NEET PG Pathology Sample Paper-1

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 42-year-old male presenting with subacute hepatic failure undergoes a core needle biopsy. Histopathological evaluation demonstrates extensive hepatocytes with swollen, pale, finely granular cytoplasm. Special staining and electron microscopy confirm that this appearance is driven by massive, compensatory hypertrophy and structural fragmentation of the smooth endoplasmic reticulum (SER) secondary to chronic xenobiotic exposure. Which of the following molecular hallmarks is most classically associated with this specific cellular adaptation?

(A) Induction of the Cytochrome P450 monooxygenase enzyme system

(B) Accelerated ubiquitin-mediated proteasomal degradation of actin filaments

(C) Decreased intracellular pH leading to clumping of nuclear chromatin

(D) Direct transdifferentiation of hepatocytes into biliary epithelial cells

Q2. A molecular biology lab investigates the mechanistic triggers of cell death. They expose a cell line to a targeted toxin that selectively causes permeabilization of the outer mitochondrial membrane without causing immediate ATP depletion. This leads to the cytosolic release of Cytochrome c and Smac/DIABLO. Which of the following downstream events will directly occur to initiate the execution phase of this pathway?

(A) Activation of Caspase-8 via the Fas-associated death domain (FADD)

(B) Binding of Cytochrome c to Apaf-1, forming an apoptosome that recruits Caspase-9

(C) Cleavage of Gasdermin D to form membrane pores and initiate pyroptosis

(D) Upregulation of FLIP to block the death-inducing signaling complex (DISC)

Q3. A 62-year-old female presents with persistent, localized pain in her right thigh. Imaging reveals a well-circumscribed, deeply seated soft tissue mass. Biopsy reveals a malignant mesenchymal tumor. Cytogenetic analysis identifies a characteristic $t(12;16)(q13;p11)$ chromosomal translocation. This structural mutation leads to the formation of a chimeric fusion protein that alters transcription factors crucial for adipocyte differentiation. What is the most likely diagnosis?

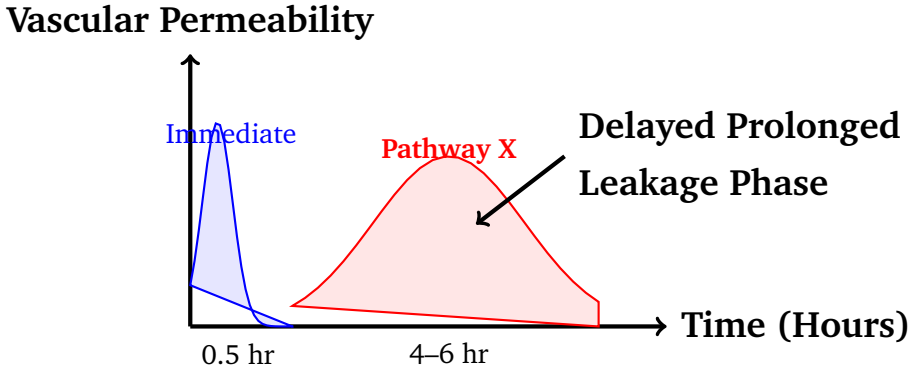
(A) Myxoid Liposarcoma

(B) Synovial Sarcoma

(C) Alveolar Rhabdomyosarcoma

(D) Ewing Sarcoma

Q4. An experimental pathology study maps the timeline of vascular permeability alterations during an acute inflammatory response following a localized thermal injury. The diagram below tracks the endothelial response profile over time. Identify the specific cellular mechanism labeled as **Pathway X** that accounts for the prolonged, delayed leakage phase shown in the curve:



(A) Histamine-mediated transient endothelial cell contraction in postcapillary venules

(B) Direct, severe endothelial cell necrosis and detachment affecting venules and capillaries

(C) VEGF-induced transient transcellular transport through intra-cytoplasmic vesiculovacuolar organelles

(D) Rapid marginations of platelets forming a temporary, leaky hemostatic plug

Q5. A 28-year-old male with a history of recurrent soft tissue abscesses is found to have a defect in leukocyte rolling along the vascular endothelium. Functional assays reveal that his leukocytes lack the sialyl-Lewis X modified glycoprotein ligands required to bind to selectins. Which clinical phenotype and primary molecular deficiency best describe this patient's condition?

(A) Leukocyte Adhesion Deficiency Type 1 (LAD-1); defect in CD18 β_2-integrin subunit

(B) Leukocyte Adhesion Deficiency Type 2 (LAD-2); defect in GDP-fucose transporter

(C) Chediak-Higashi Syndrome; defect in vesicle trafficking regulatory protein (LYST)

(D) Chronic Granulomatous Disease; defect in NADPH oxidase subunit gp91phox

Q6. During a routine autopsy of an 80-year-old male who died of ischemic heart disease, the prosector notes a deeply brownish-pigmented myocardium. Microscopic examination of the cardiomyocytes reveals abundant, fine, perinuclear, golden-brown cytoplasmic granules that do not stain with Prussian blue. Which of the following biochemical pathways is responsible for the formation of this pigment?

(A) Incomplete lysosomal degradation of lipid peroxidation products from autophagocytosed membranes

(B) Intracellular polymerization of homogentisic acid secondary to an enzyme deficiency

(C) Excess systemic systemic absorption of ferric iron depositing as crystalline polymers

(D) Defective breakdown of porphyrin rings leading to systemic hematoidin deposits

Q7. A 35-year-old female with an autoimmune connective tissue disease is found to have extensive, coarse calcifications within her damaged mitral valve leaflets and scarred subcutaneous nodules, despite maintaining normal serum calcium and phosphorus concentrations. Which statement best summarizes the underlying pathogenesis of this finding?

(A) Hyperparathyroidism driving precipitation of calcium salts in alkaline environments

(B) Membrane injury causing calcium influx, matrix vesicle formation, and nucleation of crystalline calcium phosphate

(C) Systemic vitamin D intoxication driving metastatic deposits in healthy tissues

(D) Decreased osteoclastic resorption leading to passive accumulation of hydroxyapatite

Q8. A 52-year-old male chronic smoker presents with a cough and hemoptysis. A bronchoscopy is performed, and a biopsy of the main stem bronchus demonstrates that the normal pseudostratified ciliated columnar epithelium has been replaced by stratified squamous epithelium. Which molecular mechanism is responsible for this adaptive transformation?

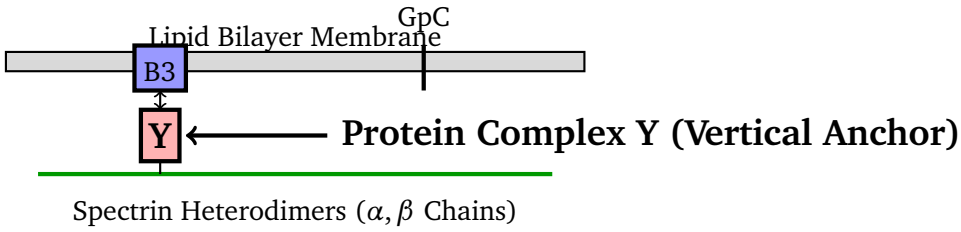
(A) Differentiated columnar cells undergoing direct phenotypic transdifferentiation into squamous cells

(B) Genetic mutation of the p53 gene driving clonal malignant proliferation

(C) Reprogramming of local tissue stem cells or undifferentiated reserve cells mediated by cytokines and growth factors

(D) Increased rates of apoptosis among ciliated cells paired with selective necrosis of basal cells

Q9. A 24-year-old female presents with severe fatigue and mild scleral icterus. Her peripheral blood smear shows numerous microspherocytes, and the osmotic fragility test is markedly positive. The diagram below illustrates the horizontal and vertical structural connectivity of the red blood cell cytoskeleton. Identify the classic structural protein component labeled as **Protein Complex Y** whose vertical tethering defect results in this patient's clinical presentation:



(A) Spectrin α-β horizontal cross-linking dimer

(B) Ankyrin (interacting with Band 3 and Spectrin)

(C) Protein 4.1R complex stabilizing the actin junctional node

(D) Tropomodulin capping filament head

Q10. A 65-year-old male presents with generalized lymphadenopathy, splenomegaly, and a profound leukocytosis of $120,000/\mu$L. The differential count reveals a predominance of mature-appearing lymphocytes along with numerous smudge cells. Flow cytometry demonstrates a clonal population of B cells expressing CD5, CD19, CD20 (weak), and CD23. Which of the following molecular aberrations or cytogenetic updates is most frequently associated with a poor prognosis in this disease entity?

(A) Isolated deletion of 13q14 ($del(13q)$)

(B) Deletion of 17p ($del(17p)$) involving the TP53 gene locus

(C) Trisomy 12q

(D) $t(11;14)(q13;q32)$ leading to Cyclin D1 overexpression

Q11. A 9-year-old boy is evaluated for bleeding from his gums and epistaxis. Laboratory results show a prolonged bleeding time, normal prothrombin time (PT), and a prolonged activated partial thromboplastin time (aPTT). Platelet aggregation studies show completely absent aggregation in response to ristocetin, which is not corrected by adding normal pooled plasma. However, aggregation in response to ADP, epinephrine, and collagen is normal. What is the defective or deficient molecule?

(A) Glycoprotein Ib-IX-V complex (GPIb)

(B) Glycoprotein IIb-IIIa complex (GPIIb/IIIa)

(C) von Willebrand Factor (vWF)

(D) Dense granule Adenosine Triphosphate (ATP) storage pool

Q12. A 38-year-old male with long-standing poorly controlled celiac disease presents with progressive dyspnea, microcytic anemia, and severe glossitis. Serum studies show low iron and low ferritin. He is placed on therapeutic oral iron supplementation, but follow-up counts at 4 weeks show minimal hematological response. A duodenal biopsy confirms persistent villous atrophy. Which segment of the gastrointestinal tract is the primary site for iron absorption, and which regulatory hormone inhibits iron export by triggering the degradation of ferroportin?

(A) Ileum; Erythropoietin

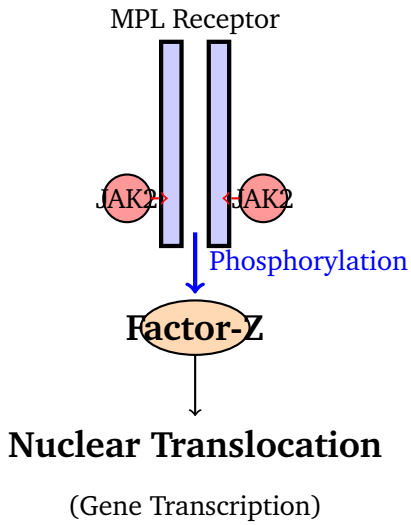
(B) Jejunum; Hepcidin

(C) Duodenum; Hepcidin

(D) Stomach; Gastrin

Q13. A bone marrow biopsy from an asymptomatic 58-year-old male with persistent thrombocytosis ($890,000/\mu$L) reveals dense clusters of atypical, hyperlobulated, giant megakaryocytes with a "staghorn" appearance, without significant reticulin fibrosis. The diagnostic workup includes molecular screening for mutations in Janus Kinase 2 (JAK2), Calreticulin (CALR), and Myeloproliferative Leukemia Virus Oncogene (MPL). The schematic below tracks the signaling pathway downsteam of these mutations. Identify the

downstream transcription factors labeled as **Factor-Z** that are constitutively phosphorylated in this condition:



(A) STAT3 and STAT5 proteins

(B) Smad2 and Smad3 complexes

(C) NF-κB p65 subunit

(D) c-Myc proto-oncogene products

Q14. A 29-year-old male presenting with dark urine in the morning is evaluated for paroxysmal nocturnal hemoglobinuria (PNH). Flow cytometry confirms the absence of GPI-anchored proteins on his granulocytes. Deficiencies in which specific membrane-bound regulatory proteins explain his intravascular hemolysis and propensity for atypical venous thrombosis?

(A) CD55 (Decay-Accelerating Factor) and CD59 (Membrane Attack Complex Inhibitor)

(B) CD11a and CD18 integrity molecules

(C) CD16 and CD32 Fc-gamma receptors

(D) CD4 prototypic markers and CD8 costimulatory anchors

Q15. A 64-year-old male presents with severe chest pain and expires shortly after arrival. Autopsy reveals a massive transmural myocardial infarction involving the anterior wall of the left ventricle. Histopathological evaluation of the

infarcted zone shows extensive coagulative necrosis, loss of cardiomyocyte nuclei, and dense neutrophilic infiltration. Based on the cellular kinetics of myocardial injury repair, what is the estimated age of this myocardial infarction at the time of death?

(A) 4 to 12 hours

(B) 1 to 3 days

(C) 7 to 10 days

(D) 2 to 3 weeks

Q16. A 54-year-old male smoker undergoes an endoscopic ultrasound-guided biopsy of a suspicious indurated mass located in the head of the pancreas. Histopathological examination reveals well-formed malignant glands embedded within an abundant, dense, collagenous stroma (desmoplasia). Molecular profiling identifies a point mutation in codon 12 of the KRAS gene. Which of the following best describes the immediate downstream biochemical consequence of this specific KRAS mutation?

(A) Persistent binding of GTP due to loss of intrinsic GTPase activity, leading to constitutive downstream RAF/MAPK signaling

(B) Accelerated inactivation of tyrosine kinases via rapid phosphorylation loops

(C) Absolute blockade of the PI3K/Akt pathway due to competitive inhibition

(D) Failure of RAS to translocate to the plasma membrane for activation

Q17. A 32-year-old female presents with malar rash, arthralgias, and marked proteinuria. A renal biopsy is performed, and light microscopy demonstrates diffuse hypercellularity of the glomeruli with thickened capillary walls showing prominent "wire-loop" lesions. Subendothelial electron-dense deposits are identified on electron microscopy. Immunofluorescence reveals a coarse granular "full house" pattern. What is the correct classification of this lupus nephritis lesion according to the ISN/RPS criteria?

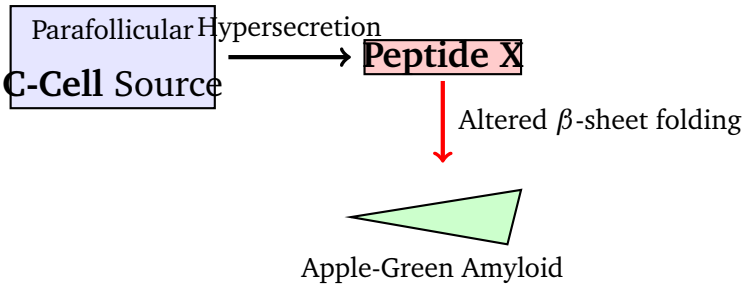
(A) Class II (Mesangial Proliferative Lupus Nephritis)

(B) Class III (Focal Lupus Nephritis)

(C) Class IV (Diffuse Lupus Nephritis)

(D) Class V (Membranous Lupus Nephritis)

Q18. A 45-year-old male undergoes a total thyroidectomy for a rapidly enlarging, firm thyroid nodule. Histopathology reveals sheets of polygonal cells separated by an abundant fibrovascular stroma that stains strongly with Congo Red, showing apple-green birefringence under polarized light. The schematic below highlights the cellular origins and biochemical pathways involved. Identify the native precursor hormone labeled as **Peptide X** that undergoes misfolding to form these amyloid deposits:



(A) Thyroglobulin precursor monomer

(B) Calcitonin

(C) Parathyroid Hormone-Related Protein (PTHrP)

(D) Islet Amyloid Polypeptide (IAPP)

Q19. A 58-year-old male with a 45 pack-year history of cigarette smoking presents with a cough, weight loss, and severe centrilobular emphysema. A lung biopsy reveals a central bronchial mass. Microscopic evaluation demonstrates sheets of small pleomorphic cells with scanty cytoplasm, fine granular chromatin ("salt and pepper"), and frequent nuclear molding. Immunohistochemical staining is strongly positive for chromogranin A, synaptophysin, and CD56. What is the fundamental cytogenetic driver or tumor suppressor loss associated with this neoplasm?

(A) Activating mutations in EGFR exons 19 or 21

(B) EML4-ALK gene inversions/fusions

(C) Concurrent obligate loss of both TP53 and RB1 tumor suppressor genes

(D) Overexpression of Cyclin D1 due to $t(11;14)$ rearrangement

Q20. A 28-year-old female presents with progressive exertional dyspnea. Her clinical evaluation confirms a diagnosis of idiopathic Pulmonary Arterial Hypertension (PAH). Histopathological examination of her small pulmonary muscular arteries demonstrates advanced lesions characterized by intimal fibrosis, medial hypertrophy, and complex endothelial-lined channels forming a web-like network ("plexiform lesions"). Mutations in which signaling pathway gene are most classically associated with this condition?

(A) BMPR2 (Bone Morphogenetic Protein Receptor Type 2)

(B) TGF-β Ligand-1

(C) Endothelin-1 Receptor Alpha

(D) Nitric Oxide Synthase 3 (NOS3)

Q21. A 62-year-old male undergoes a radical nephrectomy for a solid cortical mass in the upper pole of the left kidney. Microscopic analysis shows sheets of large polygonal cells with abundant, optical clear cytoplasm and a delicate network of branching, thin-walled prominent vasculature. Cytogenetic analysis of the tumor tissue reveals a loss of heterozygosity on the short arm of chromosome 3 ($3p$). Which protein accumulates intracellularly as a direct consequence of this genetic loss under normoxic conditions?

(A) Hypoxia-Inducible Factor 1-alpha (HIF-1α)

(B) von Hippel-Lindau tumor suppressor protein (pVHL)

(C) Ubiquitin-ligase core adaptors

(D) Fibroblast Growth Factor Receptor-1

Q22. A 48-year-old female with long-standing, poorly controlled type 2 diabetes mellitus presents with nephrotic-range proteinuria and progressive renal insufficiency. Light microscopy of a percutaneous renal biopsy demonstrates marked diffuse intercapillary glomerulosclerosis alongside distinct nodular, acellular PAS-positive spherical lesions located in the periphery of the

glomerulus. What are these characteristic nodular lesions called, and what is their primary structural composition?

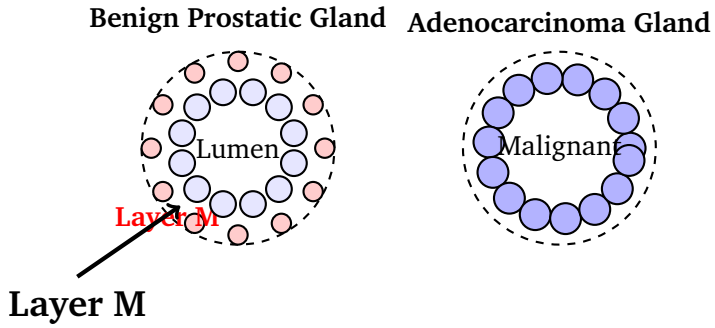
(A) Kimmelstiel-Wilson nodules; composed of mesangial matrix expansion and type IV collagen

(B) Aschoff nodules; composed of pluripotential giant cells and fibrinoid necrosis

(C) Councilman bodies; composed of condensed apoptotic hepatocyte fragments

(D) Crooke hyaline changes; composed of intermediate cytokeratin filaments

Q23. A 68-year-old male presents with urinary frequency, urgency, and a markedly elevated serum Prostate-Specific Antigen (PSA) level of 24 ng/mL. A transrectal ultrasound-guided core biopsy of the peripheral zone of the prostate is performed. The structural schematic below demonstrates the cellular architecture of a malignant gland compared to a benign gland. Identify the specific diagnostic cell layer labeled as **Layer M** that is characteristically absent in invasive prostatic adenocarcinoma:



(High Molecular Weight Cytokeratin / p63 positive)

(A) Inner cuboidal secretory luminal epithelium

(B) Intact outer myoepithelial sheath

(C) Continuous basal epithelial cell layer

(D) Dense fibroelastic muscular stroma

Q24. A 40-year-old male presents with worsening dysphagia for both solids and liquids. A barium swallow reveals a dilated proximal esophagus with se-

vere tapering at the lower esophageal sphincter, resembling a "bird's beak." Manometry confirms incomplete lower esophageal sphincter relaxation along with an aperistaltic esophageal body. What is the primary neuropathological defect responsible for this systemic motility disorder?

(A) Hypertrophy of the circular muscular layer within the gastric antrum

(B) Autoimmune-mediated or infectious destruction of inhibitory nitrergic neurons within the myenteric (Auerbach) plexus

(C) Atrophy of the mucosal Meissner plexus secondary to ischemic injury

(D) Eosinophilic infiltration into the lamina propria inducing fibrotic rings

Q25. A 26-year-old female presents with chronic bloody diarrhea, lower abdominal cramps, and tenesmus. Colonoscopy reveals continuous inflammation, erythema, and superficial mucosal ulcerations extending from the rectum up to the mid-descending colon, with an abrupt transition to normal mucosa. A mucosal biopsy confirms the presence of crypt distortion and active neutrophilic crypt abscesses without granulomas. Which of the following long-term histopathological transformations is most critical to screen for during surveillance follow-ups?

(A) Development of extensive submucosal hamartomatous polyposis

(B) Dysplastic changes within the flat mucosal surface, predisposing to invasive Colorectal Adenocarcinoma

(C) Transmural stricturing lesions prone to enteroenteric fistula formation

(D) Metaplastic transformation into heterotopic gastric mucosa

Detailed Solutions

Q1.

Solution

Concept: Barbiturates, alcohol, and various xenobiotics undergo enzymatic detoxification in the liver. This demand triggers a compensatory hypertrophy of the smooth endoplasmic reticulum (SER) where the processing enzymes reside.

Solution:

Let's analyze the adaptive cellular mechanisms in response to chronic xenobiotic load:

(a) The smooth endoplasmic reticulum houses the mixed-function oxidase system, primarily containing cytochrome P450 enzymes.

(b) Prolonged exposure to subtoxic levels of these compounds induces a feed-forward transcriptional response that expands the surface area of the SER membrane network to increase detoxification capacity.

(c) This structural expansion accounts for the swollen, finely granular, pale appearance of the cytoplasm on light microscopy. Therefore, the **Induction of the Cytochrome P450 monooxygenase enzyme system** is the classic molecular hallmark of this cellular adaptation.

Final Answer: Induction of the Cytochrome P450 monooxygenase enzyme system

Answer: (A)

Go Back to Question 1

Q2.

Solution

Concept: The intrinsic (mitochondrial) pathway of apoptosis is initiated by loss of outer mitochondrial membrane integrity, allowing the escape of pro-apoptotic intermembrane proteins into the cytosol.

Solution:

Let's trace the molecular interactions that orchestrate the initiation phase of this cell death cascade:

(a) The release of Cytochrome c into the cytosol triggers an ATP-dependent conformational assembly with apoptotic protease activating factor-1 (Apaf-1).

(b) This multi-protein complex organizes into a wheel-like heptameric structure known as the apoptosome.

(c) The assembled apoptosome serves as a docking platform that binds and activates the initiator caspase of the intrinsic pathway, Caspase-9. Thus, **Binding of Cytochrome c to Apaf-1, forming an apoptosome that recruits Caspase-9** directly follows outer membrane permeabilization.

Final Answer: Binding of Cytochrome c to Apaf-1, forming an apoptosome that recruits Caspase-9

Answer: (B)

Go Back to Question 2

Q3.

Solution

Concept: Soft tissue sarcomas frequently exhibit highly specific, diagnostic balanced chromosomal translocations that yield chimeric oncogenic fusion transcripts.

Solution:

Let's align the cytogenetic and differentiation profiles with the diagnostic entities:

(a) The balanced translocation $t(12;16)(q13;p11)$ fuses the *DDIT3* (*CHOP*) gene on chromosome 12 with the *FUS* gene on chromosome 16.

(b) The resultant FUS-DDIT3 fusion protein acts as an aberrant transcription factor that interferes with normal adipocytic differentiation, locking cells in a primitive, lipoblastic state.

(c) This specific cytogenetic hallmark is the defining molecular feature of **Myxoid Liposarcoma**. Synovial sarcoma is characterized by $t(X;18)$, Ewing sarcoma by $t(11;22)$, and alveolar rhabdomyosarcoma by $t(2;13)$ or $t(1;13)$.

Final Answer: Myxoid Liposarcoma

Answer: (A)

Go Back to Question 3

Q4.

Solution

Concept: Vascular leakage in acute inflammation occurs via distinct temporal phases depending on the nature and severity of the inciting cellular injury.

Solution:

Let's break down the kinetics of endothelial responses represented on the graph:

(a) The immediate response spike is brief (lasting 15–30 minutes) and is mediated by histamine or bradykinin causing endothelial contraction exclusively in postcapillary venules.

(b) Severe direct injuries, such as thermal burns or necrotizing bacterial toxins, precipitate a delayed, prolonged leakage curve (**Pathway X**) that peaks between 4 to 6 hours and lasts for days.

(c) This sustained phase is driven by **Direct, severe endothelial cell necrosis and detachment affecting venules and capillaries**, continuing until the structural integrity of the microvascular bed is restored via endothelial regeneration or thrombosis.

Final Answer: Direct, severe endothelial cell necrosis and detachment affecting venules and capillaries

Answer: (B)

Go Back to Question 4

Q5.

Solution

Concept: Leukocyte migration into inflamed extravascular tissues requires a highly orchestrated, sequential cascade of rolling, tight adhesion, and transmigration.

Solution:

Let's analyze the clinical presentation and specific molecular defect described:

(a) Leukocyte rolling is mediated by weak interactions between endothelial selectins (E-selectin, P-selectin) and fucosylated carbohydrate ligands, such as sialyl-Lewis X, present on passing leukocytes.

(b) Leukocyte Adhesion Deficiency Type 2 (LAD-2) results from a loss-of-function mutation in the **GDP-fucose transporter** located in the Golgi apparatus.

(c) The lack of fucose transport prevents the synthesis of sialyl-Lewis X on glycoproteins, completely abolishing selectin-mediated leukocyte rolling and leading to recurrent infections and persistent leukocytosis without pus formation. LAD-1, by contrast, is a tight adhesion defect involving the integrin β_2 subunit (CD18).

Final Answer: Leukocyte Adhesion Deficiency Type 2 (LAD-2); defect in GDP-fucose transporter

Answer: (B)

Go Back to Question 5

Q6.

Solution

Concept: Lipofuscin is an insoluble, wear-and-tear cellular pigment that accumulates over time in non-dividing, long-lived permanent tissues such as myocardial fibers and neurons.

Solution:

Let's evaluate the biogenesis of this fine, golden-brown perinuclear cardiac pigment:

(a) Subcellular organelles and membranes constantly undergo free-radical mediated lipid peroxidation during baseline metabolic functioning.

(b) When these damaged components are sequestered into autophagic vacuoles and fused with lysosomes, the altered lipid-protein polymers resist enzymatic hydrolysis.

(c) This results in the **Incomplete lysosomal degradation of lipid peroxidation products from autophagocytosed membranes**, leaving behind residual lipofuscin granules. Because it contains no iron, it yields a completely negative Prussian blue stain result.

Final Answer: Incomplete lysosomal degradation of lipid peroxidation products from autophagocytosed membranes

Answer: (A)

Go Back to Question 6

Q7.

Solution

Concept: Pathological calcification is categorized as either dystrophic calcification (occurring in damaged or necrotic tissues with normal serum calcium levels) or metastatic calcification (occurring in normal tissues secondary to systemic hypercalcemia).

Solution:

Let's delineate the mechanistic steps of calcification within injured structures:

(a) The patient demonstrates normal systemic calcium and phosphorus profiles, which classifies the valvular and subcutaneous deposits as dystrophic calcification.

(b) The initiating step is cellular and **membrane injury causing calcium influx**, which results in the concentration of calcium ions within dying cells and the formation of membrane-derived matrix vesicles.

(c) Phosphate groups generated by membrane-associated phosphatases bind these accumulated calcium ions, creating a localized high concentration that drives the nucleation of crystalline calcium phosphate (hydroxyapatite) within the extracellular matrix.

Final Answer: Membrane injury causing calcium influx, matrix vesicle formation, and nucleation of crystalline calcium phosphate

Answer: (B)

Go Back to Question 7

Q8.

Solution

Concept: Metaplasia is a reversible, adaptive cellular transition where one adult differentiated cell type is replaced by another adult cell type that is better able to withstand a hostile microenvironment.

Solution:

Let's analyze the cellular reprogramming mechanics responsible for this architectural shift:

(a) Chronic irritation from cigarette smoke damages the delicate, ciliated columnar epithelium of the respiratory tract.

(b) This stress does not cause fully differentiated, mature columnar cells to structurally alter their individual phenotypes.

(c) Instead, cytokines, chemokines, and growth factors rewrite the transcriptional programs of local tissue stem cells or undifferentiated reserve basal cells. This **Reprogramming of local tissue stem cells or undifferentiated reserve cells** changes their differentiation lineage toward a stratified squamous epithelium to provide enhanced mechanical protection.

Final Answer: Reprogramming of local tissue stem cells or undifferentiated reserve cells mediated by cytokines and growth factors

Answer: (C)

Go Back to Question 8

Q9.

Solution

Concept: The biconcave shape and mechanical flexibility of the erythrocyte depend on a specialized cytoskeleton linked to the overlying plasma membrane via vertical and horizontal structural protein interactions.

Solution:

Let's identify the protein structural defect based on the topological diagram and clinical disease markers:

(a) Hereditary spherocytosis is driven by mutations that disrupt the vertical stabilizing assemblies that link the horizontal spectrin cytoskeleton to the lipid bilayer.

(b) **Ankyrin** (**Protein Complex Y**) forms the primary vertical anchor, bridging the multipass transport protein Band 3 (B3) within the lipid bilayer to the underlying spectrin heterodimer chains.

(c) Defects in ankyrin lead to a destabilized lipid bilayer, resulting in microvesiculation, membrane loss, a decreased surface area-to-volume ratio (spherocyte formation), and an elevated osmotic fragility profile.

Final Answer: Ankyrin (interacting with Band 3 and Spectrin)

Answer: (B)

Go Back to Question 9

Q10.

Solution

Concept: Chronic Lymphocytic Leukemia (CLL) / Small Lymphocytic Lymphoma (SLL) exhibits variable clinical courses that correlate tightly with specific underlying somatic cytogenetic aberrations.

Solution:

Let's evaluate the prognostic implications of the major cytogenetic subgroups in CLL:

(a) Isolated $del(13q14)$ is the most frequent cytogenetic finding and is associated with a favorable long-term prognosis and stable disease.

(b) Conversely, a **Deletion of 17p ($del(17p)$) involving the TP53 gene locus** is a high-risk molecular marker associated with rapid disease progression, therapeutic resistance to standard chemoimmunotherapy, and a short overall survival time.

(c) Trisomy 12q carries an intermediate risk, while $t(11;14)$ is the defining genetic hallmark of Mantle Cell Lymphoma, not CLL.

Final Answer: Deletion of 17p ($del(17p)$) involving the TP53 gene locus

Answer: (B)

Go Back to Question 10

Q11.

Solution

Concept: Platelet adhesion to exposed subendothelial extracellular matrix requires the binding of specific platelet surface receptors to localized von Willebrand factor (vWF) multimeric anchors.

Solution:

Let's differentiate Bernard-Soulier syndrome from von Willebrand disease based on the platelet aggregation assay:

(a) The patient has a prolonged bleeding time and prolonged aPTT (due to vWF's role in stabilizing Factor VIII), alongside a selective failure of ristocetin-induced platelet aggregation.

(b) Ristocetin activates the interaction between the platelet **Glycoprotein Ib-IX-V complex (GPIb)** and vWF.

(c) In von Willebrand disease, adding normal pooled plasma corrects the defect by supplying exogenous vWF. Because this patient's defect **is not corrected** by normal pooled plasma, the lesion resides on the platelet surface itself. This confirms a diagnostic deficiency of the **Glycoprotein Ib-IX-V complex (GPIb)**, which is diagnostic of Bernard-Soulier Syndrome.

Final Answer: Glycoprotein Ib-IX-V complex (GPIb)

Answer: (A)

Go Back to Question 11

Q12.

Solution

Concept: Systemic iron homeostasis is regulated by modulating dietary iron absorption in the proximal small intestine and controlling iron mobilization from intracellular storage pools.

Solution:

Let's match the anatomy of iron absorption with its principal endocrine regulator:

(a) Dietary iron is primarily processed and absorbed across the enterocytes of the **Duodenum** and upper jejunum. This accounts for why celiac disease-induced villous atrophy leads to severe, refractory microcytic iron-deficiency anemia.

(b) The primary systemic hormone regulating iron kinetics is **Hepcidin**, a peptide synthesized by hepatocytes.

(c) When iron stores are elevated or systemic inflammation is present, hepcidin binds directly to the cellular iron exporter ferroportin on the basolateral membrane of enterocytes and macrophages, triggering its internal degradation to shut down iron transport into the bloodstream.

Final Answer: Duodenum; Hepcidin

Answer: (C)

Go Back to Question 12

Q13.

Solution

Concept: Essential Thrombocythemia (ET) is a clonal myeloproliferative neoplasm characterized by somatic driver mutations in *JAK2*, *CALR*, or *MPL* that induce constitutive activation of thrombopoietin receptor signaling pathways.

Solution:

Let's trace the downstream signal transduction cascade shown in the pathway schematic:

(a) Somatic mutations in *JAK2* ($V617F$), *CALR* frameshifts, or *MPL* ($W515$) induce ligand-independent, constitutive tyrosine kinase activation of the associated Janus Kinase 2 proteins.

(b) Activated JAK2 directly phosophorylates downstream **STAT3 and STAT5 proteins** (**Factor-Z**), causing them to form active homo- or heterodimers.

(c) These phosphorylated STAT dimers translocate into the nucleus, where they act as active transcription factors that drive megakaryocyte proliferation and platelet overproduction. Smad factors belong to the TGF-β pathway, while NF-κB operates primarily within inflammatory cascades.

Final Answer: STAT3 and STAT5 proteins

Answer: (A)

Go Back to Question 13

Q14.

Solution

Concept: Paroxysmal Nocturnal Hemoglobinuria (PNH) is an acquired clonal hematopoietic stem cell disorder caused by a somatic mutation in the *PIGA* gene, which is required for the synthesis of glycosylphosphatidylinositol (GPI) anchors.

Solution:

Let's identify the complement regulatory proteins that require a GPI anchor:

(a) Without a functional GPI anchor, hematopoietic lineages cannot express membrane-bound complement defense proteins on their cell surfaces.

(b) The key missing regulatory elements are **CD55 (Decay-Accelerating Factor)**, which accelerates the inactivation of C3 and C5 convertases, and **CD59 (Membrane Attack Complex Inhibitor)**, which prevents C9 polymerization into the membrane attack complex ($C5b$-9).

(c) The absence of CD55 and CD59 leaves erythrocytes vulnerable to spontaneous complement-mediated intravascular lysis, while lack of these markers on platelets and endothelial cells triggers leukocyte activation and pre-thrombotic states.

Final Answer: CD55 (Decay-Accelerating Factor) and CD59 (Membrane Attack Complex Inhibitor)

Answer: (A)

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Q15.

Solution

Concept: Myocardial infarction repair proceeds via a predictable sequence of histopathological alterations that allow the accurate timing of ischemic injuries during postmortem examination.

Solution:

Let's establish the chronological timeline of myocardial injury based on cellular changes:

(a) Between 4 to 12 hours post-infarction, changes are subtle, presenting primarily as early coagulation necrosis, edema, and wavy myocardial fibers.

(b) By **1 to 3 days**, the classic hallmarks of coagulation necrosis peak: cardiomyocytes lose their nuclei and cross-striations, and a dense, early neutrophilic infiltrate migrates into the necrotic zone to clear cellular debris.

(c) By 7 to 10 days, neutrophils have died off and are replaced by prominent macrophage infiltration and early granulation tissue. Thus, the presence of concurrent dense neutrophilic infiltration and fully formed coagulative necrosis dates the infarction to 1–3 days.

Final Answer: 1 to 3 days

Answer: (B)

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Q16.

Solution

Concept: The *KRAS* proto-oncogene encodes a small membrane-bound GTPase that acts as an on/off molecular switch in growth factor receptor signaling pathways.

Solution:

Let's analyze the biochemical consequences of the oncogenic codon 12 point mutation:

(a) Normal RAS cycles between an inactive GDP-bound state and an active GTP-bound state, returning to its inactive state via intrinsic GTPase activity stimulated by GTPase-activating proteins (GAPs).

(b) Activating point mutations in codon 12 impair this intrinsic GTPase activity and render RAS insensitive to GAP-mediated inactivation.

(c) This results in the **Persistent binding of GTP due to loss of intrinsic GTPase activity, leading to constitutive downstream RAF/MAPK signaling**. This continuous signaling drives the uninhibited cellular proliferation and desmoplastic response characteristic of pancreatic ductal adenocarcinoma.

Final Answer: Persistent binding of GTP due to loss of intrinsic GTPase activity, leading to constitutive downstream RAF/MAPK signaling

Answer: (A)

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Q17.

Solution

Concept: Lupus nephritis histopathology is categorized into distinct architectural classes based on the extent and localized distribution of immune complex deposition and glomerular hypercellularity.

Solution:

Let's evaluate the biopsy features against the ISN/RPS diagnostic criteria:

(a) The biopsy demonstrates diffuse glomerular hypercellularity involving greater than 50% of all glomeruli, alongside prominent global subendothelial thickening of the basement membrane ("wire-loop" lesions).

(b) Electron microscopy confirms extensive subendothelial electron-dense immune deposits, and immunofluorescence demonstrates a strong, pan-reactive "full house" granular pattern (staining positive for IgG, IgA, IgM, C3, and C1q).

(c) This combination of diffuse proliferation, wire-loop subendothelial deposits, and full house immunofluorescence satisfies the criteria for **Class IV (Diffuse Lupus Nephritis)**, which is the most common and severe form of renal involvement in SLE.

Final Answer: Class IV (Diffuse Lupus Nephritis)

Answer: (C)

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Q18.

Solution

Concept: Amyloidosis involves the pathological extracellular deposition of misfolded, insoluble protein polymers arranged in a stable β-pleated sheet conformation.

Solution:

Let's trace the endocrine cell lineage and the peptide precursor highlighted in the diagram:

(a) Medullary Thyroid Carcinoma is a neuroendocrine neoplasm derived from the neural crest-derived **parafollicular C-cells** of the thyroid gland.

(b) These malignant cells synthesize and secrete high amounts of the native peptide hormone **Calcitonin** (**Peptide X**).

(c) In the tumor stroma, localized high concentrations of monomeric calcitonin cause it to undergo conformational misfolding into stable β-pleated sheets. This forms localized amyloid (ACal) deposits that display characteristic apple-green birefringence under polarized light following Congo Red staining.

Final Answer: Calcitonin

Answer: (B)

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Q19.

Solution

Concept: Small Cell Lung Carcinoma (SCLC) is a high-grade, aggressive neuroendocrine malignancy that is strongly linked to heavy tobacco exposure and exhibits characteristic genomic inactivation profiles.

Solution:

Let's correlate the cytomorphology, immunohistochemical staining, and molecular drivers of this neoplasm:

(a) The presence of small pleomorphic cells with scanty cytoplasm, fine granular salt-and-pepper chromatin, nuclear molding, and positive staining for neuroendocrine markers (chromogranin A, synaptophysin, CD56) is diagnostic of SCLC.

(b) At the molecular level, SCLC does not typically rely on kinase activations such as *EGFR* mutations or *ALK* fusions, which are more common in non-smoking adenocarcinoma patients.

(c) Instead, SCLC is driven by the **Concurrent obligate loss of both TP53 and RB1 tumor suppressor genes**, which dysregulates cell cycle checkpoints and promotes rapid cellular proliferation.

Final Answer: Concurrent obligate loss of both TP53 and RB1 tumor suppressor genes

Answer: (C)

Go Back to Question 19

Q20.

Solution

Concept: Idiopathic Pulmonary Arterial Hypertension (PAH) is characterized by progressive remodeling of small pulmonary muscular arteries, leading to occlusion of the vascular lumen, increased pulmonary vascular resistance, and right heart strain.

Solution:

Let's isolate the genetic pathway linked to heritable and idiopathic forms of PAH:

(a) Advanced remodeling in PAH leads to the formation of plexiform lesions, which are complex webs of endothelial channels within the remodeled vessel wall.

(b) Idiopathic and familial PAH are most classically caused by inactivating germline mutations in the **BMPR2 (Bone Morphogenetic Protein Receptor Type 2)** gene, a member of the TGF-β receptor superfamily.

(c) A deficiency in BMPR2 signaling disrupts normal growth control mechanisms within the vascular wall, favoring the survival and proliferation of vascular smooth muscle cells and endothelial cells, which drives luminal narrowing and plexiform lesion formation.

Final Answer: BMPR2 (Bone Morphogenetic Protein Receptor Type 2)

Answer: (A)

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Q21.

Solution

Concept: Clear Cell Renal Cell Carcinoma (ccRCC) is highly associated with structural deletions or inactivating mutations on the short arm of chromosome 3 ($3p$), which contains the *VHL* tumor suppressor gene.

Solution:

Let's trace the biochemical changes that follow a loss of von Hippel-Lindau protein function under normoxic conditions:

(a) Under normal, well-oxygenated (normoxic) conditions, the von Hippel-Lindau protein (pVHL) acts as the recognition substrate for an E3 ubiquitin ligase complex. It binds to hydroxylated **Hypoxia-Inducible Factor 1-alpha (HIF-1α)** and targets it for rapid proteasomal degradation.

(b) Loss of heterozygosity on chromosome $3p$ removes functional pVHL expression.

(c) In the absence of pVHL, **Hypoxia-Inducible Factor 1-alpha (HIF-1α)** escapes degradation and stabilizes within the cytosol under normoxic conditions. It then translocates to the nucleus to drive the transcription of pro-angiogenic targets, such as VEGF and PDGF, producing the highly vascularized networks characteristic of ccRCC.

Final Answer: Hypoxia-Inducible Factor 1-alpha (HIF-1α)

Answer: (A)

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Q22.

Solution

Concept: Long-standing diabetic microvascular disease causes structural alterations in the kidney, collectively termed diabetic nephropathy.

Solution:

Let's identify the specific nodular lesions and their structural composition:

(a) The presence of distinct, acellular, PAS-positive spherical lesions in the peripheral mesangium of a diabetic patient is pathognomonic for advanced diabetic nephropathy.

(b) These structures are called **Kimmelstiel-Wilson nodules** (nodular intercapillary glomerulosclerosis).

(c) They are **composed of mesangial matrix expansion and type IV collagen**, resulting from non-enzymatic glycation of proteins and increased growth factor activity (such as TGF-β) that stimulates matrix deposition and causes progressive capillary loop occlusion.

Final Answer: Kimmelstiel-Wilson nodules; composed of mesangial matrix expansion and type IV collagen

Answer: (A)

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Q23.

Solution

Concept: The definitive diagnosis of invasive prostatic adenocarcinoma rests on evaluating glandular architecture and confirming the loss of cell layers that are present in benign prostatic tissue.

Solution:

Let's analyze the cell layer layout shown in the comparative diagram:

(a) Benign prostatic acini are lined by a dual-cell layer: an inner layer of columnar secretory luminal epithelium and an outer **Continuous basal epithelial cell layer** (**Layer M**).

(b) This outer basal layer stains positive for high-molecular-weight cytokeratin (such as CK5/6 or 34βE12) and nuclear p63.

(c) When prostatic adenocarcinoma cells invade the stroma, they form malignant glands that lack this **Continuous basal epithelial cell layer**. The complete absence of Layer M helps differentiate invasive adenocarcinoma from look-alike benign mimics like adenosis or high-grade prostatic intraepithelial neoplasia (PIN).

Final Answer: Continuous basal epithelial cell layer

Answer: (C)

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Q24.

Solution

Concept: Achalasia is a primary esophageal motility disorder characterized by a failure of the lower esophageal sphincter (LES) to relax during swallowing, paired with aperistalsis along the esophageal body.

Solution:

Let's isolate the primary neuroanatomic defect responsible for this motility pattern:

(a) Coordinated esophageal relaxation and peristalsis are mediated by inhibitory postganglionic neurons located within the myenteric (Auerbach) plexus situated between the circular and longitudinal smooth muscle layers.

(b) These inhibitory neurons release nitric oxide (NO) and vasoactive intestinal peptide (VIP) to relax the LES smooth muscle.

(c) Idiopathic achalasia is driven by the **Autoimmune-mediated or infectious destruction of inhibitory nitrergic neurons within the myenteric (Auerbach) plexus**. This loss leaves excitatory cholinergic signaling unchecked, causing sustained contraction of the LES and aperistalsis.

Final Answer: Autoimmune-mediated or infectious destruction of inhibitory nitrergic neurons within the myenteric (Auerbach) plexus

Answer: (B)

Go Back to Question 24

Q25.

Solution

Concept: Long-standing inflammatory bowel disease, particularly Ulcerative Colitis, places patients at a significantly increased risk for developing colorectal cancer.

Solution:

Let's evaluate the histopathological progression associated with neoplastic surveillance in this patient:

(a) The clinical presentation of continuous colonic inflammation starting from the rectum, paired with crypt abscesses and an absence of granulomas, confirms a diagnosis of active Ulcerative Colitis.

(b) Chronic cycles of inflammation and epithelial regeneration promote the accumulation of pro-neoplastic mutations within the mucosa.

(c) Unlike sporadic colon cancer, which typically arises from distinct adenomatous polyps, colitis-associated cancer often develops from **Dysplastic changes within the flat mucosal surface, predisposing to invasive Colorectal Adenocarcinoma**. Regular surveillance biopsies are required to detect these flat dysplastic changes early.

Final Answer: Dysplastic changes within the flat mucosal surface, predisposing to invasive Colorectal Adenocarcinoma

Answer: (B)

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Answer Key

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