NEET PG Pathology Sample Paper-7

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 female undergoing evaluation for systemic lupus erythematosus (SLE) undergoes a renal biopsy. Electron microscopy reveals dense, ribbon-like subendothelial deposits. Molecular analysis confirms an alteration in a regulatory protein that prevents the assembly of the membrane attack complex (MAC) on autologous cells by accelerating the decay of C3 and C5 convertases. Which of the following membrane-bound regulatory proteins is most likely functionally deficient or mutated in this scenario?

(A) CD55 (Decay-accelerating factor)

(B) CD59 (Protectin)

(C) Factor H

(D) Complement Receptor 1 (CR1)

Q2. During an experimental study on cellular senescence, fibroblasts are exposed to repetitive sub-lethal oxidative stress. Over time, these cells demonstrate a stable arrest in the G1 phase of the cell cycle, accompanied by increased expression of β-galactosidase. Western blot analysis reveals markedly elevated levels of a specific tumor suppressor protein that directly inhibits Cyclin-Dependent Kinases 4 and 6 (CDK4/6). Which protein is responsible for this direct inhibition?

(A) p21 (WAF1/CIP1)

(B) p16 (INK4a)

(C) p27 (Kip1)

(D) p53

Q3. A 68-year-old male with a history of long-standing poorly controlled hypertension dies suddenly from a ruptured aortic aneurysm. Autopsy reveals extensive concentric left ventricular hypertrophy. Microscopic examination of the myocardium demonstrates enlarged cardiomyocytes with boxcar-shaped nuclei. Which of the following intracellular signaling pathways is primarily responsible for mediating this specific form of pathologic myocardial adaptation?

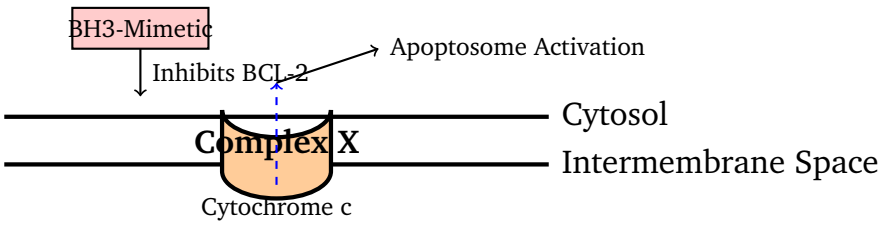
(A) Phosphoinositide 3-kinase/Akt (PI3K/Akt) pathway

(B) G-protein-coupled receptor (GPCR)-mediated calcineurin pathway

(C) Notch signaling pathway

(D) Wnt/β-catenin pathway

Q4. A clinical research team analyzes cellular apoptosis pathways in malignant lymphocytes exposed to a novel BH3-mimetic therapeutic agent. The schematic below depicts the mitochondrial outer membrane permeabilization (MOMP) cascade triggered by the drug. Identify the specific pore-forming oligomeric complex labeled as **X** in the diagram that directly mediates the release of Cytochrome c into the cytosol:



(A) BCL-2 / BCL-XL heterodimers

(B) BAX / BAK oligomers

(C) FAS / FADD death-inducing signaling complexes (DISC)

(D) Caspase-9 / Apaf-1 rings

Q5. A 29-year-old male presents with recurrent epistaxis, cutaneous ecchymoses, and delayed wound healing. Genetic screening reveals a loss-of-function mutation in the gene encoding the lysosomal trafficking regulator protein, resulting in defective phagosome-lysosome fusion. A peripheral blood smear demonstrates giant lysosomal inclusions within neutrophils. Which of the following additional clinical manifestations is most characteristically associated with this patient's underlying disease?

(A) Partial oculocutaneous albinism

(B) Severe retroperitoneal fibrosis

(C) Lytic bone lesions with hypercalcemia

(D) Recurrent thrombophlebitis migrans

Q6. An 8-year-old boy presents with severe photosensitivity, hyperpigmentation, and multiple early-onset cutaneous malignancies on sun-exposed areas. Skin biopsy shows atypical keratinocytes consistent with squamous cell carcinoma. The molecular pathology involves a defect in the nucleotide excision repair (NER) mechanism. Which of the following specific enzymatic events is compromised in this patient during the processing of UV-induced DNA damage?

(A) Cleavage of mismatched bases by a specific DNA glycosylase

(B) Endonucleolytic cleavage of the damaged DNA strand by an excinuclease

(C) Direct reversal of pyrimidine dimers by photolyase

(D) Synthesis of short RNA primers by DNA primase

Q7. A 54-year-old female diagnosed with invasive ductal carcinoma of the breast undergoes genetic sequencing of the tumor tissue. The report highlights a localized amplification of the HER2/neu (ERBB2) oncogene. This receptor belongs to the receptor tyrosine kinase family. Which downstream intracellular cascade is primarily activated upon ligand-independent homodimerization of this amplified receptor to promote uncontrolled cellular proliferation?

(A) JAK/STAT signaling pathway

(B) RAS/RAF/MEK/ERK pathway

(C) cAMP-dependent Protein Kinase A pathway

(D) TGF-β/SMAD signaling pathway

Q8. A tissue biopsy from a chronic non-healing ulcer shows dense granulation tissue containing abundant newly formed capillaries, fibroblasts, and extracellular matrix deposition. Molecular profiling indicates an upregulation of a growth factor that specifically binds to tyrosine kinase receptors on endothelial cells, inducing their migration, proliferation, and sprout formation. This factor is known to be induced by hypoxia-inducible factor 1-alpha (HIF-1α). Identify this mediator.

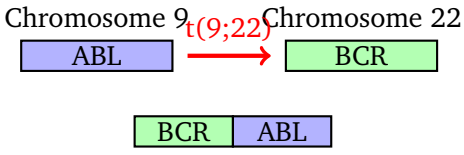
(A) Transforming Growth Factor-beta (TGF-β)

(B) Vascular Endothelial Growth Factor A (VEGF-A)

(C) Platelet-Derived Growth Factor (PDGF)

(D) Fibroblast Growth Factor 2 (FGF-2)

Q9. A 45-year-old male with long-standing fatigue and mild splenomegaly presents for evaluation. His complete blood count reveals a marked leukocytosis with a left shift, reflecting the presence of mature and maturing granulocytic precursors. The bone marrow cytogenetic analysis shows a specific reciprocal translocation. The schematic below maps the fusion gene configuration responsible for this condition. Identify the chimeric protein product derived from this chromosomal rearrangment:



Chimeric Fusion Oncogene

(A) A constitutively active receptor tyrosine kinase

(B) A constitutively active non-receptor tyrosine kinase

(C) A truncated nuclear transcription factor

(D) A defective dual-specificity phosphatase

Q10. A 35-year-old female presents with severe microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury. A peripheral blood smear confirms the presence of numerous schistocytes. Coagulation profiles (PT, aPTT, and Fibrinogen) are completely within normal reference limits. Further specialized testing demonstrates a severe reduction in ADAMTS13 protease activity. Which of the following pathophysiologic mechanisms directly causes the systemic microvascular thrombosis observed in this patient?

(A) Unchecked propagation of tissue factor-mediated extrinsic pathway cascade

(B) Accumulation of ultra-large von Willebrand factor (ULvWf) multimers inducing platelet agglutination

(C) Complement-mediated lysis of endothelial cells via defective CD59 expression

(D) Defective binding of Antithrombin III to endothelial heparan sulfate proteoglycans

Q11. A 62-year-old male with a history of recurrent deep vein thromboses presents with generalized pruritus that worsens significantly after a warm bath, accompanied by headache and erythromelalgia. Laboratory results show a hemoglobin level of 19.5 g/dL, hematocrit of 59%, white blood cell count of 14,500/μL, and a platelet count of 520,000/μL. Erythropoietin level is subnormal. Which of the following molecular abnormalities is most uniformly identified in patients with this myeloproliferative neoplasm?

(A) JAK2 V617F mutation causing hypersensitivity to erythropoietin signaling

(B) CALR frameshift mutation altering calcium homeostasis in the endoplasmic reticulum

(C) MPL W515L mutation leading to autonomous thrombopoietin receptor activation

(D) BCR-ABL1 transcript encoding a p210 oncoprotein

Q12. A bone marrow biopsy from a 72-year-old female with progressive pancytopenia and massive splenomegaly reveals extensive reticulin fibrosis and clusters of atypical, pleomorphic megakaryocytes with hyperchromatic nuclei. Many cells show a "cloud-like" nuclear morphology. Cytogenetic analysis reveals a deletion of 5q (del(5q)). What is the diagnostic significance of isolated del(5q) in the context of myelodysplastic syndromes (MDS)?

(A) It dictates a highly aggressive course with high rates of transformation to AML

(B) It represents a favorable prognostic subgroup that responds exceptionally well to lenalidomide

(C) It indicates absolute resistance to all immunomodulatory therapeutics

(D) It confirms a diagnosis of secondary acute myeloid leukemia rather than MDS

Q13. A 19-year-old male presenting with painless cervical lymphadenopathy undergoes an excisional biopsy. Histopathological evaluation reveals large, atypical lymphoid cells with bilobed or multilobed nuclei and prominent, inclusion-like "owl-eye" nucleoli. Immunohistochemical analysis displays a classic phenotype: the cells are strongly positive for CD30 and CD15, but negative for CD20 and CD45. Which variant of Hodgkin lymphoma is most likely characterized by these findings?

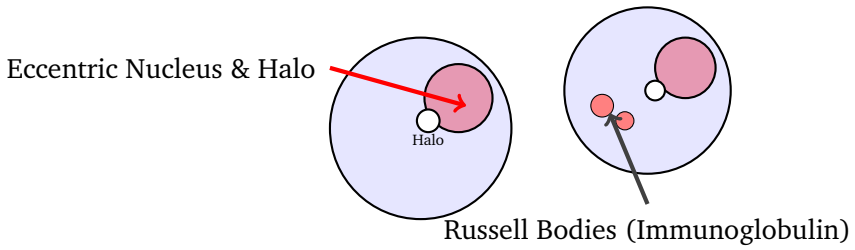
(A) Nodular lymphocyte predominant Hodgkin lymphoma

(B) Classical Hodgkin lymphoma, Mixed Cellularity subtype

(C) Classical Hodgkin lymphoma, Nodular Sclerosis subtype

(D) Lymphocyte-rich Hodgkin lymphoma

Q14. A 65-year-old male presents with bone pain, fatigue, and an elevated serum creatinine level. Serum protein electrophoresis (SPEP) reveals a prominent M-spike in the gamma globulin region. The diagram below illustrates the characteristic classic bone marrow aspirate appearance expected in this condition. Identify the key diagnostic cellular structures or features labeled with arrows:



(A) Auer rods within blast cells indicating acute promyelocytic leukemia

(B) Mott cells and Russell bodies within clonal plasma cells indicating Multiple Myeloma

(C) Reed-Sternberg cells within a polymorphous inflammatory background

(D) Gaucher cells containing crumpled tissue paper cytoplasm

Q15. A 58-year-old male presenting with gross hematuria undergoes a cystoscopy, which reveals an exophytic mass in the lateral wall of the urinary bladder. A transurethral resection of the bladder tumor (TURBT) is performed. Histopathological examination confirms an invasive urothelial carcinoma. Molecular profiling reveals an activating mutation in the FGFR3 gene along with a deletion of chromosome 9p. Which of the following statements best describes the characteristic pathway of tumorigenesis associated with these specific molecular findings?

(A) Flat non-invasive carcinoma in situ pathway with early TP53 mutations

(B) Papillary pathway originating from urothelial hyperplasia, often associated with a favorable initial prognosis but high recurrence rate

(C) Schistosoma-induced chronic inflammatory squamous metaplasia pathway

(D) Lynch-syndrome-associated microsatellite instability pathway

Q16. A 44-year-old non-smoking female presents with a progressive cough and dyspnea. A chest CT scan reveals a peripheral 3.5-cm lung mass. A wedge resection is performed, and histopathology demonstrates glandular structures invading the stroma, staining strongly positive for TTF-1 and Napsin A. Molecular analysis detects an inversion on chromosome 2p that fuses the

echinoderm microtubule-associated protein-like 4 (EML4) gene with a specific receptor tyrosine kinase gene. This patient's tumor is highly responsive to which class of targeted inhibitors?

(A) EGFR-targeted tyrosine kinase inhibitors (e.g., Erlotinib)

(B) ALK inhibitors (e.g., Crizotinib)

(C) BRAF V600E inhibitors (e.g., Vemurafenib)

(D) MEK inhibitors (e.g., Trametinib)

Q17. A 32-year-old female presents with severe epistaxis, hemoptysis, and acute renal failure. Laboratory evaluation reveals a markedly elevated serum c-ANCA (PR3-ANCA) titer. A renal biopsy shows a necrotizing crescentic glomerulonephritis with minimal immune deposition on immunofluorescence (pauci-immune status). Which of the following features, if observed in a lung biopsy from this patient, would most conclusively establish the diagnosis of Granulomatosis with Polyangiitis (GPA) over microscopic polyangiitis?

(A) Eosinophil-rich granulomatous inflammation with severe asthma history

(B) Necrotizing granulomatous vasculitis with geographic necrosis

(C) Linear deposition of IgG along the alveolar basement membrane

(D) Intra-alveolar hemorrhage without inflammation or necrosis

Q18. A 62-year-old male with chronic hepatitis C virus infection and cirrhosis presents with an elevated serum alpha-fetoprotein (AFP) level of 2400 ng/mL. A multiphase contrast-enhanced CT scan of the abdomen shows a 4-cm hypervascular mass in the right hepatic lobe that demonstrates hyperenhancement during the arterial phase and rapid "washout" during the venous phase. Which of the following histological criteria is most specific for diagnosing a well-differentiated hepatocellular carcinoma (HCC) over a benign hepatic adenoma on a core needle biopsy?

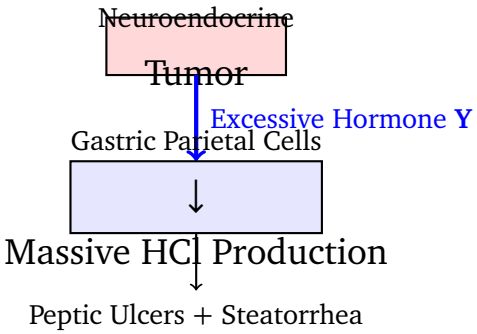
(A) Presence of normal portal tracts and bile ductules within the lesion

(B) Thickening of hepatic cords to more than 3 cells wide with diffuse reticulin framework loss

(C) Cytoplasmic accumulation of glycogen and lipid droplets

(D) Absence of cytologic atypia and mitotic figures

Q19. A 42-year-old male presenting with chronic epigastric pain and intractable diarrhea undergoes an upper GI endoscopy, revealing markedly thickened gastric folds and multiple atypical ulcers located in the second and third parts of the duodenum. The schematic diagram below outlines the physiological feedback loop altered in this condition. Identify the primary hormone-secreting tumor causing this pathology:



(Zollinger-Ellison Syndrome)

(A) Insulinoma secreting insulin

(B) Gastrinoma secreting gastrin

(C) VIPoma secreting vasoactive intestinal peptide

(D) Glucagonoma secreting glucagon

Q20. A 34-year-old female presents with a painless, rapidly growing mass in her right thyroid lobe. Fine-needle aspiration (FNA) biopsy displays sheets of polygonal cells within an abundant amyloid-containing stroma that stains positive with Congo red under polarized light (apple-green birefringence). Immunohistochemical stains show strong positivity for calcitonin. Which of the following genetic alterations is most characteristically associated with this tumor type, either sporadically or as part of a familial syndrome?

(A) RET proto-oncogene point mutations

(B) BRAF V600E mutation

(C) PAX8-PPARγ1 fusion gene

(D) RET/PTC chromosomal translocation

Q21. A 52-year-old female presents with progressive generalized muscle weakness, ptosis, and diplopia that worsens significantly toward the end of the day or after repetitive muscle use. A chest CT reveals an anterior mediastinal mass measuring 4.5 cm. A biopsy of this mass confirms a thymoma. What is the fundamental immunopathologic mechanism linking this patient's anterior mediastinal neoplasm to her neuromuscular symptoms?

(A) Tumor-mediated secretion of a paraneoplastic peptide that blocks presynaptic voltage-gated calcium channels

(B) Defective thymic central tolerance training leading to the generation of autoantibodies against postsynaptic acetylcholine receptors (AChR)

(C) Direct metastatic infiltration of the neuromuscular junctions by malignant thymocytes

(D) Molecular mimicry between thymic epithelial proteins and peripheral skeletal muscle myosin heavy chains

Q22. A 24-year-old male presents with a painless testicular mass. Serum tumor markers reveal a normal alpha-fetoprotein (AFP) level but a moderately elevated human chorionic gonadotropin (hCG) level. Radical orchiectomy is performed. Gross examination shows a well-circumscribed, homogeneous, lobulated white-pink mass lacking areas of hemorrhage or necrosis. Microscopic evaluation demonstrates nests of large, uniform cells with clear, glycogen-rich cytoplasm separated by thin fibrous septae infiltrated by T-lymphocytes. What is the most likely diagnosis?

(A) Embryonal Carcinoma

(B) Yolk Sac Tumor

(C) Seminoma

(D) Choriocarcinoma

Q23. A 63-year-old male presenting with progressive memory loss, cognitive decline, and ataxia dies within six months of symptom onset. An autopsy is

performed. Brain histology demonstrates widespread, confluent vacuolation of the neuropil within the gray matter of the cerebral cortex and basal ganglia, creating a classic "spongiform" appearance. No inflammatory infiltrates are identified. Which of the following biochemical alterations represents the primary underlying pathogenesis of this disease?

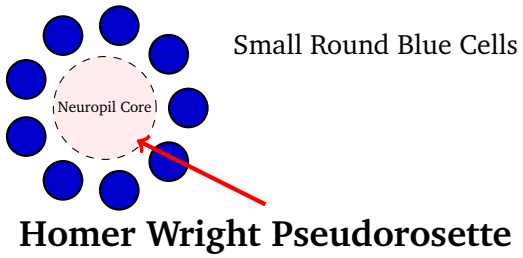
(A) Conformational change of a normal cellular protein (PrP^{C}) from an α-helical structure into an infectious β-sheet rich isoform (PrP^{Sc})

(B) Hyperphosphorylation of microtubule-associated tau proteins leading to neurofibrillary tangles

(C) Extracellular deposition of β-amyloid peptides derived from abnormal cleavage of amyloid precursor protein

(D) Ubiquitination and cytoplasmic aggregation of TDP-43 within motor neurons

Q24. A 9-month-old infant presents with a palpable abdominal mass, hypertension, and opsoclonus-myoclonus syndrome ("dancing eyes-dancing feet"). Urinary screening is markedly positive for vanillylmandelic acid (VMA) and homovanillic acid (HVA). A biopsy of the mass is performed. The structural schematic below maps the distinctive cellular arrangement seen on histopathology. Identify the diagnostic structure illustrated:



(A) Flexner-Wintersteiner rosettes containing a central true lumen

(B) Homer Wright pseudorosettes containing a central core of fibrillary neuropil

(C) Schiller-Duval bodies containing a central capillary vessel

(D) Call-Exner bodies containing eosinophilic fluid material

Q25. A 62-year-old female presents with persistent pelvic pain and abdominal distension. Imaging confirms bilateral complex ovarian masses along with extensive peritoneal carcinomatosis. A tumor biopsy reveals a high-grade serous ovarian carcinoma. Molecular screening confirms a germline mutation in the BRCA1 gene. Which of the following DNA repair mechanisms is fundamentally defective in this patient's tumor cells due to this genetic mutation?

(A) Mismatch repair (MMR)

(B) Base Excision Repair (BER)

(C) Homologous recombination DNA repair (HRR)

(D) Non-homologous end joining (NHEJ)

Detailed Solutions

Q1.

Solution

Concept: The complement system is strictly regulated by membrane-bound and soluble proteins to prevent collateral damage to autologous tissues. Regulatory proteins target the assembly and stability of critical amplification enzymes ($C3$ and $C5$ convertases).

Solution:

Let's evaluate the functions of the listed regulatory proteins:

(a) **CD55 (Decay-accelerating factor / DAF)** is a glycosylphosphatidylinositol (GPI)-anchored membrane protein that physically binds to $C3$ and $C5$ convertases ($C4b2a$ and $C3bBb$). It accelerates their dissociation (decay), preventing downstream cleavage cascades and stopping the formation of the membrane attack complex (MAC).

(b) CD59 (Protectin) operates downstream of CD55 by binding the $C5b-8$ complex, explicitly preventing the recruitment and polymerization of $C9$ pores. It does not accelerate convertase decay.

(c) Factor H is a soluble plasma regulator that works similarly to CD55 but is not a membrane-bound component of the host cell surface.

Final Answer: CD55 (Decay-accelerating factor)

Answer: (A)

Go Back to Question 1

Q2.

Solution

Concept: Cellular senescence induced by stress is controlled by key tumor suppressor networks that arrest cell cycle progression at specific checkpoints.

Solution:

Let's analyze the inhibitors governing the G1-to-S phase transition:

(a) The INK4 family of cyclin-dependent kinase inhibitors specifically targets the $CDK4$ and $CDK6$ kinases, preventing them from complexing with Cyclin D.

(b) **p16 (INK4a)** is the hallmark protein upregulated during stress-induced cellular senescence. By directly binding and blocking $CDK4/6$, p16 keeps the Retinoblastoma (Rb) protein hypophosphorylated, ensuring it binds tightly to and suppresses the $E2F$ transcription factor, forcing permanent G1 phase arrest.

(c) p21 (WAF1/CIP1) is activated primarily via p53 pathways and targets a broader range of CDKs ($CDK2$, $CDK1$), rather than selectively acting as a dedicated $CDK4/6$ inhibitor.

Final Answer: p16 (INK4a)

Answer: (B)

Go Back to Question 2

Q3.

Solution

Concept: Myocardial hypertrophy can be physiologic (adaptive) or pathologic (maladaptive). Each type is driven by distinct intracellular signaling pathways responding to different mechanical or chemical stressors.

Solution:

Let's break down the molecular mechanisms of cardiac hypertrophy:

(a) Pathologic hypertrophy, caused by chronic hemodynamic overloads like systemic hypertension, is initiated by mechanical stretch and neurohumoral factors (e.g., Angiotensin II, Endothelin-1).

(b) These factors stimulate **G-protein-coupled receptors (GPCRs)**, activating downstream cascades that elevate intracellular calcium levels. This calcium excess activates **calcineurin**, a phosphatase that dephosphorylates the transcription factor NFAT, driving it into the nucleus to induce pathologic gene patterns.

(c) Physiological hypertrophy (e.g., seen in trained athletes) is conversely mediated by growth factors (IGF-1) acting through the PI3K/Akt pathway.

Final Answer: G-protein-coupled receptor (GPCR)-mediated calcineurin pathway

Answer: (B)

Go Back to Question 3

Q4.

Solution

Concept: The intrinsic apoptotic pathway centers around Mitochondrial Outer Membrane Permeabilization (MOMP). This critical event is governed by a balance between pro-apoptotic and anti-apoptotic members of the BCL-2 protein family.

Solution:

Let's analyze the components involved in pore formation as depicted in the diagram:

(a) BH3-mimetics act by neutralizing anti-apoptotic proteins like BCL-2 or BCL-XL, which normally keep pro-apoptotic effectors sequestered in an inactive state.

(b) Once free from inhibition, the core pro-apoptotic executioner proteins **BAX and BAK** change confirmation and assemble into high-molecular-weight oligomeric structures within the mitochondrial outer membrane.

(c) This specific **BAX / BAK oligomer complex** forms physical channels (Complex X) that breach the membrane, permitting the escape of Cytochrome c into the cytosol to kickstart the apoptosome assembly.

Final Answer: BAX / BAK oligomers

Answer: (B)

Go Back to Question 4

Q5.

Solution

Concept: Chediak-Higashi syndrome is a rare autosomal recessive disorder caused by a mutation in the *LYST* gene, which regulates intracellular lysosomal trafficking and vesicle fusion.

Solution:

Let's connect the cellular trafficking defect to its characteristic clinical signs:

(a) Defective *LYST* expression stops the normal transport and fusion of protein-containing vesicles, leading to the formation of massive, non-functional megagranules (giant lysosomal inclusions) inside neutrophils, platelets, and melanocytes.

(b) Because melanocytes cannot properly distribute melanin-containing melanosomes to surrounding keratinocytes, patients present with **Partial oculocutaneous albinism**.

(c) The leukocyte defects also compromise microbial killing, predisposing individuals to recurrent pyogenic infections, alongside bleeding tendencies from abnormal platelet dense granules.

Final Answer: Partial oculocutaneous albinism

Answer: (A)

Go Back to Question 5

Q6.

Solution

Concept: Xeroderma Pigmentosum is an autosomal recessive disease caused by inherited mutations in genes regulating the Nucleotide Excision Repair (NER) pathway, leading to extreme UV vulnerability.

Solution:

Let's trace the enzymatic steps involved in standard NER function:

(a) Ultraviolet radiation creates covalent linkages between adjacent pyrimidines, forming cyclobutane pyrimidine dimers or 6-4 photoproducts that distort the DNA double helix.

(b) In humans, repairing these bulky lesions relies on NER. The key step involves structural recognition of the distortion followed by **Endonucleolytic cleavage of the damaged DNA strand by an excinuclease** complex. This excinuclease clips the phosphodiester backbone on both the 5' and 3' sides of the lesion.

(c) A defect in this endonucleolytic excision phase prevents removal of the mutated patch, causing rapid mutation accumulation and early-onset skin malignancies. (Note: Human cells lack photolyases, ruling out direct reversal mechanisms).

Final Answer: Endonucleolytic cleavage of the damaged DNA strand by an excinuclease

Answer: (B)

Go Back to Question 6

Q7.

Solution

Concept: The HER2/neu (*ERBB2*) proto-oncogene encodes a 185-kDa transmembrane receptor tyrosine kinase belonging to the EGFR family. Amplification of this gene drives over-expression, leading to autonomous signaling.

Solution:

Let's analyze the intracellular pathway activated by HER2:

(a) When *HER2* is amplified, the high concentration of receptors on the cell surface promotes spontaneous, ligand-independent homodimerization and heterodimerization (typically with HER3).

(b) This dimerization induces cross-phosphorylation of internal tyrosine kinase domains. These phosphorylated residues recruit adaptor proteins (like Grb2 and SOS) that activate the classic **RAS/RAF/MEK/ERK pathway** (mitogen-activated protein kinase cascade).

(c) This signaling cascade directly targets nuclear transcription factors to upregulate cyclins, driving uninhibited cell proliferation and survival in breast adenocarcinomas.

Final Answer: RAS/RAF/MEK/ERK pathway

Answer: (B)

Go Back to Question 7

Q8.

Solution

Concept: Angiogenesis is a vital component of granulation tissue formation during wound healing. It is tightly regulated by specific growth factors responding to local environmental cues such as tissue hypoxia.

Solution:

Let's isolate the primary growth factor involved in blood vessel sprout formation:

(a) In a healing ulcer, rapid tissue proliferation causes localized hypoxia. This low-oxygen environment stabilizes the transcription factor **Hypoxia-Inducible Factor 1-alpha (HIF-1α)**.

(b) HIF-1α translocates to the nucleus and directly upregulates the transcription of **Vascular Endothelial Growth Factor A (VEGF-A)**.

(c) VEGF-A is secreted into the extracellular space, where it binds to tyrosine kinase receptors ($VEGFR-2$) on nearby endothelial cells. This interaction triggers endothelial migration, proliferation, and assembly into new functional capillary loops.

Final Answer: Vascular Endothelial Growth Factor A (VEGF-A)

Answer: (B)

Go Back to Question 8

Q9.

Solution

Concept: Chronic Myelogenous Leukemia (CML) is molecularly defined by the Philadelphia chromosome, which results from a reciprocal translocation between chromosomes 9 and 22, designated as $t(9;22)(q34;q11)$.

Solution:

Let's characterize the biochemical properties of the resulting fusion protein:

(a) The translocation fuses the *BCR* gene from chromosome 22 to the *ABL1* gene on chromosome 9, producing a chimeric *BCR-ABL1* fusion gene.

(b) The wild-type *ABL1* gene encodes a non-receptor tyrosine kinase that is normally tightly regulated via auto-inhibition.

(c) The structural fusion with the BCR sequence replaces the auto-inhibitory N-terminus of ABL1, converting it into a **constitutively active non-receptor tyrosine kinase**. This mutant enzyme continually phosphorylates downstream substrates without requiring external upstream signaling, driving massive myeloid precursor proliferation.

Final Answer: A constitutively active non-receptor tyrosine kinase

Answer: (B)

Go Back to Question 9

Q10.

Solution

Concept: Thrombotic Thrombocytopenic Purpura (TTP) is a life-threatening microangiopathy caused by a functional deficiency in the metalloprotease ADAMTS13, leading to platelet-rich microvascular thrombi.

Solution:

Let's look at the pathophysiology of thrombus formation in TTP:

(a) Vascular endothelial cells normally synthesize and secrete von Willebrand factor (vWF) as ultra-large, highly adhesive protein multimers.

(b) In healthy vessels, the ADAMTS13 protease continuously cleaves these ultra-large multimers into smaller, less active fragments to prevent spontaneous clotting.

(c) A severe deficiency in ADAMTS13 activity leads to the **Accumulation of ultra-large von Willebrand factor (ULvWf) multimers inducing platelet agglutination**. These long strings tether to endothelial surfaces under high shear stress conditions, capturing and aggregating passing platelets. This process creates widespread microthrombi that fragment red blood cells into schistocytes and consume platelets.

Final Answer: Accumulation of ultra-large von Willebrand factor (ULvWf) multimers inducing platelet agglutination

Answer: (B)

Go Back to Question 10

Q11.

Solution

Concept: Polycythemia Vera (PV) is a clonal myeloproliferative neoplasm characterized by autonomous erythroid production that occurs independently of systemic erythropoietin levels.

Solution:

Let's evaluate the primary genetic driver of PV:

(a) The clinical constellation of panmyelosis (elevated hemoglobin, hematocrit, WBC, and platelets) paired with low serum erythropoietin and post-bath pruritus (aquagenic pruritus) is highly specific for Polycythemia Vera.

(b) Virtually > 95% of PV patients carry a somatic **JAK2 V617F mutation** within the pseudokinase domain of the Janus Kinase 2 protein.

(c) This mutation eliminates normal auto-inhibitory control, causing downstream hematopoietic receptors to become hypersensitive. This drives continuous, ligand-independent intracellular signaling, allowing erythroid precursors to proliferate without requiring normal levels of erythropoietin.

Final Answer: JAK2 V617F mutation causing hypersensitivity to erythropoietin signaling

Answer: (A)

Go Back to Question 11

Q12.

Solution

Concept: Myelodysplastic Syndromes (MDS) are clonal stem cell disorders marked by cytopenias, ineffective hematopoiesis, and dysplastic cell morphology. Specific cytogenetic findings dictate prognosis and direct therapy.

Solution:

Let's analyze the clinical impact of an isolated 5q deletion:

(a) MDS presenting with an isolated deletion of chromosome 5q—often termed the "5q minus syndrome"—has unique clinico-pathological properties, including macrocytic anemia and an abundance of hypolobated, "cloud-like" megakaryocytes.

(b) In the context of MDS, an isolated del(5q) abnormality **represents a favorable prognostic subgroup that responds exceptionally well to lenalidomide**.

(c) Lenalidomide works by targeting the altered protein degradation pathways unique to del(5q) clones, inducing selective cytotoxicity against the mutant cell line and restoring normal bone marrow function.

Final Answer: It represents a favorable prognostic subgroup that responds exceptionally well to lenalidomide

Answer: (B)

Go Back to Question 12

Q13.

Solution

Concept: Hodgkin Lymphoma is divided into Classical Hodgkin Lymphoma (CHL) and Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL). These divisions are based on distinct cellular morphologies and immunohistochemical profiles.

Solution:

Let's look at the immunophenotypic signature described:

(a) The classic Reed-Sternberg (RS) cell is a large lymphoid cell with a multi-lobed nucleus and prominent inclusion-like nucleoli ("owl-eye" appearance).

(b) In all subtypes of **Classical Hodgkin Lymphoma**, these malignant cells display a specific cell-surface marker profile: they are strongly positive for **CD30** and **CD15**, while typically lacking standard B-cell markers like CD20 and pan-leukocyte markers like CD45.

(c) Since the prompt lists subtypes belonging to Classical Hodgkin Lymphoma alongside a specific phenotypic match, we evaluate the cellular background. However, the presence of these definitive classical markers ($CD30^+$, $CD15^+$, $CD20^-$, $CD45^-$) immediately rules out NLPHL (which has $CD20^+$, $CD45^+$ "popcorn cells"). Among classical choices, the question specifies a general archetype matching **Classical Hodgkin Lymphoma** properties. Mixed Cellularity contains abundant classical RS cells in a varied inflammatory background.

Final Answer: Classical Hodgkin lymphoma, Mixed Cellularity subtype

Answer: (B)

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Q14.

Solution

Concept: Multiple Myeloma is a malignant neoplasm of clonal plasma cells that accumulate within the bone marrow, producing excessive amounts of a single monoclonal immunoglobulin (M-spike).

Solution:

Let's interpret the bone marrow aspirate features outlined in the diagram:

(a) The diagram displays typical neoplastic plasma cells characterized by an eccentric nucleus, clumped "clock-face" chromatin, and a prominent perinuclear clear zone (halo) representing the Golgi apparatus.

(b) When plasma cells synthesize massive amounts of immunoglobulin that cannot be properly secreted, the proteins accumulate within the cytoplasm, forming large, eosinophilic, round inclusions called **Russell bodies**.

(c) Cells packed with multiple Russell bodies are termed **Mott cells**. Identifying these expanded clonal plasma cell features confirms a diagnosis of **Multiple Myeloma**.

Final Answer: Mott cells and Russell bodies within clonal plasma cells indicating Multiple Myeloma

Answer: (B)

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Q15.

Solution

Concept: Urothelial (transitional cell) carcinoma of the bladder develops through two separate, well-defined genetic pathways: the papillary pathway and the flat non-invasive (carcinoma in situ) pathway.

Solution:

Let's map the molecular profile to its corresponding pathway:

(a) The presence of an activating mutation in the **FGFR3** gene paired with a loss/deletion of chromosome **9p** (containing the tumor suppressor *CDKN2A*) is characteristically associated with the **papillary pathway**.

(b) This pathway typically originates from urothelial hyperplasia, forming exophytic, branching structures. Clinically, these tumors are often low-grade initially and hold a **favorable initial prognosis, but carry a very high rate of local recurrence** within the bladder.

(c) Conversely, the flat carcinoma in situ pathway skips hyperplastic stages, is driven by early *TP53* and *RB* alterations, and tends to be high-grade and highly invasive from the outset.

Final Answer: Papillary pathway originating from urothelial hyperplasia, often associated with a favorable initial prognosis but high recurrence rate

Answer: (B)

Go Back to Question 15

Q16.

Solution

Concept: Lung adenocarcinomas often express specific driver oncogene alterations that serve as excellent targets for precision tyrosine kinase inhibitors.

Solution:

Let's identify the targeted therapy that addresses this specific gene rearrangement:

(a) The patient has a lung adenocarcinoma (glandular histology, $TTF-1^+$, $NapsinA^+$) that develops in a non-smoker.

(b) The chromosome 2p inversion fuses the 5' portion of the *EML4* gene with the 3' portion of the **ALK (Anaplastic Lymphoma Kinase)** receptor tyrosine kinase gene, creating an oncogenic *EML4-ALK* fusion product.

(c) This chimeric protein undergoes constitutive autophosphorylation, activating survival pathways. Tumors positive for this alteration show excellent clinical responses to specialized **ALK inhibitors (e.g., Crizotinib)**.

Final Answer: ALK inhibitors (e.g., Crizotinib)

Answer: (B)

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Q17.

Solution

Concept: Granulomatosis with Polyangiitis (GPA, formerly Wegener's) and Microscopic Polyangiitis (MPA) are both systemic, small-vessel, pauci-immune necrotizing vasculitides that can affect the kidneys and lungs.

Solution:

Let's differentiate GPA from MPA based on histological criteria:

(a) Both conditions cause a crescentic, pauci-immune glomerulonephritis and can induce pulmonary hemorrhage.

(b) The key histological distinction is that GPA is characterized by **necrotizing granulomatous inflammation with geographic necrosis** and multinucleated giant cells within the parenchymal lesions. MPA, by definition, lacks granulomas.

(c) (Note: Eosinophil-rich granulomas with asthma point toward Eosinophilic Granulomatosis with Polyangiitis / Churg-Strauss, while linear IgG lines define Goodpasture syndrome).

Final Answer: Necrotizing granulomatous vasculitis with geographic necrosis

Answer: (B)

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Q18.

Solution

Concept: Differentiating well-differentiated Hepatocellular Carcinoma (HCC) from benign hepatic lesions like hepatocellular adenoma on core needle biopsies requires evaluating structural and reticulin scaffolding criteria.

Solution:

Let's isolate the specific histological hallmarks of malignant transformation in hepatocytes:

(a) Hepatocellular adenomas preserve a regular, single- or double-cell thick hepatic cord layout and maintain their underlying reticulin matrix framework, though they lack normal portal tracts.

(b) Well-differentiated HCC is characterized by a significant structural abnormality: the **thickening of hepatic cords to more than 3 cells wide, accompanied by a diffuse loss of the reticulin framework**.

(c) This widened trabecular growth architecture indicates malignant proliferation, overriding the delicate scaffolding of normal liver plates.

Final Answer: Thickening of hepatic cords to more than 3 cells wide with diffuse reticulin framework loss

Answer: (B)

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Q19.

Solution

Concept: Zollinger-Ellison Syndrome (ZES) is a clinical syndrome caused by a neuroendocrine tumor that secretes massive quantities of a hormone that drives hyperchlorhydria.

Solution:

Let's trace the endocrine feedback loop shown in the diagram:

(a) The patient presents with classic signs of ZES: thickened gastric folds (due to trophic effects), atypical ulcers in distal duodenal regions, and steatorrhea (caused by excess gastric acid inactivating pancreatic enzymes).

(b) This syndrome is caused by a **gastrinoma**, a neuroendocrine tumor usually located in the pancreas or duodenum.

(c) The tumor secretes excessive amounts of **gastrin (Hormone Y)**, which binds to CCK2 receptors on gastric parietal cells, driving uninhibited, massive hydrochloric acid production.

Final Answer: Gastrinoma secreting gastrin

Answer: (B)

Go Back to Question 19

Q20.

Solution

Concept: Medullary Thyroid Carcinoma (MTC) is a neuroendocrine tumor originating from the calcitonin-secreting parafollicular C-cells of the thyroid gland.

Solution:

Let's link the diagnostic histopathology with the corresponding genetic alterations:

(a) The presence of polygonal cells within an amyloid stroma (derived from altered calcitonin prohormone deposits) that shows apple-green birefringence under polarized light, combined with calcitonin positivity, is pathognomonic for Medullary Thyroid Carcinoma.

(b) MTC is strongly associated with activating **RET proto-oncogene point mutations**.

(c) These mutations occur germline in familial syndromes (MEN 2A and 2B) or somatically in approximately 50% of sporadic MTC cases. (Note: *BRAF* mutations and *RET/PTC* translocations are instead characteristic of papillary thyroid carcinoma).

Final Answer: RET proto-oncogene point mutations

Answer: (A)

Go Back to Question 20

Q21.

Solution

Concept: Myasthenia Gravis is a classic autoantibody-mediated autoimmune disease that shares a deep immunopathologic link with thymic abnormalities, such as thymic hyperplasia or thymomas.

Solution:

Let's trace the immunological link between the thymus and the neuromuscular junction:

(a) The patient presents with symptoms of Myasthenia Gravis (fluctuating muscle weakness, ptosis, diplopia) alongside an anterior mediastinal mass confirmed as a thymoma.

(b) The normal thymus coordinates central tolerance by training developing T-cells to recognize self-antigens. Neoplastic thymic epithelial cells inside a thymoma fail to express these self-antigens properly, causing a **defective thymic central tolerance training**.

(c) This selection failure permits autoreactive T-helper cells to escape into the periphery. These cells then stimulate B-lymphocytes to synthesize **autoantibodies directed against postsynaptic acetylcholine receptors (AChR)** at the neuromuscular junction, blocking neuromuscular transmission.

Final Answer: Defective thymic central tolerance training leading to the generation of autoantibodies against postsynaptic acetylcholine receptors (AChR)

Answer: (B)

Go Back to Question 21

Q22.

Solution

Concept: Seminoma is the most common type of testicular germ cell tumor, presenting typically as a painless, uniform mass in young adult males.

Solution:

Let's evaluate the clinical, serological, and histological markers:

(a) Serology shows a normal alpha-fetoprotein (AFP) level, which is a key diagnostic point because **pure seminomas never produce AFP**. They can, however, produce modest amounts of hCG if syncytiotrophoblastic giant cells are present within the tumor.

(b) Grossly, the tumor is classic for a seminoma: homogeneous, lobulated, and notably lacking the extensive hemorrhage or necrosis typical of embryonal carcinomas or choriocarcinomas.

(c) Microscopic analysis reveals the classic architectural pattern: large, uniform cells with clear, glycogen-rich cytoplasm and distinct cell borders, organized into nests separated by delicate fibrous septae that are heavily infiltrated by T-lymphocytes.

Final Answer: Seminoma

Answer: (C)

Go Back to Question 22

Q23.

Solution

Concept: Creutzfeldt-Jakob Disease (CJD) is a rapidly progressive, fatal neurodegenerative condition classified as a transmissible spongiform encephalopathy.

Solution:

Let's analyze the molecular transformation driving this pathology:

(a) The combination of rapid cognitive decline, memory loss, and ataxia over a short six-month window, paired with a brain biopsy showing vacuolation of the gray matter without inflammation, is pathognomonic for CJD.

(b) The core pathogenesis relies on a **conformational change of a normal cellular prion protein (PrP^C) from an α-helical structure into an infectious, protease-resistant β-sheet rich isoform (PrP^{Sc})**.

(c) Once formed, the abnormal PrP^{Sc} protein acts as a template, forcing neighboring normal PrP^C proteins to misfold into the toxic β-sheet shape. These collect into aggregates that damage neurons, producing the classic spongiform vacuolation.

Final Answer: Conformational conversion of the normal cellular prion protein (PrP^C), which is predominantly α-helical, into the pathogenic infectious isoform (PrP^{Sc}), characterized by a β-pleated sheet-rich structure.

Answer: (A)

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Q24.

Solution

Concept: Neuroblastoma is a common extracranial solid tumor of infancy derived from neural crest cells in the sympathetic chain or adrenal medulla. It is characterized by specific small, round, blue cell architectures.

Solution:

Let's analyze the structural design shown in the diagram:

(a) The infant displays classic clinical features of neuroblastoma, including an abdominal mass, catecholamine overproduction (elevated urinary VMA and HVA), and opsoclonus-myoclonus paraneoplastic syndrome.

(b) The histopathology diagram illustrates tumor cells organized in a concentric ring around a central core filled with pink, fibrillary extensions.

(c) This specific arrangement is a **Homer Wright pseudorosette**, which contains a central core of fibrillary neuropil rather than a true vascular or empty lumen. Flexner-Wintersteiner rosettes, by contrast, contain a true lumen and are typical of retinoblastomas.

Final Answer: Homer Wright pseudorosettes containing a central core of fibrillary neuropil

Answer: (B)

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Q25.

Solution

Concept: The *BRCA1* and *BRCA2* genes encode essential tumor suppressor proteins that coordinate the repair of severe chromosomal damage to maintain genomic stability.

Solution:

Let's isolate the specific DNA repair pathway dependent on BRCA1 function:

(a) High-grade serous ovarian carcinomas in patients with *BRCA1* mutations result from an inability to repair double-strand DNA breaks cleanly.

(b) The BRCA1 protein plays a critical role in **Homologous recombination DNA repair (HRR)**, an error-free pathway that uses an undamaged sister chromatid template to repair double-strand breaks.

(c) When *BRCA1* is mutated, cells are forced to rely on error-prone pathways like non-homologous end joining (NHEJ). This leads to a rapid accumulation of chromosomal abnormalities and accelerates malignant transformation.

Final Answer: Homologous recombination DNA repair (HRR)

Answer: (C)

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Answer Key

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