**

(73)What are practical therapeutic implications of ability of P_{53} gene to control Apoptosis?

- **Irradiation**
- **Chemotherapy**

mediate their effects by inducing DNA damage and subsequent Apoptosis.

(74)Which genes are lost in colon carcinoma?

- **APC genes**

(75)Which types of carcinoma occurs when there is mutation in beta catenin gene?

- **Carcinoma colon**
- **Hepatoblastoma**

(76)Which carcinoma occurs when there is mutation in E-cadherin?

- **Gastric carcinoma**

(77)Which genes function as Tumor suppressors?

- **$INK4_a$/ARF- Bladder carcinoma, Head and neck tumors, Cholangiocarcinoma, ALL**
- **TGF beta pathway- Pancreatic carcinoma ,Colon carcinoma**
- **PTEN - Breast carcinoma, Endometrium carcinoma, Thyroid carcinoma**
- **NF_1 - Neurofibromatosis 1**
- **NF_2 - Neurofibromatosis 2**
- **VHL -Hereditary renal cell carcinoma -Pheochromocytomas**

-Hemangioblastoma

- **PTCH** -Basal cell carcinoma
- **WT_1** - Wilm's tumor

(78)What is mechanism of cellular aging?

- **Normal human cells -60 to 70 doubling**
- **As senescent –cells lose ability to divide. This is due to shortening of telomeres at end of chromosomes.**

(79)Which are potent angiogenic factors in tumor?

- **Basic fibroblast growth factor**
- **VEGF**

(80)Which are angiogenetic inhibitors in tumor?

- **Angiostatin**
- **Endostatin**
- **Vasculostatin**

(81)What is the role of P_{53} gene in Angiogenesis?

- **P_{53} stimulates expression of angiogenic molecules such as Thrombospondin-1 and repress expression of Pro-angiogenic like VEGF balancing process of Angiogenesis.**

(82)Which family of glycoprotein is responsible for cell to cell adhesion?(Cohesiveness of cell)

- **E-Cadherin**

(83)Which groups of proteases are responsible for tumor cell invasion?

- **Matrix metalloproteinases**

- **Cathepsin D**
- **Urokinase plasminogen activator**

(84)What is role of MMP-9 in tumor invasion?

- **It cleaves type-IV collagen of epithelial and vascular basement membrane mainly of breast, colon and stomach.**

(85)Which groups help tumor cells to migrate?

- **Cytokines**
- **Growth factors (IGF_c I & II)**

(86)Which blood cells are more vulnerable to attach to tumor cells?

- **Platelets**

(87)Which molecule is used by tumor cells to migrate to specific tissues?

- **CD 44**

(88)Where does Prostatic carcinoma commonly metastasize?

- **Bone**

(89) Where does Bronchogenic carcinoma commonly metastasize?

- **Adrenal and Brain**

(90)Where does Neuroblastoma commonly metastasize?

- **Liver and Bones**

(91)Which molecules play important role in metastasis? Give examples.

- **Cytokines**
- **E.g. Breast cancer cells have chemokines receptors $CXCR_4$ and CCR_7 .**
- **Tissues highly expressing these receptors are common sites of metastasis in Breast carcinoma.**

(92)Which tissue is nonpermissive of metastasis?

- **Skeletal muscle**

(93)What are metastasis suppressor genes? Give examples.

- **A gene whose lose promotes development of metastasis without effect on primary tumor.**
- **E.g. mir 335, mir 126 -> suppress breast cancer metastasis**

(94)What is metastatic Oncogene? Give example.

- **Gene favoring development of metastasis without effect upon the primary tumor.**
- **E.g. SNAIL, TWIST -> promotes epithelial mesenchymal transformation.**

(95)What is Genomic Instability?

- **It occurs when both copies of DNA repair genes are lost leading to cancer.**
- **3 defects.**
    1. **Mismatch repair.**
    2. **Nucleotide excision repair.**
    3. **Recombination repair.**

(96)Give examples of cancer occurring due to DNA mismatch repair.

- **Hereditary Nonpolyposis Colon Cancer Syndrome -> Germline mutation in MSG 2 & MLH 1 gene.**

(97)What are Microsatellites?

- **They are tandem repeats of one to six nucleotides found throughout the genome.**

(98)What is Xeroderma Pigmentosusm?

- **Inherited disorder of defective DNA repair.**
- **Increased risk of skin cancer.**

- **DNA Nucleotide excision repair defect.**

(99)What are examples of DNA Recombination Repair defect?

- **Bloom syndrome(developmental defect)**
- **Ataxia tengiectasia (neural signs)**
- **Fanconi anemia (Bone marrow Aplasia)**

(100)Which gene is mutated in Fanconi Anemia?

- **BRCA 2**

(101) Which cancers occur due to mutation in BRCA-1?

- **Epithelial ovarian cancer**
- **Prostate cancer**

(102) Which cancers occur due to mutation in BRCA-2 gene?

- **Breast Ca**
- **Ovary Ca**
- **Prostate Ca**
- **Pancreas Ca**
- **Bileduct Ca**
- **Stomach Ca**
- **Melanocytes**

(103) Which factors favour cancer cell motility?

- **Cleavage of collagen IV --- Releases VEGT**
- **Enzymatic degradation of laminin 5 by MMPs--- Proteolytic fragments**

(104) Which growth factors promote tumor cells?

- **PDGF**
- **TGF-β**

- **bFCF**

(105) What is Warburg effect?

- **Even in presence of ample oxygen, cancer cells shift their glucose metabolism away from mitochondria to glycolysis.**

(106) What is principle of PET scanning?

- **Glucose hunger of tumor cells is used to visualize tumors in PET scanning.**
- **18F – fluorodeoxyglucose - a nonmetabolizable derivative of glucose in injected which is preferentially taken by tumor cells.**

(107) What is Autophagy?

- **Normal cells in oxygen and glucose deprivation arrest their growth and canabolise their own organelles, proteins and membranes as energy source.**

(108) Which genes promote Autophagy?

- **Tumor suppressor gene like PTEN.**

(109) Which oncogen is activated by which translocation in CML?

- **(9;22) (q34;q11)**
- **ABL 9q34, BCR 22q11**

(110) Which oncogen is activated by which translocation in Acute leukemias (ALL & AML) ?

- **(8;21) (q22;q22)**
- **AML – 8q22**
- **ETO -- 21q22**
- **PML – 15q22**
- **RARA – 17q21**

(111) Which oncogen is activated by which translocation in Burkitt's lymphoma?

- **(8;14) (q24;q32)**
- **C-MYC 8q24**
- **IGH 14q32**

(112) Which oncogen is activated by which translocation in Ewing's sarcoma?

- **(11;22) (q24;q22)**
- **FLI1 11q24**
- **EWSR1 22q12**

(113) Which oncogen is activated by which translocation in prostatic adenocarcinoma?

- **(21;21) (q22;q22) ERG (21q22.2)**
- **(7;21) (p22;q22) ETV1 (7p21.2)**
- **(17;21) (p21;q22) ETV4 (17q21)**

(114) Which chromosomal rearrangements activate proto-oncogens?

- **Translocations**
- **Inversions**

(115) What is Philadelphia chromosome?

- **Characteristic of CML**
- **Subset of ALL**
- **Eg of oncogen formed by fusion of two separate genes**

(116) Give examples of cancers caused due to chromosomal deletions?

- **Chromosome 13q14 – retinoblastoma**
- **17p, 5q, 18q – Colorectal carcinoma**
- **3p – Small cell lung carcinoma**

(117) Give examples of tumors caused due to gene amplification?

- **N-MYC – Neuroblastoma**

- **ERBB2 – Breast cancer**
- **C-MYC**
- **L-MYC** } **Small cell carcinoma of Lung**
- **N-MYC**

(118) What is Epigenetics?

- **Reversible, heritable changes in gene expression occurring without mutation due to modification of histones and DNA methylation.**

(119) What is genomic printing?

- **Methylation participates in the phenomenon in which the maternal or paternal allele of gene or chromosome is modified by methylation and inactivated.**

(120) What is miRNAs?

- **Small noncoding single strandard RNAs of approx 22 nucleotides in length incorporated in RNA- induced silencing complex.**
- **Control cell growth, differentiation and cell survival.**
- **Either lead to over-expression of oncogen or suppress action of tumor suppression gene.**

(121) Give example of miRNA mediated down-regulation.

- **Increased expression of BCL2**

(122) Give examples of miRNA mediated up-regulation.

- **RAS and MYC oncogenes in lung tumors and B-cell leukemias.**

(123) What is multistep Carcinogenesis?

- **Each cancer must result from accumulation of multiple mutations. This is known as multistep carcinogenesis.**

(124) Give examples of multi-step carcinogenesis.

- **Colon Ca**
- **APC at 5q21 – Mucosa at risk**
- **APC β-catenin**
- **KRAS at 12p12 – Adenocarcinoma**
- **P53 at 17p13 – Carcinoma**

(125) What are steps involved in chemical carcinogenesis?

- **Initiation**
- **Initiation causing permanent DNA damage (mutation)**
- **Promoters inducing tumors**

(126) What are targets of chemical carcinogenesis?

- **DNA, RNA and Proteins**

(127) What are direct acting chemical carcinogenesis?

- **They don't require metabolic conversion to become carcinogenic.**
- **Eg., Dimethyl Sulphate**

(128) What are indirect acting chemical carcinogenesis?

- **Chemical requiring metabolic conversion to be an ultimate carcinogen.**
- **Eg., Polycyclic hydrocarbons**

(129) Which carcinogen cause carcinoma of Lung in cigarette smoking?

- **Benzopyrene**

(130) Give few examples of Natural chemical carcinogens.

- **Alfatoxin B**
- **Safrole**
- **Betel nuts**
- **Grisefulvin**

(131)Which are common Molecular targets of Chemical Carcinogens?

- **RAS**
- **P53**

(132) What is Aflatoxin B1?

- **A naturally occuring chemical carcinogen produced by some strains of Aspergillus which grows on improperly stored grains and nuts.**

(133)What is role of Aflatoxin?

- **Produce mutation of P53 gene G:C → T:A transmission in codon 249 causing Hepatocellular carcinoma.**

(134)Which chemical carcinogens are potential at work place and home?

- **Vinyl chloride**
- **Arsenic**
- **Nickel**
- **Chromium**
- **Insecticide**
- **Fungicides**

(135)Which chemical carcinogen is used as food preservative?

- **Nitrites → causing nitrosylation of amines in food → Nitrosamines are carcinogenic.**

(136)What are Promoters?

- **They are agents that do not cause mutation but stimulate division of mutated cells.**
- **E.g. Phenols, drugs, hormones**

(137)What is Radiation Carcinogenesis?

- **Cancer caused by Radiant energy like ultraviolet rays of sunlight (skin carcinoma) or ionizing electromagnetic radiation.**

(138)Which cancers are caused by Ultraviolet rays?

- **Squamous cell carcinoma**
- **Basal cell carcinoma**
- **Melanoma of skin**

(139)Which wavelength of Ultraviolet rays is responsible for cancers?

- **UVB (280-320 nm)**

(140)What is mechanism of causing cancer by UVB light rays?

- **Its formation of pyrimidine dimers in DNA.**

(141)Which cancers are caused by ionizing radiation?

- **Acute and chronic myeloid leukemia**
- **Thyroid cancer at young age**
- **Carcinoma of breast, lung and salivary glands**

(142)Which cancer is caused by HTLV -1 virus? How?

- **T cell leukemia / lymphoma through TAX gene.**

(143)Which is oncogenic RNA virus?

- **HTLV-1**

(144)Which are oncogenic DNA viruses?

- **HPV**
- **Epstein Barr virus**
- **Hepatitis B virus**
- **Kaposi sarcoma- herpes virus**
- **Merkel cell polyoma virus**

(145)Which HPV viruses are responsible for Squamous cell papillomas (warts)?

- **HPV 1, 2,4 and 7**

(146)Which HPV viruses cause Squamous cell carcinoma of cervix and anorectal regions?

- **HPV 16 and 18**

(147)Which viral genes are responsible for oncogenic potentials of HPV?

- **E_6 and E_7**

(148)Which cancers are caused by Epstein Barr virus?

- **Burkitt's lymphoma**
- **B cell lymphoma**
- **Hodgkin lymphoma**
- **Nasopharyngeal carcinoma**
- **Gastric carcinoma**

(149)Which genes of EBV acts as oncogene in B cell lymphoma?

- **LMP- 1**
- **EBNA-2**

(150)Which oncogene of EBV is responsible for Burkitt's lymphoma?

- **C-MYC**

(151) Which oncogene of EBV virus are responsible for nasopharyngeal carcinoma?

- **LMP-1**
- **VEGF**
- **FGF2**
- **MMP9**
- **COX-2**

(152) Which oncogenic virus is responsible for Hepatocellular carcinoma?

- **HBV**
- **HCV**

(153) Which gene in HBV acts as oncogene for Hepatocellular carcinoma?

- **HBx**

(154)Which virus neither DNA nor RNA acts as viral oncogene? How?

- **HCV through HCV core protein**

(155)Which cancers are caused by H. pylori?

- **Gastric Adenocarcinoma**
- **Gastric Lymphoma**

(156) Which gene of H. pylori acts as oncogene?

- **Cag A**

(157) What are tumor antigens?

- **Antigens that elicit immune response against tumors.**
- **Two types:**
  1) Tumor specific- Present only on tumor cells
  2) Tumor associated – Present on tumor cells and also on some normal cells

(158) Which cells are major immune defense mechanism against tumor cells?

- **Cytotoxic T- lymphocytes**

(159) Which oncogene products or mutated tumor suppressor gene is recognized by CD8 or cytotoxic T cells?

- **Oncogene products- Mutated RAS BCR/ABL fusion proteins**
- **Tumor suppressor gene –Mutated p53 protein**

(160) Give examples of over expressed or aberrantly expressed cellular proteins acting as tumor antigen.

- **Over expressed- Tyrosinase**
  gp 100
  MART in melanoma
- **Aberrantly expressed – MAGE**
  BAGE } **Cancer testis antigen**

(161) Which tumor antigens are produced by oncogenic viruses?

- **Tumor antigens produced by oncogenic viruses are as follow:**
  - **Human Papilloma Virus- E6**
  - **In Cervical Carcinoma- E7 Proteins**
  - **In EBV induced lymphoma- EBNA Proteins**

(162) Which are oncofetal tumor antigens?

- **Oncofetal tumor antigens are as follow:**
  - **Carcinoembyonic Antigen**
  - **α- fetoprotein**

(163) Which glycolipids act as tumor antigens?

- **Glycolipids which act as tumor antigens are as follow:**
  - **GM2, CD2, CD3- Involved in melanoma.**

(164) Which glycoproteins act as tumor antigens?

- **Glycoproteins which act as tumor antigens are as follow:**
  - **CA-125- Ovarian cancer**
  - **CA19-9- Ovarian cancer**
  - **MUC-1- Breast cancer**

(165) What are differentiation antigens?

- **Differentiation antigens are tumor antigens normally present on cells of origin.**

(166) Give examples of differentiation tumor antigens.

- **Example of differentiation tumor antigen is: CD-20- B- cell lymphoma**

(167) Which type of malignancy is common in AIDS?

- **Malignancy common in AIDS is: Lymphoma**

(168) Which growth factor is immunosuppressant?

- **Growth factor which act as immunosuppressant is: TGF-β**

(169) What is cachexia?

- **Cachexia is defined as:**
  Individuals with cancer suffer from progressive loss of body fat and lean body mass accompanied by weakness, anorexia and anemia.

(170) Which factors are responsible for cachexia?

- **Factors responsible for cachexia are as follow:**
  - **Tumor Necrosis Factor**
  - **IL-1**
  - **Interferon-ϒ**

(171) What are paraneoplastic syndromes?

- **Paraneoplastic syndromes are defined as:**
  Symtom complexes in cancer bearing individuals that cannot be explained, indigenous to tissue from which tumor arose.

(172) Which cancers are associated with Cushing's syndrome?

- **Cancers associated with Cushing's syndrome are:**
  Small cell carcinoma of lung, Pancreatic carcinoma
- **Are due to ACTH**

(173) Which cancers are associated with hypercalcemia?

- **Cancers associated with hypercalcemia are:**
  Squamous cell carcinoma of lung, Breast carcinoma, Renal cell carcinoma
- **Are due to parathyroid hormone related protein, TGF-α, TNF, IL-1.**

(174) Which cancers are associated with hypoglycemia?

- **Cancers associated with hypoglycemia are:**
  Adult T-cell Leukemia, Ovarian carcinoma, Fibrosarcoma
- **Are due to insulin or insulin-like substance.**

(175) Which tumors are associated with carcinoid syndrome?

- **Tumors associated with carcinoid syndrome are:**
  Hepatocellular carcinoma, Pancreatic carcinoma
- **Are due to serotonin and bradykinin.**

(176) Which cancers are associated with Myasthenia and CNS and peripheral nervous system?

- **Cancers associated with Myasthenia and CNS and peripheral nervous system are:**
  Bronchogenic carcinoma, Breast carcinoma.
- **Causes may be immunological.**

(177) Which dermatological cancers are associated with which cancers?

- **Dermatological cancers associated with cancers are:**
  - **Acanthosis Nigricans- Gastric carcinoma, Lung carcinoma, Uterine carcinoma**
  - **Dermatomyositis- Bronchogenic carcinoma, Breast carcinoma.**
- **Are due to immunological causes or EGF.**

(178) Which bone and soft tissue tumors are associated with which cancers?

- **Bone and soft tissue tumors associated with cancers are:**
  - **Hypertrophic osteoarthropathy- Bronchogenic carcinoma.**

(179) Which vascular and hematologic conditions are associated with which cancers?

- **Vascular and hematologic conditions associated with cancers are:**
  - **Venous thrombosis- Pancreatic carcinoma**
  - **Red cell aplasia- Thymic neoplasms.**

(180) What is grading of cancers?

- **Grading of cancers is based on the degree of differentiation of tumor cells, the number of mitosis and architectural features.**

(181) What is staging of cancers?

- **Staging of cancers is based on the size of primary lesion, its extent and spread to regional lymph nodes and the presence or absence of blood borne metastasis.**

(182) Which system is generally used for staging of cancers?

- **System generally used for staging of cancers is:**
  American Joint Committee System based on TNM
  - **T for primary Tumor**
  - **N for regional lymph Node involvement**
  - **M for Metastasis.**

(183) How is staging of cancer done?

- **Staging of cancer is done according to increase in size of primary tumor.**
- **T_0 - In situ tumor and than T_1 to T_4 – According to increase in size.**
- **N_1 to N_3 - According to involvement and increasing number and range of lymph nodes.**
- **M_1 –M_2 – According to presence of metastasis.**

(184) Give examples of some mimicking carcinomas.

- **Examples of some mimicking carcinomas are:**
  - **Radiation changes in skin or mucosa are similar to cancer.**
  - **Healing fracture can mimic carcinoma.**

(185) Which fixative is generally used for electron microscopy?

- **Fixative generally used for electron microscopy is: Glutraldehyde.**

(186) What is anaplasia?

- **Anaplasia is defined as:**
  Cancer cells having lowered cohesiveness and exhibit a range of morphologic changes.

(187) What is the base of immunochemistry?

- **Bases of immunohistochemistry are:**
  - **Availability of specific antibodies in undifferentiated carcinomas.**
    E.g. Cytokeratins- Epithelial origin.
    Desmin- Muscle origin.
  - **Determination of site of origin in metastatic tumors.**
    E.g. PSA- Carcinoma prostate
    Thyroglobulin- Thyroid carcinoma.
  - **Detection of molecules having prognostic or therapeutic significance.**
    E.g. ER-PR status in breast carcinoma.

(188) What is flow cytometry?

- **Flow cytometry can measure membrane antigens and DNA content of tumor cells.**
- **It is useful in identification and classification of tumors arising from T and B lymphocytes.**

(189) Which are molecular techniques for detection of carcinomas?

- **Molecular techniques for detection of carcinomas are:**
  - **Cytogenetic analysis. E.g. Round cell tumor.**
  - **FISH (Fluorescent In Situ Hybridization)**
  - **PCR (Polymerase Chain Reaction)**
  - **Special Karyotyping**
  - **Comparative Genomic Hybridization (Microarray Format)**
  - **DNA microarrays**

(190) What is proteomics?

- **Proteomics is defined as:**
  A technique used to obtain profiles and proteins contained in tissues, serum and other body fluids.

(191) Give examples of hormones acting as tumor markers.

- **Examples of hormones acting as tumor markers are:**
  - **HCG- Trophoblastic tumors**
  - **Calcitonin- Medullary carcinoma of thyroid**
  - **Catecholamines- Pheochromocytoma**

(192) Which oncofetal antigens are acting as tumor markers?

- **Oncofetal antigens acting as tumor markers are:**
  - **α- fetoprotein- Liver cell carcinomas**
  - **CEA- Carcinoma of colon, lung, stomach and pancreas.**

(193) Which isoenzymes act as tumor markers?

- **Isoenzymes acting as tumor markers are:**
  - **PSA- Prostatic carcinoma**
  - **Neuron-specific enolase- Small cell carcinoma of lung, Neuroblastoma**

(194) Which proteins act as tumor markers?

- **Proteins acting as tumor markers are: Immunoglobulins- Multiple myeloma**

(195) Which mucins and glycoproteins act as tumor markers?

- **Mucins and glycoproteins acting as tumor markers are:**
  - **CA-125- Ovarian carcinoma**
  - **CA-19-9- Colon carcinoma, Pancreatic carcinoma**
  - **CA- 15-3- Breast carcinoma.**

(196) Which molecular markers act as tumor markers?

- **Molecular markers acting as tumor markers are:**
  - **APC, RAS in stool and serum- Colon carcinoma**
  - **RAS in stool and serum- Pancreatic carcinoma**
  - **RAS in sputum and serum- Lung carcinoma**
  - **RAS in urine- Bladder carcinoma.**

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REPAIR

(1) What is difference between regeneration and healing?

- **Regeneration is restitution of lost tissue**
- **Healing is restoring original structure with collagen deposition and scar formation.**

(2) What is regeneration?

- **Growth of cells and tissues to replace lost structures of skin epithelial and hematopoietic cells.**

(3) What is healing ?

- **Tissue response to wound inflammatory process and cell necrosis. Eg. Atherosclerosis.**

(4) What is organization?

- **In parenchymal organ, replacement of inflammatory infiltrate with granulation tissue and fibrosis.**

(5) What is required for regeneration?

- **Extracellular Matrix scaffold as they provide framework for cell migration and maintain cell polarity. They are also source of agent critical for tissue repair.**

(6) On what is size of cell population determined?

- **Cell proliferation**
- **Cell differentiation**
- **Cell death**

(7) Give examples of physiologic proliferation.

- **Endometrial cells due to estrogen in menstrual cycle**
- **Thyroid stimulating hormone causing enlargement of thyroid in pregnancy**

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(8) Mention stages of Cell cycle.

- **G_1 – Presynthetic**
- **S – DNA synthesis**
- **G_2 – Premitotic**
- **M – Mitotic**

(9) What are labile tissues?

- **Continuously dividing tissues are labile tissue**
- **Eg. Skin, Oral cavity, Vagina and Cervix**
  Lining mucosa of all glands in body
  GIT, Urinary bladder.

(10) What are quiescent or stable cell?

- **Cells that have low level of replication and can replicate when stimulated.**
- **Eg. Parenchymal cells of Liver, Kidney and Pancreas**

(11) What are permanent cells?

- **Cannot undergo mitotic division eg neuron, skeletal and cardiac muscle cells.**

(12) What are basic characteristics of stem cells?

- **Prolonged self renewal capacity**
- **Asymmetric replication**

(13) Which are different types of stem cells?

- **Embryonic**
- **Adult**

(14) What are embryonic stem cells?

- **Pluripotent cells giving rise to the all tissue of human body.**

(15) From which cells Embryonic cells are isolated?

- **Normal blastocyst – structure formed at 32 cell stage of embryonic development**

(16) To what is pluripotency of embryonic stem cell related?

- **Expression of unique transcription factors**
- **Examples: Na-nog, WNT-B-catenin**

(17) what is knockout mice?

- **A specific gene inactivated or deleted from cultured ES.**
- **Injected into blastocyst**
- **Implanted in uterus of surrogate mother**
- **Develop in full embryos**

(18) What are adult stem cells?

- **Any tissues in adult animals contain reservoirs of stem cells → Adult stem cells**

(19) What are tissue stem cells?

- **Adult stem cells located outside bonemarrow.**

(20) What are niches?

- **Sites where stem cells are located.**

(21) Give examples of Niches?

- **Isthmus of stomach glands.**
- **At base of crypts of colon.**
- **Bulge area of hair follicles.**
- **Limbus of cornea.**
- **Bone marrow.**

(22)What are Hematopoetic Stem Cells?

- **Derived from Bonemarrow.**
- **Generate all blood cells and reconstitute Bonemarrow.**

(23)From where hematopoetic stem cells are collected?

- **Bonemarrow.**
- **Umbilical cord.**
- **Circulating blood receiving cytokines.**
  e.g. Granulocyte Macrophage colony stimulating factor.

(24)What are Bonemarrow Stromal cells?

- **Stem cells from Bonemarrow generating various tissue like Chondrocytes, Osteoblasts, Adipocytes, Myoblast and endothelial cell precursors.**

(25)What is Transdifferentiation?

- **A change in stem cell differentiation from one cell type to other.**

(26)What is developmental plasticity?

- **Multiplicity of Stem cell differentiation .**

(27)What are Multipotent Adult Progenitor Cells?

- **Cells with broad developmental capability.**
- **Isolated from postnatal human and rodent Bonemarrow.**
- **Can differentiate into mesodermal, endodermal and neuroectodermal cells.**
- **Isolated from Muscle, Brain, Skin.**
- **Closely related to Embryonal Stem cells.**

(28)Where are tissue Stem Cells present in Liver?

- **Canals of Henry.**

(29)Where are tissue Stem cells present in Brain?

- **Olfactory bulb.**

- **Dentate gyrus of Hippocampus.**

(30)Where are tissue Stem cells located in Skeletal and Cardiac muscle?

- **Beneath myocyte basal lamina.**
- **Self renewing epithelial cell also contain stem cells.**

(31) Name of the growth factors.

- **EGF**
- **PDGF**
- **FGF 1, FGF 2**
- **Keratinocytes**
- **TNF**
- **Interferons**
- **Interleukins**

(32) Function and location of EGF and TGF.

- **Both helps in mitogenesis for epithelial cells, hepatocytes and fibroblast**
- **Found in sweat, saliva, urine and intestinal contents**
- **In wounds produced by keratinocytes and macrophages**

(33) Function and location of Hepatocyte Growth Factor

- **Isolated from platelets and serum**
- **Mitogenic on hepatocytes and biliary epithelium**
- **Epithelial cells of lungs, mammary glands and skin**
- **Produced by fibroblast and endothelial cells.**

(34) Vascular endothelial Growth Factor (VEGF)

- **VEGF A to D and placental growth factor induces blood vessel formation and growth (Angiogenesis)**

(35) Platelet Derived Growth Factor

- **There are 3 isoforms : AA, AB, BB**
- **Stored in α platelet granules**
- **Causes migration and proliferation of fibroblast, smooth muscle cells and monocytes.**

(36) Fibroblast Growth factor (FGF)

- **Contains acidic and basic members**
- **Angiogenesis and wound repair**
- **Skeletal muscle development**
- **Lung maturation**
- **Hematopoeisis**

(37) Transforming growth factor (TGF) – ß

- **There are 3 isoforms – $ß_1$, $ß_2$, $ß_3$**
- **Growth inhibitor for most epithelial cell and leucocytes**
- **Potent fibrogenic agents stimulates fibroblast Chemotaxis – enhance production of collagen, fibronectin**
- **Strong anti-inflammatory effect**

(38) What is autocrine signaling?

- **Cells producing signal act on themselves**

(39) What are examples of autocrine signaling?

- **Liver regeneration**
- **Proliferation of antigen stimulated lymphocytes**

(40) What is Paracrine signaling?

- **One cell type producing ligand which acts on adjacent target cell.**

(41) What is Paracrine signaling?

- **One cell type producing ligand which acts as adjacent target cells.**

(42) Examples of paracrine signaling.

- **Connective tissue repair in wound healing.**
- **Hepatocyte replication in liver regeneration.**

(43) What is juxtacrine signaling?

- **A special type of paracrine signaling occurring when signaling molecule is anchored in cell membranes and binds a receptor in plasma membrane.**

(44) What is endocrine signaling?

- **Hormones are synthesized by cells of endocrine organs and act on target cell.**

(45) Give examples of receptors with tyrosine kinase activity.

- **EGF , TGF- α, HGF, PDGF, VEGF, FGF**

(46) Give examples of receptors lacking tyrosine kinase activity.

- **IL-2, IL-3, Interferon- α, ß, ϒ.**

(47) What are seven transmembrane G- protein coupled receptors?

- **It contains 7- transmembrane α- helixs**
- **Constituents largest family**
- **Vasopressin, Serotonin, Histamine, Epinephrine**

(48) What are steroid hormone receptors?

- **Diffuse through cell membrane and bind to receptor in nucleus mostly Thyroid hormone, Vit-D.**

(49) What are PPaRs?

- **Peroxisome Proliferator- activated receptors, Steroid hormone receptors involved in broad ranges of cell differentiation and adipogenesis.**

(50) What are transcription factors?

- **Many signal transducter system used by growth factors to transfer information to nucleus and modulate gene expression.**

(51) Give examples of transcription factors

- **C-myc , c-JUN : cell proliferation**
- **P-53 - cell inhibitors**

(52) Which organ has remarkable capacity to regenerate?

- **Liver (theory of prometheus) – 60% liver resection can result in double regeneration.**

(53) What is compensatory growth or compensatory hyperplasia?

- **Restoration of liver mass achieved without regrowth of lobes but enlargement of lobes.**

(54) How does hepatocytes replicate ?

- **By combined action of cytokines and polypeptide growth hormones, hepatocytes replicate.**

(55) What are actions of Extracellular matrix in tissue repair and regeneration?

- **It gives mechanical support**
- **Control cell growth through INTEGRIN receptors.**
- **Maintenance of cell differentiation through INTEGRINS**
- **Scaffolding**
- **Establishment of tissue microenvironments**
- **Storage and presentation of regulatory molecules. Eg. Secretion of Growth factor like FGF & HGF**

(56) What is Extracellular matrix composed of?

- **Three groups of macromolecules:**
- **Fibrous structural protein – collagen and elastin providing tensile strength and recoil.**

- **Adhesion glycoprotein - connect matrix elements to each other and to cells**
- **Proteoglycans and hyaluronan**

  Forming two forms of ECM
  - **Interstitial matrix – found in spaces between cell and connective tissue, consisting of mainly collagen, elastin, fibronectin**
  - **Basement membrane – consists of nonfibrillar collagen laminin, heparin sulfate**

(57) How many types of collagen are there?

- **27 types of collagen are there.**

(58) Which are fibrillar collagen?

- **I, II, III, V and XI are fibrillar collagen.**

(59) Which type of collagen is seen in Basement membrane?

- **Type IV with laminin is seen in basement membrane.**

(60) Which vitamin is needed for formation of collagen?

- **Vitamin C is needed for collagen.**

(61)What happens in Scurvy?

- **Due to lack of Vitamin C there is improper wound healing.**

(62)Which effect occur due to lack of Fibrillar Collagen?

- **Ehler Danlos Syndrome.**
- **Osteogenesis Imperfecta (Type I).**
- **Stickler Syndrome(1X).**

(63)Which genetic disease occur when there is no collagen (Type IV) in Bonemarrow?

- **Alport Syndrome.**

(64) What is action of Elastin?

- **Allows tissue to expand and recoil.**

(65)Where is Elastin mainly seen?

- **Large blood vessels like Aorta.**
- **Uterus.**
- **Skin.**
- **Ligaments.**

(66)What is Fibrillin?

- **It is a glycoprotein associated with extracellular membrane.**
- **Serves as scaffolding for deposition of glycoprotein.**

(67)What is Marfans's Syndrome?

- **Inherited defect of fibrillin resulting in formation of abnormal elastic fibers with changes in Cardiovascular System (Aortic Dissection) and skeleton.**

(68)Which are Cell Adhesion Proteins?

- **Immunoglobulin**
- **Cadherins**
- **Integrins**
- **Selectins**
- **Mostly acts as receptors.**
- **Bond to same cell type or different cell type.**

(69) Function of Integrin?

- **Bind to extracellular membrane proteins like Fibronectin, Laminin, Osteoprotein providing connection beyween cell and extracellular membrane.**
- **To other Cell Adhesion molecule providing cell to cell interaction.**

(70) Function of Fibronectin.

- **Binds to collagen, fibrin and procollagens.**

(71) Different forms of fibronectin.

- **Plasma fibronectin - binds to fibrin stabilizing blood clot, filling wounds.**
- **Tissue fibronectin**

(72) What is action of cadherin and integrins?

- **They links cell surface with cytoskeleton through binding to actin and intermediate filaments.**

(73) What is cadherin?

- **Calcium dependant adherence protein participate in interactions between cells of same type.**

(74) What type of junction are formed by cadherin?

- **Zonula adherens – small spotlike junction located near apical surface of cells.**
- **Desmosome – strong and extensive present in epithelial and muscle cells.**

(75) How does linkage of cadherin occurs to cytoskeleton ?

- **It occurs through 2 classes of catenin : ß-catenin and α-catenin.**

(76) Role of cadherin in cancer.

- **Diminished function of E-cadherin in breast and gastric cancer.**
- **ß-catenin – acts in WNT pathway participating in stem cell homeostasis and regeneration – alteration and mutation – Gastrointestinal and Liver cancer.**

(77) Other families of adhesion protein.

- **SPARC (secreted protein acidic and rich in cysteine) – also known as osteonectin – tissue remodeling**
- **Thrombospondins – inhibit angiogenesis**

- **Osteoporin – regulates calcification**
- **Tenascin – morphogenesis and cell adhesion**

(78) What are GAGS ?

- **Glycosaminoglycans present in Extracellular matrix**
- **It is formed of polymers and disaccharides.**

(79) Which GAG is not linked with protein ?

- **Hyaluronan**

(80) What are function of GAGs?

- **To organize Extracellular matrix**
- **Regulate connective tissue structure and permeability**
- **Modulators in inflammation, cell growth etc.**

(81) Which are structurally distinct families of GAGs?

- **Produced and assemble in golgi apparatus and RER:**
  - ✓ **Heparan sulfate**
  - ✓ **Chondroitin sulfate**
  - ✓ **Keratan sulfate**
- **Hyaluronan : Product in plasma membrane by enzyme hyaluronan synthetase**

(82) What is significance of hyaluronan?

- **Found in Extracellular matrix of heart valves, skin and skeletal tissues.**
- **Synovial fluid, vitreous of eye, umbilical cord**
- **Provide resilience and lubrication to many types of connective tissue, Example: Cartilages in joints**
- **Concentration increase in: RA (Rheumatoid arthiritis), Scleroderma, Psoriasis, Osteoarthritis.**

(83) When does healing occur by scar formation?

- **When tissue injury is severe or chronic and results in damage of both parenchyma and stromal framework→ Repair occur by deposition of collagen and other extracellular metrix.**

(84) What are the features of repair by connective tissue deposition?

- **Inflammation**
- **Angiogenesis**
- **Migration and proliferation of fibroblasts**
- **Scar formation**
- **Connective tissue remodelling**

(85) What is angiogenesis?

- **Formation of new blood vessels.**
- **Involves- i) Branching and extension of adjacent preexisting vessels**
  ii) Recruitment of endothelial progenitor cells from Bonemarrow

(86) Which growth factor plays important role in angiogenesis?

- **VEGF (Vascular Endothelial Growth Factor)**
  Through VEGFR (Vascular Endothelial Growth Factor Receptor)

(87) Example of Physiologic angiogenesis.

- **Proliferative endometrium**

(88) Pathological angiogenesis Occurs in

- **Chronic inflammation**
- **Wound healing**
- **Tumors**
- **Diabetic Retinopathy**

(89) Which substances stabilize angiogenesis?

- **Angiopoetins – 1 & 2**

- **PDGF (Platelet Derived Growth Factor)**
- **TGF-ß (Tumor Growth Factor- ß)**
  (by recruiting pericytes and smooth muscle cells)

(90) Which ECM proteins regulate angiogenesis?

- **Integrins**
- **Matricellular protein etc, Thrombospondin, SPARC (Secreted protein acidic and rich in cysteine), Teracin-C.**
- **Proteinases**

(91)What is Endostatin?

- **Inhibitor of endothelial proliferation and angiogenesis.**
- **Fragment of Collagen.**

(92)What are different phases of wound healing?

- **Inflammation : Platelet adhesion, aggregation and formation of clot leading to inflammation.**
- **Proliferation : Formation of granulation tissue, proliferation and migration of connective tissue and reepithelization of wound surface.**
- **Maturation: ECM deposition, tissue remodelling and wound contraction.**

(93)What does a blood clot contain?

- **Entrapped red cells.**
- **Fibrin.**
- **Fibronectin.**
- **Complements.**

(94)What is Granulation Tissue?

- **Hallmark of repair.**
- **Fibroblast and vascular endothelial cells proliferate in first 24 to 72 hours of repair forming granulation tissue.**

(95) What is characteristic histological picture of Granulation tissue?

- **Presence of small blood vessels and proliferation of fibroblasts.**

(96)What are key cellular constitutes of tissue repair?

- **Macrophages → Clear extracellular debris, fibrin → Promote angiogenesis and ECM.**

(97) What is importance of Tumor Growth Factor- β (TGF- β)?

- **Most fibrogenic agent.**

(98)What are Matrix Metallo Proteinase (MMP)?

- **Family of enzymes with more than 20 members.**
- **180 residue Zinc protease domain.**
- **Cause degradation of collagen and other ECM.**

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