МИНИСТЕРСТВО ОБРАЗОВАНИЯ И НАУКИ КЫРГЫЗСКОЙ РЕСПУБЛИКИ
ОШСКИЙ ГОСУДАРСТВЕННЫЙ УНИВЕРСИТЕТ

МЕЖДУНАРОДНЫЙ МЕДИЦИНСКИЙ ФАКУЛЬТЕТ

Кафедра патологий, базисной и клинической фармакологии

УТВЕРЖДЕНО
на заседании кафедры
протокол № от «__» _____ 2025г.
Заведующий кафедры
к.б.н., доцент А.А.Момунова

СОГЛАСОВАНО
Председатель УМС факультета
к.э.н., доцент Базиева А.М.
«11» 11 2025 г.

ФОНД ТЕСТОВЫХ ЗАДАНИЙ

для итогового контроля по дисциплине

«Патология 3»

На 2025-2026 учебный год
Направление: 560001- ЛЕЧЕБНОЕ ДЕЛО (GM)

Курс: 3 **Семестр: 5**

Сетка часов

Наименование дисциплины	Всего	Кредит	Аудиторные занятия (60 ч.)		СРС	СРСП
			Лекции	Практические		
Базисная фармакология	150 ч.	5 кр.	24 ч.	36 ч.	81 ч.	9 ч.
Кол-во тестовых вопросов	500					

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г.Ош – 2025г.

ЭКСПЕРТНОЕ ЗАКЛЮЧЕНИЕ БАНКА ТЕСТОВЫХ ЗАДАНИЙ

кафедры «Патологии, базисной и клинической фармакологии»

от «22» октября 2025 г.

на разработанные тестовые задания по дисциплине

«Патология 3.»

наименование дисциплины

PhD. Исмагилов И.Д., преп. Мурзагишева А.М., преп. Зубаиров Ж.Т.

/указать должность, ученую степень, Ф.И.О. автора (авторов)/

Тестовые задания проверены членом экспертной группы тестологов

_____

/указать должность, ученую степень, Ф.И.О./

Направления проведения оценки структуры и содержания тестового задания

№	Направление экспертизы	Оценка экспертов	
1	Соответствие задания программам и стандартам обучения	Соответствует	Не соответствует
		✓	
2	Включение в тесты только наиболее важных, базовых знаний	Соответствует	Не соответствует
		✓	
3	Ясность смысла тестовой ситуации и представления ТЗ	ясно	Не ясно
		✓	
4	Правильность ответа на вопрос ТЗ	Соответствует	Не соответствует
		✓	
5	Значимость содержания тестового задания (0-сомнительный, 1-допустимый, 2-важный, 3-существенный)	3 балл(ов)	
6	Соответствие необходимое число заданий по каждому разделу дисциплины исходя из его важности и числа часов, отведенных на его изучение в программе.	Соответствует	Не соответствует
		✓	

Членом экспертной группы выявлены следующие недостатки в тестовом задании _____

Членом экспертной группы внесены следующие исправления (корректировки) в тестовое задание _____

На основании представления тестовых заданий автором (авторами) и проведенной проверки сделала следующее заключение:

1) Содержание тестовых заданий **соответствует** (**не соответствует**) содержанию УМКД *(нужное подчеркнуть)*

2) Представленные тестовые задания в следующем объеме 500 вопросов: **соответствуют** (**не соответствуют**) требованиям, предъявляемым к количеству, уровням сложности и формам заданий для составления тестов. *(нужное подчеркнуть)*

Тестолог Мурзагишева А.М. _____ 22.10.25
подпись дата

Ознакомлен зав. кафедрой _____ 24.10.25
подпись дата

Pathology Question Bank - 500 Multiple Choice Questions Based on Robbins, Cotran & Kumar Pathologic Basis of Disease, 11th Edition

Note: Questions incorporate Team-Based Learning (TBL), Problem-Based Learning (PBL), Challenge-Based Learning (CBL), and Research-Based Learning (RBL) methodologies.

Topic 1: Endocrine System I - Thyroid Gland (30 questions)

Question 1 (PBL Clinical Scenario) A 45-year-old woman presents with palpitations, weight loss, and heat intolerance. Laboratory tests show TSH <0.01 mU/L and elevated free T4. Physical examination reveals a diffusely enlarged thyroid gland with a bruit. What is the most likely underlying pathological mechanism?
A) Follicular epithelial cell hyperplasia due to TSH receptor antibodies
B) Autonomous thyroid nodule secreting excess hormone
C) Thyroid hormone resistance syndrome
D) Exogenous thyroid hormone administration
E) Pituitary adenoma secreting TSH

Question 2 (CBL Histological Challenge) During a thyroidectomy for multinodular goiter, the pathologist observes follicles of varying sizes filled with colloid, areas of fibrosis, and calcification. Some follicles show flattened epithelium while others show hyperplastic changes. This pattern is most characteristic of:
A) Hashimoto thyroiditis
B) Follicular adenoma
C) Multinodular goiter
D) Papillary thyroid carcinoma
E) Graves disease

Question 3 (RBL Research Application) Recent studies have identified the role of pendrin (SLC26A4) in thyroid physiology. A mutation in this transporter would most directly affect which thyroid function?
A) Iodide uptake from blood
B) Iodide efflux into follicular lumen
C) Thyroglobulin synthesis
D) T4 to T3 conversion
E) TSH receptor signaling

Question 4 (TBL Team Discussion) A patient presents with a thyroid mass. Fine needle aspiration shows cells with nuclear grooves, nuclear pseudoinclusions, and powdery chromatin. The team must determine the most appropriate next step. What is the most likely diagnosis based on these cytological features?
A) Follicular adenoma
B) Papillary thyroid carcinoma
C) Medullary thyroid carcinoma
D) Anaplastic thyroid carcinoma
E) Hashimoto thyroiditis

Question 5 (PBL Pathophysiology) A 35-year-old patient develops hypothyroidism following radioiodine treatment for Graves disease. The mechanism of hypothyroidism in this case is:
A) Autoimmune destruction of thyroid tissue
B) Radiation-induced DNA damage to follicular cells
C) Decreased iodide uptake by thyroid gland
D) TSH receptor blocking antibodies
E) Thyroid hormone resistance

Question 6 (CBL Complex Case) A 28-year-old woman presents with fatigue, weight gain, and cold intolerance. Thyroid function tests show elevated TSH and low free T4. Anti-TPO antibodies are positive. Ultrasound shows a hypoechoic, heterogeneous thyroid gland. What histological feature would you expect to find?
A) Lymphoid follicles with germinal centers and Hurthle cell metaplasia
B) Uniform follicular hyperplasia with minimal colloid
C) Follicular epithelial dysplasia with nuclear atypia
D) Amyloid deposition between follicles
E) Extensive fibrosis with calcification

Question 7 (RBL Molecular Mechanism) The RET/PTC rearrangement commonly found in papillary thyroid carcinoma results in:
A) Loss of tumor suppressor function
B) Constitutive activation of tyrosine kinase signaling
C) Defective DNA repair mechanisms
D) Resistance to apoptosis
E) Enhanced angiogenesis

Question 8 (TBL Diagnostic Challenge) A team is evaluating a thyroid nodule with the following characteristics: encapsulated, uniform follicular architecture, no nuclear features of papillary carcinoma, and questionable capsular invasion. The most appropriate classification is:
A) Follicular adenoma
B) Follicular carcinoma
C) Follicular variant of papillary carcinoma
D) Atypical follicular lesion
E) Invasive follicular carcinoma

Question 9 (PBL Clinical Integration) A patient with a history of neck irradiation in childhood presents with a thyroid nodule. Which type of thyroid cancer has the strongest association with radiation exposure?
A) Follicular carcinoma
B) Papillary carcinoma
C) Medullary carcinoma
D) Anaplastic carcinoma
E) Primary thyroid lymphoma

Question 10 (CBL Advanced Pathology) Calcitonin levels are markedly elevated in a patient with a thyroid mass. Histological examination would most likely reveal:
A) Sheets of follicular cells with colloid
B) Papillary structures with psammoma bodies
C) Nests of cells with amyloid deposition
D) Spindle cells with extensive necrosis
E) Lymphoid infiltrate with germinal centers

Question 11 (RBL Epidemiological Data) Population studies show that the incidence of thyroid cancer has increased significantly over the past decades, primarily due to an increase in which subtype?
A) Follicular carcinoma
B) Papillary microcarcinoma
C) Medullary carcinoma
D) Anaplastic carcinoma
E) Primary thyroid lymphoma

Question 12 (TBL Differential Diagnosis) A patient presents with rapid thyroid enlargement, dysphagia, and hoarseness. The mass is firm and fixed. The team suspects anaplastic carcinoma. Which microscopic feature would confirm this diagnosis?
A) Well-differentiated follicular structures
B) Papillary architecture with nuclear grooves
C) Pleomorphic cells with extensive mitoses and necrosis
D) Uniform small round cells with salt-and-pepper chromatin
E) Lymphoid infiltrate with Hurthle cell changes

Question 13 (PBL Hormonal Regulation) A patient with goiter lives in an iodine-deficient area. The pathophysiological mechanism leading to goiter formation is:
A) Direct toxic effect of iodine deficiency on thyroid cells
B) Compensatory TSH elevation leading to thyroid hyperplasia
C) Autoimmune reaction triggered by iodine deficiency
D) Genetic predisposition activated by environmental factors
E) Decreased thyroid hormone degradation

Question 14 (CBL Molecular Pathology) A familial case of medullary thyroid carcinoma is identified. Genetic testing would most likely reveal a mutation in which gene?
A) BRAF
B) RAS
C) RET
D) PIK3CA
E) TP53

Question 15 (RBL Treatment Response) Studies show that patients with BRAF V600E mutation-positive papillary thyroid carcinoma have different clinical outcomes. This mutation is associated with:
A) Better response to radioiodine therapy
B) Lower risk of recurrence
C) More aggressive tumor behavior
D) Improved overall survival
E) Higher iodide uptake

Question 16 (TBL Case Analysis) A 60-year-old patient presents with a rapidly growing thyroid mass and cervical lymphadenopathy. FNA shows lymphoid cells with plasmacytic differentiation. The most likely diagnosis is:
A) Hashimoto thyroiditis
B) Primary thyroid lymphoma
C) Metastatic lymphoma
D) Poorly differentiated thyroid carcinoma
E) Medullary thyroid carcinoma

Question 17 (PBL Immunological Mechanism) In Graves disease, the thyroid-stimulating immunoglobulin (TSI) acts by:
A) Blocking TSH receptor function
B) Destroying thyroid follicular cells
C) Mimicking TSH action at the receptor level
D) Preventing thyroid hormone synthesis
E) Increasing thyroid hormone degradation

Question 18 (CBL Histochemical Analysis) Congo red staining is positive in the stroma of a thyroid tumor. This finding is most characteristic of:
A) Papillary thyroid carcinoma
B) Follicular thyroid carcinoma
C) Medullary thyroid carcinoma
D) Anaplastic thyroid carcinoma
E) Thyroid lymphoma

Question 19 (RBL Prognostic Factors) Research indicates that the TNM staging system for thyroid cancer considers age as a critical factor. For papillary and follicular carcinomas, the age cutoff that affects staging is:
A) 45 years
B) 50 years
C) 55 years
D) 60 years
E) 65 years

Question 20 (TBL Morphological Recognition) The pathology team is examining a thyroid specimen with enlarged follicles containing abundant colloid and flattened epithelium. This appearance is most consistent with:
A) Active thyroid tissue under TSH stimulation
B) Suppressed thyroid tissue in hyperthyroidism
C) Thyroid tissue in hypothyroidism
D) Neoplastic transformation
E) Inflammatory thyroid disease

Question 21 (PBL Clinical Correlation) A patient with thyrotoxicosis has a thyroid scan showing decreased uptake throughout the gland. The most likely diagnosis is:
A) Graves disease
B) Toxic multinodular goiter
C) Thyroiditis with thyrotoxicosis
D) Toxic adenoma
E) TSH-secreting pituitary adenoma

Question 22 (CBL Advanced Immunology) Hashimoto thyroiditis is characterized by the presence of which specific antibodies?
A) TSH receptor antibodies
B) Thyroglobulin and thyroid peroxidase antibodies
C) Thyroid hormone receptor antibodies
D) Sodium-iodide symporter antibodies
E) Calcitonin antibodies

Question 23 (RBL Genetic Analysis) Familial adenomatous polyposis (FAP) patients have an increased risk of developing which thyroid tumor?
A) Papillary carcinoma
B) Follicular carcinoma
C) Medullary carcinoma
D) Cribriform-morular variant of papillary carcinoma
E) Anaplastic carcinoma

Question 24 (TBL Microscopic Features) During microscopic examination, psammoma bodies are identified in a thyroid tumor. These calcified structures are most characteristically seen in:
A) Follicular adenoma
B) Follicular carcinoma
C) Papillary carcinoma
D) Medullary carcinoma
E) Anaplastic carcinoma

Question 25 (PBL Pathophysiological Consequences) Severe hypothyroidism in infancy leads to cretinism. The primary reason for irreversible mental retardation is:
A) Direct toxic effect of TSH on brain tissue
B) Impaired myelination during critical developmental period
C) Chronic hypoglycemia affecting brain metabolism
D) Accumulation of thyroid hormone precursors
E) Secondary adrenal insufficiency

Question 26 (CBL Diagnostic Imaging) A thyroid ultrasound shows multiple hypoechoic nodules with microcalcifications and irregular margins. These features are most suggestive of:
A) Colloid nodules
B) Follicular adenomas
C) Papillary thyroid carcinoma
D) Hashimoto thyroiditis
E) Subacute thyroiditis

Question 27 (RBL Therapeutic Implications) Recent studies on aggressive variants of papillary thyroid carcinoma show that which histological variant has the worst prognosis?
A) Follicular variant
B) Tall cell variant
C) Solid variant
D) Cribriform-morular variant
E) Warthin-like variant

Question 28 (TBL Laboratory Integration) A patient has elevated calcitonin levels. The team must determine the source. Calcitonin is primarily secreted by which thyroid cells?
A) Follicular cells
B) C cells (parafollicular cells)
C) Hurthle cells
D) Stromal fibroblasts
E) Endothelial cells

Question 29 (PBL Complications Management) A patient develops thyroid storm following surgery. The pathophysiological mechanism involves:
A) Sudden release of preformed thyroid hormones
B) Autoimmune destruction of remaining thyroid tissue
C) Parathyroid gland damage during surgery
D) Recurrent laryngeal nerve injury
E) Postoperative infection

Question 30 (CBL Research Protocol) A research study is investigating the role of microRNAs in thyroid cancer. Which microRNA dysregulation is most commonly associated with papillary thyroid carcinoma?
A) miR-221/222 overexpression
B) miR-181a underexpression
C) miR-15a overexpression
D) miR-124 underexpression
E) miR-200c overexpression

Topic 2: Endocrine System II - Adrenal, Pituitary, Parathyroid Glands (30 questions)

Question 31 (PBL Clinical Case) A 40-year-old woman presents with moon face, purple striae, and hypertension. Laboratory tests show elevated cortisol levels that do not suppress with low-dose dexamethasone but do suppress with high-dose dexamethasone. What is the most likely diagnosis?
A) Primary adrenal adenoma
B) Adrenal carcinoma
C) Pituitary adenoma secreting ACTH
D) Ectopic ACTH syndrome
E) Primary bilateral adrenal hyperplasia

Question 32 (CBL Pathological Analysis) Histological examination of an adrenal tumor shows cells arranged in nests and cords with eosinophilic cytoplasm, nuclear pleomorphism, and frequent mitoses. Weiss criteria evaluation suggests malignancy. This tumor is most likely:
A) Adrenal adenoma
B) Adrenal carcinoma
C) Pheochromocytoma
D) Metastatic carcinoma
E) Adrenal lymphoma

Question 33 (RBL Molecular Genetics) Li-Fraumeni syndrome patients have an increased risk of developing adrenocortical carcinoma due to mutations in which gene?
A) BRCA1
B) TP53
C) RB1
D) VHL
E) MEN1

Question 34 (TBL Diagnostic Challenge) A patient presents with episodic hypertension, palpitations, and diaphoresis. 24-hour urine catecholamines are elevated. The tumor is most likely located in which anatomical region?
A) Anterior pituitary
B) Adrenal cortex
C) Adrenal medulla
D) Sympathetic ganglia
E) Posterior pituitary

Question 35 (PBL Hormonal Regulation) A patient with Addison's disease would be expected to have which laboratory pattern?
A) Low cortisol, low ACTH
B) High cortisol, low ACTH
C) Low cortisol, high ACTH
D) High cortisol, high ACTH
E) Normal cortisol, high ACTH

Question 36 (CBL Advanced Pathophysiology) The "rule of 10s" for pheochromocytomas states that approximately 10% are bilateral, 10% are malignant, and 10% occur in which location?
A) Children
B) Extra-adrenal locations
C) Association with other endocrine tumors
D) Familial cases
E) Asymptomatic presentations

Question 37 (RBL Clinical Research) Studies show that germline mutations in which gene are most commonly associated with hereditary pheochromocytoma-paraganglioma syndrome?
A) RET
B) VHL
C) SDHB
D) NF1
E) MEN1

Question 38 (TBL Histological Recognition) The pathology team observes cells with abundant eosinophilic, granular cytoplasm arranged in nests (Zellballen pattern) separated by fibrovascular septa. This pattern is characteristic of:
A) Adrenal adenoma
B) Adrenal carcinoma
C) Pheochromocytoma
D) Neuroblastoma
E) Ganglioneuroma

Question 39 (PBL Pituitary Disorders) A 25-year-old woman presents with amenorrhea and galactorrhea. MRI shows a pituitary microadenoma. The tumor is most likely secreting:
A) Growth hormone
B) Prolactin
C) ACTH
D) TSH
E) FSH/LH

Question 40 (CBL Endocrine Pathology) A patient with acromegaly undergoes pituitary surgery. Histological examination of the adenoma would most likely show:
A) Chromophobe cells with sparse granules
B) Acidophilic cells with abundant cytoplasm
C) Basophilic cells with PAS-positive granules

D) Mixed chromophilic and chromophobic cells
E) Oncocytic cells with mitochondrial accumulation

Question 41 (RBL Genetic Syndromes) Multiple endocrine neoplasia type 1 (MEN1) is associated with tumors in which three primary locations?
A) Pituitary, adrenal, thyroid
B) Pituitary, parathyroid, pancreatic islets
C) Thyroid, parathyroid, adrenal medulla
D) Pituitary, thyroid, pancreatic islets
E) Parathyroid, thyroid, adrenal cortex

Question 42 (TBL Laboratory Correlation) A patient has elevated parathyroid hormone (PTH) and hypercalcemia. The team must differentiate between primary hyperparathyroidism and malignancy-associated hypercalcemia. Which additional test would be most helpful?
A) Serum phosphate level
B) PTH-related peptide (PTHrP)
C) 25-hydroxyvitamin D
D) Alkaline phosphatase
E) Serum magnesium

Question 43 (PBL Parathyroid Pathology) An 80% parathyroidectomy is performed for parathyroid hyperplasia. The histological features that distinguish hyperplasia from adenoma include:
A) Cellular pleomorphism
B) Increased mitotic activity
C) Involvement of multiple glands
D) Presence of fat cells
E) Capsular invasion

Question 44 (CBL Adrenal Insufficiency) A patient with chronic adrenal insufficiency develops an acute adrenal crisis. The precipitating factor is most commonly:
A) Sudden cessation of steroid replacement
B) Physical or emotional stress
C) Dietary sodium restriction
D) Excessive fluid intake
E) Drug interactions

Question 45 (RBL Therapeutic Response) Research on pheochromocytoma treatment shows that preoperative alpha-blockade is essential because:
A) It prevents tumor growth
B) It reduces catecholamine synthesis
C) It prevents hypertensive crisis during surgery
D) It improves tumor localization
E) It reduces postoperative complications

Question 46 (TBL Morphological Features) Waterhouse-Friderichsen syndrome is characterized by:
A) Chronic adrenal atrophy with fibrosis
B) Bilateral adrenal hyperplasia
C) Acute bilateral adrenal hemorrhage
D) Unilateral adrenal tumor
E) Adrenal calcification

Question 47 (PBL Diagnostic Workup) A patient presents with hirsutism, acne, and irregular menses. Laboratory studies show elevated testosterone and DHEA-S. The most appropriate imaging study would be:
A) Pituitary MRI
B) Adrenal CT scan
C) Ovarian ultrasound
D) Thyroid ultrasound
E) Parathyroid scan

Question 48 (CBL Hormone Pathways) Congenital adrenal hyperplasia due to 21-hydroxylase deficiency results in:
A) Excess cortisol and aldosterone production
B) Deficient cortisol and excess androgen production
C) Excess cortisol and deficient androgen production
D) Normal cortisol and excess aldosterone production
E) Deficient all steroid hormone production

Question 49 (RBL Population Studies) Epidemiological studies show that primary aldosteronism (Conn syndrome) is more common than previously thought. The most frequent cause is:
A) Unilateral aldosterone-producing adenoma
B) Bilateral adrenal hyperplasia
C) Glucocorticoid-remediable aldosteronism
D) Adrenal carcinoma E) Ectopic aldosterone production

Question 50 (TBL Pituitary Anatomy) The posterior pituitary (neurohypophysis) releases hormones that are synthesized in:
A) Anterior pituitary cells
B) Hypothalamic nuclei
C) Posterior pituitary cells
D) Pineal gland E) Median eminence

Question 51 (PBL Clinical Syndromes) A patient presents with diabetes insipidus, visual field defects, and headaches. MRI shows a suprasellar mass. The most likely diagnosis is:
A) Pituitary adenoma
B) Craniopharyngioma
C) Meningioma
D) Glioma
E) Metastatic tumor

Question 52 (CBL Histochemical Staining) Chromogranin A immunostaining would be positive in which adrenal tumor?
A) Adrenal adenoma
B) Adrenal carcinoma
C) Pheochromocytoma
D) Metastatic carcinoma
E) Primary adrenal lymphoma

Question 53 (RBL Prognostic Markers) The PASS (Pheochromocytoma of the Adrenal Gland Scaled Score) system is used to assess:
A) Hormone secretion levels
B) Tumor size and location
C) Malignant potential
D) Response to treatment
E) Genetic predisposition

Question 54 (TBL Case Discussion) A patient has a pituitary mass and elevated IGF-1 levels. The team discusses the pathophysiology of acromegaly. Growth hormone excess primarily affects which type of bone growth?
A) Linear growth in children
B) Appositional bone growth
C) Endochondral ossification
D) Bone remodeling only
E) Trabecular bone density

Question 55 (PBL Electrolyte Disorders) A patient with hyperaldosteronism would be expected to have which electrolyte pattern?
A) Hypernatremia, hyperkalemia
B) Hyponatremia, hypokalemia
C) Hypernatremia, hypokalemia
D) Hyponatremia, hyperkalemia
E) Normal sodium, hyperkalemia

Question 56 (CBL Familial Syndromes) MEN2A syndrome is characterized by medullary thyroid carcinoma, pheochromocytoma, and:
A) Parathyroid adenomas
B) Pancreatic islet cell tumors
C) Adrenal cortical tumors
D) Pituitary adenomas
E) Mucosal neuromas

Question 57 (RBL Treatment Outcomes) Long-term studies of patients with Cushing's disease show that the most effective treatment modality is:
A) Medical therapy with ketoconazole
B) Bilateral adrenalectomy
C) Transsphenoidal pituitary surgery
D) Radiation therapy
E) Combination medical therapy

Question 58 (TBL Differential Diagnosis) The team evaluates a patient with hypercalcemia and suppressed PTH. The most likely cause is:
A) Primary hyperparathyroidism
B) Malignancy-associated hypercalcemia
C) Secondary hyperparathyroidism
D) Tertiary hyperparathyroidism
E) Familial hypocalciuric hypercalcemia

Question 59 (PBL Adrenal Imaging) A patient with suspected primary aldosteronism undergoes adrenal venous sampling. This procedure is performed to:
A) Measure aldosterone production rates
B) Differentiate unilateral from bilateral disease
C) Assess adrenal vascular anatomy
D) Guide biopsy procedures
E) Monitor treatment response

Question 60 [PBL] A 30-year-old woman presents 6 months postpartum with fatigue, inability to lactate, and amenorrhea. Laboratory shows low cortisol, TSH, and LH/FSH. What is the most likely diagnosis?
A) Postpartum depression
B) Sheehan's syndrome
C) Lymphocytic hypophysitis
D) Pituitary adenoma
E) Hypothalamic dysfunction

Topic 3: Diabetes Mellitus and Complications (29 questions)

Question 61 (PBL Clinical Presentation) A 12-year-old child presents with polyuria, polydipsia, weight loss, and ketoacidosis. Laboratory tests show glucose 450 mg/dL, ketones positive, and pH 7.25. The underlying pathophysiological mechanism is:
A) Insulin resistance with relative insulin deficiency
B) Autoimmune destruction of pancreatic beta cells
C) Genetic defect in insulin receptor function
D) Pancreatic beta cell exhaustion
E) Medication-induced hyperglycemia

Question 62 (CBL Histopathological Analysis) Pancreatic islet examination in a patient with type 1 diabetes would most likely show:
A) Beta cell hyperplasia with increased islet size
B) Lymphocytic infiltration with beta cell destruction
C) Amyloid deposition between beta cells
D) Fibrosis with preserved islet architecture
E) Increased alpha cell proportion only

Question 63 (RBL Genetic Research) HLA associations with type 1 diabetes show the strongest risk is conferred by which alleles?
A) HLA-DR3/DR4
B) HLA-B27
C) HLA-A1/A2
D) HLA-DQ6
E) HLA-DR2

Question 64 (TBL Pathophysiology Discussion) The team discusses insulin resistance in type 2 diabetes. Which tissue is primarily responsible for postprandial glucose disposal?
A) Liver
B) Skeletal muscle
C) Adipose tissue
D) Brain
E) Kidney

Question 65 (PBL Metabolic Complications) A 55-year-old diabetic patient presents with altered consciousness and severe dehydration. Laboratory tests show glucose 800 mg/dL, serum osmolality 350 mOsm/kg, and negative ketones. This condition is:
A) Diabetic ketoacidosis
B) Hyperosmolar hyperglycemic state
C) Hypoglycemic coma
D) Lactic acidosis
E) Alcoholic ketoacidosis

Question 66 (CBL Advanced Pathology) Diabetic nephropathy progression involves several histological changes. The earliest change detectable by light microscopy is:
A) Glomerular basement membrane thickening
B) Mesangial matrix expansion
C) Nodular glomerulosclerosis (Kimmelstiel-Wilson lesions)
D) Arteriolar hyalinosis
E) Tubular atrophy and interstitial fibrosis

Question 67 (RBL Clinical Trials) The DCCT (Diabetes Control and Complications Trial) demonstrated that intensive glycemic control:
A) Prevents the development of type 1 diabetes
B) Reduces microvascular complications in type 1 diabetes
C) Prevents macrovascular disease in type 2 diabetes
D) Eliminates the need for insulin therapy
E) Reverses established diabetic complications

Question 68 (TBL Laboratory Integration) A patient has fasting glucose 110 mg/dL and HbA1c 6.2%. The team must classify this patient's glucose status. This pattern is consistent with:
A) Normal glucose tolerance
B) Impaired fasting glucose
C) Prediabetes
D) Type 2 diabetes
E) Type 1 diabetes

Question 69 (PBL Vascular Complications) Diabetic retinopathy pathogenesis involves multiple mechanisms. The initial change that occurs in retinal capillaries is:
A) Capillary basement membrane thickening
B) Loss of pericytes
C) Endothelial cell proliferation
D) Hard exudate formation
E) Neovascularization

Question 70 (CBL Diagnostic Challenge) A 55-year-old diabetic presents with progressive kidney disease. Renal biopsy shows nodular glomerulosclerosis and arteriolar hyalinosis. Which mechanism best explains these findings?
a) Immune complex deposition
b) Hyperglycemia-induced mesangial expansion
c) Hypertensive nephrosclerosis
d) Acute tubular necrosis
e) Interstitial nephritis
) Hyperglycemia-induced mesangial expansion

Question 71 (RBL Molecular Mechanisms) Advanced glycation end products (AGEs) contribute to diabetic complications through:
A) Direct cytotoxic effects only
B) Protein cross-linking and inflammatory responses
C) Inhibition of insulin signaling
D) Enhanced glucose uptake
E) Improved endothelial function

Question 72 (TBL Histological Features) The pathology team examines a pancreatic islet from a patient with type 2 diabetes. Which finding is most characteristic?
A) Complete absence of beta cells
B) Amyloid deposition (amylin)
C) Extensive lymphocytic infiltration
D) Beta cell hyperplasia
E) Increased vascularity

Question 73 (PBL Neuropathy Mechanisms) Diabetic neuropathy pathogenesis involves multiple pathways. Which metabolic pathway contributes to nerve damage through osmotic stress?
A) Polyol pathway
B) Protein kinase C pathway
C) AGE formation pathway
D) Hexosamine pathway
E) Inflammatory cytokine pathway

Question 74 (CBL Renal Pathology) A diabetic patient develops progressive kidney disease. Which urinalysis finding indicates early diabetic nephropathy?
A) Gross proteinuria (>300 mg/day)
B) Microalbuminuria (30-300 mg/day)
C) Hematuria
D) Pyuria
E) Glycosuria

Question 75 (RBL Epidemiological Studies) Population studies show that which ethnic group has the highest prevalence of type 2 diabetes?
A) Caucasians
B) African Americans
C) Native Americans
D) Asian Americans
E) Hispanic Americans

Question 76 (TBL Clinical Correlation) A diabetic patient develops sudden vision loss. Fundoscopy reveals dot-blot hemorrhages, cotton wool spots, and neovascularization. Virtual case studies suggest which pathophysiologic mechanism?
a) Osmotic lens swelling
b) Retinal capillary occlusion and ischemia
c) Optic nerve inflammation
d) Vitreous hemorrhage
e) Macular edema formation

Question 77 (PBL Metabolic Syndrome) The metabolic syndrome includes diabetes along with other features. Which combination defines this syndrome?
A) Diabetes, hypertension, dyslipidemia, central obesity
B) Diabetes, nephropathy, neuropathy, retinopathy
C) Diabetes, ketoacidosis, dehydration, electrolyte imbalance
D) Diabetes, autoimmune thyroiditis, adrenal insufficiency
E) Diabetes, gastroparesis, autonomic neuropathy

Question 78 (CBL Pancreatic Pathology) Pancreatic transplantation can cure type 1 diabetes. However, chronic rejection of pancreatic allografts typically shows:
A) Acute tubular necrosis
B) Chronic pancreatitis with fibrosis
C) Recurrent autoimmune insulitis
D) Vascular thrombosis
E) Ductal adenocarcinoma

Question 79 (RBL Therapeutic Research) Studies on incretin-based therapies show that GLP-1 agonists work primarily by:
A) Increasing insulin synthesis
B) Decreasing insulin resistance
C) Glucose-dependent insulin secretion and delayed gastric emptying
D) Inhibiting glucagon secretion only
E) Promoting beta cell regeneration

Question 80 (TBL Autoimmune Markers) The team evaluates autoimmune markers in diabetes. Which antibody is most specific for type 1 diabetes?
A) Anti-GAD (glutamic acid decarboxylase)
B) Anti-IA2 (tyrosine phosphatase)
C) Anti-ZnT8 (zinc transporter 8)
D) Anti-insulin antibodies
E) All are equally specific

Question 81 (PBL Acute Complications) A diabetic patient presents with fruity breath odor and deep, rapid breathing (Kussmaul respirations). The underlying acid-base disturbance is:
A) Metabolic alkalosis with respiratory compensation
B) Respiratory acidosis with metabolic compensation
C) Metabolic acidosis with respiratory compensation
D) Respiratory alkalosis with metabolic compensation
E) Mixed acid-base disorder

Question 82 (CBL Cardiovascular Risk) Diabetes is considered a coronary heart disease equivalent because diabetic patients have:
A) Similar cardiovascular risk to patients with known coronary disease
B) Higher cardiovascular risk than any other condition
C) Lower cardiovascular risk due to medical management
D) Risk that varies with glycemic control only
E) Risk limited to microvascular disease

Question 83 (RBL Genetic Susceptibility) Twin studies show that type 2 diabetes concordance in identical twins is approximately:

A) 25%
B) 50%
C) 75%
D) 90%
E) 100%

Question 84 (TBL Diagnostic Criteria) The team reviews diagnostic criteria for diabetes. Which HbA1c level confirms diabetes diagnosis?
A) ≥5.7%
B) ≥6.0%
C) ≥6.5%
D) ≥7.0%
E) ≥8.0%

Question 85 (PBL Gestational Diabetes) Gestational diabetes mellitus occurs due to:
A) Autoimmune destruction of beta cells during pregnancy
B) Pregnancy hormones causing insulin resistance
C) Fetal glucose consumption
D) Maternal dietary changes
E) Placental insulin degradation

Question 86 (CBL Skin Manifestations) A diabetic patient develops thick, waxy, induration of skin on the back of hands and fingers. This finding is called:
A) Diabetic dermopathy
B) Necrobiosis lipoidica
C) Acanthosis nigricans
D) Diabetic scleredema
E) Limited joint mobility syndrome

Question 87 (RBL Prevention Studies) The Finnish Diabetes Prevention Study showed that type 2 diabetes can be prevented by:
A) Pharmacological intervention only
B) Lifestyle modifications including diet and exercise
C) Genetic screening and counseling
D) Early insulin therapy
E) Bariatric surgery

Question 88 (TBL Pancreatic Islet Biology) The team studies islet cell types. Which cell type secretes glucagon?
A) Alpha cells
B) Beta cells
C) Delta cells
D) PP cells
E) Epsilon cells

Question 89 (PBL Hypoglycemia) A diabetic patient on insulin develops severe hypoglycemia. The physiological response includes release of:
A) Insulin and C-peptide
B) Glucagon and epinephrine
C) Cortisol and growth hormone
D) Both B and C
E) Somatostatin and GLP-1

Topic 4: Musculoskeletal System I - Osteoporosis, Osteomalacia, Rickets (29 questions)

Question 90 (PBL Clinical Case) A 65-year-old postmenopausal woman suffers a hip fracture after a minor fall. DEXA scan shows T-score of -2.8. The primary mechanism underlying her bone loss is:
A) Decreased osteoblast activity
B) Increased osteoclast activity due to estrogen deficiency
C) Defective collagen synthesis
D) Impaired calcium absorption
E) Vitamin D deficiency

Question 91 (CBL Bone Histology) Bone biopsy from an osteoporotic patient would show:
A) Increased bone mass with normal architecture
B) Decreased bone mass with preserved architecture
C) Normal bone mass with abnormal mineralization
D) Increased bone mass with abnormal architecture
E) Decreased bone mass with defective mineralization

Question 92 (RBL Molecular Mechanisms) The RANKL/RANK/OPG pathway regulates bone remodeling. Osteoprotegerin (OPG) functions as:
A) An osteoclast activator
B) A decoy receptor that inhibits osteoclast formation
C) An osteoblast growth factor
D) A calcium channel blocker
E) A collagen synthesis enhancer

Question 93 (TBL Risk Factor Analysis) The team evaluates risk factors for osteoporosis. Which factor has the greatest impact on peak bone mass?
A) Genetics
B) Calcium intake
C) Exercise
D) Vitamin D status
E) Hormonal factors

Question 94 (PBL Metabolic Bone Disease) A child presents with bowing deformities of legs, delayed tooth eruption, and growth retardation. Laboratory tests show elevated alkaline phosphatase, elevated PTH, and low 25-hydroxyvitamin D. The diagnosis is:
A) Osteoporosis
B) Osteomalacia
C) Rickets
D) Osteogenesis imperfecta
E) Hyperparathyroidism

Question 95 (CBL Radiological Correlation) Looser zones (pseudofractures) on radiographs are pathognomonic for:
A) Osteoporosis
B) Osteomalacia
C) Paget disease
D) Osteosarcoma
E) Osteomyelitis

Question 96 (RBL Vitamin D Metabolism) The rate-limiting step in vitamin D metabolism occurs in which organ?
A) Skin (7-dehydrocholesterol to vitamin D3)
B) Liver (25-hydroxylation)
C) Kidney (1α-hydroxylation)
D) Intestine (absorption)
E) Parathyroid glands (PTH secretion)

Question 97 (TBL Laboratory Integration) A patient has low serum calcium, high PTH, high alkaline phosphatase, and low 25-hydroxyvitamin D. The team determines this pattern is most consistent with:
A) Primary hyperparathyroidism
B) Secondary hyperparathyroidism due to vitamin D deficiency
C) Tertiary hyperparathyroidism
D) Hypoparathyroidism
E) Pseudohypoparathyroidism

Question 98 (PBL Pediatric Case) An exclusively breastfed infant with limited sun exposure develops craniotabes, delayed fontanelle closure, and rachitic rosary. The underlying deficiency is:
A) Calcium
B) Phosphate
C) Vitamin D
D) Vitamin C
E) Protein

Question 99 (CBL Bone Quality Assessment) The difference between osteoporosis and osteomalacia can be distinguished by:
A) Bone mineral density measurement only
B) Serum calcium levels only
C) Bone biopsy showing mineralization defects in osteomalacia
D) Age of patient only
E) Gender of patient only

Question 100 (RBL Therapeutic Research) Bisphosphonate therapy for osteoporosis works by:
A) Stimulating osteoblast activity
B) Inhibiting osteoclast activity
C) Improving calcium absorption
D) Increasing vitamin D synthesis
E) Enhancing collagen production

Question 101 (TBL Genetic Disorders) The team discusses hereditary bone diseases. Osteogenesis imperfecta is caused by mutations affecting:
A) Calcium channels
B) Vitamin D receptors
C) Type I collagen
D) Alkaline phosphatase
E) Growth hormone receptors

Question 102 (PBL Hormonal Effects) Postmenopausal osteoporosis occurs primarily due to:
A) Decreased calcium intake
B) Reduced physical activity
C) Loss of estrogen's inhibitory effect on bone resorption
D) Age-related decrease in growth hormone
E) Impaired vitamin D metabolism

Question 103 (CBL Drug-Induced Bone Disease) Long-term corticosteroid therapy causes bone loss through which mechanism?
A) Increased osteoblast activity
B) Decreased osteoclast activity
C) Impaired intestinal calcium absorption and increased bone resorption
D) Enhanced vitamin D metabolism
E) Stimulated parathyroid hormone secretion

Question 104 (RBL Prevention Strategies) Population studies show that peak bone mass is typically achieved by which age?
A) 20 years
B) 30 years
C) 40 years
D) 50 years
E) 60 years

Question 105 (TBL Diagnostic Methods) The team compares diagnostic methods for osteoporosis. DEXA scan measures:
A) Bone quality
B) Bone mineral density
C) Bone turnover markers
D) Fracture risk only
E) Calcium content only

Question 106 (PBL Renal Bone Disease) A 65-year-old postmenopausal woman presents with hip fracture after minor trauma. DEXA scan shows T-score of -2.8. 3D bone models reveal loss of trabecular connectivity. Which pathophysiologic mechanism best explains these findings?
a) Decreased bone mineralization
b) Increased bone resorption relative to formation
c) Defective collagen synthesis
d) Impaired calcium absorption
e) Vitamin D deficiency

Question 107 (CBL Biochemical Markers) Which biochemical marker is most specific for bone formation?
A) Alkaline phosphatase
B) Osteocalcin
C) Procollagen type I N-terminal propeptide (PINP)
D) Parathyroid hormone
E) 25-hydroxyvitamin D

Question 108 (RBL Fracture Healing) Research on fracture healing shows that the initial phase involves:
A) Osteoblast proliferation
B) Cartilage formation
C) Inflammatory response and hematoma formation
D) Bone remodeling
E) Calcium deposition

Question 109 (TBL Age-Related Changes) The team discusses age-related bone changes. Which change occurs earliest in aging?
A) Decreased bone mineral density
B) Reduced osteoblast function
C) Increased osteoclast activity
D) Impaired calcium absorption
E) Changes in bone architecture

Question 110 (PBL Nutritional Factors) A patient with malabsorption syndrome develops bone disease. Which nutrients are most critical for bone health?
A) Calcium and phosphorus only
B) Vitamin D and calcium only
C) Calcium, phosphorus, vitamin D, and magnesium
D) Protein and vitamin C only

Question 111 (CBL Secondary Osteoporosis) Which condition is most commonly associated with secondary osteoporosis in young adults?
A) Hypogonadism
B) Hyperthyroidism
C) Cushing's syndrome
D) Diabetes mellitus
E) Rheumatoid arthritis

Question 112 (RBL Exercise Physiology) Weight-bearing exercise prevents bone loss through:
A) Increased calcium absorption
B) Mechanical stimulation of osteoblasts (Wolff's law)
C) Enhanced vitamin D synthesis
D) Improved hormonal balance
E) Better nutrition absorption

Question 113 (TBL Pathological Fractures) The team evaluates pathological fractures. Which site is most commonly affected in osteoporotic fractures?
A) Skull B) Vertebral compression fractures
C) Long bone shaft

D) Ribs
E) Pelvis

Question 114 (PBL Calcium Homeostasis) A patient has hypocalcemia with normal PTH levels. The most likely diagnosis is:
A) Primary hypoparathyroidism
B) Pseudohypoparathyroidism
C) Vitamin D deficiency
D) Magnesium deficiency
E) Chronic kidney disease

Question 115 (CBL Bone Biopsy) Tetracycline labeling in bone biopsy is used to assess:
A) Bone mineralization rate
B) Osteoclast activity
C) Bone formation rate
D) Calcium content
E) Collagen structure

Question 116 (RBL Gender Differences) Studies show that men develop osteoporosis less frequently than women primarily because:
A) Higher peak bone mass and gradual bone loss B) Better calcium absorption C) More physical activity D) Different genetic factors E) Hormonal protection throughout life

Question 117 (TBL Treatment Monitoring) The team discusses monitoring osteoporosis treatment. Which parameter best indicates treatment response?
A) Serum calcium levels
B) Bone mineral density changes
C) Alkaline phosphatase levels
D) Pain assessment
E) Fracture rate

Question 118 (PBL Vitamin D Deficiency) Adult vitamin D deficiency (osteomalacia) differs from childhood deficiency (rickets) primarily in:
A) Serum biochemistry
B) Underlying mechanism
C) Growth plate involvement
D) Bone mineralization defects
E) Response to treatment

Topic 5: Musculoskeletal System II - Osteomyelitis, Bone Tumors, Arthritis (30 questions)

Question 119 (PBL Infectious Disease) A 10-year-old boy develops fever, bone pain, and limping after a minor injury. X-rays show lytic lesions in the distal femur metaphysis. Blood cultures are positive for Staphylococcus aureus. The most likely diagnosis is:
A) Septic arthritis
B) Acute hematogenous osteomyelitis
C) Chronic osteomyelitis
D) Bone tumor with secondary infection
E) Cellulitis with bone involvement

Question 120 (CBL Radiological Pathology) Brodie's abscess is a characteristic finding in:
A) Acute osteomyelitis
B) Chronic osteomyelitis
C) Septic arthritis
D) Bone tumor
E) Stress fracture

Question 121 (RBL Microbiological Research) In adults, which organism is the most common cause of vertebral osteomyelitis?
A) Staphylococcus aureus
B) Streptococcus pyogenes
C) Escherichia coli
D) Pseudomonas aeruginosa
E) Salmonella species

Question 122 (TBL Histological Analysis) The pathology team examines bone tissue showing necrotic bone (sequestrum) surrounded by new bone formation (involucrum). This pattern is characteristic of:
A) Acute osteomyelitis
B) Chronic osteomyelitis
C) Osteosarcoma
D) Paget disease
E) Fibrous dysplasia

Question 123 (PBL Bone Tumor Classification) A 16-year-old athlete presents with knee pain and swelling. X-rays show a mixed lytic and sclerotic lesion in the distal femur with a "sunburst" appearance and Codman's triangle. The most likely diagnosis is:
A) Osteochondroma
B) Giant cell tumor
C) Osteosarcoma
D) Ewing sarcoma
E) Chondrosarcoma

Question 124 (CBL Tumor Pathology) The pathognomonic microscopic feature of osteosarcoma is:
A) Giant cells with many nuclei
B) Cartilaginous matrix
C) Malignant cells producing osteoid
D) Small round blue cells
E) Spindle cells in fascicles

Question 125 (RBL Genetic Alterations) Ewing sarcoma is characterized by which chromosomal translocation?
A) t(11;22)(q24;q12) EWS-FLI1
B) t(12;16)(q13;p11) FUS-CHOP
C) t(2;13)(q35;q14) PAX3-FOXO1
D) t(X;18)(p11;q11) SYT-SSX
E) t(17;22)(q22;q13) COL1A1-PDGFB

Question 126 (TBL Age-Related Tumors) The team discusses age distribution of bone tumors. Which primary bone tumor is most common in patients over 60 years old?
A) Osteosarcoma
B) Chondrosarcoma
C) Ewing sarcoma
D) Giant cell tumor
E) Osteochondroma

Question 127 (PBL Metastatic Disease) A 55-year-old woman with breast cancer develops back pain and pathological fracture. Which bones are most commonly affected by metastatic disease?
A) Long bones of extremities
B) Skull and facial bones
C) Spine, pelvis, and ribs
D) Hands and feet
E) Sternum and clavicle

Question 128 (CBL Benign Bone Lesions) An osteochondroma differs from other bone tumors because it:
A) Never undergoes malignant transformation
B) Has a cartilaginous cap continuous with the parent bone

C) Occurs only in flat bones
D) Is always symptomatic
E) Requires immediate surgical removal

Question 129 (RBL Tumor Biology) Multiple hereditary exostoses (osteochondromas) are associated with mutations in which genes?
A) TP53 and RB1
B) EXT1 and EXT2
C) NF1 and NF2
D) APC and KRAS
E) BRCA1 and BRCA2

Question 130 (TBL Diagnostic Imaging) The team evaluates bone tumor imaging. Which imaging finding is most suggestive of malignancy?
A) Well-defined borders
B) Sclerotic rim
C) Cortical destruction and soft tissue mass
D) Pedunculated growth
E) Homogeneous density

Question 131 (PBL Arthritis Classification) A 35-year-old woman presents with symmetric polyarthritis affecting hands and feet, morning stiffness lasting 2 hours, and positive rheumatoid factor. The underlying pathological mechanism is:
A) Crystal deposition in joints
B) Autoimmune synovial inflammation
C) Infectious arthritis
D) Degenerative joint disease
E) Metabolic bone disease

Question 132 (CBL Synovial Pathology) Histological examination of rheumatoid synovium shows:
A) Acute neutrophilic inflammation only
B) Chronic lymphoplasmacytic inflammation with pannus formation
C) Granulomatous inflammation
D) Fibrosis without inflammation
E) Normal synovial architecture

Question 133 (RBL Autoimmune Mechanisms) The shared epitope in HLA-DR4 and HLA-DR1 associated with rheumatoid arthritis is located in:
A) α1 domain
B) β1 domain
C) α2 domain
D) β2 domain
E) Transmembrane region

Question 134 (TBL Joint Destruction) The team discusses joint destruction in rheumatoid arthritis. Which enzyme is primarily responsible for cartilage degradation?
A) Collagenase
B) Hyaluronidase
C) Elastase
D) Matrix metalloproteinases
E) Cathepsins

Question 135 (PBL Crystal Arthropathy) A 45-year-old man develops sudden onset severe pain in the first metatarsophalangeal joint. Synovial fluid analysis shows needle-shaped, negatively birefringent crystals. The diagnosis is:
A) Rheumatoid arthritis
B) Septic arthritis
C) Gout
D) Pseudogout
E) Reactive arthritis

Question 136 (CBL Crystal Identification) Pseudogout is caused by calcium pyrophosphate dihydrate crystals that are:
A) Needle-shaped and negatively birefringent
B) Rod-shaped and positively birefringent
C) Rectangular and negatively birefringent
D) Needle-shaped and positively birefringent
E) Amorphous and non-birefringent

Question 137 (RBL Metabolic Arthritis) Hyperuricemia leading to gout can result from which metabolic defect?
A) Hypoxanthine-guanine phosphoribosyltransferase (HPRT) deficiency
B) Glucose-6-phosphatase deficiency
C) Adenosine deaminase deficiency
D) Purine nucleoside phosphorylase deficiency
E) Thymidine kinase deficiency

Question 138 (TBL Osteoarthritis Pathology) The team examines osteoarthritic cartilage. Which change occurs earliest in osteoarthritis?
A) Complete cartilage loss
B) Subchondral bone sclerosis
C) Osteophyte formation
D) Surface fibrillation and loss of proteoglycans
E) Synovial inflammation

Question 139 (PBL Septic Arthritis) A 25-year-old sexually active male develops acute monoarthritis of the knee with purulent effusion. Gram stain shows gram-negative diplococci. The most likely organism is:
A) Staphylococcus aureus
B) Streptococcus pyogenes
C) Neisseria gonorrhoeae
D) Haemophilus influenzae
E) Escherichia coli

Question 140 (CBL Juvenile Arthritis) Still's disease (systemic juvenile idiopathic arthritis) is characterized by:
A) Symmetric polyarthritis only
B) Fever, rash, lymphadenopathy, and arthritis
C) Sacroiliac joint involvement
D) Association with HLA-B27
E) Positive rheumatoid factor

Question 141 (RBL Therapeutic Targets) Anti-TNF-α therapy in rheumatoid arthritis works by:
A) Stimulating cartilage regeneration
B) Blocking inflammatory cytokine signaling
C) Enhancing bone formation
D) Improving joint lubrication
E) Preventing crystal formation

Question 142 (TBL Spinal Arthritis) The team evaluates a patient with chronic back pain and stiffness. X-rays show sacroiliac joint fusion and bamboo spine. The diagnosis is:
A) Rheumatoid arthritis
B) Osteoarthritis
C) Ankylosing spondylitis
D) Psoriatic arthritis
E) Reactive arthritis

Question 143 (PBL Bone Tumor Staging) A patient with osteosarcoma undergoes staging studies. Which factor most significantly affects prognosis?
A) Tumor size

B) Presence of metastases at diagnosis
C) Patient age
D) Tumor location
E) Histological grade

Question 144 (CBL Giant Cell Tumor) Giant cell tumor of bone typically:
A) Occurs in children and adolescents
B) Affects the metaphysis of long bones
C) Extends to the epiphysis and joint surface
D) Has a high rate of malignant transformation
E) Shows characteristic calcification patterns

Question 145 (RBL Bone Healing) Research on osteomyelitis treatment shows that chronic infection persists due to:
A) Antibiotic resistance only
B) Poor vascularization and biofilm formation
C) Immunosuppression
D) Inadequate surgical debridement
E) Wrong antibiotic choice

Question 146 (TBL Tumor Markers) The team discusses bone tumor markers. Which serum marker is elevated in osteosarcoma?
A) PSA
B) AFP
C) Alkaline phosphatase
D) LDH
E) Both C and D

Question 147 (PBL Reactive Arthritis) A patient develops arthritis, urethritis, and conjunctivitis following a gastrointestinal infection. This triad suggests:
A) Rheumatoid arthritis
B) Systemic lupus erythematosus
C) Reactive arthritis (Reiter's syndrome)
D) Behçet's disease
E) Inflammatory bowel disease arthritis

Question 148 (CBL Chondrosarcoma) Which feature helps distinguish chondrosarcoma from enchondroma?
A) Location in bone
B) Cartilaginous matrix
C) Cellular atypia and infiltrative growth
D) Size of lesion
E) Age of patient

Topic 6: Skin and Soft Tissue - Inflammatory Diseases, Skin Tumors (29 questions)

Question 149 (PBL Dermatopathology) A 30-year-old woman presents with erythematous, scaly plaques on extensor surfaces of elbows and knees. Skin biopsy shows psoriasiform hyperplasia with parakeratosis and Munro microabscesses. The diagnosis is:
A) Eczematous dermatitis
B) Psoriasis
C) Lichen planus
D) Seborrheic dermatitis
E) Contact dermatitis

Question 150 (CBL Inflammatory Pathways) The pathogenesis of psoriasis involves which primary immune mechanism?
A) Type I hypersensitivity reaction B) Th17/IL-23 axis activation
C) Type III immune complex deposition
D) Th2-mediated allergic response
E) Complement-mediated tissue damage

Question 151 (RBL Genetic Susceptibility) Genome-wide association studies have identified which gene as having the strongest association with psoriasis?
A) PSORS1 (HLA-Cw6)
B) IL23R
C) TNF-α
D) STAT3
E) TLR4

Question 152 (TBL Histological Patterns) The pathology team examines a skin biopsy showing a band-like lymphocytic infiltrate at the dermoepidermal junction with basal cell vacuolization. This pattern is characteristic of:
A) Psoriasis
B) Lichen planus
C) Atopic dermatitis
D) Contact dermatitis
E) Seborrheic dermatitis

Question 153 (PBL Allergic Dermatitis) A patient develops a vesicular eruption on hands after exposure to poison ivy. The underlying mechanism is:
A) Type I (IgE-mediated) hypersensitivity
B) Type II (antibody-mediated) hypersensitivity
C) Type III (immune complex) hypersensitivity
D) Type IV (T-cell mediated) hypersensitivity
E) Non-immunologic toxic reaction

Question 154 (CBL Melanocytic Lesions) A dermatologist performs a biopsy of a pigmented lesion showing asymmetry, irregular borders, and color variation. Histology shows atypical melanocytes with pagetoid spread. The most important prognostic factor is:
A) Degree of pigmentation
B) Breslow thickness
C) Presence of ulceration
D) Mitotic rate

Question 155 (RBL Melanoma Genetics) Which gene mutation is most commonly found in melanomas arising from sun-exposed skin?
A) BRAF
B) NRAS
C) KIT
D) GNAQ
E) BAP1

Question 156 (TBL Skin Cancer Prevention) The team discusses UV radiation and skin cancer. Which type of UV radiation is primarily responsible for melanoma development?
A) UVA (315-400 nm)
B) UVB (280-315 nm)
C) UVC (200-280 nm)
D) Both UVA and UVB
E) Infrared radiation

Question 157 (PBL Non-Melanoma Skin Cancer) A 70-year-old farmer presents with a pearly, nodular lesion on his nose with telangiectasias and central ulceration. The most likely diagnosis is:
A) Squamous cell carcinoma
B) Basal cell carcinoma
C) Melanoma
D) Seborrheic keratosis
E) Actinic keratosis

Question 158 (CBL Tumor Pathology) Basal cell carcinoma rarely metastasizes because:

A) It grows very slowly
B) The basement membrane remains intact
C) Tumor cells have limited invasive capacity
D) It occurs in sun-protected areas
E) It responds well to local treatment

Question 159 (RBL Carcinogenesis) Human papillomavirus (HPV) is associated with which skin malignancy?
A) Melanoma
B) Basal cell carcinoma
C) Squamous cell carcinoma
D) Merkel cell carcinoma
E) Dermatofibrosarcoma protuberans

Question 160 (TBL Precancerous Lesions) The team evaluates actinic keratoses. These lesions are considered precancerous because they can progress to:
A) Basal cell carcinoma
B) Squamous cell carcinoma
C) Melanoma
D) Sebaceous carcinoma
E) Merkel cell carcinoma

Question 161 (PBL Autoimmune Skin Disease) A patient presents with tense bullae on normal-appearing skin. Direct immunofluorescence shows linear IgG and C3 deposition at the dermoepidermal junction. The diagnosis is:
A) Pemphigus vulgaris
B) Bullous pemphigoid
C) Dermatitis herpetiformis
D) Linear IgA disease
E) Epidermolysis bullosa

Question 162 (CBL Blistering Disorders) The difference between pemphigus and pemphigoid lies in:
A) Age of onset B) Level of blister formation C) Immunofluorescence pattern D) Response to treatment E) Associated malignancies

Question 163 (RBL Wound Healing) Studies on wound healing show that the inflammatory phase is characterized by:
A) Collagen synthesis
B) Epithelialization
C) Neutrophil and macrophage infiltration
D) Angiogenesis
E) Tissue remodeling

Question 164 (TBL Infectious Dermatology) The team examines a skin biopsy showing pseudoepitheliomatous hyperplasia with microabscesses containing broad-based budding yeasts. The organism is most likely:
A) Candida albicans
B) Blastomyces dermatitidis
C) Histoplasma capsulatum
D) Sporothrix schenckii
E) Cryptococcus neoformans

Question 165 (PBL Vascular Tumors) A newborn presents with a rapidly growing red nodule on the scalp that appeared shortly after birth. The lesion is most likely:
A) Port-wine stain
B) Infantile hemangioma
C) Congenital hemangioma
D) Pyogenic granuloma
E) Kaposi sarcoma

Question 166 (CBL Soft Tissue Sarcomas) Dermatofibrosarcoma protuberans is characterized by which chromosomal abnormality?
A) t(X;18)(p11;q11)
B) t(12;22)(q13;q12)
C) t(17;22)(q22;q13)
D) Ring chromosome 22
E) t(11;22)(q24;q12)

Question 167 (RBL Photobiology) Research on photoaging shows that chronic UV exposure primarily damages which skin component?
A) Epidermis only
B) Dermal collagen and elastic fibers
C) Subcutaneous fat
D) Hair follicles
E) Sweat glands

Question 168 (TBL Melanoma Staging) The team discusses melanoma staging. Which factor is NOT included in the TNM staging system for melanoma?
A) Breslow thickness
B) Mitotic rate
C) Presence of ulceration
D) Degree of pigmentation
E) Lymph node involvement

Question 169 (PBL Drug Reactions) A patient develops a widespread maculopapular eruption with fever and eosinophilia after starting allopurinol. This reaction pattern suggests:
A) Type I hypersensitivity
B) Drug rash with eosinophilia and systemic symptoms (DRESS)
C) Stevens-Johnson syndrome
D) Fixed drug eruption
E) Urticaria

Question 170 (CBL Keratinization Disorders) Ichthyosis vulgaris is caused by mutations in which gene encoding a key protein in keratinization?
A) Keratin 1
B) Keratin 10
C) Filaggrin
D) Loricrin
E) Involucrin

Question 171 (RBL Tumor Immunology) A patient presents with chronic eczematous dermatitis resistant to topical steroids. Virtual skin biopsy shows epidermal spongiosis, dermal inflammation, and eosinophils. Patch testing reveals multiple contact allergies. Which pathophysiologic mechanism explains this presentation?
a) Type I hypersensitivity
b) Type II hypersensitivity
c) Type III hypersensitivity
d) Type IV hypersensitivity
e) Non-immunologic irritation

Question 172 (TBL Adnexal Tumors) The team evaluates a skin tumor with ductal differentiation and positive CEA staining. This tumor is most likely:
A) Sebaceous adenoma
B) Pilomatrixoma
C) Eccrine poroma
D) Trichoepithelioma
E) Syringoma

Question 173 (PBL Pigmentation Disorders) A patient presents with hypopigmented patches showing loss of melanocytes on biopsy. The most likely diagnosis is:
A) Vitiligo
B) Albinism
C) Melasma
D) Post-inflammatory hypopigmentation
E) Pityriasis alba

Question 174 (CBL Connective Tissue Tumors) A slow-growing, painless nodule on the back shows spindle cells arranged in a storiform pattern. The tumor is positive for CD34. The diagnosis is:
A) Dermatofibroma
B) Dermatofibrosarcoma protuberans
C) Neurofibroma
D) Leiomyoma
E) Fibrous histiocytoma

Question 175 (RBL Therapeutic Targets) Targeted therapy for advanced melanoma includes inhibitors of which pathway?
A) EGFR signaling
B) BRAF/MEK pathway
C) PI3K/AKT pathway D) PD-1/PD-L1 immune checkpoint
E) Both B and D

Question 176 (TBL Nail Pathology) The team examines a nail biopsy showing melanocytes at the dermoepidermal junction with pagetoid spread. This finding in the nail unit suggests:
A) Subungual hematoma
B) Nail melanoma
C) Bacterial infection
D) Fungal infection E) Psoriatic nail changes

Question 177 (PBL Genetic Skin Disorders) Xeroderma pigmentosum patients develop multiple skin cancers due to defects in:
A) Melanin synthesis
B) DNA repair mechanisms
C) Immune surveillance
D) Keratinocyte differentiation
E) Collagen synthesis

Topic 7: Nervous System I - Trauma, Stroke, Infections (29 questions)

Question 178 (PBL Traumatic Brain Injury) A 25-year-old motorcyclist suffers head trauma and initially loses consciousness for 5 minutes, then has a lucid interval before deteriorating neurologically. CT scan shows a lens-shaped hyperdense lesion. The most likely diagnosis is:
A) Subdural hematoma
B) Epidural hematoma
C) Subarachnoid hemorrhage
D) Intracerebral hemorrhage
E) Diffuse axonal injury

Question 179 (CBL Cerebrovascular Pathology) A 65-year-old hypertensive patient develops sudden onset right hemiplegia and aphasia. CT scan shows a hypodense area in the left middle cerebral artery territory. The underlying pathological process is:
A) Hemorrhagic transformation
B) Ischemic infarction
C) Vasogenic edema
D) Arteriovenous malformation
E) Cerebral aneurysm

Question 180 (RBL Stroke Mechanisms) The penumbra in acute stroke represents:
A) Irreversibly damaged brain tissue
B) Normal brain tissue
C) Potentially salvageable ischemic tissue
D) Hemorrhagic transformation
E) Areas of luxury perfusion

Question 181 (TBL Intracranial Pressure) The team discusses intracranial pressure regulation. According to the Monro-Kellie doctrine, increased intracranial pressure results from increased volume of:
A) Brain tissue only
B) Blood only
C) CSF only
D) Brain tissue, blood, or CSF
E) Extracellular fluid only

Question 182 (PBL CNS Infections) A 20-year-old college student presents with fever, headache, neck stiffness, and petechial rash. CSF analysis shows neutrophilic pleocytosis, low glucose, and high protein. Gram stain shows gram-negative diplococci. The most likely organism is:
A) Streptococcus pneumoniae
B) Neisseria meningitidis
C) Haemophilus influenzae
D) Listeria monocytogenes
E) Staphylococcus aureus

Question 183 (CBL Neuropathological Changes) Histological examination of brain tissue following ischemic stroke would show which changes at 24-48 hours?
A) No visible changes
B) Neuronal eosinophilia and nuclear pyknosis
C) Extensive necrosis with cavitation
D) Gliosis and scar formation
E) Hemorrhagic transformation

Question 184 (RBL Cerebral Aneurysms) Berry aneurysms most commonly occur at which location?
A) Anterior communicating artery
B) Middle cerebral artery bifurcation
C) Posterior communicating artery
D) Basilar artery tip

Question 185 (TBL Blood-Brain Barrier) The team discusses blood-brain barrier disruption in various pathological conditions. Which condition typically causes the most severe barrier breakdown?
A) Ischemic stroke
B) Brain tumor
C) Multiple sclerosis
D) Alzheimer's disease
E) Meningitis

Question 186 (PBL Viral Encephalitis) A patient presents with behavioral changes, memory loss, and temporal lobe abnormalities on MRI. CSF shows lymphocytic pleocytosis. The most likely viral etiology is:
A) Cytomegalovirus
B) Herpes simplex virus type 1
C) Varicella-zoster virus
D) Epstein-Barr virus

Question 187 (CBL Hydrocephalus) Communicating hydrocephalus results from:
A) Obstruction within the ventricular system

B) Impaired CSF absorption at arachnoid villi
C) Overproduction of CSF
D) Congenital absence of foramina
E) Tumor blocking CSF flow

Question 188 (RBL Traumatic Axonal Injury) Diffuse axonal injury occurs due to:
A) Direct impact forces
B) Rotational and shearing forces
C) Hypoxic-ischemic injury
D) Inflammatory mediators
E) Secondary edema formation

Question 189 (TBL Cerebral Edema) The team evaluates different types of cerebral edema. Vasogenic edema is characterized by:
A) Intracellular water accumulation
B) Extracellular fluid accumulation due to blood-brain barrier disruption
C) CSF accumulation in ventricles
D) Protein accumulation in neurons
E) Lipid accumulation in myelin

Question 190 (PBL Fungal Infections) An immunocompromised patient develops CNS infection with narrow-budding yeasts visible on India ink preparation. The most likely organism is:
A) Candida albicans
B) Aspergillus fumigatus
C) Cryptococcus neoformans
D) Histoplasma capsulatum
E) Blastomyces dermatitidis

Question 191 (CBL Vascular Malformations) Arteriovenous malformations (AVMs) differ from cavernous malformations in:
A) Age of presentation
B) Presence of high-flow arteriovenous shunting
C) Risk of hemorrhage
D) Location in brain
E) Treatment options

Question 192 (RBL Neuroprotection) Research on neuroprotective strategies in stroke shows that excitotoxicity is mediated primarily through:
A) GABA receptors
B) NMDA glutamate receptors
C) Dopamine receptors
D) Acetylcholine receptors
E) Serotonin receptors

Question 193 (TBL CSF Analysis) The team interprets CSF findings. Which pattern is characteristic of viral meningitis?
A) Neutrophilic pleocytosis, low glucose, high protein
B) Lymphocytic pleocytosis, normal glucose, mildly elevated protein
C) No cells, normal glucose, normal protein
D) Eosinophilic pleocytosis, low glucose, high protein
E) Red cells, xanthochromia, elevated protein

Question 194 (PBL Spinal Cord Injury) A patient suffers complete spinal cord transaction at T10. Which function would be preserved?
A) Voluntary motor function below the lesion
B) Sensation below the lesion
C) Autonomic reflexes below the lesion
D) All functions below the lesion
E) No functions below the lesion

Question 195 (CBL Prion Diseases) Creutzfeldt-Jakob disease is characterized by:
A) Viral inclusion bodies
B) Amyloid plaques only
C) Spongiform changes and prion protein accumulation
D) Inflammatory infiltrates
E) Demyelination

Question 196 (RBL Stroke Prevention) Population studies show that which risk factor has the highest attributable risk for stroke?
A) Hypertension
B) Diabetes mellitus
C) Atrial fibrillation
D) Smoking
E) Hyperlipidemia

Question 197 (TBL Intracranial Hemorrhage) The team discusses spontaneous intracerebral hemorrhage. Which location is most commonly associated with hypertensive hemorrhage?
A) Cerebral cortex
B) Basal ganglia (putamen)
C) Cerebellum
D) Brainstem
E) Subarachnoid space

Question 198 (PBL Brain Abscesses) A patient with congenital heart disease develops a brain abscess. The most likely route of infection is:
A) Direct extension from sinusitis
B) Post-traumatic implantation
C) Hematogenous spread
D) Post-surgical contamination
E) CSF shunt infection

Question 199 (CBL Cerebral Autoregulation) Normal cerebral blood flow is maintained over a range of blood pressures through:
A) Cardiac output regulation
B) Cerebrovascular autoregulation
C) CSF pressure changes
D) Venous return mechanisms
E) Respiratory compensation

Question 200 (RBL Therapeutic Hypothermia) Studies on therapeutic hypothermia in brain injury show its neuroprotective effects are primarily due to:
A) Reduced cerebral blood flow
B) Decreased metabolic demand and excitotoxicity
C) Improved cardiac output
D) Enhanced drug delivery
E) Increased CSF production

Question 201 (TBL Neuroimaging Correlation) The team correlates CT and MRI findings with pathology. Hemorrhage appears hyperdense on CT due to:
A) Protein content
B) Hemoglobin iron content
C) Cellular debris
D) Calcium deposits
E) Contrast enhancement

Question 202 (PBL Tuberculous Meningitis) A patient from an endemic area presents with chronic meningitis. CSF shows lymphocytic pleocytosis, low glucose, and high protein. Acid-fast stains are positive. The typical distribution of infection is:
A) Convexity of brain
B) Basal cisterns and cranial nerves
C) Spinal cord only
D) Cerebellum

E) Brain stem only

Question 203 (CBL Neurocritical Care) Brain death determination requires absence of:
A) Cortical function only
B) Brainstem reflexes only
C) Spinal reflexes only
D) Both cortical and brainstem function
E) Cardiovascular reflexes

Question 204 (RBL Stroke Thrombolysis) Research on stroke thrombolysis shows that tissue plasminogen activator (tPA) must be administered within which time window for optimal benefit?
A) 1 hour
B) 3 hours (now extended to 4.5 hours)
C) 6 hours
D) 12 hours
E) 24 hours

Question 205 (TBL Secondary Brain Injury) The team discusses secondary brain injury mechanisms. Which factor contributes most to secondary injury after trauma?
A) Initial impact forces
B) Hypoxia and hypotension
C) Skull fractures
D) Scalp lacerations
E) CSF leaks

Question 206 (PBL Neurosurgical Emergencies) A patient presents with sudden severe headache described as "worst headache of my life." CT scan is normal, but CSF shows xanthochromia. The most likely diagnosis is:
A) Migraine headache
B) Subarachnoid hemorrhage
C) Meningitis
D) Epidural hematoma
E) Brain tumor

Topic 8: Nervous System II - Neurodegenerative Diseases, CNS Tumors (30 questions)

Question 207 (PBL Alzheimer's Disease) A 75-year-old woman presents with progressive memory loss and cognitive decline over 3 years. Brain biopsy would most likely show:
A) Lewy bodies and alpha-synuclein deposits
B) Neurofibrillary tangles and amyloid plaques
C) TDP-43 inclusions
D) Prion protein deposits
E) Huntingtin aggregates

Question 208 (CBL Protein Aggregation) The major component of neurofibrillary tangles in Alzheimer's disease is:
A) Amyloid beta protein
B) Hyperphosphorylated tau protein
C) Alpha-synuclein
D) TDP-43
E) Huntingtin

Question 209 (RBL Genetic Risk Factors) The strongest genetic risk factor for late-onset Alzheimer's disease is:
A) Presenilin 1 mutations
B) APP mutations
C) APOE ε4 allele
D) Tau mutations
E) α-synuclein mutations

Question 210 (TBL Amyloid Processing) The team discusses amyloid pathology. Amyloid beta peptide is generated from amyloid precursor protein (APP) by which enzymes?
A) α-secretase and γ-secretase
B) β-secretase and γ-secretase
C) α-secretase and β-secretase
D) Caspases
E) Matrix metalloproteinases

Question 211 (PBL Parkinson's Disease) A 65-year-old man presents with tremor, rigidity, and bradykinesia. The underlying pathology primarily affects which brain region?
A) Cerebral cortex
B) Hippocampus
C) Substantia nigra
D) Cerebellum
E) Thalamus

Question 212 (CBL Lewy Body Pathology) Lewy bodies in Parkinson's disease contain which major protein component?
A) Tau
B) Amyloid beta
C) Alpha-synuclein
D) Neurofilament
E) Huntingtin

Question 213 (RBL Dopamine Pathways) The motor symptoms in Parkinson's disease result from degeneration of which dopaminergic pathway?
A) Mesocortical pathway
B) Mesolimbic pathway
C) Nigrostriatal pathway
D) Tuberoinfundibular pathway

Question 214 (TBL Brain Tumors) The team evaluates a brain tumor in a 45-year-old adult. Which primary brain tumor is most common in adults?
A) Meningioma
B) Glioblastoma multiforme
C) Oligodendroglioma
D) Ependymoma
E) Medulloepithelioma

Question 215 (PBL Pediatric Brain Tumors) A 7-year-old child presents with hydrocephalus and ataxia. MRI shows a posterior fossa mass. The most likely diagnosis is:
A) Glioblastoma
B) Meningioma
C) Medulloepithelioma
D) Oligodendroglioma

Question 216 (CBL Glioma Grading) WHO grading of astrocytomas is based on:
A) Tumor size only
B) Location in brain
C) Cellular atypia, mitoses, endothelial proliferation, and necrosis
D) Patient age
E) Contrast enhancement pattern

Question 217 (RBL Molecular Markers) IDH1 mutation status in gliomas is important because it:
A) Determines treatment response only
B) Indicates better prognosis
C) Affects tumor location
D) Changes histological appearance
E) Increases malignancy grade

Question 218 (TBL Meningioma Pathology) The team examines a meningioma. These tumors characteristically:
A) Always invade brain parenchyma
B) Arise from arachnoid cap cells
C) Are highly malignant
D) Occur only in children
E) Metastasize frequently

Question 219 (PBL Huntington's Disease) A patient with Huntington's disease would show which characteristic brain changes?
A) Hippocampal sclerosis
B) Caudate and putamen atrophy
C) Cerebellar atrophy
D) Frontal lobe atrophy only
E) Brainstem atrophy

Question 220 (CBL Trinucleotide Repeats) Huntington's disease is caused by expansion of which trinucleotide repeat?
A) CGG repeats
B) GAA repeats
C) CAG repeats
D) CTG repeats
E) AAG repeats

Question 221 (RBL Prion Diseases) Sporadic Creutzfeldt-Jakob disease is characterized by:
A) Viral infection
B) Bacterial infection
C) Abnormal prion protein conformation
D) Autoimmune process
E) Toxic exposure

Question 222 (TBL CSF Biomarkers) The team discusses CSF biomarkers for Alzheimer's disease. Which pattern is characteristic?
A) High amyloid beta, high tau
B) Low amyloid beta, high tau
C) High amyloid beta, low tau
D) Low amyloid beta, low tau
E) Normal amyloid beta and tau

Question 223 (PBL ALS Pathology) Amyotrophic lateral sclerosis (ALS) primarily affects which cell types?
A) Upper motor neurons only
B) Lower motor neurons only
C) Both upper and lower motor neurons
D) Sensory neurons only
E) Interneurons only

Question 224 (CBL TDP-43 Pathology) TDP-43 inclusions are characteristic of which neurodegenerative disease?
A) Alzheimer's disease
B) Parkinson's disease
C) Huntington's disease
D) Frontotemporal dementia and ALS
E) Multiple sclerosis

Question 225 (RBL) Research on Parkinson's disease pathogenesis reveals that α-synuclein aggregation follows which anatomical progression pattern?
a) Cortex to brainstem
b) Brainstem to cortex (Braak staging)
c) Random distribution
d) Symmetrical progression
e) Subcortical nuclei only

Question 226 (TBL Tumor Markers) The team discusses immunohistochemical markers for brain tumors. GFAP positivity indicates:
A) Neuronal differentiation
B) Astrocytic differentiation
C) Oligodendroglial differentiation
D) Meningothelial differentiation
E) Ependymal differentiation

Question 227 (PBL Multiple Sclerosis) Multiple sclerosis plaques show which histological features?
A) Neuronal loss only
B) Demyelination with relative axonal preservation
C) Complete tissue necrosis
D) Vascular proliferation
E) Amyloid deposition

Question 228 (CBL Oligodendroglioma) The characteristic "fried egg" appearance in oligodendroglioma is due to:
A) Cellular atypia
B) Fixation artifact creating perinuclear halos
C) Mitotic activity
D) Vascular proliferation
E) Calcification

Question 229 (RBL Dementia Subtypes) Frontotemporal dementia differs from Alzheimer's disease by:
A) Earlier onset and behavioral changes
B) Later onset and memory loss
C) Motor symptoms
D) Visual hallucinations
E) Cerebellar involvement

Question 230 (TBL Blood-Brain Barrier) The team discusses tumor treatment barriers. Which brain tumor typically disrupts the blood-brain barrier most severely?
A) Low-grade astrocytoma
B) Oligodendroglioma
C) Glioblastoma multiforme
D) Meningioma
E) Schwannoma

Question 231 (PBL Pick Disease) Pick disease is characterized by:
A) Amyloid plaques and tangles
B) Lewy bodies
C) Pick bodies containing tau
D) TDP-43 inclusions only
E) Prion protein deposits

Question 232 (CBL Ependymoma) Ependymomas characteristically show which microscopic feature?
A) Perivascular pseudorosettes
B) Homer Wright rosettes
C) Flexner-Wintersteiner rosettes
D) True rosettes and perivascular pseudorosettes
E) No specific rosette formation

Question 233 (RBL) Virtual brain tissue analysis reveals spongiform changes, neuronal loss, and absence of inflammation. Prion protein immunostaining is positive. Which mechanism explains the pathogenesis of prion diseases?
a) Viral infection
b) Protein misfolding and propagation
c) Autoimmune destruction
d) Genetic mutation

e) Toxic exposure

Question 234 (TBL Normal Pressure Hydrocephalus) The team evaluates normal pressure hydrocephalus. The classic triad includes:
A) Headache, nausea, papilledema
B) Gait disturbance, urinary incontinence, dementia
C) Memory loss, personality change, aphasia
D) Tremor, rigidity, bradykinesia
E) Weakness, sensory loss, reflex changes

Question 235 (PBL Brain Metastases) Which primary tumor most commonly metastasizes to the brain?
A) Breast carcinoma
B) Lung carcinoma
C) Melanoma
D) Renal cell carcinoma
E) Colon carcinoma

Question 236 (CBL Schwannoma) Vestibular schwannomas (acoustic neuromas) arise from:
A) Cochlear nerve
B) Vestibular portion of cranial nerve VIII
C) Facial nerve
D) Trigeminal nerve
E) Glossopharyngeal nerve

Topic 9: Endocrine + Musculoskeletal (20 questions)

Question 237 (TBL Integrated Case) A 45-year-old woman presents with fatigue, weight gain, and bone pain. Laboratory tests show elevated TSH, low free T4, elevated PTH, and low 25-hydroxyvitamin D. The team must identify the primary disorder and its consequences:
A) Primary hypothyroidism with secondary hyperparathyroidism
B) Secondary hypothyroidism with primary hyperparathyroidism
C) Vitamin D deficiency causing both thyroid and parathyroid dysfunction
D) Primary hyperparathyroidism with concurrent thyroid disease
E) Multiple endocrine neoplasia syndrome

Question 238 (PBL Complex Pathophysiology) A patient with chronic kidney disease develops bone disease, secondary hyperparathyroidism, and thyroid dysfunction. Which mechanism best explains this constellation of findings?
A) Direct toxic effects of uremia on endocrine organs
B) Impaired vitamin D metabolism affecting multiple systems
C) Autoimmune destruction of endocrine glands
D) Genetic predisposition to multiple endocrine disorders
E) Drug-induced endocrine dysfunction

Question 239 (CBL Histological Integration) A bone biopsy from an osteoporotic patient with hyperparathyroidism shows increased osteoclast activity and fibrosis. This pattern is characteristic of:
A) Primary osteoporosis
B) Osteomalacia
C) Osteitis fibrosa cystica
D) Paget disease
E) Metastatic bone disease

Question 240 (RBL Molecular Mechanisms) The calcium-sensing receptor (CaSR) regulates both parathyroid and thyroid C-cell function. Mutations in this receptor cause:
A) Multiple endocrine neoplasia syndromes
B) Familial hypocalciuric hypercalcemia
C) Autoimmune polyglandular syndrome
D) Pseudohypoparathyroidism
E) DiGeorge syndrome

Question 241 (TBL Clinical Correlation) A patient with Graves' disease develops osteoporosis. The team discusses the mechanism by which hyperthyroidism affects bone:
A) Direct toxic effects of thyroid hormones on osteoblasts
B) Increased bone turnover with net bone loss
C) Impaired calcium absorption
D) Secondary hyperparathyroidism
E) Vitamin D deficiency

Question 242 (PBL Diagnostic Challenge) A 30-year-old woman presents with kidney stones, bone pain, and depression. Serum calcium is 11.5 mg/dL, PTH is elevated. Which additional test would best differentiate primary hyperparathyroidism from other causes?
A) 24-hour urine calcium
B) Vitamin D levels
C) Bone densitometry
D) Parathyroid imaging
E) Phosphate levels

Question 243 (CBL Endocrine Interactions) Cushing's syndrome can cause secondary osteoporosis through which mechanisms?
A) Decreased osteoblast function and increased bone resorption
B) Impaired calcium absorption only
C) Secondary hyperparathyroidism only
D) Vitamin D deficiency only
E) Increased physical activity

Question 244 (RBL Therapeutic Research) Studies on bisphosphonate therapy show that these drugs can cause which rare but serious complication?
A) Hypercalcemia
B) Osteonecrosis of the jaw
C) Hyperparathyroidism
D) Thyroid dysfunction
E) Adrenal insufficiency

Question 245 (TBL Integrated Physiology) The team analyzes the relationship between insulin resistance and bone metabolism. Diabetes mellitus affects bone through:
A) Increased bone formation
B) Decreased bone formation and impaired bone quality
C) No significant effects on bone
D) Improved bone mineralization
E) Enhanced fracture healing

Question 246 (PBL Case Synthesis) A patient with MEN1 syndrome presents with bone disease, kidney stones, and psychiatric symptoms. This constellation suggests:
A) Pituitary adenoma
B) Primary hyperparathyroidism
C) Pancreatic islet cell tumor
D) Adrenal adenoma
E) Thyroid carcinoma

Question 247 (CBL Pathological Comparison) The difference between osteoporosis and osteopetrosis is:
A) Age of onset only
B) Genetic versus acquired etiology
C) Decreased versus increased bone density
D) Location of bone involvement
E) Response to treatment

Question 248 (RBL Population Studies) Epidemiological studies show that which factor most strongly predicts fracture risk independent of bone mineral density?
A) Age
B) Gender
C) Previous fracture history
D) Physical activity level
E) Calcium intake

Question 249 (TBL Laboratory Integration) A patient has normal serum calcium but elevated alkaline phosphatase and osteocalcin. This pattern suggests:
A) Normal bone metabolism
B) High bone turnover state
C) Vitamin D deficiency
D) Hypoparathyroidism
E) Malabsorption syndrome

Question 250 (PBL Clinical Decision Making) A postmenopausal woman with osteoporosis also has hyperthyroidism. The treatment priority should be:
A) Treat osteoporosis first
B) Treat hyperthyroidism first
C) Treat both conditions simultaneously
D) Monitor without treatment
E) Calcium supplementation only

Question 251 (CBL Histochemical Analysis) TRAP (tartrate-resistant acid phosphatase) staining is used to identify:
A) Osteoblasts
B) Osteocytes
C) Osteoclasts
D) Chondrocytes
E) Fibroblasts

Question 252 (RBL Genetic Research) Mutations in the RANKL gene would most likely cause:
A) Increased bone formation
B) Osteopetrosis due to defective osteoclast function
C) Accelerated bone resorption
D) Normal bone metabolism
E) Defective mineralization

Question 253 (TBL System Integration) The team evaluates a patient with both thyroid cancer and hyperparathyroidism. This combination suggests:
A) Coincidental diseases
B) MEN2A syndrome
C) Autoimmune polyglandular syndrome
D) Radiation-induced tumors
E) Paraneoplastic syndrome

Question 254 (PBL Complications Management) A patient with severe osteoporosis develops a bisphosphonate-related atypical fracture. The pathophysiology involves:
A) Oversuppression of bone remodeling
B) Drug-induced osteomalacia
C) Secondary hyperparathyroidism
D) Vitamin D toxicity
E) Calcium malabsorption

Question 255 (CBL Differential Diagnosis) Brown tumors in hyperparathyroidism can be distinguished from true bone tumors by:
A) Location in bone
B) Radiological appearance only
C) Resolution with parathyroid treatment
D) Histological features only
E) Age of patient

Question 256 (RBL Treatment Outcomes) Long-term studies of parathyroidectomy for primary hyperparathyroidism show that bone mineral density:
A) Continues to decline
B) Remains stable
C) Improves significantly
D) Shows variable response
E) Deteriorates initially then improves

Topic 10: Hematopoietic and Lymphoid System I - Anemias, Spleen Pathology (30 questions)

Question 257 (PBL Anemia Classification) A 25-year-old vegetarian woman presents with fatigue and pallor. Laboratory tests show Hb 8.5 g/dL, MCV 68 fL, serum iron 40 μg/dL, TIBC 450 μg/dL, ferritin 8 ng/mL. The diagnosis is:
A) Chronic disease anemia
B) Iron deficiency anemia
C) Thalassemia minor
D) Sideroblastic anemia
E) Megaloblastic anemia

Question 258 (CBL Bone Marrow Pathology) Bone marrow examination in iron deficiency anemia would show:
A) Increased iron stores and ringed sideroblasts
B) Decreased iron stores and micronormoblasts
C) Normal iron stores and megaloblasts
D) Increased iron stores and normal erythropoiesis
E) Decreased iron stores and hypercellular erythropoiesis

Question 259 (RBL Molecular Mechanisms) Hepcidin regulation of iron metabolism works by:
A) Enhancing iron absorption in duodenum
B) Blocking ferroportin and reducing iron export from cells
C) Increasing transferrin synthesis
D) Stimulating erythropoietin production
E) Enhancing iron storage in ferritin

Question 260 (TBL Laboratory Integration) The team evaluates different causes of microcytic anemia. Which laboratory finding best distinguishes thalassemia from iron deficiency?
A) Serum iron levels
B) RBC count relative to hemoglobin level
C) Reticulocyte count
D) Hemoglobin electrophoresis
E) Bone marrow iron stores

Question 261 (PBL Hemolytic Anemia) A 30-year-old African American man develops anemia after taking antimalarial medication. Blood smear shows bite cells and Heinz bodies. The underlying defect is:
A) Membrane protein abnormality
B) Enzyme deficiency (G6PD)
C) Hemoglobin structural variant
D) Autoimmune hemolysis
E) Mechanical fragmentation

Question 262 (CBL Red Cell Morphology) Spherocytes on blood smear are most characteristic of:
A) Iron deficiency anemia
B) Megaloblastic anemia
C) Hereditary spherocytosis or autoimmune hemolysis

D) Thalassemia
E) Sickle cell disease

Question 263 (RBL Genetic Disorders) Sickle cell disease is caused by a point mutation in the β-globin gene resulting in:
A) Valine substituted for glutamic acid at position 6
B) Lysine substituted for glutamic acid at position 6
C) Glutamic acid substituted for valine at position 6
D) Deletion of glutamic acid at position 6
E) Insertion at position 6

Question 264 (TBL Hemoglobin Disorders) The team discusses thalassemia pathophysiology. In β-thalassemia major, the primary problem is:
A) Defective α-globin chain synthesis
B) Defective β-globin chain synthesis with excess α-chains
C) Hemoglobin instability
D) Abnormal oxygen affinity
E) Increased hemoglobin F production

Question 265 (PBL Megaloblastic Anemia) A 65-year-old patient presents with anemia, glossitis, and neurological symptoms. Laboratory tests show MCV 115 fL, hypersegmented neutrophils, and low vitamin B12. The underlying mechanism is:
A) Iron deficiency
B) Folate deficiency
C) Impaired DNA synthesis
D) Hemolysis
E) Chronic disease

Question 266 (CBL Bone Marrow Morphology) In megaloblastic anemia, bone marrow examination shows:
A) Micronormoblasts with decreased iron
B) Megaloblasts with nuclear-cytoplasmic asynchrony
C) Ringed sideroblasts
D) Increased plasma cells
E) Fibrosis and decreased cellularity

Question 267 (RBL Vitamin Metabolism) Pernicious anemia results from:
A) Dietary vitamin B12 deficiency
B) Intrinsic factor deficiency due to autoimmune gastritis
C) Folate deficiency
D) Terminal ileum disease
E) Transcobalamin deficiency

Question 268 (TBL Hemolysis Evaluation) The team evaluates a patient with suspected hemolysis. Which laboratory finding is most specific for intravascular hemolysis?
A) Elevated indirect bilirubin
B) Decreased haptoglobin
C) Hemoglobinuria
D) Elevated LDH
E) Increased reticulocytes

Question 269 (PBL Autoimmune Hemolysis) A patient develops anemia with positive direct antiglobulin test (DAT). The blood smear shows spherocytes and polychromasia. This pattern suggests:
A) Hereditary spherocytosis
B) Warm autoimmune hemolytic anemia
C) Cold agglutinin disease
D) Drug-induced hemolysis
E) Microangiopathic hemolytic anemia

Question 270 (CBL Spleen Pathology) Hypersplenism is characterized by:
A) Splenomegaly with pancytopenia
B) Normal spleen size with thrombocytosis
C) Splenomegaly with polycythemia
D) Asplenia with normal blood counts
E) Normal spleen function with anemia

Question 271 (RBL Splenic Function) The spleen's role in immunity includes:
A) Antibody production by marginal zone B cells
B) Removal of encapsulated bacteria
C) Processing of particulate antigens
D) All of the above functions
E) T cell development only

Question 272 (TBL Post-Splenectomy Changes) Following splenectomy, the blood smear would characteristically show:
A) Howell-Jolly bodies and target cells
B) Bite cells and Heinz bodies
C) Spherocytes and polychromasia
D) Schistocytes and thrombocytopenia
E) Hypersegmented neutrophils

Question 273 (PBL Thrombotic Thrombocytopenic Purpura) A patient presents with thrombocytopenia, microangiopathic hemolytic anemia, fever, neurological symptoms, and renal dysfunction. The underlying pathophysiology involves:
A) Autoimmune platelet destruction
B) ADAMTS13 deficiency leading to unusually large vWF multimers
C) Disseminated intravascular coagulation
D) Heparin-induced thrombocytopenia
E) Primary bone marrow failure

Question 274 (CBL Microangiopathic Hemolysis) Schistocytes (fragmented red cells) on blood smear are most commonly seen in:
A) Iron deficiency anemia
B) Megaloblastic anemia
C) Thrombotic thrombocytopenic purpura
D) Autoimmune hemolytic anemia
E) Hereditary spherocytosis

Question 275 (RBL Erythropoietin Regulation) Erythropoietin production is primarily regulated by:
A) Hemoglobin levels
B) Tissue oxygen tension
C) Iron availability
D) Reticulocyte count
E) Bone marrow cellularity

Question 276 (TBL Anemia of Chronic Disease) The team discusses anemia of chronic disease. The characteristic laboratory pattern includes:
A) Low serum iron, low TIBC, normal/high ferritin
B) Low serum iron, high TIBC, low ferritin
C) High serum iron, low TIBC, high ferritin
D) Normal serum iron, normal TIBC, low ferritin
E) High serum iron, high TIBC, normal ferritin

Question 277 (PBL Paroxysmal Nocturnal Hemoglobinuria) A patient develops intravascular hemolysis, thrombosis, and pancytopenia. Flow cytometry shows absence of CD55 and CD59 on red cells. The diagnosis is:
A) Autoimmune hemolytic anemia
B) Thrombotic thrombocytopenic purpura
C) Paroxysmal nocturnal hemoglobinuria

D) Aplastic anemia
E) Myelodysplastic syndrome

Question 278 (CBL Splenic Marginal Zone) The splenic marginal zone is important for:
A) Red cell destruction only
B) Platelet sequestration only
C) Response to polysaccharide antigens
D) Hematopoiesis in adults
E) Iron storage

Question 279 (RBL Glucose-6-Phosphate Dehydrogenase) G6PD deficiency protects against which infectious disease?
A) Tuberculosis
B) Malaria
C) HIV infection D) Hepatitis B E) Influenza

Question 280 (TBL Reticulocyte Response) The team evaluates reticulocyte counts in different anemias. Which condition typically shows an inappropriately low reticulocyte response?
A) Acute blood loss
B) Hemolytic anemia
C) Iron deficiency anemia
D) Hereditary spherocytosis
E) Sickle cell disease

Question 281 (PBL Alpha Thalassemia) Hemoglobin Bart's (γ4) in newborns indicates:
A) β-thalassemia major
B) α-thalassemia (deletion of 3 or 4 α-globin genes)
C) Sickle cell disease
D) Hereditary persistence of fetal hemoglobin
E) Normal variant

Question 282 (CBL Sideroblastic Anemia) Ringed sideroblasts in the bone marrow are characteristic of:
A) Iron deficiency anemia
B) Megaloblastic anemia
C) Sideroblastic anemia
D) Aplastic anemia
E) Chronic disease anemia

Question 283 (RBL Lead Poisoning) Lead poisoning causes anemia through which mechanism?
A) Iron deficiency
B) Inhibition of heme synthesis enzymes
C) Hemolysis
D) Folate deficiency
E) Erythropoietin suppression

Question 284 (TBL Hemoglobin Variants) The team discusses hemoglobin electrophoresis patterns. Hemoglobin S has which electrophoretic mobility?
A) Same as HbA
B) Faster than HbA
C) Slower than HbA
D) Does not migrate
E) Variable mobility

Question 285 (PBL Aplastic Anemia) A patient presents with pancytopenia and a hypocellular bone marrow. The most likely diagnosis is:
A) Acute leukemia
B) Myelodysplastic syndrome
C) Aplastic anemia
D) Myelofibrosis
E) Metastatic disease

Question 286 (CBL Splenectomy Indications) Splenectomy is most beneficial in which condition?
A) Sickle cell disease
B) Hereditary spherocytosis with severe hemolysis
C) Iron deficiency anemia
D) Megaloblastic anemia
E) Anemia of chronic disease

Topic 11: Hematopoietic and Lymphoid System II - Leukemias, Lymphomas, Myelomas (30 questions)

Question 287 (PBL Acute Leukemia) A 5-year-old child presents with fever, bruising, and bone pain. Laboratory tests show WBC 50,000/μL with 80% blasts, thrombocytopenia, and anemia. Flow cytometry shows CD19+, CD10+, TdT+. The diagnosis is:
A) Acute myeloid leukemia
B) B-cell acute lymphoblastic leukemia
C) T-cell acute lymphoblastic leukemia
D) Chronic lymphocytic leukemia
E) Hodgkin lymphoma

Question 288 (CBL Blast Morphology) Auer rods in leukemic blasts are pathognomonic for:
A) B-cell acute lymphoblastic leukemia
B) T-cell acute lymphoblastic leukemia
C) Acute myeloid leukemia
D) Chronic myeloid leukemia
E) Chronic lymphocytic leukemia

Question 289 (RBL Cytogenetics) The Philadelphia chromosome t(9;22)(q34;q11) creating BCR-ABL fusion is characteristic of:
A) Acute lymphoblastic leukemia B) Chronic myeloid leukemia C) Acute myeloid leukemia D) Chronic lymphocytic leukemia E) Multiple myeloma

Question 290 (TBL Leukemia Classification) The team discusses FAB classification of acute myeloid leukemia. M3 (acute promyelocytic leukemia) is associated with which chromosomal abnormality?
A) t(8;21)(q22;q22)
B) t(15;17)(q22;q12)
C) inv(16)(p13;q22)
D) t(9;11)(p22;q23)
E) t(6;9)(p23;q34)

Question 291 (PBL Chronic Myeloid Leukemia) A 45-year-old patient presents with splenomegaly and leukocytosis with left shift including basophils. Cytogenetics shows t(9;22). The phase of disease is most likely:
A) Chronic phase
B) Accelerated phase
C) Blast crisis
D) Remission
E) Cannot determine from information given

Question 292 (CBL Lymphoma Morphology) Reed-Sternberg cells are pathognomonic for:
A) Non-Hodgkin lymphoma
B) Hodgkin lymphoma
C) Acute lymphoblastic leukemia
D) Chronic lymphocytic leukemia
E) Multiple myeloma

Question 293 (RBL Oncogenes) The MYC oncogene is characteristically involved in which lymphoma?
A) Follicular lymphoma
B) Mantle cell lymphoma
C) Burkitt lymphoma
D) Marginal zone lymphoma
E) Hodgkin lymphoma

Question 294 (TBL Lymphoma Staging) The team discusses Ann Arbor staging for lymphomas. Stage II disease indicates:
A) Single lymph node region
B) Two or more lymph node regions on same side of diaphragm
C) Lymph node regions on both sides of diaphragm
D) Extranodal involvement
E) Bone marrow involvement

Question 295 (PBL B-cell Lymphomas) A 60-year-old patient presents with painless lymphadenopathy. Lymph node biopsy shows small cleaved cells with t(14;18) translocation. The diagnosis is:
A) Chronic lymphocytic leukemia
B) Mantle cell lymphoma
C) Follicular lymphoma
D) Diffuse large B-cell lymphoma
E) Burkitt lymphoma

Question 296 (CBL Immunophenotyping) CD5+ B-cell lymphomas include:
A) Follicular lymphoma and marginal zone lymphoma
B) Chronic lymphocytic leukemia and mantle cell lymphoma
C) Burkitt lymphoma and diffuse large B-cell lymphoma
D) Primary effusion lymphoma and plasmablastic lymphoma
E) Hodgkin lymphoma variants

Question 297 (RBL Tumor Suppressors) The p53 tumor suppressor gene is commonly mutated in which hematologic malignancy?
A) Chronic myeloid leukemia in chronic phase
B) Hairy cell leukemia
C) Chronic lymphocytic leukemia with poor prognosis
D) Follicular lymphoma
E) Hodgkin lymphoma

Question 298 (TBL Multiple Myeloma) The team evaluates a patient with back pain, anemia, and hypercalcemia. Serum protein electrophoresis shows an M-spike. Bone marrow shows 40% plasma cells. The diagnosis is:
A) Monoclonal gammopathy of undetermined significance
B) Solitary plasmacytoma
C) Multiple myeloma
D) Waldenström macroglobulinemia
E) AL amyloidosis

Question 299 (PBL Plasma Cell Disorders) The difference between multiple myeloma and MGUS (monoclonal gammopathy of undetermined significance) includes:
A) Presence of M-protein
B) Percentage of bone marrow plasma cells and end-organ damage
C) Age of patient
D) Type of immunoglobulin produced
E) Bone marrow cellularity

Question 300 (CBL Cytochemistry) Tartrate-resistant acid phosphatase (TRAP) positivity is characteristic of:
A) Chronic lymphocytic leukemia
B) Prolymphocytic leukemia
C) Hairy cell leukemia
D) Large granular lymphocyte leukemia
E) Adult T-cell leukemia

Question 301 (RBL Viral Oncogenesis) Human T-lymphotropic virus type 1 (HTLV-1) is associated with which malignancy?
A) Burkitt lymphoma
B) Primary effusion lymphoma
C) Adult T-cell leukemia/lymphoma
D) Anaplastic large cell lymphoma
E) Hodgkin lymphoma

Question 302 (TBL T-cell Lymp\
homas) The team discusses peripheral T-cell lymphomas. Which is the most common type in Western countries?
A) Anaplastic large cell lymphoma
B) Angioimmunoblastic T-cell lymphoma
C) Peripheral T-cell lymphoma, not otherwise specified
D) Extranodal NK/T-cell lymphoma
E) Adult T-cell leukemia/lymphoma

Question 303 (PBL Chronic Lymphocytic Leukemia) A 70-year-old patient has lymphocytosis with small, mature lymphocytes and smudge cells. Flow cytometry shows CD19+, CD5+, CD23+. The prognosis is best predicted by:
A) Age and gender
B) Lymphocyte count
C) ZAP-70 expression and IGHV mutation status
D) Lymph node size
E) Hemoglobin level

Question 304 (CBL Bone Marrow Fibrosis) Primary myelofibrosis is characterized by:
A) Decreased reticulin and collagen fibers
B) Increased reticulin and collagen fibers with JAK2 mutations
C) Normal bone marrow architecture
D) Hypocellular bone marrow
E) Sheets of plasma cells

Question 305 (RBL JAK-STAT Pathway) JAK2 V617F mutation is found in which myeloproliferative neoplasms?
A) Polycythemia vera only
B) Essential thrombocythemia only
C) Primary myelofibrosis only
D) All three classical myeloproliferative neoplasms
E) Chronic myeloid leukemia

Question 306 (TBL Polycythemia Vera) The team evaluates a patient with elevated hematocrit, splenomegaly, and pruritus after bathing. Which test distinguishes primary from secondary polycythemia?
A) Hemoglobin level
B) Erythropoietin level
C) JAK2 mutation analysis
D) Oxygen saturation
E) Red cell mass

Question 307 (PBL Waldenström Macroglobulinemia) A patient presents with fatigue, bleeding, and visual disturbances. Serum shows IgM monoclonal protein. Bone marrow contains lymphoplasmacytic cells. The clinical syndrome is due to:
A) Hyperviscosity from IgM paraprotein
B) Bone destruction
C) Hypercalcemia
D) Renal failure
E) Immune suppression

Question 308 (CBL Histologic Subtypes) Nodular lymphocyte predominant Hodgkin lymphoma differs from classical Hodgkin lymphoma by:
A) Age of onset
B) Presence of LP (popcorn) cells instead of Reed-Sternberg cells
C) Stage at presentation
D) Response to treatment
E) Site of involvement

Question 309 (RBL Therapeutic Targets) Rituximab (anti-CD20) is effective in which hematologic malignancies?
A) T-cell lymphomas
B) B-cell lymphomas and some leukemias
C) Hodgkin lymphoma
D) Acute myeloid leukemia
E) Multiple myeloma

Question 310 (TBL Minimal Residual Disease) The team discusses monitoring treatment response. Minimal residual disease is most accurately assessed by:
A) Complete blood count only
B) Bone marrow morphology only
C) Flow cytometry and molecular techniques
D) Physical examination only
E) Imaging studies only

Question 311 (PBL Richter Transformation) A patient with chronic lymphocytic leukemia develops rapidly enlarging lymph nodes and systemic symptoms. This most likely represents:
A) Disease progression
B) Infection
C) Transformation to diffuse large B-cell lymphoma
D) Treatment resistance
E) Second primary malignancy

Question 312 (CBL Myelodysplastic Syndromes) Myelodysplastic syndromes are characterized by:
A) Hypocellular bone marrow with pancytopenia
B) Hypercellular bone marrow with dysplastic changes and cytopenias
C) Normal bone marrow with peripheral blasts
D) Bone marrow fibrosis
E) Plasma cell infiltration

Question 313 (RBL Epigenetic Modifications) DNA methyltransferase inhibitors (5-azacytidine, decitabine) are used to treat:
A) Acute lymphoblastic leukemia
B) Chronic myeloid leukemia
C) Myelodysplastic syndromes
D) Hodgkin lymphoma
E) Multiple myeloma

Question 314 (TBL Lymphoma Genetics) The team discusses lymphoma-associated translocations. The t(11;14)(q13;q32) translocation involves which genes?
A) BCL2 and IGH
B) CCND1 and IGH
C) MYC and IGH
D) BCL6 and IGH
E) ALK and NPM1

Question 315 (PBL Aggressive Lymphomas) A patient presents with a rapidly growing mediastinal mass and superior vena cava syndrome. The most likely diagnosis is:
A) Hodgkin lymphoma
B) Primary mediastinal large B-cell lymphoma
C) Follicular lymphoma
D) Marginal zone lymphoma
E) Small lymphocytic lymphoma

Question 316 (CBL Bone Marrow Transplant) Graft-versus-host disease following allogeneic stem cell transplantation primarily affects:
A) Bone marrow only
B) Liver, skin, and gastrointestinal tract
C) Central nervous system
D) Kidneys and lungs
E) Heart and skeletal muscle

Topic 12: Hemostasis Pathology (29 questions)

Question 317 (PBL Bleeding Disorders) A 8-year-old boy presents with prolonged bleeding after tooth extraction and easy bruising. Family history reveals affected males on maternal side. Laboratory tests show prolonged aPTT, normal PT, and normal platelet count. The diagnosis is:
A) Hemophilia A (Factor VIII deficiency)
B) Hemophilia B (Factor IX deficiency)
C) von Willebrand disease
D) Thrombocytopenic purpura
E) Vitamin K deficiency

Question 318 (CBL Coagulation Pathways) The intrinsic pathway of coagulation is assessed by which laboratory test?
A) Prothrombin time (PT)
B) Activated partial thromboplastin time (aPTT)
C) Bleeding time
D) Platelet aggregometry
E) Fibrinogen level

Question 319 (RBL von Willebrand Factor) von Willebrand factor functions include:
A) Platelet adhesion to subendothelium
B) Carrying and protecting Factor VIII
C) Facilitating platelet aggregation under high shear
D) All of the above functions
E) Inhibiting platelet function

Question 320 (TBL Platelet Disorders) The team evaluates a patient with mucocutaneous bleeding and prolonged bleeding time despite normal platelet count. This pattern suggests:
A) Thrombocytopenic purpura
B) Qualitative platelet disorder
C) Coagulation factor deficiency
D) Fibrinolytic disorder
E) Vascular disorder

Question 321 (PBL Thrombocytopenia) A 30-year-old woman presents with petechiae and menorrhagia. Platelet count is 15,000/μL. Bone marrow shows increased megakaryocytes. The most likely diagnosis is:
A) Aplastic anemia
B) Acute leukemia
C) Immune thrombocytopenic purpura (ITP)
D) Thrombotic thrombocytopenic purpura
E) Drug-induced bone marrow suppression

Question 322 (CBL Anticoagulant Mechanisms) Heparin-induced thrombocytopenia (HIT) occurs due to:
A) Direct bone marrow suppression

B) Antibodies against heparin-platelet factor 4 complexes
C) Increased platelet consumption
D) Vitamin K antagonism
E) Disseminated intravascular coagulation

Question 323 (RBL Fibrinolytic System) Tissue plasminogen activator (tPA) converts plasminogen to plasmin, which:
A) Activates coagulation factors
B) Inhibits platelet aggregation
C) Degrades fibrin clots
D) Promotes thrombosis
E) Stabilizes clots

Question 324 (TBL Disseminated Intravascular Coagulation) The team evaluates DIC. Which laboratory pattern is characteristic?
A) Prolonged PT/aPTT, low platelets, low fibrinogen, elevated D-dimers
B) Normal PT/aPTT, normal platelets, normal fibrinogen
C) Shortened PT/aPTT, high platelets, high fibrinogen
D) Prolonged PT only, normal aPTT, normal platelets
E) Normal PT/aPTT, low platelets only

Question 325 (PBL Warfarin Therapy) A patient on warfarin therapy has PT/INR of 8.0 and is bleeding. The mechanism of warfarin action involves:
A) Direct thrombin inhibition
B) Platelet aggregation inhibition
C) Vitamin K antagonism affecting factors II, VII, IX, X D) Heparin cofactor activation
E) Fibrinolytic activation

Question 326 (CBL Hypercoagulable States) Factor V Leiden mutation causes thrombophilia by:
A) Increasing factor V activity
B) Resistance to activated protein C
C) Decreasing antithrombin levels
D) Increasing fibrinogen levels
E) Activating platelets

Question 327 (RBL Protein C Pathway) The protein C anticoagulant pathway is activated by:
A) Tissue factor
B) Thrombin-thrombomodulin complex
C) Activated platelets
D) Endothelial damage
E) Factor Xa

Question 328 (TBL Antiphospholipid Syndrome) The team evaluates a patient with recurrent thrombosis and pregnancy losses. Laboratory tests show lupus anticoagulant and anticardiolipin antibodies. This syndrome is characterized by:
A) Bleeding tendency
B) Arterial and venous thrombosis
C) Platelet dysfunction
D) Factor deficiencies
E) Fibrinolytic disorders

Question 329 (PBL) A patient presents with bleeding episodes and normal coagulation studies except for prolonged bleeding time. Platelet aggregation shows absent response to ristocetin but normal response to other agonists. What is the diagnosis?
a) von Willebrand disease type 1
b) von Willebrand disease type 2B
c) Bernard-Soulier syndrome
d) Glanzmann thrombasthenia
e) Platelet storage pool disease

Question 330 (CBL Platelet Function Tests) Platelet aggregometry measures platelet response to various agonists. Which agonist specifically tests ADP receptor function?
A) Collagen
B) Epinephrine
C) ADP
D) Ristocetin
E) Arachidonic acid

Question 331 (RBL Thrombopoietin) Thrombopoietin regulates:
A) Platelet function only
B) Megakaryocyte development and platelet production
C) Coagulation cascade
D) Fibrinolysis
E) Endothelial function

Question 332 (TBL Bernard-Soulier Syndrome) The team discusses inherited platelet disorders. Bernard-Soulier syndrome involves deficiency of which platelet glycoprotein?
A) GPIIb/IIIa B) GPIb/IX/V complex C) GPVI D) GPIa/IIa E) All glycoproteins

Question 333 (PBL Glanzmann Thrombasthenia) A patient has a lifelong bleeding disorder with normal platelet count but absent platelet aggregation to all agonists except ristocetin. The defective protein is:
A) von Willebrand factor
B) Factor VIII
C) GPIIb/IIIa (αIIbβ3 integrin)
D) GPIb/IX/V complex
E) Platelet factor 4

Question 334 (CBL Hemophilia Genetics) Hemophilia A and B are X-linked recessive disorders. Female carriers typically have:
A) Normal factor levels and no bleeding
B) 50% factor levels and mild bleeding tendency
C) Severe bleeding like affected males
D) Complete factor deficiency
E) Enhanced clotting tendency

Question 335 (RBL Gene Therapy) Recent advances in hemophilia treatment include gene therapy targeting:
A) Platelet production
B) Factor VIII or IX gene replacement
C) von Willebrand factor
D) Fibrinogen synthesis
E) Protein C production

Question 336 (TBL Thrombophilia Testing) The team discusses when to test for inherited thrombophilia. Testing is most appropriate in:
A) All patients with venous thrombosis
B) Young patients with unprovoked thrombosis or family history
C) Elderly patients with provoked thrombosis
D) Patients with arterial thrombosis only
E) Asymptomatic family members

Question 337 (PBL Vitamin K Deficiency) A newborn develops bleeding with prolonged PT and aPTT. The most likely cause is:
A) Hemophilia A
B) von Willebrand disease
C) Vitamin K deficiency
D) Immune thrombocytopenic purpura
E) Disseminated intravascular coagulation

Question 338 (CBL Fibrinogen Disorders) Dysfibrinogenemia differs from afibrinogenemia by:
A) Fibrinogen concentration
B) Functional abnormality versus absence of fibrinogen
C) Inheritance pattern
D) Clinical severity
E) Laboratory detection methods

Question 339 (RBL Antiplatelet Therapy) Aspirin inhibits platelet function by:
A) Blocking ADP receptors
B) Irreversibly acetylating cyclooxygenase-1
C) Inhibiting GPIIb/IIIa
D) Blocking thrombin receptors
E) Enhancing cAMP levels

Question 340 (TBL Massive Transfusion) The team manages a patient requiring massive blood transfusion. Which coagulation abnormality develops first?
A) Factor deficiency
B) Thrombocytopenia
C) Fibrinogen deficiency
D) Protein C deficiency
E) Antithrombin deficiency

Question 341 (PBL Prothrombin Gene Mutation) The G20210A prothrombin gene mutation increases thrombosis risk by:
A) Decreasing prothrombin function
B) Increasing prothrombin levels
C) Affecting protein C activity
D) Reducing factor V function
E) Enhancing fibrinolysis

Question 342 (CBL Scott Syndrome) Scott syndrome is a rare bleeding disorder involving:
A) Platelet adhesion defects
B) Defective platelet procoagulant activity
C) Factor VIII deficiency
D) von Willebrand factor absence
E) Fibrinogen abnormalities

Question 343 (RBL Direct Oral Anticoagulants) Direct oral anticoagulants (DOACs) work by:
A) Vitamin K antagonism
B) Direct inhibition of thrombin or factor Xa
C) Platelet inhibition
D) Enhancing fibrinolysis
E) Protein C activation

Question 344 (TBL Microangiopathic Hemolytic Anemia) The team evaluates a patient with thrombocytopenia, hemolytic anemia, and renal dysfunction. The underlying mechanism involves:
A) Immune platelet destruction
B) Bone marrow failure
C) Microvascular thrombosis with mechanical hemolysis
D) Primary coagulation factor deficiency
E) Antibody-mediated hemolysis

Question 345 (PBL Hemostatic Plug Formation) The sequence of events in primary hemostasis includes:
A) Vasoconstriction, platelet adhesion, aggregation, and plug formation
B) Fibrin formation, platelet activation, vasoconstriction
C) Coagulation cascade activation, fibrinolysis, repair
D) Endothelial activation, complement fixation, inflammation
E) Thrombosis, embolization, resolution

Topic 13: Pediatric Pathology - Congenital Anomalies, Neonatal Diseases (30 questions)

Question 346 (PBL Congenital Heart Disease) A newborn presents with cyanosis and a heart murmur. Echocardiography shows the aorta and pulmonary artery arising from the right ventricle with a ventricular septal defect. The diagnosis is:
A) Tetralogy of Fallot
B) Transposition of great arteries
C) Double outlet right ventricle
D) Truncus arteriosus
E) Hypoplastic left heart syndrome

Question 347 (CBL Neural Tube Defects) Maternal folate deficiency during pregnancy increases the risk of which congenital anomaly?
A) Congenital heart disease
B) Neural tube defects (spina bifida, anencephaly)
C) Cleft lip and palate
D) Limb malformations
E) Chromosomal abnormalities

Question 348 (RBL Teratogen Exposure) Maternal alcohol consumption during pregnancy can cause fetal alcohol spectrum disorders characterized by:
A) Cardiac anomalies only
B) Growth restriction, facial dysmorphism, and neurodevelopmental defects
C) Limb defects only
D) Renal anomalies
E) Chromosomal abnormalities

Question 349 (TBL Down Syndrome) The team evaluates a newborn with Down syndrome (trisomy 21). Which cardiac anomaly is most commonly associated?
A) Ventricular septal defect
B) Endocardial cushion defect (atrioventricular canal)
C) Tetralogy of Fallot
D) Coarctation of aorta
E) Patent ductus arteriosus

Question 350 (PBL Respiratory Distress Syndrome) A premature infant born at 28 weeks gestation develops respiratory distress shortly after birth. The underlying pathophysiology involves:
A) Congenital heart disease
B) Surfactant deficiency leading to alveolar collapse
C) Infection
D) Aspiration
E) Congenital diaphragmatic hernia

Question 351 (CBL Hyaline Membrane Disease) Histological examination of lungs from an infant with respiratory distress syndrome shows:
A) Bacterial pneumonia
B) Hyaline membranes lining alveolar ducts and sacs
C) Meconium aspiration
D) Pulmonary hemorrhage
E) Normal lung architecture

Question 352 (RBL Surfactant Biology) Pulmonary surfactant is primarily produced by which cells?
A) Alveolar macrophages
B) Type I pneumocytes
C) Type II pneumocytes
D) Bronchial epithelial cells
E) Pulmonary capillary endothelium

Question 353 (TBL TORCH Infections) The team discusses TORCH infections in neonates. Which organism most commonly causes congenital hearing loss?
A) Toxoplasma gondii
B) Rubella virus
C) Cytomegalovirus
D) Herpes simplex virus
E) Syphilis

Question 354 (PBL Necrotizing Enterocolitis) A premature infant develops abdominal distension, feeding intolerance, and bloody stools. X-rays show pneumatosis intestinalis. The diagnosis is:
A) Hirschsprung disease
B) Necrotizing enterocolitis
C) Meconium ileus
D) Pyloric stenosis
E) Intussusception

Question 355 (CBL Congenital Diaphragmatic Hernia) Congenital diaphragmatic hernia most commonly occurs on which side?
A) Right side
B) Left side
C) Bilateral
D) Posterior
E) Anterior

Question 356 (RBL Genetic Counseling) Advanced maternal age (>35 years) increases the risk of which chromosomal abnormality?
A) Turner syndrome
B) Klinefelter syndrome
C) Trisomy 21 (Down syndrome)
D) Cri-du-chat syndrome
E) Williams syndrome

Question 357 (TBL Phenylketonuria) The team discusses newborn screening for phenylketonuria (PKU). This condition results from deficiency of which enzyme?
A) Tyrosinase
B) Phenylalanine hydroxylase
C) Homogentisic acid oxidase
D) Branched-chain amino acid decarboxylase
E) Ornithine transcarbamylase

Question 358 (PBL Cystic Fibrosis) A newborn presents with meconium ileus. Genetic testing confirms cystic fibrosis. The defective protein is:
A) α1-antitrypsin
B) CFTR (cystic fibrosis transmembrane conductance regulator)
C) Dystrophin
D) Huntingtin
E) Factor VIII

Question 359 (CBL Potter Sequence) Potter sequence (oligohydramnios sequence) results from severe oligohydramnios and includes:
A) Cardiac defects
B) Growth restriction, pulmonary hypoplasia, and facial deformities
C) Neural tube defects
D) Limb malformations only
E) Chromosomal abnormalities

Question 360 (RBL Fetal Growth) Intrauterine growth restriction (IUGR) can result from:
A) Maternal factors (hypertension, smoking)
B) Placental factors (placental insufficiency)
C) Fetal factors (chromosomal abnormalities)
D) All of the above factors
E) Genetic factors only

Question 361 (TBL Hypoxic-Ischemic Encephalopathy) The team evaluates a term infant with birth asphyxia who develops seizures. The brain regions most vulnerable to hypoxic-ischemic injury are:
A) Cerebellum and brainstem
B) Hippocampus, basal ganglia, and watershed areas
C) Frontal lobes only
D) Spinal cord
E) Peripheral nerves

Question 362 (PBL Congenital Hypothyroidism) A newborn is diagnosed with congenital hypothyroidism on screening. If untreated, this condition leads to:
A) Diabetes mellitus
B) Cretinism with mental retardation and growth failure
C) Cardiac arrhythmias
D) Liver disease
E) Renal failure

Question 363 (CBL Holoprosencephaly) Holoprosencephaly is characterized by:
A) Incomplete separation of cerebral hemispheres
B) Absence of cerebellum
C) Spina bifida
D) Hydrocephalus only
E) Cerebellar malformation

Question 364 (RBL Maternal Diabetes) Maternal diabetes during pregnancy increases the risk of which fetal complications?
A) Macrosomia and hypoglycemia
B) Cardiac and neural tube defects
C) Respiratory distress syndrome
D) All of the above complications
E) Growth restriction only

Question 365 (TBL Hirschsprung Disease) The team discusses Hirschsprung disease. This condition results from:
A) Intestinal atresia
B) Absence of ganglion cells in intestinal wall
C) Malrotation
D) Meconium plug
E) Inflammatory bowel disease

Question 366 (PBL Congenital Adrenal Hyperplasia) A female newborn presents with ambiguous genitalia and salt-wasting. The most likely enzyme deficiency is:
A) 11β-hydroxylase
B) 17α-hydroxylase
C) 21-hydroxylase
D) 3β-hydroxysteroid dehydrogenase
E) Aromatase

Question 367 (CBL Osteogenesis Imperfecta) Osteogenesis imperfecta type II (lethal form) is characterized by:
A) Blue sclerae only
B) Severe bone fragility with intrauterine or neonatal death
C) Mild bone fragility
D) Dentinogenesis imperfecta only
E) Joint laxity only

Question 368 (RBL Prematurity Complications) Intraventricular hemorrhage in premature infants most commonly originates from:
A) Choroid plexus

B) Germinal matrix
C) Cerebral cortex
D) Cerebellum
E) Brainstem

Question 369 (TBL Tracheoesophageal Fistula) The team evaluates a newborn with excessive salivation and choking with feeds. The most common type of tracheoesophageal fistula is:
A) Esophageal atresia with proximal fistula
B) Esophageal atresia with distal fistula
C) H-type fistula without atresia
D) Esophageal atresia without fistula
E) Double fistula

Question 370 (PBL Retinopathy of Prematurity) A premature infant develops retinal changes due to oxygen therapy. The pathophysiology involves:
A) Direct toxic effects of oxygen
B) Abnormal retinal vascularization and neovascularization
C) Infection
D) Genetic factors
E) Nutritional deficiency

Question 371 (CBL Congenital Infections) Congenital toxoplasmosis characteristically causes:
A) Chorioretinitis, hydrocephalus, and intracranial calcifications
B) Cataracts and hearing loss
C) Cardiac defects
D) Limb malformations
E) Liver disease only

Question 372 (RBL Chromosomal Analysis) Karyotype analysis of a newborn with Turner syndrome typically shows:
A) 47,XXY
B) 45,X or mosaicism
C) 47,XYY
D) 46,XX
E) Trisomy 18

Question 373 (TBL Galactosemia) The team discusses galactosemia. This condition can cause:
A) Hepatomegaly and cataracts
B) Mental retardation if untreated
C) Ovarian dysfunction in females
D) All of the above complications
E) Renal disease only

Question 374 (PBL) A newborn presents with projectile vomiting and palpable abdominal mass. Virtual case analysis shows pyloric stenosis. Which pathophysiologic mechanism explains hypertrophic pyloric stenosis?
a) Congenital absence of pyloric muscle
b) Muscular hypertrophy causing outlet obstruction
c) Neural innervation defect
d) Inflammatory stenosis
e) Vascular malformation

Question 375 (CBL Maple Syrup Urine Disease) Maple syrup urine disease results from deficiency of:
A) Phenylalanine hydroxylase
B) Branched-chain α-keto acid dehydrogenase
C) Tyrosinase
D) Homogentisic acid oxidase
E) Cystathionine synthase

Topic 14: Environmental and Nutritional Diseases (30 questions)

Question 376 (PBL Alcohol-Related Disease) A 45-year-old construction worker presents with progressive dyspnea and cough. Chest CT shows bilateral upper lobe fibrosis and hilar lymphadenopathy. Lung biopsy reveals silicotic nodules with birefringent particles. Which pathophysiologic mechanism explains silicosis?
a) Direct toxic injury to pneumocytes
b) Macrophage activation and fibroblast proliferation
c) Immune-mediated lung injury
d) Infectious complications
e) Genetic susceptibility

Question 377 (CBL Tobacco-Related Pathology) Cigarette smoking is the primary risk factor for which type of lung cancer?
A) Adenocarcinoma
B) Squamous cell carcinoma
C) Large cell carcinoma
D) Small cell carcinoma
E) All types equally

Question 378 (RBL Carbon Monoxide Poisoning) Carbon monoxide toxicity occurs because CO has which property relative to oxygen?
A) Lower affinity for hemoglobin
B) 200-fold higher affinity for hemoglobin
C) Same affinity for hemoglobin
D) Irreversibly binds to hemoglobin
E) Blocks oxygen transport by other mechanisms

Question 379 (TBL Air Pollution) The team discusses particulate matter (PM2.5) health effects. Fine particles primarily affect:
A) Upper respiratory tract only B) Cardiovascular and respiratory systems C) Gastrointestinal system D) Nervous system only E) Skin and eyes only

Question 380 (PBL Lead Poisoning) A child presents with developmental delays, abdominal pain, and anemia. Blood lead level is elevated. Lead toxicity primarily affects:
A) Liver only
B) Kidneys only
C) Nervous system, hematopoietic system, and kidneys
D) Lungs only
E) Heart only

Question 381 (CBL) AI algorithms for environmental health risk assessment focus on which data integration approach?
a) Exposure monitoring + health outcomes
b) Geographic information systems + epidemiologic data
c) Biomarker analysis + environmental measurements
d) Multi-source data fusion with predictive modeling
e) Population surveillance + individual risk factors

Question 382 (RBL Mercury Toxicity) Methylmercury toxicity primarily affects which organ system?
A) Liver
B) Kidneys
C) Central nervous system
D) Lungs
E) Heart

Question 383 (TBL Occupational Lung Disease) The team evaluates pneumoconioses. Silicosis is characterized by:
A) Upper lobe fibrosis and hilar adenopathy
B) Lower lobe fibrosis
C) Pleural disease only

D) No pulmonary changes
E) Acute respiratory failure

Question 384 (PBL Vitamin Deficiencies) A patient presents with bleeding gums, petechiae, and poor wound healing. The deficiency is most likely:
A) Vitamin A
B) Vitamin B12
C) Vitamin C (scurvy)
D) Vitamin D

Question 385 (CBL Protein-Energy Malnutrition) Kwashiorkor differs from marasmus by:
A) Adequate calories but protein deficiency with edema
B) Both calorie and protein deficiency without edema
C) Vitamin deficiencies only
D) Mineral deficiencies only
E) No clinical differences

Question 386 (RBL Vitamin A Deficiency) Vitamin A deficiency can cause:
A) Night blindness and xerophthalmia
B) Keratinization of epithelial surfaces
C) Increased susceptibility to infections
D) All of the above effects
E) Bleeding disorders only

Question 387 (TBL Obesity Pathophysiology) The team discusses obesity-related diseases. Which condition is NOT directly associated with obesity?
A) Type 2 diabetes mellitus
B) Cardiovascular disease
C) Osteoarthritis
D) Sleep apnea
E) Osteoporosis

Question 388 (PBL Radiation Injury) A patient receives high-dose radiation therapy. Acute radiation syndrome affects which organ systems first?
A) Nervous system
B) Hematopoietic and gastrointestinal systems
C) Cardiovascular system
D) Respiratory system
E) Genitourinary system

Question 389 (CBL Chemical Carcinogenesis) Aflatoxin B1 exposure is associated with which cancer?
A) Lung cancer
B) Hepatocellular carcinoma
C) Bladder cancer
D) Leukemia
E) Brain tumors

Question 390 (RBL) Research on vitamin D deficiency reveals that insufficient sunlight exposure affects which physiologic process?
a) 7-dehydrocholesterol conversion in skin
b) 25-hydroxylation in liver
c) 1α-hydroxylation in kidneys
d) Vitamin D receptor binding
e) Calcium absorption in intestine

Question 391 (TBL Drug-Induced Liver Injury) The team evaluates hepatotoxic drugs. Acetaminophen overdose causes liver injury through:
A) Direct hepatotoxicity
B) Formation of toxic metabolite NAPQI
C) Immune-mediated injury
D) Cholestatic injury
E) Viral reactivation

Question 392 (PBL Heat-Related Illness) A construction worker develops altered mental status, hyperthermia, and anhidrosis on a hot day. The diagnosis is:
A) Heat exhaustion
B) Heat stroke
C) Heat cramps
D) Dehydration
E) Hypoglycemia

Question 393 (CBL Cold Injury) Frostbite pathophysiology involves:
A) Direct cellular freezing only
B) Vascular injury and thrombosis
C) Reperfusion injury
D) All of the above mechanisms
E) Infection only

Question 394 (RBL Electromagnetic Radiation) Ionizing radiation increases cancer risk primarily through:
A) Direct cell membrane damage
B) DNA damage and chromosomal aberrations
C) Protein denaturation
D) Mitochondrial dysfunction
E) Immune suppression only

Question 395 (TBL Pesticide Exposure) The team discusses organophosphate poisoning. The mechanism involves:
A) Cholinesterase inhibition
B) Sodium channel blockade
C) GABA receptor antagonism
D) Dopamine depletion
E) Serotonin excess

Question 396 (PBL Vitamin D Deficiency) An elderly homebound patient develops bone pain and muscle weakness. Laboratory tests show low 25-hydroxyvitamin D. Contributing factors include:
A) Limited sun exposure
B) Decreased dietary intake
C) Impaired skin synthesis with aging
D) Reduced renal 1α-hydroxylase activity
E) All of the above factors

Question 397 (CBL Iron Overload) Hereditary hemochromatosis causes iron accumulation primarily in:
A) Heart, liver, and pancreas
B) Lungs and kidneys
C) Brain and spleen
D) Muscles and bones
E) Skin and eyes

Question 398 (RBL Wilson Disease) Wilson disease involves defective copper metabolism due to mutations in:
A) Ceruloplasmin gene
B) ATP7B gene (copper transporter)
C) Copper oxidase gene
D) Metallothionein gene
E) Transferrin gene

Question 399 (TBL Eating Disorders) The team evaluates anorexia nervosa complications. Which finding is most common?
A) Hyperkalemia
B) Bradycardia and hypothermia

C) Hypertension
D) Hyperglycemia
E) Thrombocytosis

Question 400 (PBL) A patient presents with night blindness and dry eyes. Dietary history reveals inadequate intake of dark leafy vegetables and dairy products. Which vitamin deficiency is most likely?
a) Vitamin A
b) Vitamin D
c) Vitamin E
d) Vitamin K
e) Vitamin C

Question 401 (CBL) AI systems for monitoring air pollution health effects focus on which endpoints as most predictive?
a) Respiratory symptoms and function
b) Cardiovascular events
c) Inflammatory biomarkers
d) Mortality outcomes
e) Comprehensive multi-organ effects

Question 402 (RBL Bisphenol A (BPA)) BPA is an endocrine disruptor that primarily affects:
A) Thyroid function only
B) Reproductive hormones and development
C) Adrenal function only
D) Growth hormone
E) Parathyroid hormone

Question 403 (TBL Global Warming) The team discusses health impacts of climate change. Which effect is most direct?
A) Increased infectious disease transmission
B) Heat-related illness and death
C) Food and water insecurity
D) Air quality deterioration
E) Mental health impacts

Question 404 (PBL Micronutrient Deficiencies) A patient with chronic malabsorption develops night blindness, delayed wound healing, and recurrent infections. These symptoms suggest deficiency of:
A) Zinc and vitamin A
B) Iron and folate
C) Vitamin B12 and thiamine
D) Calcium and vitamin D
E) Magnesium and potassium

Question 405 (CBL Food Safety) Foodborne illness from Salmonella typically presents with:
A) Bloody diarrhea and fever
B) Neurological symptoms
C) Hepatitis
D) Respiratory symptoms
E) Skin rash

Topic 15: Immune-Related Diseases Revisited - Systemic Autoimmune Disorders (29 questions)

Question 406 (PBL Systemic Lupus Erythematosus) A 25-year-old woman presents with fatigue, joint pain, malar rash, and proteinuria. Laboratory tests show positive ANA, anti-dsDNA, and low complement levels. The diagnosis is:
A) Rheumatoid arthritis
B) Systemic lupus erythematosus
C) Scleroderma
D) Sjögren's syndrome
E) Mixed connective tissue disease

Question 407 (CBL Lupus Nephritis) The most common and severe form of lupus nephritis is:
A) Minimal mesangial (Class I)
B) Mesangial proliferative (Class II)
C) Focal proliferative (Class III)
D) Diffuse proliferative (Class IV)
E) Membranous (Class V)

Question 408 (RBL Autoantibody Production) Anti-dsDNA antibodies in SLE are produced by:
A) T cells
B) Plasma cells derived from activated B cells
C) Natural killer cells
D) Macrophages
E) Neutrophils

Question 409 (TBL Complement System) The team discusses complement deficiencies in autoimmune disease. Which complement component deficiency is strongly associated with SLE?
A) C1q, C1r, C1s (early classical pathway)
B) C3 deficiency
C) C5 deficiency
D) Factor B deficiency
E) Properdin deficiency

Question 410 (PBL Antiphospholipid Syndrome) A patient with SLE develops recurrent thrombosis and pregnancy losses. Additional testing shows anticardiolipin antibodies and lupus anticoagulant. The underlying mechanism involves:
A) Platelet activation
B) Antibodies against phospholipid-protein complexes affecting coagulation
C) Factor deficiencies
D) Enhanced fibrinolysis
E) Vascular inflammation only

Question 411 (CBL Drug-Induced Lupus) Which medication is most commonly associated with drug-induced lupus?
A) Penicillin
B) Hydralazine
C) Aspirin
D) Metformin
E) Furosemide

Question 412 (RBL HLA Associations) The strongest HLA association with systemic lupus erythematosus is:
A) HLA-B27
B) HLA-DR2 and HLA-DR3
C) HLA-DR4
D) HLA-DQ2
E) HLA-A1

Question 413 (TBL Scleroderma Classification) The team discusses systemic sclerosis subtypes. Limited cutaneous systemic sclerosis (lcSSc) is associated with which antibody?
A) Anti-Scl-70 (topoisomerase I)
B) Anti-centromere antibody
C) Anti-RNA polymerase III
D) Anti-Th/To
E) Anti-PM-Scl

Question 414 (PBL Raynaud Phenomenon) A patient with scleroderma develops digital ulcers and Raynaud phenomenon. The pathophysiology involves:
A) Arterial obstruction only
B) Venous thrombosis
C) Vasospasm and structural vascular changes
D) Hyperviscosity
E) Embolic phenomena

Question 415 (CBL Pulmonary Hypertension) In systemic sclerosis, pulmonary arterial hypertension results from:
A) Left heart failure
B) Pulmonary embolism
C) Vasculopathy affecting pulmonary vessels
D) Pneumonia
E) Pleural effusions

Question 416 (RBL Fibrosis Mechanisms) Progressive systemic sclerosis involves excessive collagen deposition due to:
A) Increased collagen synthesis by activated fibroblasts
B) Decreased collagen degradation
C) Growth factor dysregulation (TGF-β, PDGF)
D) All of the above mechanisms
E) Genetic collagen abnormalities only

Question 417 (TBL Sjögren's Syndrome) The team evaluates a patient with dry eyes and mouth. Salivary gland biopsy shows lymphocytic infiltration. Which antibodies are most specific?
A) Rheumatoid factor
B) Anti-SSA/Ro and anti-SSB/La
C) ANA
D) Anti-dsDNA
E) Anti-centromere

Question 418 (PBL CREST Syndrome) A patient presents with calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasias. This constellation is called:
A) Diffuse systemic sclerosis
B) Limited cutaneous systemic sclerosis (CREST)
C) Mixed connective tissue disease
D) Overlap syndrome
E) Undifferentiated connective tissue disease

Question 419 (CBL Inflammatory Myopathies) Polymyositis differs from dermatomyositis by:
A) Muscle enzyme elevation patterns
B) Absence of skin manifestations
C) Age of onset
D) Response to treatment
E) Associated malignancies

Question 420 (RBL Muscle Biopsy) Muscle biopsy in polymyositis characteristically shows:
A) Perifascicular atrophy
B) Endomysial inflammatory infiltrate
C) Perimysial inflammation
D) Normal muscle architecture
E) Neurogenic atrophy

Question 421 (TBL Mixed Connective Tissue Disease) The team discusses MCTD. This condition is defined by the presence of which antibody?
A) Anti-dsDNA
B) Anti-Sm
C) Anti-U1-RNP
D) Anti-SSA/Ro
E) Anti-Scl-70

Question 422 (PBL Behçet's Disease) A patient presents with recurrent oral ulcers, genital ulcers, skin lesions, and uveitis. This combination suggests:
A) Systemic lupus erythematosus
B) Crohn's disease
C) Behçet's disease
D) Aphthous stomatitis
E) Herpes simplex infection

Question 423 (CBL Vasculitis Classification) Giant cell arteritis primarily affects which type of vessels?
A) Small vessels (capillaries, venules)
B) Medium-sized arteries
C) Large arteries (aorta and major branches)
D) Veins only
E) Lymphatic vessels

Question 424 (RBL Temporal Arteritis) Giant cell (temporal) arteritis can cause which serious complication?
A) Stroke B) Blindness due to ischemic optic neuropathy C) Myocardial infarction D) Kidney failure E) Liver failure

Question 425 (TBL Polyarteritis Nodosa) The team evaluates a patient with necrotizing vasculitis affecting medium-sized arteries. Which laboratory finding supports the diagnosis?
A) ANCA positivity
B) Hepatitis B surface antigen positivity
C) Anti-dsDNA positivity
D) Rheumatoid factor positivity
E) Complement deficiency

Question 426 (PBL ANCA-Associated Vasculitis) A patient presents with pulmonary-renal syndrome. Laboratory tests show c-ANCA (PR3-ANCA) positivity. The diagnosis is:
A) Microscopic polyangiitis
B) Eosinophilic granulomatosis with polyangiitis
C) Granulomatosis with polyangiitis (Wegener's)
D) Polyarteritis nodosa
E) Henoch-Schönlein purpura

Question 427 (CBL Goodpasture Syndrome) Anti-glomerular basement membrane (anti-GBM) disease affects:
A) Kidneys only
B) Lungs only
C) Both kidneys and lungs
D) Liver and kidneys
E) Heart and lungs

Question 428 (RBL Complement Pathways) Alternative complement pathway activation is important in which renal disease?
A) Post-infectious glomerulonephritis
B) Membranoproliferative glomerulonephritis type II
C) Minimal change disease
D) IgA nephropathy
E) Focal segmental glomerulosclerosis

Question 429 (TBL Immunosuppressive Therapy) The team discusses treatment of autoimmune diseases. Methotrexate primarily works by:
A) B cell depletion
B) T cell costimulation blockade
C) Folate antagonism affecting DNA synthesis
D) TNF-α inhibition

E) Complement inhibition

Question 430 (PBL Systemic Sclerosis Complications) A patient with diffuse systemic sclerosis develops acute kidney injury with hypertension. This suggests:
A) Lupus nephritis
B) Scleroderma renal crisis
C) Drug-induced nephrotoxicity
D) Urinary tract infection
E) Diabetic nephropathy

Question 431 (CBL Autoimmune Hepatitis) Type 1 autoimmune hepatitis is associated with which antibodies?
A) Anti-mitochondrial antibodies
B) Anti-smooth muscle and anti-nuclear antibodies C) Anti-LKM1 antibodies
D) Anti-centromere antibodies
E) Anti-dsDNA antibodies

Question 432 (RBL Molecular Mimicry) Molecular mimicry as a mechanism of autoimmunity involves:
A) Cross-reactivity between pathogen and self-antigens
B) Polyclonal B cell activation
C) Regulatory T cell dysfunction
D) Complement deficiency
E) Apoptosis defects

Question 433 (TBL Overlap Syndromes) The team discusses patients with features of multiple autoimmune diseases. Which combination is most commonly seen?
A) SLE and rheumatoid arthritis
B) Systemic sclerosis and polymyositis
C) Sjögren's syndrome and primary biliary cirrhosis
D) All of the above combinations
E) Autoimmune diseases don't overlap

Question 434 (PBL Antineutrophil Cytoplasmic Antibodies) p-ANCA (perinuclear pattern) is most commonly directed against which antigen?
A) Proteinase 3 (PR3)
B) Myeloperoxidase (MPO)
C) Elastase
D) Lactoferrin
E) Cathepsin G

Topic 16: Neoplasia Revisited - Molecular Oncology and Targeted Therapy (30 questions)

Question 435 (PBL Oncogene Activation) A 45-year-old woman is diagnosed with breast cancer. Molecular analysis shows HER2/neu amplification. This oncogene encodes:
A) A transcription factor
B) A growth factor receptor with tyrosine kinase activity
C) A cell cycle protein
D) An apoptosis inhibitor
E) A DNA repair enzyme

Question 436 (CBL Tumor Suppressor Genes) The p53 tumor suppressor gene is mutated in over 50% of human cancers. p53 functions as:
A) A growth factor receptor
B) A cell cycle checkpoint protein and guardian of the genome
C) An oncogene
D) A DNA polymerase
E) A growth factor

Question 437 (RBL DNA Repair Mechanisms) BRCA1 and BRCA2 mutations predispose to breast and ovarian cancer because these genes are involved in:
A) Cell cycle regulation
B) Apoptosis
C) Homologous recombination DNA repair
D) Transcription
E) Protein synthesis

Question 438 (TBL Knudson Two-Hit Hypothesis) The team discusses hereditary cancer syndromes. Knudson's two-hit hypothesis explains:
A) Oncogene activation
B) Tumor suppressor gene inactivation in hereditary cancers
C) DNA repair mechanisms
D) Metastatic potential
E) Drug resistance

Question 439 (PBL Colorectal Cancer Progression) The adenoma-carcinoma sequence in colorectal cancer involves sequential genetic alterations. The earliest change is typically:
A) p53 mutation
B) K-RAS mutation
C) APC gene inactivation
D) DCC loss
E) Microsatellite instability

Question 440 (CBL Microsatellite Instability) Hereditary nonpolyposis colorectal cancer (HNPCC) is caused by mutations in:
A) APC gene
B) p53 gene
C) DNA mismatch repair genes (MLH1, MSH2, MSH6, PMS2)
D) K-RAS gene
E) BRCA1 gene

Question 441 (RBL Targeted Therapy) Imatinib (Gleevec) is effective in chronic myeloid leukemia because it:
A) Inhibits BCR-ABL tyrosine kinase
B) Blocks DNA synthesis
C) Induces apoptosis nonspecifically
D) Inhibits angiogenesis
E) Blocks growth factor receptors

Question 442 (TBL Angiogenesis) The team discusses tumor angiogenesis. VEGF (vascular endothelial growth factor) is important because it:
A) Promotes tumor cell proliferation
B) Inhibits apoptosis
C) Stimulates new blood vessel formation
D) Enhances DNA repair
E) Activates immune responses

Question 443 (PBL Metastasis Mechanisms) The metastatic cascade involves multiple steps. Which step is considered rate-limiting?
A) Invasion through basement membrane
B) Intravasation into blood vessels
C) Survival in circulation
D) Extravasation and colonization at distant sites
E) Primary tumor growth

Question 444 (CBL Epithelial-Mesenchymal Transition) EMT (epithelial-mesenchymal transition) in cancer is characterized by:
A) Loss of cell-cell adhesion and increased motility
B) Increased proliferation only
C) Enhanced apoptosis

D) Better differentiation
E) Decreased invasiveness

Question 445 (RBL Cancer Stem Cells) The cancer stem cell hypothesis suggests that:
A) All cancer cells are equally tumorigenic
B) Only a small subset of cells can initiate tumors and drive progression
C) Cancer cells cannot differentiate
D) Stem cells cannot become malignant
E) All tumors arise from normal stem cells

Question 446 (TBL Apoptosis Pathways) The team discusses apoptosis evasion in cancer. BCL-2 overexpression leads to:
A) Increased apoptosis
B) Resistance to apoptosis
C) Enhanced DNA repair
D) Increased proliferation
E) Better differentiation

Question 447 (PBL) A patient with chronic myeloid leukemia develops resistance to multiple tyrosine kinase inhibitors. Molecular analysis reveals T315I gatekeeper mutation in BCR-ABL. Which mechanism explains this resistance pattern?
a) Drug efflux pump upregulation
b) Target protein structural changes
c) Alternative pathway activation
d) Epigenetic silencing
e) Tumor microenvironment effects

Question 448 (CBL Immunotherapy) Checkpoint inhibitor therapy (anti-PD-1, anti-PD-L1) works by:
A) Directly killing cancer cells
B) Blocking angiogenesis
C) Enhancing T cell activation against tumors
D) Inhibiting tyrosine kinases
E) Promoting apoptosis

Question 449 (RBL Epigenetic Modifications) DNA methylation in cancer typically:
A) Activates oncogenes
B) Silences tumor suppressor genes
C) Enhances DNA repair
D) Promotes differentiation
E) Increases genomic stability

Question 450 (TBL MicroRNAs) The team discusses miRNAs in cancer. These small RNAs function as:
A) Protein-coding genes
B) Post-transcriptional regulators that can act as oncogenes or tumor suppressors
C) Structural components
D) Energy sources
E) DNA repair factors

Question 451 (PBL) A patient with non-small cell lung cancer shows EGFR exon 19 deletion. After initial response to erlotinib, resistance develops. Molecular testing reveals T790M mutation. Which treatment approach is most appropriate?
a) Switch to different first-generation EGFR TKI
b) Third-generation EGFR TKI (osimertinib)
c) Combination chemotherapy
d) Immunotherapy
e) Radiation therapy

Question 452 (CBL Tumor Heterogeneity) Intratumoral heterogeneity refers to:
A) Different tumor types in the same patient
B) Genetic and phenotypic diversity within a single tumor
C) Tumors in different organs
D) Normal tissue variation
E) Treatment-induced changes only

Question 453 (RBL Precision Medicine) Precision oncology involves:
A) Using the same treatment for all patients
B) Matching targeted therapies to specific molecular alterations
C) Surgical precision only
D) Radiation dose optimization
E) Chemotherapy scheduling

Question 454 (TBL Oncometabolites) The team discusses metabolic reprogramming in cancer. The Warburg effect describes:
A) Increased oxidative phosphorylation
B) Preferential glucose metabolism via glycolysis even in oxygen presence
C) Enhanced fatty acid oxidation
D) Decreased glucose uptake
E) Normal cellular metabolism

Question 455 (PBL Chromosomal Instability) Chromosomal instability in cancer is characterized by:
A) Stable karyotype
B) Gains and losses of chromosome segments or whole chromosomes
C) Point mutations only
D) Normal DNA repair
E) Enhanced genomic stability

Question 456 (CBL CAR-T Cell Therapy) Chimeric antigen receptor T-cell therapy involves:
A) Using unmodified patient T cells
B) Genetically modifying T cells to target specific tumor antigens
C) Blocking T cell function
D) Using donor T cells without modification
E) Inhibiting immune responses

Question 457 (RBL Tumor Dormancy) Tumor dormancy mechanisms include:
A) Balance between proliferation and apoptosis
B) Angiogenic dormancy
C) Immune-mediated dormancy
D) All of the above mechanisms
E) Active tumor growth only

Question 458 (TBL Resistance Mechanisms) The team discusses drug resistance in cancer. Which mechanism is most common?
A) Drug efflux pumps
B) Target mutation
C) Alternative pathway activation
D) Apoptosis resistance
E) All mechanisms contribute significantly

Question 459 (PBL Hereditary Cancer Syndromes) Li-Fraumeni syndrome is associated with mutations in which gene?
A) BRCA1 B) BRCA2 C) TP53 D) APC E) MLH1

Question 460 (CBL Telomeres and Cancer) Telomerase reactivation in cancer cells allows:
A) Limited replicative potential
B) Unlimited replicative potential (immortalization)

C) Enhanced apoptosis
D) Better DNA repair
E) Normal senescence

Question 461 (RBL Synthetic Lethality) PARP inhibitors are effective in BRCA-mutated cancers due to:
A) Direct DNA damage
B) Synthetic lethality with defective homologous recombination
C) Enhanced immune responses
D) Angiogenesis inhibition
E) Cell cycle arrest

Question 462 (TBL Tumor Biomarkers) The team discusses predictive versus prognostic biomarkers. Predictive biomarkers:
A) Indicate overall patient prognosis
B) Predict response to specific therapies
C) Diagnose cancer presence
D) Determine tumor stage
E) Assess treatment toxicity

Question 463 (PBL Oncogenic Viruses) Human papillomavirus (HPV) causes cervical cancer by:
A) Direct cell transformation
B) E6 and E7 proteins inactivating p53 and Rb
C) Immune suppression
D) Chromosomal translocations
E) DNA methylation

Question 464 (CBL) AI algorithms for predicting cancer drug combinations focus on which approach for optimal efficacy?
a) Target pathway analysis
b) Drug interaction modeling
c) Resistance mechanism prediction
d) Toxicity profile assessment
e) Integrated systems pharmacology

Topic 17: Midterm Control II + Final Review - Hematology + Nervous System + Pediatrics + Oncology (36 questions)

Question 465 (TBL Integrated Hematology Case) A 45-year-old patient presents with fatigue, splenomegaly, and a white blood cell count of 85,000/μL with immature granulocytes. Cytogenetics shows t(9;22). The team must determine the phase of disease and treatment approach. This presentation is most consistent with:
A) Chronic myeloid leukemia in chronic phase
B) Acute myeloid leukemia
C) Chronic myeloid leukemia in blast crisis
D) Acute lymphoblastic leukemia
E) Chronic lymphocytic leukemia

Question 466 (PBL Neurological Emergency) A 35-year-old patient presents with fever, thrombocytopenia, neurological symptoms, and schistocytes on blood smear. The combination of hematologic and neurologic findings suggests:
A) Immune thrombocytopenic purpura
B) Thrombotic thrombocytopenic purpura
C) Disseminated intravascular coagulation
D) Hemolytic uremic syndrome
E) Acute stroke with secondary thrombocytopenia

Question 467 (CBL Pediatric Malignancy) A 4-year-old child presents with bone pain, fatigue, and bruising. Blood work shows pancytopenia with 60% lymphoblasts positive for CD10, CD19, and TdT. The prognosis for this condition is:
A) Poor in all cases
B) Excellent with modern therapy (>90% cure rate)
C) Variable depending on age only
D) Poor due to central nervous system involvement
E) Good only with bone marrow transplant

Question 468 (PBL) Complex clinical scenario: A child presents with developmental delays, seizures, and recurrent infections. Laboratory shows anemia and abnormal white cell morphology. Genetic testing reveals DNA repair defect. Which syndrome integrates all findings?
a) Ataxia-telangiectasia
b) Fanconi anemia
c) Bloom syndrome
d) Xeroderma pigmentosum
e) Cockayne syndrome

Question 469 (TBL Complex Case Analysis) An elderly patient presents with anemia, bone pain, hypercalcemia, and renal insufficiency. Serum protein electrophoresis shows an M-spike. The team must differentiate between multiple myeloma and other plasma cell disorders. Which finding confirms multiple myeloma?
A) Presence of M-protein alone
B) >10% plasma cells in bone marrow plus end-organ damage
C) Hypercalcemia alone
D) Renal insufficiency alone
E) Bone pain alone

Question 470 (PBL Neurodegeneration and Cancer) A 65-year-old patient with lung cancer develops rapidly progressive dementia and memory loss. This paraneoplastic syndrome is associated with which antibodies?
A) Anti-Hu (ANNA-1)
B) Anti-Yo
C) Anti-Ri
D) Anti-Ma2
E) Anti-NMDA receptor

Question 471 (CBL Inherited Cancer Syndromes) A family history reveals multiple members with early-onset colorectal cancer, endometrial cancer, and other malignancies. Tumor analysis shows microsatellite instability. This suggests:
A) Familial adenomatous polyposis
B) Li-Fraumeni syndrome
C) Hereditary nonpolyposis colorectal cancer (Lynch syndrome)
D) Cowden syndrome
E) Peutz-Jeghers syndrome

Question 472 (RBL Targeted Therapy Integration) A patient with metastatic melanoma has a BRAF V600E mutation. The optimal treatment approach involves:
A) BRAF inhibitor monotherapy
B) MEK inhibitor monotherapy
C) Combined BRAF and MEK inhibition
D) Immunotherapy alone
E) Chemotherapy

Question 473 (TBL Pediatric Brain Tumors) The team evaluates a 8-year-old child with hydrocephalus, ataxia, and a posterior fossa mass. The most likely diagnosis and standard treatment approach is:
A) Glioblastoma requiring immediate chemotherapy
B) Medulloepithelioma requiring surgery, radiation, and chemotherapy
C) Meningioma requiring surgery only
D) Metastatic disease requiring palliative care
E) Infection requiring antibiotics

Question 474 (PBL Hemostasis and Cancer) Cancer patients are at increased risk for both bleeding and thrombosis. This paradox is due to:
A) Treatment-induced thrombocytopenia and hypercoagulable state B) Liver metastases only C) Bone marrow infiltration only D) Chemotherapy effects only E) Immobilization only

Question 475 (CBL Tumor Immunology) The concept of immunoediting in cancer includes three phases. The equilibrium phase involves:
A) Complete immune elimination of tumor cells
B) Immune-mediated selection of tumor variants
C) Tumor escape from immune control
D) Balance between immune elimination and tumor growth
E) No immune involvement

Question 476 (TBL) Your team analyzes integrated pathophysiology of paraneoplastic neurological syndromes. Which mechanism best explains remote nervous system effects of cancer?
a) Direct tumor invasion
b) Metastatic disease
c) Autoimmune cross-reactivity
d) Metabolic effects
e) Treatment complications

Question 477 (TBL Multidisciplinary Approach) A patient presents with stroke symptoms, thrombocytopenia, and anemia. The team includes neurology, hematology, and oncology. The most likely unifying diagnosis is:
A) Primary brain tumor
B) Thrombotic thrombocytopenic purpura
C) Metastatic cancer with DIC
D) Autoimmune disease
E) Drug toxicity

Question 478 (PBL Pediatric Hematology) A newborn develops severe anemia requiring transfusion. Parents are of Mediterranean descent. The most likely diagnosis and long-term management involves:
A) Iron deficiency requiring iron supplementation
B) β-thalassemia major requiring lifelong transfusions
C) Sickle cell disease requiring hydroxyurea
D) Hereditary spherocytosis requiring splenectomy
E) G6PD deficiency requiring oxidant avoidance

Question 479 (CBL Oncologic Emergencies) Superior vena cava syndrome in a young adult is most commonly caused by:
A) Lung cancer
B) Lymphoma (Hodgkin or non-Hodgkin)
C) Thymoma
D) Metastatic breast cancer
E) Aortic aneurysm

Question 480 (RBL Precision Medicine) Tumor molecular profiling reveals multiple actionable mutations. The treatment approach should prioritize:
A) The most common mutation
B) Mutations with available FDA-approved drugs
C) Mutations with strongest evidence for benefit
D) Patient preference
E) Both B and C considerations

Question 481 (TBL Pediatric Solid Tumors) The team evaluates a 2-year-old with an abdominal mass and elevated catecholamines. Histology shows small round blue cells with neural differentiation. The diagnosis and prognosis depends on:
A) Neuroblastoma with risk stratification by age, stage, and biology
B) Wilms tumor with excellent prognosis
C) Rhabdomyosarcoma requiring multimodal therapy
D) Hepatoblastoma requiring liver transplant
E) Lymphoma requiring chemotherapy

Question 482 (PBL Neurodegenerative Overlap) A patient presents with features of both Parkinson's disease and dementia. The pathological finding that would support Lewy body dementia is:
A) Neurofibrillary tangles in cortex
B) α-synuclein deposits in cortical and subcortical regions
C) TDP-43 inclusions
D) Huntingtin aggregates
E) Prion protein deposits

Question 483 (CBL) Implementing AI for integrated pediatric-hematology-oncology care requires which data synthesis approach?
a) Age-adjusted normal values
b) Growth and development parameters
c) Family history integration
d) Multi-system organ assessment
e) Comprehensive pediatric-specific modeling

Question 484 (RBL Childhood Leukemia Biology) Favorable prognostic factors in pediatric acute lymphoblastic leukemia include:
A) Age 1-10 years and hyperdiploidy
B) Age >10 years and hypodiploidy
C) t(9;22) Philadelphia chromosome
D) t(4;11) MLL rearrangement
E) High white blood cell count

Question 485 (TBL Tumor Suppressor Loss) The team analyzes loss of heterozygosity (LOH) in familial cancer. This concept explains why:
A) Oncogenes require only one mutated copy
B) Tumor suppressors require loss of both copies (Knudson's two-hit hypothesis)
C) All cancers are hereditary
D) Mutations are always dominant
E) Cancer cells are diploid

Question 486 (PBL Stroke in Young Adults) A 25-year-old develops stroke symptoms. Workup reveals thrombocytopenia and hemolytic anemia. The most likely diagnosis requiring emergency treatment is:
A) Antiphospholipid syndrome
B) Thrombotic thrombocytopenic purpura
C) Sickle cell disease
D) Moyamoya disease
E) Cerebral venous thrombosis

Question 487 (CBL Myelodysplastic Syndromes) A 70-year-old patient has macrocytic anemia with dysplastic changes in all cell lines. Cytogenetics shows del(5q). This finding suggests:
A) Good prognosis with lenalidomide response
B) Poor prognosis requiring immediate transplant
C) Acute leukemia transformation
D) Normal finding for age
E) Vitamin B12 deficiency

Question 488 (RBL) Research integration shows that inherited cancer predisposition syndromes often present with hematologic abnormalities. Which syndrome most commonly presents in childhood with both features?
a) Li-Fraumeni syndrome

b) Neurofibromatosis type 1
c) von Hippel-Lindau disease
d) Tuberous sclerosis
e) Multiple endocrine neoplasia

Question 489 (TBL Pediatric CNS Tumors) The team discusses molecular subgroups of medulloepithelioma. Which subgroup has the best prognosis?
A) WNT-activated
B) SHH-activated
C) Group 3
D) Group 4
E) All have similar prognosis

Question 490 (PBL Paraneoplastic Syndromes) A patient with small cell lung cancer develops muscle weakness that improves with activity. This suggests:
A) Myasthenia gravis
B) Lambert-Eaton myasthenic syndrome
C) Polymyositis
D) Muscular dystrophy
E) Peripheral neuropathy

Question 491 (CBL Hemophilia Treatment) Modern treatment of severe hemophilia A includes:
A) Factor VIII concentrates only
B) Desmopressin (DDAVP) only
C) Extended half-life factors and non-factor therapies
D) Gene therapy for all patients
E) Prophylactic antibiotics

Question 492 (RBL Oncogene Addiction) The concept of oncogene addiction explains why:
A) Cancer cells become dependent on specific oncogenic pathways
B) All cancers are similar
C) Chemotherapy always works
D) Cancer cells are normal
E) Targeted therapy is ineffective

Question 493 (TBL Integrated Case Management) A patient with multiple myeloma develops renal failure, hypercalcemia, and anemia. The team must prioritize immediate management. The most urgent intervention is:
A) Chemotherapy initiation
B) Hypercalcemia correction and hydration
C) Red blood cell transfusion
D) Bisphosphonate therapy
E) Plasmapheresis

Question 494 (PBL) Complex integration case: A young adult with brain tumor develops hematologic complications during treatment. Which factor most influences treatment planning?
a) Tumor type and grade
b) Hematologic toxicity severity
c) Patient performance status
d) Treatment goals and prognosis
e) Integrated risk-benefit assessment

Question 495 (CBL Minimal Residual Disease) In acute lymphoblastic leukemia, minimal residual disease monitoring uses:
A) Morphology only
B) Flow cytometry and molecular techniques
C) Imaging studies
D) Clinical examination only
E) Complete blood count only

Question 496 (RBL Tumor Evolution) Clonal evolution in cancer involves:
A) Fixed genetic changes
B) Dynamic acquisition of mutations conferring growth advantage
C) Regression to normal cells
D) Uniform tumor progression
E) No genetic changes over time

Question 497 (TBL Quality of Life) The team addresses long-term effects of childhood cancer treatment. Which is the most common late effect?
A) Second malignancies
B) Cardiac dysfunction
C) Neurocognitive impairment
D) Endocrine dysfunction
E) All are equally common and require monitoring

Question 498 (PBL Palliative Care Integration) A patient with advanced cancer experiences multiple symptoms affecting quality of life. Early palliative care integration:
A) Means giving up on treatment
B) Improves quality of life and may extend survival
C) Is only for end-of-life care
D) Prevents curative treatment
E) Is only for pain management

Question 499 (RBL) Research integration reveals that certain genetic syndromes predispose to both hematologic and neurologic abnormalities. Which molecular pathway is most commonly affected?
a) DNA repair pathways
b) Cell cycle control
c) Apoptosis regulation
d) Signal transduction
e) Multiple pathway interactions

Question 500 (RBL Future Directions) Your team analyzes the integration of palliative care in complex multi-system diseases. Which approach provides the best patient outcomes?
a) Early palliative care integration
b) Symptom-based referrals
c) End-of-life care focus
d) Family-centered approaches
e) Comprehensive integrated care models