

NEET PG Pathology Sample Paper-10

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 58-year-old chronic alcoholic presents with hepatomegaly. A liver biopsy reveals macrovesicular steatosis. Which of the following is the primary mechanism leading to the intracellular accumulation of lipids in this condition?
- (A) Decreased synthesis of fatty acids
(B) Decreased conversion of fatty acids to triglycerides
(C) Decreased synthesis of apoproteins (apoE/apoB-100)
(D) Increased oxidation of fatty acids in mitochondria
- Q2.** During an experiment, cells are exposed to a toxic agent that selectively inhibits ATP synthesis. Which of the following downstream cellular alterations will occur first as a direct consequence of this metabolic failure?
- (A) Ribosomal detachment from the rough endoplasmic reticulum
(B) Influx of sodium and water into the cytoplasm
(C) Efflux of calcium into the extracellular space
(D) Autophagy of damaged mitochondria
- Q3.** A 62-year-old male with a history of long-standing uncontrolled hypertension dies of an acute myocardial infarction. At autopsy, the left ventricular wall



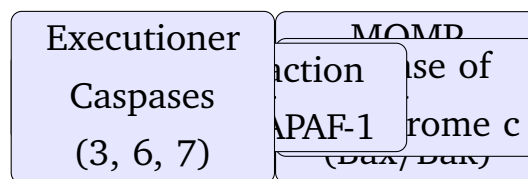
measures 2.2 cm in thickness (normal: 1.1–1.2 cm). Which of the following cellular changes best describes this adaptive process in the myocardium?

- (A) Increase in the size of individual myocytes driven by gene expression changes
- (B) Increase in the absolute number of myocardial cells via mitotic division
- (C) Synthesis of structural proteins leading to numeric hyperplasia
- (D) Metaplastic transformation of connective tissue into functional muscle fibers

Q4. Which of the following cellular pathways is considered the primary executioner mechanism during the intrinsic (mitochondrial) pathway of apoptosis?

- (A) Activation of Caspase-8 by Fas-FasL interaction
- (B) Release of Cytochrome c into the cytosol and subsequent activation of Caspase-9
- (C) Direct cleavage of nuclear DNA by Granzyme B
- (D) Translocation of Bax and Bak to form inhibitory homodimers on the outer membrane

Q5. Refer to the schematic pathway represented below:



In this intrinsic apoptotic cascade, what specific molecular complex or molecule does "X" represent?

- (A) Apoptosome (heptameric complex activating Caspase-9)
- (B) Disc Complex (FADD bound to procaspase-8)
- (C) Inflammasome (caspase-1 activating complex)
- (D) Necrosome (RIPK1-RIPK3 complex)



- Q6.** A tissue biopsy from a patient with chronic granulomatous disease shows persistent localized inflammation. Under the microscope, large multinucleated Langhans giant cells are observed. These specific giant cells are formed by the fusion of which of the following cell lineages?
- (A) Neutrophilic myeloblasts
 - (B) Activated T-helper lymphocytes
 - (C) Epithelioid macrophages
 - (D) Plasma cells derived from B-lymphocytes
- Q7.** A 23-year-old female sustains a deep laceration on her forearm which is closed with sutures. Over the next few weeks, tissue repair progresses dynamically. Which of the following growth factors plays the most critical role in stimulating both collagen synthesis and inhibiting the degradation of the extracellular matrix during scar formation?
- (A) Vascular Endothelial Growth Factor (VEGF)
 - (B) Transforming Growth Factor-beta ($TGF-\beta$)
 - (C) Epidermal Growth Factor (EGF)
 - (D) Tumor Necrosis Factor-alpha ($TNF-\alpha$)
- Q8.** A 54-year-old male is diagnosed with an adenocarcinoma of the colon. Genetic analysis reveals a point mutation in the KRAS gene that abolishes its intrinsic GTPase activity. Which of the following downstream events is the direct result of this specific mutation?
- (A) Persistent activation of the MAP kinase signaling pathway
 - (B) Constitutional inactivation of the Wnt/ β -catenin pathway
 - (C) Overexpression of the p53 tumor suppressor protein
 - (D) Epigenetic silencing of mismatch repair genes (MLH1/MSH2)
- Q9.** A 3-year-old boy is brought to the clinic due to fatigue and mild pallor. Peripheral blood smear reveals microcytic hypochromic red blood cells with prominent basophilic stippling and target cells. Hemoglobin electrophoresis



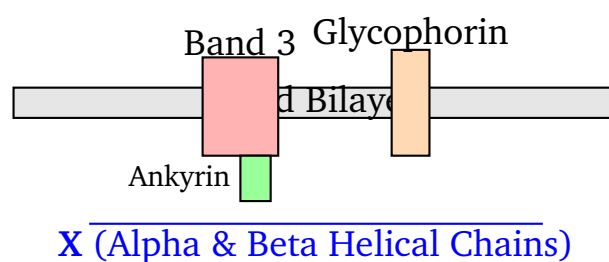
demonstrates a significant elevation of HbA2 (5.5%) and slightly increased HbF. What is the most likely diagnosis?

- (A) Iron deficiency anemia
- (B) β -Thalassemia minor
- (C) α -Thalassemia trait
- (D) Anemia of chronic disease

Q10. A 28-year-old pregnant female at 32 weeks of gestation presents with severe fatigue and glossitis. Her complete blood count shows Hemoglobin: 8.2 g/dL, MCV: 118 fL, and a normal platelet count. A peripheral blood smear exhibits macro-ovalocytes and hypersegmented neutrophils. Which of the following metabolic findings would uniquely confirm a deficiency of Vitamin B12 over Folic Acid in this patient?

- (A) Elevated serum homocysteine levels
- (B) Decreased serum folate levels
- (C) Elevated urinary and serum methylmalonic acid (MMA) levels
- (D) Increased mean corpuscular volume

Q11. Refer to the simplified schematic diagram of an erythrocyte membrane architecture shown below:



A molecular defect causing a quantitative deficiency or structural abnormality in the skeletal protein labeled "X" is the most common underlying cause of which hereditary hemolytic state?

- (A) Paroxysmal Nocturnal Hemoglobinuria
- (B) Hereditary Spherocytosis



- (C) Glucose-6-Phosphate Dehydrogenase Deficiency
- (D) Sickle Cell Anemia

Q12. A 62-year-old male presents with generalized lymphadenopathy, splenomegaly, and a total leukocyte count of $85,000/\mu\text{L}$. Flow cytometry of the peripheral blood lymphocytes reveals a clonal population of mature B cells expressing CD5, CD19, CD20 (weak), and CD23. What is the most characteristic morphological feature seen on the peripheral blood smear of this patient?

- (A) Auer rods within blast cells
- (B) Reed-Sternberg cells
- (C) Pelger-Huët anomalies
- (D) Smudge cells (basket cells)

Q13. A 45-year-old male presents with fatigue, massive splenomegaly, and early satiety. His CBC shows a total WBC count of $150,000/\mu\text{L}$ with a full spectrum of granulocytic cells (myelocytes, metamyelocytes, bands, and mature neutrophils) and a blast count of 2%. Cytogenetic analysis confirms the presence of a $t(9;22)(q34;q11)$ translocation. Which of the following diagnostic parameters would typically be decreased or absent in this condition?

- (A) Serum uric acid level
- (B) Leukocyte Alkaline Phosphatase (LAP) score
- (C) Vitamin B12 binding capacity
- (D) Bone marrow cellularity

Q14. A 14-year-old boy presents with an expanding, painless mass involving his right mandible. A biopsy of the lesion reveals a diffuse infiltration of intermediate-sized B lymphocytes with high mitotic activity interspersed with pale, tingible-body macrophages. This classic histopathological appearance is known as a "starry sky" pattern. Which of the following genetic alterations is characteristically associated with this neoplasm?

- (A) $t(8;14)$ translocation leading to MYC overexpression

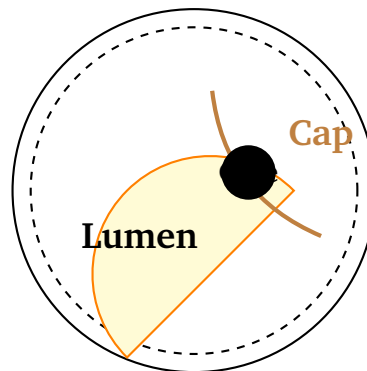


- (B) t(14;18) translocation leading to BCL2 overexpression
- (C) t(11;14) translocation leading to Cyclin D1 overexpression
- (D) Deletion of 17p leading to loss of p53 function

Q15. A 58-year-old male with a history of long-standing atherosclerosis suddenly collapses and dies. Autopsy reveals a massive abdominal aortic aneurysm rupture. Histological evaluation of the aortic wall away from the rupture site would most likely demonstrate which of the following degenerative features?

- (A) Dense concentric calcification of the tunica adventitia
- (B) Cystic medial degeneration with loss of smooth muscle cells and elastic fibers
- (C) Hyaline arteriosclerosis of the vasa vasorum
- (D) Hyperplastic arteriosclerosis with "onion-skin" remodeling

Q16. Refer to the cross-sectional diagram of a coronary artery lumen undergoing remodeling:



If this advanced fibrofatty plaque becomes unstable and undergoes sudden rupture with superimposed subocclusive thrombosis, which clinical acute coronary syndrome is most typically induced if the distal perfusion is partially maintained via collaterals?

- (A) Unstable Angina or Non-ST-segment Elevation Myocardial Infarction (NSTEMI)
- (B) Chronic Stable Angina Pectoris



- (C) Acute transmural ST-segment Elevation Myocardial Infarction (STEMI)
- (D) Calcific Monckeberg medial sclerosis

Q17. A 65-year-old heavy smoker presents with chronic cough, progressive exertional dyspnea, and significant weight loss. A chest X-ray reveals a 4 cm central hilar mass obstructing the right main bronchus. Sputum cytology reveals clusters of large, pleomorphic cells with abundant cytoplasm, hyperchromatic nuclei, distinct intercellular bridges, and focal concentric whorls of dense eosinophilic material. What is the correct histopathological diagnosis?

- (A) Small cell lung carcinoma
- (B) Adenocarcinoma of the lung
- (C) Squamous cell carcinoma of the lung
- (D) Large cell neuroendocrine carcinoma

Q18. A 42-year-old male presents with hemoptysis, chronic sinusitis, and hematuria. Laboratory analysis is notable for an elevated serum c-ANCA (PR3-ANCA) titer. A renal biopsy shows crescentic necrotizing glomerulonephritis. What is the most probable diagnosis?

- (A) Microscopic polyangiitis
- (B) Granulomatosis with polyangiitis (Wegener's)
- (C) Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
- (D) Anti-GBM antibody disease (Goodpasture's syndrome)

Q19. A 35-year-old female undergoes a total thyroidectomy for a cold nodule detected in her right thyroid lobe. Microscopic examination displays sheets of cells showing crowded nuclei with a clear, ground-glass appearance ("Orphan Annie eyes"), prominent nuclear grooves, and scattered laminated calcified structures. What are these characteristic calcified structures called?

- (A) Asbestos bodies
- (B) Councilman bodies

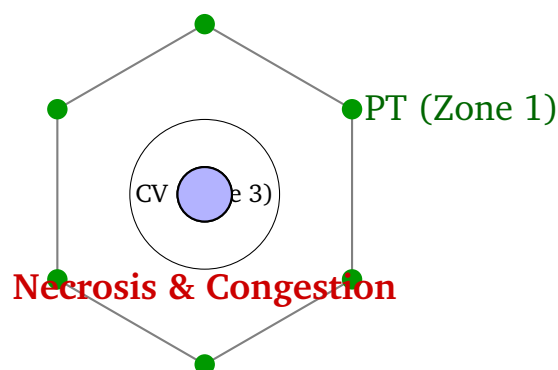


- (C) Psammoma bodies
- (D) Mallory-Denk bodies

Q20. A 48-year-old male presents with persistent epigastric pain that improves immediately after taking meals. An upper gastrointestinal endoscopy identifies a well-demarcated 1.5 cm ulcerated lesion in the first part of the duodenum. A biopsy from the ulcer edge is positive for *Helicobacter pylori*. Which of the following pathological mechanisms is predominantly responsible for the duodenal ulceration caused by this pathogen?

- (A) Hypersecretion of gastric acid secondary to antral inflammation and D-cell inhibition
- (B) Direct mucosal invasion and systemic dissemination by the bacteria
- (C) Autoimmune destruction of the duodenal enterocytes by cross-reactive antibodies
- (D) Ischemic necrosis of the mucosa due to localized microvascular thrombosis

Q21. Refer to the schematic visualization of a hepatic lobule microarchitecture from a patient presenting with severe chronic right-sided congestive heart failure:



Which descriptive gross pathological term corresponds to the liver appearance resulting from this centrilobular congestion (Zone 3) contrasted against normal or fatty peripheral zones (Zone 1)?

- (A) Cirrhosis
- (B) Nutmeg liver

- (C) Peliosis hepatis
- (D) Budd-Chiari liver

Q22. A 52-year-old female presents with progressive difficulty swallowing solid food, skin tightening over her fingers, and severe heartburn. A biopsy from her lower esophagus shows extensive interstitial fibrosis of the lamina propria and submucosa with severe atrophy of the muscularis propria. Which autoantibody profile is most highly specific for the systemic condition causing these findings?

- (A) Anti-dsDNA antibodies
- (B) Anti-Scl-70 (anti-topoisomerase I) antibodies
- (C) Anti-Jo-1 antibodies
- (D) Anti-Smith (Sm) antibodies

Q23. A 10-year-old boy presents with periorbital edema, smoke-colored urine, and mild hypertension. He had a severe sore throat 2 weeks ago that resolved without antibiotics. Urinalysis shows dysmorphic RBCs and RBC casts. A renal biopsy undergoes immunofluorescence microscopy, revealing a characteristic granular, "starry sky" deposition of IgG and C3 along the glomerular basement membrane. What is the primary ultrastructural find expected on electron microscopy?

- (A) Diffuse effacement of podocyte foot processes
- (B) Subendothelial electron-dense deposits
- (C) Subepithelial electron-dense deposits ("humps")
- (D) Splitting of the glomerular basement membrane ("tram-tracking")

Q24. A 55-year-old male presents with a painless enlarging mass in his right testicle. After an orchidectomy, gross examination reveals a well-circumscribed, homogeneous, fleshy, lobulated white-tan tumor without areas of hemorrhage or necrosis. Histopathology shows nests of uniform, large cells with clear cytoplasm rich in glycogen, separated by thin fibrous septa infiltrated by lymphocytes. What is the correct diagnosis?



- (A) Yolk sac tumor
- (B) Choriocarcinoma
- (C) Seminoma
- (D) Embryonal carcinoma

Q25. A 63-year-old postmenopausal female presents with abnormal uterine bleeding. An endometrial biopsy confirms endometrial adenocarcinoma. Which of the following underlying conditions or risk factors is most strongly correlated with the development of Type I (endometrioid) endometrial carcinoma via prolonged unopposed estrogen stimulation?

- (A) Multiparity
- (B) Obesity
- (C) Combined oral contraceptive use
- (D) Early menopause



Detailed Solutions

Q1.

Solution

Concept:

Alcoholic liver disease begins with hepatic steatosis, characterized by abnormal accumulation of lipid droplets within hepatocytes. Chronic ethanol consumption disrupts cellular metabolic pathways by heavily increasing the NADH/NAD⁺ ratio via the actions of alcohol dehydrogenase and acetaldehyde dehydrogenase. This altered redox state suppresses mitochondrial fatty acid oxidation and shifts the metabolic pathway toward increased triglyceride synthesis and deposition.

Solution:

- (a) Chronic ethanol metabolism generates excess NADH. This high NADH/NAD⁺ ratio inhibits β -oxidation of fatty acids in the mitochondria, because key enzymes like 3-hydroxyacyl-CoA dehydrogenase require NAD⁺ as a cofactor.
- (b) Excess hydrogen ions from ethanol oxidation are used for lipid synthesis, promoting the conversion of fatty acids into triglycerides within the cytoplasm of hepatocytes.
- (c) Concurrently, ethanol intake alters lipid export by impairing the synthesis and secretion of apoproteins, particularly Apolipoprotein B-100 and ApoE, which are necessary to form Very Low-Density Lipoproteins (VLDL) for lipid transport out of the liver.
- (d) Decreased conversion of fatty acids to triglycerides is incorrect, as triglyceride synthesis is actually accelerated in chronic alcoholism.
- (e) Fatty acid synthesis is stimulated rather than decreased, as high acetyl-CoA levels driven by acetate production provide substrates for lipogenesis.

Final Answer: The primary mechanism is decreased synthesis of apoproteins.

Answer: (C)

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Q2.

Solution**Concept:**

Ischemic or toxic cellular injury leads to mitochondrial dysfunction, resulting in the rapid depletion of Adenosine Triphosphate (ATP). Cells rely heavily on oxidative phosphorylation to generate ATP to maintain homeostatic ion gradients. When ATP synthesis fails, active transport mechanisms across the plasma membrane stop working, initiating a predictable sequence of reversible structural alterations before irreversible damage occurs.

Solution:

- (a) The primary consequence of ATP depletion is the failure of the active ATP-dependent sodium-potassium pump ($Na^+/K^+-ATPase$). This pump normally moves three sodium ions out of the cell and two potassium ions into the cell against concentration gradients.
- (b) When this pump fails, sodium ions accumulate inside the cytoplasm, while potassium ions diffuse out of the cell down their concentration gradient.
- (c) The intracellular accumulation of sodium increases the intracellular osmotic pressure, drawing water into the cell. This causes rapid cellular swelling (hydropic change) and cisternae dilation of the endoplasmic reticulum.
- (d) Ribosomal detachment from the rough endoplasmic reticulum occurs later, as structural alteration from swelling and altered pH disrupts ribosome binding to the translocon.
- (e) Calcium efflux is prevented; instead, calcium floods into the cytoplasm due to the failure of ATP-driven Ca^{2+} pumps. Autophagy is a delayed response to persistent nutrient or metabolic stress.

Final Answer: The alteration that occurs first is the influx of sodium and water into the cytoplasm.

Answer: (B)

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Q3.

Solution**Concept:**

Hypertrophy is an adaptive cellular response characterized by an increase in the size of individual cells, leading to an increase in the overall size of the affected organ. This process occurs in non-dividing permanent tissues, such as cardiac myocytes and skeletal muscle cells, which have minimal regenerative capacity and cannot undergo mitotic division to handle increased mechanical or hemodynamic workloads.

Solution:

- (a) Long-standing uncontrolled hypertension forces the left ventricle to pump blood against elevated systemic vascular resistance. This chronic pressure overload increases mechanical stress on the ventricular wall.
- (b) In response to mechanical stretch, growth factors (TGF- β , IGF-1) and vasoactive agents (angiotensin II, endothelin-1) stimulate intracellular signaling cascades within cardiac myocytes.
- (c) These signaling pathways induce the transcription of structural proteins, leading to an increase in the number of myofilaments and sarcomeres per cell. This expands the volume of individual myocytes without cellular division.
- (d) Mitotic division does not occur in adult cardiac myocytes, making numeric hyperplasia an incorrect description of myocardial adaptation to chronic workload.
- (e) Metaplasia refers to the reversible replacement of one adult cell type by another cell type, which does not characterize the increased muscular thickness seen in hypertensive heart disease.

Final Answer: The adaptive process is an increase in the size of individual myocytes driven by gene expression changes.

Answer: (A)

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Q4.

Solution**Concept:**

Apoptosis, or programmed cell death, occurs via two main pathways: the extrinsic (death receptor) pathway and the intrinsic (mitochondrial) pathway. The intrinsic pathway is triggered by intracellular stress, DNA damage, or loss of survival signals. This leads to mitochondrial outer membrane permeabilization (MOMP), regulated by the balance between pro-apoptotic and anti-apoptotic proteins of the Bcl-2 family.

Solution:

- (a) When cells experience stress, pro-apoptotic proteins Bax and Bak oligomerize to form channels in the outer mitochondrial membrane, causing the release of mitochondrial intermembrane proteins into the cytosol.
- (b) Cytochrome c is released from mitochondria into the cytoplasm, where it binds to Apoptotic Protease Activating Factor-1 (APAF-1) in the presence of dATP to form a wheel-like heptameric complex called the apoptosome.
- (c) The apoptosome binds and activates the initiator caspase, pro-caspase-9. Active caspase-9 then cleaves and activates executioner caspases (caspase-3 and caspase-7), which carry out coordinated protein degradation.
- (d) Activation of Caspase-8 by Fas-FasL interaction belongs exclusively to the extrinsic pathway of apoptosis, not the mitochondrial pathway.
- (e) Direct cleavage of nuclear DNA by Granzyme B is a mechanism utilized by cytotoxic T lymphocytes to induce apoptosis independently of traditional upstream initiator complexes.

Final Answer: The primary executioner mechanism is the release of Cytochrome c into the cytosol and subsequent activation of Caspase-9.

Answer: (B)

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Q5.

Solution**Concept:**

The intrinsic pathway of apoptosis relies on the formation of specific macromolecular complexes within the cytosol to amplify apoptotic signals. Following mitochondrial outer membrane permeabilization (MOMP) mediated by Bax and Bak, key proteins are released into the cytoplasm. This initiates a structural cascade that converts inactive pro-caspases into functional, active executioner enzymes.

Solution:

- (a) Cellular injury or DNA damage activates the pro-apoptotic Bcl-2 proteins Bax and Bak, which permeabilize the outer mitochondrial membrane.
- (b) Permeabilization allows Cytochrome c to exit the mitochondrial intermembrane space and enter the cytosol.
- (c) Once inside the cytosol, Cytochrome c binds to Apoptotic Protease Activating Factor-1 (APAF-1). This binding induces a conformational change, forming a wheel-like heptameric structure.
- (d) This heptameric macromolecular complex is called the apoptosome, represented by "X" in the provided schematic pathway diagram.
- (e) The apoptosome recruits and cleaves pro-caspase-9 into active caspase-9, which then directly activates executioner caspases-3, 6, and 7. The DISC complex functions in the extrinsic pathway, while the inflammasome activates caspase-1 during pyroptosis.

Final Answer: The molecular complex represented by X is the Apoptosome.

Answer: (A)

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Q6.

Solution**Concept:**

Granulomatous inflammation is a specialized form of chronic inflammation characterized by collections of activated macrophages that develop an altered, epithelial-like appearance. This response is driven by a cellular immune reaction against persistent, poorly degradable antigens, or in conditions like chronic granulomatous disease where phagocytes lack functional NADPH oxidase to destroy engulfed pathogens.

Solution:

- (a) During persistent antigen exposure, macrophages engulfing the antigen present fragments to $CD4^+$ T-helper cells, which release cytokines like Interferon-gamma ($IFN-\gamma$).
- (b) $IFN-\gamma$ activates macrophages, transforming them into epithelioid cells characterized by abundant cytoplasm, vesicular nuclei, and elongated cell boundaries.
- (c) Under the sustained influence of these cytokines, multiple epithelioid macrophages fuse together to form multinucleated giant cells.
- (d) In Langhans giant cells, the nuclei are arranged in a horseshoe-shaped or peripheral configuration along the cell border, which is highly characteristic of granulomas.
- (e) Neutrophilic myeloblasts are precursors of granulocytes, while activated T-lymphocytes and plasma cells secrete regulatory proteins and antibodies, but do not fuse to form giant cells.

Final Answer: The giant cells are formed by the fusion of Epithelioid macrophages.

Answer: (C)

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Q7.

Solution**Concept:**

Wound healing and scar formation involve a sequence of inflammation, proliferation, and tissue remodeling. During the repair phase, the extracellular matrix (ECM) is synthesized and modified to restore tissue continuity. This balance between matrix production and degradation is tightly regulated by polypeptide growth factors secreted by macrophages, platelets, and endothelial cells at the injury site.

Solution:

- (a) Transforming Growth Factor-beta ($TGF-\beta$) is the most critical cytokine involved in tissue fibrosis and scar stabilization during the late stages of wound healing.
- (b) $TGF-\beta$ acts directly on fibroblasts to stimulate the transcription of genes encoding extracellular structural components, heavily increasing collagen and fibronectin synthesis.
- (c) Concurrently, $TGF-\beta$ reduces ECM degradation by downregulating the expression of matrix metalloproteinases (MMPs) and upregulating tissue inhibitors of metalloproteinases (TIMPs).
- (d) Vascular Endothelial Growth Factor (VEGF) primarily drives angiogenesis and increases vascular permeability, but does not directly stimulate collagen deposition.
- (e) Epidermal Growth Factor (EGF) promotes the migration and proliferation of epithelial cells, while Tumor Necrosis Factor-alpha ($TNF-\alpha$) acts primarily as a pro-inflammatory signaling cytokine.

Final Answer: The growth factor playing the most critical role is Transforming Growth Factor-beta.

Answer: (B)

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Q8.

Solution**Concept:**

The KRAS gene encodes a small GTPase protein that acts as an essential molecular switch in growth factor signaling pathways. Normally, KRAS cycles between an active GTP-bound state and an inactive GDP-bound state. This conversion is regulated by its intrinsic GTPase activity, which hydrolyzes GTP to GDP to terminate growth signaling downstream of epidermal growth factor receptors.

Solution:

- (a) Point mutations in codons 12, 13, or 61 of the KRAS gene impair its intrinsic GTPase activity, rendering the protein unable to hydrolyze bound GTP into GDP
- (b) As a result, the mutant KRAS protein remains locked in its active, GTP-bound conformation, sending continuous stimulatory signals to downstream effectors independent of external growth factor stimulation.
- (c) This constitutional activation downstream shifts the Mitogen-Activated Protein (MAP) kinase pathway into a persistent on-state, driving cell proliferation and survival.
- (d) Inactivation of the Wnt/ β -catenin pathway is characteristic of APC gene alterations, not KRAS mutations.
- (e) KRAS mutations do not cause p53 overexpression, which typically occurs due to TP53 gene mutations, nor do they directly induce epigenetic silencing of DNA mismatch repair genes.

Final Answer: The direct result is the persistent activation of the MAP kinase signaling pathway.

Answer: (A)

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Q9.

Solution**Concept:**

Thalassemias are hereditary hemolytic anemias caused by mutations that reduce the synthesis of α -globin or β -globin polypeptide chains. This imbalance leads to defective hemoglobin synthesis and ineffective erythropoiesis. Hemoglobin electrophoresis serves as the definitive diagnostic tool to differentiate various types of thalassemias from other microcytic hypochromic anemias based on the percentages of specific hemoglobin variants.

Solution:

- (a) Adult hemoglobin consists primarily of HbA ($\alpha_2\beta_2$). When β -globin chain synthesis is reduced, as in β -thalassemia minor, there is a compensatory increase in the synthesis of delta and gamma chains.
- (b) This shift causes a diagnostic rise in HbA_2 ($\alpha_2\delta_2$) levels above the normal range ($> 3.5\%$), typically reaching 4% to 8%, along with a mild elevation in HbF ($\alpha_2\gamma_2$).
- (c) Peripheral blood smears in these patients characteristically demonstrate microcytic hypochromic red blood cells, target cells, and basophilic stippling caused by precipitated RNA aggregates.
- (d) Iron deficiency anemia also causes microcytic hypochromic cells, but presents with normal or decreased levels of HbA_2 and low serum ferritin.
- (e) α -Thalassemia trait shows a normal or reduced percentage of HbA_2 because α -chain deficiency limits the formation of both HbA and HbA_2 .

Final Answer: The most likely diagnosis is β -Thalassemia minor.

Answer: (B)

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Q10.

Solution**Concept:**

Megaloblastic anemias are macrocytic disorders caused by impaired DNA synthesis, most commonly due to Vitamin B12 (cobalamin) or Folic Acid (folate) deficiencies. Both vitamins serve as coenzymes in the pathway that converts homocysteine to methionine, meaning a deficiency in either leads to elevated serum homocysteine levels and similar megaloblastic changes in the bone marrow and peripheral blood.

Solution:

- (a) Vitamin B12 acts uniquely as a cofactor for the mitochondrial enzyme methylmalonyl-CoA mutase, which converts methylmalonyl-CoA to succinyl-CoA during fatty acid and amino acid catabolism.
- (b) When Vitamin B12 is deficient, this metabolic pathway is blocked, leading to an accumulation of methylmalonic acid (MMA) in both serum and urine.
- (c) Folic acid does not participate in the conversion of methylmalonyl-CoA to succinyl-CoA. Therefore, MMA levels remain entirely normal in isolated folate deficiency.
- (d) Elevated serum homocysteine occurs in both deficiencies, making it an unhelpful marker for distinguishing between the two causes of macrocytic anemia.
- (e) Decreased serum folate levels confirm a folate deficiency, while an increased mean corpuscular volume (MCV) is a general indicator of macrocytosis seen in both conditions.

Final Answer: The finding that uniquely confirms Vitamin B12 deficiency is elevated urinary and serum methylmalonic acid levels.

Answer: (C)

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Q11.

Solution**Concept:**

Hereditary spherocytosis is an inherited hemolytic state caused by diverse molecular defects in proteins that anchor the red blood cell plasma membrane to its underlying cytoskeleton. The normal biconcave erythrocyte shape requires a highly stable, flexible structural grid to withstand structural stress during passage through tortuous splenic cords. Quantitative deficiencies or functional mutations in these core skeletal proteins destroy this mechanical linkage.

Solution:

- (a) The primary skeletal protein grid element labeled X represents spectrin, which is composed of intertwined alpha and beta helical chains forming a horizontal dimeric/tetrameric structural network beneath the lipid bilayer.
- (b) Spectrin is vertically tethered to the plasma membrane transmembrane proteins, such as Band 3 and Glycophorin, via linking complexes containing ankyrin, protein 4.2, and protein 4.1.
- (c) Deficiencies or vertical assembly defects in spectrin disrupt the mechanical stability of the lipid bilayer, causing the erythrocyte to shed small microvesicles during circulatory stress.
- (d) Loss of membrane surface area relative to intracellular volume forces the cell to assume its lowest energy physical state, which is a rigid, non-deformable sphere (spherocyte).
- (e) These abnormal spherocytes lack standard deformability, leading to selective trapping, physical micro-fragmentation, and phagocytosis by macrophages within the splenic cords.

Final Answer: The hereditary hemolytic state is Hereditary Spherocytosis.

Answer: (B)

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Q12.

Solution**Concept:**

Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) is a neoplastic disorder characterized by the progressive accumulation of morphologically mature but functionally incompetent B lymphocytes. The disease typically displays a highly distinct immunophenotypic profile on flow cytometry, expressing characteristic pan-B cell markers alongside an unusual T-cell surface antigen.

Solution:

- (a) The clonal proliferation of small, mature B-lineage lymphocytes uniquely co-expresses the T-cell marker CD5 along with regular B-cell surface antigens CD19, CD23, and weak expression of CD20.
- (b) These neoplastic lymphocytes are morphologically fragile and susceptible to physical disruption during the mechanical preparation of a standard peripheral blood film.
- (c) The physical shearing forces applied during film smearing cause these fragile cells to rupture, leaving behind characteristic crushed nuclear remnants known as smudge cells or basket cells.
- (d) Auer rods are crystalline cytoplasmic inclusions composed of azurophilic granule components found exclusively within malignant myeloblasts in acute myeloid leukemia.
- (e) Reed-Sternberg cells represent giant, multi-nucleated neoplastic B cells characteristic of Hodgkin lymphoma, while Pelger-Huët anomalies describe structural nuclear hyposegmentation seen in myelodysplastic syndromes.

Final Answer: The characteristic morphological feature is Smudge cells (basket cells).

Answer: (D)

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Q13.

Solution**Concept:**

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm initiated by the formation of the BCR-ABL1 fusion gene on the Philadelphia chromosome, t(9;22)(q34;q11). This chromosomal rearrangement produces a constitutively active tyrosine kinase that drives the uncontrolled proliferation of the entire granulocytic lineage within the active bone marrow spaces.

Solution:

- (a) Chronic myeloid leukemia leads to a massive expansion of mature and maturing neutrophils, metamyelocytes, myelocytes, and promyelocytes, creating an extraordinarily hypercellular bone marrow and high peripheral leukocytosis.
- (b) Despite the vast numeric abundance of mature neutrophils, these neoplastic cells possess severe functional and biochemical defects, including a dramatic reduction or total absence of the secondary granule enzyme leukocyte alkaline phosphatase.
- (c) Measuring the overall activity of this enzyme yields a low Leukocyte Alkaline Phosphatase (LAP) score, which serves as a clinical milestone to distinguish CML from a neutrophilic leukemoid reaction.
- (d) Serum uric acid is markedly elevated due to the high turnover rate of the massive numbers of proliferating nucleic acids.
- (e) Vitamin B12 binding capacity is heavily increased due to hypersecretion of transcobalamin I by the expanded granulocytic mass, and bone marrow cellularity approaches maximum capacity.

Final Answer: The diagnostic parameter that is typically decreased or absent is the Leukocyte Alkaline Phosphatase score.

Answer: (B)

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Q14.

Solution**Concept:**

Burkitt lymphoma is a highly aggressive B-cell non-Hodgkin lymphoma characterized by an exceptionally rapid cellular proliferation rate. The classic histopathological configuration exhibits a cohesive sheet of medium-sized monomorphic neoplastic B lymphocytes interspersed with pale, clear macrophages containing engulfed cellular debris, establishing a diagnostic starry sky appearance.

Solution:

- (a) The pathognomonic driver of Burkitt lymphoma is a reciprocal chromosomal translocation involving the MYC proto-oncogene located on chromosome 8q24.
- (b) The most frequent variant is the t(8;14)(q24;q32) translocation, which translocates the MYC gene adjacent to the highly active immunoglobulin heavy-chain (IGH) locus on chromosome 14.
- (c) This juxtaposition leads to continuous, unregulated overexpression of the MYC transcription factor, which activates gene programs for metabolic reprogramming, rapid cellular growth, and intense mitotic activity.
- (d) The extreme rate of proliferation is matched by a high rate of spontaneous apoptosis, yielding cellular debris that is cleared by tingible-body macrophages.
- (e) The t(14;18) translocation is associated with BCL2 overexpression in follicular lymphoma, whereas the t(11;14) alteration shifts Cyclin D1 expression in mantle cell lymphoma.

Final Answer: The genetic alteration associated with this neoplasm is the t(8;14) translocation leading to MYC overexpression.

Answer: (A)

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Q15.

Solution**Concept:**

An abdominal aortic aneurysm (AAA) is a permanent pathological dilation of the aortic wall, occurring secondary to severe, chronic atherosclerotic degradation. The structural integrity of the aorta depends entirely on the mechanical properties of its tunica media, which must resist continuous arterial pressure waves through a complex lattice of elastic fibers and smooth muscle cells.

Solution:

- (a) Chronic plaque buildup blocks the physical diffusion of oxygen and nutrients from the aortic lumen into the internal layers of the thick vessel wall.
- (b) This local ischemia induces an inflammatory infiltrate within the tunica media, activating macrophages that release matrix metalloproteinases (MMPs) that actively degrade structural elastin and collagen.
- (c) Severe loss of smooth muscle cells combined with structural destruction of the elastica network leads to a classic histopathological lesion termed cystic medial degeneration.
- (d) This degenerative weakening of the structural matrix compromises the tensile strength of the media, allowing the arterial wall to thin out and dilate under systemic pressure.
- (e) Concentric calcification of the adventitia is not a primary degenerative driving feature, while hyaline and hyperplastic arteriosclerosis are microvascular lesions seen primarily within systemic small arteries.

Final Answer: The degenerative feature is cystic medial degeneration with loss of smooth muscle cells and elastic fibers.

Answer: (B)

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Q16.

Solution**Concept:**

Acute coronary syndromes (ACS) are triggered by sudden mechanical disruptions of advanced, vulnerable atherosclerotic plaques. A plaque with a thin fibrous cap covering a soft lipid-rich necrotic core is unstable and susceptible to physical rupture under hemodynamic stress, exposing highly thrombogenic core components to passing blood elements.

Solution:

- (a) Superficial or deep rupture of the fibrous cap exposes core collagen and tissue factor directly to circulating platelets, initiating immediate platelet aggregation and an integrated coagulation cascade.
- (b) This rapid cascade results in the acute formation of a superimposed subocclusive intraluminal thrombus at the site of the ruptured plaque.
- (c) If the resulting thrombus remains subocclusive, or if strong collateral blood flow partially maintains distal tissue perfusion, myocardial cell necrosis is limited to the subendocardial zone.
- (d) This clinical scenario manifests as unstable angina or a Non-ST-segment Elevation Myocardial Infarction (NSTEMI), where full transmural ischemic necrosis is avoided.
- (e) Complete occlusive thrombosis without collateral flow leads directly to a transmural STEMI, while stable angina involves a fixed, unruptured plaque.

Final Answer: The clinical acute coronary syndrome is Unstable Angina or Non-ST-segment Elevation Myocardial Infarction.

Answer: (A)

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Q17.

Solution**Concept:**

Squamous cell carcinoma of the lung is a malignant epithelial neoplasm showing an intimate structural association with a long-standing history of tobacco smoking. It typically arises centrally within the major segmental bronchi, where chronic irritation from inhaled carcinogens induces squamous metaplasia of the normal respiratory mucosa, progressing over time to dysplasia and invasive carcinoma.

Solution:

- (a) Sputum cytology and tissue biopsy demonstrate diagnostic architectural features of differentiation toward a squamous epithelium lineage.
- (b) These distinct features include the presence of well-formed intercellular bridges (desmosomes) connecting adjacent pleomorphic cells, along with intracellular accumulation of dense keratin.
- (c) Neoplastic cells that produce abundant keratin frequently arrange themselves into focal, concentric laminated whorls called keratin pearls or squamous eddies.
- (d) Small cell lung carcinoma is a neuroendocrine tumor exhibiting small cells with minimal cytoplasm, fine nuclear chromatin, and no squamous differentiation or keratin production.
- (e) Adenocarcinoma displays distinct glandular differentiation or mucin production and typically arises within peripheral lung fields, while large cell carcinoma lacks these specific patterns.

Final Answer: The histopathological diagnosis is Squamous cell carcinoma of the lung.

Answer: (C)

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Q18.

Solution**Concept:**

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis, is a systemic necrotizing vasculitis that predominantly targets small-to-medium vessels. It characteristically involves a classic clinical triad affecting the upper respiratory tract, the lower respiratory tract, and the renal microvasculature.

Solution:

- (a) The presence of chronic sinusitis, saddle-nose deformities, pulmonary lesions causing hemoptysis, and focal necrotizing glomerulonephritis points directly to a systemic vasculitic process.
- (b) The highly specific serological marker for this disease is the cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA), which targets neutrophil proteinase 3 (PR3-ANCA).
- (c) In the kidneys, the aggressive vascular inflammation triggers necrosis of the glomerular tuft, leading to a rapid influx of inflammatory cells into Bowman's space to form crescents.
- (d) Microscopic polyangiitis is also a small-vessel vasculitis but is typically associated with p-ANCA (MPO-ANCA) and lacks granulomatous upper airway involvement.
- (e) Churg-Strauss syndrome features prominent eosinophilia and severe asthma, while Goodpasture's syndrome involves linear anti-GBM antibodies without upper respiratory tract necrotizing granulomas.

Final Answer: The diagnosis is Granulomatosis with polyangiitis.

Answer: (B)

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Q19.

Solution**Concept:**

Papillary thyroid carcinoma is the most common malignant neoplasm of the thyroid gland. Its diagnosis relies heavily on characteristic nuclear features rather than architectural patterns alone. These diagnostic nuclear markers include optially clear, ground-glass nuclei, nuclear grooves, and prominent intranuclear inclusions.

Solution:

- (a) The clear, empty-appearing nuclei are termed Orphan Annie eye nuclei and represent a primary diagnostic feature of papillary thyroid carcinoma.
- (b) Due to the papillary growth architecture, local tips of the papillae can undergo focal ischemic necrosis and subsequent dystrophic calcification over time.
- (c) These areas of calcification accumulate in concentric, laminated spherical structures known as psammoma bodies, which are highly visible on light microscopy.
- (d) Asbestos bodies are iron-coated asbestos fibers found within lung tissue following occupational exposure.
- (e) Councilman bodies represent apoptotic hepatocytes seen in acute viral or toxic hepatitis, while Mallory-Denk bodies are cytokeratin aggregates found in alcoholic steatohepatitis.

Final Answer: The calcified structures are Psammoma bodies.

Answer: (C)

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Q20.

Solution**Concept:**

Peptic ulcer disease involving the first part of the duodenum is strongly correlated with chronic localized infection by the spiral bacterium *Helicobacter pylori*. The colonization of the gastric mucosa by this pathogen alters regular hormone feedback pathways that control gastric acid secretion, shifting the balance of acid delivery to the duodenum.

Solution:

- (a) *Helicobacter pylori* colonizes the gastric antrum, triggering an inflammatory response that damages local somatostatin-producing delta cells (D-cells).
- (b) The loss of somatostatin removes the normal inhibitory brake on G-cells, leading to unregulated hypersecretion of gastrin into the systemic circulation.
- (c) High gastrin levels drive gastric parietal cells to produce and secrete massive amounts of hydrochloric acid, overwhelming the natural buffering capacity of the duodenum.
- (d) The excessive acid load enters the proximal duodenum, causing mucosal injury and peptic ulceration.
- (e) *Helicobacter pylori* remains non-invasive within the superficial mucous gel layer; it does not directly invade the deep tissue or cause structural microvascular thrombosis.

Final Answer: The mechanism is hypersecretion of gastric acid secondary to antral inflammation and D-cell inhibition.

Answer: (A)

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Q21.

Solution**Concept:**

Chronic right-sided congestive heart failure causes a systemic backup of venous blood, significantly increasing hydrostatic pressure within the inferior vena cava and hepatic veins. This backward pressure is transmitted directly to the central veins of the liver lobules, inducing persistent passive congestion and cellular hypoxia that selectively damages the parenchyma furthest from the oxygenated arterial supply.

Solution:

- (a) The structural microarchitecture of the hepatic lobule determines its vulnerability to ischemic injury. Central vein areas (Zone 3) receive the least oxygenated blood compared to the periportal areas (Zone 1).
- (b) Severe chronic venous congestion leads to blood pooling and high pressure in Zone 3, causing localized hemorrhagic necrosis and fatty change of surrounding hepatocytes.
- (c) Grossly, these congested, dark red-brown necrotic centrilobular zones contrast sharply against the surrounding pale, unaffected, or fatty periportal parenchymal tissue.
- (d) This alternating mottled pattern mimics the speckled internal appearance of a grated nutmeg seed, leading to the pathognomonic gross pathological term nutmeg liver.
- (e) Peliosis hepatis is characterized by cyclic, irregular sinusoidal dilations forming blood-filled spaces, while Budd-Chiari syndrome results from acute thrombotic occlusion of the major hepatic veins.

Final Answer: The descriptive gross pathological term is Nutmeg liver.

Answer: (B)

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Q22.

Solution**Concept:**

Systemic sclerosis (scleroderma) is a chronic multisystem autoimmune disease characterized by widespread microvascular injury, immunological activation, and extensive interstitial fibrosis of the skin and internal organs. The disease is split into diffuse and limited clinical subsets based on the physical extent of cutaneous involvement and specific underlying circulating autoantibodies.

Solution:

- (a) The clinical presentation of dysphagia, proximal dermal tightening over the fingers (sclerodactyly), and severe gastrointestinal reflux indicates systemic sclerosis affecting the esophageal smooth muscle layer.
- (b) Chronic fibrotic replacement of the lamina propria combined with severe muscularis propria atrophy decreases lower esophageal sphincter pressure, destroying normal peristaltic functionality.
- (c) The diffuse systemic sclerosis variant is strongly linked with the presence of anti-Scl-70 antibodies, which directly target the nuclear enzyme DNA topoisomerase I.
- (d) This specific autoantibody profile carries a high diagnostic specificity for diffuse disease and correlates with an increased risk of developing progressive pulmonary fibrosis.
- (e) Anti-dsDNA and anti-Smith antibodies are highly specific serological markers for systemic lupus erythematosus, whereas anti-Jo-1 antibodies track with polymyositis and dermatomyositis.

Final Answer: The highly specific autoantibody profile is Anti-Scl-70 antibodies.

Answer: (B)

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Q23.

Solution**Concept:**

Poststreptococcal glomerulonephritis (PSGN) is an immunologically mediated glomerular disease that develops weeks after a group A beta-hemolytic streptococcal infection. Nephritogenic bacterial antigens plant themselves within the glomerular tuft, inducing a type III hypersensitivity reaction characterized by local immune complex assembly and subsequent complement cascade activation.

Solution:

- (a) The classical clinical presentation includes periorbital edema, gross hematuria yielding smoke-colored urine, and mild hypertension following a documented pharyngeal or cutaneous streptococcal illness.
- (b) Immunofluorescence microscopy confirms a coarse, granular starry sky deposition pattern of immunoglobulin G and complement component C3 along the capillary walls.
- (c) Diagnostic electron microscopy reveals large, prominent electron-dense deposits located strictly within the subepithelial space, projecting outward like distinct humps.
- (d) These subepithelial humps represent aggregated lattices of antigen-antibody complexes that have slowly crossed the glomerular basement membrane.
- (e) Diffuse effacement of podocyte foot processes describes minimal change disease, subendothelial deposits characterize membranoproliferative glomerulonephritis type I, and basement membrane splitting indicates Alport syndrome or MPGN.

Final Answer: The primary ultrastructural finding is subepithelial electron-dense deposits.

Answer: (C)

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Q24.

Solution**Concept:**

Seminoma is the most common malignant germ cell tumor of the testis, peaking in incidence during the third and fourth decades of life. On gross examination, it typically presents as a well-circumscribed, uniform, lobulated fleshy mass that notably lacks areas of extensive hemorrhage or ischemic tissue necrosis.

Solution:

- (a) Histopathological evaluation reveals a monomorphic population of large, uniform polygonal cells arranged in distinct nests or sheets separated by delicate fibrous tissue stroma.
- (b) Individual tumor cells display distinct, well-demarcated borders, large vesicular nuclei with prominent nucleoli, and abundant clear cytoplasm containing high concentrations of glycogen.
- (c) The thin fibrous connective tissue septa separating these cellular sheets are characteristically infiltrated by a prominent reactive population of small T lymphocytes.
- (d) This combination of uniform clear cells, lymphoid-rich stroma, and a fleshy homogeneous gross appearance is pathognomonic for a testicular seminoma.
- (e) Yolk sac tumors display primitive reticular networks with Schiller-Duval bodies, embryonal carcinomas show highly pleomorphic sheets with necrosis, and choriocarcinomas present with cytotrophoblasts and syncytiotrophoblasts.

Final Answer: The correct diagnosis is Seminoma.

Answer: (C)

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Q25.

Solution**Concept:**

Endometrial carcinoma is classified into two distinct biological types based on clinical, metabolic, and genetic profiles. Type I (endometrioid) carcinoma represents the most common form, developing via an atypical endometrial hyperplasia pathway driven by prolonged, unmitigated exposure to estrogen.

Solution:

- (a) Estrogen acts as a potent mitogen for endometrial glandular tissue. Any physiological state that increases circulating estrogen levels without a balancing luteal phase progesterone exposure increases cancer risk.
- (b) Obesity is a major risk factor because adipose tissue contains high levels of the aromatase enzyme, which peripheralizes adrenal androgens into active estrone.
- (c) This continuous peripheral production creates a chronic state of unmitigated estrogen stimulation on the sensitive endometrial lining, driving glandular hyperplasia and transformation.
- (d) Multiparity is protective because the high-progesterone state of pregnancy interrupts estrogen stimulation, and oral contraceptives deliver balancing progestins that thin the endometrium.
- (e) Early menopause reduces the total duration of the lifetime ovulatory estrogen window, meaning it acts as a protective factor rather than a metabolic driver.

Final Answer: The condition most strongly correlated is Obesity.

Answer: (B)

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Answer Key

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

