ABSITE SLAYER

SECOND EDITION

DALE A. DANGLEBEN
FIRAS G. MADBAK

Mc Graw Hill

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Dedication

This work is dedicated to my father, Arthur Charles Dangleben, who told me that education was the gateway to a better future. Rest in peace, Dad.

Dale A. Dangleben, MD, FACS

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INTRODUCTION: GENERAL TEST-TAKING TIPS

1. A good night's sleep before exams brings renewed spirit and concentration to complete the task.
2. Simple meditation or yoga on the morning of the exam can help with stress and anxiety release and promote focus.
3. Do not carb-load for breakfast because you may crash and get fatigued during the exam, so balance it out.
4. It is not a one-night preparation, nor one week, nor one month. It is a continuous year-round schedule.
5. Do not second-guess yourself.
6. Do not choose an answer because you have not heard of it.
7. There is no 100% item on test. Each year a pattern is seen: some commonly asked questions do not show up, but common things are common. You have to know the basics.
8. Do not overthink the questions. Keep it simple.
9. The night before the test should not be devoted to an "all-nighter" or intense review. Read a few things to ease your conscience, but spend time having a good meal and, more importantly, getting a good night's sleep.
10. Beware of the urge to change answers. Statistically, your first answer is correct more often than a changed answer.
11. If you know an answer is correct but can't remember why, the reason may not matter. For the sake of the test, so you don't get too hung up on one single question, just answer the question and move on.
12. Don't get bogged down by wordy or long questions. Often the last sentence or 2 tells the primary question being asked.
13. The best prep for the ABSITE is RESIDENCY and a small amount of daily formal study.

    Always do what you do in real life: stabilize patients before the operating room, never send an unstable patient to the CT scanner, and always remember to differentiate sick patients from nonsick patients.
14. "Get to 2": these exams are usually about narrowing down the answers to 2 likely choices. Then go back to look for the clues to sort out these final options.
15. Study hard in order to treat your patients in the best way possible, not to take an exam.
16. As noted in tip #9, it is a bad idea to try to study the night before an ABSITE exam. This can lead to finding information that you have not totally mastered and may affect your confidence for the exam. If you are going to review a topic, choose a topic in which you are well versed to boost your confidence for the exam.
17. Layer your clothing for the exam. You never know what the room temperature will be like.
18. Eat breakfast, but avoid eating heavy foods. Bring snacks to the test.

19. Questions are generally "fluff free." There is little fluff in the questions. If they wanted you to know more, they would have told you! The absence of clues toward a particular decision is a clue that you should NOT be moving in that direction.
20. Consider bringing Tylenol and ibuprofen for muscle aches or headaches.
21. The test writers love the "thoughtless trap." For example, they will give you a patient with colon cancer who needs an operation, but they will also mention the patient had an MI last week. You have to factor the MI into your decision. Read the questions carefully: there is usually more than enough time.
22. Remember, the ABSITE is an endurance test. Pace yourself wisely and take a short break if necessary to get back on track.
23. They want you to get it right! Only a handful of questions are designed to separate out the ninety-ninth percentile from the ninety-eighth percentile.

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CHAPTER 1

Cell Biology

Christie Buonpane

Test Taking Tip

Often, complex cell biology is hidden within a question seemingly about a clinical scenario. If you can parse the implied question from the background without wasting time on superfluous information, you will have the best chance at efficiently making progress through tough questions.

CELL MEMBRANE

Which cell wall component increases membrane fluidity?
Cholesterol

What are the 3 main lipid classes found in the cell membrane?
Phospholipids, cholesterol, and glycolipids

What percentages of protein, carbohydrate, and lipid compose the plasma membrane?
Protein: 60%, carbohydrate: 1% to 10%, and lipid: 40%

What are the most common phospholipids in the plasma membrane?
Phosphatidylethanolamine and phosphatidylcholine

Which portion of the cell wall provides capacitance (ability to store charge)?
Lipid portion of plasma membrane

Which portion provides the ability to resist charge?
Protein portion

What is the difference between surface antigens in the ABO system and the HLA system?
ABO = glycolipids
HLA = glycoproteins

Name the adhesion molecules that anchor a cell to other cells:
Desmosomes

Name the adhesion molecules that anchor a cell to extracellular matrix molecules:
Hemidesmosomes

Cell-cell occluding junctions that form a water-impermeable barrier:
Tight junctions

Toxic portion of lipopolysaccharide complex:
Lipid A

What synthesizes cAMP and serves as a second messenger to activate various cell enzymes and processes?
Adenylate cyclase

CELL STRUCTURES

Name the thin filaments that interact with myosin to cause muscle contraction:
Actin

Name the thick filaments that slide along actin utilizing ATP:
Myosin

Intermediate filament found in hair and nails:
Keratin

Intermediate filament found in muscle:
Desmin

Intermediate filament found in fibroblasts:
Vimentin

Form specialized cellular structures such as mitotic spindles, cilia, and neuronal axons; form lattice inside the cell to aid in transport of organelles in cell:
Microtubules

Specialized microtubule that forms spindle fibers during cell division:
Centriole

Structural component of cell that synthesizes exported proteins:
Rough endoplasmic reticulum

Structural component of cell that detoxifies drugs and is involved with lipid/steroid synthesis:
Smooth endoplasmic reticulum

Structural component of a cell that uses carbohydrates to modify proteins and targets proteins to lysosomes:
Golgi apparatus

Structure inside the cell that has a double membrane with an outer membrane that is continuous with the rough endoplasmic reticulum:
Nucleus

Structure inside the nucleus with no membrane where ribosomes are made:
Nucleolus

Cell structure responsible for energy production:
Mitochondria

GENETICS

Consists of proteins, histones, and double-stranded helical DNA:
Chromosomes

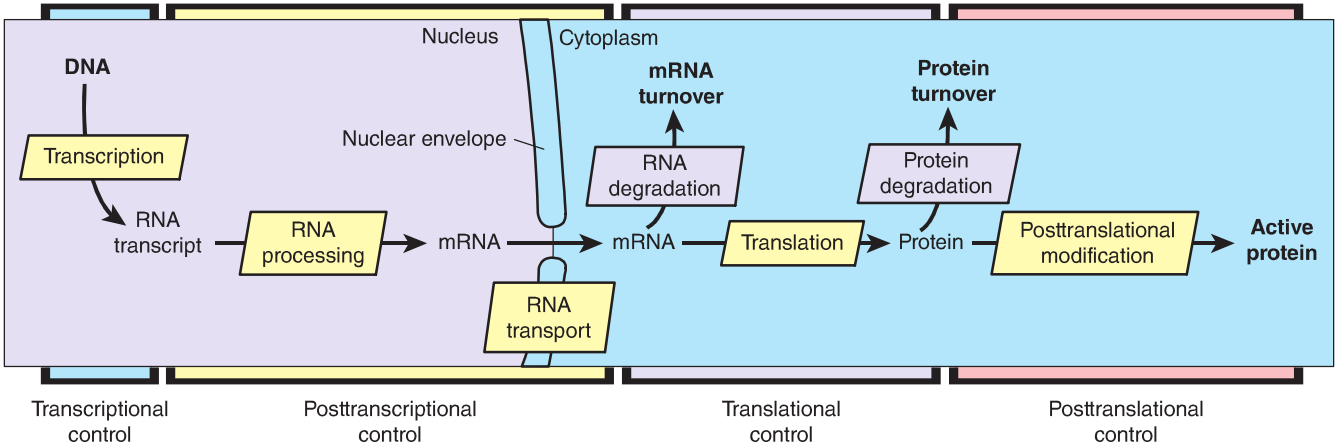

FIGURE 1-1. Four major steps in the control of eukaryotic gene expression. Transcriptional and posttranscriptional control determine the level of mRNA that is available to make a protein, whereas translational and posttranslational control determine the final outcome of functional proteins. Note that posttranscriptional and posttranslational controls consist of several steps. *(Reproduced with permission from Brunicardi FC, Andersen DK, Billiar TR, et al: Schwartz's Principles of Surgery, 11th ed. New York, NY: McGraw Hill; 2019.)*

Adenine and guanine are examples of:
Purines

Cytosine, thymidine, and uracil are examples of:
Pyrimidines

Process by which ribosomes use mRNA as a template for synthesis of proteins:
Translation

Process by which RNA polymerase uses a DNA strand for synthesis of mRNA:
Transcription

Place where transcription takes place:
Nucleus

Sequence of the start codon:
AUG

Coils of DNA that are the basic units of DNA packaging:
Nucleosomes

Small basic proteins that nonspecifically bind with DNA segments:
Histones

Formed by the coiling of 6 or more nucleosomes by the histone H1:
Solenoids

Proteins are synthesized from:
mRNA

Enzyme involved in the unwinding of DNA:
DNA helicase

Enzyme used to catalyze the formation of the RNA primers used to initiate DNA synthesis:
DNA primase

Enzyme that links DNA fragments by degrading RNA primers:
DNA ligase

Type of mutation that results in a single amino acid change from a point mutation:
Missense mutation

Type of mutation resulting in a change in a single base pair:
Point mutation

Type of mutation occurring from a point mutation that results in replacement of an amino acid with a stop codon:
Nonsense mutation

Type of mutation that occurs with the addition or deletion of a few base pairs:
Frameshift mutation

Technique by which DNA can be amplified a billion-fold by utilizing synthesized primers/oligonucleotides to complement a strand of DNA:
Polymerase chain reaction

Noncoding regions that interrupt eukaryotic genes:
Introns

Process by which introns are removed from an RNA transcript:
Splicing

RECEPTORS AND SIGNALS

Platelet-derived growth factor, epidermal growth factor, and transforming growth factor alpha belong to this receptor family:
Tyrosine kinase receptor

Activated by calcium and diacylglycerol:
Protein kinase C

Activated by cAMP:
Protein kinase A

Enzyme that converts membrane phosphoinositols into IP3 and DAG:
Phospholipase C

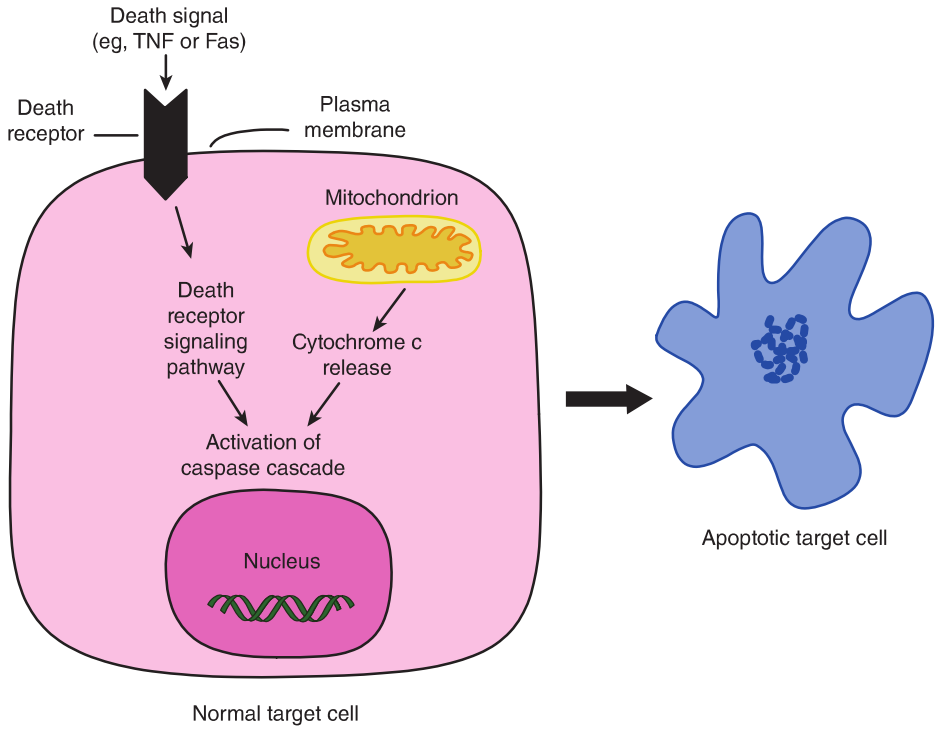

FIGURE 1-2. A simplified view of the apoptosis pathways. Extracellular death receptor pathways include the activation of Fas and tumor necrosis factor receptors and consequent activation of the caspase pathway. The intracellular death pathway indicates the release of cytochrome c from mitochondria, which also triggers the activation of the caspase cascade. During apoptosis, cells undergo DNA fragmentation, nuclear and cell membrane breakdown, and are eventually digested by other cells. *(Reproduced with permission from Brunicardi FC, Andersen DK, Billiar TR, et al: Schwartz's Principles of Surgery, 11th ed. New York, NY: McGraw Hill; 2019.)*

Mediates release of calcium from sarcoplasmic reticulum in muscle, endoplasmic reticulum, and mitochondria:
IP3

Works with calcium to activate protein kinase C:
DAG

Enzyme that breaks down ATP to cAMP with release of pyrophosphate:
Adenylate cyclase

Most critical component in neovascularization in tumor metastases:
VEGF receptor

Cellular process under the precise control of different extracellular and intracellular signals and follows a fixed sequence of events leading to cell death:
Apoptosis

Steroid hormones bind receptor in:
Cytoplasm

Thyroid hormone binds receptor in:
Nucleus

Examples of cAMP-dependent hormones:
TSH, ACTH

CELL TRANSPORT

Type of cell transport that uses concentration gradient as a driving force:
Diffusion (CO_2, O_2, and urea)

Type of diffusion that utilizes a carrier and is saturable:
Facilitated diffusion

Type of cell transport that requires ATP for energy:
Active transport

CELLULAR METABOLISM

In glycolysis, 1 glucose molecule generates:
2 ATP and 2 pyruvate molecules

Name of cycle where NADH and $FADH_2$ are created from the 2 pyruvate molecules produced from the breakdown of glucose:
Krebs cycle

Overall number of ATP generated from 1 molecule of glucose:
38 ATP: 36 from Krebs cycle + 2 ATP from glycolysis

Process by which amino acids and lactic acid via the Cori cycle are converted into glucose:
Gluconeogenesis

Largest site of gluconeogenesis:
Liver

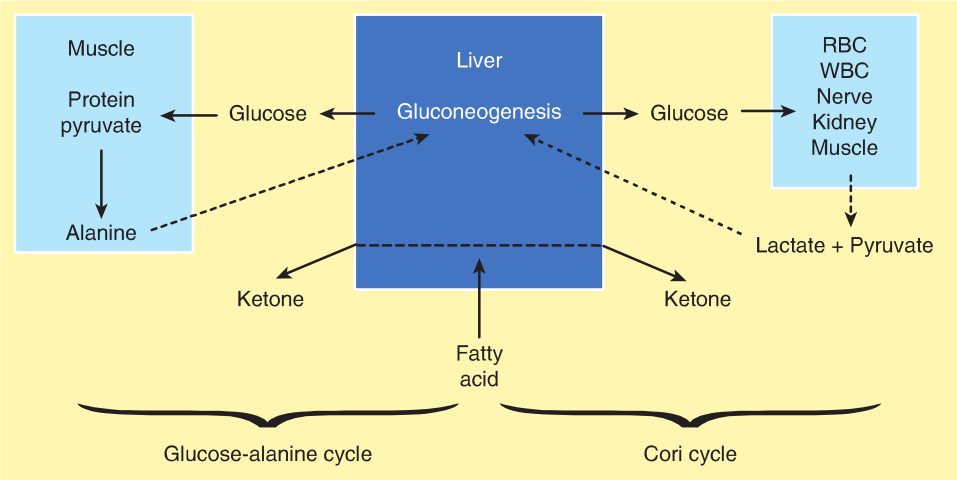

FIGURE 1-3. The recycling of peripheral lactate and pyruvate for hepatic gluconeogenesis is accomplished by the Cori cycle. Alanine within skeletal muscles can also be used as a precursor for hepatic gluconeogenesis. During starvation, such fatty acid provides fuel sources for basal hepatic enzymatic function. RBC, red blood cell; WBC, white blood cell. *(Reproduced with permission from Brunicardi FC, Andersen DK, Billiar TR, et al: Schwartz's Principles of Surgery, 11th ed. New York, NY: McGraw Hill; 2019.)*

What can be used for gluconeogenesis?
Yes: lactic acid, amino acids, glycerol
No: free fatty acids, lipids

Name the breakdown product of fat metabolism that cannot be converted back into pyruvate:
Acetyl CoA

Lipases act on lipids to form:
Fatty acids and monoacylglycerols

Fatty acid utilization:
Short chain = direct transport to liver
Long chain = packaged into micelles into lymph

CELL CYCLE

Most variable part of the cell cycle that determines cell cycle length:
G1

Part of cell cycle where protein synthesis and DNA replication occur:
S

Growth factors affect the cell during this phase of the cell cycle:
G1

Phase that helps maintain genomic stability:
G2

Part of cycle where cell divides:
M

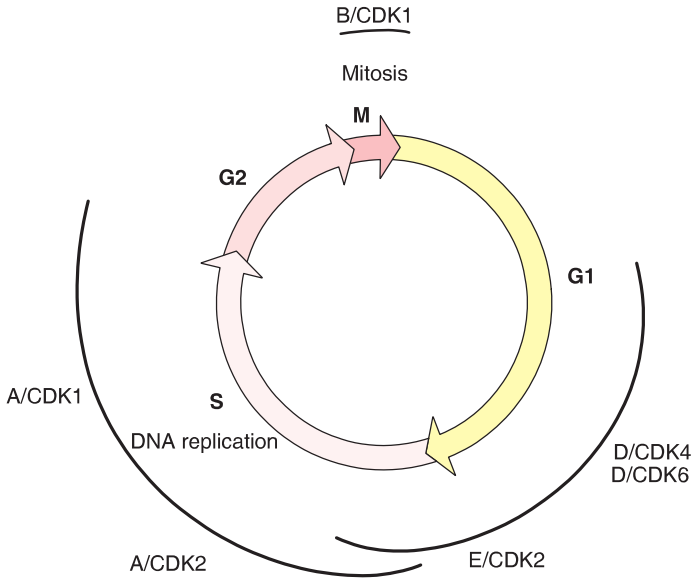

FIGURE 1-4. The cell cycle and its control system. M is the mitosis phase, when the nucleus and the cytoplasm divide; S is the phase when DNA is duplicated; G1 is the gap between M and S; G2 is the gap between S and M. A complex of cyclin and cyclin-dependent kinase (CDK) controls specific events of each phase. Without cyclin, CDK is inactive. Different cyclin/CDK complexes are shown around the cell cycle. A, B, D, and E stand for cyclin A, cyclin B, cyclin D, and cyclin E, respectively. *(Reproduced with permission from Brunicardi FC, Andersen DK, Billiar TR, et al: Schwartz's Principles of Surgery, 11th ed. New York, NY: McGraw Hill; 2019.)*

Tumor cells are most sensitive to radiation during this stage of the cell cycle:
M

Phase of mitosis where chromosomes shorten, nucleolus and nuclear envelope disappear, and spindle apparatus forms:
Prophase

Phase of mitosis where centromeres align on the equatorial plate, spindle fibers attach to the centromeres, and centromeres duplicate:
Metaphase

Phase of mitosis where chromatids migrate to opposite poles:
Anaphase

Phase when nucleolar and nuclear envelope re-form and chromosomes decondense:
Telophase

MULTIPLE CHOICE QUESTIONS

1. **Erythrocytes use glycolysis primarily as a source of energy in the form of**
   A. ATP to power active membrane transport
   B. ATP to maintain cytoskeleton integrity
   C. NADH to power protein synthesis
   D. NADPH to initiate DNA replication
   E. NADH to reduce oxidized glutathione

2. A defect in cholesterol metabolism or other sources of bile would cause difficulties in digestion because bile is needed for

A. Emulsification of dietary fat for easier access of stomach lipases
B. Denaturation of dietary proteins for easier digestion by proteases
C. Micelle incorporation of lipids for easier digestion by lipases
D. Neutralization of stomach acid
E. Stimulation of pancreatic secretions

3. Cyclins are proteins that serve as signals to control progression of cells around the cell cycle. Cyclin signals are transmitted via

A. Histone acetylases
B. Protein kinases
C. DNA methylases
D. Specific proteases
E. Small interfering RNAs (siRNA)

4. Which of the following is a correct match?

A. G cell—pepsinogen
B. Chief cell—gastrin
C. Parietal cell—HCl and intrinsic factor
D. Mucous cells—cholecystokinin

5. Platelet activation, muscle contraction, pancreatic secretion, and glycogen degradation act via which intracellular signal mechanism?

A. cAMP second messenger signaling
B. Calmodulin-induced calcium release
C. Protein kinase A activation
D. IP3- and DAG-induced activation of protein kinase C

6. Base deficit and serum lactate correlate with mortality in trauma by reflecting which of the following systemic changes from normal physiology?

A. Myoglobin-induced ATN progressing to renal failure
B. Hypoperfused end organs relying on energy generated via anaerobic metabolism
C. Skeletal muscle sarcomere-unregulated release of calcium and diacylglycerol
D. Injured organ trauma-induced apoptosis releasing corresponding intravascular waste cellular products

7. Which of the following clinical scenarios regarding metabolism is false or implausible?

A. An elderly patient on indomethacin, oxazepam, aspirin, and acetaminophen becomes jaundiced after overwhelming UDP-glucuronic acid transferase enzymes
B. A 26-year-old female on oral contraceptives conceives after a course of antibiotics
C. A 56-year-old with atrial fibrillation on warfarin is admitted with spontaneous hematemesis after starting ciprofloxacin/metronidazole therapy for diverticulitis
D. A traumatically injured 38-year-old with no past medical history develops coma and cerebral infarction from profound hypoglycemia within 30 minutes of injury

8. Which mechanism explains ultraviolet light as a risk factor for skin cancers?

A. UV-B light is absorbed by DNA strands, causing pyrimidine dimers
B. Increased number of melanocytes after prolonged tanning leads to proliferation errors
C. Vitamin D activation includes free radicals as a side product
D. Sunlight induces collagen breakdown, leading to sheer stress injury

9. Select the incorrect statement from the following.

A. Aerobic metabolism provides the most efficient, most proliferative process to convert glucose into ATP in humans
B. Hepatocyte metabolism of toxins includes cytochrome P-450 enzymes, UDP-glucuronyl transferases, glutathione S-transferases, and sulfotransferases
C. The entirety of chromosomal DNA is contained within the nucleus in formation with histone proteins
D. Phase I reactions change endogenous substances' solubility, while phase II reactions change their chemical structure

10. Which of the following is true?

A. The Na/K ATPase transports 3 Na+ in for every 2 K+ out
B. Na+ is the most common intracellular cation
C. Cl- is the most common extracellular anion
D. K+ is high in concentration in the extracellular fluid

11. Once the Golgi apparatus modifies proteins with carbohydrates, it then transports them to the cell membrane and they are:

A. Secreted
B. Targeted to lysosomes
C. Both
D. Neither

12. Choose the answer with the correct pairing:

A. Mitochondria: major site of ATP production
B. Krebs cycle: occurs in the nucleus
C. Gluconeogenesis: occurs in the mitochondrial matrix
D. Free fatty acids: substrate for gluconeogenesis

13. Microtubules are involved in:

A. Muscle contraction
B. Transport of organelles
C. Formation of hair and nails
D. Engulfment of particles for degradation

14. Protein kinase A:

A. Is an intracellular enzyme activated by Ca++
B. Hydroxylates enzymes and proteins
C. Is an intracellular enzyme activated by cAMP
D. Is an intracellular enzyme activated by diacylglycerol (DAG)

15. What is the correct action of tight junctions?

A. Allow communication between cells
B. Composed of connexon subunits
C. Include occludin and claudin proteins
D. Stabilize cell-to-cell adhesion and are attached to the actin cytoskeleton

ANSWERS

1. **Answer: A.** B would be correct if it listed NADPH instead of ATP. C is incorrect because the cell does not make its own proteins. D is incorrect because RBCs lack nuclei and therefore do not replicate any DNA. E would be correct if it listed NADPH instead of NADH.
2. **Answer: C.** The stomach does not produce lipases. Bile micelle incorporation is not related to protease activity. Bile does not affect the acidic pH of stomach effluent. Pancreas secretions are stimulated by hormones, not bile.
3. **Answer: B.** Histone acetylases and DNA methylases play a role in DNA configuration, while proteases are not involved in cell messaging. siRNA is part of gene expression, not directly related to cell messaging.
4. **Answer: C.** G cell = gastrin, chief cell = pepsinogen, parietal cell = HCl and intrinsic factor, mucous cell = mucus/bicarbonate.
5. **Answer: D.** B is incorrect because IP3 binding to endoplasmic reticulum releases calcium. A and C are incorrect because they belong to the protein kinase A system.
6. **Answer: B.** Lactate production is associated with hypoperfusion in trauma. Myoglobin can cause ATN or renal failure in trauma but should not directly alter BD or lactate. Sarcomere release of calcium is implicated in malignant hyperthermia.
7. **Answer: D.** D is the incorrect scenario. Glycogen stores can supply the necessary glucose for anaerobic metabolism even in intense need for 20 to 90 minutes, after which it is depleted; thus, anaerobic metabolism would attempt to meet the needs of the patient in scenario D.
8. **Answer: A.** B is incorrect because melanocyte number is constant as part of neural crest migration as an embryo. C is incorrect because free radicals are not involved. D is incorrect because collagen is unrelated to DNA sequence.
9. **Answer: D.** Phase I reactions change chemical structure, while phase II reactions change solubility.
10. **Answer: C.** The Na/K ATPase transports 3 Na+ out for every 2 K+ in. K+ is the most common intracellular cation. K+ is low in concentration in the extracellular fluid (4 mEq/L).
11. **Answer: C.** The proteins are secreted or targeted to lysosomes.
12. **Answer: A.** Mitochondria are the major site for ATP production. The Krebs cycle occurs in the mitochondrial matrix. Gluconeogenesis occurs in the cytoplasm. Free fatty acids cannot be used for gluconeogenesis because acetyl CoA cannot be converted back to pyruvate.
13. **Answer: B.** Microtubules are involved in the formation of specialized cell structures such as cilia and axons, transport of organelles within the cell, and cell division. Actin and myosin are involved in muscle contraction. Intermediate filaments such as keratin

are involved in the formation of hair and nails. Phagosomes and endosomes engulf particles for degradation.

14. **Answer: C.** Protein kinase A is an intracellular enzyme activated by cAMP. It phosphorylates other enzymes and proteins, not hydroxylates. Protein kinase C is activated by Ca++ and DAG.

15. **Answer: C.** Gap junctions allow communication between cells and are made up of 2 connexon subunits. Tight junctions include proteins such as occludin and claudin and form a water-impermeable barrier between cells. Adherens junctions stabilize cell-to-cell adhesion and are attached to the actin cytoskeleton.

CHAPTER 2

Hematology

Christine Du

Test Taking Tip

Hematology requires lots of memorization. Important topics to look over include bleeding disorders and the various anticoagulants. These are basic questions you don't want to miss.

THE COAGULATION PATHWAY

Sequence of the intrinsic pathway of coagulation:
Prekallikrein + HMW kininogen + factor XII + exposed collagen → activates factor XI → activates factor IX, combines with factor VIII → activates factor X, combines with factor V → converts prothrombin (factor II) into thrombin. Thrombin converts fibrinogen into fibrin.

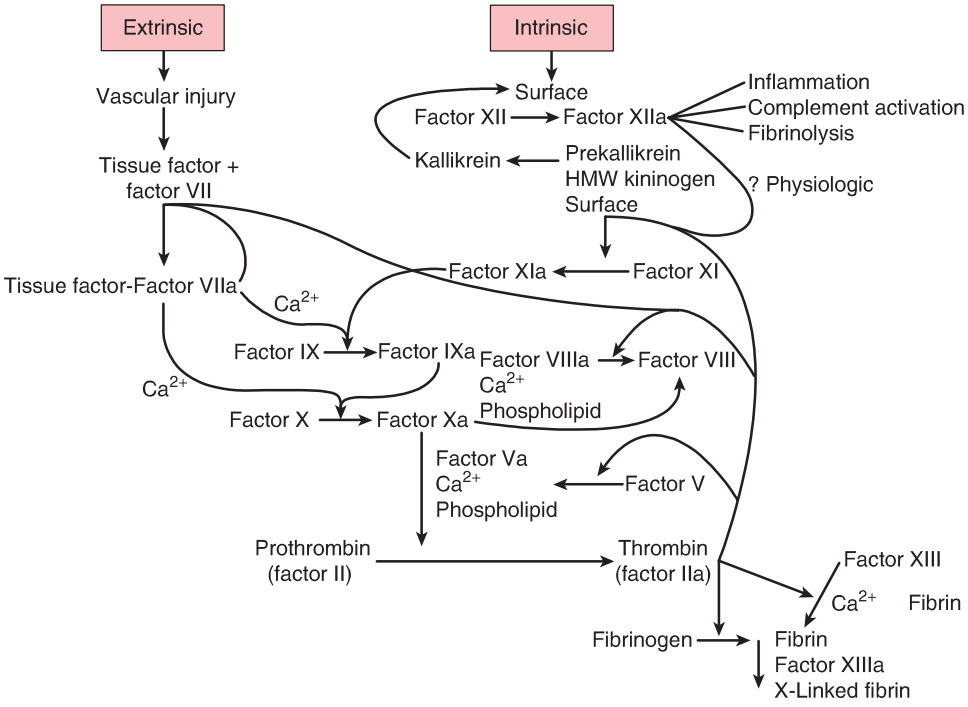

FIGURE 2-1. Schematic of the coagulation system. HMW, high molecular weight. *(Reproduced with permission from Brunicardi FC, Andersen DK, Billiar TR, et al: Schwartz's Principles of Surgery, 9th ed. New York, NY: McGraw Hill; 2010.)*

Sequence of the extrinsic pathway of coagulation:
Factor VII + tissue factor → activates factor X, combines with factor V → converts prothrombin into thrombin. Thrombin converts fibrinogen into fibrin.

Which factor is the convergence point and common to both the extrinsic and intrinsic pathways of coagulation?
Factor X

What does the prothrombin complex consist of?
Factor V, X, platelet factor 3, and prothrombin catalyze the formation of thrombin

What function does thrombin have?
Activates factors V and VIII, activates platelets, and converts fibrinogen into fibrin and fibrin split products

Which factor has the shortest half-life?
Factor VII

What factor can be used to differentiate a consumptive coagulopathy from hepatocellular disease?
Factor VIII:C; consumptive coagulopathy will have reduced levels of all factors, and hepatocellular disease will have reduced levels of all factors except factor VIII

Which factors are known as the labile factors (activity lost in stored blood)?
Factors V and VIII

What function does factor XIII have?
Cross-links fibrin

What does protein C do?
Degrades fibrinogen and factors V and VIII (vitamin K dependent)

What does protein S do?
Acts as protein C cofactor (vitamin K dependent)

What does Von Willebrand factor (vWF) do?
Links collagen to the GpIb receptor on platelets

What is the function of antithrombin III?
Binds heparin, inhibits factors IX, X, XI, and thrombin

Where does tissue plasminogen activator come from, and what does it do?
Released from endothelium, and it converts plasminogen into plasmin

What does plasmin do?
Degrades fibrinogen, fibrin, and factors V and VIII

What is the natural inhibitor of plasmin called, and where does it come from?
Alpha-2 antiplasmin; comes from the endothelium

What are the vitamin K–dependent factors?
Factors II, VII, IX, and X and proteins C and S

What function does tissue factor pathway inhibitor have?
Inhibits factor X

LABORATORY TESTS AND DATA

PT measures the function of these factors:
Factors II, V, VII, and X and fibrinogen

What 2 factors are not measured by the PTT?
Factors VII and XIII

PTT measures the function of these factors:
Factors II, V, VIII, IX, X, XI, and XII and fibrinogen

What is the normal value for bleeding time, and what does it imply?
Normal bleeding time ranges from 3 to 9 minutes and implies platelet counts >50,000/mL and normal platelet function

What test aids in detecting circulating anticoagulants, qualitative abnormalities of fibrin, inhibition of fibrin polymerization, and measures the clotting time of plasma?
Thrombin time

Patients bleeding after a large number of blood transfusions should be considered to have:
Dilutional thrombocytopenia (vs. hemolytic transfusion reaction)

What factors are common to both PT and PTT?
Factors II, V, and X and fibrinogen

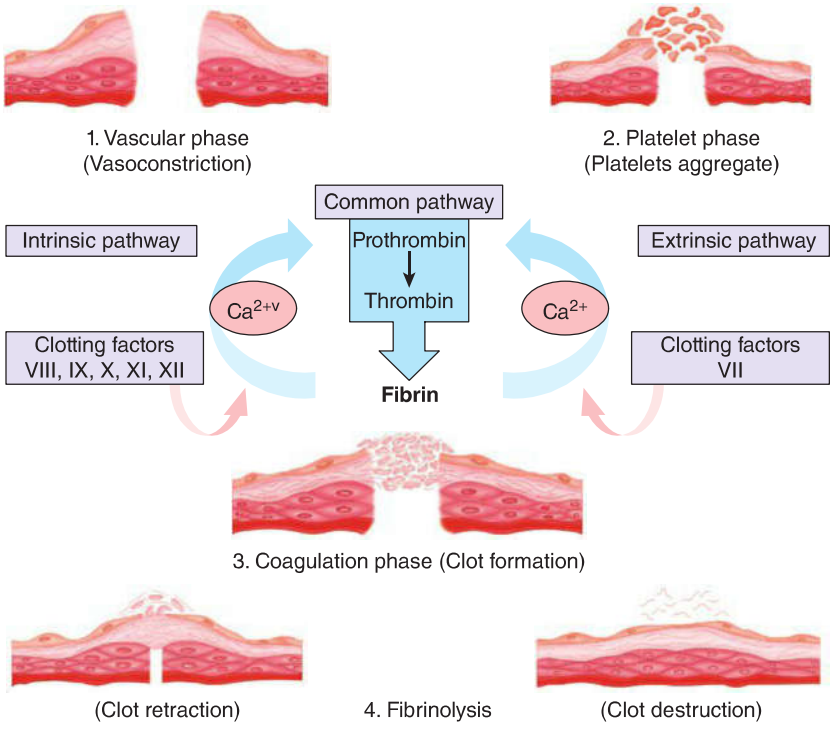

FIGURE 2-2. Biology of hemostasis. The 4 physiologic processes that interrelate to limit blood loss from an injured vessel are illustrated and include vascular constriction, platelet plug formation, fibrin clot formation, and fibrinolysis. *(Reproduced with permission from Brunicardi FC, Andersen DK, Billiar TR, et al: Schwartz's Principles of Surgery, 9th ed. New York, NY: McGraw Hill; 2010.)*

How many hours must elapse after the last dose of IV heparin before the PT can be reliably measured?
Minimum of 5 hours

Sequence of physiologic reactions that mediate hemostasis following vascular injury:
1. Vasoconstriction
2. Platelet activation/adherence/aggregation
3. Thrombin generation

HYPERCOAGULABILITY DISORDERS

What is Virchow triad?
Stasis, endothelial injury, and hypercoagulability

What is the most common cause of acquired hypercoagulability?
Smoking

What is the most common inherited hypercoagulable state?
Factor V Leiden

What is the treatment for hyperhomocysteinemia?
Vitamin B-12 and folate

Name the prothrombin gene defect causing spontaneous venous thrombosis:
Prothrombin gene defect G20210A

PLATELET FUNCTION AND DYSFUNCTION

What is the normal life span of a platelet?
7 to 10 days

Formation of a platelet plug requires these 2 electrolytes:
Calcium and magnesium

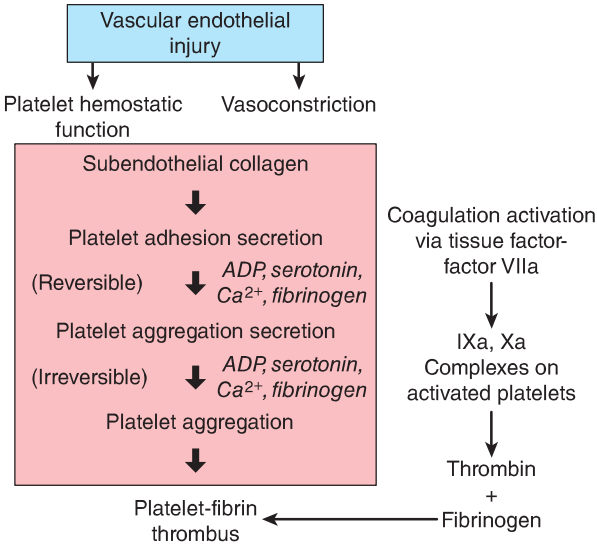

FIGURE 2-3. Schematic of platelet activation and thrombus function. ADP, adenosine diphosphate. *(Reproduced with permission from Brunicardi FC, Andersen DK, Billiar TR, et al: Schwartz's Principles of Surgery, 9th ed. New York, NY: McGraw Hill; 2010.)*

Platelet count needed before surgery:
>50,000/mL

Platelet count associated with spontaneous bleeding:
<20,000/mL

Platelet count when prophylactic platelet transfusions should be given:
<10,000/mL

Time to formation of a platelet plug is measured by this test:
Bleeding time

Inhibits platelet aggregation by inhibiting prostaglandin synthesis (PGG_2, $PGGH_2$) from arachidonic acid:
NSAIDs (ASA, ibuprofen, etc.)

Uremia leads to a downregulation of:
GpIb, GpIIb/IIIA, and vWF

Initial treatment of choice for uremic coagulopathy:
Dialysis

Drug that can be given to help correct platelet dysfunction from uremia, bypass, or ASA:
Desmopressin (DDAVP)

DDAVP and conjugated estrogens stimulate the release of:
Factor VII and vWF

RED BLOOD CELL/BLOOD PRODUCTS

Cause of microcytic anemia in a man or postmenopausal woman until proven otherwise:
Colon cancer

What is the normal life span of a red blood cell?
120 days

The electrolyte most likely to fall after infusion of stored blood:
Ionized calcium (citrate in stored blood binds serum calcium)

How long can PRBCs be stored?
~42 days or 6 weeks

Most common blood product to contain bacterial contamination:
Platelets

What type of bacteria is usually found in contaminated platelets?
Gram-positive organisms

Most common bacteria found with blood product contamination:
Gram-negative rods (*Escherichia coli*)

What types of infectious diseases can be transmitted by transfusion?
Hepatitis B and C, HIV, HTLV I and II, Chagas disease, malaria, and "theoretical risk" of Creutzfeldt-Jacob disease

True or False: Washed red blood cells can be given safely to patients who have had severe allergic/anaphylactic reactions to plasma
True, because there are barely any plasma proteins in washed red blood cells

The use of transfusion with leukocyte-reduced packed red blood cells is justified in:
Patients with multiple reactions despite premedication with antipyretics needing long-term platelet support, and transplant candidates in order to prevent formation of HLA antibodies

What are the laboratory criteria for diagnosis of a hemolytic transfusion reaction?
Hemoglobinuria with free hemoglobin concentrations >5 mg/dL, serologic confirmation of incompatibility, and positive direct antiglobulin test results

Approximate formula to convert Hct into Hgb:
Hct/3 = Hgb

1 U PRBC should increase the Hgb and Hct by:
1 g/dL and Hct by ~3% to 4%

Which blood type is the universal donor?
O negative

What happens during a type and screen?
Patient's blood is screened for antibodies and blood type is determined

What happens for a type and cross?
Recipient's serum is checked for preformed antibodies against donor's antigens in PRBC

What fluid cannot be infused with PRBC and why?
Lactated Ringer (LR); calcium in LR may result in coagulation within the IV line

What is the most common cause of transfusion hemolysis?
Clerical error leading to ABO incompatibility

Symptoms of transfusion reaction:
Fever, chills, nausea, hypotension, lumbar/chest pain, abnormal bleeding, and pain at infusion site

Treatment of transfusion hemolysis:
Stop transfusion; fluids; furosemide (Lasix); alkalinize urine with bicarbonate; pressors as needed

CLOTTING DISORDERS AND TREATMENT

How long does it take for vitamin K to take effect?
6 hours

How long do the effects of FFP last?
6 hours

How long does it take for FFP to work?
Immediately

What does cryoprecipitate contain?
vWF, factor VIII, and fibrinogen

What does FFP contain?
All factors, including labile factors V and VIII; AT-III; and proteins C and S

What is the best method for detecting patients at risk for bleeding?
A complete history and physical examination

True or False: A normal circumcision rules out a bleeding disorder
False. Newborns may not bleed at circumcision because of clotting factors from the mother (factor VIII crosses the placenta)

What percentage of patients with a bleeding disorder is picked up by abnormal bleeding from tonsillectomy or tooth extraction?
99%

What is the most common congenital bleeding disorder?
Von Willebrand disease

This factor is deficient in hemophilia A:
Factor VIII

Preoperative treatment for hemophilia A:
Factor VIII infusion to 100% normal preoperative levels

Coagulation study that is elevated in hemophilia A:
PTT

Factor deficient in hemophilia B:
Factor IX

Inheritance of hemophilia A and B:
Sex-linked recessive

What is the treatment for hemarthrosis in a patient with hemophilia A?
Initial therapy includes factor VIII, joint rest, cold packs (3–5 days), and a compression dressing (3–5 days), followed by active range-of-motion exercises 24 hours after factor VIII therapy

How long does it take for desmopressin to reach its maximal procoagulant effect?
1 to 2 hours

Deficiency in Von Willebrand disease:
vWF and factor VIII:C

Inheritance of Von Willebrand disease:
Autosomal dominant for types 1 and II; autosomal recessive for type III

Treatment of Von Willebrand disease:
DDAVP or cryoprecipitate

For what type of Von Willebrand disease is desmopressin or DDAVP specifically contraindicated?
Type 2B

Name of syndrome for deficiency of factor XI? Treatment?
Rosenthal syndrome; plasma

What is the eponym for the deficiencies of factors VII and X? Treatment?
Stuart-Prower deficiency; plasma

What receptor deficiency is found in Glanzmann thrombocytopenia?
GpIIb/IIIa receptor deficiency; the platelets cannot bind to each other

What is the treatment for Glanzmann thrombocytopenia?
Platelets

What receptor deficiency is found in Bernard-Soulier disease?
GpIb receptor deficiency; the platelets cannot bind to collagen

What is the treatment for Bernard-Soulier disease?
Platelets

Mechanism by which DIC occurs:
Thromboplastic materials are introduced into the circulation that leads to activation of the coagulation system with protective or secondary fibrinolysis

What is the most important component in the treatment of DIC?
Correcting the underlying cause

Examples of fast DIC:
Amniotic fluid embolus, placenta abruption, septic abortion, septicemia, massive tissue injury, incompatible blood transfusion, purpura fulminans

Examples of slow DIC:
Liver disease, Kasabach-Merritt syndrome, acute promyelocytic leukemia, dead fetus syndrome, transfusion of activated prothrombin complex concentrates, carcinomas

Postoperative patients with untreated polycythemia vera are at risk for:
Postoperative thrombosis, bleeding, combination of thrombosis and bleeding, or infection

What are the desired platelet counts and hematocrit in a patient with polycythemia vera before an elective operation?
Plt $<$400,000/mL and Hct $<$48%

ANTICOAGULATION

Heparin binds to this protein for its anticoagulation effects:
Anti-thrombin III; heparin-antithrombin III complex then binds factor IX, X, and XI

What is the half-life of heparin?
90 minutes

What is the dose of protamine to reverse 100 U or 1 mg of heparin?
1 to 1.5 mg

What signs are seen in a protamine reaction?
Bradycardia, hypotension, and decreased heart function

Name the diagnosis: A patient is given Coumadin for a PE; 3 days later his skin sloughs off his arms and legs:
Warfarin-induced skin necrosis

Reason that warfarin-induced skin necrosis occurs:
Proteins C and S have a shorter half-life than factors II, VII, IX, and X. Coumadin leads to a decrease in proteins C and S before the other factors, leading to a hypercoagulable state.

Patients with this deficiency are at increased risk for warfarin-induced skin necrosis:
Protein C deficiency

Mechanisms where extracorporeal circulation may lead to bleeding:
Inadequate reversal of heparin, overadministration of protamine, or thrombocytopenia

Mechanism where extracorporeal circulation may lead to clotting:
Activation of factor XII

What is the desired activated clotting time for routine anticoagulation?
150 to 200 seconds

What is the desired activated clotting time for cardiopulmonary bypass?
400 seconds

What surgical procedures require an INR <1.2?
Neurosurgical procedures, operations on the prostate or eye, or blind needle aspiration

What INR is a contraindication to intramuscular injection?
INR >1.5

What are the absolute contraindications to the use of thrombolytics?
Recent CVA (<2 months), intracranial pathology, and active internal bleeding

What is Argatroban?
A synthetic direct thrombin inhibitor derived from L-arginine. Metabolized in the liver.

What is hirudin?
An irreversible direct thrombin inhibitor derived from leeches

What is bivalirudin?
A reversible direct thrombin inhibitor

What is ancrod?
Malayan pit viper venom that stimulates tPA release

What is the length of anticoagulation treatment for a first, second, or third episode of DVT? For significant PE?
Coumadin for 6 months, 1 year, and lifetime, respectively; lifetime anticoagulation for those who had a significant PE

What are the indications for an IVC filter?
Patients who have undergone a pulmonary embolectomy; patients with documented PE while anticoagulated; patients with free-floating femoral, iliofemoral, IVC DVT; patients with contraindication to anticoagulation; patients at high risk for DVT (head injured/orthopedic injured on prolonged bed rest)

MULTIPLE CHOICE QUESTIONS

1. **What is the first step in hemostasis?**
   A. Platelet aggregation
   B. Vascular vasodilation
   C. Vascular vasoconstriction
   D. Fibrin formation

2. What is the most common congenital hypercoagulability disorder?

A. Prothrombin gene defect G20210 A
B. Protein C deficiency
C. Protein S deficiency
D. Factor V Leiden

3. What blood product listed does not carry the risk of HIV and hepatitis B or C?

A. Whole blood
B. Albumin
C. Platelets
D. Fresh frozen plasma

4. What drug can be used to treat bleeding with transurethral prostate resection?

A. Hirudin
B. Ancrod
C. Aminocaproic acid
D. Urokinase

5. A 45-year-old male with the diagnosis of antithrombin III deficiency develops a DVT. What do you have to administer to the patient prior to starting heparin?

A. Cryoprecipitate
B. Platelets
C. Fresh frozen plasma
D. DDAVP

6. A 55-year-old male was placed on a heparin drip for a lower extremity DVT. Three days later he had a platelet count of 52,000 (decreased from 180,000). You suspect heparin-induced thrombocytopenia (HIT). What antibody has he developed?

A. IgG PF4 Ab
B. IgM PF4 Ab
C. IgG PAF Ab
D. IgM PAF Ab

7. All of the following are relative contraindications to thrombolytic therapy except:

A. Pregnancy
B. Recent surgery (<10 days)
C. Recent trauma
D. Recent CVA (<2 months)
E. Liver disease

8. A 36-year-old female is 32 weeks pregnant and has been diagnosed with a lower extremity DVT. The treatment that is absolutely contraindicated is:

A. IV heparin only
B. Arixtra (fondaparinux)
C. Fragmin (dalteparin)
D. IV heparin transitioned to Coumadin
E. Lovenox (enoxaparin)

9. This class of antibiotics can induce a platelet disorder:

A. Fluoroquinolones
B. Cephalosporins
C. Carbapenems
D. Aminoglycosides

10. Of the following scenarios, which patient has indication for an IVC filter?

A. A 36-year-old male who has a recurrent DVT while on Coumadin with an INR 1.5
B. A 42-year-old female with an upper extremity DVT
C. A 28-year-old female who is 27 weeks pregnant
D. A 67-year-old male with a PE while on therapeutic Coumadin
E. A 50-year-old male who has factor V Leiden

11. Heparin is cleared by the:

A. Liver
B. Endothelium
C. Proteinase enzymes in the blood
D. Reticuloendothelial system

12. What is the mechanism of action of clopidogrel (Plavix)?

A. Inhibits platelet aggregation
B. Activates antithrombin III
C. ADP receptor antagonist
D. Inhibits cAMP phosphodiesterase

13. What is the mechanism of action of heparin?

A. Inhibits platelet aggregation
B. Activates antithrombin III
C. ADP receptor antagonist
D. Inhibits cAMP phosphodiesterase

14. What is the mechanism of action of cilostazol (Pletal)?

A. Inhibits platelet aggregation
B. Activates antithrombin III
C. ADP receptor antagonist
D. Inhibits cAMP phosphodiesterase

15. In relation to the hemoglobin-oxygen dissociation curve, how is stored blood hemoglobin affected by the affinity of oxygen?

A. It has low 2,3-DPG; therefore, the curve shifts left, increasing its affinity to oxygen
B. It has low 2,3-DPG; therefore, the curve shifts right, decreasing its affinity to oxygen
C. It has high 2,3-DPG; therefore, the curve shifts left, increasing its affinity to oxygen
D. It has high 2,3-DPG; therefore, the curve shifts right, decreasing its affinity to oxygen

ANSWERS

1. **Answer: C.** When there is disruption at the endothelium causing bleeding, the first step in hemostasis is vasoconstriction followed by the adherence of platelets to the injured site by the link of glycoprotein receptor 1b (platelet surface) to the vessel wall by circulation vWF. This expresses the surface receptor glycoprotein IIb/IIIa on the platelet. Platelets aggregate, forming a platelet plug, and this is followed ultimately by fibrin formation.
2. **Answer: D.** Factor V Leiden (resistance to activated protein C) is reportedly present in 20% to 60% of cases of venous thrombosis. It is present in 1% to 2% of the population. Compared to other hypercoagulable disorders, it is of lower risk in forming thrombus and more likely the thrombus will be venous rather than arterial.
3. **Answer: B.** Albumin carries the theoretical risk of Creutzfeldt-Jakob disease.
4. **Answer: C.** Aminocaproic acid is a lysine analogue that inhibits fibrinolysis. It competitively binds to the lysine-binding sites of a fibrin clot, blocking the binding of plasminogen.
5. **Answer: C.** Fresh frozen plasma is needed to be administered with patients who are antithrombin III deficient so that the mechanism of heparin (i.e., activating antithrombin III, thereby inactivating factor Xa and thrombin) is effective.
6. **Answer: A.** HIT develops when the body forms antibodies, usually IgG, against heparin when it is bound to platelet factor 4 protein. With HIT, both arterial and venous thromboses can form.
7. **Answer: D.** Absolute contraindications to thrombolytic therapy include active internal bleeding, recent CVA (<2 months), and intracranial pathology.
8. **Answer: D.** Coumadin is teratogenic and crosses the placenta.
9. **Answer: B.** Penicillins and cephalosporins can bind platelets and increase bleeding time.
10. **Answer: D.** Indications for an IVC filter include patients who have a contraindication to anticoagulation; a pulmonary embolus while on therapeutic anticoagulation; free-floating iliofemoral, IVC or femoral DVT; and patients who have had a pulmonary embolectomy.
11. **Answer: D.** Heparin is cleared by the reticuloendothelial system.
12. **Answer: C.** Clopidogrel is an ADP receptor antagonist.
13. **Answer: B.** Heparin activates antithrombin III.
14. **Answer: A.** Cilostazol inhibits platelet aggregation.
15. **Answer: A.** Stored blood is low in 2,3-DPG; therefore, the hemoglobin–oxygen dissociation curve shifts to the left, increasing hemoglobin affinity to oxygen.

CHAPTER 3

Transplant and Immunology

Patty T. Liu

Test Taking Tips

Topics related to transplant are usually memorization-based and make up a very small percentage.

Quickly review the mechanism of action and side effects of transplant medications and the types of rejection the night before the test.

INTERLEUKINS

Name the cells of origin and functions of the following interleukins:

Interleukin-1
- Mononuclear phagocytes, T and B cells, NK cells, fibroblasts, neutrophils, smooth muscle cells
- Proliferation of T and B cells; fever, inflammation; endothelial cell activation; increases liver protein synthesis

Interleukin-2
- Activated T cells
- T-cell growth factor, cytotoxic T-cell generation; B-cell proliferation/differentiation; growth/activation of NK cells

Interleukin-4
- CD4+ T cells, mast cells
- B-cell activation/differentiation, T- and mast-cell growth factor

Interleukin-5
- T cells
- Eosinophil proliferation/activation

Interleukin-6
- Mononuclear phagocytes, T cells, endothelial cells
- B-cell proliferation/differentiation; T-cell activation; increases liver acute-phase reactants; fever, inflammation

Interleukin-8
- Lymphocytes, monocytes, multiple other cell types
- Stimulates granulocyte activity, chemotactic activity; potent angiogenic factor

Interleukin-10
- Mononuclear phagocyte, T cells
- B-cell activation/differentiation, inhibition, mononuclear phagocytes

Interleukin-12
- Mononuclear phagocytes, dendritic cells
- IFN-γ synthesis, T-cell cytolytic function, CD4+ T-cell differentiation

INTERFERONS AND OTHER CHEMOKINES

What cells produce interferon-γ and what are its functions?
- NK and T cells
- Increases expression of class I and class II MHC, activates macrophages and endothelial cells, augments NK activity, antiviral

What cells produce interferon-α and β and what are their functions?
- Mononuclear phagocyte-α; fibroblast-β
- Mononuclear phagocyte increases class I MHC expression, antiviral, NK-cell activation

What cells produce tumor necrosis factor-α and β and what are their functions?
- NK and T cells, mononuclear phagocyte
- B-cell growth/differentiation, enhance T-cell function, macrophage activator, neutrophil activator

What cells produce transforming growth factor-β and what are its functions?
- T cells, mononuclear phagocyte
- T-cell inhibition

What cells produce lymphotoxin and what are its functions?
- T cells
- Neutrophil activator, endothelial activation

IMMUNOSUPPRESSANTS

What was the first effective clinical immunosuppressive maintenance regimen for the transplantation of solid organs? (It was introduced in 1962.)
Azathioprine and corticosteroids

What 2 commercially available polyclonal lymphocyte-depleting agents are used for induction therapy?
Horse anti-thymocyte globulin; rabbit anti-thymocyte globulin (most commonly used)

What is OKT3?
A very potent murine monoclonal antibody that binds to CD3, a site associated with the TCR, that blocks cell-mediated cytotoxicity by inhibiting the function of naive T cells and established cytotoxic lymphocytes. Approved for use in 1985 for steroid-resistant rejection of kidney, liver, and heart transplants, but withdrawn from market in 2010 due to availability of other treatments with similar efficacy and fewer side effects.

What may be seen with the first or second dose of OKT3?
Acute cytokine release syndrome; avoid with concomitant administration of steroids or indomethacin

What 2 monoclonal antibodies block the IL-2 receptor to prevent rejection and became available in 1998?
Basiliximab (Simulect) – chimeric murine-human antibody mainly used for induction therapy in liver and kidney transplant

Table 3-1 Summary of the Main Immunosuppressive Drugs

Drug	Mechanism of Action	Adverse Effects	Clinical Uses	Dosage
Cyclosporine (CSA)	Binds to cyclophilin	Nephrotoxicity	Improved bioavailability of microemulsion form	PO 8–10 mg/kg/d (given in 2 divided doses)
	Inhibits calcineurin and IL-2 synthesis	Tremor		
	Undergoes hepatic metabolism and biliary excretion	Hypertension Hirsutism	Used as mainstay of maintenance protocols	
		Gingival hyperplasia		
Tacrolimus (FK506)	Binds to FKBP	Nephrotoxicity	Improved patient and graft survival in (liver) primary and rescue therapy	PO 0.15–0.3 mg/kg/d (given in 2 divided doses)
	Inhibits calcineurin and IL-2 synthesis	Hypertension		IV 0.05–0.1 mg/kg/d
		Neurotoxicity (tremors, headache)		
		GI toxicity (nausea, diarrhea) Diabetogenic	Used as mainstay of maintenance, like CSA	
Mycophenolate mofetil	Antimetabolite	Leukopenia	Effective for primary and rescue therapy (kidney transplants)	PO 1 g bid
	Inhibits enzyme necessary for de novo purine synthesis	GI toxicity (diarrhea)	Has replaced azathioprine	
Sirolimus	Inhibits lymphocyte effects driven by IL-2 receptor via mTOR pathway	Thrombocytopenia	May allow early withdrawal of steroids and decreased calcineurin doses	PO 2–4 mg/d, adjusted to trough drug levels
		Increased cholesterol and triglycerides		
		Impaired wound healing		
Corticosteroids	Multiple actions	Cushingoid state	Used in induction, maintenance, and treatment of acute rejection	Varies from mg to several grams per day
	Anti-inflammatory	Glucose intolerance		Maintenance doses, 5–10 mg/d
	Inhibits lymphokine production	Osteoporosis		
Azathioprine	Antimetabolite	Myelosuppression (thrombocytopenia, neutropenia, anemia)	Used as alternate agent to mycophenolate in maintenance protocols or during pregnancy	PO 1–3 mg/kg/d for maintenance
	Interferes with DNA and RNA synthesis by inhibiting de novo purine synthesis	GI toxicity (N/V, diarrhea)		
		Liver dysfunction		

FKBP, FK506-binding protein; IL, interleukin; mTOR, mammalian Target of Rapamycin.

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Daclizumab (Zenapax) – humanized antibody, withdrawn from market in 2009 for prevention of transplant rejection

What is rituximab?
An anti-CD20 monoclonal antibody; CD20 is a surface molecule expressed on B cells

What is alemtuzumab?
A humanized anti-CD52 monoclonal antibody (Campath 1H) that can be used for induction therapy or to treat acute rejection

What are the antiinflammatory effects of glucocorticoids?
Inhibition of cytokine gene transcription in macrophages; inhibition of cytokine secretion (IL-1, IL-6, TNF); suppression of the production and effect of T-cell cytokines; inhibition of the ability of macrophages to respond to lymphocyte-derived signals (migration inhibition factor, macrophage activation factor); suppression of prostaglandin synthesis

RENAL TRANSPLANT

What are the indications for kidney transplant?
Irreversible renal failure from diabetes; hypertension; glomerulonephritis; cystic kidney disease; and to lesser extent: autoimmune diseases such as lupus, IgA nephropathy, and Goodpasture syndrome; congenital renal dysplasia; hereditary diseases such as Fabry disease and Alport syndrome

Define the stages of chronic kidney disease (CKD) and at what stage(s) patients are referred for transplant:
Stage 1: GFR >90 mL/min
Stage 2: GFR 60 to 89 mL/min
Stage 3: GFR 30 to 59 mL/min
Stage 4: GFR 15 to 29 mL/min
Stage 5: GFR <15 mL/min
Refer CKD stage 4 and 5 patients for transplant

What is the most common reason for kidney transplant?
Diabetes (35%)

What are the 3 anastomoses of a heterotopic kidney transplant?
Renal artery to iliac artery; renal vein to iliac vein; ureter to bladder

If the choice of a left or right donor kidney is available, which one is preferred and why?
The left kidney; longer renal vein allows for an easier anastomosis

Why is the external iliac artery preferred over the internal iliac artery for vascular anastomosis during a renal transplantation?
The external iliac artery requires less dissection and there is less of a chance for anastomotic narrowing over the internal iliac artery

What complications can arise if accessory renal arteries are ligated instead of reconstructed in a donor kidney?
Renal infarcts/necrosis; ureteral necrosis; urinary fistula formation

What is the expected time period for return of normal renal function after renal transplantation?
Living donor 3 to 5 days; cadaveric 7 to 15 days

What drug is used routinely by most centers for prophylaxis against urinary tract infections and *Pneumocystis jiroveci* (*carinii*)?
Trimethoprim-sulfamethoxazole

What is the most common cause of sudden cessation of urinary output in the immediate postoperative period following a renal transplant?
The presence of a blood clot in the bladder or urethral catheter; can be relieved by irrigation

How is the definitive diagnosis of a primary infection with polyomavirus (type BK) made in a patient with a kidney transplant?
Allograft biopsy to demonstrate nuclear inclusions in tubular epithelial cells using special staining and the absence of rejection or drug toxicity

What is the mainstay of treatment of posttransplant lymphoproliferative disorder (PTLD)?
Decreasing the level of immunosuppression

REJECTION AFTER RENAL TRANSPLANT

What kind of rejection results from preformed antibodies against the donor organ characterized by the transplanted kidney turning blue within minutes of revascularization?
Hyperacute rejection

When does acute cellular rejection after renal transplantation occur?
The first few weeks to months after transplantation and occasionally years later

What is the red flag that indicates rejection following renal transplantation?
Increasing creatinine

What are the classic signs and symptoms of acute cellular rejection after renal transplantation?
Malaise, fever, oliguria, hypertension, tenderness and swelling over the allograft, elevated creatinine

When does chronic allograft nephropathy occur?
Often after years of stable function; may be accelerated in allografts that have had multiple or incompletely treated episodes of acute rejection

GRAFT AND PATIENT SURVIVAL AND COMPLICATION RATES

What is the 1-year graft survival for a living donor kidney compared to a standard-criteria cadaveric kidney?
98% for a living donor kidney; 93% for a standard-criteria cadaveric kidney

What is the 5-year graft survival for a living donor kidney compared to a standard-criteria cadaveric kidney?
85% for a living donor kidney; 75% for a standard-criteria cadaveric kidney

Table 3-2 Causes of Increased Serum Creatinine Early after Kidney Transplant

Cause	Characteristics	Diagnosis	Treatment
Hypovolemia	• Decreased CVP • Decreasing urine output • Low blood pressure • Low Hgb if due to bleeding	• Check Hgb and CVP	• Rehydrate with appropriate fluids
Vascular thrombosis	• Sudden drop in urine output • Dark hematuria • Tender, swollen graft	• Ultrasound with Doppler	• Re-explore for thrombectomy or nephrectomy
Bladder outlet obstruction	• Clots in urinary catheter • Sudden drop in urine output	• Distended bladder on examination or by ultrasound	• Irrigate or change bladder catheter —
Ureter obstruction	—	• Euvolemic • Ultrasound showing hydroureter • Possible lymphocele on ultrasound	• Do percutaneous nephrostogram • Drainage of lymphocele (if it is the cause of ureter obstruction)
Drug toxicity	• High CSA or FK506 level	• Check drug levels	• Decrease dosage of drugs
Acute rejection	• May have risk factors such as low drug levels, high PRA	• Kidney biopsy	• Administer bolus steroid or antilymphocyte treatment • Begin plasmapheresis (and IVIG if humoral rejection)

CSA, cyclosporin A; CVP, central venous pressure; Hgb, hemoglobin; IVIG, intravenous immunoglobulin; PRA, panel reactive antibody.
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What is the 1-year patient survival rate after a living donor kidney transplant compared to a standard-criteria cadaveric kidney transplant?
99% for a living donor kidney transplant; 96% for a standard-criteria cadaveric kidney transplant

What is the 5-year patient survival rate after a living donor kidney transplant compared to a standard-criteria cadaveric kidney transplant?
92% for a living donor kidney transplant; 85% for a standard-criteria cadaveric kidney transplant

LIVER TRANSPLANT

What is the most frequent vascular complication with liver transplantation?
Hepatic artery thrombosis; can manifest as rapid or indolent worsening of graft function or as necrosis of the bile duct and dehiscence of the biliary-enteric anastomosis

What is the treatment for a post-op bile leak seen in a patient after liver transplantation?
Stenting of the anastomosis by ERCP. Surgical exploration and revision of the anastomosis if suspect complete disruption or experiencing peritonitis; if leak secondary to ischemic bile duct injury as a result of early hepatic artery thrombosis, treatment is urgent retransplantation.

What is the MELD score?
Model for End-stage Liver Disease is the formula currently used to assign points for prioritizing position on the waiting list for cadaveric liver transplant; MELD is based on INR, bilirubin, and creatinine, with extra points for the presence of liver cancer

What 3 laboratory values is the MELD score based on?
Total bilirubin; international normalized ratio; creatinine

What are the indications for a liver transplant?
Liver failure from noncholestatic cirrhosis (hepatitis B, hepatitis C, alcoholic, cryptogenic); cholestatic cirrhosis (primary biliary cirrhosis, primary sclerosing cholangitis, Caroli disease, and biliary atresia); fulminant liver failure; Budd-Chiari; inborn errors of metabolism; malignant tumors (hepatocellular carcinoma)

How is the liver transplant placed (orthotopic or heterotopic)?
Orthotopic

What are the options for biliary drainage for liver transplantation?
Donor common bile duct to recipient common bile duct end-to-end; Roux-en-Y choledochojejunostomy

What is chronic liver rejection called?
Vanishing bile duct syndrome

What are the red flags indicating rejection of a liver transplant?
Increased serum bilirubin, LFTs, and alkaline phosphatase

Where is the site of rejection with a liver transplant?
The biliary epithelium is involved with rejection first, followed by the vascular endothelium

True or False: Renal function in a patient with hepatorenal syndrome does not improve after liver transplantation.
False; renal function improves in patients with hepatorenal syndrome after liver transplantation

What must be excluded on imaging on initial workup in all liver transplant candidates?
Extrahepatic metastases; macrovascular invasion of the liver

Hepatic portoenterostomy is otherwise known as:
The Kasai procedure

What are indications for liver transplantation in a patient with biliary atresia?
Failure of the Kasai procedure; failure to thrive; recurrent cholangitis; typical signs of end-stage liver disease

What are the components of the Child-Turcotte-Pugh score?
Encephalopathy, ascites, total bilirubin, INR, serum albumin

PANCREAS TRANPLANT

What are the indications for pancreas transplant?
Type 1 diabetes associated with renal failure or frequent severe episodes of hypoglycemic unawareness

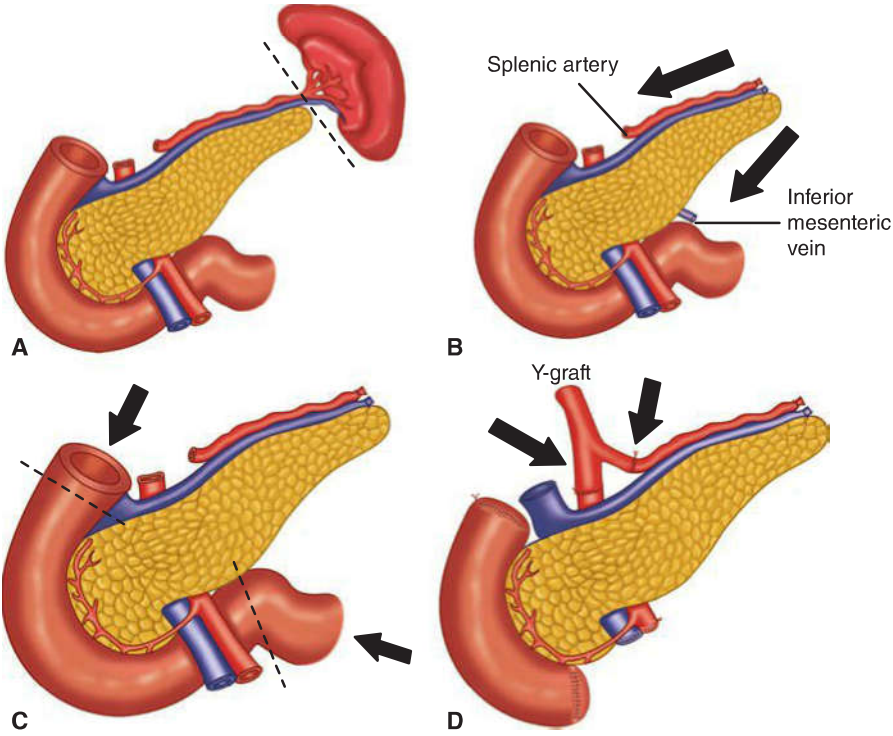

FIGURE 3-1. Bench preparation of pancreas graft. Steps include the following: (A) removal of the spleen; (B) removal of tissue along the superior and inferior aspect of the tail of the pancreas; (C) trimming of excess duodenum; and (D) ligation of vessels at the root of the mesentery and placement of arterial Y-graft. *(Reproduced with permission from Brunicardi FC, Andersen DK, Billiar TR, et al: Schwartz's Principles of Surgery, 9th ed. New York, NY: McGraw Hill; 2010.)*

What are the options for exocrine drainage of pancreas transplant?
Enteric/bowel drainage and bladder drainage

What is the associated electrolyte complication with a bladder-drained pancreas transplant?
Loss of bicarbonate

Where is the anastomosis of the exocrine duct with an enteric-drained pancreas transplant?
To the jejunum; the advantage is that endocrine function drains from the portal vein directly to the liver and pancreatic contents stay within the GI tract (no need to replace bicarbonate)

What are the options for venous drainage of pancreas transplant?
Systemic – donor portal vein to recipient iliac vein
Portal – donor portal vein to recipient SMV

What are the red flags indicating rejection of a pancreas transplant?
Graft tenderness, elevated serum amylase and lipase, decreased urinary amylase in bladder-drained pancreas transplant

Why should a kidney and pancreas be transplanted together if possible?
Can diagnose rejection earlier because elevated serum creatinine is a better indicator of rejection; better survival of graft associated with kidney-pancreas than pancreas alone

Why is hyperglycemia not a good indicator for rejection surveillance?
Appears relatively late with pancreatic rejection

If a combined kidney-pancreas transplant is performed, which organ is usually transplanted first?
The pancreas is usually transplanted first to minimize ischemia time for the pancreas

What is the most commonly used transplant site for pancreatic islet transplantation?
The liver (via portal vein embolization)

HEART TRANSPLANT

What are the indications for heart transplant?
Age birth to 65 years with terminal acquired heart disease class IV of the New York Heart Association classification (inability to do any physical activity without discomfort = 10% of surviving 6 months)

What are contraindications for heart transplant?
Active infection; poor pulmonary function; increased pulmonary artery resistance

What are the red flags of rejection of a heart transplant?
Fever, hypotension or hypertension, increased T4/T8 ratio

What are the tests for rejection of a heart transplant?
Endomyocardial biopsy

LUNG TRANSPLANT

What are the indications for lung transplant?
Disease that substantially limits activities of daily living and is likely to result in death within 12 to 18 months: pulmonary fibrosis, COPD, eosinophilic granuloma, primary pulmonary HTN, Eisenmenger syndrome, cystic fibrosis

What are the contraindications for lung transplant?
Current smoking; active infection

What are the donor requirements for lung transplant?
55 years of age or younger; clear CXR, PA oxygen tension = 300 on 100% oxygen and 5 cm PEEP; no purulent secretions on bronchoscopy

What are the necessary anastomoses in a lung transplant?
Anastomoses of the bronchi, pulmonary artery, and pulmonary veins; bronchial artery is not necessary

What are the postoperative complications following lung transplantation?
Bronchial necrosis/stricture; reperfusion injury; pulmonary edema; rejection

What are the red flags of rejection for a lung transplant?
Decreased arterial oxygen tension; fever; increased fatigability, infiltrate on x-ray

What is chronic lung rejection called?
Obliterative bronchiolitis

INTESTINAL TRANSPLANT

What are the transplant anastomoses in an intestinal transplantation?
Donor SMA to recipient aorta; donor SMV to recipient portal vein

What is the most common indication for intestinal transplant?
Inability to sustain successful TPN because of lack of IV access sites or severe complications from chronic TPN (liver failure)

Name another common immunologic problem other than rejection following intestinal transplantation.
Graft-versus-host disease from large lymphoid tissue in transplanted intestines

What is the most common cause of death after small bowel transplantation?
Sepsis and multiorgan failure

How is rejection surveillance conducted on transplanted intestine?
Endoscopic biopsies

What is the largest lymphoid organ in the human body?
The intestine

POTPOURRI

What is the leading cause of chronic rejection and subsequent graft loss?
Inadequately treated acute rejection

What is the primary cause of late renal allograft loss?
Chronic rejection

What is the most common cause of renal failure in African Americans?
Hypertensive nephrosclerosis

How long is the projected extension in life in a patient with a kidney transplant compared to the same patient on dialysis?
10 years

What are the 3 most common causes of renal failure treated by kidney transplantation?
Diabetes mellitus (37%); hypertension (22%); glomerular diseases (14%)

Absolute contraindication to transplantation.
Infection or malignancy that cannot be eradicated

After the successful treatment of cancer, what is the usual required time period without evidence of disease before transplantation?
2 years

What GFR is required before a patient can become eligible to be listed for a cadaveric kidney?
GFR $<$20 mL/min

What does a positive cross-match signify?
The presence of donor-reactive antibodies, detected by incubation of recipient serum with donor lymphocyte cells in the presence of complement; thus the cross-match is incompatible and the transplant should not proceed

What does a high panel-reactive antibody signify?
A lower likelihood of being cross-match-compatible with a donor

What is the most common cancer after transplantation?
Squamous cell skin cancer

MULTIPLE CHOICE QUESTIONS

1. **Pancreatic transplantation is considered a lifesaving procedure in which of the following patients?**
   A. 32-year-old female on dialysis secondary to diabetic nephropathy
   B. 46-year-old male with high insulin requirements to maintain normoglycemia
   C. 37-year-old female with episodes of severe hypoglycemic unawareness
   D. 21-year-old female with brittle diabetes

2. **Which virus is associated with PTLD?**
   A. EBV
   B. HSV
   C. RSV
   D. HIV

3. **Which of the following is a complication of calcineurin inhibitors that is LESS pronounced in sirolimus?**
   A. Hyperlipidemia
   B. Thrombocytopenia
   C. Rash
   D. Nephrotoxicity

4. **If a patient has tertiary hyperparathyroidism, when should he or she undergo total parathyroidectomy with autotransplantation?**
   A. In 3 months if moderate hypercalcemia persists
   B. In 12 months if hypercalcemia and elevated PTH levels persist
   C. In 6 months if PTH levels are twice normal
   D. Immediately after transplant if PTH levels are greater than normal

5. **Which of the following are the most common indications for liver transplantation in adults and children, respectively?**
   A. Autoimmune hepatitis and inborn errors of metabolism
   B. Malignant neoplasms and biliary atresia
   C. Cholestatic cirrhosis and viral hepatitis
   D. Noncholestatic cirrhosis and biliary atresia

6. **In the Child-Turcotte-Pugh score, which of the following would be assigned the highest point value in a patient with cryptogenic cirrhosis?**
   A. INR—2.2
   B. Ascites—moderate
   C. Albumin—2.7
   D. Encephalopathy—none

7. Which of the following is the active component of azathioprine?

A. 12-mercaptoprimer
B. 3-mercaptopurine
C. 6-mercaptopyrimidine
D. 6-mercaptopurine

8. In a patient who has recently undergone a cadaveric renal transplant, which of the following is a correct pairing between a virus and the appropriate medication to treat it?

A. HSV—ritonavir
B. CMV—ganciclovir
C. EBV—lamivudine
D. CMV—acyclovir

9. What is the number-one cause of early mortality after lung transplantation?

A. Pneumonia
B. Acute rejection
C. Bronchopleural fistula
D. Reperfusion injury

10. Which of the following regarding secondary complications of diabetes and pancreas transplantation is FALSE?

A. Diabetic retinopathy can stabilize after pancreas transplantation
B. Vascular disease can stabilize after pancreas transplantation
C. Diabetic neuropathy can improve after pancreas transplantation.
D. Pancreas transplantation can prevent recurrence of diabetic nephropathy in renal allograft

11. What is the number-one risk factor for primary nonfunction after liver transplantation?

A. Macrosteatosis
B. Microsteatosis
C. Cold ischemia time
D. Donor age

12. All of the following statements regarding cross-matches for kidney transplantation are true EXCEPT

A. Cross-match is performed by mixing donor lymphocytes with recipient serum
B. A positive cross-match is an absolute contraindication to kidney transplantation
C. Cross-match is done prior to kidney transplantation to prevent graft loss from hyperacute rejection
D. A positive cross-match means the donor and recipient are compatible

13. Which of the following impairs wound healing the MOST?

A. Tacrolimus
B. Mycophenolate
C. Sirolimus
D. Prednisone

14. You just completed a living donor kidney transplant and are called to the recovery room because your patient stopped making urine. What is the NEXT best step?

A. Irrigate Foley catheter
B. Give bolus of fluid
C. Obtain ultrasound of the transplant kidney
D. Take patient back to operating room for re-exploration

15. Which of the following patients with hepatocellular carcinoma could be considered a candidate for liver transplant based on imaging?

A. A single tumor in the left lobe, 5.5 cm in diameter
B. Two tumors, both in right lobe, 3.5 cm and 2.5 cm in diameter
C. Three tumors, 1 in right and 2 in left lobe, 2.5 cm, 2.8 cm, and 1.0 cm in diameter
D. None of the above

16. Which of the following is the best measure of the liver's synthetic function?

A. Albumin
B. Bilirubin
C. INR
D. AST and ALT

17. Which medication is paired incorrectly with the corresponding side effect?

A. Tacrolimus – tremor
B. Mycophenolate – leukopenia
C. Cyclosporine – hirsutism
D. Azathioprine – diabetogenic

ANSWERS

1. **Answer: C.** 37-year-old female with episodes of severe hypoglycemic unawareness. Over time, patients with multiple episodes of hypoglycemia may not experience typical symptoms. Therefore, hypoglycemia can become severe, resulting in neurologic injury.
2. **Answer: A.** EBV. Immunosuppression allows B cells that are infected with EBV to proliferate.
3. **Answer: D.** Nephrotoxicity. Sirolimus can be used for immunosuppression in patients with renal transplants if there is evidence of calcineurin inhibitor–induced nephropathy on biopsies.
4. **Answer: B.** In 12 months if hypercalcemia and elevated PTH levels persist. A diagnosis of tertiary hyperparathyroidism warrants surgical correction so that consequences (osteomalacia and renal osteodystrophy) of the disease do not ensue.
5. **Answer: D.** Noncholestatic cirrhosis (65%) in adults—includes viral hepatitis (B and C), alcoholic and cryptogenic cirrhosis; biliary atresia (58%) in children.

Although the diseases listed are the most common indications for liver transplants, there are many others. They include:

- Cholestatic liver disease/cirrhosis (e.g., primary biliary cirrhosis, primary sclerosing cholangitis, Caroli disease, and biliary atresia)