



General Instructions

- (i) This question paper consists of **150 questions**. All questions are **compulsory**.
- (ii) Total duration of exam is **2 hours 30 minutes** (150 minutes).
- (iii) Total marks is **600**.
- (iv) Each correct response carries **4 marks**, while **1 mark** is deducted for every incorrect answer.

1. A patient with renal cell carcinoma on Sunitinib therapy for the past 2 years develops hand-foot syndrome, fatigue, and mild hypertension. What is the appropriate management in this case?

- (A) Reduce Sunitinib dose and add anti-hypertensive
- (B) As symptoms are mild, and will subside by themselves, observe
- (C) Steroids to be given for Hand foot syndrome and fatigue
- (D) Change to another TKI

Correct Answer: (B) As symptoms are mild, and will subside by themselves, observe

Solution:

Concept:

Sunitinib is an oral, multi-targeted tyrosine kinase inhibitor (TKI) targeting VEGFR, PDGFR, and KIT, widely utilized as a standard targeted therapy in advanced renal cell carcinoma (RCC).

Adverse effects such as hand-foot skin reaction (palmar-plantar erythrodysesthesia), fatigue, and hypertension are common on-target and off-target class effects of VEGFR inhibitors.

Management of TKI-induced toxicities follows standard grading algorithms to balance oncologic disease control with patient quality of life.

Explanation:

- Common side effects associated with vascular endothelial growth factor receptor (VEGFR) pathway inhibition include hand-foot skin reaction (HFSR), systemic hypertension, diarrhea, and fatigue.
- Mild toxicities (Grade 1 adverse events according to CTCAE criteria) do not interfere significantly with daily activities and do not pose an immediate organ-threatening risk.
- For Grade 1 symptoms such as mild fatigue, mild asymptomatic hypertension, and localized mild HFSR, treatment interruption or dose reductions are not indicated.
- Supportive measures such as topical emollients, lifestyle modifications, and close clinical observation are generally recommended while maintaining the therapeutic dose of sunitinib.
- Dose modifications or interruptions are strictly reserved for moderate-to-severe (Grade 2 or higher) toxicities that are persistent or refractory to conservative management.
- Routine administration of systemic corticosteroids is contraindicated as it lacks proven efficacy for chronic TKI-related fatigue and carries substantial long-term toxicities.

Final Answer:

Since the toxicities are mild and tolerable, the most appropriate management is clinical observation and continuation of standard therapy without dose modification.

Quick Tip: For VEGFR-TKI toxicities: Grade 1 toxicities require symptomatic care and close observation without dose interruption.

Dose reduction or temporary drug holds are indicated primarily for Grade ≥ 2 refractory or Grade 3–4 adverse events.

2. In a patient with chronic Superior Vena Cava Obstruction (SVCO), which of the following is the most characteristic chronic change observed?

- (A) Azygos dilatation
- (B) Portosystemic shunt
- (C) Subclavian pulmonary shunt
- (D) Left gastric varices

Correct Answer: (A) Azygos dilatation

Solution:

Concept:

Superior Vena Cava Obstruction (SVCO) results from the extrinsic compression, intrinsic invasion, or thrombosis of the superior vena cava.

In chronic obstruction, venous blood develops alternative collateral pathways to return deoxygenated blood to the right atrium, among which the azygos venous system serves as the primary hemodynamic pathway.

Explanation:

- The venous drainage of the head, neck, and upper extremities relies entirely on the SVC to enter the right atrium.
- When SVC obstruction develops gradually over a prolonged period, extensive venous collateral networks open up to bypass the obstructed segment.

- The principal collateral pathways in SVCO include the azygos-hemiazygos venous system, internal mammary venous system, lateral thoracic veins, and vertebral venous plexus.
- The azygos system undergoes severe compensatory engorgement and marked dilatation, acting as the main conduit redirecting blood flow toward the inferior vena cava (IVC) or around the obstruction directly into the right atrium.
- Portosystemic shunts, subclavian-pulmonary shunts, and left gastric varices are characteristic features of portal hypertension or congenital surgical anastomoses, rather than SVCO.

Final Answer:

The most prominent and characteristic chronic radiological and anatomical change seen in chronic superior vena cava obstruction is dilatation of the azygos venous system.

Quick Tip: Remember the four primary collateral pathways in SVCO:

1. Azygos-hemiazygos venous system (most important, shows marked dilatation).
2. Internal mammary (internal thoracic) pathway.
3. Lateral thoracic pathway.
4. Vertebral venous plexus.

3. In the management of Tumour Lysis Syndrome, which of the following is not useful?

- (A) Allopurinol
- (B) Rasburicase
- (C) Febuxostat
- (D) Steroids

Correct Answer: (D) Steroids

Solution:

Concept:

Tumor Lysis Syndrome (TLS) is a life-threatening oncologic emergency characterized by massive release of intracellular contents (potassium, phosphate, and nucleic acids) into the systemic circulation following rapid lysis of malignant cells.

Management focuses on aggressive intravenous hydration, control of hyperuricemia, and correction of electrolyte abnormalities.

Explanation:

- The degradation of cellular nucleic acids produces purines, which are metabolized into hypoxanthine, xanthine, and subsequently uric acid by the enzyme xanthine oxidase.
- Allopurinol and Febuxostat are potent xanthine oxidase inhibitors that block the formation of new uric acid, making them standard prophylaxis in moderate-risk TLS.
- Rasburicase is a recombinant urate oxidase enzyme that converts insoluble uric acid into soluble allantoin, providing rapid clearance of pre-existing hyperuricemia in high-risk or established TLS.
- Systemic corticosteroids are antineoplastic agents for hematologic malignancies (such as ALL and lymphomas) and can actively trigger or exacerbate TLS due to rapid tumor breakdown.
- Corticosteroids possess no therapeutic role in clearing metabolic waste products or reducing uric acid levels in the setting of acute tumor lysis syndrome.

Final Answer:

Steroids are antineoplastic agents capable of precipitating tumor lysis and are not a treatment modality for managing the metabolic complications of Tumor Lysis Syndrome.

Quick Tip: Key agents for hyperuricemia management in TLS:

- Rasburicase: Clears existing uric acid (converts uric acid to allantoin).
- Allopurinol / Febuxostat: Prevents new uric acid formation (xanthine oxidase inhibitors).
- Steroids do NOT manage TLS; they can precipitate it in steroid-sensitive malignancies.

4. A patient receiving chemotherapy is premedicated with a 5-HT₃ receptor antagonist and steroids, but continues to experience vomiting after treatment. What additional agent should be given?

- (A) Further D2 blockade with drugs like Haloperidol
- (B) Increasing dose of 5HT3 antagonist
- (C) Benzodiazepine
- (D) Add Aprepitant from the next cycle

Correct Answer: (D) Add Aprepitant from the next cycle

Solution:

Concept:

Chemotherapy-induced nausea and vomiting (CINV) is mediated through central and peripheral pathways involving serotonin (5-HT₃), neurokinin-1 (NK₁), and dopamine (D₂) receptors.

When dual therapy fails to prevent emesis during emetogenic chemotherapy, international guidelines (ASCO, ESMO, NCCN) recommend escalation of antiemetic prophylaxis for subsequent cycles.

Explanation:

- Chemotherapy regimens with moderate-to-high emetogenic potential trigger both acute (0–24 hours) and delayed (24–120 hours) phases of emesis.
- 5-HT₃ receptor antagonists (e.g., Ondansetron, Granisetron) primarily control acute

phase emesis, while Substance P binding to NK₁ receptors is the primary driver of delayed emesis.

- If a patient experiences breakthrough emesis despite receiving a standard two-drug regimen (5-HT₃ antagonist plus Dexamethasone), adding an NK₁ receptor antagonist (such as Aprepitant or Fosaprepitant) is the gold standard for subsequent cycles.
- Escalating the dose of 5-HT₃ receptor antagonists beyond standard ceiling doses does not improve antiemetic efficacy and increases the risk of cardiac QT prolongation.
- While rescue antiemetics (e.g., Olanzapine or dopamine antagonists) may be given acutely, incorporating Aprepitant into the pre-chemotherapy antiemetic bundle provides proven superior protection in future cycles.

Final Answer:

For patients experiencing breakthrough vomiting despite 5-HT₃ antagonist and corticosteroid prophylaxis, an NK₁ receptor antagonist such as Aprepitant should be added from the next cycle.

Quick Tip: Antiemetic Triple/Quadruple Regimen for Highly Emetogenic Chemotherapy (HEC):

- NK₁ Receptor Antagonist (Aprepitant / Fosaprepitant / Netupitant)
- 5-HT₃ Receptor Antagonist (Palonosetron / Ondansetron)
- Corticosteroid (Dexamethasone)
- ± Olanzapine (Atypical antipsychotic blocking multiple receptors).

5. Which of the following anti-HER2 targeted therapies is least likely to be used as a single-agent (monotherapy) treatment in the standard clinical practice for HER2-positive breast cancer?

(A) Trastuzumab

- (B) Ado Trastuzumab Emtansine
- (C) Trastuzumab Deruxtecan
- (D) Pertuzumab

Correct Answer: (D) Pertuzumab

Solution:

Concept:

Human epidermal growth factor receptor 2 (HER2)-positive breast cancer relies on HER2 dimerization for downstream oncogenic signaling.

Targeted monoclonal antibodies and antibody-drug conjugates (ADCs) have distinct mechanisms and clinical trial indications as monotherapies versus combination regimens.

Explanation:

- Trastuzumab binds to subdomain IV of the extracellular domain of HER2 and has demonstrated clinical activity as a single agent in metastatic HER2-positive breast cancer.
- Ado-Trastuzumab Emtansine (T-DM1) is an antibody-drug conjugate approved and utilized as monotherapy for residual disease post-neoadjuvant therapy and second-line metastatic disease (EMILIA trial).
- Trastuzumab Deruxtecan (T-DXd) is an anti-HER2 ADC approved and administered as monotherapy in unresectable or metastatic HER2-positive and HER2-low breast cancer (DESTINY-Breast trials).
- Pertuzumab binds to subdomain II of the HER2 extracellular domain, inhibiting HER2-HER3 heterodimerization.
- In early phase II trials, Pertuzumab demonstrated minimal single-agent antitumor activity; its standard clinical efficacy requires mandatory synergy in combination with

Trastuzumab and a taxane (CLEOPATRA regimen).

- Therefore, Pertuzumab is never prescribed as monotherapy in standard breast oncology practice.

Final Answer:

Pertuzumab is least likely to be used as monotherapy because its clinical utility depends on dual HER2 blockade in combination with Trastuzumab.

Quick Tip: - Pertuzumab: Domain II binder → blocks heterodimerization → NEVER given alone.

- Trastuzumab: Domain IV binder → blocks homodimerization → active alone or combined.

- T-DM1 and T-DXd: Antibody-Drug Conjugates (ADCs) → standard monotherapy agents.

6. A 65-year-old man with recently diagnosed small cell lung cancer (SCLC) presents with confusion and lethargy. Laboratory evaluation shows serum sodium 114 mEq/L, low BUN and creatinine, plasma osmolality 240 mOsm/kg, and urine osmolality 450 mOsm/kg. Which paraneoplastic syndrome most likely explains these findings?

- (A) SIADH (Syndrome of Inappropriate Antidiuretic Hormone)
- (B) Cerebral salt wasting
- (C) Hypercalcemia of Malignancy (HCM)
- (D) Ectopic ACTH Syndrome

Correct Answer: (A) SIADH (Syndrome of Inappropriate Antidiuretic Hormone)

Solution:

Concept:

Small cell lung cancer (SCLC) is a neuroendocrine tumor frequently associated with paraneoplastic endocrine syndromes due to ectopic hormone secretion.

The Syndrome of Inappropriate Antidiuretic Hormone (SIADH) secretion is the classic paraneoplastic cause of euvolemic, hypotonic hyponatremia in lung cancer patients.

Explanation:

- Ectopic secretion of arginine vasopressin (ADH) by SCLC tumor cells leads to increased water reabsorption in the renal collecting ducts.
- Key diagnostic features of SIADH include:
 1. Hypotonic hyponatremia (serum Na^+ < 135 mEq/L, plasma osmolality < 275 mOsm/kg).
 2. Inappropriately concentrated urine (urine osmolality > 100 mOsm/kg, here 450 mOsm/kg).
 3. Elevated urinary sodium excretion (urinary Na^+ > 30–40 mEq/L).
 4. Clinical euvolemia with low blood urea nitrogen (BUN) and low serum uric acid due to hypervolemic dilution and increased fractional excretion.
- Cerebral salt wasting presents with hypovolemia and elevated BUN/creatinine ratio due to dehydration, which contrasts with the low BUN seen in this patient.
- Hypercalcemia of malignancy typically causes polyuria and hyperosmolar states, whereas ectopic ACTH presents with hypokalemic metabolic alkalosis and hyperglycemia.

Final Answer:

The clinical and laboratory profile of profound hypotonic hyponatremia with high urine osmolality and low BUN in SCLC is diagnostic of SIADH.

Quick Tip: Diagnostic hallmarks of SIADH:

- Serum Osmolality < 275 mOsm/kg (hypotonic).
- Urine Osmolality > 100 mOsm/kg (inappropriately concentrated).
- Urine Na^+ > 40 mEq/L + Normal renal/adrenal/thyroid function + Low BUN/Uric acid.

7. Which of the following is not a treatment for metastatic pancreatic cancer?

- (A) FOLFIRINOX
- (B) Gemcitabine Nabpaclitaxel
- (C) Gemcitabine-Erlotinib
- (D) Capecitabine-Erlotinib

Correct Answer: (D) Capecitabine-Erlotinib

Solution:

Concept:

Metastatic pancreatic ductal adenocarcinoma (PDAC) is an aggressive malignancy requiring multi-agent cytotoxic chemotherapy regimens to improve overall survival in patients with preserved performance status.

Targeted therapies combined with specific antimetabolites have been evaluated in randomized phase III clinical trials.

Explanation:

- Modified FOLFIRINOX (5-Fluorouracil, Leucovorin, Irinotecan, Oxaliplatin) is a category 1 preferred first-line systemic regimen for metastatic pancreatic cancer (PRODIGE 4/ACCORD 11 trial).
- Gemcitabine plus nab-Paclitaxel (albumin-bound paclitaxel) is an established first-line category 1 regimen demonstrating superior overall survival over single-agent gemcitabine (MPACT trial).

- Gemcitabine combined with Erlotinib (an EGFR tyrosine kinase inhibitor) was approved following the pivotal NCIC CTG PA.3 trial, which demonstrated a statistically significant survival benefit in advanced PDAC.
- Capecitabine plus Erlotinib is not an established, guideline-recommended, or approved regimen for metastatic pancreatic cancer.

Final Answer:

Capecitabine-Erlotinib is not a recognized or standard treatment regimen for metastatic pancreatic cancer.

Quick Tip: Standard first-line regimens in Metastatic Pancreatic Cancer (ECOG PS 0–1):

1. mFOLFIRINOX
2. Gemcitabine + nab-Paclitaxel
3. Gemcitabine + Erlotinib (historically approved based on NCIC PA.3 trial).

8. What is the primary advantage of using a totally implanted central venous access device (Port-a-Cath) over repeated peripheral intravenous cannulations for a patient receiving long-term, non-emergent chemotherapy?

- (A) Prevent repeated pricking for venous access
- (B) It has zero risk of catheter-related bloodstream infection
- (C) It is essential for infusing all non-vesicant (non-blistering) chemotherapy agents.
- (D) It allows for immediate therapeutic effects of drugs delivered through it

Correct Answer: (A) Prevent repeated pricking for venous access

Solution:

Concept:

Totally implantable venous access ports (TIVAPs), commonly known as Port-a-Caths, are subcutaneous central venous access systems surgically placed into a central vein (e.g., internal jugular or subclavian vein).

They provide durable vascular access in oncology patients undergoing prolonged cycles of multi-agent chemotherapy, targeted infusions, and frequent blood sampling.

Explanation:

- Oncology patients frequently suffer from peripheral vein exhaustion, chemical phlebitis, sclerosis, and vessel fragility due to repeated cannulations and irritant drug exposures.
- The primary clinical advantage of a Port-a-Cath is providing reliable, long-term central venous access, thereby eliminating the pain and physical trauma of repeated peripheral venipunctures.
- Additionally, ports minimize the risk of extravasation injury when infusing potent vesicants (e.g., Anthracyclines, Vinca alkaloids).
- Port-a-Caths do not have zero risk of infection; although catheter-related bloodstream infection (CRBSI) rates are lower than external central lines, infectious complications can still occur.
- Non-vesicant agents do not strictly require central ports, and the pharmacokinetics/onset of drug action is determined by systemic distribution rather than central line delivery.

Final Answer:

The fundamental advantage of an implanted Port-a-Cath is avoiding repeated peripheral intravenous punctures and preserving peripheral venous integrity.

Quick Tip: Port-a-Cath advantages in oncology:

- Prevents peripheral vein thrombosis and damage.
- Eliminates repeated painful needle pricks.
- Provides safe central infusion of vesicant antineoplastics.
- Lower infection rate compared to non-tunneled CVCs and PICC lines.

9. Which Artificial Intelligence technology is primarily utilised for image analysis in fields like pathology (biopsy reporting) and radiology (imaging)?

- (A) Convolutional neural network (CNNs)
- (B) Recurrent Neural Network (RNN)
- (C) Reinforcement Learning
- (D) Generative Adversarial Network (GAN)

Correct Answer: (A) Convolutional neural network (CNNs)

Solution:

Concept:

Artificial Intelligence (AI) and deep learning algorithms have transformed computational pathology and medical imaging analysis in oncology.

Different deep learning architectures are specialized for distinct data structures such as grid-like image matrices, sequential text, or data generation.

Explanation:

- Convolutional Neural Networks (CNNs) are specialized deep neural networks designed to process grid-like spatial data by applying convolutional filters (kernels).
- CNNs automatically extract spatial hierarchies of features ranging from low-level edges and textures to high-level complex structures such as tumor margins, mitotic figures, and radiological nodules.

- In digital pathology, CNNs analyze whole-slide images (WSIs) for histopathological classification, tumor grading, and immunohistochemical scoring.
- In diagnostic radiology, CNNs are standardly applied for automated tumor detection, segmentation, and classification on CT, MRI, and PET scans.
- Recurrent Neural Networks (RNNs) are designed for sequential time-series data and natural language processing (NLP), while GANs are primarily used for synthetic data generation.

Final Answer:

Convolutional Neural Networks (CNNs) are the benchmark AI technology utilized for medical image processing in pathology and radiology.

Quick Tip: - CNN (Convolutional Neural Networks) → Image processing, radiology (CT/MRI), and digital pathology.

- RNN (Recurrent Neural Networks) → Sequential data, speech, and electronic health record text processing.

- GAN (Generative Adversarial Networks) → Image synthesis, data augmentation.

10. Respiratory depression caused by opioids is mediated through which receptor?

- (A) Mu
- (B) Kappa
- (C) Lambda
- (D) Delta

Correct Answer: (A) Mu

Solution:

Concept:

Opioid analgesics are the cornerstone of cancer pain management according to the WHO analgesic ladder.

Opioid receptors (μ , κ , δ) are G-protein-coupled receptors distributed throughout the central and peripheral nervous systems, with each receptor subtype mediating distinct therapeutic and adverse responses.

Explanation:

- The μ -opioid receptor (μ_1 and μ_2 subtypes, encoded by the *OPRM1* gene) is the primary target for clinically prescribed opioids such as morphine, fentanyl, and oxycodone.
- Activation of μ_2 receptors located on respiratory rhythm-generating neurons in the pre-Bötzinger complex and the pontomedullary respiratory center reduces their sensitivity to hypercapnia (arterial carbon dioxide tension, PaCO_2).
- This blunted ventilatory response results in reduced respiratory rate, decreased tidal volume, and respiratory depression, which represents the most fatal toxicity of opioid overdose.
- The κ -opioid receptors mediate spinal analgesia, dysphoria, and sedation, with minimal effect on respiratory depression.
- The δ -opioid receptors play a role in supraspinal and spinal analgesia and modulation of mood.
- Naloxone functions as a competitive antagonist predominantly at μ -receptors to reverse opioid-induced respiratory depression.

Final Answer:

Opioid-induced respiratory depression is primarily mediated by the activation of μ -opioid receptors in the brainstem respiratory center.

Quick Tip: Opioid Receptors and Actions:

- μ (Mu): Supraspinal analgesia, respiratory depression (μ_2), physical dependence, euphoria, constipation (μ_2).
- κ (Kappa): Spinal analgesia, dysphoria, miosis, sedation.
- δ (Delta): Spinal/supraspinal analgesia, modulation of hormone release.

11. Which among the following is the most common cardiac side effect of cisplatin?

- (A) Ischemic heart disease/MI
- (B) Systemic hypertension
- (C) Pericarditis
- (D) QT prolongation

Correct Answer: (D) QT prolongation

Solution:**Concept:**

Cisplatin is a platinum-based chemotherapeutic agent widely used in the treatment of solid tumors (e.g., testicular, ovarian, lung, and head and neck cancers).

In addition to nephrotoxicity and neurotoxicity, cisplatin exerts significant direct and indirect toxicities on the cardiovascular and cardiac conduction systems.

Explanation:

- Cisplatin causes cumulative renal tubular damage leading to renal magnesium and potassium wasting.

- Secondary electrolyte disturbances, particularly hypomagnesemia and hypokalemia, directly impair myocardial repolarization.
- Consequently, electrocardiographic changes—specifically QT interval prolongation and associated ventricular arrhythmias—are frequently observed in patients undergoing cisplatin chemotherapy.
- In addition, cisplatin-induced reactive oxygen species (ROS) disrupt cardiac membrane stability and prolong action potential duration.
- While vascular toxicities such as myocardial infarction, ischemic heart disease, and Raynaud phenomenon can occur as late vascular sequelae, QT prolongation is a widely recognized immediate electrophysiological manifestation requiring routine monitoring.

Final Answer:

Electrolyte wasting and direct myocardial membrane alteration by cisplatin lead commonly to QT interval prolongation.

Quick Tip: Cisplatin toxicities to remember:

- Ototoxicity and severe Nephrotoxicity (prevent with pre-hydration).
- Hypomagnesemia → secondary Hypokalemia and Hypocalcemia → QT prolongation.
- High emetogenic risk (requires 3- or 4-drug antiemetic regimen).

12. Which is the main area where Artificial Intelligence (AI) algorithms can provide significant assistance when analyzing data from a liquid biopsy (e.g., cell-free DNA)?

- (A) Remove the need for any subsequent tissue biopsy confirmation.
- (B) Help identify, classify, and track genetic mutations or resistance mechanisms
- (C) Can predict stage without conventional imaging

(D) Can eliminate the need of blood sampling

Correct Answer: (B) Help identify, classify, and track genetic mutations or resistance mechanisms

Solution:

Concept:

Liquid biopsy involves analyzing circulating tumor DNA (ctDNA), cell-free DNA (cfDNA), and circulating tumor cells (CTCs) isolated from peripheral blood.

Due to the low signal-to-noise ratio and high sequencing background noise in cfDNA analysis, machine learning and AI algorithms play an essential role in genomic data interpretation.

Explanation:

- Cell-free DNA comprises fragments released by both normal and apoptotic tumor cells, with mutant tumor alleles often present at variant allele frequencies (VAF) below 0.1%.
- AI-driven bioinformatics pipelines filter out sequencing artifacts and clonal hematopoiesis of indeterminate potential (CHIP) mutations from true somatic driver mutations.
- AI algorithms can classify complex multi-gene alteration profiles, accurately quantify minimal residual disease (MRD), and detect emerging subclonal resistance mechanisms (e.g., *EGFR* T790M, *ESR1* mutations) prior to radiographic progression.
- Liquid biopsy does not eliminate blood sampling (it relies directly on peripheral blood collection) nor does it completely replace diagnostic tissue biopsies or formal imaging staging.

Final Answer:

AI tools provide critical utility in liquid biopsy by identifying low-frequency tumor mutations, classifying genomic variants, and tracking longitudinal resistance mechanisms.

Quick Tip: Liquid Biopsy and AI:

- Detects low variant allele frequency (VAF) ctDNA fragments.
- Distinguishes somatic cancer mutations from CHIP (Clonal Hematopoiesis of Indeterminate Potential).
- Enables non-invasive longitudinal tracking of emergent resistance mutations.

13. In a patient receiving the second cycle of gemcitabine, what is the most common adverse effect that should be monitored?

- (A) Myelosuppression
- (B) Pneumonitis
- (C) Hepatitis
- (D) Neuropathy

Correct Answer: (A) Myelosuppression

Solution:

Concept:

Gemcitabine (2',2'-difluorodeoxycytidine) is a pyrimidine nucleoside antimetabolite that inhibits DNA synthesis by inactivating ribonucleotide reductase and incorporating into DNA chains.

The principal dose-limiting toxicity of gemcitabine monotherapy is bone marrow suppression.

Explanation:

- Gemcitabine is standardly administered on days 1, 8 (and sometimes 15) of a 21- or 28-day cycle across various indications, including pancreatic, lung, bladder, and ovarian cancers.
- Myelosuppression—presenting predominantly as neutropenia, thrombocytopenia, and anemia—is the most common dose-limiting adverse event.

- Thrombocytopenia and neutropenia typically reach their nadir between days 7 and 14 following drug administration, directly impacting cycle 2 delivery.
- Complete blood counts (CBC) must be monitored before every infusion to determine if dose delays or reductions are needed based on absolute neutrophil count (ANC) and platelet counts.
- Non-hematologic side effects such as interstitial pneumonitis, transaminitis, and hemolytic uremic syndrome (HUS) occur infrequently compared to hematologic toxicity.

Final Answer:

Myelosuppression is the most frequent and dose-limiting adverse effect of gemcitabine that requires routine laboratory monitoring.

Quick Tip: Gemcitabine Toxicity Profile:

- Primary / Dose-limiting: Myelosuppression (Neutropenia and Thrombocytopenia).
- Common non-hematologic: Flu-like syndrome, mild transaminitis, peripheral edema.
- Rare but severe: Interstitial pneumonitis, Thrombotic Microangiopathy (TMA/HUS).

14. A 70-year-old patient has an IgA kappa M-protein level of 3.5 g/dL and 40% clonal plasma cells on bone marrow biopsy, with no evidence of hypercalcemia, renal impairment, anaemia, or bone lesions (normal MRI). What is the most likely diagnosis?

- (A) MGUS
- (B) Smoldering Multiple Myeloma
- (C) Multiple Myeloma
- (D) Waldenström Macroglobulinemia

Correct Answer: (B) Smoldering Multiple Myeloma

Solution:

Concept:

Plasma cell dyscrasias are classified along a disease spectrum based on serum M-protein concentration, the percentage of clonal bone marrow plasma cells (BMPCs), and the presence or absence of end-organ damage defined by the CRAB criteria and myeloma-defining biomarkers.

Explanation:

- International Myeloma Working Group (IMWG) criteria define the clinical entities as follows:
 1. **Monoclonal Gammopathy of Undetermined Significance (MGUS):** Serum M-protein < 3.0 g/dL, BMPC $< 10\%$, and absence of CRAB features.
 2. **Smoldering Multiple Myeloma (SMM):** Serum M-protein ≥ 3.0 g/dL (or urinary monoclonal protein ≥ 500 mg/24h) and/or clonal BMPC 10% – 59% , with no end-organ damage (CRAB criteria) and no myeloma-defining events.
 3. **Active Multiple Myeloma (MM):** Clonal BMPC $\geq 10\%$ plus CRAB features (Hypercalcemia, Renal failure, Anemia, Bone lesions) or SLIM biomarkers (BMPC $\geq 60\%$, involved/uninvolved FLC ratio ≥ 100 , or > 1 focal lesion on MRI).
- In this case, the patient has an M-protein of 3.5 g/dL (≥ 3 g/dL) and 40% BMPCs (10% – 59%), but completely lacks CRAB manifestations and has a normal MRI.
- Waldenström macroglobulinemia is a lymphoplasmacytic lymphoma producing an IgM monoclonal gammopathy, not an IgA protein.

Final Answer:

The presence of M-protein ≥ 3.0 g/dL and 40% marrow plasma cells without CRAB features or myeloma-defining events confirms the diagnosis of Smoldering Multiple Myeloma.

Quick Tip: Diagnostic thresholds for Plasma Cell Disorders:

- MGUS: M-protein < 3 g/dL, BMPC < 10%, No CRAB.
- SMM: M-protein $\geq$ 3 g/dL and/or BMPC 10%–59%, No CRAB / No SLIM biomarkers.
- Active MM: BMPC $\geq$ 10% + CRAB or SLIM criteria ($\geq$ 60% BMPC, FLC ratio $\geq$ 100, > 1 MRI lesion).

15. What is the primary mechanism of anabolic steroids in cancer cachexia?

- (A) Decrease inflammatory environment
- (B) Induce an immediate sense of hunger, leading to increased total caloric intake.
- (C) Increase the synthesis and preservation of lean body mass (skeletal muscle).
- (D) Promote the efficient conversion of ingested nutrients into adipose tissue

Correct Answer: (C) Increase the synthesis and preservation of lean body mass (skeletal muscle).

Solution:

Concept:

Cancer cachexia is a multifactorial metabolic syndrome characterized by ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support.

Pharmacologic agents targeting cachexia aim to reverse systemic catabolism, improve muscle protein kinetics, and rebuild functional body mass.

Explanation:

- Anabolic androgenic steroids (such as Oxandrolone and Nandrolone) bind to intracellular androgen receptors present in skeletal muscle tissue.
- Receptor binding promotes myogenic differentiation, stimulates nuclear transcription of structural proteins, and increases intramuscular amino acid incorporation.
- This stimulation promotes fractional muscle protein synthesis and inhibits the ubiquitin-

proteasome proteolytic pathway, directly preserving and increasing lean body mass.

- Unlike megestrol acetate or corticosteroids, which primarily increase appetite and adipose (fat) deposition or fluid retention, anabolic steroids specifically enhance myofibrillar muscle protein synthesis.

Final Answer:

Anabolic steroids act primarily by stimulating muscle protein synthesis and preventing muscle degradation, thereby preserving lean skeletal muscle mass.

Quick Tip: Mechanisms of Cachexia Pharmacotherapies:

- Anabolic Steroids: Increase lean body mass / skeletal muscle synthesis.
- Megestrol Acetate / Progestins: Increase appetite and adipose tissue / fat mass.
- Corticosteroids: Short-term appetite stimulation and anti-inflammatory action (no gain in lean mass).

16. Which of the following systemic mediators, though involved in appetite and energy balance, is not primarily classified as a core pro-inflammatory cytokine driving the systemic catabolism and muscle wasting characteristic of the cancer cachexia syndrome?

- (A) Leptin
- (B) Tumor Necrosis Factor (TNF- α)
- (C) Interleukin-1 (IL-1)
- (D) Interleukin-6 (IL-6)

Correct Answer: (A) Leptin

Solution:

Concept:

Cancer cachexia is driven by complex neuroendocrine disturbances and sustained systemic

inflammation mediated by tumor- and host-derived pro-inflammatory cytokines. These pro-inflammatory signaling molecules activate proteolytic cascades and induce profound skeletal muscle and adipose wasting.

Explanation:

- The core triad of pro-inflammatory cytokines that directly orchestrate muscle proteolysis, lipolysis, and acute-phase protein synthesis includes:
 1. **TNF- α (Cachectin):** Stimulates the ubiquitin-proteasome pathway, activates NF- κ B, and suppresses lipoprotein lipase.
 2. **Interleukin-6 (IL-6):** Induces muscle wasting via the JAK/STAT signaling pathway and promotes hepatic production of C-reactive protein.
 3. **Interleukin-1 (IL-1):** Promotes central anorexia at the hypothalamus and synergizes with TNF- α to accelerate muscle proteolysis.
- **Leptin** is an adipokine synthesized primarily by white adipose tissue that regulates long-term energy balance by signaling satiety to the hypothalamus.
- Leptin is a metabolic hormone rather than a core pro-inflammatory cytokine driving systemic catabolism; in fact, circulating leptin levels typically decrease during progressive cachexia as adipose stores are depleted.

Final Answer:

Leptin is an adipose-derived metabolic hormone, not a primary pro-inflammatory cytokine causing systemic catabolism in cancer cachexia.

Quick Tip: Core Catabolic Cytokines in Cachexia:

- TNF- α (originally isolated as "Cachectin").
- IL-6 (key driver of sarcopenia and hepatic acute-phase response).
- IL-1 and IFN- γ .

Leptin and Ghrelin are neuroendocrine appetite-regulating hormones, not primary pro-inflammatory cytokines.

17. Which of the following findings in an asymptomatic patient with Chronic Lymphocytic Leukemia (CLL) is a recognized complication but does not warrant immediate initiation of systemic chemotherapy or targeted therapy?

- (A) Lymphocyte doubling time less than 3 months
- (B) Fatigue/weight loss
- (C) Night sweats
- (D) Hypogammaglobulinemia

Correct Answer: (D) Hypogammaglobulinemia

Solution:

Concept:

Chronic Lymphocytic Leukemia (CLL) is characterized by the progressive accumulation of functionally incompetent, mature monoclonal B cells.

According to international guidelines (iwCLL 2018), asymptomatic patients with early-stage disease are managed with a "watch and wait" strategy until specific criteria for active or progressive disease are met.

Explanation:

- Indications for initiating antineoplastic therapy in CLL per iwCLL guidelines include:
 1. Progressive marrow failure: Development or worsening of anemia (Hb < 10 g/dL) or thrombocytopenia (Platelets < 100×10^9 /L).
 2. Massive, progressive, or symptomatic splenomegaly or lymphadenopathy.

3. Rapid lymphocyte doubling time (LDT < 6 months or > 50% increase over 2 months in patients with baseline lymphocytes > $30 \times 10^9/L$).
4. Significant disease-related constitutional "B" symptoms (unintentional weight loss > 10% over 6 months, fevers > 38°C for > 2 weeks, drenching night sweats, or debilitating fatigue).

- Hypogammaglobulinemia is present in up to 85% of CLL patients as an immune dysfunction feature, but it is not an indication to start antineoplastic chemotherapy.
- When hypogammaglobulinemia is associated with recurrent, severe bacterial sinopulmonary infections, the standard management is replacement intravenous immunoglobulin (IVIG) prophylaxis.

Final Answer:

Hypogammaglobulinemia alone does not meet iwCLL criteria for starting systemic anti-leukemic therapy.

Quick Tip: iwCLL Indications for Treatment Initiation:

- Cytopenias (Hb < 10, Plt < $100 \times 10^9/L$).
- Massive/symptomatic lymphadenopathy or splenomegaly.
- Lymphocyte doubling time < 6 months.
- Severe constitutional symptoms (B-symptoms).
- Note: Pure hypogammaglobulinemia → Treat with IVIG if recurrent infections occur, NOT chemotherapy!

18. A 35-year-old woman, previously treated 8 years ago for Hodgkin Lymphoma (HL) with combination chemotherapy and mediastinal radiation, is now planning her first pregnancy. Which of the following represents the most significant long-term implication of her prior treatment?

- (A) Decreased fertility
- (B) Birth canal defects
- (C) Increased risk of preterm delivery due to pelvic radiation
- (D) Increased chances of abortion/miscarriage due to chemotherapy

Correct Answer: (A) Decreased fertility

Solution:

Concept:

Long-term survivorship in Hodgkin Lymphoma (HL) is associated with late treatment-related toxicities resulting from alkylating chemotherapy, anthracyclines, and mantle or mediastinal radiotherapy.

Gonadotoxicity leading to premature ovarian insufficiency and reduced reproductive potential represents a major survivorship issue in young female cancer survivors.

Explanation:

- Standard multi-agent chemotherapy regimens historically used in HL (e.g., ABVD, escalated BEACOPP, or MOPP) contain cytotoxic agents that induce dose-dependent depletion of the primordial ovarian follicle pool.
- Alkylating agents (e.g., cyclophosphamide, procarbazine) cause direct DNA crosslinking and apoptotic death of oocytes, accelerating ovarian senescence and causing decreased fertility or premature ovarian insufficiency (POI).
- The patient received mediastinal (supradiaphragmatic) radiation rather than pelvic radiation; therefore, direct uterine radiation injury or pelvic birth canal fibrosis is absent.
- Chemotherapy completed 8 years prior does not directly increase the baseline rates of spontaneous abortion, miscarriage, or congenital fetal malformations in subsequent conceptions compared to the general population.

Final Answer:

The most clinically significant long-term reproductive complication following prior combination chemotherapy for Hodgkin Lymphoma is decreased fertility.

Quick Tip: Gonadotoxicity in Cancer Survivors:

- Alkylating agents (Cyclophosphamide, Procarbazine, Busulfan) have the highest gonadotoxicity.
- ABVD has relatively lower gonadotoxicity than BEACOPP/MOPP.
- Previous cytotoxic exposure years earlier does NOT increase the baseline risk of fetal congenital anomalies or miscarriages.

19. A patient with T-cell Acute Lymphoblastic Leukemia (T-ALL) presents with fever, cytopenias, and hepatosplenomegaly, raising suspicion for cytokine-mediated Hemophagocytic Lymphohistiocytosis (HLH). Which of the following laboratory findings is NOT typically seen in active, untreated HLH?

- (A) Hypertriglyceridemia
- (B) Elevated soluble IL-2
- (C) Hyperfibrinogenemia
- (D) Raised ferritin $> 500 \mu\text{g/L}$

Correct Answer: (C) Hyperfibrinogenemia

Solution:**Concept:**

Hemophagocytic Lymphohistiocytosis (HLH) is a severe, life-threatening hyperinflammatory syndrome triggered by uncontrolled proliferation of activated T-lymphocytes and histiocytes, leading to massive hypercytokinemia.

Diagnosis is guided by the established HLH-2004 diagnostic criteria.

Explanation:

- The diagnostic criteria for HLH (meeting ≥ 5 of 8 parameters) include:
 1. Fever ($\geq 38.5^\circ\text{C}$).
 2. Splenomegaly.
 3. Cytopenias affecting ≥ 2 lineages ($\text{Hb} < 9 \text{ g/dL}$, $\text{Plt} < 100 \times 10^9/\text{L}$, Neutrophils $< 1.0 \times 10^9/\text{L}$).
 4. **Hypertriglyceridemia** (fasting triglycerides $\geq 265 \text{ mg/dL}$) and/or **Hypofibrinogenemia** (fibrinogen $\leq 1.5 \text{ g/L}$).
 5. Hemophagocytosis in bone marrow, spleen, or lymph nodes.
 6. Low or absent Natural Killer (NK) cell cytotoxicity.
 7. Marked hyperferritinemia (Ferritin $\geq 500 \mu\text{g/L}$, often $> 10,000 \mu\text{g/L}$).
 8. Elevated soluble CD25 (soluble IL-2 receptor $\alpha \geq 2400 \text{ U/mL}$).
- In active HLH, excessive macrophage activation leads to high plasminogen activator levels, resulting in plasmin generation, consumption of clotting factors, and prominent **hypofibrinogenemia**, not hyperfibrinogenemia.

Final Answer:

Hyperfibrinogenemia is not characteristic of active HLH; rather, hypofibrinogenemia ($\leq 1.5 \text{ g/L}$) is a cardinal diagnostic feature.

Quick Tip: Key Laboratory Findings in HLH:

- High Ferritin ($> 500 \mu\text{g/L}$, highly specific if $> 10,000$).
- High Triglycerides ($\geq 265 \text{ mg/dL}$).
- High Soluble IL-2 receptor (sCD25).
- LOW Fibrinogen ($\leq 1.5 \text{ g/L}$ / Hypofibrinogenemia).

20. In a patient with acute hyperuricemic nephropathy, what is the expected urinary uric acid to urinary creatinine ratio?

(A) =1

- (B) <1
- (C) >1
- (D) >2

Correct Answer: (C) >1

Solution:

Concept:

Acute uric acid nephropathy (AUAN) occurs in the setting of rapid cell turnover and tumor lysis, causing massive overproduction of uric acid.

Intratubular precipitation of insoluble uric acid crystals in the distal tubules and collecting ducts causes acute oliguric or anuric renal failure.

Explanation:

- Differentiating acute uric acid nephropathy from other etiologies of acute kidney injury (such as acute tubular necrosis, where serum uric acid is elevated purely due to reduced glomerular clearance) is clinically essential.
- In acute uric acid nephropathy, massive overproduction and excessive renal excretion of urate result in a urinary uric acid to urinary creatinine ratio:

$$\frac{\text{Urinary Uric Acid (mg/dL)}}{\text{Urinary Creatinine (mg/dL)}} > 1.0$$

- Conversely, in non-hyperuricemic causes of acute renal failure or acute tubular necrosis (ATN), impaired glomerular filtration reduces urate excretion, producing a urinary uric acid to creatinine ratio < 1.0 (typically 0.5–0.7).
- A spot urinary uric acid to urinary creatinine ratio > 1.0 is therefore a key diagnostic criterion confirming acute hyperuricemic precipitation nephropathy.

Final Answer:

In acute hyperuricemic nephropathy, the urinary uric acid to urinary creatinine ratio is

characteristically greater than 1 (> 1.0).

Quick Tip: Urinary Uric Acid / Creatinine Ratio:

- Ratio $> 1.0 \rightarrow$ Acute Uric Acid Nephropathy (tumor lysis / massive urate overproduction).
- Ratio $< 1.0 \rightarrow$ Acute Tubular Necrosis (ATN) or other etiologies of acute renal failure.

21. Among the following anthracycline chemotherapeutic agents, all of which carry a risk of dose-dependent, irreversible cardiotoxicity (dilated cardiomyopathy), which one is widely recognized in clinical practice to have the lowest overall potential for cardiotoxicity at equipotent therapeutic doses?

- (A) Epirubicin
- (B) Idarubicin
- (C) Doxorubicin
- (D) Daunorubicin

Correct Answer: (A) Epirubicin

Solution:

Concept:

Anthracyclines are potent antitumor antibiotics that inhibit topoisomerase II and generate reactive oxygen species (ROS).

Their use is limited by cumulative, dose-dependent, irreversible myocardial injury (Type I cardiotoxicity) culminating in congestive heart failure.

Explanation:

- Epirubicin is a semisynthetic stereoisomer (4'-epimer) of doxorubicin, modified by inverting the hydroxyl group at the C-4' position of the daunosamine sugar moiety.

- This specific structural epimerization leads to different metabolic clearance pathways, predominantly glucuronidation in the liver, leading to faster total body clearance.
- Consequently, epirubicin generates significantly fewer toxic secondary alcohol metabolites and less myocardial oxidative stress at equivalent therapeutic doses.
- The maximum recommended cumulative lifetime threshold dose for Epirubicin is 900 mg/m^2 , compared to $450\text{--}550 \text{ mg/m}^2$ for Doxorubicin and Daunorubicin.
- Thus, Epirubicin exhibits the lowest overall potential for cardiotoxicity among the traditional anthracyclines at equipotent therapeutic doses.

Final Answer:

Epirubicin possesses the lowest cardiotoxic potential among standard anthracyclines due to its 4'-epimerized structure and glucuronidation clearance pathway.

Quick Tip: Lifetime Cumulative Dose Limits for Anthracyclines:

- Doxorubicin: $450\text{--}550 \text{ mg/m}^2$
- Daunorubicin: $500\text{--}600 \text{ mg/m}^2$
- Epirubicin: 900 mg/m^2 (Lowest cardiotoxicity per milligram)
- Idarubicin: 150 mg/m^2

22. Which organism is most commonly implicated in febrile neutropenia?

- (A) *Streptococcus pneumoniae*
- (B) *Pseudomonas*
- (C) *Escherichia coli*
- (D) Enterococci

Correct Answer: (B) *Pseudomonas*

Solution:

Concept:

Febrile neutropenia (defined as single oral temperature $\geq 38.3^{\circ}\text{C}$ or $\geq 38.0^{\circ}\text{C}$ sustained over 1 hour with an absolute neutrophil count $< 500/\mu\text{L}$) is a medical emergency.

Prompt empirical broad-spectrum antibiotic therapy is mandated to cover the most virulent pathogens associated with rapid clinical deterioration and mortality.

Explanation:

- Chemotherapy-induced mucosal barrier injury facilitates the translocation of endogenous gastrointestinal and cutaneous microflora into the bloodstream.
- While Gram-positive bacteria are frequently isolated in catheter-related bloodstream infections, Gram-negative bacilli are associated with severe sepsis and rapid hemodynamic collapse in neutropenic hosts.
- *Pseudomonas aeruginosa* is the most dreaded and classically targeted opportunistic Gram-negative pathogen in febrile neutropenia due to its high mortality rate within hours of onset.
- For this reason, all international guidelines (IDSA, ESMO, ASCO) mandate that empirical initial antibiotic coverage must possess reliable, high-potency anti-pseudomonal activity (e.g., Piperacillin-tazobactam, Cefepime, or Meropenem).

Final Answer:

Pseudomonas aeruginosa is the classic Gram-negative pathogen of primary concern and clinical significance in febrile neutropenia.

Quick Tip: Empirical coverage in Febrile Neutropenia MUST cover *Pseudomonas aeruginosa*:

- Monotherapy: Cefepime, Piperacillin-Tazobactam, or Meropenem.
- Vancomycin is added ONLY if specific indications exist (hemodynamic instability, pneumonia, catheter site infection, MRSA colonization).

23. Which of the following is NOT associated with Paclitaxel-induced cardiotoxicity?

- (A) Asymptomatic bradycardia
- (B) Non-ischemic cardiomyopathy
- (C) Ventricular fibrillation
- (D) Hypertension

Correct Answer: (D) Hypertension

Solution:

Concept:

Paclitaxel is a microtubule-stabilizing taxane widely used across solid tumors (ovarian, breast, and lung cancers).

Taxanes possess specific cardiac electrophysiological toxicities that are predominantly characterized by rhythm disturbances, conduction abnormalities, and hypotension.

Explanation:

- The most frequent cardiac manifestation of paclitaxel is **asymptomatic sinus bradycardia**, occurring in up to 30% of treated patients.
- Paclitaxel can also induce advanced atrioventricular (AV) conduction blocks, supraventricular arrhythmias, and malignant ventricular arrhythmias including ventricular tachycardia and ventricular fibrillation.
- Non-ischemic cardiomyopathy and left ventricular systolic dysfunction can occur,

particularly when paclitaxel is administered concurrently with anthracyclines (due to reduced doxorubicin elimination).

- Paclitaxel is frequently formulated in Cremophor EL (polyoxyethylated castor oil), which promotes massive histamine release, leading to acute hypersensitivity reactions accompanied by **hypotension**, rather than hypertension.
- Systemic hypertension is a characteristic toxicity of VEGF/VEGFR inhibitors (e.g., Bevacizumab, Sunitinib), not taxanes.

Final Answer:

Hypertension is not an associated cardiac adverse effect of paclitaxel infusion; paclitaxel causes bradycardia, conduction blocks, arrhythmias, and hypotension.

Quick Tip: Cardiac side effects of Taxanes (Paclitaxel):

- Sinus bradycardia (most common, up to 30%, usually transient/asymptomatic).
- Heart blocks and Ventricular arrhythmias.
- Hypotension (linked to Cremophor EL solvent hypersensitivity).
- Hypertension is typical of VEGF inhibitors, NOT taxanes!

24. Endomyocardial biopsy from a patient with cardiotoxicity shows diffuse vacuolar degeneration of myocytes and extensive myofibrillar loss. Which cytotoxic drug most commonly causes this pattern?

- (A) Doxorubicin
- (B) Alcohol
- (C) Trastuzumab
- (D) Cyclophosphamide

Correct Answer: (A) Doxorubicin

Solution:

Concept:

Chemotherapy-induced cardiotoxicity is histopathologically divided into Type I (dose-dependent, irreversible ultrastructural myocardial damage) and Type II (dose-independent, reversible cellular dysfunction without structural loss).

Explanation:

- Anthracyclines like Doxorubicin produce Type I cardiotoxicity via topoisomerase II β inhibition and iron-mediated generation of reactive oxygen species (ROS).
- This oxidative stress causes severe, permanent lipid peroxidation of the mitochondrial and sarcoplasmic membranes of cardiomyocytes.
- On endomyocardial biopsy and electron microscopy (Billingham criteria), anthracycline toxicity is characterized by:
 1. Diffuse sarcoplasmic vacuolar degeneration (swollen sarcoplasmic reticulum and mitochondria).
 2. Extensive myofibrillar loss and dropout.
 3. Disruption and lysis of sarcomeres followed by interstitial fibrosis.
- Trastuzumab causes Type II cardiotoxicity, which produces no characteristic ultrastructural myofibrillar loss and is typically reversible.
- High-dose cyclophosphamide cardiotoxicity causes acute hemorrhagic myopericarditis with endothelial necrosis, microthrombi, and interstitial hemorrhage rather than isolated myofibrillar dropout.

Final Answer:

The classic endomyocardial biopsy pattern of diffuse myocyte vacuolization and extensive

myofibrillar loss is pathognomonic for doxorubicin-induced cardiomyopathy.

Quick Tip: Types of Cardiotoxicity:

- Type I (Anthracyclines/Doxorubicin): Dose-dependent, permanent, myocyte vacuolization and myofibrillar loss on biopsy.
- Type II (Trastuzumab): Dose-independent, reversible, normal biopsy (no structural myofibrillar destruction).
- Cyclophosphamide: Acute hemorrhagic myopericarditis with microthrombi.

25. A trigger point injection is a minimally invasive intervention primarily used to treat which type of pain syndrome?

- (A) Focal muscle pain
- (B) Neuropathic pain
- (C) Dermatomal pain
- (D) Radicular or dermatomal pain

Correct Answer: (A) Focal muscle pain

Solution:

Concept:

Myofascial pain syndrome is a common chronic musculoskeletal pain disorder encountered in cancer patients and palliative care populations.

It is characterized by hyperirritable spots located within taut bands of skeletal muscle fibers, known clinically as myofascial trigger points.

Explanation:

- Myofascial trigger points are discrete, focal, hyperalgesic nodules in muscle tissue that cause local muscle tenderness and characteristic referred pain patterns upon mechanical stimulation.

- A trigger point injection involves inserting a small needle directly into the palpable taut muscular band and infiltrating local anesthetics (e.g., Lidocaine or Bupivacaine) with or without a corticosteroid.
- The injection disrupts the dysfunctional motor endplates, inactivates sustained sarcomere contraction, interrupts the local pain-spasm cycle, and provides prompt relief for focal muscle pain.
- Neuropathic, dermatomal, and radicular pain syndromes arise from peripheral nerve damage or spinal nerve root compression; these conditions require neuromodulatory pharmacotherapy, epidural steroid injections, or targeted nerve blocks rather than trigger point injections.

Final Answer:

Trigger point injections are indicated specifically for the treatment of localized myofascial trigger points presenting as focal muscle pain.

Quick Tip: Interventional Pain Strategies:

- Trigger Point Injection → Myofascial / Focal Muscle Pain.
- Epidural / Selective Nerve Root Block → Radicular / Dermatomal Neuropathic Pain.
- Celiac Plexus / Splanchnic Neurolysis → Visceral Upper Abdominal Cancer Pain.

26. Among the following functional pancreatic neuroendocrine tumors (pNETs), which one carries the highest intrinsic risk of malignancy or metastasis at diagnosis?

- (A) Gastrinoma
- (B) Insulinoma
- (C) Glucagonoma
- (D) VIPoma

Correct Answer: (A) Gastrinoma

Solution:

Concept:

Pancreatic neuroendocrine tumors (pNETs) are categorized into functional and non-functional tumors based on hormone hypersecretion.

The malignant potential and likelihood of distant metastases vary significantly among different functional neuroendocrine tumor subtypes.

Explanation:

- **Gastrinoma (Zollinger-Ellison syndrome):** Between 60% and 90% of gastrinomas are malignant, with a high proportion demonstrating locoregional lymph node metastases or hepatic dissemination at the time of initial diagnosis.
- **Insulinoma:** In contrast to gastrinomas, insulinomas are benign in over 90% of cases, with malignant potential documented in less than 10% of patients.
- **Glucagonoma and VIPoma:** Both of these rare neuroendocrine tumors have high malignancy rates (50%–80%), but gastrinoma is the most prevalent and consistently documented highly malignant functional pNET in clinical practice.
- Gastrinomas typically arise within the "gastrinoma triangle" (Passaro triangle) and often require aggressive surgical resection and targeted somatostatin analog therapy due to high metastatic incidence.

Final Answer:

Gastrinomas carry a high intrinsic malignant and metastatic propensity (60%–90%) at presentation among functional pancreatic neuroendocrine neoplasms.

Quick Tip: Malignancy rates in Functional pNETs:

- Insulinoma: ~ 10% malignant (mostly benign).
- Gastrinoma: 60%–90% malignant (high rate of liver/nodal metastases).
- VIPoma / Glucagonoma: 60%–80% malignant.

27. Which of the following statements is TRUE regarding the transdermal fentanyl patch in the management of chronic cancer pain?

- (A) It is generally avoided in patients who are severely cachectic
- (B) It is recommended as first-line opioid for acute breakthrough pain
- (C) Initiation leads to immediate response necessitating stopping other drugs
- (D) It is safe to use in opioid-naïve patients at the lowest dose

Correct Answer: (A) It is generally avoided in patients who are severely cachectic

Solution:

Concept:

Transdermal fentanyl patches provide sustained, continuous systemic opioid delivery for stable chronic cancer pain through a subcutaneous dermal depot.

Proper patient selection and awareness of its unique pharmacokinetics are vital for safe therapeutic outcomes.

Explanation:

- Transdermal fentanyl relies on the presence of a viable subcutaneous fat depot to form a drug reservoir from which fentanyl is slowly released into the systemic circulation.
- In severely cachectic patients, the depletion of subcutaneous adipose tissue and poor peripheral cutaneous perfusion lead to erratic, unpredictable drug absorption and suboptimal analgesia.

- Transdermal fentanyl has a slow onset of action (12–24 hours to reach steady therapeutic serum concentrations); therefore, it is completely inappropriate for managing acute breakthrough pain episodes.
- It is strictly contraindicated in opioid-naïve patients due to the high risk of fatal respiratory depression; patients must be opioid-tolerant before patch initiation.
- Previous baseline analgesia must be gradually transitioned and maintained during the first 12 to 24 hours of patch application until steady therapeutic plasma levels are achieved.

Final Answer:

Transdermal fentanyl patches should be avoided in severely cachectic patients because loss of subcutaneous adipose tissue disrupts drug depot formation and absorption kinetics.

Quick Tip: Key Transdermal Fentanyl Rules:

- Contraindicated in opioid-naïve patients (must be opioid-tolerant: ≥ 60 mg oral morphine equivalent/day for ≥ 1 week).
- Delayed onset (12–24 hours) and prolonged offset (16–24 hours elimination half-life).
- Avoid in severe cachexia or uncontrolled pyrexia (heat increases absorption rate dangerously).

28. A 55-year-old patient with metastatic melanoma on Ipilimumab (CTLA-4 inhibitor) develops Grade 4 diarrhea (>10 stools/day). What is the most appropriate initial management step for this immune-related adverse event (irAE)?

- (A) Discontinue and start corticosteroids with taper over 4–8 weeks
- (B) Discontinue and taper over 7 days to preserve drug function
- (C) Restart immunotherapy once resolved
- (D) Reduce dose

Correct Answer: (A) Discontinue and start corticosteroids with taper over 4–8 weeks

Solution:

Concept:

Immune checkpoint inhibitors, particularly cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) blockers like Ipilimumab, can precipitate severe autoimmune toxicities known as immune-related adverse events (irAEs).

Immune-mediated colitis/enteritis is graded according to Common Terminology Criteria for Adverse Events (CTCAE) to dictate immunosuppressive interventions.

Explanation:

- Grade 4 diarrhea/colitis is defined as > 10 stools per day over baseline, incontinence, life-threatening hemodynamic consequences, or urgent intervention indicated.
- According to ASCO/ESMO/NCCN guidelines, Grade 4 immune-mediated enterocolitis requires permanent discontinuation of the offending checkpoint inhibitor.
- High-dose systemic corticosteroid therapy must be initiated immediately (intravenous Methylprednisolone 1–2 mg/kg/day or equivalent).
- Once clinical improvement to Grade 1 or baseline is achieved, corticosteroids must be tapered slowly over a minimum of 4 to 8 weeks.
- A rapid taper (e.g., ≤ 7 days) results in a high incidence of rebound inflammatory colitis.
- If steroid-refractory colitis persists after 48 to 72 hours, biologics such as Infliximab or Vedolizumab should be promptly administered.

Final Answer:

The standard of care for Grade 4 immune-mediated diarrhea is permanent discontinuation

of immunotherapy and prompt initiation of high-dose corticosteroids tapered over 4 to 8 weeks.

Quick Tip: Management of Immune Checkpoint Inhibitor Colitis:

- Grade 1: Continue therapy, symptomatic care.
- Grade 2: Withhold ICI, start oral steroids (0.5–1 mg/kg/day).
- Grade 3–4: Permanently discontinue CTLA-4 inhibitor, IV Methylprednisolone (1–2 mg/kg/day), taper over 4–8 weeks.
- Steroid-refractory (no improvement in 48–72h) → Add Infliximab or Vedolizumab.

29. A 70-year-old male with lung cancer presents with facial swelling, distended neck veins, and dyspnea that worsen when lying down. Physical findings suggest Superior Vena Cava Obstruction (SVCO). What is the most appropriate initial diagnostic or therapeutic step?

- (A) Start palliative radiotherapy immediately
- (B) Immediate initiation of high-dose corticosteroids
- (C) Schedule a conventional X-ray and MRI
- (D) Perform a contrast-enhanced CT scan of the chest

Correct Answer: (D) Perform a contrast-enhanced CT scan of the chest

Solution:

Concept:

Superior Vena Cava Obstruction (SVCO) is a common oncologic presentation resulting from mediastinal tumor bulk compression, direct vascular invasion, or intraluminal thrombosis. Accurate imaging is the critical first step to delineate the precise anatomy of obstruction, assess thrombus burden, and establish histological tissue diagnosis before starting definitive therapy.

Explanation:

- Contrast-enhanced computed tomography (CECT) of the chest and neck is the gold-standard imaging modality for evaluating suspected SVCO.

- CECT precisely demonstrates the level and degree of caval narrowing, collateral vessel architecture, the underlying primary tumor mass, and the presence or absence of intraluminal thrombosis.
- In the absence of acute stridor, airway compromise, or cerebral edema, SVCO is not an immediate life-threatening emergency requiring blind emergency radiotherapy.
- Immediate emergency radiotherapy without obtaining tissue biopsy and anatomical mapping can obscure diagnostic histopathology and compromise definitive systemic therapy planning (e.g., chemotherapy for small cell lung cancer or lymphoma).
- Thus, performing a diagnostic CECT scan of the chest is the mandatory initial step.

Final Answer:

A contrast-enhanced CT (CECT) scan of the chest is the most appropriate initial diagnostic step to characterize superior vena cava obstruction.

Quick Tip: Approach to SVCO:

- Step 1: Contrast-enhanced CT (CECT) of the chest (diagnostic gold standard).
- Step 2: Establish histological tissue diagnosis before radiation (unless stridor/cerebral edema).
- Emergency treatment (Stenting / RT) is reserved for acute airway compromise or cerebral edema.

30. A patient receiving an Irinotecan-based chemotherapy regimen develops diarrhea (requiring hospitalization and IV fluids) two days after drug administration. After ruling out infection, what is the most appropriate specific treatment for this late-onset Irinotecan-induced diarrhea?

- (A) Loperamide
- (B) Atropine

- (C) Methylprednisolone
(D) Octreotide

Correct Answer: (A) Loperamide

Solution:

Concept:

Irinotecan (a topoisomerase I inhibitor) induces two distinct types of diarrhea: acute (cholinergic-mediated) and late-onset (secretory and inflammatory-mediated by its active metabolite SN-38).

The management strategies for acute versus late-onset irinotecan diarrhea differ fundamentally.

Explanation:

- **Acute diarrhea** occurs within 24 hours of infusion, accompanied by cholinergic symptoms (sweating, abdominal cramps, salivation), and is treated with intravenous or subcutaneous **Atropine**.
- **Late-onset diarrhea** occurs > 24 hours post-infusion (typically day 5 to 7, or two days after as in this vignette) due to direct mucosal toxicity of biliary-excreted active SN-38 metabolite.
- High-dose **Loperamide** is the specific, first-line treatment of choice for late-onset irinotecan-induced diarrhea:
 - Loading dose: 4 mg at the first loose bowel movement.
 - Maintenance dose: 2 mg every 2 hours until diarrhea-free for 12 consecutive hours.
- Octreotide is reserved as a second-line intervention for loperamide-refractory diarrhea or patients presenting with severe dehydration and sepsis.

Final Answer:

High-dose Loperamide is the established first-line specific treatment for late-onset irinotecan-

induced diarrhea.

Quick Tip: Irinotecan Diarrhea Management:

- Acute Diarrhea (< 24 hours, cholinergic) → Atropine (0.25–1.0 mg IV/SC).
- Late Diarrhea (> 24 hours, SN-38 mediated) → High-dose Loperamide (4 mg then 2 mg q2h).
- Refractory late diarrhea → Octreotide (100–150 μ g SC TID).

31. Which of the following is least likely to be the underlying cause of Superior Vena Cava Obstruction (SVCO)?

- (A) Lymphoma
- (B) Thymic Carcinoma
- (C) Non–Small Cell Lung Carcinoma (NSCLC)
- (D) Carcinoma Breast

Correct Answer: (B) Thymic Carcinoma

Solution:

Concept:

Malignancy is responsible for over 85%–90% of cases of Superior Vena Cava Obstruction (SVCO).

The relative incidence reflects the prevalence of intrathoracic tumors and their anatomical proximity to the superior vena cava in the middle and anterior mediastinum.

Explanation:

- Non–Small Cell Lung Carcinoma (NSCLC) is the most common malignant cause, accounting for approximately 50% of all SVCO cases.
- Small Cell Lung Cancer (SCLC) represents approximately 20%–25% of cases.

- Non-Hodgkin Lymphoma and Hodgkin Lymphoma account for approximately 10%–15% of SVCO presentations, particularly in younger cohorts with bulky mediastinal adenopathy.
- Metastatic Carcinoma of the Breast is a well-established cause of secondary mediastinal lymphadenopathy causing extrinsic caval compression.
- Thymic Carcinomas are extremely rare anterior mediastinal neoplasms with an annual incidence of less than 0.15 per 100,000 individuals, making them the least likely cause of SVCO among the listed options.

Final Answer:

Thymic Carcinoma is the least common cause of SVCO due to its extremely low absolute population incidence compared to lung cancer, lymphoma, and metastatic breast cancer.

Quick Tip: Etiology of Malignant SVCO:

1. Lung Cancer: ~ 70%–80% (NSCLC > 50%, SCLC ~ 20%).
2. Lymphoma: ~ 10%–15%.
3. Metastatic malignancies (Breast, Germ cell tumors): ~ 5%.
4. Rare mediastinal tumors (Thymic carcinoma): < 1%.

32. What is the most likely cause of hypercalcemia in a patient with lymphoma?

- (A) 1,25-dihydroxy vitamin D
- (B) ACTH
- (C) Transforming Growth Factor (TGF)-Beta
- (D) Parathyroid hormone

Correct Answer: (A) 1,25-dihydroxy vitamin D

Solution:

Concept:

Hypercalcemia of malignancy (HCM) occurs through distinct humoral and osteolytic pathophysiological mechanisms.

In Hodgkin and Non-Hodgkin lymphomas, hypercalcemia is predominantly driven by tumor-mediated production of active vitamin D metabolites.

Explanation:

- Lymphoma cells and tumor-infiltrating macrophages aberrantly express the enzyme 1α -hydroxylase (CYP27B1).
- This enzyme converts circulating 25-hydroxyvitamin D [calcidiol] into its active form, **1,25-dihydroxyvitamin D** [calcitriol], in an uncontrolled, non-PTH-regulated manner.
- Elevated calcitriol levels enhance fractional intestinal absorption of calcium and phosphate while simultaneously stimulating osteoclast-mediated bone resorption.
- Unlike solid tumors (e.g., squamous cell carcinomas), which classically cause hypercalcemia via Parathyroid Hormone-related Protein (PTHrP), lymphomas characteristically exhibit hypervitaminosis D.
- Ectopic PTH production is exceptionally rare, and ACTH does not directly mediate calcium mobilization.

Final Answer:

The predominant humoral mechanism of hypercalcemia in lymphoma is the autonomous extra-renal synthesis of 1,25-dihydroxyvitamin D (calcitriol).

Quick Tip: Mechanisms of Hypercalcemia of Malignancy:

- Solid tumors (Squamous cell of lung/H&N, Renal): PTHrP mediated (80%).
- Osteolytic bone metastases (Breast, Myeloma): Local osteolytic cytokines (20%).
- Lymphomas (Hodgkin / NHL): Calcitriol ($1,25-(\text{OH})_2\text{D}_3$) mediated (< 1%).

33. Which of the following statements is not true regarding testicular tumors?

- (A) Approximately 90–95% of all testicular tumors are Germ Cell Tumors (GCTs)
- (B) Choriocarcinoma is the most common subtype, with a prevalence of 50% among GCTs
- (C) Antitumor antibiotics are often used as a component of curative treatment regimens
- (D) Platinum-based chemotherapy is the cornerstone of systemic treatment for metastatic disease

Correct Answer: (B) Choriocarcinoma is the most common subtype, with a prevalence of 50% among GCTs

Solution:

Concept:

Testicular germ cell tumors (GCTs) represent the vast majority of primary testicular neoplasms and are among the most curable solid malignancies with modern multi-agent platinum-based chemotherapy.

Explanation:

- Germ cell tumors account for 90%–95% of all primary malignant testicular neoplasms, with sex cord-stromal tumors (Leydig and Sertoli cell tumors) comprising the remainder.
- Testicular GCTs are broadly divided into seminomas and non-seminomatous germ cell tumors (NSGCTs).
- **Seminoma** is the single most common histological subtype, accounting for approximately 50% of all germ cell tumors.

- Pure **Choriocarcinoma** is the rarest subtype, representing less than 1% of primary testicular GCTs, characterized by aggressive hematogenous dissemination and elevated serum β -hCG.
- Antitumor antibiotics like **Bleomycin** (as part of the standard BEP regimen: Bleomycin, Etoposide, Cisplatin) and platinum agents are fundamental cornerstones of curative chemotherapy.

Final Answer:

Statement (B) is false; Seminoma is the most common subtype (50%), whereas Choriocarcinoma represents < 1% of testicular GCTs.

Quick Tip: Testicular Germ Cell Tumors Key Facts:

- Seminoma is the most common subtype (~ 50%).
- Pure choriocarcinoma is the rarest (< 1%) and most aggressive.
- Curative chemotherapy: BEP (Bleomycin [antitumor antibiotic], Etoposide, Cisplatin [platinum]).

34. A lady with ovarian carcinoma on chemotherapy (Khorana score = 2) presents with right calf swelling. Ultrasound shows small saphenous vein thrombophlebitis but no deep vein thrombosis (DVT). What is the next step in management?

- (A) Monitor carefully for venous thromboembolism (VTE) and continue chemotherapy
- (B) Start aspirin and observe
- (C) Direct oral anticoagulants (DOACs) for 3 months
- (D) Start low molecular weight heparin and compression stockings

Correct Answer: (D) Start low molecular weight heparin and compression stockings

Solution:

Concept:

Cancer-associated superficial vein thrombosis (SVT) carries a high risk of propagation into the deep venous system and subsequent pulmonary embolism.

In active malignancy receiving chemotherapy, superficial thrombophlebitis requires anticoagulation along with symptomatic measures.

Explanation:

- Active malignancy is a major prothrombotic state that significantly increases the likelihood of SVT progressing to proximal deep vein thrombosis (DVT) or pulmonary embolism (PE).
- According to international guidelines (CHEST, ITAC, ESMO), patients with cancer and superficial vein thrombosis of the lower extremity should receive therapeutic or prophylactic anticoagulation.
- Low Molecular Weight Heparin (LMWH, such as Enoxaparin or Dalteparin) or Fondaparinux for at least 45 days is standardly recommended to prevent thrombus extension.
- Concomitant use of graduated compression stockings and leg elevation relieves local pain, inflammation, and venous stasis edema.
- Observation alone or aspirin monotherapy is inadequate in cancer patients with active ongoing chemotherapy who harbor an elevated thromboembolic risk.

Final Answer:

The recommended management for superficial vein thrombosis in a cancer patient on chemotherapy is therapeutic LMWH combined with compression stockings.

Quick Tip: Management of Cancer-Associated Thrombophlebitis:

- High risk of DVT/PE propagation.
- Anticoagulation: LMWH (or Fondaparinux) for ≥ 45 days.
- Graduated compression stockings for symptomatic relief.

35. What is the most useful method for fertility preservation in female cancer patients before initiating chemotherapy?

- (A) Ovarian tissue preservation
- (B) Oocyte cryopreservation
- (C) Ovarian transposition (Oophoropexy) to move the ovaries out of the radiation field
- (D) Administration of GnRH agonists to temporarily suppress the ovaries

Correct Answer: (B) Oocyte cryopreservation

Solution:

Concept:

Fertility preservation is an essential consideration for adolescent and young adult (AYA) patients prior to receiving gonadotoxic chemotherapy or pelvic radiation.

Established reproductive technologies offer proven, high-success methods for preserving future biological parenthood.

Explanation:

- **Oocyte (and embryo) cryopreservation** is the gold-standard, first-line, and most established fertility preservation strategy endorsed by ASCO and ASRM for post-pubertal female cancer patients.
- Controlled ovarian stimulation using antagonist protocols with random-start stimulation allows mature oocyte retrieval within 10–14 days, avoiding unnecessary cancer treatment delays.

- **Ovarian tissue cryopreservation** is primarily indicated for prepubertal girls or when chemotherapy cannot be delayed by two weeks for ovarian stimulation.
- **Ovarian transposition (oophoropexy)** is specific for pelvic radiation, not systemic chemotherapy.
- **GnRH agonists** (e.g., Goserelin) provide medical ovarian suppression during chemotherapy to reduce premature ovarian failure, but they do not replace established cryopreservation methods for guaranteed reproductive preservation.

Final Answer:

Oocyte (or embryo) cryopreservation is the most established and standard method for preserving fertility prior to gonadotoxic chemotherapy in post-pubertal females.

Quick Tip: Fertility Preservation Guidelines (ASCO/ESMO):

- First-line standard for post-pubertal women: Oocyte / Embryo Cryopreservation.
- Pre-pubertal girls / Urgent treatment: Ovarian Tissue Cryopreservation.
- Pelvic RT protection: Oophoropexy (Ovarian Transposition).

36. Which of the following anticancer drugs carries the highest risk of infertility in patients?

- (A) Cyclophosphamide
- (B) Methotrexate
- (C) Busulfan
- (D) Adriamycin

Correct Answer: (A) Cyclophosphamide

Solution:

Concept:

Chemotherapy-induced gonadotoxicity is directly related to the drug class, cumulative dose, and age of the patient.

Alkylating agents cause cell-cycle non-specific covalent cross-linking of DNA, exerting severe cytotoxicity against both dividing spermatogonia and non-dividing primordial ovarian follicles.

Explanation:

- **Cyclophosphamide** is an oxazaphosphorine alkylating agent with the highest documented clinical risk of causing permanent azoospermia in males and irreversible premature ovarian failure in females.
- In females, cyclophosphamide induces apoptosis in the quiescent primordial follicle reserve, causing profound cortical follicular atrophy and persistent amenorrhea in a cumulative dose-dependent manner.
- While Busulfan is also an alkylating agent, cyclophosphamide is by far the most widely utilized high-gonadotoxicity agent in general oncology and hematology regimens.
- Antimetabolites (e.g., Methotrexate) and Anthracyclines (e.g., Adriamycin / Doxorubicin) carry intermediate to low risks of permanent sterilizing gonadotoxicity compared to alkylators.

Final Answer:

Cyclophosphamide carries the highest risk of permanent infertility due to alkylation-mediated depletion of gonadal germ cells and follicles.

Quick Tip: Gonadotoxic Risk Hierarchy of Antineoplastics:

- High Risk (> 80% infertility): Alkylating agents (Cyclophosphamide, Ifosfamide, Busulfan, Chlorambucil, Procarbazine).
- Intermediate Risk (20%–80%): Cisplatin, Carboplatin, Doxorubicin.
- Low/Minimal Risk (< 20%): Methotrexate, 5-FU, Vincristine, Bleomycin.

37. What is the empirical antibiotic regimen for febrile neutropenia in patients at high risk of infections?

- (A) Meropenem alone
- (B) Ceftriaxone
- (C) Piperacillin + Gentamicin
- (D) Vancomycin alone

Correct Answer: (C) Piperacillin + Gentamicin

Solution:

Concept:

High-risk febrile neutropenia (MASCC score < 21 or anticipated prolonged profound neutropenia > 7 days) requires immediate broad-spectrum intravenous empirical antibiotic therapy.

Coverage must encompass Gram-negative bacilli, particularly *Pseudomonas aeruginosa*, as well as common Gram-positive pathogens.

Explanation:

- Combination therapy with an antipseudomonal β -lactam/penicillin (e.g., Piperacillin-Tazobactam) plus an Aminoglycoside (e.g., Gentamicin or Amikacin) is a classic guideline-recommended empirical regimen for high-risk, clinically unstable neutropenic patients.

- This combination provides rapid synergistic bactericidal killing against resistant Gram-negative bacilli, including *Pseudomonas aeruginosa* and Enterobacterales.
- Ceftriaxone lacks antipseudomonal activity and is inadequate for empirical treatment in high-risk neutropenia.
- Vancomycin alone lacks essential Gram-negative spectrum coverage and should not be used as single-agent empirical therapy.
- Monotherapy with Piperacillin-Tazobactam, Cefepime, or Meropenem is standard, but when combination therapy is selected for high-risk patients, an antipseudomonal penicillin plus an aminoglycoside represents the standard synergistic pairing.

Final Answer:

Combination therapy of Piperacillin plus Gentamicin provides the necessary synergistic broad-spectrum antipseudomonal coverage for high-risk febrile neutropenia.

Quick Tip: Empirical Regimens in Febrile Neutropenia:

- High-Risk Patients (MASCC < 21): IV Antipseudomonal β -lactam (Piperacillin-Tazobactam / Cefepime / Meropenem) $\pm$ Aminoglycoside (Gentamicin).
- Low-Risk Patients (MASCC $\geq$ 21): Oral Ciprofloxacin + Amoxicillin-Clavulanate.

38. A patient with Medullary Thyroid Carcinoma (MTC) undergoes total thyroidectomy and central neck dissection. Which of the following findings is least likely to be an indication for postoperative radiotherapy (RT)?

- (A) Bulky neck nodes
- (B) Extrathyroid extension
- (C) High calcitonin

(D) Residual disease

Correct Answer: (C) High calcitonin

Solution:

Concept:

Medullary Thyroid Carcinoma (MTC) arises from calcitonin-producing parafollicular C-cells of the thyroid.

Primary curative therapy is complete surgical excision; external beam radiation therapy (EBRT) has no role for isolated biochemical elevation in the absence of locoregional structural disease.

Explanation:

- External beam radiation therapy (EBRT) in MTC is reserved for locoregional disease control in patients at high risk of local recurrence.
- Standard clinical indications for adjuvant postoperative neck radiotherapy include:
 1. Gross or microscopic residual disease (R1 or R2 resection).
 2. Extensive extrathyroidal extension (invasion into trachea, larynx, esophagus, or recurrent laryngeal nerve).
 3. Extensive or bulky locoregional lymph node metastases with extracapsular extension.
- An elevated postoperative serum calcitonin or carcinoembryonic antigen (CEA) indicates residual or metastatic disease (biochemical persistence), but high calcitonin alone—without demonstrable locoregional anatomical disease—is NOT an indication for neck radiotherapy.
- Systemic therapy (e.g., RET inhibitors like Selpercatinib/Cabozantinib) or imaging surveillance is indicated for persistent calcitonin elevation.

Final Answer:

Elevated serum calcitonin level in isolation is a biochemical biomarker and is least likely to

serve as an indication for postoperative radiation therapy in MTC.

Quick Tip: Indications for Postoperative Radiotherapy in MTC:

- Positive surgical margins / Gross residual disease (R2/R1).
- T4 disease with extensive extrathyroidal soft tissue invasion.
- Bulky lymph nodes with extracapsular spread.
- High calcitonin alone without structural target is NOT an indication for EBRT!

39. CDK 4/6 inhibitors act on which phase of the cell cycle?

- (A) G0 to G1
- (B) S to G2
- (C) G2 to M
- (D) G1 to S

Correct Answer: (D) G1 to S

Solution:

Concept:

Cyclin-dependent kinases 4 and 6 (CDK 4/6) are serine/threonine kinases that form active catalytic complexes with D-type cyclins.

These complexes regulate cell cycle progression through the critical restriction point (*R*-point) between the growth (G_1) phase and DNA synthesis (*S*) phase.

Explanation:

- In response to mitogenic and estrogenic signaling in ER-positive breast cancer, Cyclin D binds to and activates CDK4 and CDK6.
- The active Cyclin D–CDK4/6 complex phosphorylates the Retinoblastoma tumor

suppressor protein (Rb).

- Phosphorylation of Rb (pRb) causes it to release the E2F transcription factors, which subsequently transcribe genes required for DNA replication, driving cell cycle transition from G_1 phase into S phase.
- CDK 4/6 inhibitors (e.g., Palbociclib, Ribociclib, Abemaciclib) selectively inhibit CDK4 and CDK6 catalytic activity, preventing Rb phosphorylation and arresting cells at the G_1 to S checkpoint.

Final Answer:

CDK 4/6 inhibitors prevent the phosphorylation of Rb, thereby arresting the cell cycle specifically at the G_1 to S transition phase.

Quick Tip: Cell Cycle Targets:

- CDK 4/6 Inhibitors (Palbociclib, Ribociclib, Abemaciclib): $G_1 \rightarrow S$ checkpoint.
- Antimetabolites (5-FU, Gemcitabine, Methotrexate): S phase.
- Taxanes and Vinca Alkaloids: M phase (Mitotic spindle).
- Bleomycin and Etoposide: $G_2 \rightarrow M$ transition.

40. Which of the following statements regarding the characteristics of chronic cancer-related pain is NOT true?

- (A) Dull persistent pain managed by standard analgesics
- (B) Cancer pain is often a mixture of nociceptive (somatic/visceral) and neuropathic components
- (C) Pain should be managed according to the WHO analgesic ladder, stepping up from non-opioids to strong opioids as needed
- (D) Breakthrough pain is a transient, severe flare-up of pain that must be treated with immediate-release opioids

Correct Answer: (A) Dull persistent pain managed by standard analgesics

Solution:

Concept:

Cancer-related pain is a complex, progressive, multidimensional symptom involving nociceptive, visceral, and neuropathic mechanisms.

Palliative pain management follows structured international guidelines to achieve comprehensive relief across all severity spectrums.

Explanation:

- Chronic cancer pain is rarely simple or mild; it encompasses severe somatic pain, visceral capsule stretch, inflammatory hyperalgesia, and neuropathic nerve infiltration.
- It is not adequately managed simply with standard over-the-counter simple analgesics (e.g., paracetamol or NSAIDs) as the disease progresses; instead, it often necessitates potent Step 3 opioids (Morphine, Fentanyl, Oxycodone) and adjuvant medications.
- Cancer pain frequently exhibits mixed pathophysiology combining nociceptive and neuropathic elements (Statement B is true).
- The World Health Organization (WHO) 3-step analgesic ladder represents the global standard framework for pain escalation (Statement C is true).
- Breakthrough pain is defined as a transitory increase in pain occurring against a background of controlled chronic pain, requiring immediate-release, rapid-onset opioids (Statement D is true).

Final Answer:

Statement (A) is not true because chronic cancer pain is heterogeneous and typically requires escalation to opioid-based regimens rather than simple standard analgesics alone.

Quick Tip: Cancer Pain Management Principles:

- WHO Ladder: Step 1 (Non-opioid) → Step 2 (Weak opioid) → Step 3 (Strong opioid ± Adjuvants).
- Breakthrough pain: Use immediate-release opioids calculated at 10%–1/6th of total 24-hour baseline opioid dose.

41. Which hepatic benign lesion has malignant potential?

- (A) Focal nodular hyperplasia
- (B) Hepatic adenoma
- (C) Benign micronodules
- (D) Hemangioma

Correct Answer: (B) Hepatic adenoma

Solution:

Concept:

Benign liver lesions are common incidental findings on abdominal imaging.

Distinguishing lesions with true malignant transformation potential from entirely indolent lesions is critical for determining surgical resection versus conservative observation.

Explanation:

- **Hepatic Adenoma (Hepatocellular Adenoma):** A benign monoclonal neoplasm composed of hepatocytes, most commonly associated with oral contraceptive use, anabolic steroid exposure, and metabolic syndrome.
- Hepatic adenomas possess significant malignant potential to transform into Hepatocellular Carcinoma (HCC), particularly β -catenin-mutated adenomas, lesions > 5 cm in diameter, and those arising in male patients.
- Furthermore, hepatic adenomas carry a substantial risk of spontaneous rupture and

life-threatening intraperitoneal hemorrhage.

- **Focal Nodular Hyperplasia (FNH):** A polyclonal regenerative response to an underlying vascular malformation characterized by a central fibrous scar; it has zero malignant potential.
- **Hepatic Hemangioma:** The most common benign liver lesion, composed of cavernous vascular spaces, with no malignant potential.

Final Answer:

Hepatic adenoma is the benign liver lesion with established potential for malignant transformation into hepatocellular carcinoma.

Quick Tip: Benign Liver Lesions Summary:

- Hepatic Adenoma: Malignant transformation risk (~ 5%–10%) + Risk of rupture/bleeding → Surgical resection if > 5 cm or in males.
- Focal Nodular Hyperplasia (FNH): Central stellate scar, strictly benign → Conservative observation.
- Hemangioma: Peripheral nodular puddling on dynamic CT/MRI, strictly benign.

42. An adult patient successfully treated for Acute Myeloid Leukemia (AML) with allogeneic hematopoietic stem cell transplantation (HSCT) 8 years ago presents with persistent symptoms including xerostomia, dysphagia, and generalized fatigue. No evidence of disease recurrence or acute infection is found. What is the most likely long-term complication causing this constellation of symptoms?

- (A) Radiation-induced esophageal effect
- (B) GVHD affecting salivary gland
- (C) Post-transplant infection (viral, fungal)
- (D) Secondary malignancy due to immunosuppression

Correct Answer: (B) GVHD affecting salivary gland

Solution:

Concept:

Chronic Graft-versus-Host Disease (cGVHD) is a major late immune-mediated complication following allogeneic hematopoietic stem cell transplantation (HSCT), occurring months to years post-transplant.

It results from donor-derived T-cell and B-cell dysregulation leading to chronic inflammation and extensive multiorgan fibrosis.

Explanation:

- Chronic GVHD frequently presents with autoimmune-like features mimicking systemic sclerosis or Sjögren syndrome.
- Salivary and lacrimal glands are classic target organs: immune-mediated lymphocytic infiltration and periductal fibrosis destroy salivary acini, resulting in severe **xerostomia** (dry mouth) and mucosal atrophy.
- Esophageal involvement in chronic GVHD causes mucosal desquamation, webbing, and fibrous esophageal strictures, leading to persistent **dysphagia**.
- The combination of xerostomia (which impairs bolus transit) and esophageal chronic GVHD directly explains dysphagia and fatigue.
- Radiation-induced acute effects occur early post-transplant conditioning, and infectious causes typically present acutely with fever and specific localizing signs rather than an indolent 8-year course.

Final Answer:

The clinical features of xerostomia and dysphagia 8 years post-allogeneic HSCT are classic manifestations of chronic Graft-versus-Host Disease (cGVHD) affecting the salivary glands and

esophagus.

Quick Tip: Chronic GVHD Classic Organ Manifestations:

- Oral / Salivary: Xerostomia (Sjögren-like sicca syndrome), oral lichenoid plaques.
- GI / Esophageal: Dysphagia, esophageal webs, and strictures.
- Skin: Sclerodermatous changes, vitiligo, lichen planus-like lesions.
- Eyes: Keratoconjunctivitis sicca (dry eyes).

43. A patient receiving treatment for Acute Lymphoblastic Leukemia (ALL) develops pancreatitis. Which of the following antileukemic agents is the most common cause of this complication?

- (A) L-Asparaginase
- (B) Vincristine
- (C) Daunorubicin
- (D) Dexamethasone

Correct Answer: (A) L-Asparaginase

Solution:

Concept:

L-Asparaginase (derived from *E. coli* or *Erwinia*) and its pegylated form (Pegaspargase) are essential antineoplastic agents in the multi-agent induction regimens for Acute Lymphoblastic Leukemia (ALL).

By depleting circulating plasma asparagine, asparaginase starves leukemic lymphoblasts of an essential amino acid, but it also carries distinct, organ-specific non-hematologic toxicities.

Explanation:

- Asparaginase inhibits protein synthesis across all organ systems, with prominent effects on pancreatic acinar cells and the liver.

- **Acute Pancreatitis** is a well-recognized and potentially life-threatening complication of L-asparaginase therapy, occurring in 5%–10% of treated patients.
- Pathophysiologically, asparaginase causes intracellular zymogen activation and severe pancreatic acinar cell injury, leading to elevated amylase/lipase, pancreatic necrosis, and pseudocyst formation.
- Development of severe or necrotizing asparaginase-associated pancreatitis necessitates permanent discontinuation of the drug.
- Other classic toxicities of asparaginase include hepatotoxicity, thrombosis (antithrombin III depletion), and hypersensitivity/anaphylaxis.
- Vincristine causes peripheral neuropathy/ileus, Daunorubicin causes cardiotoxicity/myelosuppression, and Dexamethasone rarely induces pancreatitis compared to asparaginase.

Final Answer:

L-Asparaginase is the antileukemic agent most commonly implicated in drug-induced acute pancreatitis in ALL patients.

Quick Tip: L-Asparaginase / Pegaspargase Toxicities to Remember:

- Acute Pancreatitis (requires monitoring of amylase/lipase).
- Thrombosis (decreased Antithrombin III and Protein C/S synthesis).
- Hepatotoxicity (hyperbilirubinemia and transaminitis).
- Hypersensitivity reactions (develop anti-asparaginase neutralizing antibodies).

44. A patient with BRCA-mutated ovarian cancer was diagnosed in January 2024 and completed chemotherapy in July 2024. In February 2025, her CA-125 levels are elevated, and recurrence

is noted on imaging. The patient is asymptomatic. What is the next step in management?

- (A) Platinum chemotherapy
- (B) Non-platinum chemotherapy
- (C) Olaparib (PARP inhibitor, as patient is BRCA mutant)
- (D) Observation and follow-up

Correct Answer: (A) Platinum chemotherapy

Solution:

Concept:

Recurrent epithelial ovarian carcinoma is classified based on the Platinum-Free Interval (PFI)—the time elapsed between completion of the last platinum-based therapy and radiographic/biochemical disease recurrence.

The PFI guides subsequent treatment selection and platinum rechallenge.

Explanation:

- In this patient, primary platinum-based chemotherapy was completed in July 2024, and disease recurrence was documented in February 2025.
- The Platinum-Free Interval (PFI) is approximately 7 months (from July 2024 to February 2025).
- A PFI $\geq$ 6 months defines platinum-sensitive recurrent ovarian cancer.
- The standard of care for platinum-sensitive relapse is rechallenge with a platinum-based combination doublet (e.g., Carboplatin plus Pegylated Liposomal Doxorubicin, Carboplatin plus Gemcitabine, or Carboplatin plus Paclitaxel).
- **BRCA mutation** status confers extreme platinum sensitivity and homologous recombination deficiency (HRD).

- While PARP inhibitors (such as Olaparib) are standard, they are utilized as maintenance therapy following response to platinum rechallenge in this setting, or after prior frontline platinum therapy; cytotoxic platinum rechallenge must precede second-line PARP maintenance.

Final Answer:

Because the platinum-free interval is > 6 months, the disease is platinum-sensitive, and the next step is platinum-based combination chemotherapy.

Quick Tip: Ovarian Cancer Recurrence Rules:

- Platinum-Sensitive ($\text{PFI} \geq 6$ months) $\rightarrow$ Rechallenge with Platinum-based doublet chemotherapy (followed by PARP inhibitor maintenance).
- Platinum-Resistant ($\text{PFI} < 6$ months) $\rightarrow$ Non-platinum single agent (e.g., Paclitaxel, PLD, Topotecan) $\pm$ Bevacizumab.
- Platinum-Refractory (Progressing during therapy) $\rightarrow$ Non-platinum regimen.

45. What is the treatment of opioid induced constipation?

- (A) Stimulant laxative like senna
- (B) Naloxone
- (C) Peripheral mu antagonist like Methylnaltrexone
- (D) Dietary modification alone

Correct Answer: (A) Stimulant laxative like senna

Solution:

Concept:

Opioid-induced constipation (OIC) is the most prevalent, persistent adverse effect of chronic

opioid therapy in cancer patients.

Unlike opioid-induced sedation or nausea, tolerance does not develop to constipation, requiring routine prophylactic and active pharmacologic laxative management.

Explanation:

- Opioids stimulate μ -opioid receptors located in the myenteric and submucosal plexuses of the enteric nervous system, causing decreased peristalsis, increased non-propulsive segmental contractions, and increased fluid absorption.
- First-line prophylactic and therapeutic standard of care is a **stimulant laxative** (e.g., Senna, Bisacodyl), with or without an osmotic laxative (e.g., Polyethylene Glycol [PEG] or Lactulose).
- Stimulant laxatives directly promote colonic motility and counteract opioid-induced intestinal hypomotility.
- Dietary fiber and fluid modifications alone are generally ineffective and can worsen obstructive symptoms in opioid-induced dysmotility.
- Peripherally Acting μ -Opioid Receptor Antagonists (PAMORAs, such as Methylnaltrexone, Naloxegol) are second-line rescue agents indicated specifically for refractory OIC when standard laxatives fail.
- Systemic Naloxone crosses the blood-brain barrier and precipitates acute opioid withdrawal and reversal of analgesia.

Final Answer:

The first-line pharmacological treatment and prophylaxis for opioid-induced constipation is a stimulant laxative such as senna.

Quick Tip: Stepwise Management of Opioid-Induced Constipation (OIC):

1. First-line: Stimulant laxative (Senna / Bisacodyl) ± Osmotic laxative (PEG).
2. Avoid bulk-forming fiber (can cause fecal impaction).
3. Refractory to standard laxatives: Add a PAMORA (Methylnaltrexone SC or Naloxegol PO).

46. How is the presence of an invasive fungal infection most commonly evaluated using non-culture-based serum testing?

- (A) 1,3 Beta D-glucan assay
- (B) Galactomanan antigen assay
- (C) Cryptococcal antigen test
- (D) Polymerase Chain Reaction

Correct Answer: (A) 1,3 Beta D-glucan assay

Solution:

Concept:

Invasive fungal infections (IFIs) are a major cause of morbidity and mortality in neutropenic and immunocompromised cancer patients.

Because blood cultures lack rapid sensitivity, non-culture-based serological biomarker assays allow early non-invasive diagnostic screening.

Explanation:

- (1 → 3)- β -D-Glucan (BDG) is a major cell wall polysaccharide component present in almost all clinically relevant pathogenic fungi, including *Candida* spp., *Aspergillus* spp., *Pneumocystis jirovecii*, and *Fusarium* spp. (exceptions: Mucorales and *Cryptococcus*).
- The serum BDG assay functions as a widely utilized broad-spectrum, pan-fungal non-culture-based screening test with high negative predictive value.

- In contrast, the **Galactomannan assay** is genus-specific, detecting polysaccharide antigen primarily released by *Aspergillus* species.
- The **Cryptococcal antigen (CrAg)** lateral flow assay specifically detects the glucuronoxylomannan capsule of *Cryptococcus neoformans/gattii*.
- Thus, the (1 → 3)- β -D-glucan assay is the most comprehensive general non-culture test for invasive fungal disease.

Final Answer:

The 1,3 Beta D-glucan (BDG) assay is the primary non-culture-based serum biomarker used for general evaluation of invasive fungal infections.

Quick Tip: Non-Culture Fungal Biomarkers:

- 1,3- β -D-Glucan (BDG): Broad pan-fungal marker (*Candida*, *Aspergillus*, *Pneumocystis*). Negative in Mucorales and *Cryptococcus*.
- Galactomannan: Specific for *Aspergillus* (serum and BAL).
- Cryptococcal Antigen (CrAg): Highly sensitive/specific for *Cryptococcus*.

47. Which antidepressant is associated with the least sexual dysfunction?

- (A) Venlafaxine
- (B) Fluoxetine
- (C) Escitalopram
- (D) Bupropion

Correct Answer: (D) Bupropion

Solution:

Concept:

Depression and adjustment disorders are highly prevalent in cancer patients undergoing active treatment and survivorship.

Antidepressant selection in psycho-oncology requires minimizing adverse quality-of-life side effects such as fatigue, weight changes, and sexual dysfunction.

Explanation:

- Selective Serotonin Reuptake Inhibitors (SSRIs, like Fluoxetine and Escitalopram) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs, like Venlafaxine) increase serotonergic transmission at 5-HT₂ receptors.
- Stimulation of post-synaptic 5-HT₂ receptors in the central nervous system inhibits sexual desire, impairs arousal, and delays or prevents orgasm/ejaculation, resulting in treatment-emergent sexual dysfunction in up to 50%–70% of patients.
- **Bupropion** is a Norepinephrine-Dopamine Reuptake Inhibitor (NDRI) with no direct serotonergic activity.
- Because it enhances dopaminergic neurotransmission in the mesolimbic reward pathways, Bupropion carries the lowest incidence of sexual dysfunction among standard antidepressants and is frequently used to treat or avoid SSRI-induced sexual adverse effects.

Final Answer:

Bupropion has the lowest rate of sexual dysfunction among standard antidepressants due to its selective norepinephrine and dopamine reuptake inhibition.

Quick Tip: Antidepressant Profiles:

- High sexual dysfunction: SSRIs (Fluoxetine, Paroxetine, Escitalopram), SNRIs (Venlafaxine).
- Lowest sexual dysfunction: Bupropion (NDRI), Mirtazapine (α_2 -antagonist/5-HT₂ blocker).

48. All are used in the treatment of hypercalcemia except:

- (A) Denosumab
- (B) Bisphosphonates
- (C) Steroids
- (D) Hydration with diuretic

Correct Answer: (C) Steroids

Solution:

Concept:

Hypercalcemia of malignancy (HCM) is an acute medical emergency managed primarily by restoring intravascular volume, enhancing renal calcium clearance, and suppressing osteoclast-mediated bone resorption.

Explanation:

- **Intravenous Hydration and Loop Diuretics:** Aggressive isotonic saline (0.9% NaCl) hydration expands intravascular volume and enhances calciuresis. Loop diuretics (e.g., Furosemide) are added after volume repletion to promote renal calcium excretion.
- **Intravenous Bisphosphonates:** Potent nitrogen-containing bisphosphonates (e.g., Zoledronic acid 4 mg IV, Pamidronate) bind hydroxyapatite crystals and inhibit osteoclast-mediated bone breakdown, serving as standard therapy.
- **Denosumab:** A fully human monoclonal antibody against Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) that potently blocks osteoclast maturation, highly

effective for bisphosphonate-refractory hypercalcemia.

- While systemic corticosteroids (e.g., Prednisone) inhibit 1α -hydroxylase in rare calcitriol-mediated conditions (such as lymphoma or sarcoidosis), they have no efficacy in standard humoral hypercalcemia of malignancy driven by PTHrP or direct osteolytic metastasis from epithelial carcinomas.
- Therefore, steroids are not a universal primary therapy for non-hematologic hypercalcemia of malignancy.

Final Answer:

Systemic steroids are ineffective for the broad majority of solid tumor-related hypercalcemia cases and are not a standard universal hypercalcemia agent compared to hydration, bisphosphonates, and denosumab.

Quick Tip: Hypercalcemia of Malignancy Management:

1. Immediate: IV Normal Saline hydration (200–300 mL/hr) $\pm$ Furosemide (after euvolemia).
2. Definitive: IV Zoledronic acid (4 mg) or Pamidronate.
3. Refractory: Denosumab (120 mg SC).
4. Calcitonin: Rapid onset, short duration (tachyphylaxis in 48h).

49. Which of the following genetic abnormalities commonly found in Multiple Myeloma is not classified as a high-risk feature?

- (A) t (4:14)
- (B) t (11;14)
- (C) t (14:16)
- (D) Del 17p

Correct Answer: (B) t (11;14)

Solution:

Concept:

Risk stratification in Multiple Myeloma (MM) relies heavily on interphase fluorescence in situ hybridization (FISH) cytogenetics to predict disease biology, treatment response, and progression-free survival (mSMART and Revised-ISS criteria).

Explanation:

- High-risk cytogenetic abnormalities defined by IMWG and R-ISS criteria include:
 1. del(17p): Loss of the *TP53* tumor suppressor gene locus (highest risk).
 2. t(4; 14)(p16; q32): Upregulation of *FGFR3* and *MMSET/WHSC1*.
 3. t(14; 16)(q32; q23): Overexpression of the *MAF* oncogene.
 4. t(14; 20) and gain/amp(1q21).
- t(11; 14)(q13; q32) involves translocation of the immunoglobulin heavy chain (*IgH*) locus to the *CCND1* locus, causing cyclin D1 overexpression.
- Translocation t(11; 14) is classified as a standard-risk cytogenetic abnormality and uniquely confers high sensitivity to the BCL-2 inhibitor Venetoclax.

Final Answer:

Translocation t(11; 14) is a standard-risk cytogenetic feature in multiple myeloma, whereas t(4; 14), t(14; 16), and del(17p) are high-risk features.

Quick Tip: Cytogenetic Risk Stratification in Multiple Myeloma (IMWG/mSMART):

- High-Risk: del(17p), t(4; 14), t(14; 16), t(14; 20), 1q gain/amplification.
- Standard-Risk: t(11; 14), t(6; 14), hyperdiploidy, trisomies.
- Note: t(11; 14) predicts responsiveness to Venetoclax (BCL-2 inhibitor).

50. A 50-year-old female patient with a weight of 55kg and a serum creatinine of 0.8mg/dL requires Carboplatin treatment with a target Area Under the Curve (AUC) of 5. What is the total calculated dose of Carboplatin required?

- (A) 490 mg
- (B) 385 mg
- (C) 560 mg
- (D) 625 mg

Correct Answer: (A) 490 mg

Solution:

Concept:

Carboplatin dosing is uniquely determined using target Area Under the Curve (AUC) based on renal clearance according to the mathematically derived Calvert Formula.

Key Formula or Approach:

1. Calvert Formula:

$$\text{Total Carboplatin Dose (mg)} = \text{Target AUC} \times (\text{GFR} + 25)$$

2. Cockcroft-Gault Equation for Creatinine Clearance (Female):

$$\text{CrCl (mL/min)} = \frac{(140 - \text{Age}) \times \text{Weight (kg)}}{72 \times \text{Serum Creatinine (mg/dL)}} \times 0.85$$

Explanation:

- Given clinical parameters:
 - Age = 50 years
 - Weight = 55 kg
 - Serum Creatinine = 0.8 mg/dL
 - Target AUC = 5 mg/mL · min

- Step 1: Calculate the patient's Creatinine Clearance (CrCl):

$$\text{CrCl} = \frac{(140 - 50) \times 55}{72 \times 0.8} \times 0.85$$

$$\text{CrCl} = \frac{90 \times 55}{57.6} \times 0.85 = \frac{4950}{57.6} \times 0.85 \approx 85.94 \times 0.85 = 73.05 \text{ mL/min}$$

- Step 2: Calculate the Carboplatin dose using the Calvert formula:

$$\text{Dose} = 5 \times (73.05 + 25) = 5 \times 98.05 = 490.25 \text{ mg} \approx 490 \text{ mg}$$

Final Answer:

Applying the Cockcroft-Gault clearance (73.05 mL/min) into the Calvert formula yields a total carboplatin dose of approximately 490 mg.

Quick Tip: Calvert Dosing of Carboplatin:

- Formula: Dose = AUC × (GFR + 25).
- Always multiply by 0.85 for female patients when calculating CrCl via Cockcroft-Gault.
- Maximum GFR is capped at 125 mL/min in standard practice.

51. Which is true regarding timing of doxorubicin induced cardiotoxicity?

- (A) Develops by 1 month of stopping therapy
- (B) May develop upto 1 year post stopping therapy
- (C) May develop decades after stopping therapy
- (D) May develop only during the infusion

Correct Answer: (B) May develop upto 1 year post stopping therapy

Solution:

Concept:

Anthracycline-induced cardiotoxicity (Type I cardiotoxicity) is categorized chronologically into acute, early-onset chronic, and late-onset chronic cardiotoxicity.

Explanation:

- **Acute toxicity:** Occurs in < 1% of patients during or immediately after drug infusion, manifesting as transient arrhythmias or pericarditis (usually self-limiting).
- **Early-onset chronic progressive cardiotoxicity:** This is the most common presentation of anthracycline cardiomyopathy, typically manifesting clinically within 1 year post-cessation of chemotherapy.
- Patients develop progressive decline in left ventricular ejection fraction (LVEF), asymptomatic ventricular remodeling, and overt dilated cardiomyopathy during this first year of monitoring.
- Routine serial echocardiography or MUGA scans are specifically recommended at baseline and at 3, 6, and 12 months following completion of anthracycline therapy to identify this early-onset cardiomyopathy window.

Final Answer:

Early-onset chronic doxorubicin-induced cardiotoxicity classically manifests clinically up to 1 year following the completion of treatment.

Quick Tip: Chronology of Anthracycline Cardiotoxicity:

- Acute: During / within hours of infusion (arrhythmias, transient).
- Early-onset Chronic: Within 1 year post-treatment (most frequent presentation of cardiomyopathy).
- Late-onset Chronic: > 1 year to decades later (especially pediatric survivors).

52. Which of the following metastatic sites in Gestational Trophoblastic Neoplasia is not

considered high-risk?

- (A) Lung
- (B) Brain
- (C) Gastrointestinal tract
- (D) Kidney

Correct Answer: (A) Lung

Solution:

Concept:

Gestational Trophoblastic Neoplasia (GTN) includes invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT).

Risk stratification uses the FIGO/WHO prognostic scoring system to categorize patients into low-risk (score ≤ 6) and high-risk (score ≥ 7) disease to determine single-agent versus multi-agent chemotherapy.

Explanation:

- The FIGO/WHO prognostic scoring system assigns risk scores based on the specific anatomical site of metastatic disease:
 1. **Lungs:** Assigned a score of 0 (Low risk), as pulmonary metastases respond favorably to standard chemotherapy without altering prognostic tier.
 2. **Spleen and Kidney:** Assigned a score of 1.
 3. **Gastrointestinal (GI) tract:** Assigned a score of 2 (due to high risk of life-threatening hemorrhage).
 4. **Brain and Liver:** Assigned a score of 4 (High risk / adverse sites requiring intensive multi-agent regimens like EMA-CO).
- Pulmonary involvement is the most common site of metastasis in GTN (present in up to 80% of metastatic cases) and carries an excellent prognosis with single-agent Methotrexate or Actinomycin-D in the absence of other high-risk factors.

Final Answer:

Metastasis to the lung is assigned a FIGO score of 0 and is not considered a high-risk metastatic site in GTN.

Quick Tip: FIGO/WHO GTN Metastatic Site Scoring:

- Score 0: Lung (Low risk).
- Score 1: Spleen, Kidney.
- Score 2: Gastrointestinal tract.
- Score 4: Brain, Liver (High risk → EMA-CO regimen).

53. A patient with non-small cell lung cancer develops anemia and nephrotoxicity after the third cycle of Pemetrexed-Cisplatin chemotherapy. Which of the following drugs is most likely responsible for these adverse effects?

- (A) Cisplatin
- (B) Pemetrexed
- (C) Paclitaxel
- (D) Carboplatin

Correct Answer: (A) Cisplatin

Solution:**Concept:**

Cisplatin is an inorganic platinum coordination complex that forms intrastrand and interstrand DNA crosslinks.

Dose-limiting toxicities of cisplatin include cumulative nephrotoxicity, peripheral sensory neuropathy, ototoxicity, and severe emesis.

Explanation:

- **Nephrotoxicity:** Cisplatin preferentially accumulates in renal proximal convoluted tubule and collecting duct epithelial cells at concentrations five times higher than in serum.
- It induces direct tubular epithelial necrosis, mitochondrial dysfunction, renal vasoconstriction, and impaired glomerular filtration rate (GFR).
- **Anemia:** Cisplatin-induced damage to peritubular interstitial cells in the renal cortex leads to severe suppression of endogenous erythropoietin (EPO) synthesis, resulting in disproportionately severe, normocytic normochromic anemia.
- Pemetrexed is an antifolate that causes myelosuppression, but its toxicities are significantly ameliorated by folic acid and vitamin B₁₂ supplementation, and it is not primarily nephrotoxic.
- The concurrent presentation of worsening renal dysfunction and disproportionate anemia is the hallmark manifestation of cisplatin toxicity.

Final Answer:

Cisplatin is the primary causative agent responsible for both renal tubular injury (nephrotoxicity) and secondary erythropoietin deficiency anemia.

Quick Tip: Cisplatin Toxicity Profile:

- Nephrotoxicity (Proximal tubular necrosis → Prevent with vigorous IV Saline pre/post-hydration).
- Disproportionate Anemia (destruction of peritubular EPO-producing cells).
- Ototoxicity (High-frequency sensorineural hearing loss).
- Hypomagnesemia and Hypokalemia due to renal tubular wasting.

54. What is the ideal management for Stage IB2 cervix cancer?

- (A) Radical hysterectomy
- (B) Radical hysterectomy f/b Radiation therapy and brachytherapy
- (C) Chemo Radiation therapy followed by brachytherapy
- (D) Neo adjuvant chemo followed by surgery

Correct Answer: (A) Radical hysterectomy

Solution:

Concept:

Cervical cancer management is stage-dependent, guided by the Revised FIGO 2018 staging system.

In FIGO 2018, Stage IB is subclassified by maximum clinical tumor dimension: Stage IB1 (< 2 cm), Stage IB2 (≥ 2 cm to < 4 cm), and Stage IB3 (≥ 4 cm).

Explanation:

- For **Stage IB2** cervical cancer (invasive carcinoma ≥ 2 cm and < 4 cm confined to the cervix), radical surgical resection represents the primary standard of care for operable candidates.
- The procedure of choice is a **Type C (Piver-Rutledge Class III) Radical Hysterectomy** with bilateral pelvic lymphadenectomy (and sentinel lymph node mapping).
- Primary surgery allows accurate pathological assessment of surgical margins, parameter invasion, and nodal involvement without exposing the patient to the dual morbidity of upfront chemoradiation.
- For Stage IB3 (≥ 4 cm, formerly Stage IB2 in FIGO 2009), concurrent chemoradiation (CCRT) with weekly cisplatin followed by intracavitary brachytherapy is the preferred standard.

- Dual-modality therapy (radical surgery followed by routine adjuvant radiation) is avoided whenever possible due to increased risk of bladder, rectal, and lower extremity lymphedema.

Final Answer:

The ideal primary management for FIGO 2018 Stage IB2 (2– < 4 cm) cervical cancer is Type C Radical Hysterectomy with bilateral pelvic lymphadenectomy.

Quick Tip: FIGO 2018 Cervical Cancer Stage IB Management:

- Stage IB1 (< 2 cm): Radical Hysterectomy / Trachelectomy (fertility-sparing).
- Stage IB2 (2 to < 4 cm): Radical Hysterectomy + Pelvic Lymphadenectomy.
- Stage IB3 ($\geq$ 4 cm): Definitive Concurrent Chemoradiation (CCRT) + Brachytherapy.

55. A 78-year-old male with metastatic prostate cancer presents with multiple vertebral lytic lesions, including an L1 vertebral collapse causing spinal cord compression and mild neurological deficit. What is the appropriate management for this condition?

- (A) Spinal RT with boost to L1
- (B) Spine stabilization surgery
- (C) Immobilisation with brace and zoledronic acid
- (D) Continue chemotherapy

Correct Answer: (B) Spine stabilization surgery

Solution:

Concept:

Metastatic Epidural Spinal Cord Compression (MESCC) with mechanical spinal instability is an acute oncologic emergency requiring urgent multidisciplinary evaluation.

Management algorithms incorporate neurological status, oncologic radiosensitivity, mechanical

stability (Spinal Instability Neoplastic Score [SINS]), and patient performance status.

Explanation:

- The patient exhibits mechanical structural collapse of the L1 vertebra causing true thecal sac compression and progressive neurological deficits.
- According to the landmark randomized trial by Patchell et al., direct surgical decompression with instrumented spine stabilization surgery followed by postoperative radiotherapy is significantly superior to radiotherapy alone.
- Surgical stabilization restores spinal column mechanical stability, relieves immediate osseous canal compromise, and significantly improves ambulatory rates and sphincter function compared to radiation monotherapy.
- Radiotherapy alone cannot correct mechanical vertebral collapse or structural bony retropulsion into the spinal canal.
- Intravenous high-dose dexamethasone should be administered immediately alongside urgent surgical consultation for spinal stabilization.

Final Answer:

In the presence of pathological vertebral collapse, mechanical spinal instability, and neurological deficit, spine stabilization surgery is the primary treatment of choice.

Quick Tip: Indications for Surgery in Metastatic Cord Compression (Patchell Criteria):

1. Spinal column instability or bony retropulsion/collapse.
2. Progressive neurological deficit during or after RT.
3. Radioresistant tumor histology (e.g., RCC, melanoma).
4. Unknown primary needing diagnostic tissue.

56. A patient treated for acute lymphoblastic leukemia (ALL) with both systemic chemotherapy and prophylactic cranial radiotherapy present 2 years later with headache and diplopia. What is the most likely cause?

- (A) Leukemia recurrence
- (B) Radiation-induced second malignancy
- (C) Pituitary adenoma
- (D) Cerebrovascular side effect

Correct Answer: (A) Leukemia recurrence

Solution:

Concept:

The central nervous system (CNS) represents an anatomical sanctuary site in Acute Lymphoblastic Leukemia (ALL) due to limited penetration of standard systemic chemotherapeutic agents across the blood-brain barrier.

Relapse in ALL occurs most frequently within the first 2 to 3 years following initial complete remission.

Explanation:

- Isolated or combined CNS relapse occurs in up to 5%–10% of ALL patients and characteristically manifests within the first 2 to 3 years of therapy completion.
- Leukemic leptomeningeal infiltration causes increased intracranial pressure (headache, vomiting, papilledema) and cranial neuropathies (diplopia secondary to Cranial Nerve VI / abducens nerve palsy).
- A diagnostic lumbar puncture with CSF cytology/flow cytometry and neuroimaging (MRI brain/spine) is urgently required to confirm blast recurrence in the subarachnoid space.

- Radiation-induced secondary solid malignancies of the CNS (e.g., meningiomas, gliomas) possess a long latency period, typically presenting 10–20 years post-irradiation.
- Thus, acute subacute neurological deterioration 2 years post-therapy is most likely attributable to leukemic CNS recurrence.

Final Answer:

The presentation of headache and diplopia 2 years after ALL treatment is most commonly due to central nervous system leukemic recurrence.

Quick Tip: CNS Relapse in ALL:

- Timing: Peak incidence within 2–3 years.
- Classic signs: Morning headache, vomiting, diplopia (CN VI palsy), facial weakness (CN VII palsy).
- Diagnosis: CSF pleocytosis with leukemic blasts on cytopspin / flow cytometry.
- Radiation second cancers take > 10 years to develop.

57. Which malignant tumor is primarily defined by the recurrent chromosomal translocation t(11;22) (q24;q12)?

- (A) Ewing Sarcoma
- (B) Clear Cell Sarcoma
- (C) Desmoplastic Small Round Cell Tumor
- (D) Rhabdomyosarcoma

Correct Answer: (A) Ewing Sarcoma

Solution:

Concept:

Small round blue cell tumors of bone and soft tissue are defined by distinct, pathognomonic

reciprocal chromosomal translocations resulting in aberrant chimeric transcription factor fusion oncoproteins.

Explanation:

- **Ewing Sarcoma** is genetically defined by the chromosomal translocation $t(11;22)(q24;q12)$ in approximately 85%–90% of cases.
- This reciprocal translocation fuses the 5' transactivation domain of the *EWSR1* gene on chromosome 22q12 with the 3' DNA-binding domain of the *FLI1* ETS-family transcription factor gene on chromosome 11q24.
- The resulting *EWSR1-FLI1* fusion oncoprotein functions as a potent driver of tumorigenesis and serves as the definitive diagnostic biomarker on RT-PCR or FISH.
- **Clear Cell Sarcoma** is characterized by $t(12;22)(q13;q12)$ generating the *EWSR1-ATF1* fusion.
- **Desmoplastic Small Round Cell Tumor (DSRCT)** is characterized by $t(11;22)(p13;q12)$ generating the *EWSR1-WT1* fusion.
- **Alveolar Rhabdomyosarcoma** is defined by $t(2;13)(q35;q14)$ [*PAX3-FOXO1*] or $t(1;13)(p36;q14)$ [*PAX7-FOXO1*].

Final Answer:

The balanced chromosomal translocation $t(11;22)(q24;q12)$ is pathognomonic for Ewing Sarcoma.

Quick Tip: Classic Sarcoma Translocations:

- Ewing Sarcoma: $t(11;22)(q24;q12) \rightarrow EWSR1-FLI1$.
- DSRCT: $t(11;22)(p13;q12) \rightarrow EWSR1-WT1$.
- Synovial Sarcoma: $t(X;18)(p11;q11) \rightarrow SS18-SSX$.
- Myxoid Liposarcoma: $t(12;16)(q13;p11) \rightarrow FUS-DDIT3$.

58. What is the most common mutation seen in malignant melanoma?

- (A) BAP1
- (B) BRAF
- (C) NF1
- (D) NRAS

Correct Answer: (B) BRAF

Solution:

Concept:

Cutaneous malignant melanoma pathogenesis involves constitutive hyperactivation of the Mitogen-Activated Protein Kinase (MAPK) signaling pathway (RAS-RAF-MEK-ERK cascade). Somatic driver mutations in this pathway are therapeutically targetable with small-molecule kinase inhibitors.

Explanation:

- Somatic activating mutations in the **BRAF** gene are present in approximately 40%–60% of all cutaneous melanomas, making it the single most common driver mutation.
- More than 80%–90% of **BRAF** mutations involve a single valine-to-glutamic acid substitution at codon 600 (**BRAF V600E**), followed by **BRAF V600K** (10%–20%).
- This mutation locks the BRAF kinase in a constitutively active conformation, driving

uncontrolled cell cycle progression and proliferation independent of upstream RAS signaling.

- Other recurrent driver mutations in melanoma occur at lower frequencies: *NRAS* (15%–20%), *NF1* (10%–15%), and *KIT* (2%–5%, enriched in mucosal and acral lentiginous melanomas).
- *BAP1* mutations are characteristic of uveal melanoma and hereditary tumor syndromes.

Final Answer:

BRAF mutations (predominantly V600E) represent the most frequent genetic alterations in cutaneous malignant melanoma.

Quick Tip: Genomic Subtypes of Cutaneous Melanoma (TCGA):

1. *BRAF* mutated: ~ 50% (Target with Dabrafenib + Trametinib).
2. *NRAS* mutated: ~ 20%.
3. *NF1* mutated: ~ 15%.
4. Triple Wild-Type: ~ 15% (Check for *KIT* mutations in acral/mucosal sites).

59. In carcinoma vulva, which of the following is not a prognostic factor?

- (A) Tumor grade
- (B) Depth of invasion
- (C) Positive lymph nodes
- (D) Lymphovascular space invasion (LVSI)

Correct Answer: (A) Tumor grade

Solution:

Concept:

Vulvar squamous cell carcinoma (VSCC) staging and prognosis are primarily determined by locoregional tumor burden, inguino-femoral lymph node status, and anatomical depth characteristics according to FIGO/AJCC systems.

Explanation:

- **Inguino-femoral Lymph Node Status:** The single most powerful independent prognostic indicator in vulvar carcinoma is the presence, number, size, and extracapsular spread of positive inguino-femoral lymph node metastases.
- **Depth of Stromal Invasion:** Crucial parameter defining Stage IA (≤ 1 mm depth of invasion, where nodal dissection can be safely omitted due to $< 1\%$ risk of metastases) versus deeper lesions (> 1 mm) that require lymphadenectomy.
- **Lymphovascular Space Invasion (LVSI):** A validated adverse histological feature strongly associated with nodal metastasis and locoregional recurrence.
- **Tumor Histologic Grade:** While routinely reported on pathology, histological differentiation/grade (well, moderate, poorly differentiated) has repeatedly failed in multivariate analyses to demonstrate independent prognostic value for survival or nodal involvement.
- Consequently, histological grade is omitted from the FIGO staging system and does not dictate adjuvant therapy algorithms.

Final Answer:

Tumor histologic grade is not an independent prognostic factor in vulvar squamous cell carcinoma.

Quick Tip: Prognostic Factors in Vulvar Cancer:

- Most important: Inguinofemoral lymph node status (number, size, extracapsular extension).
- Key surgical determinant: Depth of invasion (> 1 mm mandates groin lymph node dissection).
- Tumor grade is NOT an independent prognostic factor.

60. Based on the clinical image, what is the T stage of this tumor?



- (A) T4b
- (B) T4a
- (C) T2
- (D) T3

Correct Answer: (A) T4b

Solution:

Concept:

The AJCC/UICC TNM staging system for breast cancer categorizes primary tumor extent (T stage) based on maximum dimensions and local invasion into overlying skin or underlying chest wall structures.

Explanation:

- The clinical photograph demonstrates cutaneous erythema, edema, and prominent dermal pore accentuation resembling the skin of an orange, pathognomonicly termed *peau d'orange*.

- Peau d'orange develops when malignant tumor emboli obstruct subdermal lymphatic drainage, causing cutaneous interstitial lymphedema and tethering at hair follicles.
- According to AJCC 8th edition staging rules:
 1. **T4a:** Extension to the chest wall (ribs, intercostal muscles, or serratus anterior muscle; pectoralis muscle invasion alone does not qualify).
 2. **T4b:** Ulceration and/or macroscopic skin edema (including peau d'orange) and/or ipsilateral satellite skin nodules that do not meet the criteria for inflammatory breast cancer.
 3. **T4c:** Both T4a and T4b features simultaneously present.
 4. **T4d:** Inflammatory carcinoma (diffuse erythema/edema involving $\geq 1/3$ of the breast).
- Therefore, localized peau d'orange and skin infiltration is classified as T4b.

Final Answer:

The presence of peau d'orange and skin involvement corresponds to stage T4b in the AJCC breast cancer staging classification.

Quick Tip: AJCC Breast Cancer T4 Subcategories:

- T4a: Chest wall fixation / deep extension.
- T4b: Skin ulceration, peau d'orange / skin edema, or satellite skin nodules.
- T4c: Both T4a and T4b.
- T4d: Inflammatory breast cancer (involves $\geq 1/3$ of breast skin).

61. Which of the following is not a laboratory criterion of Tumor Lysis Syndrome (TLS)?

- (A) Serum potassium > 8 mEq/L
- (B) Serum uric acid > 8 mg/dL

(C) Serum calcium < 7 mg/dL

(D) Serum phosphate < 4.5 mg/dL

Correct Answer: (D) Serum phosphate < 4.5 mg/dL

Solution:

Concept:

The Cairo-Bishop definition is the internationally recognized consensus classification system used to diagnose and grade Laboratory Tumor Lysis Syndrome (LTLS) and Clinical Tumor Lysis Syndrome (CTLS).

Explanation:

- Laboratory TLS (Cairo-Bishop criteria) requires ≥ 2 of the following metabolic abnormalities occurring simultaneously within 3 to 7 days after starting cytotoxic therapy:
 1. **Hyperuricemia:** Serum Uric Acid ≥ 8.0 mg/dL (or $\geq 476 \mu\text{mol/L}$) or a 25% increase from baseline.
 2. **Hyperkalemia:** Serum Potassium ≥ 6.0 mEq/L (or ≥ 6.0 mmol/L) or a 25% increase from baseline.
 3. **Hyperphosphatemia:** Serum Phosphate ≥ 4.5 mg/dL (or ≥ 1.45 mmol/L in adults; ≥ 6.5 mg/dL in children) or a 25% increase from baseline.
 4. **Hypocalcemia:** Corrected Serum Calcium ≤ 7.0 mg/dL (or ionized $\text{Ca}^{2+} < 1.12$ mg/dL) or a 25% decrease from baseline.
- In TLS, massive cellular lysis releases intracellular inorganic phosphate into the bloodstream, producing elevated serum phosphate (≥ 4.5 mg/dL), NOT low phosphate (< 4.5 mg/dL).

Final Answer:

A serum phosphate level < 4.5 mg/dL is normal and is not a criterion; elevated phosphate (≥ 4.5 mg/dL) defines TLS.

Quick Tip: Cairo-Bishop Laboratory TLS Criteria (≥ 2 required):

- Uric acid ≥ 8.0 mg/dL (or $\uparrow 25\%$).
- Potassium ≥ 6.0 mEq/L (or $\uparrow 25\%$).
- Phosphate ≥ 4.5 mg/dL (or $\uparrow 25\%$).
- Calcium ≤ 7.0 mg/dL (or $\downarrow 25\%$).

Mnemonic: "PUCK" - Phosphate $\uparrow$, Uric acid $\uparrow$, Calcium $\downarrow$, Potassium $\uparrow$.

62. Which of the following is not a clinical manifestation of Tumor Lysis Syndrome (TLS)?

- (A) Seizures
- (B) Respiratory failure
- (C) Renal failure / Creatinine increase
- (D) Arrhythmia

Correct Answer: (B) Respiratory failure

Solution:

Concept:

Clinical Tumor Lysis Syndrome (CTLS) is diagnosed when Laboratory TLS is accompanied by life-threatening end-organ clinical sequelae directly induced by electrolyte shifts and metabolic crystallization.

Explanation:

- According to the Cairo-Bishop staging classification, Clinical TLS is defined by the presence of Laboratory TLS along with at least one of the following specific clinical toxicities:
 1. **Renal failure:** Serum creatinine ≥ 1.5 times the upper limit of normal (or oliguria/anuria).
 2. **Cardiac arrhythmias / Sudden death:** Induced by severe hyperkalemia or hypocalcemia.
 3. **Seizures, tetany, or neuromuscular irritability:** Precipitated by severe hypocalcemia.

- Direct acute respiratory failure is not a defining diagnostic criterion of Clinical TLS in consensus scoring systems.
- Although pulmonary edema can develop secondary to severe oliguric renal failure or excessive fluid administration, respiratory failure per se is not an intrinsic defining clinical criterion of TLS.

Final Answer:

Respiratory failure is not a formal diagnostic clinical component of the Cairo-Bishop criteria for Clinical Tumor Lysis Syndrome.

Quick Tip: Cairo-Bishop Clinical TLS Criteria (LTLS + ≥ 1 of):

1. Renal Insufficiency (Creatinine $\geq 1.5 \times$ ULN).
2. Cardiac Arrhythmia / Sudden death.
3. Seizures / Neuromuscular irritability.

63. Which of the following chemotherapy agents has the least gonadotoxic risk in females?

- (A) Methotrexate
- (B) Busulfan
- (C) Cyclophosphamide
- (D) Ifosfamide

Correct Answer: (A) Methotrexate

Solution:

Concept:

The degree of chemotherapy-induced premature ovarian insufficiency (POI) depends primarily

on whether the cytotoxic agent targets actively dividing cells versus resting, non-dividing primordial follicles.

Explanation:

- **Alkylating agents** (e.g., Cyclophosphamide, Ifosfamide, Busulfan, Melphalan) are cell-cycle non-specific agents that directly crosslink DNA in non-dividing, resting primordial follicles in the ovarian cortex.
- This induces massive apoptosis of the permanent ovarian follicular reserve, resulting in a high risk of permanent amenorrhea and infertility (> 80%).
- **Methotrexate** is an S-phase cell cycle-specific antimetabolite that competitively inhibits dihydrofolate reductase (DHFR).
- Because primordial oocytes are arrested in the dictyotene stage of prophase I (non-replicating phase), they are inherently resistant to S-phase-specific antimetabolites.
- Consequently, Methotrexate is classified in the low / negligible gonadotoxic risk category (< 20% incidence of permanent ovarian failure).

Final Answer:

Methotrexate has the least gonadotoxic risk in females among the options, as it is an S-phase specific antimetabolite that spares non-dividing primordial follicles.

Quick Tip: Gonadotoxicity Risk Stratification in Females:

- High Risk (> 80%): Alkylating agents (Cyclophosphamide, Busulfan, Ifosfamide, Procarbazine).
- Intermediate Risk (20%–80%): Doxorubicin, Cisplatin, Carboplatin.
- Low/Minimal Risk (< 20%): Methotrexate, 5-Fluorouracil, Vincristine, Bleomycin.

64. What is the most likely cause of male infertility after chemotherapy?

- (A) Cyclophosphamide
- (B) Vincristine
- (C) Paclitaxel
- (D) Bleomycin

Correct Answer: (A) Cyclophosphamide

Solution:

Concept:

Chemotherapy-induced male gonadotoxicity involves cytotoxic damage to the germinal epithelium of the seminiferous tubules, resulting in oligospermia or permanent azoospermia. Alkylating agents exhibit the highest degree of cumulative, irreversible germ cell toxicity in post-pubertal and adult males.

Explanation:

- Cyclophosphamide generates active phosphoramidate mustard metabolites that crosslink DNA within dividing and stem-cell spermatogonia.
- Cumulative cyclophosphamide doses exceeding 7.5 g/m^2 (or $> 400 \text{ mg/kg}$) result in irreversible germinal aplasia, leading to Sertoli-cell-only syndrome and permanent azoospermia in over 80%–90% of treated males.
- In contrast, Vinca alkaloids (Vincristine), Taxanes (Paclitaxel), and Antitumor antibiotics (Bleomycin) carry substantially lower gonadotoxic potential, with recovery of spermatogenesis typically occurring within 1 to 3 years following treatment cessation.
- Therefore, semen cryopreservation (sperm banking) prior to starting cyclophosphamide-containing chemotherapy is mandatory standard practice.

Final Answer:

Cyclophosphamide is the most common and potent cause of permanent male infertility following chemotherapy.

Quick Tip: Male Gonadotoxicity Rules:

- Cyclophosphamide: Cumulative dose $> 7.5 \text{ g/m}^2 \rightarrow$ Permanent azoospermia in $> 85\%$.
- Leydig cells are relatively resistant (testosterone production usually preserved).
- Sperm cryopreservation must ALWAYS be offered prior to initiation of alkylating therapy.

65. Which cell type is most sensitive to chemotherapy-induced cytotoxicity, leading to azoospermia in males?

- (A) Leydig cell
- (B) Spermatogonial cell
- (C) Germ cell
- (D) Sertoli cell

Correct Answer: (B) Spermatogonial cell

Solution:**Concept:**

The testicular parenchyma consists of somatic supporting cells (Sertoli cells and Leydig cells) and germline cells at various stages of differentiation within the seminiferous tubules. Cellular sensitivity to radiation and cytotoxic antineoplastic agents is directly proportional to mitotic rate and proliferative activity (Bergonié-Tribondeau Law).

Explanation:

- **Spermatogonial Stem Cells (Type A and Type B spermatogonia)** are actively dividing, mitotically active germline precursors located at the basement membrane of the seminiferous tubules.

- Due to their rapid cellular proliferation kinetics, spermatogonia are the most sensitive target cells damaged by cytotoxic chemotherapy and ionising radiation.
- Destruction and depletion of the self-renewing spermatogonial stem cell pool halts downstream spermatogenesis, directly producing azoospermia.
- **Sertoli cells** (which provide structural/nutritional support) and **Leydig cells** (which synthesize testosterone in the interstitium) are quiescent, non-dividing somatic cells that are highly resistant to chemotherapy-induced cell death.
- Consequently, chemotherapy typically results in exocrine testicular failure (azoospermia/infertility) while endocrine function (normal serum testosterone and secondary sexual characteristics) remains intact.

Final Answer:

Spermatogonial cells are the most sensitive cell type in the testes to chemotherapy-induced cytotoxicity, leading to profound depletion of sperm production.

Quick Tip: Testicular Cell Sensitivity:

- Spermatogonia: Extremely sensitive (rapidly dividing → azoospermia).
- Sertoli Cells: Chemotherapy-resistant (somatic support).
- Leydig Cells: Chemotherapy-resistant (endocrine testosterone production preserved).

66. TLS (Tumour Lysis Syndrome) occurs within how many days of chemotherapy?

- (A) 1-5 days
- (B) 5-10 days
- (C) More than 20 days

(D) 1 month

Correct Answer: (A) 1-5 days

Solution:

Concept:

Tumor Lysis Syndrome (TLS) occurs when highly chemosensitive, rapidly proliferating tumor cells undergo massive apoptotic breakdown immediately following the initiation of cytotoxic antineoplastic therapy.

The chronological onset reflects the rapid cell-kill kinetics of induction chemotherapy.

Explanation:

- According to the standardized Cairo-Bishop definition, Laboratory TLS typically manifests within 12 to 72 hours (1 to 5 days) after starting chemotherapy.
- Peak elevations in intracellular electrolytes and metabolites occur sequentially:
 1. Serum Potassium rises rapidly within 12–24 hours.
 2. Serum Phosphorus and Uric Acid peak between 24–72 hours (days 1 to 3).
 3. Secondary Hypocalcemia and Acute Kidney Injury manifest between 48–96 hours (days 2 to 4).
- Because the vast majority of metabolic derangements occur within the first 5 days, intensive clinical monitoring, hydration, and urate-lowering therapy are concentrated during this critical 1–5 day window.
- TLS rarely develops beyond 7 days post-chemotherapy unless new cytotoxic treatments are administered.

Final Answer:

Tumor Lysis Syndrome classically develops within 1 to 5 days following the initiation of

chemotherapy.

Quick Tip: Timeline of TLS:

- Typical onset: 12–72 hours post-chemo.
- Critical monitoring window: Days 1 to 5.
- Serial labs (K^+ , Uric acid, PO_4^{3-} , Ca^{2+} , Creatinine) must be monitored every 4–8 hours in high-risk patients during the first 48–72 hours.

67. What is the most suitable line for short term chemo administration?

- (A) PICC
- (B) CVC
- (C) Peripheral iv line
- (D) Port-a-Cath

Correct Answer: (C) Peripheral iv line

Solution:

Concept:

Vascular access device selection in oncology depends on the duration of therapy, frequency of administration, vessel characteristics, and whether the chemotherapeutic agent is a vesicant, irritant, or non-vesicant drug.

Explanation:

- For short-term chemotherapy administration (e.g., a few single-day cycles, adjuvant regimens of brief duration, or non-vesicant drug infusions), a simple peripheral intravenous (IV) line / cannula is the most suitable and cost-effective vascular access.
- Peripheral lines do not require invasive surgical placement, carry zero risk of procedural

pneumothorax or hemothorax, and have a minimal overall risk of long-term central venous stenosis.

- **Peripherally Inserted Central Catheters (PICC):** Ideal for intermediate-term chemotherapy (e.g., weeks to 3–6 months) or continuous outpatient infusional regimens.
- **Totally Implanted Port (Port-a-Cath):** Preferred for long-term chemotherapy (> 6 months), multi-cycle regimens, and long-term surveillance blood sampling.
- **Non-tunneled Central Venous Catheter (CVC):** Indicated for acute, short-term inpatient intensive care or stem cell transplantation conditioning, but inappropriate for routine outpatient chemotherapy.

Final Answer:

A peripheral IV line is the most suitable, least invasive access for short-term chemotherapy administration.

Quick Tip: Vascular Access Selection Guide:

- Short-term / Brief treatment: Peripheral IV Line.
- Intermediate-term (1–6 months): PICC Line.
- Long-term (> 6 months / Vesicant regimens): Totally Implanted Port (Port-a-Cath).

68. A patient with Hodgkin Lymphoma presents with right cervical and mediastinal lymph node enlargement, associated with B symptoms and splenic involvement. What is the stage according to the Ann Arbor staging system?

- (A) II BES
- (B) III BES
- (C) III BS

(D) II BS

Correct Answer: (B) III BES

Solution:

Concept:

The Cotswolds-modified Ann Arbor staging system is the anatomical staging classification used for Hodgkin Lymphoma.

The diaphragm serves as the primary anatomical dividing landmark to determine disease stage.

Explanation:

- In the Ann Arbor classification:
 1. **Stage I:** Involvement of a single lymph node region or lymphoid structure.
 2. **Stage II:** Involvement of two or more lymph node regions on the same side of the diaphragm.
 3. **Stage III:** Involvement of lymph node regions or lymphoid structures on both sides of the diaphragm.
 4. **Stage IV:** Disseminated involvement of one or more extralymphatic organs.
- In this patient:
 - Right cervical and mediastinal lymph nodes are located above the diaphragm.
 - The spleen is anatomically and functionally considered a lymphoid organ located below the diaphragm, denoted by the suffix "S".
 - Because disease is present on both sides of the diaphragm (cervical/mediastinal nodes above, spleen below), this is Stage III.
- Systemic B symptoms (fever $> 38^{\circ}\text{C}$, drenching night sweats, $> 10\%$ weight loss) are denoted by suffix "B".
- Extralymphatic contiguous extension or splenic notation is classified as Stage III BES (or

Stage III BS).

Final Answer:

Lymphoid involvement above the diaphragm (cervical, mediastinal) and below the diaphragm (spleen), along with B-symptoms, is classified as Stage III BES.

Quick Tip: Ann Arbor Staging Suffixes:

- A: Asymptomatic / No B symptoms.
- B: B-symptoms present (Fever, Night sweats, Weight loss > 10%).
- S: Splenic involvement (counts as lymphoid tissue below diaphragm → makes disease at least Stage III if nodes above diaphragm are involved).
- E: Extranodal contiguous extension.

69. The most appropriate management plan for a patient with massive pulmonary thromboembolism (PTE) presenting with hypoxia but normal blood pressure (normotensive), who is currently on Sunitinib for renal cell carcinoma, is:

- (A) Start warfarin and consider for thrombolysis
- (B) Start DOAC with apixaban
- (C) Start low molecular weight heparin and continue for 6 months
- (D) Thrombolysis with alteplase and anticoagulation with low molecular weight heparin

Correct Answer: (C) Start low molecular weight heparin and continue for 6 months

Solution:

Concept:

Cancer-Associated Thrombosis (CAT) presenting as Pulmonary Embolism (PE) is risk-stratified based on hemodynamic stability into high-risk (massive / hypotensive shock) and intermediate-risk (submassive / normotensive with RV strain or hypoxia).

Management must balance effective clot resolution against hemorrhagic risks from concomitant targeted VEGF TKIs.

Explanation:

- The patient is normotensive (hemodynamically stable); therefore, by definition, this is intermediate-risk (submassive) pulmonary embolism, not high-risk hemodynamically unstable PE.
- Systemic thrombolysis (e.g., with Alteplase) is strictly reserved for high-risk PE with sustained hemodynamic shock or hypotension (Systolic BP < 90 mmHg), because thrombolysis in normotensive cancer patients carries a high risk of catastrophic major bleeding without proven mortality benefit.
- According to international clinical guidelines (ASCO, ITAC, CHEST, ESMO), therapeutic anticoagulation with Low Molecular Weight Heparin (LMWH) for at least 6 months is the standard of care for cancer-associated venous thromboembolism.
- While DOACs are options in cancer-associated thrombosis, Sunitinib interacts with CYP3A4 and P-glycoprotein pathways and carries an inherent bleeding risk, making LMWH the safest and most established agent.

Final Answer:

Because the patient is normotensive, systemic thrombolysis is not indicated; therapeutic LMWH anticoagulation for 6 months is the standard management.

Quick Tip: Pulmonary Embolism in Cancer Management:

- Massive PE with Shock (BP < 90 mmHg) → Systemic Thrombolysis + Anticoagulation.
- Submassive / Normotensive PE (Stable BP) → Therapeutic Anticoagulation (LMWH or DOAC) for ≥ 6 months without thrombolysis.

70. What is the primary accepted mechanism of anthracycline cardiotoxicity?

- (A) Inhibition of Topoisomerase II in cardiocytes
- (B) Damage by reactive oxygen radicals
- (C) Endothelial damage
- (D) Direct interference with L-type calcium channels

Correct Answer: (B) Damage by reactive oxygen radicals

Solution:

Concept:

Anthracyclines (such as Doxorubicin and Daunorubicin) are potent antineoplastic agents whose clinical application is limited by cumulative, dose-dependent myocardial damage.

Extensive preclinical and clinical evidence establishes oxidative stress and free radical generation as the primary classic mediator of anthracycline-induced cardiomyocyte apoptosis.

Explanation:

- Anthracyclines possess a quinone moiety that undergoes one-electron enzymatic reduction by mitochondrial enzymes (e.g., NADH dehydrogenase) to form a semiquinone radical.
- In the presence of molecular oxygen, the semiquinone radical rapidly transfers its electron to oxygen, generating superoxide anions ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2), and hydroxyl radicals ($OH^\bullet$).
- Furthermore, doxorubicin forms high-affinity complexes with intracellular free iron (Fe^{3+}), catalyzing Haber-Weiss and Fenton reactions that massively amplify reactive oxygen species (ROS) formation.
- Cardiomyocytes are particularly vulnerable to ROS damage because they possess

exceptionally low levels of antioxidant protective enzymes (such as catalase and glutathione peroxidase).

- Unchecked ROS induce lipid peroxidation of the mitochondrial inner membrane (specifically cardiolipin), opening mitochondrial permeability transition pores and triggering irreversible cardiomyocyte apoptosis.
- The cardioprotective efficacy of Dexrazoxane (an intracellular iron chelator) directly proves the fundamental role of iron-mediated free radical generation in anthracycline cardiotoxicity.

Final Answer:

The generation of reactive oxygen species (free radicals) causing oxidative membrane damage is the primary accepted classic mechanism of anthracycline-induced cardiotoxicity.

Quick Tip: Pathophysiology of Anthracycline Cardiotoxicity:

- Classical Mechanism: Iron-dependent Free Radical / ROS generation → lipid peroxidation of cardiolipin.
- Molecular Target: Topoisomerase II β in quiescent cardiomyocytes → triggers mitochondrial failure.
- Protection: Dexrazoxane (Iron chelator / Topo II β modulator).

71. Which of the following statements best defines the concept of the Ceiling Effect in pharmacology?

- (A) Adding further dose will be less likely to produce effects
- (B) The lowest dose of a drug required to achieve a therapeutic effect
- (C) The point at which a drug's absorption rate equals its elimination rate
- (D) An adverse drug reaction that is unpredictable and not dose-related

Correct Answer: (A) Adding further dose will be less likely to produce effects

Solution:

Concept:

In pharmacodynamics, the dose-response relationship dictates how increasing drug concentrations correlate with therapeutic efficacy.

The ceiling effect ($E_{\max}$) refers to the phenomenon where a drug reaches its maximal achievable biological response, beyond which dose escalation produces no further therapeutic benefit.

Explanation:

- The ceiling effect occurs when all available specific target receptors are fully occupied (receptor saturation) or downstream post-receptor intracellular signaling pathways are maximally activated.
- Once the ceiling threshold is reached, escalating the dosage further yields diminishing or no incremental therapeutic efficacy, while significantly increasing the incidence and severity of dose-dependent toxicities.
- In analgesic pharmacology, non-opioids (e.g., Paracetamol, NSAIDs) and partial μ -opioid agonists (e.g., Buprenorphine) exhibit a prominent ceiling effect for analgesia.
- In contrast, pure μ -opioid receptor full agonists (such as Morphine, Hydromorphone, and Fentanyl) do not possess a true pharmacological ceiling effect for pain relief, allowing continuous titration against escalating pain severity.
- Option (B) defines the minimum effective concentration/threshold dose, Option (C) defines steady-state pharmacokinetics, and Option (D) describes idiosyncratic adverse reactions.

Final Answer:

The ceiling effect is defined as the pharmacodynamic plateau where administering additional

doses will not produce greater therapeutic effects.

Quick Tip: Ceiling Effect in Analgesic Pharmacology:

- Full μ -Agonists (Morphine, Fentanyl, Oxycodone): NO ceiling effect for analgesia (dose titrated to relief or toxicity).
- Partial Agonists / Mixed Agonists (Buprenorphine, Pentazocine): HAVE a ceiling effect for analgesia and respiratory depression.
- NSAIDs / Acetaminophen: HAVE a definite ceiling effect.

72. An elderly man with bone metastasis, receiving intravenous opioids, with respiratory rate of 8/min. Which of the following should not be administered?

- (A) Pentazocine
- (B) Nalbuphine
- (C) Fentanyl
- (D) Buprenorphine

Correct Answer: (C) Fentanyl

Solution:

Concept:

Opioid-induced respiratory depression (OIRD) is defined by a significant reduction in respiratory rate (typically < 10 breaths/min) accompanied by sedation and hypercapnia. Recognizing acute opioid toxicity and avoiding administration of additional full μ -opioid agonists is critical to prevent fatal respiratory arrest.

Explanation:

- A respiratory rate of 8 breaths/min in a cancer patient receiving systemic opioids indicates severe, life-threatening opioid-induced central respiratory depression mediated by μ_2 -opioid receptors in the brainstem.

- **Fentanyl** is a high-potency, pure μ -opioid full agonist (approximately 50 to 100 times more potent than morphine). Administering additional fentanyl in the setting of existing severe bradypnea will worsen respiratory depression, precipitate hypercapnic respiratory failure, and cause fatal cardiac arrest.
- Immediate management of OIRD requires withholding all further μ -agonist opioids, providing supportive airway and oxygen therapy, and titrating the competitive opioid receptor antagonist **Naloxone** in dilute aliquots (0.04–0.1 mg IV every 2 minutes) to reverse respiratory depression without abruptly precipitating severe pain crisis.
- Pentazocine, Nalbuphine, and Buprenorphine possess mixed agonist-antagonist or partial agonist properties and are not pure full μ -agonists, though they are also avoided during active full-agonist maintenance.

Final Answer:

Fentanyl, as a potent pure μ -opioid receptor agonist, must not be administered to a patient already experiencing severe opioid-induced respiratory depression.

Quick Tip: Opioid-Induced Respiratory Depression (OIRD) Management:

- Diagnostic sign: Respiratory Rate < 10/min + Pinpoint pupils + Sedation.
- Immediate action: Stop all pure μ -agonists (Fentanyl, Morphine).
- Antidote: Dilute Naloxone (0.04–0.08 mg IV aliquots titrated to normalize ventilation without provoking acute withdrawal storm).

73. Which of the following is included in the Khorana Score?

- (A) Pre chemo HB
- (B) Performance status
- (C) History of previous VTE

(D) D-dimer level

Correct Answer: (A) Pre chemo HB

Solution:

Concept:

The Khorana Risk Score (KRS) is a validated predictive risk-assessment model used to estimate the risk of cancer-associated venous thromboembolism (VTE) in ambulatory cancer patients prior to starting systemic chemotherapy.

Explanation:

- The Khorana Score calculates VTE risk based on 5 baseline clinical and laboratory variables evaluated prior to chemotherapy initiation:
 1. **Primary Site of Cancer:** - Very High Risk (2 points): Stomach, Pancreas. - High Risk (1 point): Lung, Lymphoma, Gynecologic, Bladder, Testicular.
 2. **Pre-chemotherapy Platelet Count:** $\geq 350 \times 10^9/L$ (1 point).
 3. **Pre-chemotherapy Hemoglobin (Pre-chemo Hb):** $< 10 \text{ g/dL}$ or use of red cell growth factors / ESAs (1 point).
 4. **Pre-chemotherapy Leukocyte Count (WBC):** $> 11 \times 10^9/L$ (1 point).
 5. **Body Mass Index (BMI):** $\geq 35 \text{ kg/m}^2$ (1 point).
- Patients with a Khorana score ≥ 2 are classified as high risk for thrombosis and are candidates for primary thromboprophylaxis with direct oral anticoagulants (DOACs like Apixaban or Rivaroxaban) or LMWH.
- ECOG performance status, previous VTE history, and baseline D-dimer are not components of the classic 5-item Khorana scoring tool.

Final Answer:

Pre-chemotherapy hemoglobin ($< 10 \text{ g/dL}$) is one of the five core predictive parameters incorporated in the Khorana Score.

Quick Tip: Khorana Risk Score Parameters:

1. Cancer Site: Stomach/Pancreas (+2), Lung/Lymphoma/Gyn/GU (+1).
2. Pre-chemo Hemoglobin < 10 g/dL or ESA use (+1).
3. Platelet count $\geq 350,000/\mu\text{L}$ (+1).
4. Leukocyte count > 11,000/ μL (+1).
5. BMI $\geq 35 \text{ kg/m}^2$ (+1).

Score $\geq 2 \rightarrow$ High Risk $\rightarrow$ Consider primary DOAC prophylaxis.

74. Which of the following interventions is the most critical in Central Venous Catheter (CVC) nursing care to prevent Catheter-Related Bloodstream Infection (CRBSI)?

- (A) Sterile hand technique while handling and dressing
- (B) Flushing before and after chemo
- (C) Applying a transparent dressing and ensuring it remains clean, dry, and intact.
- (D) Using positive pressure flushing technique upon catheter disconnection.

Correct Answer: (A) Sterile hand technique while handling and dressing

Solution:

Concept:

Catheter-Related Bloodstream Infections (CRBSI) and Central Line-Associated Bloodstream Infections (CLABSI) are major causes of hospital-acquired morbidity in immunocompromised oncology patients.

Strict adherence to evidence-based aseptic bundles during catheter maintenance is the foundation of infection prevention.

Explanation:

- Microorganisms colonize central venous lines through two primary routes: extraluminal migration along the cutaneous tract (early post-insertion) and intraluminal contamination during hub handling and infusion access (predominant in maintained lines).

- Rigorous **sterile hand technique, sterile gloving, and strict hand hygiene** before any catheter manipulation or dressing change represent the single most effective barrier against introducing pathogenic skin flora (such as *Staphylococcus epidermidis* and *Staphylococcus aureus*).
- While transparent semipermeable dressings and positive-pressure flushing techniques are supportive care elements, they cannot compensate for breaches in sterile hand technique.
- CDC and INS guidelines mandate maximal sterile barrier precautions and strict aseptic non-touch techniques during all central line access and dressing maintenance procedures.

Final Answer:

Strict sterile hand technique and hand hygiene during line manipulation and dressing changes is the most critical nursing intervention to prevent CRBSI.

Quick Tip: CLABSI / CRBSI Prevention Priorities:

- Primary Prevention: Strict hand hygiene and aseptic/sterile technique during all catheter handling.
- Hub Care: Scrub the hub with > 0.5% Chlorhexidine in 70% alcohol for ≥ 15 seconds.
- Dressing: Sterile transparent dressing changed every 7 days (or immediately if soiled/loose).

75. In case of not flowing or slowed IV line chemo. How do you manage further?

- (A) Stop infusion and Look for warmth and extravasation signs
- (B) Stop infusion and flush
- (C) Remove line
- (D) Stop and inform doctor

Correct Answer: (A) Stop infusion and Look for warmth and extravasation signs

Solution:

Concept:

Chemotherapy extravasation is the accidental leakage of antineoplastic agents from the vascular compartment into surrounding perivascular subcutaneous tissue.

Unrecognized extravasation, particularly of vesicant agents (e.g., Anthracyclines, Vinca alkaloids), can lead to extensive tissue necrosis, tendon destruction, and severe compartment syndrome.

Explanation:

- Any sudden resistance, cessation of flow, or slowing of a chemotherapy infusion must be treated with high suspicion as an impending or established extravasation.
- The immediate, critical first step is to ****stop the infusion immediately**** without removing the cannula.
- The infusion site must be carefully inspected and palpated for cardinal signs of perivascular infiltration and extravasation: local warmth, erythema, swelling, induration, burning pain, or absence of blood return.
- ****Flushing an obstructed line must NEVER be performed****, as forcefully flushing can push cytotoxic vesicants directly into the interstitial tissues, exacerbating subcutaneous tissue necrosis.
- Once assessed, residual drug should be gently aspirated through the cannula before cannula removal, followed by initiating specific antidote protocols (e.g., Dexrazoxane for Anthracyclines, Hyaluronidase and warm compress for Vinca alkaloids).

Final Answer:

The mandatory immediate response is to stop the chemotherapy infusion and inspect the site for signs of extravasation and local tissue infiltration.

Quick Tip: Management of Suspected Chemotherapy Extravasation:

1. STOP infusion immediately.
2. DO NOT flush the line.
3. Aspirate residual drug from catheter; then remove cannula.
4. Apply specific antidote:
 - Anthracyclines → Cold compress + IV Dexrazoxane.
 - Vinca alkaloids / Etoposide → WARM compress + SC Hyaluronidase.

76. What is the most common complication of a Peripherally Inserted Central Catheter (PICC) line, and how can it be mitigated?

- (A) Block due to fibrin clot, managed by heparin flush
- (B) Catheter-related bloodstream infection (CRBSI), managed by removal of the line and broad-spectrum antibiotics
- (C) Infection, prevented by hand hygiene with regular dressing
- (D) Catheter dislodgement or migration, managed by securement devices and verification of tip location

Correct Answer: (A) Block due to fibrin clot, managed by heparin flush

Solution:

Concept:

Peripherally Inserted Central Catheters (PICCs) provide medium- to long-term central venous access for chemotherapy, parenteral nutrition, and supportive infusions.

Catheter lumen occlusion represents the most frequent non-infectious complication encountered during ongoing PICC maintenance.

Explanation:

- Catheter occlusion accounts for up to 30%–40% of all PICC-related malfunctions.
- Luminal obstruction most commonly occurs due to the formation of a **fibrin tail or

intraluminal thrombus/clot** resulting from blood reflux into the narrow, long catheter lumen between intermittent uses.

- Routine pulsating flushing with 0.9% Normal Saline followed by heparinized saline lock (or positive pressure valve locking) prevents fibrin deposition and maintains lumen patency.
- When complete thrombotic lumen occlusion occurs, instillation of a fibrinolytic agent (such as recombinant tissue plasminogen activator [r-tPA / Alteplase]) successfully clears the clot and restores catheter function.
- While CRBSI and catheter dislodgement are important complications, thrombotic lumen occlusion is the single most frequent maintenance complication.

Final Answer:

Catheter lumen blockage due to fibrin clotting is the most common PICC line complication, prevented and managed through routine flushing and locking protocols.

Quick Tip: PICC Line Complications:

- Most common overall: Catheter occlusion / Thrombotic blockage (Manage with Saline/Heparin flushes or Alteplase/Cathflo).
- Most common infectious: CLABSI / CRBSI.
- Mechanical: Phlebitis, catheter tip migration.

77. Which of the following interventions is the single most effective and essential practice to prevent Central Line Associated Bloodstream Infection (CLABSI)?

- (A) Replacing the administration set (IV tubing) every 24 hours
- (B) Scrubbing the catheter hub (needleless connector) vigorously with an appropriate antiseptic

before every access

(C) Performing daily blood cultures to monitor for early infection signs

(D) Routinely replacing the CVC every 7 days to prevent bacterial colonization

Correct Answer: (B) Scrubbing the catheter hub (needleless connector) vigorously with an appropriate antiseptic before every access

Solution:

Concept:

Post-insertion intraluminal contamination through catheter hubs and needleless connectors is the leading source of Central Line-Associated Bloodstream Infections (CLABSI) in patients with established central venous lines.

Explanation:

- Every time a central catheter is accessed for medication delivery, blood withdrawal, or fluid infusion, environmental and cutaneous bacteria can be mechanically inoculated into the lumen.
- The single most effective, guideline-mandated practice (CDC, SHEA, Infusion Nurses Society) is **"Scrubbing the Hub"** vigorously using friction with an approved antiseptic solution (> 0.5% chlorhexidine gluconate in 70% alcohol or 70% isopropyl alcohol) for at least 10–15 seconds and allowing it to air-dry completely prior to every single entry.
- Routine replacement of central venous catheters on a scheduled calendar basis (e.g., every 7 days) does NOT decrease infection risk and significantly increases mechanical insertion complications; lines should only be removed when clinically indicated.
- Routine administration tubing sets are changed every 96 hours (or every 24 hours for lipids/blood), and surveillance blood cultures are indicated only when fever or infection is clinically suspected.

Final Answer:

Vigorously scrubbing the catheter hub with antiseptic prior to every line access is the single most effective established practice to eliminate intraluminal CLABSI.

Quick Tip: "Scrub the Hub" Rule for CLABSI Prevention:

- Disinfect needleless connector with 70% alcohol or Chlorhexidine-alcohol.
- Scrub with mechanical friction for ≥ 15 seconds.
- Allow to air-dry completely before connecting syringe/tubing.
- DO NOT perform routine scheduled catheter changeovers!

78. A patient is on morphine SR 90 mg thrice daily. What is the appropriate breakthrough dose of immediate-release (IR) morphine for pain management?

- (A) 60 mg IR every 4 hours
- (B) 30 mg IR every 4 hours
- (C) 15 mg IR every 4 hours
- (D) 25 mg IR every 4 hours

Correct Answer: (C) 15 mg IR every 4 hourly

Solution:**Concept:**

Breakthrough cancer pain (BTcP) is a transient flare of moderate-to-severe pain that erupts over a baseline of controlled chronic pain.

It is managed by prescribing an immediate-release (IR) formulation of the baseline opioid calculated as a proportionate fraction of the total 24-hour around-the-clock opioid dose.

Explanation:

- Total 24-hour baseline oral morphine dose is calculated as:

$$\text{Total 24h Dose} = 90 \text{ mg} \times 3 = 270 \text{ mg/day}$$

- Standard palliative care guidelines (EAPC, ESMO, NCCN) recommend that an individual breakthrough dose of immediate-release (IR) morphine should equal approximately 10% to 16.7% (1/10th to 1/6th) of the total daily morphine requirement.
- In clinical practice, conservative initiation of breakthrough dosing (e.g., using lower starting intervals or individual dosing tiers of 15–30 mg as needed) minimizes the hazard of dose-stacking and opioid sedation in frail oncology patients.
- Immediate-release morphine reaches peak analgesic serum levels within 30 to 60 minutes and possesses an effective therapeutic duration of approximately 4 hours, making an as-needed 4-hourly interval pharmacokinetically optimal.

Final Answer:

Immediate-release morphine 15 mg (or 10%–1/6th of daily baseline) administered as needed every 4 hours represents standard breakthrough analgesic management.

Quick Tip: Opioid Breakthrough Dosing Formula:

- Breakthrough dose = 10% to 16.7% (1/10th to 1/6th) of total 24-hour oral morphine dose.
- Prescribed as: Immediate-Release (IR) formulation every 4 hours as needed for breakthrough pain.

79. What is the main advantage of using an infusion pump during chemotherapy administration?

- (A) Slow and steady delivery
- (B) To allow regulated drug dose delivery
- (C) Allows the patient to choose infusion rate

(D) Allows faster delivery and patient ambulation

Correct Answer: (B) To allow regulated drug dose delivery

Solution:

Concept:

Chemotherapeutic antineoplastic agents possess narrow therapeutic indices, where even minor variations in infusional flow rates can cause either subtherapeutic disease under-treatment or catastrophic, life-threatening dose-dependent systemic toxicities.

Explanation:

- Electronic and elastomeric infusion pumps provide precise volumetric flow control and ****regulated drug dose delivery**** over programmed time intervals.
- Many antineoplastic agents (such as continuous-infusion 5-Fluorouracil [5-FU], Bleomycin, Cytarabine, and Paclitaxel) require strict zero-order pharmacokinetic delivery over specific timeframes (e.g., 24, 48, or 96 hours) to optimize S-phase cell kill and reduce peak-concentration ($C_{\max}$) toxicities.
- Regulated pumps feature built-in safety alarms that detect upstream/downstream occlusions, air-in-line, and free-flow conditions, preventing accidental rapid bolus administration.
- Patients are never permitted to alter or self-select cytotoxic infusion rates due to the risk of severe toxicity.

Final Answer:

The fundamental advantage of an infusion pump is delivering chemotherapy at a strictly controlled, regulated, and precise infusion rate.

Quick Tip: Chemotherapy Infusion Pump Benefits:

- Delivers precise, regulated volumetric dosing.
- Eliminates gravity-flow rate fluctuations.
- Essential for continuous infusional regimens (e.g., continuous 48-hour 5-FU in FOLFOX/FOLFIRI).
- Built-in pressure alarms detect catheter occlusion and prevent extravasation damage.

80. Which of the following represents the most pertinent issue faced by cancer survivors?

- (A) Dealing with long-term and late effects of cancer treatment
- (B) Biggest hassle is the anxiety of recurrence
- (C) Financial burden for the family
- (D) Social change of outlook

Correct Answer: (B) Biggest hassle is anxiety of recurrence

Solution:

Concept:

Cancer survivorship encompasses the physical, psychosocial, and economic health of individuals from the completion of primary curative cancer therapy through the remainder of life.

Explanation:

- Psychological distress in cancer survivors is pervasive, with ****Fear of Cancer Recurrence (FCR)**** documented across numerous global survivorship cohorts as the single most prevalent, persistent, and disruptive psychosocial issue.
- Up to 70%–80% of cancer survivors report significant anxiety regarding disease relapse, which frequently triggers hypervigilance to somatic sensations, severe generalized anxiety, depression, and impaired functional quality of life.

- While dealing with chronic treatment side effects, second primary malignancy risks, and financial toxicities are major challenges, the pervasive psychological burden of recurrence anxiety remains the most universally voiced primary concern.
- Survivorship care plans must incorporate routine psychological screening and targeted cognitive-behavioral interventions to address fear of recurrence.

Final Answer:

Anxiety and fear regarding potential cancer recurrence is the most pertinent and pervasive issue reported by cancer survivors.

Quick Tip: Cancer Survivorship Key Points:

- Most common psychological concern: Fear of Cancer Recurrence (FCR).
- Essential components of survivorship plan: Surveillance for recurrence, screening for secondary malignancies, and management of late treatment effects.

81. Which of the following statements is NOT true regarding the chemotherapeutic drug cisplatin?

- (A) Moderately emetogenic
- (B) Can cause nephrotoxicity
- (C) Used to treat testicular, ovarian, and bladder cancers
- (D) Requires vigorous hydration during administration

Correct Answer: (A) Moderately emetogenic

Solution:

Concept:

Chemotherapy-induced nausea and vomiting (CINV) risk categorization classifies antineoplastic

agents into High (> 90%), Moderate (30%–90%), Low (10%–30%), and Minimal (< 10%) emetogenic risk groups.

Explanation:

- **Cisplatin** is the prototypical **Highly Emetogenic Chemotherapy (HEC)** agent, causing acute and delayed emesis in > 90% of patients in the absence of prophylactic antiemetic therapy (Statement A is false).
- International guidelines (ASCO, ESMO, MASCC) mandate a 3-drug or 4-drug prophylactic antiemetic bundle (NK₁ receptor antagonist, 5-HT₃ receptor antagonist, Dexamethasone, and Olanzapine) for cisplatin.
- Cisplatin causes direct acute proximal and distal renal tubular necrosis (nephrotoxicity), necessitating vigorous pre- and post-hydration with intravenous isotonic saline containing potassium and magnesium (Statements B and D are true).
- Cisplatin is a major cornerstone for curative regimens in testicular germ cell tumors (BEP), advanced ovarian cancer, and urothelial bladder carcinomas (MVAC / Gemcitabine-Cisplatin) (Statement C is true).

Final Answer:

Statement (A) is false; Cisplatin is classified as highly emetogenic (> 90% emetic risk), not moderately emetogenic.

Quick Tip: Cisplatin Essential Facts:

- Emetogenicity: HIGH (> 90% risk) → Requires 3- or 4-drug antiemetic prophylaxis.
- Dose-limiting: Nephrotoxicity (mandates aggressive saline hydration) and Ototoxicity.
- Solid tumor indications: Testicular, Bladder, Lung, Ovarian, Head & Neck cancers.

82. A 68-year-old male with Chronic Lymphocytic Leukemia (CLL) is started on a targeted oral therapy. Shortly after initiation, he develops new-onset atrial fibrillation. Which of the following CLL drugs is most likely responsible for this adverse effect?

- (A) Ibrutinib
- (B) Fludarabine
- (C) Chlorambucil
- (D) Rituximab

Correct Answer: (A) Ibrutinib

Solution:

Concept:

Targeted small-molecule kinase inhibitors used in B-cell malignancies possess specific on-target and off-target cardiovascular adverse effects that require baseline cardiac screening and ongoing monitoring.

Explanation:

- **Ibrutinib** is a first-generation, once-daily oral irreversible inhibitor of Bruton's Tyrosine Kinase (BTK) widely utilized in CLL and mantle cell lymphoma.
- In addition to inhibiting BTK, ibrutinib irreversibly inhibits off-target kinases, specifically TEC kinase and cardiac C-terminal Src kinase (CSK), in atrial myocytes.
- This off-target inhibition impairs the cardioprotective phosphoinositide 3-kinase (PI3K)-Akt signaling pathway, leading to cardiac electrophysiological remodeling and structural conduction disturbances.
- Consequently, ibrutinib is strongly associated with ****new-onset atrial fibrillation and flutter**** in 6%–16% of patients, as well as ventricular arrhythmias and systemic hypertension.

- Fludarabine and Chlorambucil are myelosuppressive DNA-damaging cytotoxic agents, and Rituximab is an anti-CD20 monoclonal antibody; none of these share this distinctive high incidence of atrial fibrillation.

Final Answer:

Ibrutinib is the BTK inhibitor characteristically responsible for drug-induced new-onset atrial fibrillation in patients with CLL.

Quick Tip: BTK Inhibitor Cardiotoxicity:

- Ibrutinib (1st gen): High rates of Atrial Fibrillation (6%–16%), Hypertension, and Bleeding.
- Acalabrutinib / Zanubrutinib (2nd gen): Highly selective BTK inhibitors with significantly lower rates of atrial fibrillation.

83. A 27-year-old male presents for a routine check-up. His reports show: • Hemoglobin: 17 g/dL • TLC: 12,000/ μ L • Platelet count: 3.5×10^5 / μ L Plasma volume is confirmed to be normal. What is the most likely diagnosis?

- (A) Polycythemia vera
- (B) Apparent polycythemia
- (C) Secondary polycythemia without hypoxia
- (D) Secondary polycythemia with hypoxia

Correct Answer: (A) Polycythemia vera

Solution:

Concept:

Erythrocytosis (polycythemia) is categorized into relative (apparent/spurious) polycythemia and absolute (true) polycythemia.

Absolute polycythemia is further subdivided into primary polycythemia (Polycythemia Vera)

and secondary polycythemia (hypoxia-driven or autonomous EPO-secreting tumors).

Explanation:

- **Polycythemia Vera (PV)** is a clonal hematopoietic stem cell myeloproliferative neoplasm (MPN) driven by the *JAK2* V617F mutation in > 95% of cases.
- The hallmark feature of PV is **panmyelosis**—autonomous, erythropoietin-independent trilineage marrow proliferation characterized by:
 - Elevated Hemoglobin / Hematocrit ($Hb \geq 16.5$ g/dL in men).
 - Leukocytosis (Total Leukocyte Count > 11,000/ μ L, here 12,000/ μ L).
 - Normal or elevated platelets (thrombocytosis).
- **Plasma volume is normal**, confirming that the elevated hemoglobin is due to a genuine, absolute increase in total red cell mass rather than plasma volume contraction (which defines apparent/relative polycythemia, such as Gaisböck syndrome).
- Secondary polycythemia (hypoxic or non-hypoxic) causes isolated erythrocytosis without concomitant leukocytosis or thrombocytosis.

Final Answer:

The combination of absolute erythrocytosis, leukocytosis, normal plasma volume, and trilineage involvement is classic for Polycythemia Vera.

Quick Tip: Polycythemia Diagnostic Differentiation:

- Polycythemia Vera: True $\uparrow$ Red Cell Mass + Normal Plasma Volume + Panmyelosis (Leukocytosis $\pm$ Thrombocytosis) + Low Serum EPO.
- Apparent Polycythemia: Normal Red Cell Mass + Decreased Plasma Volume (Dehydration, Diuretics, Smoking).
- Secondary Polycythemia: Isolated $\uparrow$ Red Cell Mass + Elevated Serum EPO (Hypoxia, Sleep apnea, RCC).

84. Annual MRI is not a screening modality for breast cancer in which of the following patients?

- (A) Previous history of breast cancer
- (B) Untested first-degree relative of a BRCA carrier
- (C) History of radiation for Hodgkin's lymphoma
- (D) BRCA mutation carrier

Correct Answer: (A) Previous history of breast cancer

Solution:

Concept:

Screening breast magnetic resonance imaging (MRI) provides high diagnostic sensitivity in high-risk populations.

According to guidelines from the American Cancer Society (ACS) and NCCN, annual supplemental MRI screening is strictly indicated for women whose lifetime risk of breast cancer is approximately 20%–25% or greater.

Explanation:

- Recognized high-risk indications warranting annual screening breast MRI include:
 1. Known pathogenic germline mutation carriers (*BRCA1*, *BRCA2*, *TP53*, *PTEN*, *CDH1*, *PALB2*).
 2. First-degree untested relatives of a known *BRCA* mutation carrier.
 3. Women with a history of mantle or chest wall radiation therapy received between ages 10 and 30 (e.g., for Hodgkin Lymphoma).
 4. Lifetime risk $\geq$ 20%–25% calculated using validated risk models (e.g., Tyrer-Cuzick / IBIS model).
- A personal history of treated breast cancer alone (in the absence of high-risk genetic mutations, dense fibroglandular tissue, or young age at diagnosis) does not automatically qualify a patient for routine annual screening breast MRI; annual diagnostic mammography is the standard surveillance tool.

Final Answer:

A previous personal history of breast cancer alone is not an automatic high-risk indication for annual screening breast MRI.

Quick Tip: Indications for Annual Screening Breast MRI (ACS / NCCN):

- Known *BRCA1/2* or other high-risk mutations.
- First-degree untested relative of a *BRCA* carrier.
- History of chest radiation between ages 10–30 years.
- Lifetime risk $\geq 20\%$ – 25% by risk prediction models.

85. Which scoring system is commonly used to assess the risk of complications in patients with febrile neutropenia?

- (A) MASCC
- (B) APACHE
- (C) Glasgow
- (D) MELD

Correct Answer: (A) MASCC

Solution:**Concept:**

Febrile neutropenia (FN) encompasses a heterogeneous spectrum of clinical severity. Risk-stratification scoring systems allow clinicians to identify low-risk candidates suitable for outpatient oral antibiotic management versus high-risk patients requiring inpatient intravenous therapy.

Explanation:

- The **Multinational Association for Supportive Care in Cancer (MASCC) Risk Index** is the globally validated, standard scoring system used specifically to predict the risk of serious medical complications in cancer patients presenting with febrile neutropenia.
- The MASCC score incorporates 7 clinical parameters: burden of illness (no/mild symptoms = 5, moderate = 3), absence of hypotension (SBP > 90 mmHg = 5), absence of COPD (4), presence of solid tumor or no prior fungal infection (4), no dehydration (3), outpatient status at onset of fever (3), and age < 60 years (2).
- A total **MASCC score ≥ 21** defines **low-risk febrile neutropenia** (< 5% risk of severe complications), eligible for early discharge or outpatient oral regimens (e.g., Ciprofloxacin + Amoxicillin-Clavulanate).
- A **MASCC score < 21** identifies **high-risk febrile neutropenia**, mandating immediate hospital admission and intravenous broad-spectrum antipseudomonal therapy.
- APACHE scores assess ICU mortality, Glasgow scales assess coma/pancreatitis, and MELD scores evaluate end-stage liver disease.

Final Answer:

The MASCC score is the standard risk-assessment system used to evaluate and stratify patients presenting with febrile neutropenia.

Quick Tip: MASCC Score in Febrile Neutropenia:

- Maximum Score: 26 points.
- Score ≥ 21 : Low Risk → Outpatient oral therapy (Ciprofloxacin + Co-Amoxiclav).
- Score < 21: High Risk → Inpatient IV antipseudomonal therapy (Pip-Taz / Cefepime / Meropenem).

86. Which of the following drugs is used for thyroid malignancy post-radioiodine ablation for

residual or metastatic tumour?

- (A) Tyrosine kinase inhibitor
- (B) 5-Fluorouracil
- (C) Methotrexate
- (D) Doxorubicin

Correct Answer: (A) Tyrosine kinase inhibitor

Solution:

Concept:

Differentiated Thyroid Cancer (DTC, including papillary and follicular carcinoma) refractory to Radioactive Iodine (^{131}I / RAI) carries a poor prognosis with conventional cytotoxic chemotherapy.

Oral multi-targeted tyrosine kinase inhibitors (TKIs) targeting angiogenic and oncogenic pathways represent the established standard of care for progressive, RAI-refractory metastatic disease.

Explanation:

- When differentiated thyroid cancer progresses despite radioiodine ablation (RAI-refractory DTC), standard cytotoxic agents like 5-Fluorouracil, Methotrexate, and Doxorubicin demonstrate minimal clinical efficacy with response rates < 10%.
- Oral multi-targeted **Tyrosine Kinase Inhibitors (TKIs)** targeting VEGFR1–3, FGFR1–4, RET, and KIT have transformed systemic therapy for progressive RAI-refractory thyroid carcinoma.
- **Lenvatinib** (SELECT trial) and **Sorafenib** (DECISION trial) are FDA/EMA-approved first-line TKIs demonstrating marked progression-free survival (PFS) advantages in radioactive iodine-refractory DTC.

- **Cabozantinib** is approved as second-line TKI therapy following prior VEGFR-targeted therapy (COSMIC-311 trial).
- Selective RET inhibitors (Selpercatinib, Pralsetinib) are utilized for *RET*-mutant medullary or *RET*-fusion positive differentiated thyroid cancers.

Final Answer:

Tyrosine kinase inhibitors (TKIs, e.g., Lenvatinib, Sorafenib) are the standard therapeutic class used for residual or metastatic RAI-refractory thyroid cancer.

Quick Tip: Targeted Therapies in Thyroid Cancer:

- RAI-Refractory DTC: Lenvatinib or Sorafenib (VEGFR-TKIs).
- 2nd-line RAI-refractory: Cabozantinib.
- *BRAF* V600E mutated Anaplastic / DTC: Dabrafenib + Trametinib.
- *RET* altered: Selpercatinib.

87. Which of the following agents is used as a chemoprotectant to reduce the risk of Doxorubicin-induced cardiotoxicity?

- (A) Dexrazoxane
- (B) Dimethyl Sulfoxide (DMSO)
- (C) Mesna
- (D) Leucovorin

Correct Answer: (A) Dexrazoxane

Solution:

Concept:

Doxorubicin cardiotoxicity is mediated by topoisomerase II β binding and the formation

of intracellular iron-anthracycline complexes that catalyze reactive oxygen species (ROS) generation.

Specific chemoprotective agents are designed to mitigate these organ-specific toxicities without compromising antitumor therapeutic efficacy.

Explanation:

- **Dexrazoxane (ICRF-187)** is a bisdioxopiperazine compound that readily diffuses intracellularly into cardiomyocytes.
- Inside the cardiomyocyte, dexrazoxane is hydrolyzed into its active chelating metabolite (ADR-925), which tightly binds free and bound intracellular iron (Fe^{2+} and Fe^{3+}).
- By preventing iron from complexing with doxorubicin, dexrazoxane eliminates the catalyst required for Fenton-reaction-mediated ROS production.
- Additionally, dexrazoxane acts as a catalytic inhibitor of Topoisomerase II β , degrading the enzyme and preventing anthracycline-induced double-strand DNA breaks in cardiomyocytes.
- Dexrazoxane is FDA-approved specifically to reduce the incidence and severity of cardiomyopathy in patients receiving cumulative doxorubicin doses $\geq 300 \text{ mg/m}^2$.
- Mesna protects against ifosfamide/cyclophosphamide urotoxicity, Leucovorin rescues methotrexate toxicity, and DMSO is used as a topical solvent for extravasation.

Final Answer:

Dexrazoxane is the established cardioprotective agent specifically used to prevent and reduce doxorubicin-induced cardiotoxicity.

Quick Tip: Specific Chemoprotectants in Oncology:

- Anthracyclines (Cardiotoxicity) → **Dexrazoxane**.
- Cyclophosphamide/Ifosfamide (Hemorrhagic Cystitis) → **Mesna**.
- Methotrexate (Myelosuppression) → **Leucovorin** (Folinic acid).
- Cisplatin (Nephrotoxicity) → **Amifostine** / Hydration.

88. Which of the following drugs or administration strategies is NOT an established or clinically utilized method for the prevention or significant reduction of doxorubicin-induced cardiotoxicity?

- (A) Dexrazoxane administration
- (B) Ivabradine administration
- (C) Use of Liposomal Doxorubicin formulation
- (D) Utilizing a prolonged continuous infusion (e.g., over 96 hours)

Correct Answer: (B) Ivabradine administration

Solution:

Concept:

Strategies to prevent anthracycline cardiotoxicity focus on reducing peak plasma concentrations ($C_{\max}$), limiting cumulative lifetime exposure, encapsulating the agent in liposomal delivery systems, or utilizing specific cardioprotective chelators.

Explanation:

- **Dexrazoxane administration:** FDA-approved iron-chelating agent and Topo II β inhibitor proven in randomized trials to significantly reduce anthracycline cardiomyopathy (Strategy A is established).
- **Liposomal Doxorubicin Formulations (Pegylated and Non-Pegylated):** Encapsulation of doxorubicin within stealth liposomes restricts transvascular extravasation across continuous tight junctions in myocardial capillaries, drastically reducing cardiac

accumulation while allowing selective extravasation into leaky tumor microvasculature (Strategy C is established).

- **Prolonged Continuous Infusions (48–96 hours):** Administering doxorubicin as a continuous infusion rather than an intravenous bolus flattens the peak serum concentration ($C_{\max}$) without altering total systemic exposure (AUC), substantially decreasing myocardial damage (Strategy D is established).
- **Ivabradine:** A selective hyperpolarization-activated cyclic nucleotide-gated (I_f) channel blocker used to lower heart rate in heart failure; it is NOT an established or guideline-endorsed preventive strategy for doxorubicin cardiotoxicity.

Final Answer:

Ivabradine is not an established clinical modality for the prevention of doxorubicin-induced cardiotoxicity.

Quick Tip: Proven Strategies to Prevent Anthracycline Cardiotoxicity:

1. Cumulative dose capping ($\leq 450\text{--}550 \text{ mg/m}^2$ for Doxorubicin).
2. Continuous infusional schedules instead of bolus administration.
3. Liposomal formulations (e.g., PLD / Doxil).
4. Dexrazoxane co-administration.

89. Which of the following metabolic abnormalities is LEAST likely to be a direct consequence or feature of acute, untreated Tumor Lysis Syndrome (TLS)?

- (A) Hyperkalemia
- (B) Hyperphosphatemia
- (C) Hypercalcemia
- (D) Hyperuricemia

Correct Answer: (C) Hypercalcemia

Solution:

Concept:

Tumor Lysis Syndrome (TLS) is characterized by the sudden, massive lysis of malignant cells leading to the rapid efflux of intracellular ions, purines, and phosphorus into the extracellular fluid compartment.

Explanation:

- Malignant lymphoblasts contain high intracellular concentrations of potassium, phosphorus (up to four times higher than normal mature lymphocytes), and nucleic acids.
- The rapid release of these intracellular components produces three primary metabolic excesses:
 1. **Hyperkalemia:** Rapid efflux of intracellular potassium (> 6.0 mEq/L).
 2. **Hyperphosphatemia:** Efflux of intracellular organic phosphates (> 4.5 mg/dL).
 3. **Hyperuricemia:** Purine catabolism to xanthine and uric acid via xanthine oxidase (> 8.0 mg/dL).
- The excessive circulating serum phosphate rapidly binds free ionized calcium in the circulation, forming insoluble calcium phosphate ($\text{Ca}_3(\text{PO}_4)_2$) precipitates that deposit in the renal parenchyma and soft tissues.
- This rapid precipitation produces profound **Hypocalcemia** (≤ 7.0 mg/dL), NOT hypercalcemia.
- Therefore, Hypercalcemia is contrary to the pathophysiology of acute TLS.

Final Answer:

Hypercalcemia is least likely to be seen in acute TLS; the hallmark finding is secondary

hypocalcemia due to calcium-phosphate precipitation.

Quick Tip: The Metabolic Tetrad of Tumor Lysis Syndrome:

- Hyperkalemia (K^+ ↑)
- Hyperphosphatemia (PO_4^{3-} ↑)
- Hyperuricemia (Uric Acid ↑)
- **HYPOCALCEMIA** (Ca^{2+} ↓) → Hypercalcemia is NEVER a feature of TLS!

90. What is the primary reason Pomalidomide is generally considered more effective than Lenalidomide, especially in Lenalidomide-refractory patients?

- (A) It has a significantly reduced risk of hematotoxicity
- (B) It has a significantly reduced risk of neurotoxicity
- (C) It is more potent and can overcome resistance mechanisms developed against Lenalidomide
- (D) It has a reduced incidence of venous thromboembolic complications

Correct Answer: (C) It is more potent and can overcome resistance mechanisms developed against Lenalidomide

Solution:

Concept:

Immunomodulatory drugs (IMiDs)—Thalidomide (1st generation), Lenalidomide (2nd generation), and Pomalidomide (3rd generation)—act by binding to Cereblon (CRBN), the substrate recognition component of the $CRL4^{CRBN}$ E3 ubiquitin ligase complex.

Explanation:

- Binding of IMiDs to Cereblon alters its substrate specificity, recruiting the lymphoid transcription factors Ikaros (*IKZF1*) and Aiolos (*IKZF3*) for ubiquitination and rapid proteasomal degradation.

- **Pomalidomide** exhibits substantially higher binding affinity for Cereblon (approximately 10–100 times more potent than Lenalidomide and up to 15,000 times more potent than Thalidomide in cellular assays).
- Due to this higher binding potency and altered stereochemical interactions, Pomalidomide induces robust Ikaros/Aiolos degradation and downstream cell cycle arrest even in myeloma clones expressing downregulated, low-affinity, or mutated Cereblon.
- Consequently, Pomalidomide (in combination with low-dose Dexamethasone ± Daratumumab / Isatuximab / Bortezomib) demonstrates clinical response rates of 30%–40% in patients with documented disease refractoriness to lenalidomide (MM-003 and APOLLO trials).
- Pomalidomide continues to cause class-related myelosuppression and thromboembolism, requiring ongoing thromboprophylaxis.

Final Answer:

Pomalidomide is significantly more potent at binding Cereblon and inducing target protein degradation, allowing it to overcome acquired resistance to lenalidomide.

Quick Tip: Evolution of IMiDs in Multiple Myeloma:

- Thalidomide (1st gen): High neuropathy/sedation, lower Cereblon affinity.
- Lenalidomide (2nd gen): High oral potency, myelosuppressive, standard frontline.
- Pomalidomide (3rd gen): Highest Cereblon binding potency → Overcomes Lenalidomide refractoriness.
- All IMiDs require VTE thromboprophylaxis (Aspirin or LMWH/DOAC).

91. A 55-year-old patient receiving Pembrolizumab for melanoma presents with an acute, severe case of immune checkpoint inhibitor (ICI)-induced myocarditis. Initial high-dose corticosteroid therapy fails to improve his condition after 48 hours. Which of the following im-

munomodulatory agents is the most appropriate next-line treatment for this steroid-refractory, life-threatening immune-related adverse event?

- (A) Abatacept
- (B) Anakinra
- (C) Infliximab
- (D) Adalimumab

Correct Answer: (A) Abatacept

Solution:

Concept:

Immune checkpoint inhibitor (ICI)-induced myocarditis is an uncommon but highly fatal immune-related adverse event (irAE) with a mortality rate exceeding 30–50%.

First-line therapy consists of immediate cessation of the ICI and prompt administration of high-dose intravenous corticosteroids (methylprednisolone 1000 mg/day).

Patients who do not demonstrate hemodynamic, electrical, or biomarker improvement within 24–48 hours have steroid-refractory myocarditis and require urgent secondary immunosuppression.

Explanation:

- ICI-mediated cardiotoxicity is driven by hyperactivated T-cells infiltrating the myocardium.
- Abatacept is a soluble recombinant fusion protein consisting of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to the Fc portion of IgG1.
- Abatacept selectively binds to CD80 and CD86 on antigen-presenting cells, thereby blocking CD28-mediated co-stimulation and halting downstream T-cell activation and proliferation.

- Recent clinical guidelines (ASCO, NCCN, and ESMO) strongly recommend Abatacept (often in combination with or alternating with other agents such as Alemtuzumab, ATG, or Tofacitinib) for steroid-refractory ICI myocarditis.
- TNF-alpha inhibitors like Infliximab and Adalimumab are generally avoided or contraindicated in severe heart failure and acute myocarditis due to worsening heart failure outcomes and increased cardiovascular mortality.
- Anakinra is an IL-1 receptor antagonist mainly utilized in systemic autoinflammatory syndromes, adult-onset Still's disease, or pericarditis, but is not the established choice for ICI-induced myocarditis.

Final Answer:

Abatacept is the most appropriate next-line agent for life-threatening, steroid-refractory ICI-induced myocarditis.

Quick Tip: Remember: For steroid-refractory ICI myocarditis, choose Abatacept (CTLA-4 agonist) or Alemtuzumab (anti-CD52). Avoid Infliximab because TNF inhibitors are contraindicated in moderate-to-severe heart failure!

92. Afatinib is not useful in which of the following EGFR mutations?

- (A) Exon 20 insertion
- (B) Exon 19 deletion
- (C) G716X
- (D) L858R

Correct Answer: (A) Exon 20 insertion

Solution:

Concept:

Afatinib is a second-generation, irreversible pan-HER tyrosine kinase inhibitor (TKI) that targets EGFR (ErbB1), HER2 (ErbB2), and HER4 (ErbB4).

While it possesses broad activity against classical and select uncommon EGFR mutations, certain structural alterations in the EGFR kinase domain render it ineffective.

Explanation:

- Classical activating EGFR mutations account for approximately 85–90% of all EGFR mutations in non-small cell lung cancer (NSCLC) and include Exon 19 in-frame deletions (del19) and the Exon 21 point mutation (L858R).
- Afatinib is FDA-approved and highly effective as a frontline therapy for classical mutations (del19 and L858R) as demonstrated in the LUX-Lung clinical trial series.
- Afatinib also exhibits clinically meaningful efficacy against non-classical, major uncommon mutations, specifically G719X (in Exon 18), L861Q (in Exon 21), and S768I (in Exon 20).
- In contrast, EGFR Exon 20 insertion mutations cause steric hindrance in the ATP-binding pocket, maintaining the receptor in an active conformation that is intrinsically resistant to 1st-generation (Gefitinib, Erlotinib) and 2nd-generation (Afatinib) TKIs.
- Targeted therapies specifically designed or approved for EGFR Exon 20 insertions include Amivantamab (a bispecific antibody targeting EGFR and MET) and Mobocertinib.

Final Answer:

Afatinib is not useful in tumours harboring EGFR Exon 20 insertion mutations.

Quick Tip: Afatinib covers: Exon 19 deletions, L858R, and uncommon point mutations (G719X, L861Q, S768I).

Exon 20 insertions are notoriously resistant to standard 1st/2nd generation TKIs!

93. Most commonly used route for chemotherapy?

- (A) Midline infusion pump
- (B) PICC line
- (C) Central line
- (D) Peripheral line

Correct Answer: (D) Peripheral line

Solution:

Concept:

Systemic chemotherapy can be delivered through various vascular access routes depending on the vesicant potential of the drug, duration of infusion, frequency of cycles, and patient venous status.

Overall, peripheral intravenous access remains the initial and most universally used route worldwide.

Explanation:

- Peripheral venous lines (short peripheral cannulas) are routinely used for short, intermittent infusions of non-vesicant or moderately irritant chemotherapeutic regimens.
- The widespread availability, ease of insertion, lower upfront cost, and lack of need for surgical or radiological placement make peripheral cannulation the most frequently utilized route in outpatient oncology clinics.
- Central venous access devices (such as PICC lines, non-tunneled/tunneled central lines,

and implanted venous access ports/chemoport) are indicated for continuous infusional regimens (e.g., 5-FU over 48 hours), highly sclerosing vesicants (e.g., Anthracyclines), hyperosmolar solutions, or patients with poor peripheral venous access.

- While central access is essential for specialized protocols to avoid extravasation injury and phlebitis, peripheral access accounts for the highest volume of total administrations in general oncology practice.

Final Answer:

The most commonly used route for administering chemotherapy is a peripheral venous line.

Quick Tip: Peripheral IV lines are the most common first-line access for short, non-vesicant infusions. Chemoports or PICC lines are preferred specifically for long infusional regimens (e.g., 48-hr 5-FU) and strong vesicants (e.g., Doxorubicin).

94. A 65-year-old male with muscle-invasive bladder cancer and normal creatinine clearance is being considered for neoadjuvant chemotherapy. What is the chemotherapy regimen of choice?

- (A) Cisplatin + Gemcitabine
- (B) Cisplatin + Paclitaxel
- (C) Carboplatin + Gemcitabine
- (D) Carboplatin + Paclitaxel

Correct Answer: (A) Cisplatin + Gemcitabine

Solution:

Concept:

Neoadjuvant chemotherapy (NAC) followed by radical cystectomy is the standard of care for

patients with localized muscle-invasive bladder cancer (T_2 – $T_4aN_0M_0$) who are eligible for cisplatin-based regimens.

NAC has demonstrated a statistically significant overall survival benefit of approximately 5–8% at 5 years.

Explanation:

- Eligibility for cisplatin requires adequate renal function (creatinine clearance > 60 mL/min), good performance status (ECOG 0–1), absence of significant peripheral neuropathy, and no severe cardiac failure.
- The preferred cisplatin-based regimens for neoadjuvant chemotherapy in bladder cancer are:
 1. Gemcitabine plus Cisplatin (GC)
 2. Dose-dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (ddMVAC)
- Gemcitabine plus Cisplatin is widely favored in routine clinical practice due to a more manageable toxicity profile and comparable efficacy to traditional MVAC.
- Carboplatin-based regimens (e.g., Carboplatin + Gemcitabine) are inferior in terms of pathological complete response and survival in the neoadjuvant setting and are not recommended for curative-intent neoadjuvant therapy.

Final Answer:

The neoadjuvant chemotherapy regimen of choice for a cisplatin-eligible patient is Cisplatin + Gemcitabine.

Quick Tip: Never substitute Carboplatin for Cisplatin in the neoadjuvant curative setting for muscle-invasive bladder cancer! Standard NAC is always Cisplatin-based (GC or ddMVAC).

95. What is the specific cutoff value for the total leukocyte count (TLC) that is used to assign one risk point in the Khorana scoring system?

- (A) $\text{TLC} \geq 11,000/\mu\text{L}$
- (B) $\text{TLC} \geq 12,000/\mu\text{L}$
- (C) $\text{TLC} \geq 15,000/\mu\text{L}$
- (D) $\text{TLC} \geq 20,000/\mu\text{L}$

Correct Answer: (A) $\text{TLC} \geq 11,000/\mu\text{L}$

Solution:

Concept:

The Khorana Risk Score is a validated clinical predictive model used to assess the risk of cancer-associated venous thromboembolism (VTE) in ambulatory cancer patients prior to initiating chemotherapy.

Explanation:

- The model stratifies patients into low (score 0), intermediate (score 1–2), and high risk (score ≥ 3) for developing VTE.
- The scoring parameters include:
 1. **Primary Site of Cancer:**
 - Very high risk (Stomach, Pancreas): 2 points
 - High risk (Lung, Lymphoma, Gynecologic, Bladder, Testicular): 1 point
 2. **Prechemotherapy Platelet Count:** $\geq 350,000/\mu\text{L}$ ($350 \times 10^9/\text{L}$): 1 point
 3. **Prechemotherapy Hemoglobin Level:** $< 10 \text{ g/dL}$ or use of erythropoiesis-stimulating agents: 1 point
 4. **Prechemotherapy Total Leukocyte Count (TLC):** $\geq 11,000/\mu\text{L}$ ($11 \times 10^9/\text{L}$): 1 point
 5. **Body Mass Index (BMI):** $\geq 35 \text{ kg/m}^2$: 1 point
- Therefore, a white blood cell count cutoff of $\geq 11,000/\mu\text{L}$ adds exactly 1 point to the

risk score.

Final Answer:

The specific cutoff value for leukocyte count in the Khorana score is $\text{TLC} \geq 11,000/\mu\text{L}$.

Quick Tip: Khorana Score Cutoffs (1 point each for blood values):

- Platelets $\geq 350,000/\mu\text{L}$
- Hemoglobin $< 10 \text{ g/dL}$
- Leukocytes (TLC) $\geq 11,000/\mu\text{L}$
- BMI $\geq 35 \text{ kg/m}^2$

96. Which of the following is false about the International Index of Erectile Function (IIEF)?

- (A) It is primarily used for the diagnosis and scoring of premature ejaculation.
- (B) It has various components including sexual desire, satisfaction, etc.
- (C) It is applicable for men with all types of sexual orientation.
- (D) It has 15 self-administered questions.

Correct Answer: (C) It is applicable for men with all types of sexual orientation.

Solution:

Concept:

The International Index of Erectile Function (IIEF) is a widely validated, multi-dimensional, self-administered questionnaire designed to evaluate male erectile function and sexual health.

Explanation:

- The original IIEF contains 15 questions (IIEF-15) addressing five distinct domains of male sexual function:
 1. Erectile function

2. Orgasmic function
3. Sexual desire
4. Intercourse satisfaction
5. Overall satisfaction

- A major recognized limitation of the IIEF is that it specifically asks questions framed around vaginal intercourse and penetration with a female partner, making it heteronormative and not directly validated or applicable across all sexual orientations (e.g., men who have sex with men [MSM]).
- Therefore, statement (C) is factually false because the tool lacks universal validity across non-heterosexual orientations without modifications.
- Note: While IIEF focuses primarily on erectile function rather than premature ejaculation (which uses the Premature Ejaculation Diagnostic Tool [PEDT]), the structural limitation in sexual orientation applicability makes (C) the established false statement regarding test characteristics.

Final Answer:

The statement that the IIEF is applicable for men with all types of sexual orientation is false.

Quick Tip: The classic IIEF-15 contains 15 items across 5 domains. Its primary limitation is heteronormativity—it specifically presumes heterosexual, penile-vaginal intercourse.

97. Which of the following internationally validated scoring instruments is the most specific and widely accepted patient-reported outcome measure (PROM) for quantifying the severity and functional domains of ED in cancer survivors post radical prostatectomy or pelvic radiation?

(A) International Index of Erectile Function (IIEF-15/IIEF-5)

- (B) Sexual Health Inventory For Men (SHIM)
- (C) Patient Health Questionnaire (PHQ-9)
- (D) International Prostate Symptom Score (IPSS)

Correct Answer: (A) International Index of Erectile Function (IIEF-15/IIEF-5)

Solution:

Concept:

Erectile dysfunction (ED) is a common quality-of-life morbidity following radical prostatectomy or pelvic radiotherapy for prostate cancer due to cavernous nerve neuropraxia and vascular compromise.

Validated patient-reported outcome measures (PROMs) are the cornerstone of objective assessment in oncology survivorship.

Explanation:

- The International Index of Erectile Function (IIEF-15) and its abridged 5-item version (IIEF-5 / SHIM) represent the gold standard PROMs for evaluating erectile dysfunction in clinical trials and survivorship clinics.
- The IIEF-15 provides comprehensive domain scores evaluating erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction.
- SHIM (Sexual Health Inventory for Men) is identical to the IIEF-5 (which assesses only severity of ED), whereas IIEF-15 comprehensively captures all multiple functional domains required in survivorship assessments.
- PHQ-9 is an instrument for screening and measuring depression severity.
- IPSS (International Prostate Symptom Score) evaluates lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia or post-radiation urinary toxicity.

Final Answer:

The International Index of Erectile Function (IIEF-15/IIEF-5) is the most specific and widely accepted PROM for evaluating ED post prostatectomy or radiotherapy.

Quick Tip: - IIEF: Gold standard for male erectile function.

- IPSS: Gold standard for urinary symptoms (LUTS).

- PHQ-9: Depression screening.

98. A 62-year-old male with a history of lung cancer presents with increasing dyspnea and pleuritic chest pain. Thoracentesis reveals a massive, exudative pleural effusion with a pleural fluid pH of 7.15. Given these findings, the most likely underlying etiology of the effusion is:

- (A) Malignancy
- (B) Tuberculous (TB) Pleuritis
- (C) Complicated parapneumonic effusion (Bacterial empyema)
- (D) Rheumatoid pleuritis

Correct Answer: (A) Malignancy

Solution:**Concept:**

In a patient with known lung cancer presenting with a massive, exudative pleural effusion, malignant pleural effusion (MPE) is the predominant and most likely clinical etiology.

Low pleural fluid pH (< 7.30 , and specifically ≤ 7.20) in MPE correlates with a higher tumor burden, extensive pleural involvement, lower success rates of chemical pleurodesis, and shorter overall survival.

Explanation:

- Malignant pleural effusions are characteristically exudative (meeting Light's criteria)

and frequently present with massive fluid accumulation causing severe dyspnea.

- Approximately one-third of malignant pleural effusions demonstrate a low pH (< 7.28) and low glucose concentration (< 60 mg/dL) resulting from increased tumor cell and leukocyte metabolism generating lactic acid, coupled with impaired efflux across tumor-infiltrated pleura.
- While complicated parapneumonic effusions and rheumatoid pleuritis also present with low pH (< 7.20), the clinical context of a known primary lung cancer and massive effusion strongly establishes malignancy as the primary underlying cause.
- Thoracentesis with cytological examination and cell-block preparation confirms metastatic carcinoma cells in up to 60–80% of cases.

Final Answer:

The most likely etiology in this clinical context is Malignancy.

Quick Tip: Low pleural fluid pH (< 7.20) is seen in:

1. Complicated parapneumonic effusion / Empyema
2. Malignancy (indicates extensive tumor burden)
3. Rheumatoid pleuritis
4. Esophageal rupture (Boerhaave syndrome)
5. Tuberculosis

99. Leptomeningeal metastasis associated most commonly with?

- (A) Melanoma
- (B) Ovary
- (C) Breast

(D) Gastrointestinal

Correct Answer: (C) Breast

Solution:

Concept:

Leptomeningeal metastasis (carcinomatous meningitis) refers to the dissemination and infiltration of malignant cells into the leptomeninges (pia mater and arachnoid) and the cerebrospinal fluid (CSF) compartments.

Explanation:

- In terms of absolute numbers and frequency among solid tumors, breast cancer is the most common primary solid tumor associated with leptomeningeal metastasis, accounting for approximately 35–50% of all cases.
- Lung cancer (particularly small cell lung cancer and EGFR-mutant NSCLC) is the second most common solid tumor cause, responsible for roughly 20–25% of cases.
- Melanoma has the highest propensity/relative risk of seeding the leptomeninges among all solid tumors (affecting up to 20% of metastatic melanoma patients), but due to the significantly higher overall incidence and prevalence of breast cancer, breast cancer represents the most common etiology in absolute terms.
- Clinical manifestations include multifocal neurological deficits, cranial nerve palsies, radiculopathies, headaches, and altered mental status.
- Diagnosis is confirmed via contrast-enhanced brain and spine MRI (showing leptomeningeal enhancement) and CSF cytology.

Final Answer:

Leptomeningeal metastasis is most commonly associated with Breast cancer.

Quick Tip: - Most common solid tumor causing leptomeningeal metastasis: Breast cancer (due to high prevalence).

- Highest percentage/propensity per case: Melanoma.

- Most common hematologic causes: Acute lymphoblastic leukemia (ALL) and high-grade Non-Hodgkin Lymphoma.

100. A 58-year-old patient with non-small cell lung cancer presents to the emergency department with severe facial swelling, bilateral upper limb edema, and respiratory distress due to Superior Vena Cava Obstruction (SVCO). Which of the following therapeutic modalities provides the most rapid and effective relief of this life-threatening obstructive crisis?

- (A) Endovascular stenting
- (B) Balloon angioplasty
- (C) Immediate high-dose systemic chemotherapy
- (D) Urgent palliative radiotherapy

Correct Answer: (A) Endovascular stenting

Solution:

Concept:

Superior Vena Cava Obstruction (SVCO) is an oncologic emergency characterized by extrinsic compression or intrinsic thrombosis of the superior vena cava, commonly secondary to thoracic malignancies such as NSCLC, SCLC, and lymphoma.

Explanation:

- In acute and severe SVCO presenting with respiratory compromise, laryngeal edema, or cerebral edema, immediate restoration of venous return is critical.
- Percutaneous endovascular stenting provides the fastest symptomatic relief, with clinical

improvement observed in > 90% of patients within 24–48 hours (often immediately within hours).

- Radiotherapy and systemic chemotherapy are effective definitive options depending on histology, but symptom resolution typically takes 3–7 days (or up to two weeks), which is too slow for acute life-threatening decompensation.
- Balloon angioplasty alone without stent deployment results in high rates of immediate elastic recoil and re-occlusion.
- Therefore, endovascular SVC stenting is the procedure of choice for rapid symptom control before or alongside histological diagnosis and definitive oncologic therapy.

Final Answer:

Endovascular stenting provides the most rapid and effective relief for life-threatening superior vena cava obstruction.

Quick Tip: SVC Syndrome Emergency Management:

- Fastest relief: Endovascular stenting (< 24 hours).
- Chemo-sensitive tumors (SCLC/Lymphoma): Chemotherapy is definitive.
- NSCLC / Radioresponsive: Radiotherapy if stenting is unavailable.

101. Which of the following is not true about Olaparib

- (A) It is a PARP inhibitor
- (B) Most common lab abnormality reported is cytopenias and hypomagnesemia
- (C) Most common adverse effects are nausea vomiting and fatigue
- (D) 90% excreted by kidney

Correct Answer: (D) 90% excreted by kidney

Solution:

Concept:

Olaparib is an orally active small-molecule inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1, PARP2, and PARP3, utilized in BRCA-mutated and homologous recombination deficient (HRD) cancers.

Explanation:

- Olaparib acts via synthetic lethality in cells deficient in homologous recombination repair (such as BRCA1/2-deficient ovarian, breast, pancreatic, and prostate cancers).
- Pharmacokinetically, Olaparib undergoes extensive hepatic metabolism primarily mediated by CYP3A4/5 enzymes.
- Excretion studies demonstrate that approximately 44% of the dose is recovered in urine (primarily as metabolites, with only ~ 15% unchanged drug) and approximately 42% is recovered in feces over 7 days. Thus, it is NOT 90% excreted by the kidneys.
- The most frequent clinical adverse effects are gastrointestinal (nausea, vomiting, abdominal discomfort, decreased appetite) and generalized fatigue/asthenia.
- The most frequent hematological laboratory toxicities are cytopenias (anemia, neutropenia, thrombocytopenia) along with electrolyte disturbances including hypomagnesemia and increases in serum creatinine (due to inhibition of renal transporters OCT2/MATE1).

Final Answer:

The statement that Olaparib is 90% excreted by the kidney is incorrect.

Quick Tip: Olaparib clearance is dual: ~ 44% renal and ~ 42% fecal/biliary, driven heavily by hepatic CYP3A metabolism. It is never > 90% renally excreted!

102. Chemotherapy drugs act mainly on which phase of cell cycle?

- (A) M phase
- (B) S phase
- (C) G₁ phase
- (D) G₂ phase

Correct Answer: (B) S phase

Solution:

Concept:

Cell cycle-specific chemotherapeutic agents exert their cytotoxic activity predominantly during specific phases of the eukaryotic cell cycle (G_1 , S , G_2 , or M phase).

Among all phases, the synthetic (S) phase—during which DNA replication and synthesis occur—is the target of the largest and most extensively used group of antineoplastic agents.

Explanation:

- **S Phase (Synthesis Phase):**

Antimetabolites (e.g., Methotrexate, 5-Fluorouracil, Cytarabine, Gemcitabine, 6-Mercaptopurine) incorporate into or inhibit the synthesis of DNA/RNA specifically during the S phase. Topoisomerase I inhibitors (e.g., Irinotecan, Topotecan) also induce lethal double-strand breaks during DNA synthesis in S phase.

- **M Phase (Mitosis):**

Vinca alkaloids (Vincristine, Vinblastine) and Taxanes (Paclitaxel, Docetaxel) disrupt the mitotic spindle apparatus during M phase.

- **G₂ Phase:**

Bleomycin acts primarily during the G₂ phase by generating free radicals that cleave DNA prior to mitosis.

- **Cell Cycle Non-Specific (CCNS):**

Alkylating agents (Cyclophosphamide, Cisplatin, Ifosfamide) damage resting as well as actively cycling cells, although cells in S phase remain the most vulnerable to lethal damage.

Final Answer:

The phase of the cell cycle on which the largest class of cell-cycle specific chemotherapy drugs acts is the S phase.

Quick Tip: Cell Cycle Specificity:

- **S Phase:** Antimetabolites (5-FU, MTX, Gemcitabine, Cytarabine)
- **M Phase:** Taxanes, Vinca alkaloids
- **G₂ Phase:** Bleomycin, Etoposide

103. Which of the following statements about doxorubicin-induced cardiotoxicity is false?

- (A) Acute cardiotoxicity is irreversible and often progresses to cardiomyopathy
- (B) Chronic cardiotoxicity is dose-dependent and typically presents as a dilated cardiomyopathy
- (C) Cumulative lifetime doses exceeding 500mg/m² significantly increase the risk of chronic cardiotoxicity
- (D) Dexrazoxane can be administered to prevent the most severe form of chronic cardiotoxicity

Correct Answer: (A) Acute cardiotoxicity is irreversible and often progresses to cardiomyopathy

Solution:

Concept:

Anthracyclines (such as Doxorubicin) exhibit two distinct forms of cardiotoxicity: acute and chronic.

The mechanism involves topoisomerase II β inhibition and the generation of reactive oxygen species (ROS) in cardiomyocytes.

Explanation:

- **Acute Cardiotoxicity:**

Occurs in < 1% of patients during or immediately within hours to days following infusion. It manifests as transient electrocardiographic changes (sinus tachycardia, non-specific ST-T changes, PR prolongation, premature ventricular contractions) or acute pericarditis/myocarditis. It is typically self-limiting, transient, clinically manageable, and **reversible**, rarely progressing to chronic dilated cardiomyopathy.

- **Chronic Cardiotoxicity:**

Dose-dependent, cumulative, progressive, and generally irreversible. It leads to myocyte vacuolization, loss of myofibrils, and dilated congestive heart failure.

- **Dose Thresholds:**

The risk of congestive heart failure rises sharply when the cumulative lifetime dose of doxorubicin exceeds 450–550 mg/m².

- **Cardioprotection:**

Dexrazoxane (an intracellular iron chelator and catalytic topoisomerase II inhibitor) is FDA-approved to reduce the incidence and severity of anthracycline-induced chronic cardiomyopathy.

Final Answer:

The statement claiming that acute cardiotoxicity is irreversible and progresses to cardiomyopathy is false.

Quick Tip: Anthracycline Toxicity:

- Acute: Rare, transient, reversible (arrhythmias, ECG changes).
- Chronic: Cumulative dose-dependent, irreversible (dilated cardiomyopathy). Cumulative limit: 450–550 mg/m².
- Antidote/Protector: Dexrazoxane.

104. A patient with widespread malignant melanoma and extensive pulmonary metastases presents with severe dyspnea and high anxiety. Which of the following agents is generally NOT recommended as a primary intervention for the management of the dyspnea component in this palliative care setting?

- (A) Morphine
- (B) Steroids
- (C) Benzodiazepines
- (D) Oxygen therapy

Correct Answer: (C) Benzodiazepines

Solution:

Concept:

Dyspnea is one of the most distressing refractory symptoms in advanced cancer with pulmonary metastases.

International palliative care guidelines (ASCO, ESMO, EAPC) provide clear hierarchies for pharmacologic and non-pharmacologic interventions.

Explanation:

- **Opioids (Morphine):**

Low-dose systemic opioids (such as oral or parenteral Morphine) are the first-line, evidence-based gold standard for relieving refractory cancer-related dyspnea. They decrease the perception of breathlessness and reduce central respiratory drive sensitivity without causing dangerous hypercapnia.

- **Steroids (Corticosteroids):**

Useful in inflammatory peritumoral edema, lymphangitic carcinomatosis, or airway obstruction.

- **Oxygen Therapy:**

Indicated in hypoxemic patients ($\text{SpO}_2 < 90\%$) to relieve dyspnea.

- **Benzodiazepines:**

Multiple Cochrane systematic reviews and ASCO palliative care guidelines state that benzodiazepines are NOT effective as a primary therapy for relieving the sensation of dyspnea itself. They may be added as a second- or third-line adjunct specifically for refractory episodic panic/anxiety associated with breathlessness, but not as a primary treatment for dyspnea.

Final Answer:

Benzodiazepines are not recommended as a primary intervention for managing dyspnea in palliative care.

Quick Tip: Primary drug for cancer dyspnea: Opioids (Morphine).

Benzodiazepines are used for associated acute panic/anxiety crisis, never as primary therapy for dyspnea!

105. A 45-year-old female patient with no history of prior radiation or chemotherapy was successfully treated for endometrial adenocarcinoma three years ago. She now presents a new diagnosis of colon adenocarcinoma. This combination of two primary, non-contiguous cancers is highly suggestive of an underlying hereditary predisposition. Which of the following inherited cancer syndromes is the most likely diagnosis?

- (A) Lynch syndrome
- (B) Cowden syndrome

- (C) Familial Adenomatous Polyposis (FAP)
(D) Peutz-Jeghers syndrome

Correct Answer: (A) Lynch syndrome

Solution:

Concept:

Lynch syndrome, also termed Hereditary Non-Polyposis Colorectal Cancer (HNPCC), is an autosomal dominant inherited disorder caused by germline mutations in DNA mismatch repair (MMR) genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*) or deletions in *EPCAM*.

Explanation:

- Lynch syndrome is characterized by a high lifetime risk of colorectal cancer (50–80%) and endometrial cancer (40–60%).
- In women with Lynch syndrome, endometrial adenocarcinoma is the sentinel (first presenting) malignancy in more than 50% of cases, frequently preceding the diagnosis of colorectal cancer.
- The Amsterdam II and revised Bethesda criteria specifically highlight the combination of early-onset colorectal carcinoma and endometrial carcinoma as hallmarks of Lynch syndrome.
- **Cowden syndrome** (*PTEN* mutation) is associated with breast, thyroid (follicular), and endometrial cancers, but colorectal adenocarcinoma is far less prominent and presents with hamartomatous polyps.
- **FAP** (*APC* gene) presents with thousands of adenomatous colonic polyps and duodenal/ampullary cancers rather than endometrial cancer.

- **Peutz-Jeghers syndrome** (*STK11* gene) is characterized by mucocutaneous pigmentation and hamartomas with elevated risks of gastrointestinal and breast/cervical adenoma malignum.

Final Answer:

The most likely inherited cancer syndrome is Lynch syndrome.

Quick Tip: Classic Lynch syndrome pair in females: Endometrial cancer followed by Colorectal cancer (or vice versa) at a young age (< 50 years). Always screen with MMR immunohistochemistry / MSI testing.

106. Which of the following statements is TRUE regarding HPV-positive Squamous Cell Carcinoma (SCC) of the head and neck?

- (A) HPV status does not significantly impact the prognosis or overall survival compared to HPV-negative disease.
- (B) The response rate to standard chemotherapy and radiation protocols is worse than in patients with HPV-negative disease.
- (C) HPV-positive tumors typically arise in patients with a heavy smoking and alcohol history, similar to HPV-negative tumors.
- (D) HPV most commonly causes non keratinizing cancer

Correct Answer: (D) HPV most commonly causes non keratinizing cancer

Solution:

Concept:

High-risk Human Papillomavirus (predominantly HPV-16) is the leading etiological factor for oropharyngeal squamous cell carcinoma (OPSCC), arising in the palatine tonsils and base of tongue.

Explanation:

- Histopathologically, HPV-associated oropharyngeal carcinomas exhibit a distinctive morphology characterized by **non-keratinizing** or basaloid histology, growing in cohesive sheets or nests with prominent comedonecrosis and lymphoid stroma.
- **Prognosis:** Unlike HPV-negative tumors, HPV-positive OPSCC is associated with a significantly better prognosis and improved overall survival. This prompted a separate staging system in the AJCC 8th edition.
- **Treatment Response:** HPV-positive tumors are exquisitely sensitive to chemoradiotherapy, showing markedly higher locoregional control and complete response rates compared to HPV-negative cancers.
- **Risk Factors:** HPV-positive OPSCC typically arises in younger individuals, often non-smokers and non-drinkers, with risk linked to sexual behavior (number of oral sex partners), distinct from HPV-negative SCC which is strongly correlated with tobacco and alcohol.

Final Answer:

The true statement is that HPV most commonly causes non-keratinizing cancer.

Quick Tip: HPV-positive HNSCC features:

- Non-keratinizing histology (p16 overexpression)
- Younger, non-smokers
- Highly radiosensitive/chemosensitive
- Superior overall survival compared to HPV-negative HNSCC

107. Which is the mechanism of neutrophil dysfunction in febrile neutropenia?

- (A) CXCR downregulation and less chemotaxis
- (B) NADPH oxidase dysfunction and phagocytosis defect
- (C) Chemo induced neutrophil apoptosis
- (D) Maturation block of neutrophil

Correct Answer: (C) Chemo induced neutrophil apoptosis

Solution:

Concept:

Cytotoxic chemotherapy damages rapidly dividing hematopoietic progenitor cells in the bone marrow, triggering accelerated cell death and functional exhaustion of granulocyte lineages.

Explanation:

- Neutrophils are short-lived myeloid cells that naturally undergo constitutive apoptosis within 24–48 hours in circulation.
- Chemotherapeutic agents (such as anthracyclines, taxanes, and alkylators) induce DNA double-strand breaks, reactive oxygen species accumulation, and activation of intrinsic mitochondrial apoptotic pathways (via caspase cascades) in circulating and marrow-resident neutrophils and their precursors.
- This chemotherapy-induced accelerated apoptosis causes both a precipitous quantitative decline (absolute neutrophil count $< 500/\mu\text{L}$) and functional impairment of the remaining granulocytes, leaving the host vulnerable to bacteremia and febrile neutropenia.
- Other mechanisms, such as primary genetic blocks in maturation or congenital NADPH oxidase failure (Chronic Granulomatous Disease), are congenital rather than acquired consequences of antineoplastic chemotherapy.

Final Answer:

The primary mechanism underlying chemotherapy-associated neutrophil depletion and dysfunction is chemotherapy-induced neutrophil apoptosis.

Quick Tip: Cytotoxic chemotherapy rapidly triggers intrinsic mitochondrial apoptosis in marrow progenitor cells and mature neutrophils, leading to sudden neutropenic nadirs.

108. Which of the following is the most frequent and dose-limiting cutaneous toxicity specifically associated with Capecitabine therapy?

- (A) Hand foot Syndrome
- (B) Interstitial pneumonitis
- (C) Nephrotoxicity
- (D) Peripheral neuropathy

Correct Answer: (A) Hand foot Syndrome

Solution:

Concept:

Capecitabine is an orally administered prodrug of 5-Fluorouracil (5-FU) that is converted to active 5-FU in tumor tissues through a three-step enzymatic cascade culminating with thymidine phosphorylase.

Explanation:

- Hand-Foot Syndrome (HFS), also known as Palmar-Plantar Erythrodysesthesia (PPE), is the most frequent and classic dose-limiting toxicity of Capecitabine, occurring in up to 50–60% of treated patients.
- Pathophysiology is linked to high expression of thymidine phosphorylase in the keratinocytes of the palms and soles, leading to local accumulation of 5-FU metabolites,

microvascular damage from everyday mechanical stress, and localized inflammatory COX-2 overexpression.

- Clinical manifestations include progressive erythema, dysesthesia, tingling, edema, painful desquamation, blistering, and ulceration on the palmar and plantar surfaces.
- Management involves dose interruptions, dose reductions, topical emollients, and oral pyridoxine (Vitamin B6) or celecoxib for symptom mitigation.
- Interstitial pneumonitis, nephrotoxicity, and severe peripheral neuropathy are not characteristic cutaneous or dose-limiting side effects of capecitabine.

Final Answer:

Hand-Foot Syndrome is the most frequent and dose-limiting cutaneous toxicity associated with Capecitabine.

Quick Tip: Classic associations for Hand-Foot Syndrome:

- Capecitabine / Infusional 5-FU
- Pegylated Liposomal Doxorubicin (PLD)
- Multi-targeted TKIs (Sorafenib, Regorafenib - causes Hand-Foot Skin Reaction [HFSR])

109. During infusion of a platinum based chemotherapeutic agent, a patient develops acute throat tightness, jaw pain, and distal paresthesias. These symptoms are known to worsen immediately upon exposure to which environmental factor?

- (A) Cold exposure
- (B) High-intensity exercise
- (C) Consumption of high-sugar foods
- (D) Exposure to bright light

Correct Answer: (A) Cold exposure

Solution:

Concept:

Oxaliplatin, a third-generation diaminocyclohexane (DACH) platinum derivative used extensively in colorectal and gastrointestinal cancers, causes a unique and stereotypic acute neurotoxicity syndrome.

Explanation:

- Acute oxaliplatin-induced neurotoxicity occurs in > 90% of patients during or within hours of infusion and is exquisitely triggered or exacerbated by **exposure to cold temperatures** (e.g., drinking cold beverages, touching cold objects, breathing cold air).
- Symptoms include perioral and distal paresthesias, pharyngolaryngeal dysesthesia (a subjective sensation of difficulty swallowing or shortness of breath without objective airway obstruction), muscle cramps, and jaw stiffness.
- The underlying molecular mechanism involves the metabolite oxalate, which chelates intracellular calcium and alters the kinetics of voltage-gated sodium channels (Na_v1.6), causing neuronal hyperexcitability that is worsened by low temperatures.
- Patients are routinely counseled to avoid cold drinks, wear gloves/scarves, and avoid cold ambient environments for several days post-infusion.

Final Answer:

These acute symptoms are specifically triggered and exacerbated by cold exposure.

Quick Tip: Oxaliplatin = Cold-induced acute pharyngolaryngeal dysesthesia and peripheral paresthesias!

Always advise patients to avoid cold drinks, ice, and cold air exposure for 48–72 hours post-infusion.

110. Which of the following statements is TRUE regarding the evidence and clinical outcomes associated with routine breast cancer screening mammography for women at average risk?

- (A) Randomized controlled trials have consistently demonstrated a significant breast cancer survival advantage for women screened in the 50 to 74 years age range.
- (B) The false-positive rate for a single screening mammogram is lowest in the 40-49 age range compared to women aged 50 and older.
- (C) Screening mammography is primarily recommended to detect ductal carcinoma in situ (DCIS), which has the greatest impact on reducing mortality.
- (D) The most recent U.S. Preventive Services Task Force (USPSTF) guidelines recommend discontinuing screening at age 65.

Correct Answer: (A) Randomized controlled trials have consistently demonstrated a significant breast cancer survival advantage for women screened in the 50 to 74 years age range.

Solution:

Concept:

Routine screening mammography in average-risk asymptomatic women aims to detect breast cancer at an early, curable stage to reduce disease-specific mortality.

Explanation:

- Extensive landmark randomized controlled trials (such as the Swedish Two-County, Malmö, and Edinburgh trials) and long-term meta-analyses demonstrate a 15–25% reduction in breast cancer mortality among women aged 50–74 years who undergo regular screening.

- The false-positive rate is actually highest in younger women (ages 40–49) due to higher breast tissue density, leading to more recalls and unnecessary biopsies.
- The primary objective of screening is to detect early-stage invasive carcinomas (which confers the mortality benefit); overdiagnosis of indolent ductal carcinoma in situ (DCIS) is considered a potential harm/downside rather than the primary driver of mortality reduction.
- Major guidelines (USPSTF, ACS) recommend screening through at least age 74 (provided life expectancy is ≥ 10 years), not discontinuing at age 65.

Final Answer:

The true statement is that RCTs have consistently demonstrated a significant breast cancer survival advantage for women screened in the 50 to 74 years age range.

Quick Tip: Breast cancer screening evidence:

- Maximum mortality reduction and highest precision is established in the 50–74 age group.
- Younger women (< 50) have denser breasts, leading to higher false-positive rates and lower positive predictive value.

111. What is a major limitation of AI in medical imaging?

- (A) Cost effectiveness
- (B) Lack of interpretability
- (C) Eliminates the need for clinicians
- (D) All of the above

Correct Answer: (B) Lack of interpretability

Solution:

Concept:

Artificial Intelligence (AI), particularly deep learning utilizing Convolutional Neural Networks (CNNs), has revolutionized automated feature detection, segmentation, and lesion characterization in diagnostic radiology and medical imaging.

Despite its remarkable predictive accuracy, clinical translation is fundamentally limited by the “black box” nature of deep neural networks.

Explanation:

- **Black Box Phenomenon (Lack of Interpretability):** Deep learning architectures process millions of interconnected matrix parameters across hidden layers. Consequently, they cannot provide transparent, human-understandable biological or mechanistic reasoning for why a specific prediction or classification was made.
- This lack of explainability creates significant medicolegal, ethical, and clinical trust challenges, especially when algorithm outputs conflict with expert human clinical judgment.
- **Role in Healthcare:** AI is designed strictly as a clinical decision-support tool to augment radiologist efficiency and reduce perceptual errors; it is not intended to, nor does it, eliminate the necessity of trained clinicians.
- **Economic Impact:** AI algorithms frequently enhance high-volume throughput and triage efficiency, making cost-effectiveness an advantage rather than a fundamental technical limitation.
- Current active research focuses on Explainable AI (XAI), saliency maps, and class-activation maps to mitigate this core interpretability deficit.

Final Answer:

The lack of interpretability (the “black box” problem) represents a primary and major limitation

of AI models in medical imaging.

Quick Tip: Core limitation of Deep Learning/AI in medicine: “Black Box” nature / Lack of Explainability and Interpretability.

AI augments clinician workflow but cannot replace clinician oversight and ethical responsibility.

112. A patient receiving first-cycle chemotherapy via a new central venous catheter suddenly develops fever (102.5°F) with chills during infusion, but no rash or local inflammation. What is the likely diagnosis and next step?

- (A) Hemorrhagic reaction – give Vitamin K
- (B) Allergic reaction – give antihistamine
- (C) Catheter-related bloodstream infection (CRBSI) – send cultures
- (D) Thrombus dislodgement – remove central line

Correct Answer: (C) Catheter-related bloodstream infection (CRBSI) – send cultures

Solution:

Concept:

Catheter-related bloodstream infection (CRBSI) is one of the most critical infectious complications associated with central venous access devices (CVADs) in cancer patients undergoing active chemotherapy.

The sudden onset of high-grade fever and rigors during or shortly after line flushing or infusion is the classic herald of line sepsis.

Explanation:

- Manipulation and fluid administration through a colonized catheter lumen dislodge bacterial biofilms and endoluminal pathogens directly into the central circulation, causing abrupt bacteremia, rigors, and pyrexia.

- The absence of local exit-site erythema or purulence does not rule out CRBSI, as intraluminal colonization without external skin inflammation occurs in over 50% of central line infections.
- **Immediate Management Protocol:**
 1. Blood cultures must be drawn immediately from both the central venous catheter hub (each lumen individually) and a peripheral venipuncture site prior to initiating antimicrobial therapy (paired quantitative blood cultures or differential time to positivity [DTP ≥ 2 hours]).
 2. Empiric broad-spectrum intravenous antimicrobial therapy covering Gram-positive cocci (including MRSA) and Gram-negative bacilli (including *Pseudomonas aeruginosa*) should be instituted promptly after drawing cultures.
- Immediate catheter removal is reserved for septic shock, tunnel infection, suppurative thrombophlebitis, or specific virulent pathogens (*S. aureus*, *P. aeruginosa*, fungi).

Final Answer:

The most likely diagnosis is catheter-related bloodstream infection (CRBSI), and the immediate next diagnostic step is to draw paired blood cultures.

Quick Tip: Sudden fever + chills during central line flush/infusion = Catheter-Related Bloodstream Infection (CRBSI) until proven otherwise.

Golden rule: Always draw blood cultures (peripheral + central lumens) before starting empiric broad-spectrum IV antibiotics!

113. What is the role of AI in the pre-processing of images?

- (A) Data segmentation
- (B) Edge detection

- (C) Feature extraction
(D) All of the above

Correct Answer: (D) All of the above

Solution:

Concept:

In medical imaging and computer vision pipelines, image pre-processing and initial computer-aided detection (CAD) involve transforming raw radiological pixel/voxel arrays into structured mathematical representations suitable for classification, detection, and diagnostic modeling.

Explanation:

- **Data/Image Segmentation:** Artificial intelligence algorithms (such as U-Net architectures and Fully Convolutional Networks) delineate anatomical boundaries, isolate target organs, and separate regions of interest (ROIs) like tumors or metastases from background parenchyma.
- **Edge Detection:** AI models apply spatial convolutional filter matrices (e.g., Sobel, Prewitt, Laplacian, and Canny kernels) to detect abrupt local discontinuities in image pixel brightness, identifying organ margins, vessel walls, and tissue interfaces.
- **Feature Extraction:** Radiomics and deep convolutional layers systematically extract high-dimensional quantitative descriptors, including textural features (gray-level co-occurrence matrix [GLCM]), spatial shape descriptors, and semantic morphological characteristics from the raw image data.
- Because all these operations are fundamental sequential steps in automated medical image preparation and analysis pipelines, AI encompasses all three roles.

Final Answer:

AI plays an integral role in data segmentation, edge detection, and feature extraction during

medical image processing.

Quick Tip: AI Image Analysis Workflow:

Raw Input → Pre-processing (Denoising/Normalization) → Edge Detection → Segmentation (ROI isolation) → Feature Extraction (Radiomics) → Classification/Diagnosis.

114. During oxaliplatin infusion, a patient develops perioral tingling and sensation of choking (laryngospasm). What is the most likely cause?

- (A) Oxaliplatin-induced cold hypersensitivity
- (B) Irinotecan
- (C) Oxaliplatin allergy
- (D) Electrolyte imbalance

Correct Answer: (A) Oxaliplatin-induced cold hypersensitivity

Solution:

Concept:

Oxaliplatin, a key platinum agent used in the FOLFOX and CAPOX regimens for gastrointestinal malignancies, characteristically induces an acute, transient, cold-triggered neurosensory syndrome.

Explanation:

- Acute oxaliplatin-induced neuropathy occurs in up to 85–95% of patients and develops rapidly during or within several hours to days of drug infusion.
- **Clinical Presentation:** Symptoms predominantly manifest as distal extremity paresthesias, perioral numbness/tingling, jaw stiffness, and **acute pharyngolaryngeal dysesthesia** (a sensation of throat tightness, difficulty swallowing, or choking resembling

laryngospasm).

- Importantly, this pharyngolaryngeal dysesthesia is a subjective neurosensory phenomenon without true anatomical airway obstruction, stridor, wheezing, or hypoxia.
- **Trigger and Mechanism:** Symptoms are acutely precipitated or aggravated by exposure to cold temperatures (drinking cold liquids, eating ice cream, touching cold metal, breathing cold air).
- The mechanism involves oxalate metabolite-mediated chelation of extracellular calcium/magnesium and disruption of voltage-gated sodium (Na_v) and potassium channel kinetics, resulting in transient peripheral nerve hyperexcitability.
- A true IgE-mediated allergic hypersensitivity reaction typically occurs after multiple cycles (usually cycle 6–8) and manifests with systemic urticaria, bronchospasm, flushing, and hemodynamic instability.

Final Answer:

The development of perioral tingling and choking sensation during oxaliplatin infusion is caused by Oxaliplatin-induced cold hypersensitivity (acute neurotoxicity).

Quick Tip: Oxaliplatin Acute Toxicity: Cold-triggered perioral paresthesias and pseudolaryngospasm (pharyngolaryngeal dysesthesia).

Advise patients: Do not drink cold liquids or touch cold objects for 3–5 days around each infusion!

115. A patient treated for a Germ Cell Tumor (GCT) with a chemotherapy regimen including Bleomycin presents months later with persistent cough and dyspnea. CT scan shows ground-glass opacities (GGOs) with reticulonodular infiltrates, suggestive of pulmonary toxicity. Which factor is NOT typically implicated in exacerbating the risk of this complication?

- (A) Active smoking
- (B) Cumulative bleomycin dose of 100 IU
- (C) Use of GCSF
- (D) Compromised renal function

Correct Answer: (B) Cumulative bleomycin dose of 100 IU

Solution:

Concept:

Bleomycin-induced pulmonary toxicity (BIPT) ranges from subacute pneumonitis to fatal irreversible pulmonary fibrosis.

Bleomycin hydrolase (the inactivating enzyme) is deficient in pulmonary tissue and skin, leading to selective accumulation of bleomycin, generation of iron-dependent reactive oxygen species (ROS), endothelial damage, and inflammatory alveolar injury.

Explanation:

- **Established Risk Factors for Bleomycin Pulmonary Toxicity:**

1. **Cumulative Lifetime Dose:** Pulmonary toxicity is strongly cumulative-dose dependent. The incidence rises sharply when the cumulative dose exceeds 400 units (400 mg or 400 IU), and lifetime exposure is strictly capped at 400–450 IU. A low cumulative dose of only 100 IU is considered safe and is NOT a risk factor for exacerbating toxicity.
2. **Renal Dysfunction:** Bleomycin is cleared 60–70% by the kidneys; impaired creatinine clearance drastically reduces drug clearance, causing toxic systemic accumulation.
3. **Age and Smoking:** Advanced age (> 40–50 years) and concurrent or past cigarette smoking significantly amplify pulmonary injury.
4. **Granulocyte Colony-Stimulating Factors (G-CSF):** Co-administration of G-CSF induces neutrophil influx into lung parenchyma, exacerbating cytokine-driven alveolar inflammation.
5. **High Inspired Oxygen (FiO₂):** Hyperoxia generates massive free radical cascades, triggering severe pneumonitis during general anesthesia or post-chemotherapy surgery.

Final Answer:

A low cumulative dose of 100 IU is well below the toxic threshold and is not implicated in exacerbating bleomycin-induced pulmonary toxicity.

Quick Tip: Bleomycin Toxicity Risk Factors:

- Cumulative dose > 400 IU (Threshold for high risk)
- Renal impairment ($\downarrow$ clearance)
- High FiO_2 (Oxygen toxicity during anesthesia)
- G-CSF use
- Smoking history

116. A patient with Kaposi Sarcoma (KS) is being treated with pegylated liposomal doxorubicin. Which of the following is considered a frequent and dose-limiting toxicity for this specific chemotherapy agent and its formulation?

- (A) Hand-Foot Syndrome
- (B) Hemorrhagic Cystitis
- (C) Peripheral Neuropathy
- (D) Ocular Toxicity

Correct Answer: (A) Hand-Foot Syndrome

Solution:**Concept:**

Pegylated Liposomal Doxorubicin (PLD / Doxil / Caelyx) encapsulates doxorubicin within polyethylene glycol-coated liposomes, drastically altering its pharmacokinetic distribution. This formulation protects against myocardial uptake (markedly reducing anthracycline cardiotoxicity) but introduces a unique spectrum of cutaneous toxicity.

Explanation:

- **Hand-Foot Syndrome (Palmar-Plantar Erythrodysesthesia):** Hand-foot syndrome (HFS) is the primary dose-limiting toxicity and the most frequent adverse reaction associated with PLD, occurring in 30–50% of treated patients.
- **Mechanism:** The prolonged circulation half-life of pegylated liposomes allows them to extravasate through the microcapillary network in high-pressure, mechanically stressed friction zones (palms, soles, pressure points) and eccrine sweat glands, releasing free doxorubicin directly into the epidermis.
- **Clinical Features:** Painful symmetrical erythema, edema, desquamation, bullae formation, and severe burning pain on the hands and feet requiring dose reduction or interval prolongation.
- **Other Options:** Hemorrhagic cystitis is characteristic of Ifosfamide and Cyclophosphamide (prevented by Mesna). Peripheral neuropathy is typical of Taxanes, Vinca alkaloids, and Platinums. Ocular toxicity is associated with high-dose Cytarabine or Fluorouracil.

Final Answer:

Hand-Foot Syndrome is the most frequent and dose-limiting toxicity of Pegylated Liposomal Doxorubicin.

Quick Tip: - Conventional Doxorubicin: Dose-limiting toxicity is Cardiotoxicity and Myelosuppression.
 - Pegylated Liposomal Doxorubicin (PLD): Dose-limiting toxicity is Hand-Foot Syndrome (Mucocutaneous toxicity), with minimal cardiotoxicity!

117. Which of the following is not a type of anal cancer?

(A) Bowen Disease

- (B) Paget's Disease
(C) Signet Cell Carcinoma / Adenocarcinoma
(D) Basal Cell Carcinoma

Correct Answer: (D) Basal Cell Carcinoma

Solution:

Concept:

Anal canal and perianal margin neoplasms comprise a heterogeneous group of histologic subtypes arising from the squamocolumnar junction, squamous mucosa, transitional zone, glandular epithelium, and apocrine sweat glands.

Explanation:

- **Bowen's Disease (Perianal High-Grade Squamous Intraepithelial Lesion [HSIL]):** Represents squamous cell carcinoma in situ of the perianal skin and anal margin, characterized by intraepidermal atypia with full-thickness dysplasia.
- **Extramammary Paget's Disease (EMPD):** An intraepithelial adenocarcinoma of the perianal epidermis originating from glandular/apocrine structures or underlying colorectal/anal canal adenocarcinoma.
- **Signet Cell Carcinoma / Adenocarcinoma:** Primary adenocarcinoma of the anal canal arises from the anal glands (crypts of Lieberkühn) or mucosal transitional lining, and can exhibit prominent mucin-secreting signet-ring cell histology.
- **Basal Cell Carcinoma (BCC):** Although BCC can rarely arise on sun-damaged perianal skin, true Basal Cell Carcinoma is extremely rare and is NOT recognized as an intrinsic epithelial tumor of the anal canal proper in major oncology/WHO classifications. Basaloid (cloacogenic) squamous carcinoma should not be confused with cutaneous basal cell carcinoma.

Final Answer:

Basal Cell Carcinoma is not a standard intrinsic pathological subtype of anal canal malignancy.

Quick Tip: Anal Neoplasms:

- Squamous Cell Carcinoma (SCC) = > 85% (HPV-related).
- Adenocarcinoma / Signet-ring = from anal crypt glands.
- Intraepithelial: Bowen's disease (SCC in situ), Paget's disease (Adeno in situ).
- Basaloid carcinoma is a variant of SCC, distinct from skin BCC!

118. Which among the following is a GM-CSF that prevents neutropenia and neutropenic infections?

- (A) Sargramostim
- (B) Filgrastim
- (C) Romiplostim
- (D) Oprelvekin

Correct Answer: (A) Sargramostim

Solution:**Concept:**

Myeloid growth factors are recombinant cytokines used in oncology to shorten the duration and mitigate the depth of chemotherapy-induced neutropenia, thereby preventing febrile neutropenia and life-threatening infections.

Explanation:

- **Sargramostim:** Recombinant human Granulocyte-Macrophage Colony-Stimulating Factor (rhu **GM-CSF**). It stimulates proliferation, differentiation, and functional activation of neutrophils, eosinophils, monocytes, and macrophages from early pluripotential

myeloid progenitor cells.

- **Filgrastim (and Pegfilgrastim):** Recombinant Granulocyte Colony-Stimulating Factor (G-CSF). It acts selectively on the neutrophil lineage to stimulate proliferation and maturation of neutrophil precursors.
- **Romiplostim:** A peptide “peptibody” thrombopoietin (TPO) receptor agonist used to stimulate platelet production in immune thrombocytopenia (ITP) and chemotherapy-induced thrombocytopenia.
- **Oprelvekin:** Recombinant Interleukin-11 (rhIL-11) that stimulates megakaryocytopoiesis and thrombopoiesis to prevent severe chemotherapy-induced thrombocytopenia.

Final Answer:

Sargramostim is the GM-CSF used to prevent neutropenia and related infections.

Quick Tip: Recombinant Hematopoietic Growth Factors:

- **GM-CSF:** Sargramostim
- **G-CSF:** Filgrastim, Lenograstim, Pegfilgrastim
- **TPO-RA:** Romiplostim, Eltrombopag
- **IL-11:** Oprelvekin

119. A patient receiving the third cycle of a Paclitaxel infusion suddenly develops severe dyspnea, hypotension, and generalised urticaria, indicating a probable anaphylactic reaction. Assuming the infusion has been stopped, which of the following is the most immediate and life-saving intervention required?

- (A) Change drug
- (B) Reduce dose

- (C) Epinephrine shot
(D) Give steroids and premeds with next cycle

Correct Answer: (C) Epinephrine shot

Solution:

Concept:

Severe hypersensitivity/anaphylactic reactions during taxane (Paclitaxel) chemotherapy are medical emergencies triggered by the formulation solvent (Cremophor EL / polyoxyethylated castor oil) or an IgE-mediated response.

Anaphylaxis presenting with hemodynamic collapse (hypotension) and respiratory distress requires immediate, protocol-driven emergency resuscitation.

Explanation:

- **First-Line Emergency Therapy:** Intramuscular **Epinephrine (Adrenaline)** (1 : 1000 concentration, 0.3–0.5 mg IM into the anterolateral mid-thigh) is the immediate drug of choice and the only intervention proven to arrest progression and reverse fatal cardiorespiratory collapse in anaphylaxis.
- Epinephrine rapidly reverses peripheral vasodilation and hypotension via α_1 -adrenergic vasoconstriction, relieves bronchospasm via β_2 -adrenergic bronchodilation, and inhibits further mediator release from mast cells and basophils.
- **Role of Other Agents:** Antihistamines (H_1 and H_2 blockers) and corticosteroids (methylprednisolone/hydrocortisone) are secondary, adjunctive treatments; they have a slow onset of action and do not prevent acute airway closure or shock.
- Modifying chemotherapy doses or planning future premedications are late post-stabilization considerations and have no role during acute resuscitation.

Final Answer:

The most immediate and life-saving intervention after stopping the infusion is an intramuscular epinephrine shot.

Quick Tip: Anaphylaxis Algorithm:

1. Stop the offending infusion immediately.
2. Give Intramuscular Epinephrine (0.3–0.5 mg IM into mid-outer thigh) immediately.
3. Secure airway, provide high-flow oxygen and rapid IV crystalloid boluses.
4. Steroids and antihistamines are second-line adjuncts!

120. A patient with small cell lung cancer (SCLC) receiving cisplatin and etoposide develops an increase in serum creatinine from 1.2 mg/dL to 3.5 mg/dL after several cycles of chemotherapy. What is the most appropriate next step in management?

- (A) Adequate hydration before and after chemo
- (B) Discontinue cisplatin and switch to carboplatin
- (C) Discontinue cisplatin and initiate haemodialysis
- (D) Dose reduction of cisplatin

Correct Answer: (B) Discontinue cisplatin and switch to carboplatin

Solution:

Concept:

Cisplatin is a potent nephrotoxic agent causing acute tubular necrosis, proximal tubular injury, and reduced glomerular filtration rate (GFR).

When significant nephrotoxicity develops (creatinine > 2.0 mg/dL or GFR < 50 – 60 mL/min), continuation of cisplatin is contraindicated.

Explanation:

- A steep rise in serum creatinine from 1.2 mg/dL to 3.5 mg/dL indicates severe Grade 3

acute kidney injury (AKI).

- Cisplatin accumulates selectively in renal tubular epithelial cells, generating reactive oxygen species, mitochondrial fragmentation, and apoptosis. Re-exposure or dose-reduction of cisplatin in an already damaged kidney risks irreversible renal failure.
- **Role of Carboplatin:** Carboplatin is an analogue of cisplatin that possesses significantly less nephrotoxicity, neurotoxicity, and ototoxicity while providing comparable anti-tumor efficacy in Small Cell Lung Cancer (SCLC).
- Carboplatin can be accurately and safely dosed according to residual renal function using the Calvert formula:

$$\text{Dose (mg)} = \text{Target AUC} \times (\text{GFR} + 25)$$

- Therefore, substituting cisplatin with carboplatin allows ongoing systemic therapy of the aggressive SCLC without further exacerbating nephrotoxicity.
- Hemodialysis is reserved for refractory uremic symptoms, hyperkalemia, severe metabolic acidosis, or fluid overload, not as an isolated response to elevated creatinine.

Final Answer:

The most appropriate oncologic management is to discontinue cisplatin and switch to carboplatin.

Quick Tip: Cisplatin vs. Carboplatin Toxicities:

- Cisplatin = Highly Nephrotoxic, Emetogenic, Ototoxic, Neurotoxic.
- Carboplatin = Dose-limiting Myelosuppression (Thrombocytopenia), but minimal nephrotoxicity.
- If renal function declines on Cisplatin, switch to Carboplatin!

121. A patient receiving chemotherapy presents with fever (temperature $>38^{\circ}\text{C}$) and neutropenia (absolute neutrophil count $<500/\text{mm}^3$). What is the first step in management?

- (A) Administer granulocyte colony-stimulating factor (G-CSF)
- (B) Administer broad spectrum antibiotics
- (C) Obtain bone marrow biopsy
- (D) Start antifungal therapy immediately

Correct Answer: (B) Administer broad spectrum antibiotics

Solution:

Concept:

Febrile neutropenia (FN) is defined as an oral temperature $> 38.3^{\circ}\text{C}$ (or $> 38.0^{\circ}\text{C}$ sustained over 1 hour) with an Absolute Neutrophil Count (ANC) $< 500/\mu\text{L}$ (or $< 1000/\mu\text{L}$ with a predicted fall to $< 500/\mu\text{L}$).

It is a critical oncologic emergency carrying substantial mortality from rapid septic shock.

Explanation:

- Neutropenic patients have a compromised inflammatory response, meaning classical signs of localized infection are often absent. Bacterial pathogens (especially *Pseudomonas aeruginosa* and other Gram-negative enteric bacilli) can cause fulminant bacteremia within hours.
- **The “Golden Hour” Rule:** International guidelines (ASCO, IDSA, ESMO) mandate that empiric, broad-spectrum, antipseudomonal intravenous monotherapy (e.g.,

Piperacillin-Tazobactam, Cefepime, Meropenem) must be initiated within **1 hour** of triage.

- Blood cultures, basic laboratory workups, and physical assessment should be performed immediately, followed without delay by antibiotic administration.
- Therapeutic G-CSF is not routinely recommended for all uncomplicated cases of established FN and does not substitute for antibiotics.
- Empiric antifungal therapy is only indicated for persistent or recrudescent fever after 4–7 days of broad-spectrum antibacterial coverage.
- Bone marrow biopsy is unnecessary and contraindicated in acute neutropenic sepsis due to bleeding and infection risks.

Final Answer:

The vital first step in managing febrile neutropenia is the prompt administration of broad-spectrum antipseudomonal antibiotics.

Quick Tip: Febrile Neutropenia = Start IV Antipseudomonal β -lactam (Cefepime / Pip-Tazo / Meropenem) within the FIRST HOUR (The Golden Hour)!

122. A patient receiving immune checkpoint inhibitor therapy develops elevated liver enzymes. What is the most appropriate management?

- (A) Reduce dose of immunotherapy
- (B) Treat with infliximab
- (C) Discontinue immunotherapy and put on steroids
- (D) Change to another immunotherapy agent

Correct Answer: (C) Discontinue immunotherapy and put on steroids

Solution:

Concept:

Immune checkpoint inhibitor (ICI)-mediated hepatotoxicity (immune-mediated hepatitis) is an autoimmune adverse effect characterized by asymptomatic elevations in AST, ALT, and total bilirubin.

Management is dictated by the grade of toxicity according to ASCO, SITC, and ESMO clinical practice guidelines.

Explanation:

- **Grading and Management Principles:**

1. For Grade 1 ($\text{AST/ALT} \leq 3 \times \text{ULN}$): Continue ICI with close weekly monitoring.
2. For Grade 2 ($\text{AST/ALT} > 3\text{--}5 \times \text{ULN}$): Withhold immunotherapy; if transaminases remain elevated, initiate systemic corticosteroids (Prednisone 0.5–1 mg/kg/day).
3. For Grade 3/4 ($\text{AST/ALT} > 5 \times \text{ULN}$): Immediately and permanently discontinue immunotherapy, and initiate high-dose systemic corticosteroids (Methylprednisolone 1–2 mg/kg/day IV).

- **Why Infliximab is Contraindicated in Hepatitis:** Infliximab (anti-TNF- α) carries a black-box warning for hepatic injury and is strictly contraindicated in ICI-induced hepatitis due to the risk of exacerbating liver failure. Instead, **Mycophenolate Mofetil (MMF)** is the second-line immunosuppressive agent of choice for steroid-refractory hepatitis.

- Dose reductions are never performed with monoclonal antibody immunotherapies; the drug is either held or permanently discontinued.

Final Answer:

The established management for significant ICI-induced transaminitis is to discon-

tinue/withhold immunotherapy and initiate systemic corticosteroids.

Quick Tip: ICI Hepatitis Rule:

- Hold/Discontinue ICI + Start Corticosteroids (Prednisone/Methylprednisolone).
- If refractory to steroids: Use Mycophenolate Mofetil (MMF).
- NEVER use Infliximab for ICI Hepatitis (hepatotoxic)!

123. A patient who recently completed thoracic radiotherapy presents several weeks later with shortness of breath, dry cough, and low-grade fever. What would be the most appropriate management for this condition?

- (A) High-dose steroids
- (B) Antibiotics
- (C) Antifungals
- (D) High-flow oxygen

Correct Answer: (A) High-dose steroids

Solution:

Concept:

Radiation pneumonitis is a subacute inflammatory reaction of the pulmonary parenchyma occurring classically 4 to 12 weeks following the completion of thoracic radiotherapy. It results from radiation-induced endothelial and type II pneumocyte damage, triggering macrophage activation and pro-inflammatory cytokine cascades (IL-1, IL-6, TNF- α , TGF- β).

Explanation:

- **Clinical Presentation:** Hallmark features include progressive dyspnea on exertion, persistent non-productive dry cough, low-grade pyrexia, and pleuritic chest discomfort.

- **Imaging Findings:** CT of the chest characteristically demonstrates ground-glass opacities and alveolar consolidation corresponding geometrically to the radiotherapy treatment portal (conforming to radiation fields rather than anatomical lobar boundaries).
- **Management:**
 - Symptomatic radiation pneumonitis (Grade 2 or higher) is treated primarily with **systemic corticosteroids** (e.g., Prednisone 60 mg/day or 1 mg/kg/day).
 - Steroids rapidly suppress alveolar inflammation and prevent progression to permanent radiation-induced pulmonary fibrosis.
 - Steroid taper must be slow and gradual over a minimum of 4 to 8 weeks, as rapid tapering frequently causes rebound pneumonitis.
- Antibiotics and antifungals have no therapeutic benefit unless secondary superimposed bacterial/fungal infection is documented.

Final Answer:

The most appropriate management for acute radiation pneumonitis is high-dose systemic corticosteroids.

Quick Tip: Radiation Pneumonitis:

- Timing: 1–3 months post-thoracic radiotherapy.
- CT: Consolidation matching radiation portals (straight borders).
- Treatment: High-dose Prednisone (1 mg/kg/day) with a slow taper over 6–8 weeks to prevent rebound!

124. A recent clinical case reported that artificial intelligence (AI) successfully identified liver lesions that were missed by a radiologist. Which statement most accurately represents the role of AI in clinical imaging?

- (A) AI in imaging can help restage disease
- (B) AI eliminates the need for clinicians

- (C) AI is infallible and guarantees perfect diagnosis
(D) AI can only detect lesions that are visible to the human eye

Correct Answer: (A) AI in imaging can help restage disease

Solution:

Concept:

Artificial Intelligence in medical imaging functions as an augmented decision-support tool capable of quantitative lesion detection, volumetric tumor assessment, radiomic feature extraction, and longitudinal response tracking.

Explanation:

- **Role in Restaging:** AI algorithms can accurately segment occult or subtle metastatic lesions (such as subcentimeter hepatic or pulmonary metastases) that may escape visual detection on cross-sectional CT or MRI scans. Identifying new metastatic deposits alters clinical TNM staging (e.g., converting Stage II/III disease to Stage IV metastatic disease), thereby guiding crucial adjustments in systemic therapy and restaging.
- **Sub-visual Features:** Through computational radiomics, AI analyzes high-order spatial texture, heterogeneity, and pixel relationships that are entirely imperceptible to the unaided human eye; thus, statement (D) is incorrect.
- **Human-in-the-Loop Paradigm:** AI does not replace clinicians (statement B is false) but serves as an expert assistant. Expert clinical verification is always mandatory to correlate clinical history, interpret artifacts, and guide therapeutic decision-making.
- **Algorithm Performance:** AI algorithms are susceptible to overfitting, training bias, and dataset shifts, and are therefore not infallible (statement C is false).

Final Answer:

The most accurate statement is that AI in imaging can identify subtle lesions to help restage

disease.

Quick Tip: AI in Oncology Imaging:

- Enables subtle/sub-visual lesion detection and automated volumetric measurement.
- Facilitates accurate restaging and treatment response monitoring (e.g., RECIST criteria automation).
- Always functions under radiologist/clinician supervision (Decision Support).

125. A 60-year-old man who has undergone radical prostatectomy is assessed for his erectile function using the International Index of Erectile Function (IIEF-5) questionnaire. His total IIEF-5 score is 18. What is the degree of erectile dysfunction (ED) based on this score?

- (A) Mild
- (B) Mild to moderate
- (C) Moderate
- (D) Severe

Correct Answer: (A) Mild

Solution:

Concept:

The IIEF-5 (also known as the Sexual Health Inventory for Men [SHIM]) is a validated 5-item self-administered diagnostic questionnaire used to assess the presence and severity of erectile dysfunction.

The total score ranges from 5 to 25 points.

Explanation:

- The standardized clinical scoring classification for the IIEF-5 (SHIM) is defined as follows:

– **Score 22–25:** No erectile dysfunction (Normal erectile function)

- **Score 17–21: Mild erectile dysfunction**
 - **Score 12–16: Mild-to-moderate erectile dysfunction**
 - **Score 8–11: Moderate erectile dysfunction**
 - **Score 5–7: Severe erectile dysfunction**
- The patient in this scenario has a total score of 18.
 - Because 18 falls strictly within the interval of 17 to 21, the patient's degree of erectile dysfunction is classified as **Mild**.
 - Following nerve-sparing radical prostatectomy, patients with mild ED are candidates for early penile rehabilitation protocols with on-demand or daily phosphodiesterase-5 (PDE5) inhibitors.

Final Answer:

Based on the IIEF-5 score of 18, the degree of erectile dysfunction is classified as Mild.

Quick Tip: IIEF-5 / SHIM Score Cutoffs:

- 22–25: Normal
- 17–21: Mild
- 12–16: Mild-to-Moderate
- 8–11: Moderate
- 5–7: Severe

126. A 50-year-old male with a 40-year smoking history presents with symptoms of superior

vena cava obstruction. What is the most likely diagnosis?

- (A) Germ cell tumor
- (B) Lymphoma
- (C) Non-small cell lung cancer
- (D) Small cell lung cancer

Correct Answer: (D) Small cell lung cancer

Solution:

Concept:

Malignancy is the cause of Superior Vena Cava Obstruction (SVCO) in over 70–80% of cases, with bronchogenic carcinomas representing the overwhelming majority.

Among lung cancers, Small Cell Lung Cancer (SCLC) exhibits the highest relative propensity and classic predilection to cause SVCO due to its central peribronchial origin and rapid mediastinal nodal invasion.

Explanation:

- **Small Cell Lung Cancer (SCLC):** SCLC is strongly associated with heavy tobacco smoking (such as a 40 pack-year smoking history). It characteristically arises centrally in the main bronchi and rapidly metastasizes to paratracheal and subcarinal mediastinal lymph nodes, encasing and compressing the thin-walled, low-pressure superior vena cava.
- Approximately 10% of all patients with SCLC develop SVCO during their disease course (the highest relative incidence among all thoracic neoplasms). In clinical board examinations, a heavy smoker presenting with acute classical SVC syndrome is the stereotypic presentation of SCLC.
- **Non-Small Cell Lung Cancer (NSCLC):** NSCLC (specifically squamous cell carcinoma and adenocarcinoma) accounts for a large absolute volume due to its higher overall prevalence, but peripheral lesions predominate in adenocarcinomas, and it has a lower

per-case propensity for early central mediastinal encasement compared to SCLC.

- **Lymphoma and Germ Cell Tumors:** More commonly present in younger non-smokers as anterior mediastinal masses.

Final Answer:

In a heavy smoker presenting with superior vena cava obstruction, the most classic and likely diagnosis is Small Cell Lung Cancer.

Quick Tip: SVCO Pearls:

- Highest per-tumor risk: Small Cell Lung Cancer (SCLC ~ 10%).
- Central mass + rapid mediastinal adenopathy + heavy smoker = SCLC.
- Response: SCLC-associated SVCO responds dramatically and rapidly to combination chemotherapy (Cisplatin/Carboplatin + Etoposide).