NEET PG Pathology Sample Paper-3

Duration: 20 Minutes **Maximum Marks: 100**

Instructions

- This paper contains **25** Multiple Choice Questions.
- Each correct answer carries **+4** mark. Incorrect answer: **−1** marks. Only **one** correct option.
- Unattempted questions carry **0** marks.
- Use of mobile phones, smartwatches, or any electronic gadgets is strictly prohibited.

Q1. A 45-year-old male with a history of chronic alcohol abuse is found to have hepatomegaly. A liver biopsy reveals intracellular accumulation of triglycerides. Which of the following molecular mechanisms is primarily responsible for the impaired secretion of lipoproteins leading to this condition?

(A) Decreased synthesis of apoproteins

(B) Increased oxidation of fatty acids

(C) Inhibition of alpha-glycerophosphate activity

(D) Decreased peripheral mobilization of fatty acids

Q2. During a research experiment, cultured endothelial cells are exposed to hypoxia. A profound drop in intracellular ATP levels is noted. Which of the following downstream metabolic events occurs as a direct consequence of this energy depletion?

(A) Efflux of water into the extracellular space

(B) Activation of the Na+/K+ ATPase pump

(C) Detachment of ribosomes from the rough endoplasmic reticulum

(D) Intracellular alkalization due to lactic acid clearance

Q3. A tissue biopsy from an irradiated uterine fibroid shows cells undergoing programmed cell death. Molecular analysis demonstrates outer mitochondrial membrane permeabilization. Which of the following proteins directly forms the channel that permits the release of Cytochrome c into the cytosol?

(A) Bcl-2

(B) Bcl-xL

(C) Bak

(D) Mcl-1

Q4. An autopsy of an 82-year-old male reveals extensive, dark-brown pigment deposition within the myocardial sarcoplasm, predominantly concentrated around the nuclei. The patient had no history of iron overload. Which of the following processes best describes the origin of this pigment?

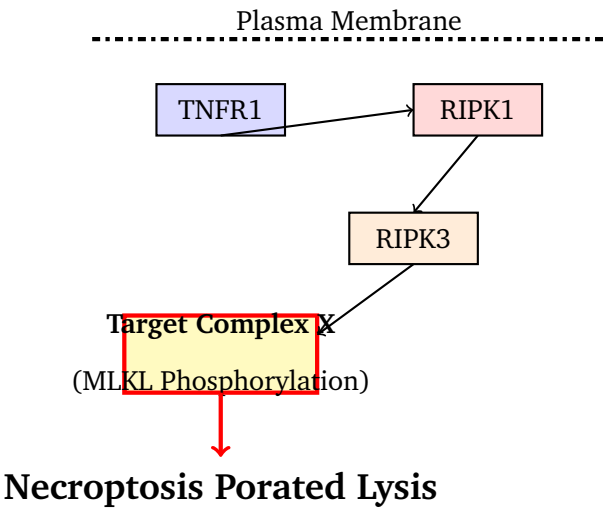
(A) Incomplete lysosomal degradation of lipid peroxidation products

(B) Polymerization of tyrosine derivatives via tyrosinase

(C) Systemic systemic congestion leading to erythrocyte breakdown

(D) Defective copper transport across cellular membranes

Q5. A clinical pathologist evaluates a lymph node biopsy under electron microscopy to characterize a pattern of necrosis. The structural overview of the cellular degeneration pathway is schematically mapped below. Identify the designated component marked as **Target Complex X** which acts as the execution platform triggering plasma membrane rupture without caspase activation:



(A) Apoptosome execution complex

(B) Pyroptosome gasdermin pore

(C) Necrosome multiprotein complex

(D) Inflammasome platform

Q6. A 28-year-old female presents with a localized skin infection. Leukocytes migrate to the site of injury. Genetic testing reveals a complete deficiency of the integrin CD18 subunit. Which step of the leukocyte adhesion cascade is most severely disrupted in this patient?

(A) Endothelial rolling

(B) Firm adhesion to endothelium

(C) Intravascular margination

(D) Selectin-mediated tethering

Q7. A biopsy of a chronic gastric ulcer reveals abundant granulation tissue at the base. Granulation tissue is composed of a specialized extracellular matrix configuration. Which collagen type is initially synthesized in highest abundance during this early proliferative phase of wound healing before being replaced?

(A) Type I Collagen

(B) Type II Collagen

(C) Type III Collagen

(D) Type IV Collagen

Q8. A 62-year-old male with long-standing cirrhosis develops a hepatic mass. Biopsy confirms hepatocellular carcinoma. Molecular profiling demonstrates an inactivating mutation in a gene responsible for halting the cell cycle when DNA damage is detected. Which of the following molecules acts as the primary gatekeeper at the G1/S checkpoint under physiological conditions?

(A) Cyclin D1

(B) Cyclin-dependent kinase 4 (CDK4)

(C) Retinoblastoma protein (Rb)

(D) E2F transcription factor

Q9. A 24-year-old female presents with severe fatigue and glossitis. Her hemoglobin is 7.2 g/dL, MCV is 118 fL, and peripheral blood smear shows hypersegmented neutrophils. Despite normal serum cobalamin levels, a metabolic block is suspected. Which of the following biochemical abnormalities is characteristically elevated in both isolated Vitamin B12 deficiency and isolated Folate deficiency?

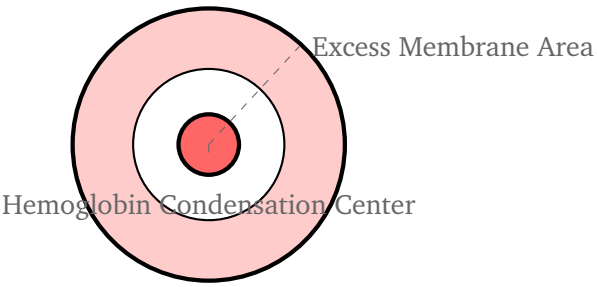
(A) Methylmalonic acid

(B) Homocysteine

(C) Propionyl-CoA

(D) Succinyl-CoA

Q10. A hematopathologist evaluates a peripheral blood film from an asymptomatic 35-year-old male during a routine checkup. The distinct erythrocyte morphologic variant illustrated in the schematic vector presentation below is observed in large numbers. Identify the matching underlying hemoglobinopathy or state linked to this cell geometry:



(A) Hereditary Spherocytosis

(B) Hemoglobin C disease / Thalassemia

(C) Glucose-6-Phosphate Dehydrogenase deficiency

(D) Microangiopathic Hemolytic Anemia

Q11. A 4-year-old boy presents with progressive pallor and splenomegaly. Laboratory evaluation reveals a normocytic hemolytic anemia with an increased mean corpuscular hemoglobin concentration (MCHC). An osmotic fragility test is positive. Which red blood cell cytoskeletal anchoring protein is most commonly defective in this condition?

(A) Ankyrin

(B) Protein 4.1

(C) Glycophorin C

(D) Actin filaments

Q12. A 68-year-old male presents with profound fatigue, bone pain, and recurrent respiratory infections. Laboratory workup reveals an IgG kappa monoclonal spike on serum protein electrophoresis, hypercalcemia, and renal insufficiency. A bone marrow biopsy is performed. Which of the following phenotypic marker profiles is typical for the neoplastic cells causing this condition?

(A) CD19+, CD20+, CD5+

(B) CD138+, CD38+, CD56+

(C) CD3+, CD4+, CD8-

(D) CD11c+, CD25+, CD103+

Q13. A 54-year-old female presents with persistent pruritus after hot showers, erythromelalgia, and splenomegaly. Her hemoglobin is 19.5 g/dL, white blood cell count is 14,500/uL, and platelet count is 520,000/uL. A bone marrow biopsy confirms polycythemia vera. Which molecular alteration drives this clonal myeloproliferative expansion?

(A) BCR-ABL1 fusion gene

(B) JAK2 V617F point mutation

(C) CALR frameshift mutation

(D) MPL W515K mutation

Q14. A 9-year-old child presents with massive mediastinal mass, superior vena cava syndrome, and a rapidly rising white blood cell count. Flow cytometry of the peripheral blasts demonstrates positivity for TdT, CD2, CD3, and CD7. The diagnosis of T-cell Acute Lymphoblastic Leukemia/Lymphoma is made. Which cytogenetic rearrangement is recurrently linked to this lineage variant?

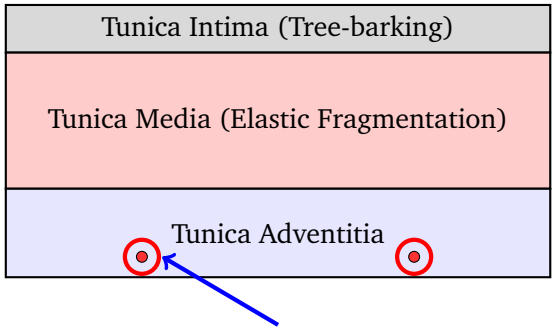
(A) t(15;17) translocation

(B) t(8;14) translocation

(C) t(11;14) translocation

(D) NOTCH1 activating mutations / TCR gene rearrangements

Q15. An autopsy specimen of a proximal aorta from a 67-year-old male with a history of untreated tertiary syphilis shows significant remodeling. The structural diagram below demonstrates the vessel wall destruction sequence. Identify the exact microscopic structural site where obliterative endarteritis directly compromises luminal flow, leading to ischemic necrosis of the tunica media:



Obliterative Endarteritis of Vasa Vasorum

(A) Internal elastic lamina

(B) Vasa vasorum lumen

(C) Endothelial surface layer

(D) Myointimal cells matrix

Q16. A 58-year-old chronic heavy smoker presents with an insidious onset of exertional dyspnea and minimal sputum production. High-resolution CT shows permanent dilation of airspaces distal to the terminal bronchioles, primarily affecting the upper lobes. What is the fundamental protease-antiprotease imbalance mechanism operating in this specific anatomical pattern of disease?

(A) Congenital deficiency of alpha-1 antitrypsin throughout the lungs

(B) Neutrophil elastase mediated destruction fueled by local oxidant inactivation of TIMPs

(C) Excessive macrophage activation secondary to CFTR channel gene mutations

(D) Eosinophilic degranulation with major basic protein destructive remodeling

Q17. A 35-year-old male presents with hemoptysis, hematuria, and rapidly progressive renal failure. A renal biopsy displays crescentic glomerulonephritis. Immunofluorescence shows linear deposition of IgG along the glomerular basement membrane. Which specific extracellular matrix component is the target autoantigen in this condition?

(A) Alpha-3 chain of Type IV Collagen

(B) Non-collagenous domain of Type I Collagen

(C) Laminin-5 structural glycoprotein

(D) Fibronectin cell-adhesion complex

Q18. A 48-year-old woman presents with an asymmetrical, painless enlargement of her thyroid gland. Histopathological examination shows dense lymphocytic infiltrates with well-formed germinal centers and abundant large epithelial cells with granular eosinophilic cytoplasm. Which autoantibody marker is most specific and pathognomonic for confirming this disease process?

(A) Anti-TSH receptor antibodies

(B) Anti-Thyroid Peroxidase (TPO) antibodies

(C) Anti-Calcium sensing receptor antibodies

(D) Anti-Thyroglobulin transcript variant antibodies

Q19. A 52-year-old male presents with persistent epigastric pain that worsens after meals. Upper endoscopy reveals a sharply demarcated, punched-out ulcer in the first part of the duodenum. Biopsies reveal no malignant architecture. Which bacterial virulence factor is primarily responsible for inducing local mucosal tissue injury and recruiting inflammatory cells in this patient's condition?

(A) CagA (Cytotoxin-associated gene A)

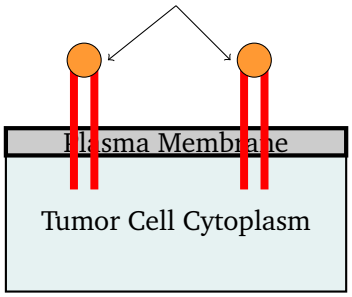
(B) VacA (Vacuolating cytotoxin A)

(C) Urease production

(D) Flagellar flagellin components

Q20. A 62-year-old woman presents with an ulcerative mass in the upper outer quadrant of her left breast. Core biopsy confirms invasive ductal carcinoma. Immunohistochemical mapping of the neoplastic cell membrane expression is illustrated below. Identify the corresponding therapeutic target receptor family designated by **Receptor Cluster Y**:

Receptor Cluster Y (HER2/neu Overexpression)



(A) Estrogen Receptor Alpha (ER)

(B) Progesterone Receptor (PR)

(C) Human Epidermal Growth Factor Receptor 2 (ErbB2)

(D) Epidermal Growth Factor Receptor 1 (EGFR)

Q21. A 63-year-old male presents with painless gross hematuria. Cystoscopy reveals a papillary exophytic mass within the urinary bladder wall. Biopsy confirms high-grade urothelial carcinoma. Which of the following molecular pathway alterations is most frequently implicated in the non-invasive papillary pathway of this malignancy?

(A) TP53 deletion mutations

(B) FGFR3 activating mutations

(C) RB1 transcriptional silencing

(D) PTEN loss of heterozygosity

Q22. A 42-year-old female presents with progressive skin tightening of her fingers, dysphagia to solids, and exertional dyspnea. Serology is positive for anti-topoisomerase I (anti-Scl-70) antibodies. Which of the following pathological changes is typically observed in the pulmonary vasculature of this patient?

(A) Granulomatous vasculitis with eosinophilic infiltration

(B) Medial hypertrophy and intimal fibrosis of small pulmonary arteries

(C) Fibrinoid necrosis of pulmonary capillaries without fibrosis

(D) Thromboangiitis obliterans of major segment arteries

Q23. A 29-year-old male with a history of intravenous drug use presents with a high-grade fever, splinter hemorrhages, and a new holosystolic murmur. Echocardiography reveals large, friable vegetations on the tricuspid valve leaflets. Which of the following histopathological features is characteristic of these vegetations?

(A) Dense collagenous organization with minimal inflammatory infiltrate

(B) Dense fibrin meshwork containing masses of proliferating bacteria and neutrophils

(C) Granulomatous nodules centered around zones of caseous necrosis

(D) Verrucous rows of sterile platelet thrombi along the lines of closure

Q24. A 3-year-old male child is brought to the clinic due to abdominal distension. Palpation reveals a large, firm, unilateral flank mass that does not cross the midline. An abdominal CT confirms a large intrarenal mass. Microscopic examination displays a triphasic pattern containing blastemal, stromal, and epithelial elements. Which of the following gene loci abnormalities is associated with this presentation?

(A) WT1 gene deletion or mutation on chromosome 11p13

(B) RB1 mutation on chromosome 13q14

(C) VHL gene inactivation on chromosome 3p25

(D) MYCN gene amplification on chromosome 2p24

Q25. A 72-year-old male presents with urinary frequency, urgency, and difficulty initiating urination. Digital rectal examination reveals a symmetrically enlarged, nodular, elastic prostate gland. A transurethral resection of the prostate (TURP) is performed. Histopathology reveals hyperplasia of both glandular epithelial cells and stromal smooth muscle elements. Which hormonal mediator is the primary driver of this hyperplastic growth within the periurethral transition zone?

(A) Estradiol

(B) Testosterone

(C) Dihydrotestosterone (DHT)

(D) Progesterone

Detailed Solutions

Q1.

Solution

Concept: Hepatic steatosis (fatty liver) in chronic alcohol abuse results from an imbalance between the synthesis/intake of lipids and their utilization or secretion. The secretion of triglycerides from hepatocytes relies heavily on packaging them into very-low-density lipoproteins (VLDLs).

Solution:

Let's analyze the pathophysiology of alcohol-induced lipid accumulation:

(a) Chronic ethanol metabolism shifts the cellular redox state by increasing the $NADH/NAD^+$ ratio, which inhibits fatty acid oxidation and promotes triglyceride synthesis.

(b) To exit hepatocytes, these accumulated triglycerides must be packaged into VLDLs, a process that requires structural lipid-binding apoproteins (primarily apolipoprotein B-100).

(c) Alcohol exerts a direct toxic effect on hepatic protein synthesis machinery, resulting in a **Decreased synthesis of apoproteins**. Without sufficient apoproteins, triglycerides cannot be assembled into exportable VLDL particles and become trapped inside the cytoplasm, leading to macrovesicular steatosis.

Final Answer: Decreased synthesis of apoproteins

Answer: (A)

Go Back to Question 1

Q2.

Solution

Concept: Hypoxic injury compromises oxidative phosphorylation in the mitochondria, leading to an acute drop in cellular adenosine triphosphate (ATP) levels. This energy failure disrupts metabolic homeostatic systems that are dependent on active transport.

Solution:

Let's track the chronological downstream events triggered by cellular ATP depletion:

(a) A drop in ATP inhibits energy-dependent ion pumps, specifically the plasma membrane Na^+/K^+ ATPase pump, leading to an intracellular accumulation of sodium and an efflux of potassium.

(b) The net gain of intracellular solute creates an osmotic gradient that drives an influx of water into the cell, resulting in early cellular swelling (hydropic degeneration), rather than water efflux.

(c) Concurrently, as the cell swells and the cisternae of the rough endoplasmic reticulum (RER) dilate due to osmotic pressure, there is a physical **Detachment of ribosomes from the rough endoplasmic reticulum**, which leads to a rapid dissociation of polysomes into monosomes and a subsequent decline in protein synthesis.

Final Answer: Detachment of ribosomes from the rough endoplasmic reticulum

Answer: (C)

Go Back to Question 2

Q3.

Solution

Concept: The intrinsic (mitochondrial) pathway of apoptosis is tightly regulated by the Bcl-2 family of proteins, which balance pro-apoptotic and anti-apoptotic signals to control outer mitochondrial membrane permeabilization (OMMP).

Solution:

Let's delineate the structural and functional divisions of the Bcl-2 protein family:

(a) Anti-apoptotic proteins (such as Bcl-2, Bcl-xL, and Mcl-1) normally preserve mitochondrial membrane integrity by binding and sequestering pro-apoptotic molecules.

(b) When cells experience irreversible DNA damage or cellular stress (e.g., from radiation), BH3-only sensors activate the pro-apoptotic executioner proteins, **Bak** and Bax.

(c) Upon activation, **Bak** (which is constitutively integrated into the outer mitochondrial membrane) undergoes a conformational change and oligomerizes with Bax to **directly form the macromolecular pores/channels** that breach the membrane, allowing Cytochrome c to escape into the cytoplasm.

Final Answer: Bak

Answer: (C)

Go Back to Question 3

Q4.

Solution

Concept: Lipofuscin is an insoluble, wear-and-tear pigment that accumulates slowly within the cytoplasm of aging, permanently differentiated post-mitotic cells, such as myocardial fibers and neurons.

Solution:

Let's analyze the biochemical origin of this endogenous pigment:

(a) Cellular metabolism produces reactive oxygen species (ROS) that chronically damage cell membranes and organelles through lipid peroxidation.

(b) These oxidized, cross-linked lipid-protein complexes are targeted for clearance and engulfed into autophagic vacuoles, which then fuse with lysosomes.

(c) Because these heavily cross-linked lipid peroxidation residues are highly resistant to standard enzymatic breakdown, they undergo **Incomplete lysosomal degradation of lipid peroxidation products**, lingering in the perinuclear space as brown, granular lipofuscin deposits (brown atrophy of the heart).

Final Answer: Incomplete lysosomal degradation of lipid peroxidation products

Answer: (A)

Go Back to Question 4

Q5.

Solution

Concept: Necroptosis is a form of programmed, caspase-independent cell death that shares biochemical upstream signaling features with apoptosis but culminates in a lytic morphological phenotype typical of necrosis.

Solution:

Let's evaluate the molecular assembly shown in the pathway schematic:

(a) Ligand binding to death receptors (such as TNFR1) under conditions where Caspase-8 is inhibited triggers the activation and phosphorylation of receptor-interacting protein kinases 1 and 3 (RIPK1 and RIPK3).

(b) RIPK1 and RIPK3 physically interact to assemble a highly stable, multiprotein signaling platform known as the **Necrosome multiprotein complex** (**Target Complex X**).

(c) Once organized, the necrosome recruits and phosphorylates the downstream executioner protein mixed lineage kinase domain-like (MLKL). Phosphorylated MLKL forms oligomers that translocate to the plasma membrane, driving pore formation, osmotic swelling, and membrane lysis.

Final Answer: Necrosome multiprotein complex

Answer: (C)

Go Back to Question 5

Q6.

Solution

Concept: Leukocyte extravasation into inflamed tissues involves a sequential cascade of steps: margination, selectin-mediated rolling, integrin-mediated firm adhesion, and transendothelial migration (diapedesis).

Solution:

Let's look at how the patient's genetic deficiency impacts the leukocyte adhesion cascade:

(a) The CD18 gene encodes the common β_2 subunit of the leukocyte integrins LFA-1 (CD11a/CD18) and Mac-1 (CD11b/CD18). A total lack of this subunit causes Leukocyte Adhesion Deficiency Type 1 (LAD-1).

(b) Selectins (E-, P-, and L-selectin) handle initial tethering and rolling, steps that remain intact in this patient.

(c) For leukocytes to stop rolling and squeeze out of the vessel, their surface integrins must bind tightly to intercellular adhesion molecule-1 (ICAM-1) on stimulated endothelial cells. Because the patient lacks functional β_2-integrins, leukocytes cannot execute **Firm adhesion to endothelium**, resulting in impaired tissue recruitment and a marked leukocytosis.

Final Answer: Firm adhesion to endothelium

Answer: (B)

Go Back to Question 6

Q7.

Solution

Concept: Wound healing and granulation tissue formation require a highly coordinated deposition, remodeling, and structural maturation of extracellular matrix components.

Solution:

Let's trace the shift in collagen types during tissue repair and structural scar maturation:

(a) Granulation tissue is an early, highly vascular proliferative matrix rich in proliferating fibroblasts, delicate capillary buds, and inflammatory cells.

(b) During this initial phase of wound healing, fibroblasts prioritize the rapid synthesis of **Type III Collagen**, which is flexible and provides a supportive scaffolding for angiogenesis and matrix accumulation.

(c) As the scar matures during the remodeling phase, metalloproteinases degrade this temporary Type III collagen network and replace it with Type I collagen, which features high tensile strength and gives mature scars their structural integrity.

Final Answer: Type III Collagen

Answer: (C)

Go Back to Question 7

Q8.

Solution

Concept: The cell cycle contains rigorous checkpoints that monitor structural DNA integrity. The restriction point at the G1/S transition controls whether a cell commits to DNA replication.

Solution:

Let's trace the molecular interactions that regulate the G1/S restriction point:

(a) Under baseline physiological conditions, the **Retinoblastoma protein (Rb)** acts as the primary molecular break or gatekeeper by binding and inactivating the E2F transcription factor family.

(b) When growth factors stimulate the cell, Cyclin D forms active complexes with CDK4 and CDK6.

(c) These active cyclin-CDK complexes phosphorylate the Rb protein. Hyperphosphorylated Rb changes shape and releases E2F, freeing the transcription factor to activate the genes required for entry into the S phase. Inactivating mutations in Rb remove this primary checkpoint, predisposing cells to malignant transformations like hepatocellular carcinoma.

Final Answer: Retinoblastoma protein (Rb)

Answer: (C)

Go Back to Question 8

Q9.

Solution

Concept: Vitamin B12 (cobalamin) and folate (Vitamin B9) are essential cofactors in one-carbon metabolism, and deficiencies in either disrupt DNA synthesis, resulting in megaloblastic anemia with hypersegmented neutrophils.

Solution:

Let's trace the pathways where cobalamin and folate overlap:

(a) In the cytosol, the conversion of homocysteine to methionine requires the enzyme methionine synthase, which utilizes both methylcobalamin (B12) and N5-methyltetrahydrofolate (folate) as cofactors. A deficiency in either vitamin stalls this reaction, causing **Homocysteine** to back up and accumulate in the blood.

(b) Inside the mitochondria, Vitamin B12 serves as an obligatory cofactor for the enzyme methylmalonyl-CoA mutase, which converts methylmalonic acid (MMA) to succinyl-CoA.

(c) Because folate does not participate in this mitochondrial mutase reaction, MMA levels remain completely normal in isolated folate deficiency. Therefore, elevated **Homocysteine** is the biochemical finding shared by both deficiency states.

Final Answer: Homocysteine

Answer: (B)

Go Back to Question 9

Q10.

Solution

Concept: Target cells (codocytes) are erythrocytes characterized by a central area of hemoglobin condensation surrounded by a clear ring and an outer hemoglobinized rim, resembling a bullseye target.

Solution:

Let's look at the membrane-to-volume kinetics that produce this target morphology:

(a) Target cells form when there is an increase in the ratio of erythrocyte surface area to intracellular hemoglobin volume (surface area-to-volume mismatch).

(b) This mismatch can be driven by a loss of intracellular hemoglobin volume (as seen in quantitative hemoglobinopathies like **Thalassemia** or iron deficiency anemia) or by an absolute increase in plasma membrane surface area (as seen in obstructive liver disease or **Hemoglobin C disease** due to structural hemoglobin mutations).

(c) Spherocytes, by contrast, exhibit a decreased surface area-to-volume ratio, resulting in a uniform round cell that lacks central pallor entirely.

Final Answer: Hemoglobin C disease / Thalassemia

Answer: (B)

Go Back to Question 10

Q11.

Solution

Concept: Hereditary spherocytosis is a congenital hemolytic disorder caused by defects in the vertical structural proteins that tether the plasma membrane lipid bilayer to the underlying spectrin cytoskeleton.

Solution:

Let's identify the primary structural culprit behind this red cell membrane defect:

(a) The patient has a normocytic hemolytic anemia, an increased MCHC (due to relative cellular dehydration as spherocytes lose membrane fragments), and a positive osmotic fragility profile.

(b) The most common molecular cause of hereditary spherocytosis (accounting for approximately 50–60% of cases) is an inherited deficiency or structural defect in **Ankyrin**.

(c) **Ankyrin** anchors the horizontal spectrin cytoskeleton to the transmembrane Band 3 complex. When ankyrin is defective, the uncoupled lipid bilayer sheds microvesicles over time. This loss of surface area forces the red cells into a fragile, spherical shape that undergoes splenic sequestration and destruction.

Final Answer: Ankyrin

Answer: (A)

Go Back to Question 11

Q12.

Solution

Concept: Multiple myeloma is a malignant neoplasm of terminally differentiated plasma cells that clonal expansions within the bone marrow, presenting clinically with bone pain, hypercalcemia, renal injury, and lytic bone lesions.

Solution:

Let's evaluate the surface marker immunophenotype that identifies plasma cell lineages:

(a) Neoplastic plasma cells emerge from mature B-lymphocytes but lose standard pan-B-cell surface markers, meaning they are typically negative for CD19 and CD20.

(b) Instead, plasma cells upregulate cell-surface glycoproteins that are highly specific for their secretory lineage, most notably **CD138** (syndecan-1) and **CD38** (cyclic ADP ribose hydrolase).

(c) Malignant plasma cell populations in multiple myeloma also frequently display aberrant expression of the neural cell adhesion molecule **CD56**. This yields a classic immunophenotypical profile of **CD138+, CD38+, CD56+**.

Final Answer: CD138+, CD38+, CD56+

Answer: (B)

Go Back to Question 12

Q13.

Solution

Concept: Myeloproliferative neoplasms (MPNs) are clonal hematopoietic stem cell disorders characterized by the autonomous overproduction of one or more mature myeloid lineages.

Solution:

Let's correlate the clinical presentation of Polycythemia Vera (PV) with its driving mutation:

(a) The patient's presentation—including panmyelosis (elevated RBCs, WBCs, and platelets), splenomegaly, post-bath pruritus (due to histamine release from basophils), and erythromelalgia—is highly classic for Polycythemia Vera.

(b) Over 95% of PV cases are driven by a somatic **JAK2 V617F point mutation** located in exon 14 of the Janus Kinase 2 gene.

(c) This mutation substitutes a valine for phenylalanine at codon 617, disrupting the auto-inhibitory domain of the kinase. This leads to constitutive, ligand-independent downstream tyrosine kinase signaling, rendering hematopoietic progenitors hypersensitive to erythropoietin (EPO) and driving uninhibited red cell expansion.

Final Answer: JAK2 V617F point mutation

Answer: (B)

Go Back to Question 13

Q14.

Solution

Concept: T-cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL) is an aggressive hematologic malignancy of immature T-lymphoblasts that typically presents in adolescents as a rapidly growing anterior mediastinal mass.

Solution:

Let's trace the molecular oncogenic mechanisms associated with the T-cell lineage:

(a) The immunophenotypic profile (TdT+, CD2+, CD3+, CD7+) confirms an immature T-cell neoplasm (T-lymphoblasts).

(b) Unlike B-ALL, which is characterized by recurrent structural translocations like $t(12;21)$ or $t(9;22)$, T-ALL is frequently driven by somatic gain-of-function **NOTCH1 activating mutations**.

(c) These mutations cause constitutive activation of the NOTCH1 signaling pathway, which interacts with structural **TCR gene rearrangements** (where T-cell receptor promoter regions accidentally drive the overexpression of proto-oncogenes), steering lymphoblasts toward malignant transformation.

Final Answer: NOTCH1 activating mutations / TCR gene rearrangements

Answer: (D)

Go Back to Question 14

Q15.

Solution

Concept: Cardiovascular syphilis characteristically targets the proximal thoracic aorta, causing luetic aortitis through an immune-mediated chronic inflammatory reaction.

Solution:

Let's trace the vascular anatomy and the ischemic cascade shown in the structural diagram:

(a) The spirochete *Treponema pallidum* invades the adventitial layer of the aorta, triggering a dense, plasma cell-rich chronic inflammatory infiltrate.

(b) This perivascular inflammation produces an **obliterative endarteritis of the vasa vasorum**, narrowing and occluding the lumens of these tiny nutrient vessels.

(c) Because the outer two-thirds of the thick aortic tunica media depends entirely on the **vasa vasorum lumen** for oxygenated blood flow, this luminal occlusion causes chronic ischemic necrosis and fragmentation of the medial elastic fibers. This weakens the vessel wall, leading to aneurysmal dilation and a wrinkled "tree-bark" intimal appearance.

Final Answer: Vasa vasorum lumen

Answer: (B)

Go Back to Question 15

Q16.

Solution

Concept: Emphysema involves the permanent enlargement of respiratory airspaces distal to terminal bronchioles due to structural destruction of the alveolar walls without obvious fibrosis.

Solution:

Let's look at how the patient's smoking habit drives this specific centrilobular lung remodeling:

(a) The high-resolution CT demonstrates a centrilobular (centriacinar) emphysema pattern that predominantly affects the upper lobes, a presentation highly characteristic of chronic cigarette smoking.

(b) Inhaled cigarette smoke irritates the airways, recruiting alveolar macrophages and neutrophils to the respiratory bronchioles. These activated neutrophils release excess amounts of **neutrophil elastase**.

(c) At the same time, reactive oxidants in tobacco smoke chemically inactivate endogenous antiproteases (such as alpha-1 antitrypsin and tissue inhibitors of metalloproteinases, or TIMPs). This creates a localized **Neutrophil elastase mediated destruction fueled by local oxidant inactivation** of protective antiproteases, leading to the targeted degradation of structural elastin fibers in the upper lobes.

Final Answer: Neutrophil elastase mediated destruction fueled by local oxidant inactivation of TIMPs

Answer: (B)

Go Back to Question 16

Q17.

Solution

Concept: Goodpasture Syndrome (Anti-Glomerular Basement Membrane disease) is an autoimmune disorder characterized by a Type II hypersensitivity reaction targeting specific basement membrane components in the kidneys and lungs.

Solution:

Let's isolate the molecular target of the autoantibodies in this condition:

(a) The patient presents with a classic pulmonary-renal syndrome (hemoptysis and hematuria) and a biopsy showing crescentic, rapidly progressive glomerulonephritis.

(b) Immunofluorescence shows a uniform, linear deposition of IgG along the glomerular basement membrane, a finding pathognomonic for anti-GBM disease.

(c) The target autoantigen is the non-collagenous domain of the **Alpha-3 chain of Type IV Collagen**. Because this specific collagen chain is highly expressed in both glomerular and pulmonary alveolar basement membranes, autoantibody binding triggers complement activation and inflammatory recruitment in both organs, causing simultaneous glomerulonephritis and alveolar hemorrhage.

Final Answer: Alpha-3 chain of Type IV Collagen

Answer: (A)

Go Back to Question 17

Q18.

Solution

Concept: Hashimoto Thyroiditis (chronic lymphocytic thyroiditis) is the most common cause of hypothyroidism in iodine-sufficient areas. It is driven by an autoimmune-mediated destruction of the thyroid gland.

Solution:

Let's match the histopathological features with the corresponding diagnostic serological markers:

(a) The histopathology—showing dense lymphocytic infiltrates, well-formed germinal centers, and Hurthle cells (large epithelial cells with granular, eosinophilic, mitochondrial-rich cytoplasm)—is diagnostic of Hashimoto Thyroiditis.

(b) While several thyroid autoantibodies can be detected during an immune response, **Anti-Thyroid Peroxidase (TPO) antibodies** are the most specific and clinically sensitive marker for this disease.

(c) TPO is an essential enzyme involved in thyroid hormone synthesis, and anti-TPO antibodies serve as a reliable serological surrogate confirming the underlying cell-mediated autoimmune destruction of the thyroid parenchyma.

Final Answer: Anti-Thyroid Peroxidase (TPO) antibodies

Answer: (B)

Go Back to Question 18

Q19.

Solution

Concept: Peptic ulcer disease in the proximal duodenum is strongly linked to *Helicobacter pylori* infection, which populates the gastric antrum and alters local mucosal defenses.

Solution:

Let's evaluate the primary tissue-destructive virulence factors of *H. pylori*:

(a) While urease production is essential for bacterial colonization (by neutralizing gastric acid), it does not directly act as the primary cytotoxin that damages mucosal cells.

(b) The major bacterial virulence factor responsible for directly inducing local mucosal cell injury and vacuolization is **VacA (Vacuolating cytotoxin A)**.

(c) VacA enters host epithelial cells and causes structural pore formation and mitochondrial dysfunction, which works alongside the immunogenic **CagA** protein to promote direct tissue remodeling, epithelial apoptosis, and neutrophil recruitment, culminating in a punched-out duodenal ulcer.

Final Answer: Vacuolating cytotoxin A (VacA)

Answer: (B)

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Q20.

Solution

Concept: Invasive ductal carcinoma of the breast is classified into therapeutic subgroups based on the expression of hormone receptors (ER, PR) and growth factor receptor amplification profiles.

Solution:

Let's identify the protein overexpressed on the cell membrane in the immunohistochemical diagram:

(a) The diagram depicts a tyrosine kinase receptor dimer that is heavily overexpressed along the plasma membrane of the breast cancer cell.

(b) This corresponds to **Human Epidermal Growth Factor Receptor 2 (ErbB2)**, commonly known as **HER2/neu**.

(c) The *HER2/neu* proto-oncogene on chromosome 17q12 encodes a 185 kDa transmembrane receptor tyrosine kinase. Amplification of this gene leads to receptor overexpression and ligand-independent dimerization, driving downstream proliferative pathways. This makes it the direct target for monoclonal antibody therapies such as trastuzumab.

Final Answer: Human Epidermal Growth Factor Receptor 2 (ErbB2)

Answer: (C)

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Q21.

Solution

Concept: Bladder cancer develops through two distinct pathways: a non-invasive papillary pathway and a flat carcinoma in situ (CIS) pathway, each driven by a unique set of genetic alterations.

Solution:

Let's analyze the molecular genetics of the urothelial carcinoma pathways:

(a) The flat invasive pathway typically arises from carcinoma in situ and is driven early on by inactivating mutations in tumor suppressor genes such as *TP53* and *RB1*.

(b) In contrast, the low-grade, non-invasive papillary pathway is characteristically driven by constitutive activation of oncogenic receptor tyrosine kinases.

(c) **FGFR3 activating mutations** (Fibroblast Growth Factor Receptor 3) are found in over 70–80% of non-invasive papillary urothelial tumors, driving ligand-independent hyperplasia and papillary exophytic growth within the bladder wall.

Final Answer: FGFR3 activating mutations

Answer: (B)

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Q22.

Solution

Concept: Systemic sclerosis (scleroderma) is a systemic connective tissue disease characterized by autoimmune-mediated vascular injury and extensive fibrosis of the skin and internal organs.

Solution:

Let's evaluate the vascular changes that occur in the lungs of scleroderma patients:

(a) The patient has diffuse systemic sclerosis, confirmed by skin tightening, dysphagia (from esophageal dysmotility), exertional dyspnea, and positive anti-topoisomerase I (anti-Scl-70) serology.

(b) The progressive dyspnea can stem from interstitial lung disease or a dedicated pulmonary vascular lesion that triggers pulmonary arterial hypertension (PAH).

(c) The classic pathohistological finding in the small pulmonary muscular arteries of these patients is **Medial hypertrophy and intimal fibrosis**. Endothelial injury triggers a proliferative remodeling cascade that thickens the vessel walls, narrows the lumens, and increases vascular resistance.

Final Answer: Medial hypertrophy and intimal fibrosis of small pulmonary arteries

Answer: (B)

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Q23.

Solution

Concept: Infective endocarditis involves the colonization of heart valves by microbial pathogens, leading to the formation of bulky, friable, destructive vegetations.

Solution:

Let's evaluate the architectural components of an active infective endocarditis vegetation:

(a) The patient's history of intravenous drug use, high fever, splinter hemorrhages, and a new tricuspid murmur point to acute infective endocarditis (typically caused by *Staphylococcus aureus*).

(b) Because these lesions are driven by active, destructive bacterial proliferation on the valve surface, histopathological evaluation reveals a **Dense fibrin meshwork containing masses of proliferating bacteria and neutrophils**.

(c) This acute inflammatory composition makes the vegetations fragile and prone to embolization, distinguishing them from the sterile, ordered platelet thrombi seen in marantic endocarditis (NBTE) or the granulomatous lesions of rheumatic heart disease.

Final Answer: Dense fibrin meshwork containing masses of proliferating bacteria and neutrophils

Answer: (B)

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Q24.

Solution

Concept: Wilms tumor (nephroblastoma) is the most common primary renal malignancy of childhood, characteristically presenting as a large, asymptomatic, unilateral flank mass.

Solution:

Let's align the histopathology and clinical presentation with the underlying genetic locus:

(a) The classic microscopic appearance of a Wilms tumor is a triphasic pattern that mimics embryonic renal development, consisting of blastemal sheets, primitive epithelial structures (abortive tubules/glomeruli), and a spindle-cell stromal background.

(b) This presentation is highly associated with structural genetic alterations at the **WT1 gene locus on chromosome 11p13**.

(c) The *WT1* gene encodes a zinc-finger transcription factor that is essential for normal urogenital development; inactivation or deletion of this gene disrupts normal mesenchymal-to-epithelial transitions, leading to the development of a nephroblastoma.

Final Answer: WT1 gene deletion or mutation on chromosome 11p13

Answer: (A)

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Q25.

Solution

Concept: Benign Prostatic Hyperplasia (BPH) is an age-related, non-malignant proliferation of epithelial and stromal elements within the periurethral transition zone of the prostate, leading to lower urinary tract symptoms (LUTS).

Solution:

Let's identify the principal androgenic hormone that drives this hyperplastic growth:

(a) While circulating testosterone enters prostatic stromal cells from the bloodstream, it is not the immediate local signaling molecule that drives cell proliferation.

(b) Inside the stromal cells, the enzyme 5-alpha reductase (primarily type 2) metabolizes testosterone into **Dihydrotestosterone (DHT)**.

(c) **DHT** is significantly more potent than testosterone because it binds to the androgen receptor with higher affinity and dissociates more slowly. Once bound, DHT acts as the primary autocrine and paracrine growth mediator, stimulating the transcription of growth factors that drive the hyperplasia of both stromal and epithelial components in the transition zone.

Final Answer: Dihydrotestosterone (DHT)

Answer: (C)

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Answer Key

Q	Ans	Q	Ans	Q	Ans	Q	Ans	Q	Ans
1	A	2	C	3	C	4	A	5	C
6	B	7	C	8	C	9	B	10	B
11	A	12	B	13	B	14	D	15	B
16	B	17	A	18	B	19	B	20	C
21	B	22	B	23	B	24	A	25	C