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CLINICAL CASES OF PHYSIOLOGY AND PATHOPHYSIOLOGY
PART 2

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SECTION BLOOD
MCQs STEP 1

1. A 48-year old woman suffering from a severe tension headache is brought to the Emergency Department after her husband discovered her unresponsive and barely breathing when he stopped at home from work during his lunch hour. A bottle of Vicodin was found next to the bathroom sink. Which of the following arterial blood gases are most consistent with her clinical presentation?
A. pH = 7.27; PaCO2 = 60 mmHg, [HCO3–] = 26 mEq/L, Anion Gap = 12 mEq/L b.
B. pH = 7.02; PaCO2 = 60 mmHg, [HCO3–] = 15 mEq/L, Anion Gap = 12 mEq/L
C. pH = 7.10; PaCO2 = 20 mmHg, [HCO3–] = 6 mEq/L, Anion Gap = 30 mEq/L d.
D. pH = 7.51; PaCO2 = 49 mmHg, [HCO3–] = 38 mEq/L, Anion Gap = 14 mEq/L e.
E. pH = 7.40; PaCO2 = 20 mmHg, [HCO3–] = 10 mEq/L, Anion Gap = 26 mEq/L
2. A 27-year-old patient with insulin-dependent diabetes mellitus told his roommate that he could not afford to refill his insulin prescription until he got a paycheck. The roommate offered to get it for him, but the patient assured him he could wait until after the weekend. When the roommate returned from a weekend trip on Sunday evening, he found the man unresponsive on the couch, and called 9-1-1. Which of the following arterial blood gases taken in the Emergency Department would be expected in diabetic coma?
A. pH = 7.22; PaCO2 = 60 mmHg, [HCO3–] = 26 mEq/L, Anion Gap = 12 mEq/L
B. pH = 7.02; PaCO2 = 60 mmHg, [HCO3–] = 15 mEq/L, Anion Gap = 12 mEq/L
C. pH = 7.10; PaCO2 = 20 mmHg, [HCO3–] = 6 mEq/L, Anion Gap = 30 mEq/L
D. pH = 7.51; PaCO2 = 49 mmHg, [HCO3–] = 38 mEq/L, Anion Gap = 14 mEq/L
E. pH = 7.40; PaCO2 = 20 mmHg, [HCO3–] = 10 mEq/L, Anion Gap = 26 mEq/L
3. A 5-year-old Egyptian boy receives a sulfonamide antibiotic as prophylaxis for recurrent urinary tract infections. Although he was previously healthy and well-nourished, he becomes progressively ill and presents to your office with pallor and irritability. A blood count shows that he is severely anemic with jaundice due to hemolysis of red blood cells. Which of the following is the simplest test for diagnosis?
A. Northern blotting of red blood cell mRNA
B. Enzyme assay of red blood cell hemolysate
C. Western blotting of red blood cell hemolysates
D. Amplification of red blood cell DNA and hybridization with allele-specific oligonucleotides (PCR-ASOs)
E. Southern blot analysis for gene deletions
4. A 2-day-old neonate becomes lethargic and uninterested in breastfeeding. Physical examination reveals hypotonia (low muscle tone), muscle twitching that suggests

seizures, and tachypnea (rapid breathing). The child has a normal heartbeat and breath sounds with no indication of cardiorespiratory disease. Initial blood chemistry values include normal glucose, sodium, potassium, chloride, and bicarbonate (HCO3–) levels; initial blood gas values reveal a pH of 7.53, partial pressure of oxygen (Po2) normal at 103 mmHg, and partial pressure of carbon dioxide (Pco2) decreased at 27 mmHg. Which of the following treatment strategies is most appropriate?

A. Administer alkali to treat metabolic acidosis

B. Administer alkali to treat respiratory acidosis

C. Decrease the respiratory rate to treat metabolic acidosis

D. Decrease the respiratory rate to treat respiratory alkalosis

E. Administer acid to treat metabolic alkalosis

5. A 45-year-old woman presents with increasing fatigue, weakness, and tingling of her arms and legs. Physical examination finds numbness and loss of balance, position, and vibratory sense in both of her lower extremities. Histologic examination of a smear made from a bone marrow aspiration reveals asynchrony in red blood cell precursors between the maturation of their nuclei and their cytoplasm. Additional workup discovers achlorhydria, and a biopsy of the antrum of her stomach reveals chronic atrophic gastritis. Which of the following is the most likely diagnosis?

A. Fanconi anemia

B. Leukoerythroblastic anemia

C. Megaloblastic anemia

D. Myelophthisic anemia

E. Sideroblastic anemia

6. A 1-year-old child recently emigrated from Africa exhibits intermittent diarrhea, pallor (pale skin), extreme tenderness of the bones, “rosary” of lumps along the ribs, nose bleeds, bruising over the eyelids, and blood in the urine. Which of the following is the most likely cause?

A. Deficiency of vitamin C due to a citrus-poor diet during pregnancy

B. Hypervitaminosis A due to ingestion of beef liver during pregnancy

C. Deficiency of vitamin C because of reliance on a milk only diet

D. Deficiency of vitamin K because of neonatal deficiency and continued poor nutrition

E. Deficiency of vitamin D due to darker skin pigmentation and poor sun exposure

7. A 61-year-old male presents to his family physician with the chief complaint of frequent diarrhea accompanied by weight loss. He reports a tendency to bruise easily and laboratory data reveal a prothrombin time of 19 seconds (normal = 11–14 seconds). The bruising and prolonged prothrombin time can be explained by a decrease in which of the following vitamins?

A. Vitamin A

B. Vitamin C
C. Vitamin D
D. Vitamin E
E. Vitamin K

8. A 66-year-old man presents for his annual physical examination. He is asymptomatic and physical examination is unremarkable. Examination of his peripheral smear, however, reveals the presence of small mononuclear cells with little cytoplasm and a mature nucleus with a prominent nuclear cleft. No "smudge cells" are seen. The presence of these "buttock cells" in the peripheral blood warrants further clinical workup to search for which one of the following malignancies?
A. Chronic lymphocytic leukemia
B. Follicular non-Hodgkin's lymphoma
C. Multiple myeloma
D. Nodular sclerosis Hodgkin's disease
E. Small-cell carcinoma of the lungs

9. A 42-year-old patient with a rare blood type is scheduled for surgery that will likely require a transfusion. Because the patient has a rare blood type, an autologous blood transfusion is planned. Prior to surgery, 1500 mL of blood is collected. The collection tubes contain calcium citrate, which prevents coagulation by which of the following actions?
A. Blocking thrombin
B. Binding factor XII c
C. Binding vitamin K
D. Chelating calcium
E. Activating plasminogen

10. A 65-year-old man presents with increasing fatigue and shortness of breath. Examination of his peripheral blood finds pancytopenia, and a few (less than 5%) immature cells are present. Some of the neutrophils are bilobed (Pelger-Huët change) and a dimorphic red blood cell population is seen. A bone marrow biopsy reveals a hypercellular marrow with about 15% of the cells being immature cells. Approximately 20% of the red cell precursors have iron deposits that encircled the nucleus. Which of the following is the most likely cause of these clinical findings?
A. Chronic blood loss
B. Iron deficiency
C. Lead poisoning
D. Myelodysplasia
E. Vitamin B12 deficiency

11. A 23-year-old woman complains of abdominal cramps and bloating that are relieved by defecation. Subsequent clinical evaluation reveals an increased maximal

acid output, decreased serum calcium and iron concentrations, and microcytic anemia. Inflammation in which area of the GI tract best explains these findings?
A. Stomach
B. Duodenum
C. Jejunum
D. Ileum
E. Colon
12. An anxious 19-year-old woman presents with perioral numbness and carpopedal spasm. Laboratory examination reveals decreased PCO2 and decreased bicarbonate. Which of the following is the most likely diagnosis?
A. Metabolic acidosis due to ketoacidosis
B. Metabolic acidosis due to renal tubular acidosis
C. Metabolic alkalosis due to thiazide diuretic
D. Respiratory acidosis due to hypoventilation
E. Respiratory alkalosis due to hyperventilation
13. A group of students in the Wilderness Medicine Club left for a Spring Break Rocky Mountain hiking trip right after their Organ Systems exam. They arrived at their lodge in Denver by 2 p.m. Mountain time, and then drove to the base camp (10,000 ft), where they camped for the night. The next day, several of the students were experiencing mental and muscle fatigue, and complained of headaches, nausea, and dyspnea, so the guide decided to acclimate at 10,000 ft. for another day. Three of the students grew impatient and announced that they were going to climb to Mt. Elbert, the highest mountain in Colorado (14,400 ft altitude, barometric pressure = 447 mmHg). About 3 hours later (less than 24 hours since they first arrived in Denver), one of the students returned in a panic to get medical help because his friends were disoriented, ataxic, short of breath, and vomiting. The guide called for the search and rescue helicopter, which located the hikers and took them to the nearest Emergency Department. A diagnostic work-up would likely show a decrease in which of the following values?
A. pH
B. $PaCO_2$
C. Pulmonary vascular resistance
D. 2,3-Bisphosphoglycerate
E. Erythropoietin
14. An adult male becomes hypotensive during surgery because of blood loss. Intravenous administration of 500 ml of which of the following solutions will have the greatest effect in restoring blood volume, and thus blood pressure to normal?
A. blood plasma
B. distilled water
C. hypoosmotic NaCl

D. isotonic dextrose solution
E. isotonic saline solution
15. Using laboratory micropuncture technique, blood plasma is collected from both the afferent arteriole and efferent arteriole of a renal cortical glomerulus. Which of the following has the lowest afferent/efferent arteriole concentration ratio?
A. albumin
B. chloride
C. glucose
D. potassium
E. sodium
16. The terminal ileum was removed from a 50year-old woman during excision of a tumor. About 3 years later, the patient was admitted to the hospital. She is very pale. Hemoglobin is 9 g/dL, MCV (mean corpuscular volume) has increased to 110 μm3 (110 fL). The provisional diagnosis is a vitamin deficiency. Which of the following vitamins is the most likely one causing the symptoms?
A. A
B. B1
C. B6
D. B12
E. K
17. Normal metabolism by the body generates large quantities of acid. In spite of this, normal blood pH is a slightly alkaline 7.4. This extracellular fluid alkalinity is maintained primarily by the body's removal of which of these?
A. Ammonia
B. Carbon dioxide
C. Keto acids such a acetoacetic acid
D. Lactic acid
E. Titratable acids such as phosphoric acid
18. You are the primary care physician for a young female college student. She has been engaged over the past 3 months in a vigorous aerobic exercise training regime that includes a significant amount of running in a hot environment. You measure her hematocrit as part of a general physical examination. Her hematocrit could well be abnormal even though she is not anemic. Which of the following choices best fits this profile?

	Total circulating erythrocyte mass	Total plasma volume	Hematocrit
(A)	Decreased	Decreased	Decreased
(B)	Increased	Decreased	Decreased
(C)	Increased	Decreased	Increased
(D)	Unchanged	Decreased	Decreased
(E)	Unchanged	Increased	Decreased

19. A patient is found to be deficient in folate. This patient is anemic, and a complete blood count indicates that the MCV is 105 fL(normal range: 80–96) and the MCHC is 34 g/dL (normal range: 32–36). The anemia is thus macrocytic, normochromic. In this patient how would you predict that the MCH (mean corpuscular hemoglobin) would compare with the normal range?

A. MCH would be elevated with respect to the normal range

B. MCH would be depressed with respect to the normal range

C. MCH would be within the normal range

D. this cannot be determined based on the information provided

20. Which of the following conditions would likely be associated with decreased levels of circulating EPO?

A. Chronic alkalosis

B. Chronic renal failure

C. Emphysema

D. Pernicious anemia

E. Pulmonary fibrosis

21. The patient is a 43-year-old male. He is anemic, with a hemoglobin level of 12.2 g/dL(normal is 15.5 g/dL). The erythrocytes are microcytic (MCV = 70 fL, with normal MCV = 80–100 fL). Which of the following would most likely be present in this patient?

A. Acute bleeding

B. Folate deficiency

C. Iron deficiency

D. Vitamin B12 deficiency

E. Vitamin K deficiency

22. Heparin is a rapidly acting, potent anticoagulant that has many important clinical uses. Which of the following is an action of heparin?

A. Activates prothrombin

B. Acts with antithrombin to inhibit thrombin activity

C. Decreases prothrombin time

D. Inhibits calcium action

E. Promotes vitamin k activity

23. Worldwide, one of the most common parasitic infections is schistosomiasis. Assume a complete blood cell count is performed in a patient with this condition. Which of the following blood cells would most likely be present in elevated amounts?
A. Eosinophils
B. Erythrocytes
C. Monocytes
D. Neutrophils
E. Platelets
24. Recovery from a severe metabolic acidosis is most dependent on which of the following?
A. The rate of ventilation to blow off excess CO_2
B. The rate of H+ secretion by the kidney
C. The rate of H+ excretion by the kidney
D. The arterial pH
E. The arterial PCO_2
25. After a rapid ascent to very high altitude, one begins to hyperventilate because of hypoxic drive. The hyperventilation will cause a decrease in the arterial PCO2. What is the renal response to this condition?
A. Increased rate of acid excretion
B. Decreased rate of acid excretion
C. Increased rate of bicarbonate reabsorption
D. Diuresis to eliminate excess fluid
E. Increased ammoniagenesis
26. A 21-year-old man with gastroenteritis developed severe vomiting with a loss of stomach acids. A metabolic alkalosis is present. Which of the following is most likely to occur?
A. The plasma bicarbonate concentration will decrease.
B. H+ will move from the plasma into the cells.
C. Peripheral chemoreceptors will stimulate pulmonary ventilation.
D. Renal H+ excretion will decrease.

ANSWERS MCQs STEP 1

1. The answer is A. Narcotics used for the treatment of severe headache may depress the medullary respiratory center causing alveolar hypoventilation, as evidenced by an elevation in arterial Paco2. The hypercapnia lowers the ratio of HCO3– to dissolved CO2 in the plasma, and thus lowers the pH according to the Henderson-Hasselbalch equation. Renal compensation for respiratory acidosis takes hours to start and days to be complete, and thus there has not been sufficient time for the body's compensatory mechanisms to take effect and for plasma [HCO3–] to rise. Thus, the scenario is most consistent with an acute, uncompensated respiratory acidosis. The slight rise in plasma bicarbonate concentration can be attributed to extracellular buffering of the excess H+.

2. The answer is C. Diabetic ketoacidosis generates a partially compensated metabolic acidosis. The primary disturbance is a decrease in the plasma [HCO3–], which lowers the ratio of HCO3– to dissolved CO2 in the plasma, and thus lowers the pH according to the Henderson-Hasselbalch equation. To compensate for the metabolic acidosis, the lungs increase the rate of alveolar ventilation, which decreases PaCO2 and thus dissolved CO2 and returns the pH toward the normal range. The differential diagnosis of metabolic acidosis is divided into high anion gap and normal anion gap (hyperchloremic) acidosis. The increased anion gap of 30 mEq/L compared to a normal value of ~12 mEq/L is consistent with an increase in ketoacids, that is, acetoacetic acid and β-hydroxybutyric acid, in the diabetic patient.

3. The answer is B. Red cell hemolysis after drug exposure suggests a red cell enzyme defect, most easily confirmed by enzyme assay to demonstrate deficient activity. A likely diagnosis here is glucose-6-phosphate dehydrogenase (G6PD) deficiency (305900), probably the most common genetic disease (it affects 400 million people worldwide). Tropical African and Mediterranean peoples exhibit the highest prevalence because the disease, like sickle cell trait, confers resistance to malaria. DNA analysis is available to demonstrate particular alleles, but simple enzyme assay is sufficient for diagnosis. More than 400 types of abnormal G6PD alleles have been described, meaning that most affected individuals are compound heterozygotes. The phenotype of jaundice and red blood cell hemolysis with anemia is triggered by a variety of infections and drugs, including a dietary substance in fava beans. Sulfonamide and related antibiotics as well as antimalarial drugs are notorious for inducing hemolysis in G6PD-deficient individuals. G6PD deficiency exhibits X-linked recessive inheritance, explaining why male offspring but not the parents become ill when exposed to antimalarials.

4. The answer is D. Brain injury or metabolic diseases that irritate the respiratory center may cause tachypnea in term infants, resulting in respiratory alkalosis. The increased respiratory rate removes ("blows off") carbon dioxide from the lung alveoli and lowers blood CO2, forcing a shift in the indicated equilibrium toward the left:

$CO_2 + H_2O \Delta H_2CO_2 \Delta H^+ + HCO_3^-$

Carbonic acid (H_2CO_2) can be ignored because negligible amounts are present at physiologic pH, leaving the equilibrium:

$CO_2 + H_2O \Delta H^+ + HCO_3^-$

The leftward shift to replenish the exhaled CO_2 of rapid breathing decreases the hydrogen ion concentration [H^+] and increases the pH ($-\log_{10}[H^+]$) to produce alkalosis (blood pH above the physiologic norm of 7.4). Other answers are eliminated because the newborn does not have acidosis, defined as a blood pH below 7.4, either from excess blood acids (metabolic acidosis) or from slower or ineffective respiration with increased [CO_2] (respiratory acidosis). The baby also does not have metabolic alkalosis, caused by loss of hydrogen ion from the kidney (e.g., with renal tubular disease) or stomach (e.g., with severe vomiting). Respiratory alkalosis is best treated by eliminating the underlying disease which will diminish the respiratory rate, elevate blood [CO_2], force the above equilibrium to the right, elevate the [H^+], and decrease the pH. The infant would prove to have a urea cycle disorder such as citrullinemia (215700) with neurologic effects (hypotonia, seizures) of high ammonia concentrations. Withdrawal of milk (protein) and other therapies decreased the ammonia, eliminated the seizures, and restored normal respiration.

5. The answer is C. The combination of clinical signs suggesting damage to both the posterior spinal cord (such as loss of vibratory and position sense) and the lateral spinal cord (such as arm and leg dystaxia and spastic paralysis) are suggestive of subacute degeneration of the spinal cord, a disorder that results from a deficiency of vitamin B12. Loss of vibratory sensation in the lower extremities is the first neurologic manifestation of this disease. These neurologic abnormalities of B12 deficiency do not occur with folate deficiency . They are thought to be the result of abnormal myelin production due to either excess methionine or abnormal fatty acid production (fatty acids with an odd number of carbons), such as propionate. There are many different causes of vitamin B12 deficiency, which also results in a megaloblastic anemia. Examples include inadequate diet, impaired absorption, bacterial overgrowth, or competitive parasitic infections. Dietary deficiencies will take years to produce deficiency states since liver stores are so great (recall that vitamin B12 is the only water soluble vitamin that is stored in the body). Dietary deficiency is seen only in strict vegetarians (diet with no animal proteins, milk, or eggs). Normally dietary B12 binds to salivary R-binders, forming a B12-R complex that is broken down by pancreatic proteases. Free B12 then binds to intrinsic factor (IF is secreted by gastric parietal cells) and the B12-IF complex is absorbed by ileal mucosal epithelial cells. B12 is then transported in blood bound to transcobalamin II. Impaired absorption occurs with deficiency of intrinsic factor (patients with pernicious anemia or gastrectomy) or malabsorptive states that involve the ileum (such as celiac disease, Crohn's disease, or

chronic pancreatitis). Pernicious anemia, an autoimmune disease, is the most common cause of vitamin B12 deficiency. Chronic pancreatitis is associated with B12 deficiency because pancreatic enzymes are necessary to enzymatically cleave the R factor from B12 in the duodenum before IF can attach to B12. Bacterial overgrowth occurs in the blind-loop syndrome or with broad-spectrum antibiotic therapy, while a competitive parasitic infection is the giant fish tapeworm, Diphyllobothrium latum. In contrast, Fanconi anemia is an autosomal recessive disorder characterized by bone marrow failure combined with certain birth defects, such as abnormalities of the radius. Leukoerythroblastic anemia refers to any space occupying lesion of the bone marrow (myelophthisic anemia) that causes immature red blood cells and immature white blood cells to appear in the peripheral blood. Finally sideroblastic anemia is characterized by the presence of numerous sideroblasts in the bone marrow and may be caused by a deficiency of pyridoxine or it may be a form of myelodysplasia.

6. The answer is C. Prolonged vitamin C deficiency (scurvy) usually occurs with severe malnutrition (famine, prisoners of war, alcoholism, extreme food fadism). Exclusive feeding of cow's milk, as may occur in areas of famine with poor supplies of maternal milk, can result in infantile scurvy with the symptoms described in the question. X-rays of the limbs are helpful in diagnosing scurvy, with a white line at the metaphysis and occasional subperiosteal hemorrhage. These radiologic features may be seen in copper deficiency associated with hyperalimentation, emphasizing the role of ascorbic acid (vitamin C) as a coenzyme for proline/lysine hydroxylases that modify collagen and also require copper. The causes of hemorrhagic disease of the newborn are desribed in the previous answer, and vitamin K deficiency is almost never seen after the newborn period because of wide dietary availability. Deficiencies of the fatsoluble vitamins A, E, and D can occur with intestinal malabsorption, but avid fetal uptake during pregnancy usually prevents infantile symptoms. Vitamin D deficiency (rickets) can also cause a series of rib lumps (rosary) and is more likely with darker skin pigmentation but has other symptoms. Hypervitaminosis A can cause liver toxicity but not bleeding, and deficiency of vitamin E can be associated with anemia in prematures but is unknown in older children and adults.

7. The answer is E. Vitamin K is a fat-soluble vitamin produced by intestinal bacteria that is essential for maintaining normal clotting of blood. The vitamin is essential for hepatic synthesis of prothrombin and factors VII, IX, and X. Common causes of vitamin K deficiency include cholestasis, and factors that limit fat absorption.

8. The answer is B. Some of the non-Hodgkin's lymphomas are associated with involvement of the peripheral blood (leukemic phase). More than half of the patients with small lymphocytic lymphoma (SLL) have involvement of the bone marrow with spillage of neoplastic cells into the peripheral blood, where they appear as mature lymphocytes, many of which are smudged. The clinical picture is then similar to that

of chronic lymphocytic leukemia (CLL). Follicular NHLs also commonly involve the bone marrow, but spillage into the peripheral blood is much less common than in SLL. Still, when the malignant small cleaved lymphocytes, which are also called centrocytes, are found within the peripheral blood, they have a characteristic cleaved appearance that is described as "buttock cells." Lymphoblastic lymphoma is another type of lymphoma that frequently involves the bone marrow and peripheral blood. The clinical picture then is similar to that of T-cell acute lymphoblastic leukemia (ALL). In contrast, multiple myeloma and Hodgkin's disease do not have malignant cells in the peripheral blood.

9. The answer is D. The citrate ion has three anionic carboxylate groups that avidly chelate calcium and reduce the concentration of free calcium in blood. Because free calcium (Ca^{2+}) is required for multiple steps in both coagulation pathways, citrate is a useful anticoagulant in vitro. The citrate ion is rapidly metabolized; thus, blood anticoagulated with citrate can be infused into the body without untoward effects. Oxalate, another calcium-chelating anticoagulant, is toxic to cells.

10. The answer is D. The myelodysplastic syndromes (MDS) are a group of disorders characterized by defective hematopoietic maturation and an increased risk of developing acute leukemia. These disorders characteristically have hypercellular bone marrows but pancytopenia in the peripheral blood. The two basic types of MDS are an idiopathic (primary) form and a therapy-related (secondary) form. Both have numerous dysplastic features affecting all blood cell lines. Red cell dysplastic features include the presence of ringed sideroblasts, megaloblastoid erythroid precursors, and misshapen erythroid precursors. A dimorphic population of red cells may be seen in the peripheral blood of some patients with some types of MDS. White cell dysplastic features include hypogranular cells or Pelger-Huët white blood cells, which are abnormal appearing neutrophils having only two nuclear lobes. Megakaryocytes may be abnormal and have only a single nuclear lobe or multiple separate nuclei, so-called "pawn ball" megakaryocytes. Chromosomal abnormalities are commonly associated with the MDSs, especially 5q_ and trisomy 8. Except for chronic myelomonocytic leukemia (CMML), which is characterized by a marked increase in the number of monocytes, the MDSs are subclassified by the number of blasts present within the bone marrow. The FAB classification of MDS is as follows: if there are less than 5% blasts present, the MDS is either refractory anemia (RA) or RA with ring sideroblasts (RARS). RA with excess blasts (RAEB, pronounced "rab") has between 5 and 20% blasts, while refractory anemia with excess blasts in transformation (RAEBIT, pronounced "rabbit") has between 20 and 30% blasts in the marrow. Acute leukemia is defined as the presence of more than 30% blasts in the marrow. The WHO (World Health Organization) has a similar classification of the MDS except that in their

classification the number of blasts in the bone marrow needed for the diagnosis of acute leukemia is only 20%.

11. The answer is B. Inflammation of the duodenum may lead to increased acid output, hypocalcemia, and microcytic anemia. Increased basal and maximal acid outputs may result from excessive stimulation of the parietal cell (e.g., hypergastrinemia) or reduced inhibitory feedback (i.e., reduced effect of enterogastrone and the enterogastric reflex). The latter may occur when the proximal small intestine is inflamed. Although calcium is absorbed along the entire length of the small intestine, it is absorbed primarily in the duodenum. Similarly, iron is absorbed primarily in the duodenum. Microcytic anemia is the result of reduced stores of iron, the most common anemia. Glucose-6-phosphatase deficiency is the most common metabolic disorder of red blood cells, and is also associated with a microcytic anemia, as is a-thalassemia

12. The answer is E. Respiratory alkalosis results from an increase in the respiratory rate that decreases blood CO2 (hypocapnia) and results in decreased arterial [H+] and [HCO3−]. The body tries to compensate for the increased pH through renal mechanisms, namely, decreased H+excretion and decreased reabsorption of HCO3−. Note that there is also no respiratory compensation for respiratory alkalosis. Causes of respiratory alkalosis include diseases or states that cause hypoxemia (such as living at high altitude), psychogenic causes, and ingestion of salicylates (which can cause a mixed respiratory alkalosis and metabolic acidosis). Respiratory acidosis is caused by a decrease in the respiratory rate, which increases blood CO2 (hypercapnia) and results in increased arterial [H+] and [HCO3−]. The body tries to compensate for the decreased Ph through renal mechanisms, namely, increased H+ excretion (through titratable H+) and increased reabsorption of HCO3−. Note that there is no respiratory compensation for respiratory acidosis. Causes of respiratory acidosis include substances that inhibit the medullary respiratory center (such as opiates, sedatives, and anesthetics), impairment of the respiratory muscles (due to neurologic diseases such as multiple sclerosis), airway obstruction, and other pulmonary diseases, such as ARDS and COPD.

13. The answer is B. Hypoxemia at high altitude stimulates the peripheral chemoreceptors to increase ventilation, causing arterial Pco2 to decrease and arterial pH to ris (respiratory alkalosis). Tissue hypoxia also stimulates erythropoietin production, which increases the number of red blood cells and the hemoglobin concentration, which increases arterial oxygen content, and thus tissue oxygen delivery. Hypoxia also increases the concentration of 2,3-bisphosphoglycerate, which decreases hemoglobin's affinity for oxygen, thereby increasing oxygen release to the tissues. Alveolar hypoxia constricts the pulmonary vessels at high altitude causing an increase in pulmonary vascular resistance and pulmonary artery pressure (pulmonary hypertension).

14. The answer is A. Intravenous solutions are distributed in the various body fluid compartments based on osmolality and their ability to penetrate the vascular wall and the cell membrane. The proteins in blood plasma will remain within the vascular compartment because of their low permeability across the vessel wall. Thus, 500 mL of blood plasma will remain in the vascular compartment. Water (choice B) passes across the cell membrane and the vascular wall easily. Hence distilled water will distribute itself between cellular and extracellular spaces, meaning only a small portion will actually contribute to blood volume, the other choices (C, D, and E) cross the vascular barrier and distribute partially to the extravascular space and thus are less effective intravascular volume expanders.

15. The answer is A. The process of glomerular ultrafiltration creates a tubular fluid that is essentially protein free. Hence, as plasma passes from the afferent arteriole, through the glomerular capillaries to the efferent arteriole, the protein albumin concentration rises as approximately 20% of the fluid is filtered out, leaving the albumin behind, giving an afferent/efferent arteriole concentration ratio of approximately 0.8. By contrast, the glomerular capillary membrane is freely permeable to water and other small particles such as glucose (choice A), chloride (choice B), potassium (choice D), and sodium (choice E), so their concentrations do not change

16. The answer is D. Deficiency of vitamin B12 results in hematological, neurological, and GI effects. The hematologic symptoms include a low red blood cell count with large-sized macrocyticred blood cells as described. Absorption of vitamin B12 is relatively complicated. The large and not very lipophilic molecule is released from food by the low pH of the stomach and pepsin digestion and binds to R protein (also called haptocorin). Pancreatic proteases digest these complexes and the liberated cobalamin (vitamin B12) now complexes with an intrinsic factor (which is produced by gastric parietal cells) and is absorbed as such in the terminal ileum. Hence, vitamin B12 absorption will be low in this patient. Liver storage is thought to be sufficient for 3–6 years so that the 3-year latency of the anemia further supports a vitamin B12 deficiency. The water-soluble vitamins B1 and B6 (choices B and C) are absorbed in the duodenum by simple diffusion. Absorption of the lipid-soluble vitamins Aand K (choices Aand E) is supported by bile-acid mixed micelles, although vitamin A and vitamin K3do not heavily rely on bile acids and can also enter the enterocytes by simple diffusion. Additionally, of the stated choices, only vitamin B12 deficiency is associated with anemia.

17. The answer is B. The vast majority of metabolic acid excretion is in the form of the volatile acid carbon dioxide which is removed via the lungs. Much smaller quantities of nonvolatile acids must be excreted in the urine. Titratable acids, such as phosphoric acid (choice E), make up a large fraction of the acids normally excreted in the urine. When stored fats are metabolized in large quantities, such as in diabetes

mellitus, keto acids such as acetoacetic acid (choice C) make up a larger portion of the renal excreted titratable acids. Likewise, when the ischemic tissues pursue anaerobic metabolism, lactic acid (choice D) makes up a larger portion of the renal excreted titratable acids. Ammonia (choice A) is not a titratable acid, but it provides a mechanism for the kidney to excrete large amounts of acid during chronic metabolic acidosis.

18. The answer is E. The central points of this question concern the definitions of hematocrit and anemia. Hematocrit is the proportion of blood that is packed cells. The hematocrit reading will be decreased by anything that lowers the number of cells, as well as by anything that increases the volume of plasma. Anemia refers to a condition in which the total circulating erythrocyte mass has decreased. In this student, a long-term regime of exercise in a warm environment has chronically increased her plasma volume, hence her hematocrit is low. However, since her total red blood cell mass is normal, there is no anemia. Choice E is correct. It is common to see a chronic increase in plasma volume develop in response to long-term exercise in a warm environment. Exercising in a warm environment places demands on the circulatory system, which must perfuse working muscles as well as skin capillary beds (to facilitate heat loss). In addition, volume is lost to sweating. Increased plasma volume helps the body meet these demands. In choice A, hematocrit could be low if erythrocyte mass decreased more than blood volume. However, this profile does not fit the question because this individual would be anemic, since erythrocyte mass is low. Choice B could not be correct since decreased plasma volume and increased red cell mass cause increased hematocrit. In choice C, the patient would not be anemic and hematocrit would be increased. However, this is not the best response since, as described above, in an individual exercising in a warm environment the hematocrit is often decreased and plasma volume is usually increased. In choice D, hematocrit would have to be increased.

19. The answer is A. These red blood cells are large (macrocytic) but have a normal hemoglobin concentration (normal MCH). Since MCH is mean hemoglobin content per red cell, this value must be elevated since the cells are large and the concentration in the cell is normal. Choice A excludes choices B–D.

20. The answer is B. EPO is a glycoprotein produced primarily in the kidney, thus EPO levels tend to be depressed in chronic renal failure. EPO is a growth factor that stimulates the production of red blood cells. Its production by the kidney is triggered by low tissue oxygenation. Any condition that decreases the oxygen-carrying capacity of the blood (such as anemia, choice D) or that causes hypoxia by decreasing lung function (such as emphysema or pulmonary fibrosis, choices C and E) will produce elevated levels of circulating EPO. Alkalosis (choice A) increases hemoglobin's affinity for oxygen, making it more difficult for tissues to extract oxygen from the

blood. In alkalosis, tissues thus tend to have lower oxygen content, with a resultant increase in circulating EPO levels.

21. The answer is C. Microcytic anemia can often be associated with defective hemoglobin synthesis. In the case of iron deficiency, heme synthesis is impaired due to the lack of iron. Acute bleeding (choice A) is normally associated with erythrocytes of normal size, since the anemia is due to simple loss of blood, with plasma expansion to maintain total volume. Both vitamin B12 and folate (choices B and D) are required for DNA synthesis. Due to the extremely active cell division required to sustain the erythrocyte pool, impaired DNA synthesis first normally manifests as a lack of erythrocyte production. Anemia due to vitamin B12 or folate deficiency is macrocytic. Vitamin K (choice E) is required for synthesis of several clotting factors. Lack of vitamin K often presents as a problem with coagulation.

22. The answer is B. Thrombin is a critical enzyme in the coagulation cascade. It not only can activate factors VIII and V, it also acts on fibrinogen to form fibrin. Thrombin is essential for clot formation. Antithrombin III modulates the coagulation cascade, serving to inhibit thrombin activity. Heparin acts as an anticoagulant because it accelerates the action of antithrombin III. Heparin does not stimulate vitamin K activity (choice E) and, in any case, anything that promoted vitamin K activity would increase coaguability, since vitamin K is necessary for synthesis of multiple coagulation factors. Activation of prothrombin (choice A) promotes coagulation. Though calcium is an essential cofactor for coagulation, heparin does not act via calcium inhibition (choice D). Because heparin inhibits thrombin action, it would prolong prothrombin time (choice C).

23. The answer is A. Eosinophils normally constitute about 2% of all blood leukocytes. These cells are phagocytic and exhibit chemotaxis. Their primary role is in fighting parasitic infection. In schistosomiasis the eosinophil attaches to the immature parasite and, by releasing various cytotoxic compounds, is able to kill the parasite. Erythrocytes (choice B) are the most numerous blood cells. They are not leukocytes, but function in blood gas transport. Erythrocyte number would not be increased in schistosomiasis. Monocytes (choice C) are leukocytes found in the blood. They are immature cells which migrate to the tissues, where they mature into macrophages. These cells are very active in phagocytosis and play a prominent role in the inflammatory response. They are not, however, particularly important in parasitic infections. Neutrophils (choice D) are another type of leukocyte that, though essential to combat bacterial infections, are not particularly sensitive to parasitic challenge. Platelets (choice E) are not leukocytes. The platelet is a cell fragment that functions in hemostasis

24. The answer is C. The rate of recovery from a severe metabolic acidosis is most dependent on the rate of H+ excretion. Pulmonary compensation occurs rapidly;

however, it can only minimize the change in pH. Pulmonary compensation cannot restore the balance after a metabolic disturbance. Recovery necessitates the excretion of the entire acid load to the system. Renal acid excretion is limited by the availability of titratable acids and ammonia for ammonium ion formation from secreted H+. The primary adaptive response of the kidney to an acidosis is ammoniagenesis. Ammoniagenesis can augment the daily excretion of acids as much as threefold. When an equivalent amount of acid is excreted, acid–base balance will be restored.

25. The answer is B. The two most important drivers of renal bicarbonate reabsorption are CO2 and H+. The hyperventilation experienced at high altitude decreases the PCO2, which generates a respiratory alkalosis. Reducing both CO2 and H+ will decrease renal H+ secretion and thus bicarbonate reabsorption. The filtered bicarbonate load will exceed the rate of H+ secretion with a loss of excess bicarbonate in the urin

26. The answer is D. The loss of gastric (hydrochloric) acid leads to an increase in the plasma bicarbonate concentration and a metabolic alkalosis. The increase in the pH will depress peripheral chemoreceptors to slow ventilation and increase the PCO2 to compensate for the increased bicarbonate. The increase in PCO2 will bring the pH nearer to 7.4 and at the same time increase renal H+ secretion. Because there is an increased level of bicarbonate in the glomerular filtrate, there will be an increase in bicarbonate reabsorption. The rate of filtration will exceed the rate of H+ secretion, and there will be a continuous loss of bicarbonate. As the plasma bicarbonate falls, the pH will continue to approach the normal of 7.4 and the ventilatory rate will increase gradually. When all the excess bicarbonate has been excreted, the plasma bicarbonate and pH will have returned to normal with a normal respiratory rate.

CLINICAL CASES

1. A 21-year-old man with insulin-dependent diabetes presents to the emergency center with mental status changes, nausea, vomiting, abdominal pain, and rapid respirations. On examination, the patient is noted to be hypotensive, breathing rapidly (tachypneic), and febrile. A fruity odor is detected on his breath. A random blood sugar is significantly elevated at 600 mg/dL. The patient also has hyperkalemia, hypomagnesemia, and elevated serum ketones. An arterial blood gas reveals a metabolic acidosis. The patient is diagnosed with diabetic ketoacidosis (DKA) and is admitted to the intensive care unit for intravenous (IV) hydration, glucose control, and correction of metabolic abnormalities.

1.1 What is the response of the kidney to metabolic acidosis?

Response of the kidney to metabolic acidosis: Increased excretion of the excess fixed hydrogen as ammonia and increased reabsorption of bicarbonate

1.2 What is the response of the kidney to a respiratory alkalosis? What is the predicted compensatory response to metabolic acidosis?

Response of the kidney to respiratory alkalosis: Decreased hydrogen excretion and decreased bicarbonate absorption

Compensatory response to metabolic acidosis: Decrease in bicarbonate and in PCO2

2. A 14-year-old boy presents to his pediatrician with a laceration on his hand that has become badly infected. Upon questioning, the boy says he has felt fatigued for some time. Physical examination reveals pallor of the mucous membranes in addition to bleeding on the inside of his cheeks. Petechiae cover his body, and patches of purpura are present on his thighs, trunk, and arms. Relevant laboratory findings are as follows:

WBC count: 2000/mm3 (N 4,500- 1 l,OOO/mm3)

Hematocrit: 22% (N Male: 41-53% Female: 36- 46%)

Platelet count: 48,000/mm3 (N150,000- 400,000/mm3)

2.1 What is the most likely diagnosis?

Aplastic anemia results from bone marrow failure or autoimmune destruction of myeloid stem cells, which leads to pancytopenia. pancytopenia affects all cell lines, resulting in neutropenia, anemia, and thrombocytopenia, all of which are seen on a complete blood count.

2.2 What is the most likely cause of this patient's condition?

Most cases of aplastic anemia are idiopathic (autoimmune). Other possible causes include the following:

• Viral agents (eg, parvovirus B19, hepatitis viruses, HIV, epstein-Barr virus).

• Drugs and chemicals (eg, alkylating and antimetabolite agents, chloramphenicol, insecticides, arsenic, and benzene).

• Radiation.

• Immune disorders (eg, systemic lupus erythematosus, graft versus host disease).

• Pregnancy.
• Hereditary transmission (eg, Fanconi anemia). Note: the diagnosis is not aplastic anemia if tumor, fibrosis, or myelodysplasia are present.

2.3 What other test can help confirm the diagnosis?

Bone marrow biopsy reveals hypocellular bone marrow (< 30% cellularity) with a fatty infiltrate.

2.4 What is the appropriate treatment for this condition?

Initial treatment is to withdraw any possible toxic agent causing the condition. Supportive care, including antibiotics for infection and blood transfusion if symptoms develop, is also important. If testing reveals severe depression of one or several cell lines, definitive therapy, including stem cell transplantation or immunosuppression, is appropriate. If possible, transfusion should be avoided before bone marrow transplantation because of the risks of alloimmunization and graft rejection.

3. A 7-month-old Greek boy is brought to his pediatrician by his parents, who have noticed that the baby has been jaundiced and dyspneic for about 2 weeks. The mother denies any previous health problems with her son. Physical examination reveals tachycardia. Laboratory tests reveal a mean corpuscular volume of 60 fL and a reticulocyte count of 0.3%. The serum iron concentration is within normal limits.

3.1 What is the most likely diagnosis?

β-thalassemia major is the homozygous form of the genetically transmitted disease β-thalassemia, where the β-globin gene of hemoglobin is mutated, resulting in microcytic anemia. It is prevalent in Mediterranean populations. By contrast, in α-thalassemia, α-globin genes in hemoglobin are deleted; this condition is most commonly present in Southeast asians and blacks.

3.2 What mutations are present in α-thalassemia and in this condition?

Humans have two α-globin genes on chromosome 16, resulting in four alpha alleles. α-thalassemia results in four types of thalassemia, depending on the number of alpha allele deletions that occur. Increasing severity results from increasing numbers of deletions. these deletions result from unequal meiotic crossover between adjacent alpha genes. humans have one β-globin gene on chromosome 11, resulting in two beta alleles. In β-thalassemia, beta allele mutations, rather than deletions, occur. these mutations can occur in the promoter, exon, intron, or polyadenylation sites. Some mutations may produce no β-globin, whereas others may produce a small amount.

3.3 What are the symptoms and signs of this condition?

Symptoms of β-thalassemia major emerge after approximately 6 months of life and are due to the decline in γ-hemoglobin production without a rise in β-hemoglobin production. the early signs and symptoms include pallor, growth retardation, hepatosplenomegaly, and jaundice.

3.4 How is this condition diagnosed?

Definitive laboratory testing using gel electrophoresis is used for diagnosis, as it can distinguish mutated and normal forms of hemoglobin. an increased concentration of fetal haemoglobin (hbF) may also be seen on electrophoresis. Notably, an increase in hBa2 is seen in β-thalassemia minor.

3.5 What is the appropriate treatment for this condition?

β-thalassemia major causes severe anemia. hbF induction may be used. treatment with repeated blood transfusions may also be required. Subsequently, iron chelation for overload is important. Splenectomy may be necessary to treat the resulting hypersplenism. Stem cell transplantation may also be used in selected cases. β-thalassemia minor is usually asymptomatic and its treatment requires only avoidance of oxidative stressors of rBCs.

4. An 8-month-old boy is brought to the pediatrician by his foster parents for a checkup. They become concerned when he continues to bleed after the heel-stick. They report that during his circumcision, he seemed to bleed for an extended amount of time as well. Physical examination is significant for multiple bruises on the child's knees and elbows. Relevant laboratory findings include a platelet count of 250,000/ mm3, a normal bleeding time, a PT of 12 seconds, and a PTT of > 120 seconds.

4.1 What is the most likely diagnosis?

Hemophilia is due to deficiencies in the intrinsic coagulation pathway (factor VIII in hemophilia a and factor IX in hemophilia B). therefore, this disease is characterized by normal bleeding time, platelet count, and prothrombin time but an elevated PTT. Von Willebrand disease is the most common hereditary bleeding disorder. It is distinguished from hemophilia by its prolonged bleeding time and usually a modest prolongation of the ptt.

4.2 What are the variants of this condition?

Hemophilia a is due to a marked deficiency of factor VIII. Hemophilia B (Christmas disease) is due to a marked deficiency of factor IX. Hemophilia B is clinically indistinguishable from hemophilia A. However, Hemophilia A is 5–10 times more prevalent.

4.3 How is this condition inherited?

Both disease variants are X-linked recessive.

4.4 What are the possible complications of this condition?

Complications include deep and delayed bleeding into joints (hemarthrosis), muscles (hematoma), and the gastrointestinal tract. the most concerning complications are bleeds in the central nervous system and oropharynx. Mucosal or cutaneous bleeding is uncommon and more characteristic of platelet dysfunction or von Willebrand disease. Transmission of blood-borne infection (specifically hIV and hepatitis C) through transfusion has been significantly reduced through modern screening technology and recombinant factors.

4.5 What are the appropriate treatments for this condition?

Clotting factor concentrate replacements can be used to prevent bleeding and limit existing hemorrhage. Both monoclonal purified and recombinant factor VIII and IX exist. Fresh frozen plasma and whole blood transfusions are used in the acute setting (but they carry the risk of encouraging the development of inhibitor antibodies to factor VIII). In mild cases of hemophilia a, desmopressin transiently increases the factor VIII level.

5. A 66-year-old postmenopausal woman presents to her physician with complaints of fatigue, dyspnea, dizziness, and tachycardia. She says she craves chewing on ice cubes. Physical examination reveals pallor of the mucous membranes of her mouth. The cells on a PBS are microcytic and hypochromic. Relevant laboratory findings are as follows:
Hemoglobin: 11 g/dL (N Male: 13.5-17.5 g/dL Female: 12.0-16.0 g/dL)
Hematocrit: 30%
Reticulocyte count: 0.2% (N 0.5-1.5% of red cells)

5.1 What is the most likely diagnosis?

Iron deficiency anemia. This diagnosis would be supported by laboratory studies demonstrating a decreased iron concentration, increased total iron binding capacity, and decreased ferritin levels. The cause for a patient's iron deficiency, however, needs to be further pursued. In addition, comorbid inflammatory conditions can raise serum ferritin, resulting in values within the normal range.

5.2 What factors can lead to this condition?

Causes of iron deficiency anemia include the following: chronic blood loss (especially gastrointestinal blood loss secondary to colon cancer); dietary deficiency (increased demand or decreased absorption); intestinal hookworm infection (this is the most common cause worldwide and should be considered in patients who have immigrated from developing countries). In general, in a postmenopausal woman and all men, one must look for GI blood loss in any newly diagnosed patient with iron deficiency anemia unless the cause of the iron loss is obvious (nose bleeds, recent trauma, etc).

5.3 Why are total iron binding capacity (TIBC) measurements important in this condition?

TIBC is high in iron deficiency anemia and low in anemia of chronic disease. Both illnesses have decreased serum iron levels. a low ferritin (< 41 ng/mL) is sensitive and specific for iron deficiency anemia. The normal iron/TIBC ratio is typically 0.25–0.45, and levels < 0.12 indicate iron deficiency. Anemia of chronic disease often has a normal iron/TIBC ratio because of the concomitant decrease of TIBC and serum iron.

What other conditions is this patient at greatly increased risk for developing?

Because of the extreme lack of iron, this patient is at risk for Plummer-Vinson syndrome. This syndrome is characterized by atrophic glossitis, esophageal webs, and anemia.

5.5 What are the common causes of microcytic, hypochromic anemia?

Microcytic anemia results from either decreased hemoglobin production or faulty hemoglobin function. Common causes include iron deficiency, thalassemia, sideroblastic anemia, and lead poisoning.

6. During the course of an annual physical examination, a previously healthy 70-year-old man mentions recent weakness and rib pain. His appetite has been good, and he has not experienced fevers, nausea, vomiting, or changes in bowel habits. Physical examination reveals splenomegaly. Results of a complete blood count are as follows:

WBC count: 10,000/mm3

Hemoglobin: 22 g/dL

Hematocrit: 62%

Platelet count: 425,000/mm3

6.1 What is the most likely diagnosis?

Polycythemia vera, also known as primary erythrocytosis. This patient's elevated hemoglobin concentration is a sign of an increased rBC count. an increased rBC mass (> 32 mL/kg in women and > 36 mL/kg in men) is diagnostic of polycythemia vera absent of secondary causes. Polycythemia vera is one of the myeloproliferative syndromes, which also include essential thrombocytosis, CML, and myeloid metaplasia.

6.2 Levels of which hormone should be measured to establish the diagnosis?

Polycythemia vera may be primary or secondary in nature. Erythropoietin levels can help distinguish between the two. Erythropoietin levels will be decreased or normal in primary polycythemia (polycythemia vera). In secondary polycythemia, increased erythropoiesis results from increased erythropoietin stimulation (eg, erythropoietin-secreting tumor, hypoxemia, altitude, or erythropoietin receptor mutations).

6.3 Which two types of carcinoma are associated with this condition?

Renal cell carcinoma and hepatocellular carcinoma. In a healthy adult, the kidneys produce a majority of the body's erythropoietin, and the liver is a secondary source.

6.4 What is a myeloproliferative disorder?

It is a disorder in which there is clinical expansion of multipotent hematopoietic stem cells. Isolated cell lines may be affected; if megakaryocyte expansion occurs, an essential thrombocytosis is seen.

6.5 How can an uncorrected ventricular septal defect (VSD) lead to this condition?

In patients with uncorrected VSD, atrial septal defect, or patent ductus arteriosus, blood is shunted from the left side of the heart to the right side, which exposes the pulmonary vasculature to systemic blood pressures. Over time, the pulmonary vasculature adapts by increasing pulmonary resistance, and blood flow through the shunt is reversed to flow from right to left. this reversal of flow is known as Eisenmenger syndrome. Right-

to-left shunts cause hypoxemia and cyanosis, a potent stimulus for erythropoietin secretion and a cause of secondary polycythemia.

6.6 What are the appropriate treatments for this condition?

Phlebotomy can reduce the risk of blood clots in patients with polycythemia to that of the normal population. In high-risk patients (the elderly or those with a history of clots), hydroxyurea may be useful for controlling the hematocrit.

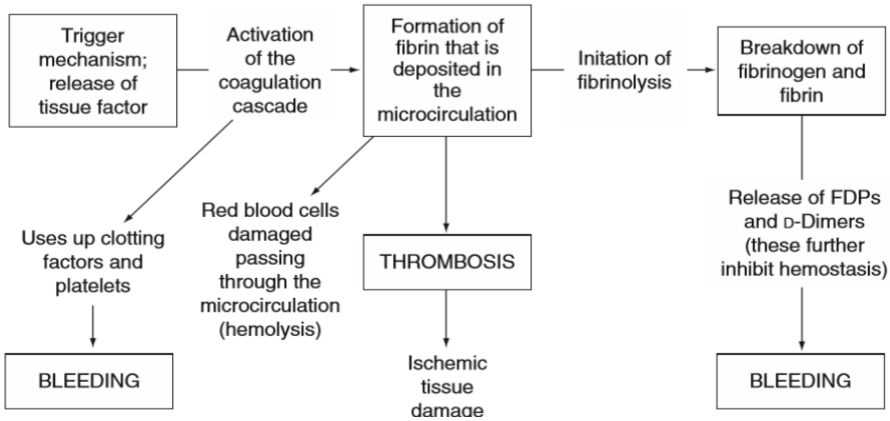
7. A 33-year-old African-American woman has been in the intensive care unit for 2 days after being admitted for treatment of a severe bacteremia. Her medical history is noncontributory. Physical examination reveals mucosal bleeding, oozing from intravenous access sites, and petechiae on her trunk and extremities. Laboratory tests reveal a prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT).

7.1 What is the most likely diagnosis?

Disseminated intravascular coagulation (DIC).

7.2 What is the pathophysiology of this condition?

DIC is a systemic process in which widespread activation of hemostasis causes thrombosis and hemorrhage. Systemic, rather than localized, clotting depletes coagulation factors.



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7.3 What are common possible causes of this condition?

Infectious causes include sepsis. Malignant causes include acute leukemia (especially acute myeloid leukemia) and other cancers (eg, prostate, causing a chronic DIC). Other causes include trauma, obstetric complications (eg, abruptio placentae, amniotic fluid embolism), and snake venom.

8. An 11-year-old girl is brought to her physician because of frequent epistaxis and “purple spots” on her body. She reports no recent history of trauma. Physical examination reveals petechiae and purpura on her arms, outer thighs, and legs. A PBS shows large platelets, but no helmet cells or schistocytes. Results of a Coombs test are positive. Relevant laboratory findings are as follows: Hemoglobin: 12.5 g/dL

Hematocrit: 36% WBC count: 5000/mm3 Platelet count: 11,000/mm3 Bleeding time: 12 minutes PT: 13 seconds PTT: 25 seconds

8.1 What is the most likely diagnosis?

Idiopathic thrombocytopenic purpura (ITP), a disease that is associated with antiplatelet antibodies, is the most likely diagnosis. The patient presents with isolated thrombocytopenia (normal WBC and hct), no coagulopathy, and given her age, ITP is the most common cause of thrombocytopenia.

8.2 What are the three main mechanisms of low platelet counts?

Thrombocytopenia may be caused by: splenic sequestration; decreased production (stem cell failure, leukemia, aplastic anemia, etOh, aspirin, clopidogrel); increased destruction (ITP, thrombotic thrombocytopenic purpura, heparin, quinidine).

8.3 What clinical findings are commonly associated with this condition?

ITP presents with mucous membrane bleeding, petechiae, and purpura. Epistaxis (nosebleed) and easy bruising are characteristic of bleeding disorders in general. ITP in childhood usually develops after a viral infection or immunization and is self-limited. Adult ITP, in contrast, is often a chronic disease.

8.4 What are the appropriate treatments for this condition?

First-line treatment is high-dose steroids. Second-line treatment includes intravenous IgG, anti-Rh, splenectomy, or rituximab (anti-CD20). Thrombopoietin receptor agonists (romiplostim) have been shown to be highly effective in raising platelets counts for long-term control, but long-term safety data and cost of therapy are limiting factors in using these modalities as first-line therapy. Acute bleeding in ITP is treated with intravenous IgG followed by platelets and pulse methylprednisolone.

SECTION RESPIRATORY SYSTEM
MCQs IFOM

1. A 95-year-old woman is transferred to the intensive care unit with a 3-day history of cough and declining mental status. Her temperature is 39.8°C (103.6°F), blood pressure is 85/50 mmHg, heart rate is 124/min, and respiratory rate is 27/min. Crackles are heard at the left lower lung base, and the patient is suffering from intermittent rigors. Blood and sputum cultures drawn at the onset of symptoms grow strains of *Klebsiella pneumoniae* that are only susceptible to an antibiotic whose mechanism of action is bactericidal against almost all gram-negative bacilli. This antibiotic acts like a detergent and binds bacterial cell membranes to increase their permeability.

Which of the following is an adverse effect of this antibiotic?

A.Granulocytopenia
B.Hearing loss
C.Hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency
D.Numbness of the extremities
E.Rhabdomyolysis

2. A 40-year-old woman undergoes a gastrectomy for gastric adenocarcinoma. Three days later, while recovering in the hospital, she experiences difficulty breathing. The operation was performed without complication. The patient has a 20-pack-year history of smoking and is taking daily broad-spectrum antibiotics, postoperatively. Her pulse is 115/min and respiratory rate is 30/min. Physical examination is significant for dullness to percussion over the right lung and decreased right breath sounds. Chest X-ray shows an elevated diaphragm on the right side as well as increased pulmonary lucency.

Which of the following is the most likely cause of this patient's symptoms?

A.Alveolar destruction
B.Decreased lung volume
C.Lung abscess
D.Lung metastasis
E.Pneumonia
F.Respiratory failure

3. A student researcher conducts a study regarding the occurrence of lung cancer in non-smoking subjects who reside with smokers. She determines that a non-smoking individual subjected to secondhand smoke at home for 10 years or more has a 50% chance of developing lung cancer. Which of the following is the probability that five randomly selected non-smoking individuals exposed to secondhand smoke for more than 10 years will all develop lung cancer?

A. 0.3%
B. 2.2%

C. 20%
D. 22%
E. 3%
F. 30%

4. 10-year-old boy is brought to his pediatrician by his mother because of uncontrolled asthma. The patient has been treated for asthma since he was 3 years old and is currently using fluticasone routinely and albuterol as needed. His only other medical problem is seasonal allergies, for which he takes fexofenadine once a day. For the past 2 weeks, he has needed to use his albuterol inhaler more than four times a day and has been having attacks that have awakened him up during the night. Temperature is 37° C (98.6° F), blood pressure is 116/72 mm Hg, pulse is 90/min, and respiratory rate is 24/min; oxygen saturation is 95% on room air. Physical examination reveals bilateral expiratory wheezes. After the patient is stabilized, the decision is made to start a long-acting beta agonist in addition to the boy's other medications.Which of the following best describes the mechanism of action of the patients new medication?

A.IgG monoclonal antibody against IgE
B.Inhibition of 5-lipoxygenase pathway
C.Inhibition of muscarinic receptors
D.Inhibition of myosin light-chain kinase
E.Inhibition of protein kinase A

5. A 31-year-old man comes to the emergency department and reports a cough that produces blood-stained mucus and shortness of breath. He also reports a 20-lb weight loss in the past month with fever, chills, blood in his urine, and generalized malaise. He denies any recent travel, tobacco use, or recreational drug use. The patient's temperature is 37.2°C (99.0°F), pulse is 90/min, respirations are 22/min, blood pressure is 112/72 mm Hg, and oxygen saturation is 96% on 2 L of oxygen. Findings from cardiac and abdominal examinations are unremarkable, but he does have intraseptal nasal ulcerations, and bilateral expiratory crackles are heard on auscultation. The patient's sputum culture is negative for acid-fast bacilli; serum blood work is positive for antineutrophil cytoplasmic autoantibodies (c-ANCA).
Which of the following would most likely be found in a renal biopsy specimen?

A. A split basement membrane
B.Necrotizing glomerulonephritis with crescent-shaped scars
C.Normal glomeruli with foot process effacement
D.Smooth linear staining on immunofluorescence
E.Wire-loop lesions with subepithelial deposits

6. A 32-year-old man with asthma is admitted to the hospital in status asthmaticus, and albuterol is administered continuously by means of a nebulizer. Four hours into his hospital course, this patient experiences acute respiratory failure; he is intubated and

transferred to the intensive care unit. After he has been receiving mechanical ventilation for 96 hours, the physician notes that this patient requires more ventilatory support and has developed a fever and purulent tracheobronchial secretions. X-ray of the chest reveals a right lower lobe infiltrate. Tracheobronchial aspiration yields a sample that is sent to the laboratory for analysis. Infection with which of the following organisms is most likely?

A. Candida albicans
B. Clostridium difficile
C. Legionella pneumophila
D. Pseudomonas aeruginosa
E. Staphylococcus epidermidis

7. A previously healthy 23-year-old man comes to the emergency department reporting right-sided chest pain that began abruptly 3 hours earlier. The patient describes the pain as a persistent stabbing sensation radiating to his right shoulder, which worsens on inspiration. He also reports an occasional cough for the past week. He had taken a 2-hour flight earlier in the day.

On physical examination, the patient is found to have a body mass index of 18.3. He is oriented to time and place but is in visible distress and looks anxious. His temperature is 36.5°C (97.7°F), blood pressure is 100/60 mm Hg, heart rate is 135, and respiratory rate is 25. Hyperresonance and decreased breath sounds are detected over the right lung field, and decreased tactile fremitus is noted. S1 and S2 are audible, and there is no jugular venous distention or tracheal deviation. The patient admits to a 7-pack-year history of smoking and has allergies to both pollen and bee stings.

Which of the following is the most likely diagnosis?

A. Asthma
B. Bronchitis
C. Emphysema
D. Pulmonary embolism
E. Spontaneous pneumothorax
F. Tension pneumothorax

8. A 37-year-old man presents to the emergency department because of severe shortness of breath, which started while he was cross-country skiing. He is active and otherwise healthy, with no significant medical history. The patient has never had an attack this severe before but says he often has similar symptoms while running or when he has a cold. Vital signs are a temperature of 97.7°F (36.5°C), blood pressure of 112/76 mm Hg, pulse of 82, respiratory rate of 22, and oxygen saturation of 93% on room air. Physical examination is significant for labored breathing with polyphonic wheezes in the lung fields bilaterally and a nasal polyp in the right nare. X-ray of the

chest shows hyperinflation without any evidence of consolidation or infiltrate.Which of the following agents would most likely precipitate a similar attack in this patient?

A. Acetaminophen
B. Aspirin
C. Captopril
D. Penicillin
E. Theophylline

9. A 48-year-old woman who is an immigrant from India comes for evaluation because of chronic cough, fatigue, and weight loss. For the past 2 months, she has been producing increasing amounts of non-foul-smelling, green-yellow sputum; she has also produced occasional blood-stained sputum. The patient denies any alcohol, drug, or cigarette use. Past medical history is noncontributory. Physical examination reveals a temperature of 38.7°C (101.7°F). The sputum is sent for microbiological diagnosis, and a chest X-ray shows a pleural effusion. Based on these results, the physician initiates treatment. At a follow-up appointment 1 month later, neurologic examination is significant for diminished sensation to light touch, pinprick, and vibration over the lower extremities bilaterally. Which of the following should administered to minimize the adverse symptoms of the patient's treatment?

A. Cobalamin
B. Pyrazinamide
C. Pyridoxine
D. Thiamine
E. Tocopherol

10. A 52-year-old woman comes for evaluation because of increasing shortness of breath with exertion over the past several years. The patient has a history of obesity, hypothyroidism, and well-controlled hypertension. She has no history of allergies/atopy and no recent respiratory infections. Her family history is significant for a father, who is living, with type 2 diabetes mellitus; her mother died of a myocardial infarction at age 63. The patient’s only medications are levothyroxine and lisinopril. Temperature is 36.7° C (98° F), blood pressure is 130/70 mm Hg, pulse is 88/min, and respiratory rate is 20/min; pulse oximetry on room air shows an oxygen saturation of 93%. She is 152.4 cm (5’) tall, and weighs 86.6 kg (191 lb); BMI 40 kg/m2. Cardiac examination is unremarkable, and the lungs are clear to auscultation bilaterally. There is no peripheral edema. Laboratory studies show:

Sodium:	135	mEq/L
Potassium:	3.8	mEq/L
Creatinine:	0.8	mg/dL
Bicarbonate:	30	mmol/L

Thyroid-stimulating hormone:	2.4	μU/mL
Glucose (fasting):	135	mg/dL
Hemoglobin:	12.1	g/dL

Results of chest x-ray study and exercise stress testing show no abnormalities. Results of pulmonary function testing are pending. Pulmonary function testing is most likely to show which of the following findings?

Option	FEV1	FVC	ERV	RV	TLC	DLCO
A	Normal	↓	↓	↓	↓	↔
B	↓	↓	↓	Normal	↓	↔
C	↓	Normal	↓	↑	↑	↓
D	↑	↑	↓	Normal	Normal	↑
E	Normal	Normal	Normal	Normal	↑	↑
F	↓	↓	↓	Normal	↓	↓

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11. A 32-year-old man presents to the local community health clinic and reports that he has increasing difficulty "catching his breath." He also reports that he has been wheezing and has a productive cough with yellow sputum. The patient does not use tobacco products. His family history includes a father with significant lung disease. His vital signs include a heart rate of 66, respiratory rate of 18, temperature of 98.5°F (36.9°C), and oxygen saturation of 97% on room air. Physical examination demonstrates expiratory wheezing bilaterally. Pulmonary function tests reveal an increase in total lung capacity and residual volume. Laboratory studies demonstrate the following: blood urea nitrogen, 17 mg/dL; creatinine, 0.8 mg/dL; and international normalized ratio, 1.3. A chest x-ray shows hyperlucency of the entire lung fields with attenuation of bronchovascular markings.

For which of the following conditions is the patient at increased risk?

A. Hematuria
B. Liver cirrhosis
C. Pancreatic insufficiency
D. Pulmonary embolism
E. Recurrent sinus infections

12. A 78-year-old woman with chronic obstructive pulmonary disease (COPD) presents with her husband to her primary care physician's office because of a 2-month history coughing up bloody sputum and an unintentional 5-lb weight loss. She has historically been compliant with her medications and appointments. Her father had lung cancer and she helped care for him for the duration of his disease. On evaluation

today, she appears well; physical examination and laboratory studies show no major abnormalities. A CT scan of the chest shows a 4-cm spiculated nodule in the left upper lobe that raises suspicion for adenocarcinoma. She requests not to be told results of her CT scan right away. When asked by the physician why she wishes to defer her diagnosis, the patient explains that she and her husband are going on a 5-day Florida vacation soon, and she knows that she will be unable to enjoy herself if she is aware of a distressing diagnosis. The patient's husband feels that the patient should learn the diagnosis now in order to have all the information before the trip.

Which of the following is the most appropriate response to this patient's request?

A."I think you may want to postpone your trip so we can confirm this diagnosis."

B."I think you should speak with a therapist to discuss your feelings about your health."

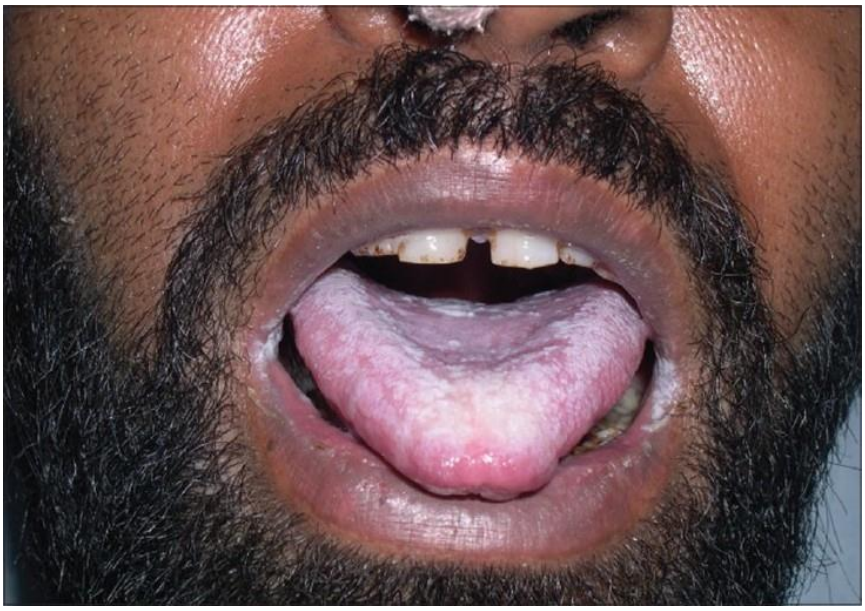
C."I understand you would like to enjoy your trip. Maybe just spend 2 days in Florida and we can come back together on Monday to discuss our plan."

D."I understand, but I really think that I should at least speak with your husband about the possible diagnosis."

E."I understand. Let's schedule an appointment for shortly after you return from your trip."

F."I'm concerned you may be in denial about the seriousness of this condition."

13. A 25-year-old man comes to the health clinic after experiencing a burning sensation in his mouth and noticing a whitish film on his tongue and the inside of his cheeks. These symptoms started 5-6 days ago. His past medical history is significant for intermittent asthma, and he was recently hospitalized for developing persistent night-time awakenings and progressive dyspnea. The patient was discharged with a new medication regimen 4 weeks ago. On examination of his oral cavity, the tongue has a coating of scrapable white plaques as shown in the image.



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Which of the following is the most appropriate treatment for this patient?

A. Albendazole

B. Amphotericin B
C. Griseofulvin
D. Nystatin
E. Oral fluconazole
F. Oral fluoride rinse
G. Terbinafine

14. An infant, born at 29 weeks' gestation, experiences difficulty breathing shortly after delivery. His mother did not receive prenatal care. Physical examination reveals tachypnea, intercostal retractions, nasal flaring, and cyanosis. On x-ray, the lungs have a diffuse ground glass appearance. He is intubated, and oxygen therapy is started.
Compared with a baby born at term, this neonate most likely has decreased levels of which of the following?

A. Phosphatidylcholine
B. Phosphatidylethanolamines
C. Phosphatidylglycerol
D. Phosphatidylinositol
E. Sphingomyelin

15. A 57-year-old man is found unconscious on the floor of his bedroom and taken to the hospital. In the following days, he develops shortness of breath and a cough productive of foul-smelling sputum. Records indicate that the patient is otherwise healthy, with no history of alcohol or tobacco use. Temperature is 38.4° C (101.2° F), heart rate is 88, blood pressure is 132/83 mm Hg, and respiratory rate is 19. On physical examination, wheezing is prominent over the posterior right lower lobe. Oral examination reveals poor dentition. After the results of a sputum culture are returned, administration of the appropriate antibiotic is started.
Which of the following organisms is most likely responsible for this patient’s condition?

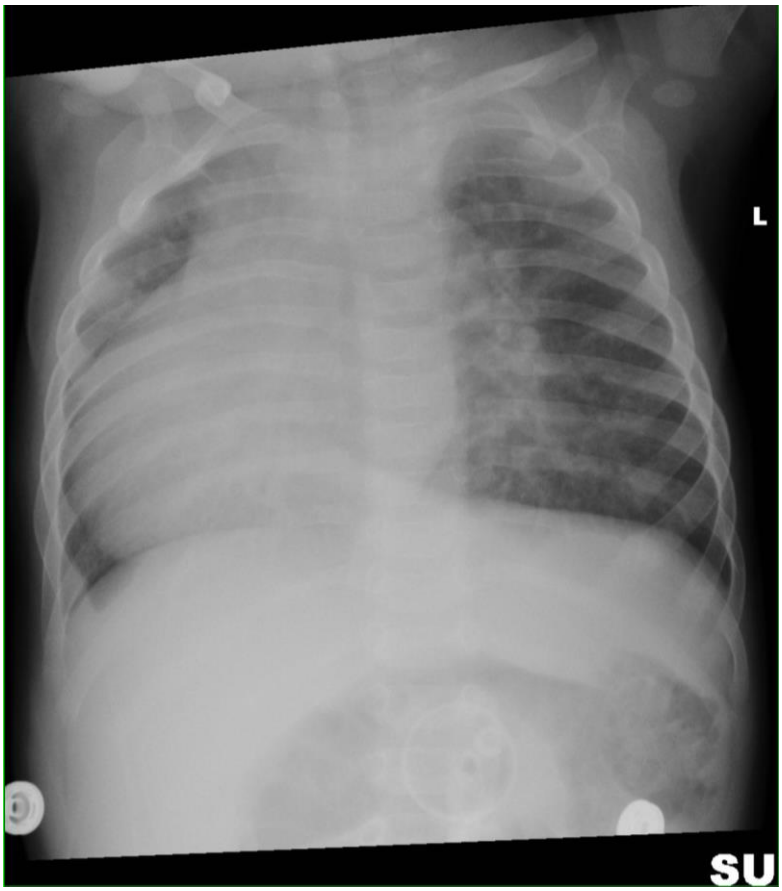
A. Klebsiella
B. Obligate intracellular bacteria
C. Peptostreptococcus
D. Pseudomonas
E. Streptococcus pneumoniae

16. A 47-year-old sole owner and operator of a pet store presents to his physician with headache, malaise, and a non-productive cough that came on suddenly and has persisted over the past 4 days. The patient takes medication to manage his hypertension and hyperlipidemia, but denies any other medical problems. His vital signs are: temperature 38.3°C (101°F), blood pressure 120/72 mm Hg, pulse 92/min, respiratory rate 26/min, and SpO2 90% on room air. Rales are auscultated bilaterally, and chest x-ray shows diffuse bilateral patchy infiltrates. The patient improves after treatment with

doxycycline. Which of the following microscopic features would most likely be seen on this patient's bronchoalveolar lavage?

A. Cytoplasmic inclusion bodies
B. Disk shapes present on silver stain
C. Gram-negative rod with bipolar staining
D. Intranuclear inclusion bodies
E. Lancet-shaped, gram-positive diplococci

17. A 2-year-old boy with a history of recurrent episodes of sinusitis is brought in by his concerned parents because he has a fever and "green, awful smelling discharge" coming from his nose. He has had clear nasal discharge for the past 2 weeks, but 2 days ago it changed to green. He has not had vomiting, diarrhea, or a rash. The parents said similar episodes have occurred several times since his birth. The boy's pulse is 99/min, blood pressure is 90/60 mm Hg, respiratory rate is 25/min, and temperature is 39.4°C (103°F). On physical examination, the physician detects tenderness to palpation over the maxillary and ethmoidal sinuses. Cardiac auscultation reveals normal sounding S1 and S2 in the right parasternal 4th intercostal space and in the right midclavicular 5th intercostal space. Lung auscultation reveals bronchovesicular breath sounds in all lung fields with crackles in the lower lung fields bilaterally. A chest x-ray is shown.



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Which of the following is most likely associated with this patient's condition?
A. Defective chloride transport
B. Elevated blood sugar
C. Infertility
D. Kyphoscoliosis
E. Tetralogy of Fallot

18. A 38-year-old Native American farmer presents to an urgent care clinic in northeastern Arizona after the sudden onset of prodromal symptoms of fever, muscle pain, cough, headache, nausea, and vomiting that have remained present for the past few hours. During physical evaluation, he has difficulty breathing. His temperature is 102.7°F (39.3°C), pulse is 120/min, respirations are 30/min, and blood pressure is 60/40 mm Hg. Laboratory tests show:
WBC: 12.5/mm3 with 7000/mm3 neutrophils
Platelet count: 90,000/mm3
Aspartate aminotransferase: 84 mU/mL
Alanine aminotransferase: 68 mU/mL
X-ray of the chest shows bilateral lung infiltrates and pleural effusions.
Which of the following is the natural reservoir for the virus causing this patient's symptoms?
A. Bats
B. Mosquitoes
C. Rodents
D. Ticks

19. A 29-year-old man with a history of cystic fibrosis comes to the emergency department because of a 1-week history of a worsening, productive cough. He has had seven episodes of pneumonia in the past year and recurrent episodes of urolithiasis and intermittent diarrhea for most of his life. He underwent a cholecystectomy 2 years ago. Family history is significant for chronic rhinosinusitis in his mother and a cousin who died of intestinal blockage at birth. The patient does not smoke or use illicit drugs. Temperature is 39° C (102° F), pulse is 98/min, respiratory rate is 21/min, and blood pressure is 129/76 mm Hg. His BMI is 17.5 kg/m2. On physical examination, the liver is palpated 3 inches below the inferior rib, and bilateral panlobular crackles are heard in the lower lung fields. Chest X-ray confirms the diagnosis of pneumonia, and a CT scan of his chest shows prominent bronchiectasis.
Which of the following antimicrobials is most effective in the treatment of this patient’s pneumonia?
A. Ampicillin
B. Cefuroxime
C. Erythromycin

D. Metronidazole
E. Piperacillin
20. A 24-year-old woman comes to the physician because of multiple episodes of difficulty breathing. She denies any chest pain, palpitations, nausea, vomiting, or headache. Medical history is significant for asthma, diagnosed in childhood. She has smoked two packs of cigarettes per day for the past 5 years. Her temperature is 98.6°F (37°C), blood pressure is 125/82 mm Hg, pulse is 70/min, respiratory rate is 22/min, and oxygen saturation is 95% on room air. Physical examination reveals labored breathing with expiratory wheezes in the lung fields bilaterally. The physician prescribes a medication that inhibits leukotriene production to manage her chronic asthma symptoms.
Which of the following medications was prescribed for this patient?
A. Albuterol
B. Ipratropium
C. Omalizumab
D. Zafirlukast
E. Zileuton
21. A 45-year-old man presents to the emergency department because of a 2-day history of coughing up blood and shortness of breath on exertion. He also reports weight loss of 7 kg (15.5 lb) and malaise over the past 2 months associated with decreased urine output. He has a history of chronic sinusitis. He does not use tobacco or alcohol and denies recent travel outside of the United States. Vital signs are within normal limits. The patient appears ill. Mild nasal crusting and bloody nasal discharge are observed. Heart sounds are normal, and crackles are heard in both lungs.
Laboratory results are as follows:
Hemoglobin: 9.5g/dL
Platelets: 400,000/mm^3
Leukocytes: 13,000/mm^3
Sodium: 140mEq/L
Potassium: 4.5mEq/L
Bicarbonate: 25mEq/L
Blood urea nitrogen: 28mg/dL
Creatinine: 2.0mg/dL
Glucose: 100 mg/dL
Which of the following is the most likely diagnosis for this patient?
A. Granulomatosis with polyangiitis
B. IgA vasculitis
C. Non–small-cell lung cancer
D. Polyarteritis nodosa

E. Thromboangiitis obliterans

22. A 32-year-old man is found unconscious on the sidewalk without evidence of trauma. He is taken by ambulance to the emergency department, where a toxicology screen is positive for high levels of ethanol and opiates. On physical examination, his pupils are constricted. His vital signs are:

Temperature: 36.1°C (97°F)
Pulse: 50/min
Blood pressure: 120/80 mm Hg
Respiratory rate: 8/min
Oxygen saturation: 93%

Arterial blood gas analysis shows:

pH: 7.29
Partial pressure of carbon dioxide: 60 mm Hg
Partial pressure of oxygen: 80 mm Hg
Bicarbonate: 24 mmol/L
Base excess: –2 mEq/L

This patient's physiologic condition has led to changes in the binding affinity of hemoglobin for oxygen.

Which of the following would change hemoglobin's affinity to bind oxygen in the same way?

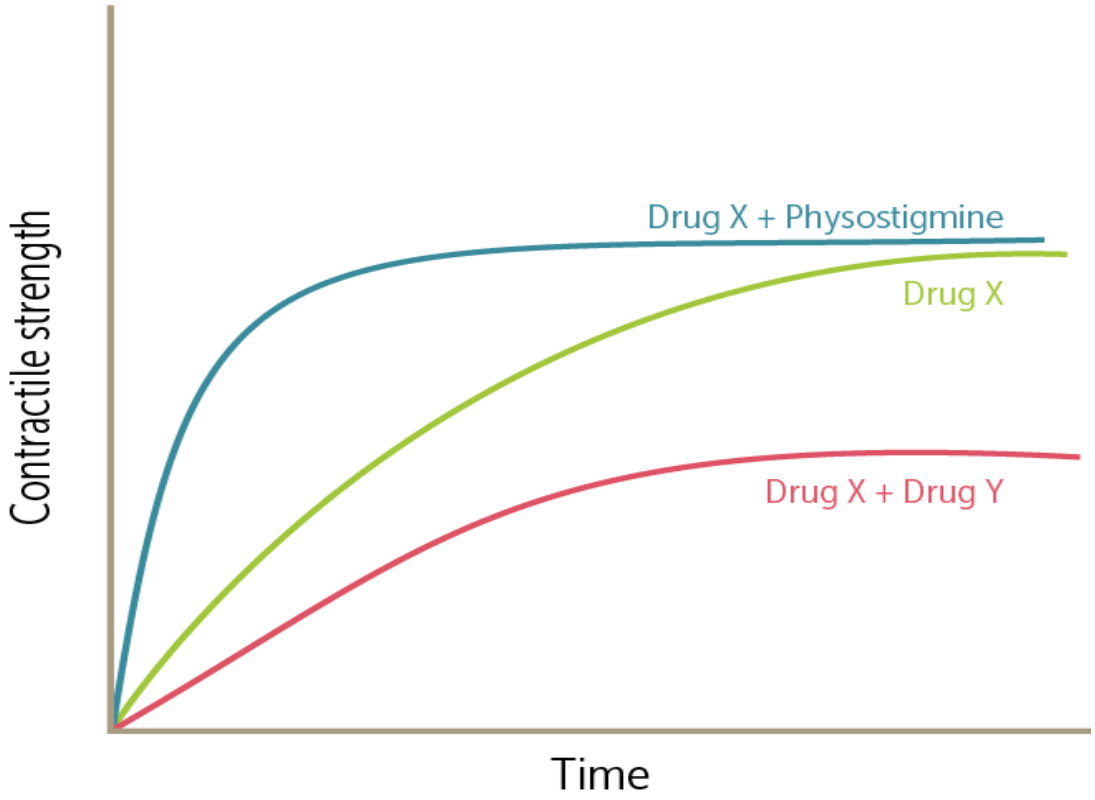
A. Decrease in hematocrit
B. Inhalation of carbon monoxide
C. Metabolic changes associated with exercise
D. Metabolic changes associated with protracted vomiting

23. A 7-year-old boy is brought to the pediatrician because of a history of chronic cough, greasy floating diarrhea, and failure to gain weight. The patient's body mass index is calculated at 17 kg/m^2, and he is in the 40th percentile for height. On auscultation, bronchial breath sounds are heard, and frequent sputum production is observed during the office visit. *Pseudomonas aeruginosa* is grown from the patient's sputum culture. The physician subsequently orders sweat testing, and the chloride content is found to be markedly elevated. Genetic testing reveals the most common mutation seen in this disease.

Which of the following is the most likely underlying cause of this patient's condition?

A. Impaired ion channel conduction
B. Impaired protein production
C. Impaired protein trafficking
D. Increased turnover of ion channels in the plasma membrane
E. Reduced ion channel response to ATP stimulation

24. An experiment to better understand the effects of certain drugs and their impact on the respiratory conduction system has been proposed. Isolates of bronchial smooth muscle are obtained and a mechanism is in place to measure the contractile strength when the isolates are exposed to certain drugs. The isolates do not have any form of innervation aside from the drugs they are exposed to. The bronchial smooth muscle is exposed to the various drug preparations being studied. A solution of acetylcholine is then added to the tissue sample to induce muscle contraction. One of the drugs, Drug Y, was mistakenly labeled and requires identification. The results of each drug on the muscle are shown below.



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If drug X is a muscarinic agonist, then Drug Y in this experiment is most likely which of the following drugs?

A. Bethanechol
B. Ipratropium
C. Methacholine
D. Neostigmine
E. Pilocarpine

25. A 25-year-old woman is brought to the emergency department after ingesting a full bottle of theophylline in a suicide attempt. Her medical history is significant for asthma that was diagnosed as a child. She presents with a tonic–clonic seizure. On physical examination, blood pressure is 80/40 mm Hg, pulse is 160/min, and respiratory rate is 30/min. The emergency medical personnel who arrived with her via ambulance report that she has been seizing since arriving 15 minutes ago.

Which of the following biochemical modifications to this patient's current condition is the most appropriate pharmacotherapy target to address the cause of this patient's presentation?

A. β1-adrenergic receptor activation
B. β1-adrenergic receptor inactivation
C. β2-adrenergic receptor activation
D. Increased intracellular cAMP through nonselective adrenergic receptors
E. Prolonged GABA receptor opening

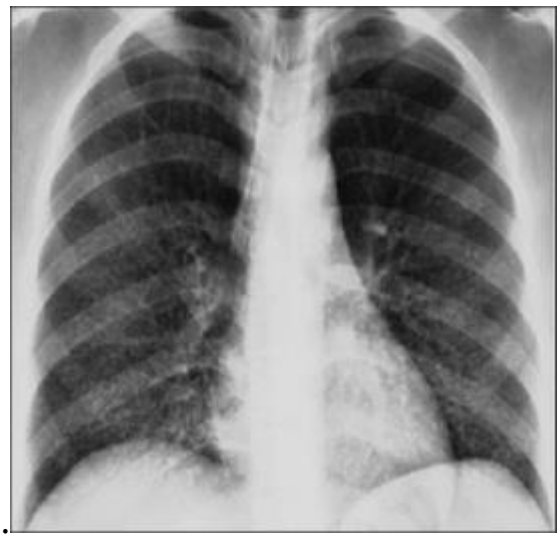
26. A 6-year-old boy is brought to his pediatrician's office with a fever and pain in the right ear. His mother states that he has been tugging at his right ear for the past 3 days and that she recorded a temperature of 102.2°F (39°C) yesterday. His appetite has been normal, and he has been tracking in the 75th percentile for height, weight, and head circumference. His medical history is significant for recurrent sinus infections over the past year. His mother's pregnancy was uncomplicated, and she obtained appropriate prenatal care. Physical examination reveals an erythematous bulging tympanic membrane in the right ear. His vital signs are: temperature, 100.4°F (38°C); blood pressure, 98/70 mm Hg; pulse, 75/min; respiratory rate, 18/min; and oxygen saturation, 97% on room air. Heart sounds are not appreciated at pulmonic, tricuspid, and mitral positions; but a regular rate and rhythm are auscultated at the aortic position. Lungs are clear to auscultation bilaterally.

This patient has an increased risk for development of which of the following complications?

A. Bronchiectasis
B. Emphysema
C. Failure to thrive
D. Heart failure
E. Mitral regurgitation
F. Pancreatic insufficiency

27. A 55-year-old woman with a history of schizophrenia is brought to the emergency department by her daughter. The patient is verbally aggressive and insists that her nurse is trying to poison her. The daughter remarks that her mother has not been adhering to her medication regimen. She is admitted to the hospital, and haloperidol is started because of her acute psychotic symptoms. During her hospital course, she is restrained with four-point soft restraints after violent outbursts toward staff. On her third day in the hospital, she reports severe right-sided chest pain that is worse during inspiration or when she attempts to cough. The patient's temperature is 37.7° C (100° F), blood pressure is 135/85 mm Hg, and pulse is 116/min. There is no tracheal deviation or jugular venous distention. On auscultation, reveals clear lungs bilaterally. The

remaining findings of the physical examination are unremarkable. A chest x-ray is shown.

. 

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Which of the following would be the most appropriate treatment for this patient?

A. Administer a β-blocker
B. Discontinue the haloperidol
C. Start administration of broad-spectrum antibiotics
D. Start intravenous administration of heparin
E. Thoracocentesis
F. Thrombolysis
G. Watchful waitin

28. A 23-year-old man comes to the emergency department because of shortness of breath and blood-tinged sputum. The patient denies any recent changes in diet, lifestyle, or travel; he also denies illicit drug use. He occasionally smokes. His vital signs show a temperature of 36.8°C (98.2°F), blood pressure of 160/90 mm Hg, heart rate of 99/min, respirations of 26/min, and an oxygen saturation rate of 88% on room air. Urinalysis is significant for the presence of protein (+2), dysmorphic red blood cells, and red blood cell casts.

Which of the following will likely be found on this patient's pulmonary function tests?

A. Decreased DLCO
B. Increased functional residual capacity
C. Increased residual volume
D. Increased total lung capacity
E. Normal FEV1:FVC

29. A 74-year-old retired shipyard laborer presents to his primary care provider with increasing shortness of breath and peripheral edema. He has no significant medical history, but his social history includes a 45–pack-year history of cigarette smoking. In addition to his work at the shipyard, he previously worked in sandblasting and fiberglass operations. He is 160 cm (5'3") tall and weighs 70 kg (154 lb). His vital

signs include a heart rate of 84/min, blood pressure of 108/68 mm Hg, and respiratory rate of 26/min. He appears to be in moderate pulmonary distress, and his chest shows an increased anteroposterior diameter with faint breath sounds and a prolonged expiratory phase. The edge of his liver is 3 cm below the right costal margin, and there is no clubbing in the fingers. Arterial blood gas analysis reveals:
Partial oxygen pressure: 60 mm Hg
Partial carbon dioxide pressure: 62 mm Hg
Bicarbonate level: 30 mEq/L
pH: 7.34
Which of the patterns of laboratory findings listed in the table would be evident on spirometry?

Choice	FEV_1	FVC	FEV_1:FVC	Total lung capacity
A	↓	↓	↓	↓
B	↓	↓	↓	↑
C	↓	↓	normal	↓
D	↓	↑	↓	↑
E	↓	↑	↑	↑

30. A 67-year-old man presents to his primary care physician with difficulty "catching his breath." His symptoms are exacerbated on exertion and his condition has progressively worsened over the past few months. The patient has a past medical history of hypertension, hyperlipidemia, and type 2 diabetes mellitus. He has a 50-pack-year history of cigarette smoking. His medications include lisinopril, hydrochlorothiazide, and metformin.
A cardiac stress test with echocardiogram reveals an ejection fraction of 65% with normal left-ventricular wall motion before and after exercise. However, the patient's mean pulmonary artery pressure is 35 mm Hg. In addition, he is short of breath after achieving 85% of his maximum target heart rate. His symptoms are relieved with administration of ipratropium, but he has no response to albuterol. Using the table provided, which of the following would be the most likely findings on pulmonary function testing for this patient?

Choice	FEV_1	FVC	FEV_1:FVC ratio	Total lung capacity
A	↑	↓	↑	↓
B	↓	↑	↓	↑
C	↓	↓	normal	↑
D	↓	↓	normal	↓
E	↓	↓	↓	↑

MCQs STEP 1

1. The majority of CO2 in the blood is carried in which of the following forms?

A. carbamino compounds

B. CO2 dissolved in solution

C. CO_3^{-2}

D. HCO_3^-

E. H_2CO_3

2. Lipoxygenase converts arachidonic acid to biologically active compounds called leukotrienes. Leukotrienes have been implicated in several disease entities, including allergic asthma, where they are presumed to mediate bronchoconstriction. Introducing leukotrienes into an airway would be expected to cause which of the following responses?

A. Decreased airway resistance

B. Decreased dead space volume

C. Increased functional residual capacity (frc)

D. Increased lung compliance

E. Increased total lung capacity

3. Figure 2-12 shows pulmonary function test tracings from a healthy person and a patient with pulmonary fibrosis. Of the following measures which would you expect to be increased in this patient, as compared to the expected norms?

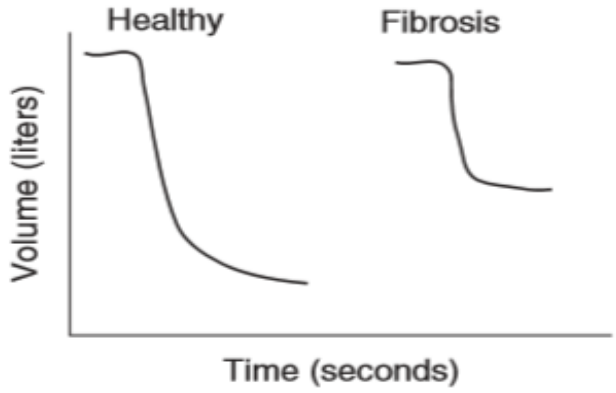


FIG. 2-12

Reproduced from materials USMLE STEP 1

A. Forced expiratory volume (FEV)/forced vital capacity (FVC)

B. FRC

C. FVC

D. Tidal volume

E. Vital capacity

4. Figure 2-13 illustrates uptake of two gases (nitrous oxide and carbon monoxide) from alveolar air to pulmonary capillary blood. Based on this information what can we conclude about carbon monoxide?

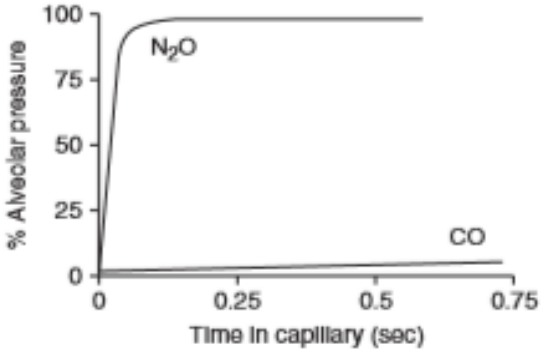


FIG. 2-13

Reproduced from materials USMLE STEP 1

A. It does not dissolve in blood
B. It does not interact with hemoglobin
C. It has equilibrated with pulmonary capillary blood
D. It is a diffusion-limited gas
E. It is a perfusion-limited gas

5. Apatient presents with long-standing emphysema. Which of the following would you expect to see in this individual?

A. Decreased physiological dead space
B. Increased fev1/fvc
C. Increased frc
D. Increased fvc
E. Increased lung elastic recoil

6. Which of the following is an adaptive response to moving from sea level to higher elevation?

A. Bronchial relaxation
B. Decreased cardiac output
C. Decreased circulating levels of epo
D. Decreased levels of 2,3-diphosphoglycerate (2,3-dpg) in erythrocytes
E. Hyperventilation

7. The graph in Figure 2-17 shows the static pressure–volume curve of a patient's lung (solid line). The broken line indicates the pressure–volume curve of a normal person for comparison. What is the approximate lung compliance of this patient over the volume range from 1 to 7 L?

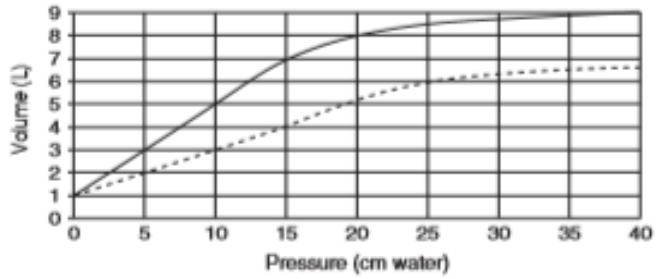


FIG. 2-17

Reproduced from materials USMLE STEP 1

A. 0.5 cm H_2O/L

B. 1 cm H_2O/L

C. 400 mL/cm H_2O

D. 800 mL/cm H_2O

E. 1000 mL/cm H_2O

8. Apatient on intensive care is ventilated with a frequency of 12 per minute and a tidal volume of 0.6 L. His arterial pH increases to >7.5. What is the most reasonable action to correct this respiratory alkalosis?

A. Decrease dead space

B. Decrease tidal volume

C. Increase minute ventilation

D. Increase oxygen fraction

E. Use positive end-expiratory pressure (peep)

9. A 3-year-old girl, who has missed several scheduled immunizations, presents to the emergency room with a fever trouble breathing. A sputum sample is brought to the laboratory for analysis. Gram stain reveals the following: rare epithelial cells, 8–10 polymorphonuclear leukocytes per highpower field, and pleomorphic gram-negative rods. As a laboratory consultant, which of the following interpretations is correct?

A. The appearance of the sputum is suggestive of h. Influenzae

B. The patient has pneumococcal pneumonia

C. The patient has vincent's disease

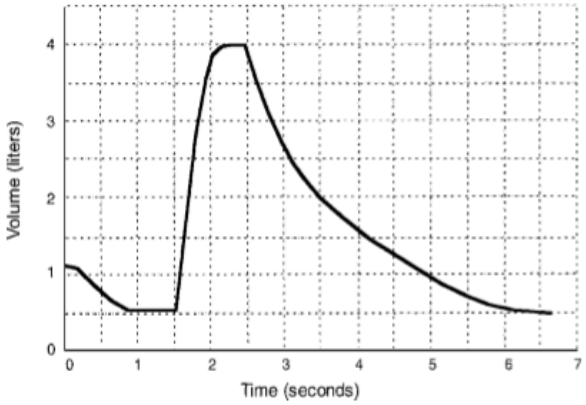
D. The sputum specimen is too contaminated by saliva to be useful

E. There is no evidence of an inflammatory response

10. A healthy middle-aged construction worker who engaged in a demolition task 10 days earlier complains of respiratory symptoms similar to those of pneumonia. No causative agent has been isolated from his sputa. The patient does not respond to any antibacterial antibiotics and dies before a definitive diagnosis was established. Microscopic examination of specimens taken of granulomatous and suppurative lesions of the lung obtained during necropsy reveal the presence of large budding yeast cells. The bud is attached to the parent cell by a broad base. Based on this information, which of the following is the most likely diagnosis?

A. Blastomycosis
B. Coccidioidomycosis
C. Cryptococcosis
D. Histoplasmosis
E. Sporotrichosis

11. An 18-year-old girl with a 9-year history of wheezing on exertion is referred for pulmonary function tests. The diagram below represents the spirometry tracing of a forced vital capacity. Her total lung capacity was 110% of predicted. Which of the following values will most likely be above normal?



Reproduced from materials USMLE STEP 1

A. Vital capacity
B. Residual volume
C. Expiratory reserve volume
D. Fev1.0/fvc
E. Maximum voluntary ventilation

12. A mother brings her 10-year-old son, who has a long-standing history of poorly controlled asthma, to the emergency department (ED). He is in a relatively early stage of what will prove to be a severe asthma attack. Arterial blood gases have not been analyzed yet, but it is obvious that the lad is in great distress. He is panting with great effort at a rate of about 160/min. Given the boy's history and the likely diagnosis, the health care team administers all the drugs listed by the stated routes, and with the expected purposes noted. The child's condition quickly improves, and the team leaves the boy with his mother while they go to care for other ED patients. Within a couple of minutes the mother comes out of her son's cubicle frantically screaming "he's stopped breathing!" Which of the listed drugs most likely caused the ventilatory arrest?

A. Albuterol, inhaled, given by nebulizer for prompt bronchodilation
B. Atropine, inhaled, given with the albuterol
C. Midazolam, iv, to normalize ventilatory rate and allay anxiety
D. Methylprednisolone (glucocorticosteroid), iv, for prompt suppression of airway inflammation
E. Normal saline, inhaled, to hydrate the airway mucosa

13. Five days after returning from a trip to mainland China a 25-yearold previously healthy woman acutely develops a cough, shortness of breath, and fever with chills, headaches, diarrhea, nausea, and vomiting. She is found to have a peripheral lymphopenia. After appropriate laboratory tests are performed the diagnosis of severe acute respiratory syndrome (SARS) is made. What type of virus is the cause of this disorder?

A. Alphavirus
B. Coronavirus
C. Filovirus
D. Flavivirus
E. Hantavirus

14. A 37-year-old man presents with a cough, fever, night sweats, and weight loss. A chest x-ray reveals irregular densities in the upper lobe of his right lung. Histologic sections from this area reveal groups of epithelioid cells with rare acid-fast bacilli and a few scattered giant cells. At the center of these groups of epithelioid cells are granular areas of necrosis. What is the source of these epithelioid cells?

A. Bronchial cells
B. Fibroblasts
C. Lymphocytes
D. Monocytes
E. Pneumocytes

15. Two siblings, ages 2 and 4, experienced fever, rhinitis, and pharyngitis that resulted in laryngotracheo bronchitis. Both had a harsh cough and hoarseness. Which of the following viruses is the leading cause of their syndrome?

A. Adenovirus
B. Group b coxsackievirus
C. Parainfluenza virus
D. Rhinovirus
E. Rotavirus

16. A patient stung by a bee is rushed into the emergency room with a variety of symptoms including increasing difficulty in breathing due to nasal and bronchial constriction. Although your subsequent treatment is to block the effects of histamine and other acute-phase reactants released by most cells, you must also block the slow-reacting substance of anaphylaxis (SRS-A), which is the most potent constrictor of the muscles enveloping the bronchial passages. An SRS-A is composed of which of the following?

A. Thromboxanes
B. Interleukins
C. Complement

D. Leukotrienes
E. Prostaglandins
17. A young boy is diagnosed with asthma. His primary symptom is frequent cough, not bronchospasm or wheezing. Other asthma medications are started, but until their effects develop fully we wish to suppress the cough without running a risk of suppressing ventilatory drive or causing sedation or other unwanted effects. Which of the following would best meet these needs?
A. Codeine
B. Dextromethorphan
C. Diphenhydramine
D. Hydrocodone
E. Promethazine

ANSWERS IFOM MCQs

1. The answer is D. This patient with a 3-day history of cough and mental decline presents with pneumonia caused by multidrug-resistant Klebsiella pneumoniae. On culture, the pathogen is only susceptible to one antibiotic, which acts as a detergent and binds bacterial cell membranes to increase their permeability. This describes the mechanism of action of polymyxins. Polymixins are predominantly used to treat severe gram-negative infections that are resistant to less toxic antimicrobials. Neurotoxicity is an adverse effect of polymyxins that can manifest as numbness of the extremities, dizziness, drowsiness, confusion, nystagmus, or blurred vision. Other adverse effects of polymyxins include nephrotoxicity, facial flushing, anaphylactoid reactions (dyspnea and tachycardia), urticaria, eosinophilia, and fever. Since the other adverse effects listed are associated with antibiotics with a different mechanism of action, these answer choices are incorrect:

Granulocytopenia is an adverse effect of both trimethoprim and dapsone. Trimethoprim inhibits bacterial dihydrofolate reductase and is used in combination with sulfonamides, causing sequential block of folate synthesis. Dapsone also inhibits folate synthesis, but it does so by inhibiting dihydropteroate synthase.

Hearing loss is an adverse effect of aminoglycosides and vancomycin. Aminoglycosides irreversibly inhibit the initiation complex through binding of the 30S subunit, cause misreading of mRNA, and also block translocation. Vancomycin inhibits cell wall peptidoglycan formation by binding the D-ala-D-ala portion of cell wall precursors.

Hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency is an adverse effect of primaquine and the sulfonamides. The mechanism of action of primaquine is not well understood, it may act by generating reactive oxygen species or by interfering with the electron transport in parasites. Sulfonamide inhibits dihydropteroate synthase, thus inhibiting folate synthesis.

Rhabdomyolysis is an adverse effect in daptomycin, which disrupts cell membranes of gram-positive cocci by creating transmembrane channels.

2. The answer is B. This woman, who is recovering from a gastrectomy has difficulty breathing, decreased breath sounds, dullness to percussion, decreased tactile fremitus, and an elevated diaphragm. These findings, together with tracheal deviation towards the side of insult, are pathognomonic for atelectasis, or alveolar collapse due to decreased lung volume. Volume loss and increased lucency of the lung are commonly seen on chest x-ray. Risk factors for atelectasis include smoking history, obesity, and the postoperative period (commonly occurring within the first 72 hours). In fact, atelectasis is one of the most common postoperative pulmonary complications, particularly following abdominal and thoracoabdominal procedures. Treatment involves decreasing pulmonary inflammation, and, as indicated, removal of the original

insult. In postoperative cases for patients without abundant secretions, continuous positive airway pressure may be beneficial. For patients with abundant secretions, chest physiotherapy and suctioning are appropriate. All patients should receive supportive care. If left untreated, this condition can progress rapidly to respiratory failure. Prevention of disease occurrence postoperatively includes proper analgesia, spirometry, and early mobility.

Types and etiologies of this condition include:

Obstructive atelectasis, or air absorption due to foreign body, mucous plug, or tumor

Compressive atelectasis resulting from an external force such as space-occupying lesion or effusion

Contraction atelectasis due to scarring of alveoli from conditions such as sarcoidosis

Adhesive atelectasis, resulting from increased surface tension due to lack of surfactant

This patient's atelectasis reflects a classic postoperative presentation. Postoperative atelectasis is usually caused by decreased compliance of lung tissue, impaired regional ventilation, retained airway secretions, and/or postoperative pain that interferes with spontaneous deep breathing and coughing.

The other choices are not the best answers for the following reasons:

Lung metastasis (gastric adenocarcinoma metastasis) do occur; however, in such cases, cough, hemoptysis, wheezing, and coin lesions on chest x-ray would be present. A cancerous plug could result in atelectasis, but this patient's x-ray rules out obstructive pathology.

A lung abscess results in a localized collection of pus within parenchyma and a cystic mass and is classically characterized by fever. Common causes include aspiration of pharyngeal contents or bronchial obstruction. On chest x-ray, air-fluid levels will often be seen, suggesting cavitation.

Respiratory failure or decompensationis a life-threatening complication of atelectasis that has been left untreated. This condition results in the inability of the respiratory system to support bodily needs. Respiration depression causes anoxia and decreased PaO_2 levels.

On examination, signs of pneumonia include bronchial breath sounds, late inspiratory crackles, egophony, whispered pectoriloquy, dullness to percussion, increased tactile fremitus, and no signs of tracheal deviation. A productive cough is usually present as is consolidation on chest x-ray due to inflammation and infection.

Alveolar destruction is common in conditions such as emphysema. Hyperinflated lungs, a flattened diaphragm, barrel chest, increased AP diameter are common signs seen on AP and lateral chest x-ray. Hyperresonance would be seen on percussion.

3. The answer is E. Probability is defined as the extent to which an outcome is likely to occur, determined by the ratio of wanted outcomes to the number of cases possible. In the this study, there is a 50% chance a non-smoking individual will develop lung

cancer after being exposed to smoke in the household for 10 or more years. The odds of all five individuals living in separate smoking households developing cancer is (0.5)^5 or 0.03 (3%). The other options are incorrect calculations. The only correct calculation to determine the chance of all of the expected outcomes occurring at the same time is to multiply the chance of each individual outcome. This calculation would be 0.5 x 0.5 x 0.5 x 0.5 x 0.5 = 0.03, or 3%.

4. The answer is D. In patients with asthma whose symptoms are not well controlled with a short-acting β2-agonist (eg, albuterol) and an inhaled glucocorticoid (eg, fluticasone), the addition of another medication is indicated. The drug of choice in this instance is a long-acting β2-agonist (LABA), such as salmeterol. Stimulation of the Gs βsub>2-receptor results in activation of adenylyl cyclase, resulting in a rise in cAMP leading to an activation of protein kinase A. The subsequent phosphorylation of myosin light-chain kinase results in its inactivation in smooth muscle, causing relaxation in the bronchioles, thus relieving asthma symptoms. It is against Food and Drug Administration (FDA) recommendations for LABAs to be used as monotherapy; LABAs must be combined with another long-acting asthma medication, such as a glucocorticoid. Because LABAs and steroids are not effective in treating symptoms of an acute asthma exacerbation, a short-acting β2-agonist, such as albuterol, must be prescribed and used on an as-needed basis.Inhibition of protein kinase A is the mechanism of action of β-blockers, which can cause constriction of smooth muscle; therefore β-blockers are relatively contraindicated for patients with asthma. Zileuton is a medication that acts by inhibition of the 5-lipoxygenase pathway, blocking the production of leukotrienes and consequently preventing bronchial hyperresponsiveness. Zileuton is not a first-line drug and is not recommended unless a patient cannot tolerate an LABA. Ipratropium bromide is an anticholinergic agent; its mechanism of action is inhibition of muscarinic receptors, which leads to bronchodilation. Although ipratropium bromide is recommended for management of chronic obstructive pulmonary disease and acute asthma exacerbations in children, it is not a first-line treatment for an asthma exacerbation. Omalizumab is a recombinant humanized IgG monoclonal antibody that binds to IgE with high affinity, preventing bronchoconstriction; however, it is only indicated if other first- and second-line therapies have failed.

5. The answer is B. This patient presents with hemoptysis, dyspnea, unexplained weight loss, fever, chills, hematuria, generalized malaise, and intranasal ulcers with no history of cocaine use or travel. Given this constellation of symptoms and a positive c-ANCA titer, the most likely diagnosis is **granulomatosis with polyangiitis** (previously known as Wegener granulomatosis). This idiopathic autoimmune disease is characterized by necrotizing, granulomatous vasculitis that affects several organs, most notably the upper respiratory tract, lungs,

and kidneys. In the kidneys, the condition manifests as a rapidly progressive **crescentic necrotizing glomerulonephritis.**
Tuberculosis (TB) can sometimes be confused with granulomatosis with polyangiitis; however, the sputum culture negative for acid-fast bacilli rules out TB. **Normal glomeruli with foot process effacement** are associated with minimal change disease, a nephrotic syndrome most often seen in children. A **split basement membrane** is associated with Alport syndrome, a nephritic syndrome caused by a genetic defect in type IV collagen and associated with sensorineural hearing loss. **Smooth linear staining on immunofluorescence** is associated with Goodpasture syndrome, which presents with hemoptysis; however, a c-ANCA titer would not be positive. **Wire-loop lesions with subepithelial deposits** are associated with systemic lupus erythematosus, but not with hemoptysis or a positive c-ANCA.

6. The answer is D. This patient is admitted to the hospital in status asthmaticus, and mechanical ventilation is initiated after he experiences acute respiratory failure. After 96 hours, the patient requires additional ventilatory support. He has also developed a fever and tracheobronchial secretions. X-ray of the chest reveals a right lower lobe infiltrate. This patient likely has ventilator-associated pneumonia (VAP), a common complication among patients requiring ventilation. Sedative medications required during intubation depress the native ciliary elevator function of natural respiration, leading to VAP. Symptoms include fever or hypothermia, new purulent sputum, or a change in respiratory support requirements. In order for VAP to be diagnosed, a patient must have been receiving mechanical ventilation for at least 48 hours. Both chronic lung disease and convalescence in the intensive care unit are risk factors for VAP. It is often caused by the gram-negative bacillus Pseudomonas aeruginosa. For this reason, empiric antibiotic therapy for VAP, such as piperacillin-tazobactam, must be prescribed to cover Pseudomonas.
Legionella pneumophila is a cause of a typical pneumonia syndrome that presents with cough, high fever, hyponatremia, and diarrhea. Candida albicans causes skin, vaginal, and oropharyngeal infections but is a very rare cause of pneumonia. Clostridium difficile presents with diarrhea in the setting of recent antibiotic use. Staphylococcus epidermidis is a cause of urinary tract infections and infections in indwelling prosthetic devices, intravenous lines, and Foley catheters.

7. The answer is E. This patient with acute pleuritic chest pain, dyspnea, and ipsilateral decreased breath sounds has most likely developed a spontaneous pneumothorax. It is not unusual for the condition to manifest in otherwise young, healthy men. Spontaneous pneumothorax occurs most commonly because of rupture of apical blebs in the pleura. The ruptured blebs lead to entry of air into the pleural space, which disrupts the negative intrapleural pressure (-5 mm Hg) and causes the lung to collapse. This results in abrupt chest pain, hyperresonant chest cavity after

collapse of the lung, decreased breath sounds secondary to decreased ventilation, decreased fremitus secondary to less solid tissue transmitting vibration, and in rare cases, hypotension caused by cardiovascular compromise. On x-ray of the chest, a linear shadow of the pleura without peripheral lung markings can be appreciated as a result of the collapse of the lung. Asthma is a chronic condition characterized by inflammation of the airways causing obstructive symptoms. Bronchitis is an inflammation of the airway, which can present with a productive cough; chest pain is not usually present. Emphysema is a type of obstructive lung disease that is due to a long history of smoking. A pulmonary embolism can develop in a patient who is in a hypercoagulable state, is sedentary for extended periods, or has endothelial damage, which can lead to endothelial dysfunction. Tension pneumothorax is caused by an acute insult/trauma to the chest that leads to trapping of air in the pleural space.

8. The answer is B. In a patient presenting with episodic wheezing, tachypnea, dyspnea, and hypoxemia, one should suspect asthma. Asthma is an obstructive lung disease that causes air trapping in the lungs from reversible bronchial hyperresponsiveness and can show up as hyperinflated lungs on a chest x-ray. Asthma is commonly triggered by exercise (especially in the cold), viral upper respiratory tract infections, allergens, and stress. Agents most commonly associated with acute asthma attacks include aspirin, food-coloring agents such as tartrazine (a yellow food dye), β-adrenergic antagonists, and sulfating agents. Aspirin-sensitive asthma is caused by cyclooxygenase (COX) inhibition, which leads to the overproduction of leukotrienes and subsequent airway constriction. The triad of aspirin sensitivity, asthma, and nasal polyps is known as Samter's triad, which is highly suggestive of aspirin-exacerbated respiratory disease. Because acetaminophen is a weak COX inhibitor, it does not shift the arachidonic acid pathway toward the overproduction of leukotrienes as aspirin does, and it does not cause bronchoconstriction and exacerbation of asthmatic symptoms. Like acetaminophen, the other drugs listed would not be expected to precipitate an acute asthma exacerbation. Captopril can cause a dry cough; penicillin can cause urticaria, angioedema, and possibly anaphylaxis; and theophylline can cause restlessness, flushing, and irritability.

9. The answer is C. This patient presents with fever, chills, weight loss, and a productive cough with hemoptysis, which is highly suggestive of Mycobacterium tuberculosis, the causative bacterial agent of tuberculosis (TB). The pleural effusion evident on the x-ray of the chest suggests pulmonary TB infection as well.

The initial treatment for TB involves the four-drug regimen of rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE regimen). Following the start of treatment, this patient presented at a follow up appointment with diminished light touch, pinprick, and vibratory sensation of the lower extremities. These symptoms, plus burning sensation in the hands and feet, are indicative of vitamin B6 deficiency. Although the RIPE

regimen drugs have several adverse effects, isoniazid is particularly known for causing neurotoxicity by inducing vitamin B6 deficiency. These symptoms can be minimized if the patient is given vitamin B6, also known as pyridoxine. Thiamine (vitamin B1), Cobalamin (vitamin B12), and Tocopherol (vitamin E) deficiency can all cause neurologic symptoms, but not that match exactly with those seen in this patient. Furthermore, these vitamins are not depleted in treatment of tuberculosis. Pyrazinamide is one of the medications used to treat tuberculosis, and administration would not prevent neurological symptoms.

10. The answer is B. This obese 52-year-old woman is experiencing chronic dyspnea without evidence of cardiac or pulmonary disease based on history and imaging (chest x-ray study and stress test show no abnormalities). This patient's dyspnea is most likely attributable to her obesity. Bicarbonate level is slightly increased (29 mmol/L), suggesting possible metabolic compensation for prolonged respiratory acidosis caused by obesity-related hypoventilation. Obesity hypoventilation syndrome is defined as obesity in conjunction with alveolar hypoventilation while awake (partial pressure of carbon dioxide ($PaCO_2$) > 45 mm Hg) that is not attributable to other causes.

FEV1: volume of air expired in 1 second after maximal inspiration

FVC: functional vital capacity or maximum volume of air that can be forcibly exhaled from lungs following a maximal inspiration

ERV: expiratory reserve volume or maximum volume of air expired after normal tidal expiration

RV: residual volume, or volume of air in lung after maximal expiration

TLC: total lung capacity (lung volume after maximal inspiration)

FRC: functional residual capacity; FRC = resting lung volume = RV+ERV. FRC is dependent on the equilibrium between the outward chest wall recoil and inward elastic recoil of lung parenchyma

Because of the increased inward recoil of the chest wall in patients with obesity secondary to increased abdominal weight, pulmonary function testing (PFT) values are characteristic of a restrictive lung disease pattern with decreased TLC and FRC and a normal FEV1/FVC ratio. Residual volume is largely unchanged in obesity, so the decrease in FRC (which is equal to ERV + RV) is characterized by a significantly decreased ERV.

Restrictive lung diseases result from either reduced lung parenchymal compliance (interstitial lung disease, pleural disease such as effusions/scarring/edema), reduced chest wall compliance (obesity), reduced chest wall musculature (ALS, muscular dystrophy), or reduced chest wall flexibility (ankylosing spondylitis, kyphoscoliosis). To distinguish between diseases involving pulmonary versus extrapulmonary (chest wall) causes of restriction, it is helpful to measure the diffusing capacity for carbon monoxide, (DLCO), which is a measure of the conductance of gas transfer from

inspired gas to the red blood cells. Among patients with a restrictive pattern, DLCO results within reference ranges suggests an extrapulmonary cause of the restriction, such as obesity, pleural effusion, pleural thickening, neuromuscular weakness, or kyphoscoliosis. A reduced DLCO suggests pulmonary parenchymal restriction due to interstitial lung disease (ILD) or pneumonitis.

Why incorrect answers are wrong:

A) This set of values represents a restrictive pattern with preserved FEV1, reduced RV, and normal DLCO, which could possibly occur in restrictive disease due to pleural cause such as empyema or large pleural effusions.

C) This set of values represents an obstructive pattern with normal FVC, reduced FEV1 and DLCO, and increased TLC. Such a set of values is characteristic of emphysema.

D & E) FEV1, FVC, and TLC may be increased in trained athletes, but increases in these values would not be characteristic of this obese patient with dyspnea on exertion.

F) This set of values represents a restrictive pattern with decreased TLC, preserved RV, and reduced ERV and DLCO. Such values would be characteristic of interstitial lung disease.

11. The answer is B. This patient presents with progressive shortness of breath and wheezing, as well as an obstructive pattern indicated by results of pulmonary function tests (ie, increased residual volume and total lung capacity). He also has hyperinflated lungs with attenuation of bronchovascular markings on a chest x-ray. Together, these findings suggest a diagnosis of emphysema. Additional history reveals that the patient has never smoked and that his father had significant lung disease. All these findings should suggest a1-antitrypsin deficiency.

α1-Antitrypsin deficiency is an inherited disorder that predisposes individuals to early-onset emphysema, usually before the age of 40 years. Classically, social history is often negative for smoking. In the lungs, decreased a1-antitrypsin leads to uninhibited elastase activity in the alveoli, which causes decreased tissue elasticity, resulting in panacinar emphysema. Individuals with a1-antitrypsin deficiency usually demonstrate panacinar emphysema that affects the lower lobes. In contrast, individuals with smoking-induced emphysema typically have centriacinar emphysema, often in the upper lobes. Patients with a1-antitrypsin deficiency are also at risk for liver cirrhosis due to the accumulation of misfolded gene products of a1-antitrypsin in the hepatocellular endoplasmic reticulum. Pancreatic insufficiency is typical of cystic fibrosis, a pulmonary disease with symptoms that begin in childhood. Hematuria with respiratory symptoms is usually seen in patients with Goodpasture syndrome. Granulomatosis with polyangiitis presents with lung pathology and recurrent sinus infections. Stasis, hypercoagulability, and endothelial damage are risk factors for pulmonary embolism.

12. The answer is E. An elderly woman presents with hemoptysis, weight loss, and CT scan results concerning for lung cancer. She requests that the physician temporarily withhold information about her CT scan until she returns from a 5-day vacation.

The patient is overall medically stable based on good general appearance, normal lab work, and stable vital signs. She has historically been compliant with treatment and appointments and will likely follow up with her doctor after her vacation. Her father had lung cancer, and she helped care for him, which suggests she is aware of what the sequelae can be (ie, she is educated about disease). In this case, therefore, the appropriate response would 1) respect the patient's desire not to learn about her diagnosis at this time, and 2) schedule a follow-up appointment now in order to ensure that the patient receives care in a prompt manner. There are two main situations in which it is justified to withhold the truth from a patient: if the physician has compelling evidence that disclosure will cause real and predictable harm (eg, disclosure that would make a depressed patient actively suicidal); or if the patient expresses an informed preference to have the truth withheld. Patients in this situation might ask that the physician instead consult family members. It is critical that the patient give thought to the implications of abdicating their role in decision-making. The principle of autonomy in medicine refers to a physician's need to respect an individual's right to self-determination and create conditions necessary for autonomous choice. If a patient makes an informed decision to have information withheld, their preference should be respected. In this situation, the patient in the vignette is aware of her decision and is making an informed choice for information to be withheld from her for just a short period. The physician should be aware that this patient has the autonomy to make this decision.

Why incorrect answers are wrong:

This patient is currently stable, so waiting five days is not likely to have a significant impact on the prognosis. The patient is indicating that she wants to go on the trip and learn of her diagnosis afterward, and that desire should be respected. There is no reason to postpone her trip to receive the diagnosis.

It is not appropriate for the physician to speak with the patient's husband about the possible diagnosis since the patient has not given permission for disclosure of the diagnosis to her husband. Even though the husband expresses the opinion that the information should not be withheld, the patient's opinion is more important.

While it may indeed be beneficial for this patient to speak with a therapist about her health and future, this is not the appropriate response by the physician at this time because the patient is making a reasonable request and intends to eventually be informed of her diagnosis.

This patient is not in denial about her condition at this point. In fact, her desire to enjoy this last trip without a distressing diagnosis may suggest that she is in fact very aware of the likely results of the CT scan.
Two days versus 5 days will likely not make much of a difference in the course of this patient's condition. This patient should be allowed to enjoy her vacation as she requests.

13. The answer is D. This patient has a history of intermittent asthma and a recent hospitalization due to progressive dyspnea. Patients with persistent asthma, which is characterized by increased frequency of daytime cough, dyspnea, and nighttime awakenings, are usually prescribed inhaled steroids, which reduce inflammation and mucus production. Steroids cause immunosuppression of not only the lungs, but also the oral cavity. This increases the risk of oral candidiasis, also known as thrush (the white, scrapable plaques seen in the image). *Candida albicans*, a yeast that is part of the normal oral flora, can become pathogenic in immunocompromised individuals. Oral nystatin preparations are the first-line treatment for candidiasis and have the least harmful adverse effects (oral nystatin has almost no systemic absorption). Nystatin functions by binding to ergosterol (the sterol specific to fungal cell membranes), forming holes and disrupting the fungal membrane. Albendazole is antihelminthic drug used to treat variety of parasitic infections that do not typically cause oropharyngeal symptoms. Amphotericin B is an antifungal that is reserved for systemic infections. Griseofulvin is used to treat topical fungal infection in skin and hair. Terbinafine is used to treat dermatophyte infections, such as onychomycosis. Oral fluconazole is reserved for treatment of moderate to severe oral candidiasis. Oral fluoride rinse can be used with inhaled steroids, as a preventive measure against oral thrush.

14. The answer is A. This premature infant presents with difficulty breathing and evidence of use of accessory muscles of respiration. An x-ray demonstrates that the lungs have a diffuse ground glass appearance. These findings indicate a diagnosis of neonatal respiratory distress syndrome (NRDS). NRDS is caused by low levels of surfactant, a naturally produced colloid that reduces surface tension in alveoli and makes it easier for infants to breathe. Phosphatidylcholine, also known as lecithin, is the dominant component of pulmonary surfactant. Pulmonary surfactant consists of phospholipids (85%), proteins (10%), and neutral lipids (5%). About 75% of the phospholipids in surfactant are composed of phosphatidylcholine. The lecithin-sphingomyelin (L/S) ratio in amniotic fluid is a marker of fetal lung maturity. The rate of sphingomyelin production is fairly stable during the pregnancy, but the lecithin concentration varies depending on the amount of surfactant, which is produced by type II pneumocytes in the 36th week of gestation. Lower lecithin (phosphatidylcholine) levels indicate that the lungs are immature. An L/S ratio of >2 to 2.5 usually indicates

fetal lung maturity. Surfactant, produced by type II pneumocytes, lines the alveoli. By reducing surface tension, surfactant prevents the alveoli from collapsing. Because premature infants can be deficient in surfactant, they are at increased risk for NRDS. If delivery can be delayed, the mother can be given glucocorticoids, which can help induce production of surfactant in the fetus.
Phosphatidylethanolamines, phosphatidylglycerol, phosphatidylinositol, and sphingomyelin are only minor components of pulmonary surfactant.

15. The answer is C. This patient has a history of unconsciousness plus fever, shortness of breath, and a productive cough with foul-smelling sputum. These findings are all consistent with aspiration pneumonia. Individuals who have lost consciousness, who are debilitated, or who have a history of alcoholism are particularly susceptible to anaerobic lung infections because of an ineffective gag reflex and increased risk of aspirating bacteria from the oral cavity. Aspiration pneumonia produces sputum that is often described as “foul smelling.” The odor is likely caused by anaerobic bacteria from the oral cavity, and patients often have poor dentition. Common oral anaerobes include Peptostreptococcus, Bacteroides fragilis, and Prevotella. Intravenous ampicillin plus sulbactam, in addition to metronidazole, are usually the first-line treatments for aspiration pneumonia. Klebsiella and Pseudomonas are less likely to be responsible for this patient's infection, since he has an intact immune system. Streptococcus pneumoniae is the most common cause of community-acquired pneumonia, but this patient’s history of unconsciousness and a cough productive of foul-smelling sputum suggest that another organism is responsible for his infection. Obligate intracellular bacteria are typically associated with "atypical" pneumonia in which findings include a nonproductive cough.

16. The answer is A. This patient presents with fever, headache, malaise, and a non-productive cough. Given his occupation as a pet-store owner, ongoing exposure to birds should be considered as a risk factor for developing psittacosis, an atypical pneumonia caused by Chlamydophila psittaci. This bacterium has been documented in over 460 species of bird. Infection is usually acquired by inhalation of dried feces that becomes aerosolized when caged birds exercise their wings or in bird-feather dust. C. psittaci infections commonly present with the symptoms demonstrated by this patient. Chest x-ray typically reveals diffuse and bilateral patchy infiltrates. Histology of the specimen obtained by bronchoalveolar lavage would show the presence of cytoplasmic inclusion bodies seen with Giemsa stain. Treatment of choice is a 10- to 14-day course of doxycycline. Intranuclear inclusions are typically seen in cytomegalovirus (CMV) and adenovirus. CMV typically occurs in immunocompromised hosts, whereas, adenovirus typically occurs in young children. Yersinia enterocolitica is seen on light microscopy as a gram-negative rod with bipolar staining and is transmitted via pet feces; however, it does not cause respiratory symptoms. Pneumocystis jirovecii is a

fungus with a fried-eggs appearance or disk shapes on methenamine silver stain. This pathogen causes bilateral and diffuse pneumonia, but typically only in immunocompromised patients. Streptococcus pneumoniae is a gram-positive lancet-shaped diplococcus and is the leading cause of community-acquired lobar pneumonia; in patients with Streptococcus pneumonia infection, lobar consolidation is seen on x-ray in contrast to the diffuse, bilateral, patchy infiltrates seen in this patient with an atypical pneumonia.

17. The answer is C. A 2-year-old boy has a fever; green, malodorous nasal discharge; and tender facial sinuses, most likely secondary to a sinus infection. He also has a history of multiple similar infections and physical exam findings that indicate his heart is on the right side of the chest (dextrocardia), which is confirmed by the chest x-ray. The combination of these symptoms is characteristic of Kartagener syndrome or primary ciliary dyskinesia (PCD), a congenital (autosomal recessive) impairment of mucociliary clearance that is caused by a defect in dynein that prevents effective movement of cilia. Movement of cilia by sliding of the dynein microtubules induces bending of the radial spokes, triggering the sliding of the vertically adjacent dynein microtubule. PCD can be caused by varying mutations in the axonemal dynein arms, inner dynein arms, assembly proteins, and radial spokes. In ciliary dyskinesia, cilia are prevented from beating normally or at all. In ciliary dysplasia, cilia are completely absent. Characteristic manifestations of PCD are caused by impaired congenital positioning of stem cells (situs inversus), impaired clearance of the respiratory tract (infections of the upper and lower respiratory tract, sinusitis, bronchiectasis), and impaired motility of sperm and fallopian tube cilia (resulting in infertility in both males and females). Additional features may include chronic otitis media, headaches, and rhinorrhea. Situs inversus occurs when major organs are reversed from their normal position, such as the heart being on the right side of the chest instead of the left. This occurs in about 50% of affected individuals. Defective chloride transport occurs in patients with cystic fibrosis and is associated with chronic respiratory infections but not with situs inversus. Elevated blood sugar is found in patients with diabetes and can cause chronic infections but is unlikely to be diagnosed at this age and is not associated with situs inversus. Kyphoscoliosis is a spinal column abnormality that is more commonly associated with cystic fibrosis. Tetralogy of fallot is a congenital cyanotic heart defect that is not associated with chronic respiratory infections or situs inversus.

18. The answer is C. This patient presents with fever, myalgia, cough, headache, nausea, and vomiting. He has dyspnea, and a chest x-ray reveals bilateral lung infiltrates and pleural effusions, indicative of pulmonary edema. His laboratory findings show leukocytosis, thromobocytopenia, and elevated liver enzyme levels. All of these point to a diagnosis of hantavirus cardiopulmonary syndrome. Hantavirus is in the bunyavirus family. Another bunyavirus, Crimean-Congo hemorrhagic fever,

might present with similar symptoms, but it has been identified only in Africa, the Middle East, and Eastern Europe. Hantavirus is found in North, Central, and South America; infections in the United States are most commonly observed in the southwestern states of Utah, New Mexico, Colorado, and Arizona where this patient lives. In contrast with most other bunyaviruses, which are transmitted by arthropod vectors (mosquitoes, ticks, or sand flies), transmission of hantavirus occurs through contact with rodents. Deer mice are the natural reservoir for the hantavirus, and transmission occurs through contact with their feces. The remaining answer choices represent common vectors and reservoirs of infectious diseases. However, this patient's geographic location and progression of symptoms are most consistent with hantavirus. Ticks are associated with a number of viral, bacterial, and protozoal diseases, including Lyme disease. Bats are associated with various pathogens, including SAR-like coronavirus and rabies virus. Mosquitoes are vectors for many infectious diseases, including malaria. Reduviid bugs are vectors for *Trypanosoma cruzi* infections, which cause Chagas disease.

19. The answer is E. The key to this question is to start with the patient's cystic fibrosis (CF), supported by his recurrent pneumonia with bronchiectasis, steatorrhea, with urolithiasis (fat binds calcium in the gut, causing increased uptake of oxalate and hyperoxaluria), family history of meconium ileus and rhinosinusitis, history of cholecystectomy (caused by insippated bile and bile acid loss with subsequent production of lithogenic bile), and his ongoing pulmonary and liver issues. The pathology stems from a defective chloride channel (CFTR mutation) which renders secretions thick and prone to blockage. This results in a myriad of pathology, including infertility, fractures and kyphoscoliosis (caused by vitamin D malabsorption), and anemia. For patients with CF who are older than 21 years of age, Pseudomonas is the most common cause of pneumonia. In patients younger than 21 with CF, the most common infective organism causing pneumonia is Staphylococcus aureus.Piperacillin is a broad-spectrum antibiotic in the penicillin class. It is susceptible to β-lactamase (a defense mechanism found in certain strains of bacteria that renders penicillins ineffective) so is commonly used with tazobactam (a β-lactamase inhibitor) to enhance its effectiveness. The other antibiotic agents listed: ampicillin, cefuroxime, erythromycin, and metronidazole are not effective against Pseudomonas aeruginosa.

20. The answer is E. Zileuton is a 5-lipoxygenase pathway inhibitor that blocks the conversion of arachidonic acid to potent bronchoconstrictors called leukotrienes. By inhibiting leukotriene production, zileuton decreases the tone of the bronchial smooth muscle, making it an effective therapy for patients with chronic asthma. Zileuton can be prescribed for adults and children ≥12 years of age, but it is not indicated for relief of acute bronchospasm. In rare cases, zileuton can cause adverse events, such as hepatotoxicity with symptoms including dark urine, clay-colored stools, jaundice, skin

bruising, tingling or numbness, and weakening of muscles.
None of the other medications listed inhibit specific enzymes as a primary mechanism of action. Omalizumab is an anti-IgE antibody that works upstream from lipoxygenase, preventing IgE from binding to mast cells and their subsequent degranulation. Albuterol and ipratropium work by modifying the sympathetic and parasympathetic receptors with the overall function of relaxing bronchial smooth muscle. Zafirlukast is a leukotriene receptor blocker and therefore works downstream from lipoxygenase.

21. The answer is A. This patient has constitutional symptoms (eg, weight loss, malaise), a history of chronic sinusitis, and new-onset hemoptysis, dyspnea, and diffuse crackles heard on lung auscultation, accompanied by decreased urine output and a high blood urea nitrogen/creatinine level. This history suggests a small-vessel vasculitis (SVV). Patients affected by a SVV have a pulmonary-renal syndrome that can present with symptoms similar to those experienced by this patient.

Pulmonary vasculature SVV, which causes diffuse alveolar hemorrhage, is characterized by hemoptysis and shortness of breath.

Renal vasculature SVV, which causes acute glomerulonephritis, is characterized by decreased urine output and elevated serum creatinine.

Although any of the antineutrophil cytoplasmic antibody (ANCA)–associated vasculitides (AAVs) may present as pulmonary-renal syndrome with pauci-immune glomerulonephritis, this patient has the characteristic history and physical examination findings ofgranulomatosis with polyangiitis(GPA): history of chronic sinusitis and nasal crusting and bloody nasal discharge, which are suggestive of destructive upper airway involvement. GPA andmicroscopic polyangiitis(MPA) are remarkably similar, differentiated only by the presence of upper or lower respiratory tract destruction and the presence of granulomatosis as determined by lung or kidney biopsy findings. Common symptoms and signs of GPA and MPA include constitutional symptoms (eg, fatigue, fever, weight loss, malaise), renal-pulmonary syndrome (eg, rhinosinusitis, cough and dyspnea, urinary abnormalities), and skin abnormalities (especially purpura). Both are ANCA positive and cause tissue necrosis without the use of immune complexes. GPA and MPA are so similar to one another that they are thought to represent a spectrum of disease. The largest group of SVVs is the AAVs, characterized by the presence of ANCA and the lack of immune complex formation. The characteristic renal involvement due to AAVs is known as pauci-immune glomerulonephritis, meaning “lack of” immune complexes. The AAVs are:

GPA, formerly known as Wegener granulomatosis

Eosinophilic granulomatosis with polyangiitis, formerly known as Churg-Strauss syndrome.

The other answer choices are incorrect.

Thromboangiitis obliterans is a medium-vessel vasculitis. It usually occurs in young males with a history of heavy tobacco use and is characterized by distal extremity gangrene and digital amputation.
Polyarteritis nodosa is a medium-vessel vasculitis. It involves the formation of immune complexes and is associated with visceral involvement and hepatitis B infection.
IgA vasculitis, also known as Henoch-Schönlein purpura, is a small-vessel vasculitis that causes arthralgia, abdominal pain, and IgA nephropathy.
Non–small-cell lung cancers most often present with cough with or without blood and in patients who have a history of tobacco use (not seen in this patient). This patient also has evidence of kidney disease (creatinine level of 2.0 mg/dL), which should prompt consideration of multisystem diseases.

22. The answer is C. This patient was found unconscious with a low respiratory rate, likely caused by ethanol and opioid intoxication resulting in respiratory depression. A low respiratory rate leads to ventilatory failure and retention of carbon dioxide, causing respiratory acidosis. These effects are signaled by the patient's low pH and elevated partial pressure of carbon dioxide on arterial blood gas analysis; his normal bicarbonate level and normal base excess rule out a metabolic component. Acidemia, as seen in this patient, is a condition that shifts the oxygen-hemoglobin dissociation curve to the right (see dotted line on image). In other words, hemoglobin's affinity for oxygen is reduced. This reduction in affinity enables increased delivery of oxygen to peripheral tissues where the pH is low. Other conditions that cause a right shift in the oxygen-hemoglobin dissociation curve include increased temperature, increased 2,3-bisphosphoglycerate (2,3-BPG), and increased metabolic demands, for example, in exercise. During exercise, lactic acid builds up in tissues and causes a metabolic acidosis that shifts the curve in the same way as respiratory acidosis. This patient's signs, symptoms and findings do not indicate inhalation of carbon monoxide (CO) and CO poisoning. CO stabilizes the relaxed form of hemoglobin so that it has increased affinity for oxygen, preventing oxygen from being unloaded to tissues. Protracted vomiting typically leads to metabolic alkalosis and an increase in pH, which causes hemoglobin to have an increased affinity for oxygen. Decreased hematocrit does not intrinsically change the affinity of hemoglobin for oxygen.

23. The answer is C. Cystic fibrosis (CF) is an autosomal recessive disease that most commonly occurs in the white population. The most common mutation of CFTR protein, delta F508 (class II) is on chromosome 7 and is found in approximately 70% of patients with CF worldwide. It is a deletion of three nucleotides for phenylalanine (hence, the F) at positions 507 and 508 (hence, the 508) of the *CFTR* gene, which causes misfolding that prevents the product's movement from the endoplasmic reticulum to the Golgi apparatus (cell trafficking). Other mutations specific to CF have been classified into five or six groups. Class I through class V mutations are

summarized in the table. Although all of the answer choices can cause CF, this is by far the most common and likely mutation in this patient.

24. The answer is C. In this experiment, isolates of the bronchial smooth muscle are exposed to various drug preparations. Drug X and Drug Y are mislabeled and must be identified through the mechanism demonstrated in the graph. To identity Drug Y, look at the mechanism of Drug X. Drug X, a muscarinic agonist, causes bronchial contraction when exposed to the smooth muscle alone, as seen by the graph. Muscarinic agonists, such as methacholine, induce bronchoconstriction through the M3 (Gq) receptor pathway, a likely mechanism for Drug X.

In the body, acetylcholine is released from postganglionic parasympathetic fibers located in the viscera of the target organ onto muscarinic receptors. A number of physiological effects are under parasympathetic control, including exocrine gland secretion (lacrimal, sweat, salivar, gastric acid), peristalsis contraction, bladder contraction, miosis (pupillary muscle contraction), eye accommodation (ciliary muscle), and insulin release. Physostigmine is an acetylcholinesterase inhibitor that increases the concentration of acetylcholine that may act on the muscarinic receptors. In patients with an atropine overdose (increased temperature, decreased secretion, flushing, blurred vision, and altered mental status), physostigmine may be used to overcome the muscarinic antagonism. Because of its large volume of distribution and penetration into the central nervous system, it is better at fixing the altered mental status as compared to other acetylcholinesterase drugs, such as pyridostigmine.

The M3 receptor is a Gq protein receptor mediated through the inositol-1,4,5-triphosphate/diacylglycerol (IP3/DAG) intracellular pathway to induce contraction of smooth muscle. Acetylcholine binds the M3 receptor inducing activation of phospholipase C (PLC) to cleave phosphatidylinositol 4,5-bisphosphate (PIP2) into IP3 and DAG. These products then carry out intracellular cascades and target functions. IP3 subsequently increased intracellular calcium ($Ca2^{+}$) ion concentrations required for smooth muscle contraction and activate protein kinase C (PKC). DAG directly activates protein kinase C (PKC). PKC is required to activate myosin light-chain kinase (MLCK) that ultimately induces the smooth muscle contraction of the target cell. In the case above, the bronchial smooth muscle is the target cell activated by the muscarinic cascade. The mechanism of the muscarinic receptor can be confirmed in the presence of physostigmine (an acetylcholinesterase inhibitor) by the synergistic effect it has on the bronchial cells. The effect is an increased strength of smooth muscle contraction from the increased acetylcholine (ACh) activating on the muscarinic receptors and the muscarinic agonist provided by Drug X.

When Drug X, a muscarinic agonist, is exposed to the cell in combination with Drug Y, the contractile response is diminished. This evidence shows that Drug Y is inhibiting the mechanism of Drug X and confirms that Drug Y is a muscarinic

antagonist. Ipratropium is a muscarinic antagonist used in the treatment of chronic obstructive pulmonary disease (COPD). By inhibiting the intrinsic smooth muscle concentration of the bronchioles, the airway remains patent. A patent airway decreases the work of breathing by providing increased airflow to the alveoli.
The other options are incorrect for the following reasons:
Methacholine is a muscarinic agonist used in the diagnosis of asthma. By activating the muscarinic receptors it would increase smooth muscle contraction of airway and decrease lumen diameter. Drug X could be methacholine, as the graph demonstrates it to increase bronchial smooth muscle contraction in the presence of acetylcholine.
Bethanechol is a direct muscarinic agonist used in the treatment of urinary retention and overflow incontinence. It is resistant to acetylcholinesterase, increasing the duration of action of the drug. Bethanechol is specific in its mechanism to targeting the muscarinic receptors of the bladder so as not to cause other systemic adverse effects. Little change would be observed in regards to bronchial smooth muscle contraction.
Pilocarpine is a muscarinic agonist used in the treatment of Sjögren syndrome. It may cause an induction of smooth muscle similar to Drug X, but the effects are more specific for exocrine gland function. The graph would show a moderate increase in smooth muscle contraction. Exposure to pilocarpine could be demonstrated by a patient with increased sweating, tear production, and salivation.
Neostigmine acetylcholinesterase inhibitor is used in the treatment of myasthenia gravis. It prolongs ACh action at the neuromuscular junction, similar to the effects observed by physostigmine in the graph. Unlike physostigmine, it does not cross the blood-brain barrier, limiting the effects on the CNS and specifically targeting peripheral muscle targets.

25. The answer is B. This patient with asthma is experiencing a tonic–clonic seizure after overdosing on theophylline in a suicide attempt. The drug theophylline is a phosphodiesterase inhibitor and adenosine receptor blocker that leads to the decreased hydrolysis of cAMP to adenosine monophosphate. An overdose of theophylline will therefore result in an elevated intracellular level of cAMP, which enhances β-adrenergic effects, leading to metabolic complications such as hypokalemia, hypomagnesemia, hypo/hypercalcemia, hyperglycemia, and metabolic acidosis. Clinically, a patient overdosing on theophylline can present with tachypnea, arrhythmia, and seizures secondary to the metabolic complications. In addition, β2-adrenergic-mediated vasodilation can contribute to hypotension and reflex tachycardia in these patients. β1-blockers such as metoprolol may therefore be given to reduce cAMP levels through inactivation of adenylate cyclase. A cardioselective β-blocker must be used in patients with asthma to avoid inducing bronchial hyperreactivity. Initial hypotension treatment would be with rapid infusion of isotonic saline. If the hypotension does not respond, alpha1-adrenergic agonists such as

phenylephrine or norepinephrine can be used. This patient's seizure should be treated with benzodiazepines. The table below details the functions of the three β-receptors. Medications that increase activation of adenylate cyclase and increase cAMP would potentiate the effects of theophylline and would be dangerous in this patient. These medications include all beta-adrenergic receptor agonists and other sympathomimetic drugs. Phosphodiesterase inhibitors such as dipyridamole (platelet de-aggregant and vasodilator, cilostazol (vasodilator used in peripheral arterial disease), milrinone (used in acutely decompensated heart failure) would prevent degradation of cAMP like theophylline and increase its toxicity. Prolonged GABA opening occurs with the use of barbiturates and would not counter the increased cAMP secondary to theophylline toxicity.

Beta-Receptor Chart

Receptor	Neurotransmitter	Result of Ligand Binding	Function
β_1	NE = Epi	Enhance adenylyl cyclase, ↑ cAMP	-Juxtaglomerular cells → ↑ renin release -Heart → ↑ inotropy, chronotropy, and dromotropy
β_2	NE « Epi	Enhance adenylyl cyclase, ↑ cAMP	-Tracheal/bronchial muscle, uterine, and vascular smooth muscle dilation -Mucous clearance -Arterioles in muscles and veins→ ↑ vascular flow to striated muscles via vasodilation -↓ gut motility & tone -Urinary bladder detrusor muscle relaxation -Skeletal muscle → promotes potassium uptake, ↑ contractility, glycogenolysis -Liver → ↑ glycogenolysis and gluconeogenesis -Induces ciliary muscle relaxation for far vision -Thickens saliva
β_3	NE » Epi	Enhance adenylyl cyclase, ↑ cAMP	-Fat cells → Activates lipolysis

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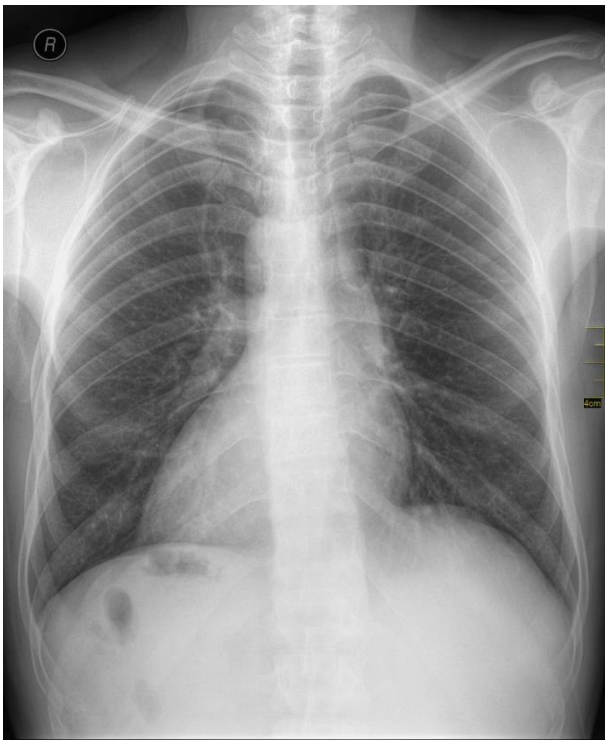
26. The answer is A. This pediatric patient is presenting with symptoms of acute otitis media of the right ear, as evidenced by ear tugging, fever, and a bulging tympanic membrane on physical examination. In addition, his history is significant for recurrent sinus infections and inaudible heart sounds on the left side of the chest, indicating that he likely has situs inversus, or dextrocardia, as shown in the image. Given these findings, this patient most likely has Kartagener syndrome. Kartagener syndrome (a subgroup of primary ciliary dyskinesia) is a condition caused by an autosomal recessive defect in the molecular motor protein dynein. This genetic defect results in immotile cilia, impairing a number of important processes. Recurrent sinusitis caused by a failure in bacteria and particle clearance

and bronchiectasis caused by a nonfunctional mucociliary elevator are both features of Kartagener syndrome. In addition, most men are infertile due to immotile sperm (azoospermia), or decreased ciliary motility. Female infertility or subfertility can also occur due to immotile cilia in the fallopian tubes, with higher rates of ectopic pregnancy. Less than 50% of women with Kartagener syndrome complete pregnancy successfully. Situs inversus has no bearing on the function of the heart itself, and therefore the patient is not at increased risk for heart failure or a murmur such as mitral regurgitation. Patients with α_1-antitrypsin deficiency present with early-onset emphysema (age ≤45), but they are predisposed to lower respiratory infections, such as bronchitis and pneumonia, rather than the sinus and ear infections experienced by this patient. Differentiating cystic fibrosis from Kartagener syndrome on the basis of clinical symptoms can be difficult because they present with the same respiratory features, such as recurrent and chronic sinopulmonary infections and bronchiectasis. However, they have different extrapulmonary features in that Kartagener syndrome is associated with situs inversus, infertility due to immotile spermatozoa, and normal growth. Cystic fibrosis, however, presents with pancreatic insufficiency, male infertility due to the absence of the vas deferens, and failure to thrive, which is not present in this patient, given his normal growth curve.



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27. The ansewer is D. This patient, who was hospitalized and restrained because of her acute psychotic symptoms, has been immobilized for several days. Her symptoms of tachycardia and sharp chest pain after this immobilization make the possibility of a pulmonary embolism (PE) very likely. This condition is characterized by acute occlusion of a pulmonary artery caused by a thrombus. Patients with a PE usually present with sudden chest pain that is worse on inspiration or coughing. This pleuritic

pain is due to the inflammation of the pleura caused by an inflammatory response to the occlusion of the vessel. Of note, on physical exam, patients will have clear lungs to auscultation which usually helps to rule out other causes of chest pain and dyspnea. The severity of the occlusion is usually assessed by its location. Occlusion at peripheral vessels usually causes less hemodynamic compromise, in contrast to central occlusion, which can cause hemodynamic instability and even sudden death.

The Virchow triad describes the three major risk factors for PE: stasis, hypercoagulability, and endothelial damage. In this patient, extended immobilization and venous stasis caused formation of deep vein thrombosis, which embolized to the lung. A PE is treated with immediate anticoagulation, such as intravenous administration of heparin, to prevent further propagation of the clot. The body's natural thrombolytic system will slowly dissolve the clot over time; therefore thrombolytics are not indicated. Patients usually receive oral anticoagulation therapy with warfarin for 6 months after the event. Antipsychotics such as haloperidol can cause extrapyramidal symptoms such as acute dystonia, akathisia, parkinsonism, and tardive dyskinesia. Discontinuing the patient's haloperidol would not alleviate her pulmonary condition. β- Blockers are indicated for patients with ischemic heart disease and have no role in management of a PE. Prophylactic antibiotics are indicated for patients who present with community-acquired pneumonia, chronic obstructive pulmonary disease, or asthma exacerbations. Patients with clinical signs of PE must immediately begin receiving anticoagulants. There should be no watchful waiting.Thrombolysis is only indicated for patients with a massive PE and signs of hypotension and right ventricular dysfunction, which are not seen in this patient. Thoracentesis is indicated for the diagnosis, and possibly treatment, of pleural effusion.

28. The answer is E. This young man with dyspnea, hemoptysis, and elevated blood pressure has proteinuria and red blood cell casts on urinalysis. These symptoms indicate a rapidly progressive glomerulonephritis, more specifically, Goodpasture syndrome. This is an idiopathic autoimmune disease in which antibodies target the non-collagenous domain of the α-3 chain of type IV collagen. Positive anti-GBM antibodies are required to confirm the diagnosis. Individuals with anti-GBM antibodies do not always progress to lung involvement, however the incidence is higher among those with a history of smoking or lung injury. Goodpasture disease carries a high risk for alveolar hemorrhage. Pulmonary function tests would show a restrictive lung disease pattern with a decreased total lung capacity, decreased forced expiratory volume in 1 second (FEV1), decreased forced vital capacity (FVC), and a normal FEV1:FVC. Treatment involves plasmapheresis, prednisone, and cyclophosphamide.

DLCO (diffusing capacity of lung for carbon monoxide) is a measure of the effectiveness of general gas diffusion across the alveolar space. Carbon monoxide is used in the determination of diffusion across the respiratory membrane as it is neither

generated nor used by the body. It is generally reduced in patients with restrictive lung disease because the alveolar-capillary membrane is either thickened or there is reduced red blood cells in the capillaries thereby reducing the capacity for carbon monoxide diffusion. However, in the case of Goodpasture syndrome, the excess hemoglobin present due to alveolar hemorrhage binds more carbon monoxide than could normally be bound by the capillaries in restrictive diseased lungs, giving a falsely elevated DLCO. Increased functional residual capacity, increased residual volume, and increased total lung capacity are all seen in obstructive lung diseases like asthma, COPD, and emphysema. Goodpasture disease shows a restrictive lung disease pattern.

29. The answer is B. This patient presents with shortness of breath and peripheral edema. He has an increased anteroposterior diameter and prolonged expiration, as well as evidence of chronic respiratory acidosis with metabolic compensation on blood gas analysis. These findings are strongly suggestive of chronic obstructive pulmonary disease (COPD). Although the patient's occupational history puts him at risk for restrictive lung disease, his physical examination findings make this diagnosis unlikely. Arterial blood gas analysis in cases of COPD shows disturbances due to impaired excretion of carbon dioxide from the lungs. The resulting gas demonstrates normal or mildly decreased pH with an elevated carbon dioxide level. Because this is a chronic process, metabolic compensation usually occurs, and patients will have an elevated bicarbonate level that brings the pH close to normal. Characteristic spirometry findings for patients with obstructive lung diseases are reductions of forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) and a decreased FEV1:FVC ratio. Total lung capacity (TLC) is increased due to lung hyperinflation, as shown in the x-ray (see image), secondary to expiratory flow limitation.

The other spirometry patterns would not be seen in a patient with an obstructive lung disease. A indicates neither an obstructive nor a restrictive pattern. FEV1 and FVC are decreased in obstructive processes; lung volumes such as the residual volume, functional residual capacity, and TLC are increased. C shows changes that are consistent with restrictive lung disease. Although the patient's occupational history would suggest restrictive lung disease, his physical findings are more consistent with obstructive lung disease. As a result of air trapping and chronic changes in pulmonary architecture, TLC is increased in obstructive processes. D is very similar to an obstructive pattern but incorrectly displays an increased FVC. Although the TLC and residual volume are both increased in obstructive processes, the greater increase is in residual volume, such that the vital capacity is actually decreased. E displays multiple errors, including an increase in the FEV1:FVC ratio, which would not be seen in an obstructive process.

30. The answer is E. This patient presents with exertional dyspnea and a long-term history of cigarette smoking, hypertension, type 2 diabetes mellitus, and

hyperlipidemia. He should first be evaluated for coronary artery disease (CAD). The patient had a normal stress test and could achieve 85% of his maximum target heart rate indicating the test was reliable (with 80% confidence) for being negative for CAD. However, he became short of breath during the stress test and was shown to have a mean pulmonary artery pressure >25 mmHg, indicating pulmonary hypertension. Administration of albuterol did not relieve the patient's symptoms, but he did improve with the administration of ipratropium, indicating that he does not have asthma but does have chronic obstructive pulmonary disease(COPD). Studies have shown that with dyspnea in the setting of COPD with a non-reversible airway, better relief is achieved with ipratropium over beta 2-agonists. Pulmonary hypertension can be seen in obstructive and restrictive lung disease; however, as this patient's symptoms resolved with ipratropium, an obstructive disease is the most likely underlying cause of his condition.

Obstructive lung diseases are characterized on pulmonary function testing as:

a decreased forced expiratory volume in one second (FEV1) due to obstruction on expiration

a decreased forced vital capacity (FVC)

a decreased FEV1:FVC ratio because the FEV1 is decreased more than the FVC

an increased total lung capacity, as air becomes trapped in the lungs due to obstruction.

The final characteristic can occur with airway constriction due to hyper-responsiveness to stimuli, or from increased compliance and loss of elastic fibers causing early airway collapse. These characteristics are seen in Choice E.

Choice A shows an increased forced expiratory volume in one second (FEV1). There are few (if any) means to increase this parameter. An increased forced vital capacity (FVC), part of Choice B, would not be seen in obstructive or restrictive diseases because it represents the volume of air that is expelled during expiration. Choice C is not correct because a reduction in FEV1 and FVC with a normal FEV1:FVC ratio are consistent with pulmonary function test findings of restrictive lung diseases. Choice D represents findings that would be seen in restrictive lung disease with the reduction in both FEV1 and FVC, a normal FEV1:FVC ratio, and overall reduced total lung capacity.

ANSWERS MCQs STEP 1

1. The answer is D. CO_2 reacts with H_2O to form H_2CO_3 (carbonic acid), in a reaction catalyzed by carbonic anhydrase. Carbonic acid then dissociates to form HCO_3^-. Approximately 90% of the
total CO_2 in the blood is carried as HCO_3^-. H_2CO_3 rapidly dissociates after being formed and a negligible fraction of blood CO_2 is carried in this form (choice D). Some CO_2 is carried bound to hemoglobin, as carbamino compounds (choice A). This is a small fraction of the total CO_2 (5%). Asimilar small fraction (5%) of total CO_2 remains dissolved in solution (choice B). Given that normal blood pH is near 7, essentially no HCO_3^- dissociates to form CO_{3-2} (choice C).

2. The answer is B. Bronchiole volume contributes to dead space volume, so increasing bronchoconstriction would decrease bronchiolar volume and thus decrease dead space volume. Bronchoconstriction is a major determinant of airway resistance to air flow. Leukotrienes, by increasing airway constriction, would increase resistance to air flow (choice A). Lung elastic tissue and alveolar surface tension determine lung compliance (choice D), which should not be affected by airway leukotrienes exposure. FRC (choice C), the point of mechanical balance between chest wall and lung, is dependent on lung compliance and, similarly, would not be affected by leukotrienes exposure. Any bronchoconstriction would slightly decrease total lung capacity (choice E).

3. The answer is A. Pulmonary fibrosis is a restrictive lung disease. Figure 2-12 illustrates pulmonary function testing data in a normal subject and a patient with fibrosis. Volume-time curves reveal FEV1 and FVC in both subjects. The FEV1/FVC ratio, which is typically about 0.8, is increased in patients with pulmonary fibrosis. Lung volumes such as vital capacity (choice E) are decreased. Patients with restrictive lung disease tend to exhibit shallow breathing, thus tidal volume is decreased (choice D). Increased elasticity causes a decrease in FRC, the mechanical balance point between lungs and chest wall (choice B). Though as noted above and illustrated in Figure 2-29 the FEV1/FVC ratio is increased in patients with pulmonary fibrosis, FVC itself is decreased (choice C).

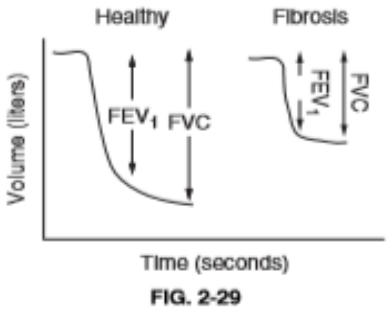

FIG. 2-29

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4. The answer is D. The plot shows that carbon monoxide fails to equilibrate with pulmonary capillary blood during the time that blood is exposed to alveolar air. Since pulmonary partial pressure rises to only a few percent of alveolar partial pressure, carbon monoxide is a diffusion-limited gas. In contrast, nitrous oxide, which does equilibrate, is a perfusion-limited gas (choice E). Carbon monoxide does cross the respiratory membrane (choice C), dissolve in pulmonary capillary blood (choice A), and binds with hemoglobin (choice B). In fact, its affinity for hemoglobin is about 250-fold greater than that of oxygen.

5. The answer is C. Destruction of lung tissue is a hallmark of emphysema. Due to this loss of elastic tissue, lung elastic recoil is decreased. Decreased elastic recoil (not increased, choice E) shifts the mechanical balance point between chest wall and lung to a higher volume—FRC is, therefore, increased. The barrel chest is characteristic of emphysema. Destruction of alveolar walls impairs gas exchange, causing an increase in physiological dead space (choice A). Tissue loss also causes a loss of radial traction with an increase in airway resistance—FVC is decreased (choice D). Emphysema is one type of chronic obstructive pulmonary disease. A decrease in the FEV1/FVC is characteristic of an obstructive disease (choice B).

6. The answer is E. At high elevation the decreased atmospheric pressure means that there is less available O_2. Decreased arterial PO_2 is sensed by peripheral chemoreceptors with a resultant increase in ventilation. Hyperventilation helps to bring alveolar and thus arterial O_2 levels back toward normal. In hypoxic conditions, erythrocyte 2,3-DPG levels (choice D) increase. This causes the oxygen-hemoglobin dissociation curve to shift to the right—thereby delivering a greater fraction of hemoglobin bound O_2 to the tissues. At high elevation EPO levels (choice C) increase because the kidneys sense low-tissue oxygenation and respond by releasing EPO into the circulation. This hormone stimulates erythrocyte production thereby increasing total blood hemoglobin levels, helping to offset the hypoxia. In low-O_2 conditions slight bronchoconstriction (choice A) can occur.

7. The answer is C. Compliance of the lung is the change in lung volume divided by the change in airway pressure ($\Delta V/\Delta P$). This patient's lungs have a compliance of 4 L/10 cm H_2O = 400 mL/cm H_2O. Lung elasticity (choices A and B) is the inverse of compliance, and this patient's lungs have an elasticity of 1.25 cm H_2O/L.

8. The answer is B. Respiratory alkalosis is due to hyperventilation, which lowers CO_2. Decreasing tidal volume will reduce alveolar ventilation and correct the respiratory alkalosis. Assuming a dead space of 150 mL, alveolar ventilation in this patient is 450 mL × 12/min = 5400 mL/min. If the tidal volume were decreased from 600 to 300 mL and the frequency increased from 12 to 24 per minute, then the alveolar ventilation would decrease to 150 ×24/min = 3600 mL/min even though the minute ventilation (12 ×600 mL/min = 24 × 300 mL/min) remains unchanged. The fraction of

O_2 (choice D) in the respiratory air does not affect respiratory volumes or frequencies in a mechanically ventilated patient. Increasing minute ventilation (choice C) or decreasing dead space (choice A) would increase alveolar ventilation and worsen respiratory alkalosis. PEEP(choice E)is positive pressure applied during the expiratory phase to prevent the collapse of alveoli and to increase FRC of the lungs. It is used primarily to improve arterial oxygenation in severely hypoxic patients.

9. The answer is A. Many sputum specimens are cultured unnecessarily. Sputum is often contaminated with saliva or is almost totally made up of saliva. These specimens rarely reveal the cause of the patient's respiratory problem and may provide laboratory information that is harmful. The sputum in the question appears to be a good specimen because there are few epithelial cells. The pleomorphic, gram-negative rods are suggestive of Haemophilus, but culture of the secretions is necessary. Normal flora from a healthy oral cavity consists of gram-positive cocci and rods, with few or no PMNs.

10. The answer is A. The key diagnostic finding is the morphology of the yeast isolated from the granulomatous, supurative lesions of the lung. Blastomyces dermatitidis, which causes blastomycosis, grows in the yeast form in infected tissues. The bud of growing yeast is attached to the parent cell by a broad base. Although the fungi that cause all other diseases listed in the question grow in yeast form in infected tissues, most buds are attached to the parent cell by a narrow base.

11. The answer is B. During a forced vital capacity (FVC), the patient is asked to breathe in as much air as possible (up to the total lung capacity), and then exhale all of the gas in her lung as fast as possible, which, in this case is 3.5 L. The FEV1.0 is the volume of gas expelled from the lung during the first second, which, in this case, is 2 L. The ratio of the FEV1.0 to the FVC in this patient is 2 L/3.5 L, which equals 0.57. Normally, FEV1.0/FVC should be $\geq$0.8. The decreased FEV1.0/FVC is indicative of an obstructive impairment. Obstructive lung diseases, such as asthma, are characterized by a greater-than-normal total lung capacity (TLC), residual volume (RV), and functional residual capacity (FRC). The inspiratory and expiratory reserves (inspiratory capacity and expiratory volume) are decreased, as is the vital capacity and the maximum voluntary ventilation.

12. The answer is C. The term asthma derives from a Greek word that means, literally, "to pant." In severe asthma attacks such as the one we describe here the hyperpnea precedes the likely development of ventilatory depression and, ultimately, ventilatory arrest. It is a sometimes successful and sometimes futile physiologic response elicited to increase ventilatory oxygen uptake and eliminate excess CO_2, although it may be insufficient to raise arterial O_2 saturation adequately and more than sufficient to induce metabolic alkalosis from excess CO_2 loss. Nonetheless, it is a "protective" response, and breathing too quickly, even inefficiently, is better than not breathing at all. This

leads to the admonition: Never give a drug that can depress ventilation or the normal ventilatory drive to an asthma patient unless he or she has a protected airway and ventilation can be controlled and supported mechanically. IV midazolam (or the IV administration of virtually any other benzodiazepine, opioid, or barbiturate) will allay anxiety, but will also tend to suppress ventilatory drive and hasten the onset of ventilatory arrest. In the scenario described here, diazepam is the wrong drug to give. Albuterol (a) or a similar β2 agonist bronchodilator, whether given by inhalation or parenterally, would not be expected to worsen the boy's ventilatory status. They should not be the only drugs relied on, but they would be appropriate adjunctive treatments, as would be all the rest for the stated purposes. As an important aside, you may recall that atropine (b) and other drugs with antimuscarinic activity have bronchodilator activity, but also tend to make airway mucus secretions more viscous, leading to airway mucus plugging. In the context of this scenario, with the administration of other drugs that we listed, and the availability of airway suctioning devices as needed, the mucus-thickening effects of an antimuscarinic should not be a problem with which we cannot easily deal by way of airway suctioning and the administration of mucus-thinning (mucolytic) drugs. Glucocorticoids (d) and nebulized saline would be valuable, if not essential, adjuncts to this boy's therapy.

13. The answer is B. Severe acute respiratory distress syndrome (SARS) is a highly contagious and very severe atypical pneumonia that was first described in the fall of 2002. The illness was particularly prevalent among the young and health care workers. In March of 2003, investigators identified the cause of SARS as a novel coronavirus (SARS-CoV). Note that the two main strains of human coronaviruses, types 229E and OC43, are major causes of the common cold. It appears that the SARS-CoV may be the first coronavirus to cause severe disease in otherwise healthy individuals as it differs from previous coronaviruses because it can infect the lower respiratory tract and spread throughout the body. Patients develop a dry cough with fever, chills, and malaise after an incubation of up to 10 days. In contrast to atypical pneumonia caused by Mycoplasma, SARS is not usually associated with a sore throat. Up to one-third of the patients improve, but the majority of patients progress to severe respiratory distress and almost 10% die from the disease. The diagnosis of SARS relies on the presence of fever and respiratory symptoms. Interestingly, the most consistent laboratory finding occurring early in the disease is peripheral lymphopenia. Examination of lung tissue from confirmed cases has revealed the presence of hyaline membrane formation, interstitial mononuclear inflammation, and desquamation of pneumocytes into the alveoli. The Center for Disease Control (CDC) has defined several criteria to be used in the diagnosis of SARS. One of the epidemiologic criteria is: "travel (including transit in an airport) within 10 days of symptom onset to an area with current, recently documented, or suspected community transmission of SARS", such as China or Hong

Kong. In contrast to Coronavirus, the Hantavirus genus belongs to the Bunyaviridae family and includes the causative agent of a group of diseases that occur throughout Europe and Asia and are referred to as hemorrhagic fever with renal syndrome. The characteristic features of this syndrome are hematologic abnormalities, renal involvement, and increased vascular permeability. Respiratory involvement is generally minimal in these diseases. Although several species of rodents in the United States are known to be infected with Hantavirus, no human cases were reported until an outbreak of severe, often fatal respiratory illness occurred in the United States in May 1993 in the Four Corners area of New Mexico, Arizona, Colorado, and Utah. This illness resulted from a new member of the genus Hantavirus that caused a severe disease characterized by a prodromal fever, myalgia, pulmonary edema, and hypotension. The main distinguishing feature of this illness, which is called Hantavirus pulmonary syndrome, is noncardiogenic pulmonary edema resulting from increased permeability of the pulmonary capillaries. Laboratory features common to both Hantavirus pulmonary syndrome and hemorrhagic fever with renal syndrome include leukocytosis, atypical lymphocytes, thrombocytopenia, coagulopathy, and decreased serum protein concentrations. Abdominal pain, which can mimic an acute abdomen, may be found in both Hantavirus pulmonary syndrome and hemorrhagic fever with renal syndrome. Dengue fever virus is a type of flavivirus, and flaviviruses are similar to alphaviruses. Dengue fever (breakbone fever) is initially similar to influenza but then progresses to a rash, muscle pain, joint pain, and bone pain. It can produce a potentially fatal hemorrhagic disorder. Ebola virus is a member of the Filoviridae family, which causes a severe hemorrhagic fever. Outbreaks occur in Africa and typically make the national news.

14. The answer is D. Granulomatous inflammation is characterized by the presence of granulomas, which by definition are aggregates of activated macrophages (epithelioid cells, not epithelial cells). These cells may be surrounded by mononuclear cells, mainly lymphocytes, and multinucleated giant cells. These cells result from the fusion of several epithelioid cells together. The source of macrophages (histiocytes) are monocytes from the peripheral blood. Granulomatous inflammation is a type of chronic inflammation initiated by a variety of infectious and noninfectious agents. Indigestible organisms or particles, or T cell–mediated immunity to the inciting agent, or both, appear essential for formation of granulomas. Tuberculosis is the classic infectious granulomatous disease and is characterized by finding rare acid-fast bacilli within areas of caseous necrosis. In addition to tuberculosis, several other infectious disorders are characterized by formation of granulomas, including deep fungal infections (coccidioidomycosis and histoplasmosis), schistosomiasis, syphilis, brucellosis, lymphogranuloma venereum, and cat-scratch disease. In sarcoidosis, a disease of unknown cause, the granulomas are noncaseating, which may assist in histologic

differentiation from tuberculosis. No organisms are found in the noncaseating granulomas of sarcoidosis.

15. The answer is C. Parainfluenza viruses are important causes of respiratory diseases in infants and young children. The spectrum of disease caused by these viruses ranges from a mild febrile cold to croup, bronchiolitis, and pneumonia. Parainfluenza viruses contain RNA in a nucleocapsid encased within an envelope derived from the host cell membrane. Infected mammalian cell culture will hemabsorb red blood cells owing to viral hemagglutinin on the surface of the cell.

16. The answer is D. Leukotrienes C4, D4, and E4 together compose the slow-reacting substance of anaphylaxis (SRS-A), which is thought to be the cause of asphyxiation in individuals not treated rapidly enough following an anaphylactic shock. SRS-Ais up to 1000 times more effective than histamines in causing bronchial muscle constriction. Anti-inflammatory steroids are usually given intravenously to end chronic bronchoconstriction and hypotension following a shock. The steroids block phospholipase A2 action, preventing the synthesis of leukotrienes from arachidonic acid. Acute treatment involves epinephrine
injected subcutaneously initially and then intravenously. Antihistamines such as diphenhydramine are administered intravenously or intramuscularly.

17. The answer is B. Dextromethorphan is a centrally acting antitussive drug that is about as efficacious a cough-suppressant as codeine. However, unlike codeine (c) and hydrocodone (d; another useful antitussive in some cases), dextromethorphan is not an opioid and lacks analgesic effects or the potential for ventilatory suppression or abuse. Diphenhydramine (c) and promethazine (e) also have antitussive action. However, they, too, can cause generalized CNS and ventilatory depression. They also exert significant antimuscarinic effects. Although that may be good in terms of inhibiting ACh-mediated bronchoconstriction, it may also cause thickening of airway mucus, favoring mechanical plugging of the airways with viscous mucus deposits that cannot be removed normally by mucociliary transport or coughing. Note warnings for all pediatric patients, specifically because of the risk of serious (and sometimes fatal) respiratory depression. This warning was not specifically targeted at pediatric patients with asthma. Nonetheless, asthma patients (and younger ones especially) are particularly vulnerable to drugs that suppress ventilatory drive, and so the warning should elicit extra vigilance.

CLINICAL CASES

1. A 7-year-old boy is brought to the emergency department (ED) after awakening in the middle of the night with difficulty breathing. He has a 2-day history of worsening productive cough and wheezing. The patient is found to have dyspnea, tachypnea, and a decreased inspiratory/expiratory ratio. Lung examination reveals diffuse rhonchi and expiratory wheezes in addition to pulsus paradoxus. He is afebrile and has no recent history of fever. This is the patient's second visit to the ED with these symptoms; his first visit was 2 years ago.

What is the most likely diagnosis?

Asthma exacerbation. Asthma is a form of obstructive lung disease

1.1 What are other obstructive lung diseases, and how do they differ from this condition?

Bronchiectasis is a disease state in which bronchi become inflamed and dilated, causing obstructed airflow and impaired clearance of secretions. It is often associated with AIDS, cystic fibrosis, and Kartagener syndrome.

Emphysema is a long-term, progressive disease in which the small airways and alveoli (which maintain the lung's functional shape) are destroyed. This is usually the result of smoking.

Chronic bronchitis is chronic inflammation of the bronchi that causes a persistent and productive cough that lasts for at least 3 months in 2 consecutive years. Smoking is almost always the cause.

1.2 What is the pathophysiology of this condition?

Acutely, bronchial hyperresponsiveness leads to episodic, reversible bronchoconstriction. Specifically, smooth muscle contraction in the airways leads to expiratory airflow obstruction. Chronically, airway inflammation leads to histologic changes in the bronchial tree.

1.3 What are common triggers of this condition?

Triggers of asthma exacerbation include stress, cold, exercise, dust and animal dander, mold, and viral upper respiratory tract infections

1.4 What is the appropriate treatment for this condition?

For acute episodes, albuterol, a β2-agonist, helps relax bronchial smooth muscle and decrease airway obstruction. However, for long-term control of persistent symptoms, inhaled corticosteroids are the best treatment.

2. A 50-year-old woman visits a community health clinic because of a 1-month history of cough productive of yellow sputum. On questioning, she says she has had several periods of cough lasting 4–6 consecutive months each year for the past 5 years. She has smoked two packs of cigarettes per day for the past 30 years. On examination, the woman's breathing is shallow, and she exhales slowly with pursed lips. Her jugular venous pulse is visible to the jawline when she is reclined at an angle of 45°. Auscultation of the chest demonstrates wheezing and distant heart sounds. A positive hepatojugular reflux is demonstrated, as is 2+ pitting edema up to her knees. X-ray of the chest is shown in Figure 14-6.

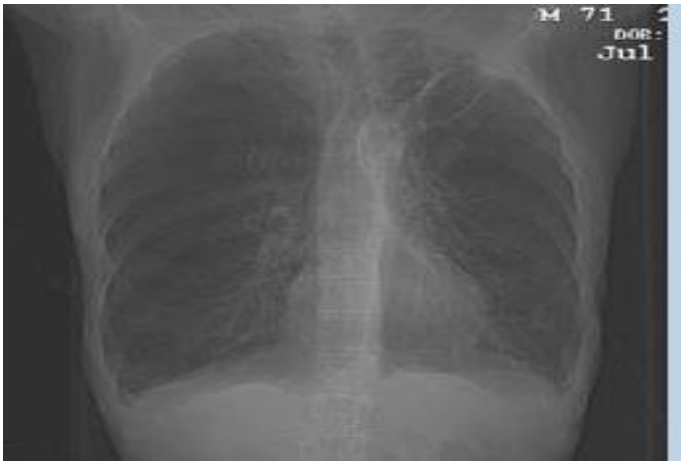


Figure 14-6. *Reproduced from Fist aid cases USMLE STEP 1*

2.1 What is the most likely diagnosis?

The history of productive cough for at least 3 consecutive months over 2 consecutive years accompanied by emphysema (suggested by pursed-lip breathing) indicates chronic obstructive pulmonary disease (COPD) with features of chronic bronchitis.

2.2 What radiologic findings can help diagnose this condition?

In patients with COPD, x-rays of the chest often reveal lung hyperinflation, flattening of the diaphragm, and decreased peripheral vascular markings.

2.3 What abnormalities would be expected on pulmonary function testing?

• In COPD, the forced expiratory volume in 1 second (FEV1) is decreased, forced vital capacity (FVC) is normal or decreased, and the FEV1/FVC ratio is <70% of predicted.
• In restrictive lung disease, decreased vital capacity and total lung capacity result in a FEV1/FVC ratio of > 80%.

2.4 How would this condition affect the patient's arterial blood gas levels (pH, PaO2, Paco2, and SaO2)?

The pH decreases as a result of respiratory acidosis. Although pH may be normal in a patient with chronic compensated COPD, it is low in a patient with an acute exacerbation. Arterial oxygen tension (PaO2) decreases, arterial carbon dioxide tension (Paco2) increases, and oxygen saturation (SaO2) decreases secondary to impaired gas exchange (from destruction of alveolar septae and pulmonary capillary bed).

2.5 How would this condition affect the patient's arterial blood gas levels (pH, PaO2, Paco2, and SaO2)?

The pH decreases as a result of respiratory acidosis. Although pH may be normal in a patient with chronic compensated COPD, it is low in a patient with an acute exacerbation. Arterial oxygen tension (PaO2) decreases, arterial carbon dioxide tension (Paco2) increases, and oxygen saturation (SaO2) decreases secondary to impaired gas exchange (from destruction of alveolar septae and pulmonary capillary bed).

3. A 62-year-old woman presents to the emergency department with acute-onset shortness of breath. She also complains of "stabbing" pleuritic right-sided chest pain. The woman had a stroke 3 months ago but is otherwise healthy. Her temperature is 36.7°C (98.1°F), blood pressure is 90/60 mm Hg, heart rate is 110/min, respiratory rate is 40/min, and oxygen saturation is 80% on room air. Physical examination

reveals jugular venous distention, and cardiovascular examination reveals a fast rate with regular rhythm and no murmurs. The woman's lungs are clear bilaterally with decreased breath sounds in the right middle lobe.

3.1 What is the most likely diagnosis?

This is a case of pulmonary embolism (also known as pulmonary thromboembolism, or PTE).

3.2 What is the Virchow triad?

The Virchow triad refers to the three factors that increase the risk for venous thrombosis: local injury to the vessel wall, hypercoagulability, and stasis. It is believed that patients with PTE are predisposed to venous thrombosis; triggers include pregnancy, limb immobility, and surgery.

3.3 What test remains the gold standard for diagnosing this condition?

Pulmonary angiography remains the most specific test available for definitively diagnosing PTE. However, because of the invasiveness of angiography, CT of the chest with thin cuts is the most frequently used diagnostic test.

3.4 What are the appropriate treatments for this condition?

PTE is treated with therapeutic levels of heparin for at least 5 days unless there is a contraindication to anticoagulation (eg, recent surgery). In most patients, warfarin and heparin may be started together and oral anticoagulation continued for at least 3 months. If there is a contraindication to anticoagulation or a high risk of recurrence of PTE, an inferior vena cava filter is recommended.

SECTION CARDIOVASCULAR SYSTEM
MCQs IFOM

1. A 67-year-old man comes to his primary care physician because of cramping and pain in the left leg that occurs during walking and is only relieved by rest. He has a 4-year history of hypertension and type 2 diabetes mellitus, and he has a 50-pack-year smoking history. His medication compliance has been poor. His father died of a myocardial infarction at age 70 years. Serum lipid panel shows a high-density lipoprotein (HDL) concentration of 33 mg/dL, a low-density lipoprotein (LDL) concentration of 186 mg/dL, and a triglyceride concentration of 172 mg/dL. Following liver function testing, the results of which are normal, the physician initiates drug therapy for he patient's condition.Three months later, the patient returns for follow-up evaluation. He is asymptomatic, but liver function test results show a serum ALT concentration of 96 U/L and a serum AST concentration of 76 U/L. Which of the following is the most likely mechanism of action of the drug prescribed to this patient?

A. Decrease in intestinal reabsorption of bile acids
B. Inhibition of HMG-CoA reductase
C. Inhibition of small intestine cholesterol absorption
D. Reduction of very-low-density lipoprotein (VLDL) synthesis
E. Upregulation of lipoprotein lipase

2. An 80-year-old man in the emergency department has persistent ventricular tachycardia despite attempted cardioversion. He is admitted to the hospital and begins receiving oral amiodarone, which resolves the arrhythmia. Weeks after his discharge home, he begins to experience drug-associated adverse effects.

Which of the following adverse effects are most likely associated with amiodarone?

A. Blurry yellow vision
B. Dyspnea on exertion and FEV1/FVC ratio < 80% on pulmonary function tests
C. Fatigue, weight gain, and constipation
D. Impotence
E. Shortened PR interval on ECG

3. A group of researchers develop a study to look into the effects of smoking and development of colon cancer. They randomly select a group of 5000 people over age 60 with a history of smoking ½-1 pack of cigarettes a day for the past 30 years. Over the next 10 years, rates of colon cancer in the study group are monitored and compared to the same age group of non-smokers in the general population. Which of the following describes this type of study?

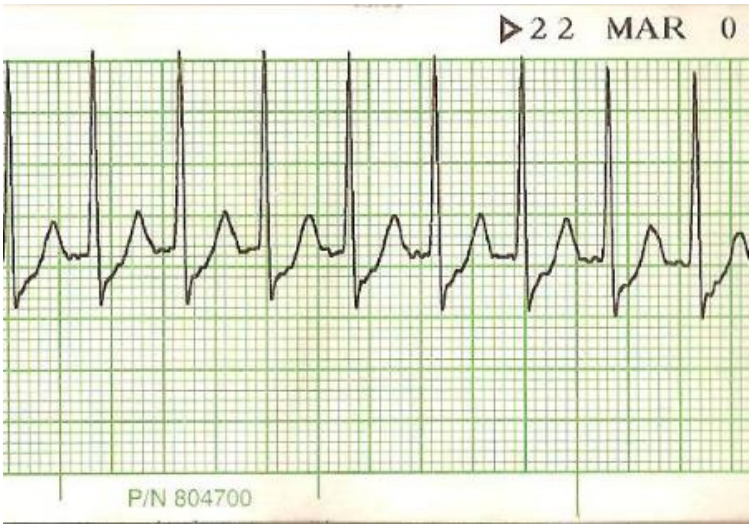
A. Case-control study
B. Cohort study
C. Cross-over study

D. Cross-sectional study
E. Double blinded clinical trial
F. Single blinded clinical trial

4. A 62-year-old man with a history of type 2 diabetes mellitus comes to the office for an annual wellness examination. He is diagnosed with hypertension and is prescribed captopril. Two weeks later, the patient returns for a follow-up visit. He has developed an annoying cough over the past 2 weeks. His temperature is 37°C (98.6°F), blood pressure is 140/85 mm Hg, and pulse is 75/min. On cardiac auscultation, heart sounds are normal with no murmurs, rubs, or gallops. Lung fields are clear to auscultation bilaterally. There is no evidence of elevated jugular venous pressure or peripheral edema. The physician discontinues the current pharmacotherapy, instead replacing it with the best available medication that does not cause the adverse effect the patient is experiencing. Compared with normal, which row in the table best represents the patient's status following administration of the new medication?

	Renin	Angiotensin I	Angiotensin II	Aldosterone	Renal Na+ Reabsorption
A.	↑	↑	↓	↓	↓
B.	↑	↑	↑	↑	↓
C.	↑	↑	↑	↓	↓
D.	↓	↓	↓	↓	↓
E.	↓	↓	↓	↓	↑

5. A 25-year-old woman with no medical history presents to the emergency department because of "a racing heartbeat." She states that her heart problems began 2 hours ago, and she appears to be worried about her condition. She reports some chest discomfort and nausea. Blood pressure is 138/80 mmHg, pulse is 170/min, and respiratory rate is 18/min. An electrocardiogram is shown.



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Which of the following interventions would most likely lead to resolution of her current arrhythmia?

A. Adenosine
B. Amiodarone
C. Flecainide
D. Lidocaine
E. Sotalol

6. A 70-year-old man comes to his cardiologist for a follow-up visit. He reports increased shortness of breath and increased swelling in both legs over the last 6 months. An echocardiogram is done in the office and reveals ejection fraction at 34%. Lisinopril is stopped and the patient is started on sacubitril/valsartan.

Which of the following best describes the mechanism of action of sacubitril?

A. Antagonism of angiotensin II receptors
B. Beta-1 adrenergic receptors blockade
C. Inhibition of Ca+ channels
D. Inhibition of neprilysin and degradation of bradykinin
E. Inhibition of sodium-potassium adenosine triphosphatase
F. Inhibits action of angiotensin converting enzyme.

7. A 3-day-old female newborn is brought to the pediatrician’s office by her parents for her first well-baby visit. The mother had an uneventful pregnancy and received adequate prenatal care. The baby was born after an uncomplicated vaginal delivery. The parents report concern over a mass on the back of their daughter's neck, which has enlarged since birth. The infant has low-set ears. On physical examination, a fluid-filled sac, 7 cm in diameter, is found on the right side of the posterior neck, and lymphedema is seen in the hands and feet.

Which of the following is the most likely diagnosis?

A. Cystic hygroma
B. Parotitis

C. Sebaceous cyst
D. Subcutaneous hemangioma
E. Teratoma
F. Thyroglossal duct cyst

8. A 53-year-old man comes to the the emergency department because of "crushing" substernal chest pain. He is diaphoretic and has lateral ST elevations on ECG. He is rushed to the cardiac catheterization laboratory, where two coronary artery stents are placed in the circumflex artery. Dual antiplatelet therapy with aspirin and clopidogrel is started. Six days later, when preparing for discharge, the patient suddenly experiences intense chest pain and lightheadedness. The following vital signs are obtained:

Temperature: 37.5°C (99.5°F)
Pulse: 125/min
Blood pressure: 85/40 mm Hg
Respiratory rate: 18/min
Oxygen saturation: 97% on room air

Auscultation of distinct heart sounds is difficult. The patient's neck veins are prominent. No other physical findings are appreciated. After a few minutes, the patient loses consciousness.

Which of the following is the most likely mechanism responsible for this patient’s sudden symptoms?

A. Interventricular septum rupture
B. Left ventricular free-wall rupture
C. Papillary muscle rupture
D. Reinfarction
E. Right ventricular free-wall rupture

9. A pharmaceutical company is investigating the effect of an experimental drug on the murine cardiac hypertrophic response. This drug binds to a myocyte transmembrane protein and activates a Gαq subunit. This interaction increases cardiac inotropy and decreases the action potential refractory period.

Increased levels of which of the following intracellular constituents are most likely responsible for this observed response?

A. Cyclic adenosine monophosphate
B. Cyclic guanosine monophosphate
C.Inositol trisphosphate
D.Nitric oxide
E. Protein kinase A
F. Sodium

10. A 65-year-old woman visits her doctor for a follow-up appointment for the management of hypertension, diagnosed 6 months ago. Since she received this diagnosis, she and her physician have begun a program of lifestyle modifications and monotherapy with enalapril. On this visit, her pulse is 78/min, respirations are 14/min, and a blood pressure is 148/96 mm Hg. An ECG tracing shows an irregular rhythm with sawtooth-patterned P waves. Given the patient's blood pressure and new-onset atrial fibrillation, the patient's physician prescribes nadolol.
What set of physiologic changes listed in the table occurs after the administration of this medication?

	Heart Rate	Contractility	Renin Release	Systemic Vascular Resistance (SVR)
A	↓	↓	↓	↔
B	↓	↓	↓	↑
C	↓	↓	↓	↓
D	↑	↑	↑	↑
E	↓	↓	↔	↔

11. A 27-year-old man is brought to the emergency department with crushing substernal chest pain radiating to his back that occurred suddenly while lifting heavy weights at the gym. He denies any history of similar pain. His blood pressure is 85/25 mm Hg, pulse is 90/min, respiratory rate is 22/min, oxygen saturation is 92%, and he is afebrile. Physical examination reveals a tall, slender man with long arms and fingers, as well as new-onset, grade IV/VI diastolic decrescendo murmur heard best at the second intercostal space right sternal border.
Which of the following is the most likely underlying cause of this patient's presenting symptoms?
A. Atherosclerosis
B. FBN1 gene mutation
C. Multiple endocrine neoplasia type 2B
D. Obliterative endarteritis of the vasa vasorum
E. Type III collagen defect
12. A 28-year-old African-American man presents with fever, weight loss, diffuse myalgias, arthralgias, and abdominal pain. On examination, his blood pressure is 168/92 mm Hg, pulse is 83, and respiratory rate is 18. He has areas of ulceration and mottled purple discoloration on his lower extremities. His medical history is otherwise significant for hepatitis B infection. Laboratory tests reveal elevations in the white blood cell count, erythrocyte sedimentation rate, and C-reactive protein level.

What histologic feature is commonly associated with this patient's disease process?

A. Caseating necrosis
B. Eosinophilic infiltrate
C. Fibrinoid necrosis
D. Granulomatous inflammation
E. Langhans giant cells
F. Onion skinning

13. A 4-year-old boy with a history of intellectual disability and seizures is brought to the physician with a 3-month history of worsening shortness of breath. During physical examination, the physician notices numerous acne-like papules on the patient's face. Echocardiography shows significant left ventricular outflow obstruction.

Which of the following is the most likely diagnosis for this patient’s heart condition?

A. Dilated cardiomyopathy
B. Lipoma
C. Myxoma
D. Rhabdomyoma
E. Transposition of the great vessels

14. A 63-year-old woman with type 2 diabetes mellitus visits her physician with complaints of chest pain on exertion. She smokes two packs of cigarettes a day. Physical examination reveals a blood pressure of 155/105 mm Hg and a heart rate of 70/min. Results of blood tests are significant for an LDL cholesterol level of 200 mg/dL and an HDL cholesterol level of >40 mg/dL. Her physician prescribes a common medication that inhibits the hepatic production of certain molecules that have been implicated in the pathogenesis of coronary artery disease. The concomitant use of a fibrate would increase the risk of which of the following adverse reactions?

A. Bilirubinuria
B. Hemoglobinuria
C. Metabolic alkalosis
D. Myoglobinuria
E. Transaminitis

15. A tall, thin 25-year-old man with a history of joint hyperflexibility visits the emergency department because he has tearing chest pain that radiates to his back. His blood pressure is 90/45 mm Hg, his pulse is 123, and his respiratory rate is 24. On physical examination, he is found to have a drop of 21 mm Hg in his systolic blood pressure during inspiration. This finding is accompanied by distended neck veins and distant heart sounds. Which of the following ECG findings would be most characteristic for this patient’s pathophysiologic process?

A. 1.5-mm ST-segment elevations in anterior leads
B. Diffuse ST-segment elevations and PR depressions

C. Low-voltage QRS complexes and oscillating QRS amplitudes
D. S1Q3T3 pattern and evidence of right ventricular strain
E. T-wave inversions in the anterior leads

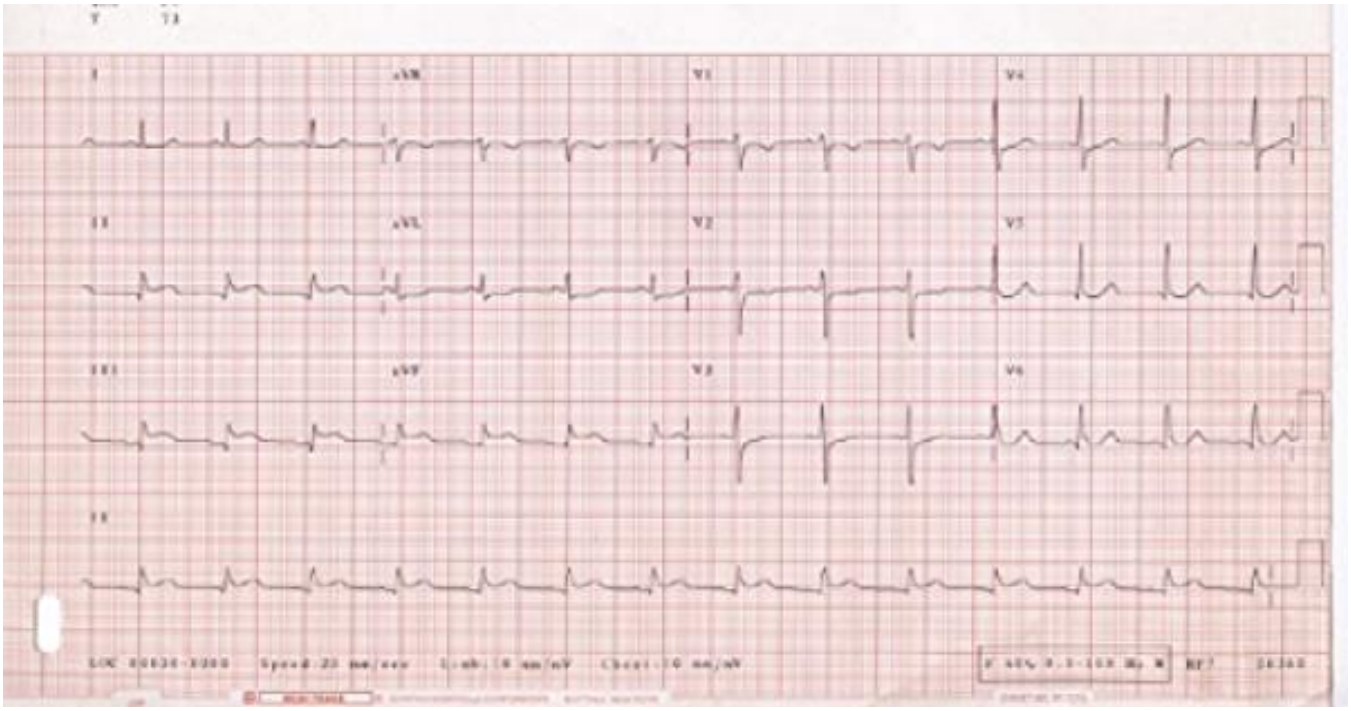
16. A 45-year-old man presents to his primary care provider for his yearly checkup. Basic lab tests, including a lipid profile, are performed before the visit. They show a low-density lipoprotein (LDL) of 174 mg/dL, high-density lipoprotein (HDL) of 46 mg/dL, and a triglyceride level of 202 mg/dL. To reduce the patient's risks for morbidity and death, his physician recommends lifestyle changes and initiates therapy with a lipid-lowering medication. The doctor warns the patient that this medication may be associated with muscle pain. By what mechanism does this intervention affect cholesterol metabolism?

A. Decreases the apparent dissociation constant of hepatic LDL cholesterol receptors
B. Decreases the maximum velocity of HMG-CoA reductase
C. Decreases the maximum velocity of hepatic LDL cholesterol receptors
D. Directly increases apparent dissociation constant for LDL receptors
E. Increases the apparent Michaelis-Menten constant of HMG-CoA reductase

17. A 67-year-old obese man comes to the emergency department because of severe substernal chest pain. He has had similar episodes in the past when climbing stairs, but they have always resolved with rest. Medical history is significant for hypertension and diabetes mellitus for which he takes lisinopril and metformin. Review of systems is positive for nausea and diaphoresis and negative for fever/chills, shortness of breath, and cough. His temperature, 37.8°C (100°F), pulse is 84/min, respirations are 18/min, blood pressure is 138/90 mm Hg, and oxygen saturation is 97% on room air. Examination reveals no murmurs or gallops, and lungs are clear without rales or wheezes. Laboratory studies show:

Leukocyte count: 5600 mm3
Hemoglobin: 16.2 g/dL
Hematocrit: 37.1%
Platelet count: 198,000/mm3
Na+: 137 mEq/L
K+: 3.5 mEq/L
Cl-: 105 mEq/L
Carbon dioxide: 22 mEq/L
Blood urea nitrogen: 14 mg/dL
Creatinine: 0.82 mg/dL
Glucose: 146 mg/dL
Troponin: 0.92 ng/mL (normal <0.01 ng/mL)

The patient’s ECG is shown in the image



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Which of the following is the most likely inciting event in the pathogenesis of this man's condition?

A. Coronary artery dissection

B. Coronary artery stenosis

C. Coronary artery vasospasm

D. Plaque rupture

E. Thromboembolic disease

18. A 64-year-old man is undergoing medication reconciliation as part of a new patient visit with an internist. One of the medications he takes inhibits the sodium-potassium-chloride cotransporter.Which of the following is a medical condition that this drug is used to treat?

A. Acute myocardial infarction

B. Dilated cardiomyopathy

C. Hypertrophic obstructive cardiomyopathy

D. Hypokalemia

E. Unstable angina pectoris

19. A researcher is conducting a population study that examines the relative risk of the occurrence of myocardial infarction in type II diabetic patients as compared with healthy patients. It is expected that the population's true mean risk value will fall within a range of values set with a specific probability. Which of the following best describes this range of values?

A. Bimodal distribution

B. Confidence interval

C. Median

D. Standard deviation
E. Standard error
F. Variance

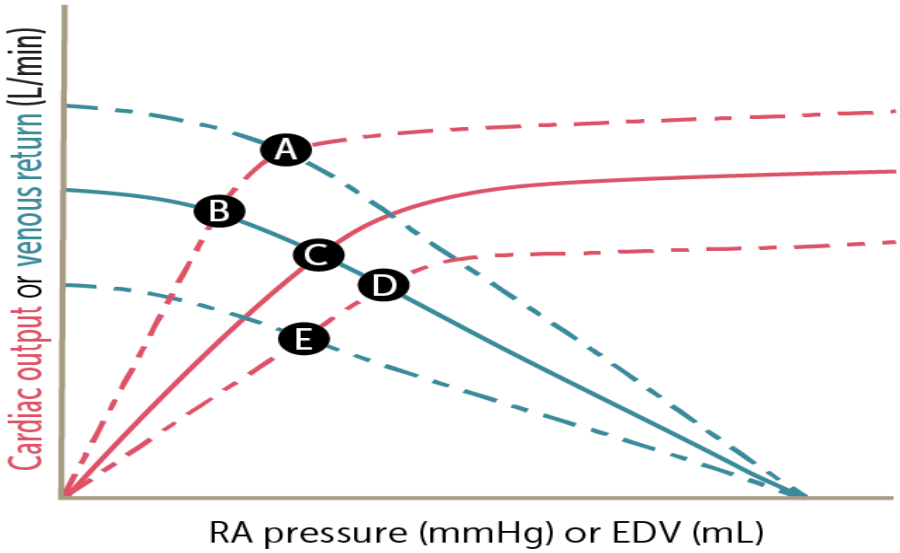
20. A 17-year-old girl is brought to her family physician by her mother. Two days ago, the patient noticed slight twitching in her arms and legs. These movements are uncontrollable and have progressively worsened since then. Four weeks ago, the patient had a mild febrile illness that was left untreated. She says she has noticed that her urine appears brown and frothy every time she goes to the bathroom. The patient is not sexually active, has no recent travel history, and has not been injured. Her temperature is 37°C (98.6°F), pulse is 88/min, respirations are 14/min, and blood pressure is 118/78 mm Hg. Physical examination reveals a patient alert and oriented ×3, pupils equally reactive to light and accommodation, and 2+ reflexes present in all extremities. Cardiac examination reveals no murmurs, rubs, or gallops. Findings on neurologic examination are within normal limits, and cranial nerves are globally intact. The thyroid is nontender and nonpalpable. The patient says she has not noticed any recent weight loss. Laboratory studies show liver function and the blood urea nitrogen concentration to be within normal ranges. Which of the following is the most likely cause of this patient's condition?

A. Elevated blood ammonia concentration
B. Generalized seizure disorder
C. Hypersensitivity cross-reaction
D. Substance intoxication
E. Subthalamic lesion
F. Triple repeat expansion

21. A 76-year-old man with a medical history of osteoarthritis, hypertension, and diabetes comes to the emergency department reporting shortness of breath and chest pain that radiates down both arms. He states that the pain started 2 hours ago and has worsened and that taking aspirin provided no relief. His current medications include metformin, lovastatin, aspirin, and sitagliptin. His temperature is 37.2°C (99°F), pulse is 100/min, respirations are 20/min, and blood pressure is 120/80 mm Hg. Coronary angiography reveals three blocked coronary arteries.Which of the following would most likely be used to reduce infection at the entry point for the cardiac angiography catheter in this patient?

A. Cefazolin
B. Ciprofloxacin
C. Gentamicin
D. Meropenem
E. Vancomycin

22. A 54-year-old man comes to the clinic with fatigue, shortness of breath, and an uncomfortable feeling of a racing heartbeat. He has a history of poorly controlled hypertension. ECG tracing reveals an irregularly irregular heartbeat. The physician prescribes a drug that inhibits myocardial sodium potassium adenosine triphosphatase. Which of the following points best depicts the change following administration of the prescribed drug (solid lines indicate normal)?



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23. A 2-year-old girl is brought to her pediatrician's office for a well-child visit. The girls mother reports that the child is doing well. She is able to climb onto and down from furniture without help, knows the names of familiar people, and speaks sentences of two to four words. She is in the 70th percentile for height and weight. Physical examination is unremarkable except for a 2/6 heart murmur best heard in left upper sternal border with wide fixed split S2.

Which of the following abnormalities explains the physical examination findings?

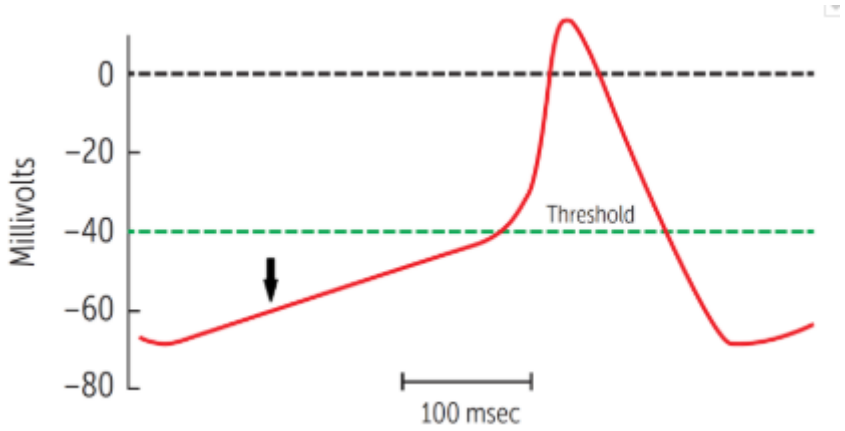
A. Aortic stenosis
B. Atrial septal defect
C. Mitral regurgitation
D. Patent ductus arteriosus
E. Transposition of great vessels
F. Ventricular septal defect

24. A 45-year-old woman is rushed to the emergency department by her husband. She started to experience palpitations, lightheadedness, and shortness of breath 1 hour ago. Her medical history is negative for any major illnesses, diagnoses, and hospitalizations. She does not take any medications. On admission, the patient's temperature is 37.6°C (99.7°F), pulse is 150/min, respiratory rate is 18/min, and blood pressure is 134/92 mm Hg. Her body mass index is 23.5 kg/m2. The attending physician immediately

administers a drug that quickly terminates the patient's tachycardia and causes flushing, bronchospasm, and a significant drop in blood pressure.
Which of the following medications was most likely administered?

A. Adenosine
B. Amiodarone
C. Ivabradine
D. Metoprolol
E. Procainamide

25. An experimental study is designed to characterize the conductance of ions across myocytes located in the sinoatrial node. An experimental animal is given a dose of norepinephrine, resulting in an increase in its heart rate. An electrophysiologic graph is mapped across the heart, and the findings from the sinoatrial nodal area are shown



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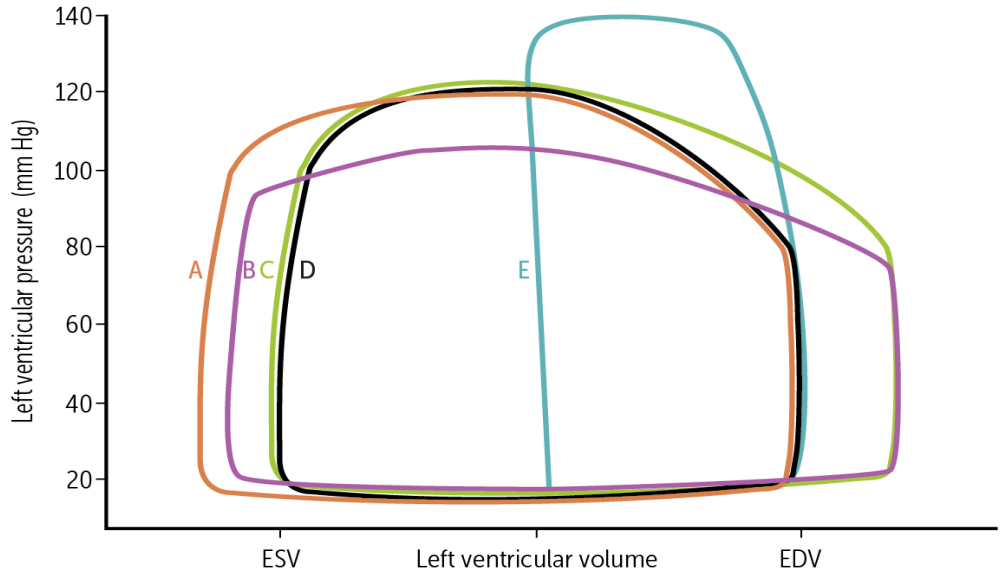
Which of the following ion/ion channels is responsible for the section of the action potential indicated by the arrow?

A. Decreased conductance of Cl-
B. Decreased conductance of HCO_3-
C. Decreased conductance of K+
D. Increased conductance of Ca_2+
E. Increased conductance of Na+

26. A 68-year-old man is brought to the emergency department because of shortness of breath and increased fatigue that has worsened during the past 3 days. He reports that over the past few weeks these symptoms have worsened with activity and when lying down, and that now he feels short of breath even at rest. He also reports having swollen ankles. He has a history of hypertension diagnosed at age 50 but takes no medications because of the expense. Temperature is 35.9° C (96.6° F), blood pressure is 164/92 mm Hg, pulse is 78/min, respiratory rate is 20/min, and oxygen saturation is 93% on room air. Bilateral crackles are heard over the lower lung fields, and there is pitting edema over lower extremities bilaterally extending to the mid calf.
Which of the following is the most likely underlying cause of these symptoms?

A. Acute damage and death of cardiomyocytes
B. Decreased pulmonary venous pressure
C. Decreased systemic vascular resistance
D. Decreased venous return to heart
E. Remodeling of cardiac myocytes as sarcomeres are added in parallel
F. Remodeling of cardiac myocytes as sarcomeres are added in series

27. A 58-year-old man is referred to the cardiac clinic because of progressive weakness, cough, and shortness of breath. He has a history of coronary artery disease and started hemodialysis 5 years ago because of end-stage renal disease. At that time, an arteriovenous (AV) fistula was constructed for access. Pulse is 97/min and blood pressure is 115/68 mm Hg. On cardiac auscultation, a systolic murmur over the apex that does not change in quality with physical maneuvers is noted.



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Which of the following changes in the left ventricular pressure-volume loop most likely reflects this patient's hemodynamic status (black line indicates normal reading)?

A.A
B.B
C.C
D.D
E.E

28. A 23-year-old man found unconscious with fresh needle tracks in his arm is brought to the emergency department by ambulance. The patient is resuscitated with naloxone and is admitted to the hospital. His temperature is 39° C (102.2° F). Upon examination, a "blowing" systolic heart murmur is heard that is loudest at the left lower sternal border. The murmur varies with respiration, becoming louder with inspiration.

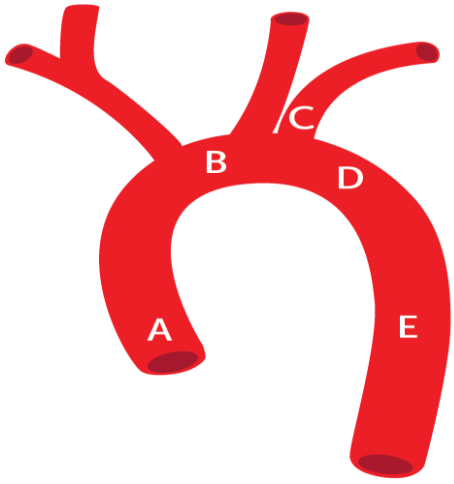
Additionally, the physician notes a prominent jugular venous pulse. Which of the following valvular abnormalities is most consistent with the murmur in this patient?

A. Aortic regurgitation
B. Aortic stenosis
C. Mitral regurgitation
D. Mitral stenosis
E.Tricuspid regurgitation
F.Tricuspid stenosis

29. A 21-year-old man comes for evaluation because of a 3-month history of occasional fainting episodes, palpitations, and lightheadedness. The patient was previously healthy and takes no medications. His family history is significant for several family members who died from sudden cardiac death before age 65. Temperature is 37° C (98.4° F), blood pressure is 123/75 mm Hg, pulse is 86/min, and respirations are 16/min. He is in not in acute distress. Physical examination shows no abnormalities. ECG shows normal sinus rhythm with a prolonged QT interval. Which of the following is the most likely diagnosis?

A. Brugada syndrome
B. Jervell and Lange-Nielsen syndrome
C. Mobitz type II atrioventricular block
D. Right bundle branch block
E. Romano-Ward syndrome
F. Wolff-Parkinson White syndrome

30. A 42-year-old woman is brought to the emergency department after being involved in a motor vehicle collision. She was a restrained passenger in a car that struck a light post while traveling at a high speed. She is conscious and reports difficulty breathing and severe pain in her chest and back. Temperature is 98.2°F (36.7°C), blood pressure is 89/52 mm Hg, and pulse is 130/min. Chest x-ray shows a widened mediastinum.



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Injury to which of the following areas in the diagram is the most likely cause of this patient’s symptoms?

A. Ascending aorta
B. Aortic arch
C. Left subclavian artery
D. Aortic isthmus
E. Descending aorta

31. A 65-year-old man is brought to the emergency department after suddenly passing out on the street. The patient is now awake and alert. His vital signs are normal. On physical examination, a crescendo-decrescendo systolic murmur with ejection click is heard at the right upper sternal border, with radiation to the neck. The patient is immediately scheduled for an echocardiogram. How does this patient's cardiac cycle differ from normal?

A. Decreased atrial filling
B. Decreased isovolumetric contraction
C. Decreased isovolumic relaxation
D. Decreased wall thickness
E. Prolonged left ventricular systole

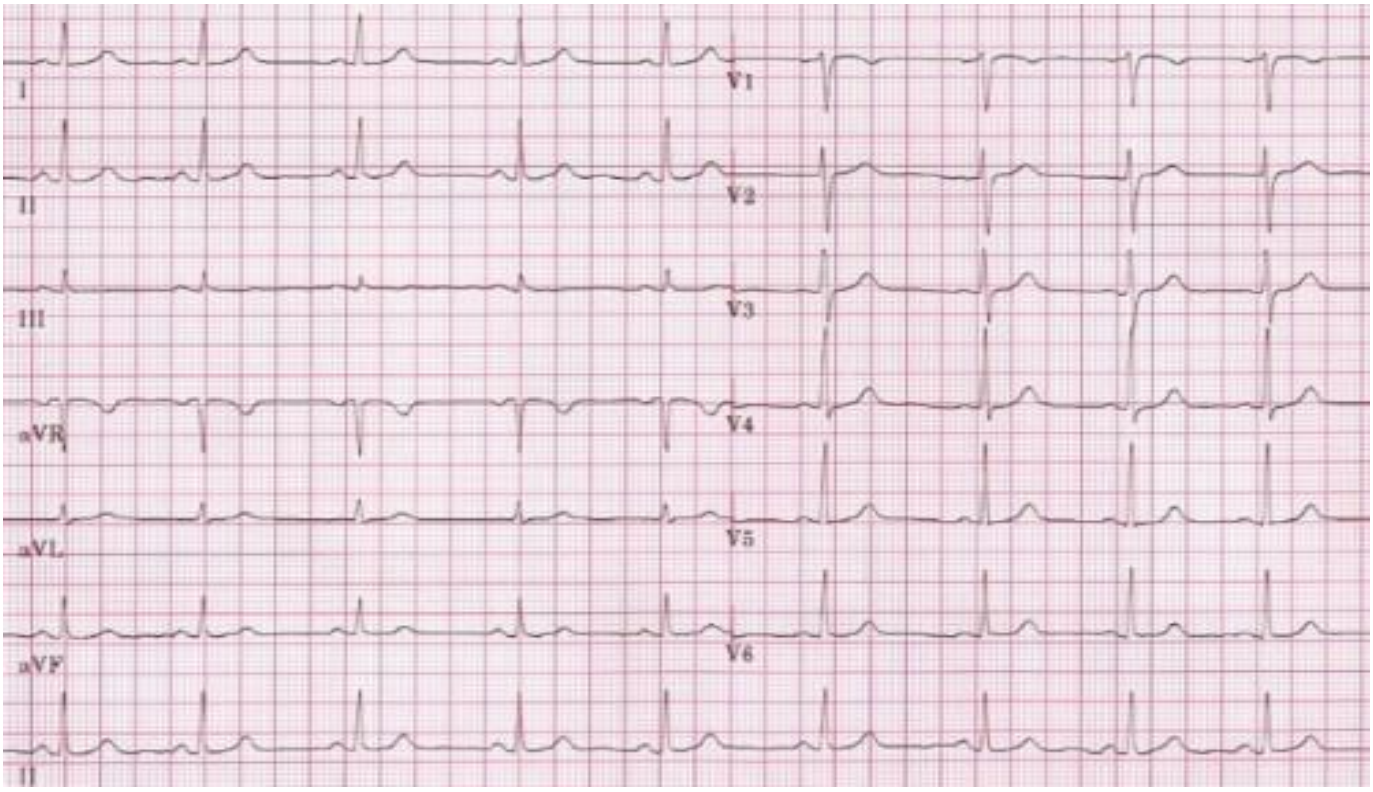
32. A 62-year-old woman comes to her primary care physician because of weakness, fatigue, and progressive shortness of breath on exertion. She has also gained 10 lb over the past few weeks. The patient is a breast cancer survivor who had received radiation therapy. Physical examination reveals hepatomegaly, jugular venous distention that fails to subside on inspiration, and abdominal pain on palpation. The patient's temperature is 101.5°F (38.5°C) and blood pressure is 115/70 mm Hg. An echocardiogram shows a reduced bi-ventricular end diastolic volume.

Which of the following is the most likely diagnosis?

A. Cardiac tamponade
B. Constrictive pericarditis
C. Dilated cardiomyopathy
D. Myocarditis
E. Systolic congestive heart failure

33. A 54-year-old man comes to the emergency department with the belief that he is having a heart attack. He reports intermittent chest pain that started about 6 hours ago and says that the pain is worse when he lies down. He denies having similar previous episodes. He sometimes wakes up with a dry cough. He claims that he has no history of tobacco use and that he drinks one glass of red wine with dinner daily. On review of systems, he denies any shortness of breath or diaphoresis. Physical examination is unremarkable, including a normal S1S2 and nontender chest wall. Breath sounds are equal bilaterally. A chest x-ray is normal. His laboratory test results include:

WBC: 6.7 K/mm3
RBC: 4.7 M/mm3
Hemoglobin: 15.1 g/dL
Hematocrit: 44.6%
Platelets: 250K/mm3
Serial troponin at 1 and 3 hours: <0.01 ng/mL
CK-MB: 4.3 ng/mL (normal range: ≤ 7.7 ng/mL, males)



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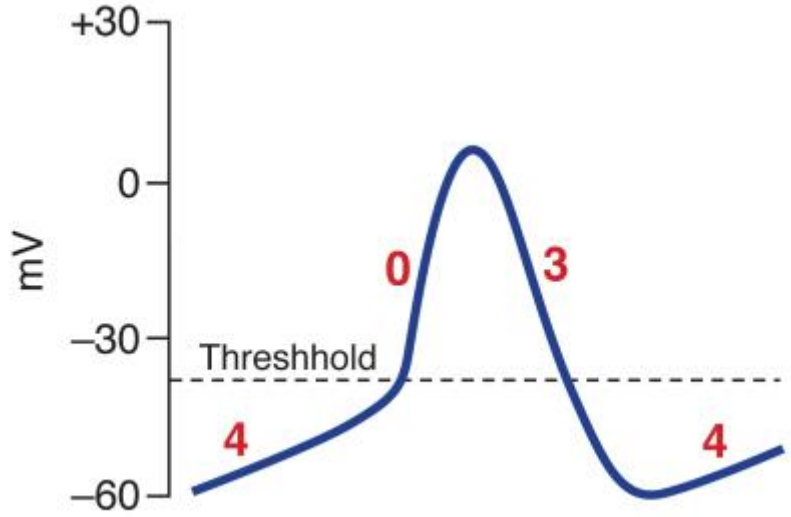
ECG is recorded and is shown in the image.
Which of the following is the most likely cause of this man's symptoms?

A. Gastroesophageal reflux disease
B. Myocardial infarction
C. Pericarditis
D. Pulmonary embolism
E. Stable angina

34. The graph illustrates a typical action potential in the sinoatrial (SA) node. Each phase of the trace can be attributed to the conductance of ions through their respective channels. Which of the following drugs has the most significant effect on the flow of ions through voltage-gated channels during phase 0 of the pacemaker action potential?



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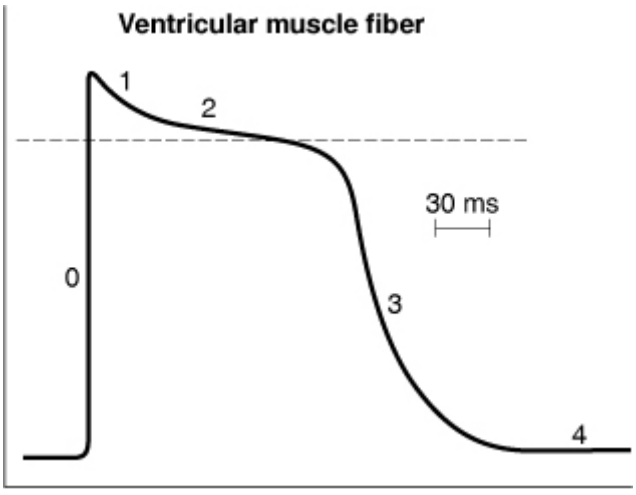
A. Adenosine
B. Atropine
C. Nifedipine
D. Procainamide
E. Propranolol
F. Verapamil

35. A 55-year-old man with a history of hypertension, diabetes mellitus type 2, and hyperthyroidism comes to the emergency department because of chest pain. An ECG reveals an acute inferior myocardial infarction (MI). Moments later, the patient becomes unresponsive. Cardiac monitoring shows ventricular fibrillation, and cardiopulmonary resuscitation (CPR) is initiated. Despite defibrillation and CPR, the patient remains in ventricular fibrillation. The physician considers administering a drug that decreases the myocardial action potential by working on phase 0.



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Which of the following drugs is most likely being considered by the physician at this time?

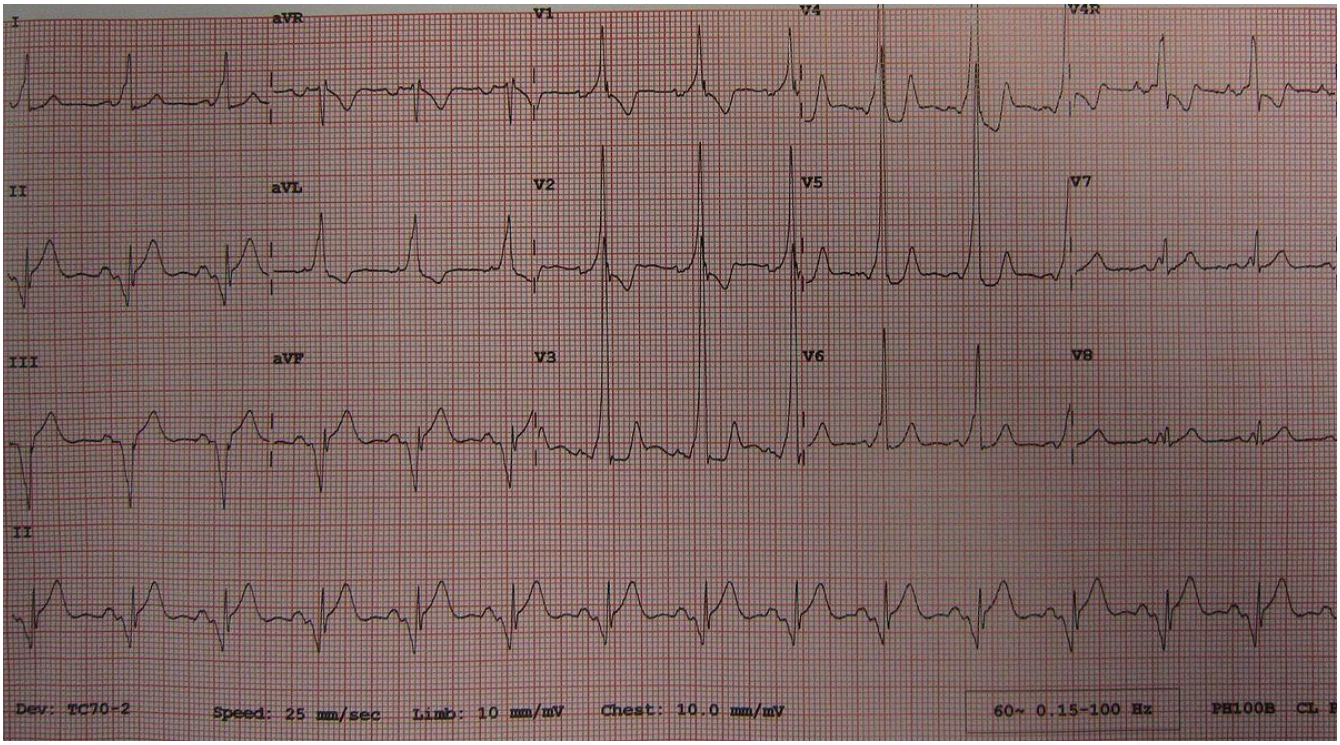
A. Diltiazem
B. Lidocaine

C. Propafenone
D. Quinidine
E. Sotalol

36. A 68-year-old man comes to his primary care physician because of a 2-month history of fatigue. He has a history of poorly controlled hypertension refractory to various medical regimens, hyperlipidemia, type 2 diabetes mellitus, and a 55-pack-year smoking history. Current medications include atorvastatin, captopril, amlodipine, hydrochlorothiazide, and metformin. On auscultation of the heart, a delayed carotid upstroke as well as a crescendo–decrescendo murmur of the left lateral neck are noted. Vital signs are within the reference ranges. Laboratory studies show:
LDL: 198 mg/dL
HDL: 27 mg/dL
Triglycerides: 175 mg/dL
Glucose (fasting): 188 mg/dL
Doppler ultrasound studies of the neck show significant narrowing of the left carotid artery, with an estimated 16-fold decrease in blood flow. Resistance in which of the following vessels is most likely to be the highest in this patient?

A. Abdominal aorta
B. Femoral artery
C. Iliac artery
D. Left circumflex artery
E. Renal artery

37. 22-year-old man comes to the emergency department because lately he sometimes feels dizzy, his heart seems to beat very rapidly for a few minutes, and then he passes out. The patient says nothing like this has ever happened to him before but does mention that his father had heart problems in the past. The physician finds an anxious-appearing young man with no murmurs, rubs, or gallops on auscultation. His pulse is 160/min, respirations are 16/min, and blood pressure is 92/48 mm Hg. An ECG is shown.



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Which of the following additional findings is most likely in this patient?

A. Delay of conduction across the atrioventricular node

B. Increased conduction across the atrioventricular node

C. Increased sympathetic tone

D. Inherited myocyte ion channel defect

E. Reduced ventricular filling during diastole

38. An 84-year-old man comes to the office of his primary care physician because of progressively worsening chest pain that occurs with activity. He has a history of coronary artery disease and has smoked one pack of cigarettes per day for the past 35 years. His father died of a stroke when the patient was a child. The patient underwent repair of an abdominal aortic aneurysm several years ago. Metoprolol is prescribed. Which set of effects listed in the table will metoprolol most likely have on this patient's heart rate, stroke volume, and mean arterial pressure?

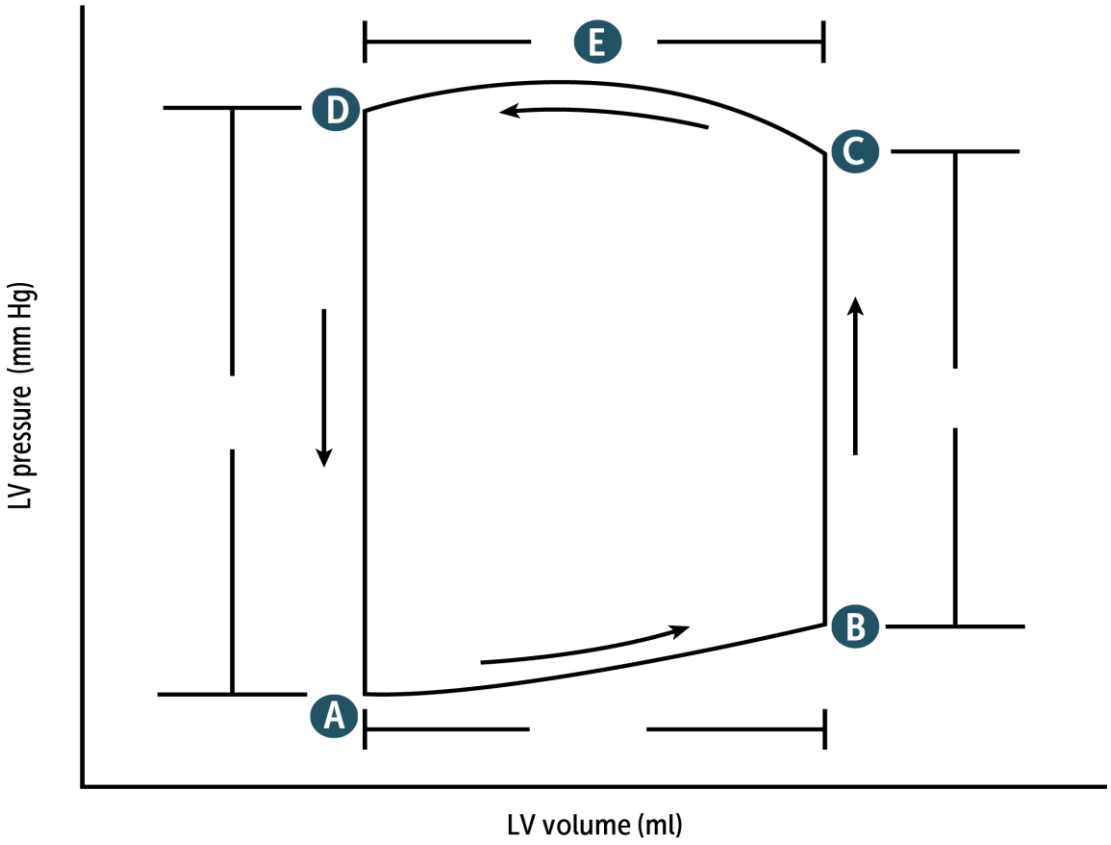
Choice	Pulse (bpm)	Stroke volume (mL)	Mean Arterial Pressure (mm Hg)
A	↓	↑	↓
B	↑	↑	↑
C	↓	↓	↓
D	↑	↓	No change
E	No change	↑	↑

39. A 62-year-old man presents to the emergency department after experiencing syncope while gardening at home. He is then admitted to the intensive care unit with a blood pressure of 80/30 mm Hg and a heart rate of 120. His temperature is 39.1°C (102.4°F). On physical examination, the patient is unresponsive, and his skin is warm and appears flushed. Initial results of laboratory testing reveal:

WBC count: 21,000/mm3
Lactate: 4.5 mmol/L
The patient is treated with fluid resuscitation, which has no effect on his vital signs.
What is the mechanism of action of the most appropriate drug to quickly compensate for this patient's hypotension?

A. Activation of the renin-angiotensin-aldosterone system
B. Parasympathetic stimulation of heart rate
C. Release of vasopressin
D. Stimulation of α1-receptors on vascular smooth muscle
E. Stimulation of β2-receptors on vascular smooth muscle

40. A 68-year-old woman who emigrated from India comes to the emergency department because of increasing difficulty breathing on exertion. She also reports coughing up blood-stained mucus during the past several weeks. She has been otherwise healthy but says that she had frequent sore throats as a child. She does not smoke or drink alcohol, and she does not take any medications. Diffuse crackles are heard on pulmonary auscultation; cardiac auscultation discloses the presence of an opening snap and diastolic rumbling murmur, best heard at the apex. The opening snap heard during cardiac auscultation of this patient best corresponds to which of the following letters on the pressure-volume loop?



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41. A 52-year-old man is referred to the cardiology clinic because of chest pain and shortness of breath during his morning walks that quickly resolves with rest. Stress echocardiography findings are consistent with exercise-induced ischemia, and the patient is sent for cardiac catheterization. During catheterization, pressure readings at one location range from 9 to 25 mm Hg. As the catheter is advanced forward, the pressure range subsequently becomes 9 to 12 mm Hg. Assuming these findings are normal, the catheter is located within which of the following cardiac structures during the first pressure reading?

A. Left ventricle

B. Pulmonary artery

C. Pulmonary artery wedge

D. Right atrium

E. Right ventricle

42. A 39-year-old woman comes to her physician after noticing the appearance of some reddish bumps on her arm. She thinks it may be acne. The patient has well-controlled hypertension and is a chronic alcoholic with a history of acute pancreatic episodes and consistently elevated hypertriglyceridemia. Her family history is significant for a brother who had a stroke at 35 years of age.On physical examination, a few small, red-yellow papules are observed on her left arm. Laboratory tests reveal a triglyceride level of 500 mg/dL. The physician prescribes a medication to lower her triglyceride level. Given the patients history of acute pancreatitis, what is the most likely adverse effect of the medication given to control her triglyceride level?

A. Cardiac arrhythmia

B. Cholesterol gallstones

C. Decreased absorption of fat-soluble vitamins

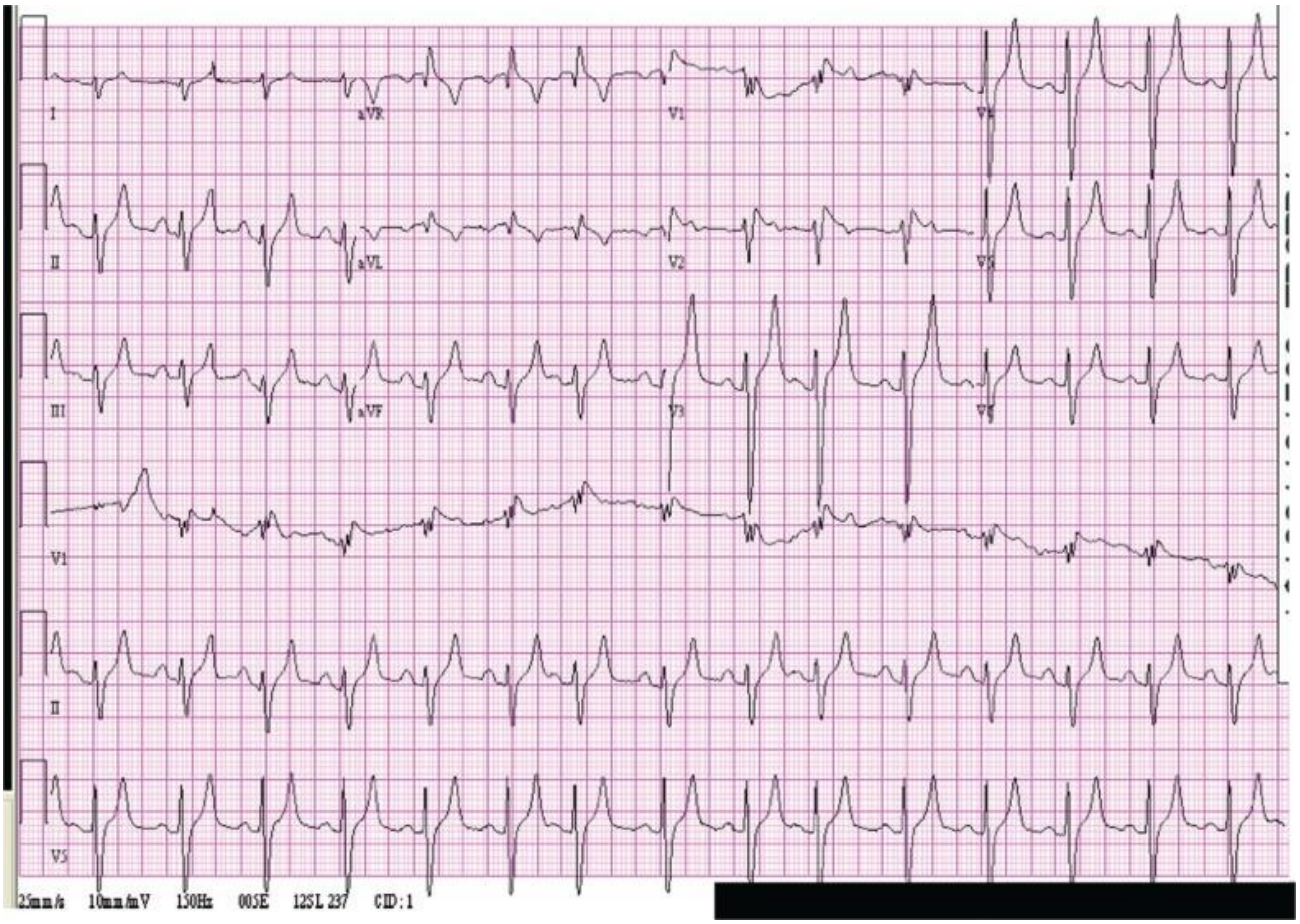
D. Edema of ankles and legs

E. Hypothyroidism

43. A 32-year-old woman calls her physician complaining of pain with urination, and says she has to urinate every 30 minutes. She reports being sexually active. The physician diagnoses her as having an uncomplicated urinary tract infection, and calls in a prescription for trimethoprim-sulfamethoxazole to the pharmacy. A week later, the patient presents to the emergency department complaining of nausea, vomiting, and fever. She tells the emergency department physician that her doctor said she had a urinary tract infection, but she never picked up the prescription because she was afraid the medicine would be too expensive. One of her friends also told her the infection would go away on its own. The physician asks for a urine sample, but the patient says she doesn’t think she can give him one, since she has been barely making any urine over the past day. Her vital signs are:

Temperature: 39.2°C(102.6°F)
Pulse: 110/min
Blood pressure: 95/60mmHg
Respiratory rate: 16/min
Oxygen saturation: 99% on room air
Examination is notable for costovertebral tenderness. Cardiac and pulmonary examinations reveal no additional pertinent findings. A basic metabolic panel shows a blood urea nitrogen level of 85 mg/dL and a serum creatinine of 3.6 mg/dL. Along with starting fluids and antibiotics, the physician orders an ECG.
Which of the following changes is the physician checking for on this patient's ECG?

A. Peaked T waves
B. QT prolongation
C. ST-segment depression
D. T-wave inversion
E. U waves



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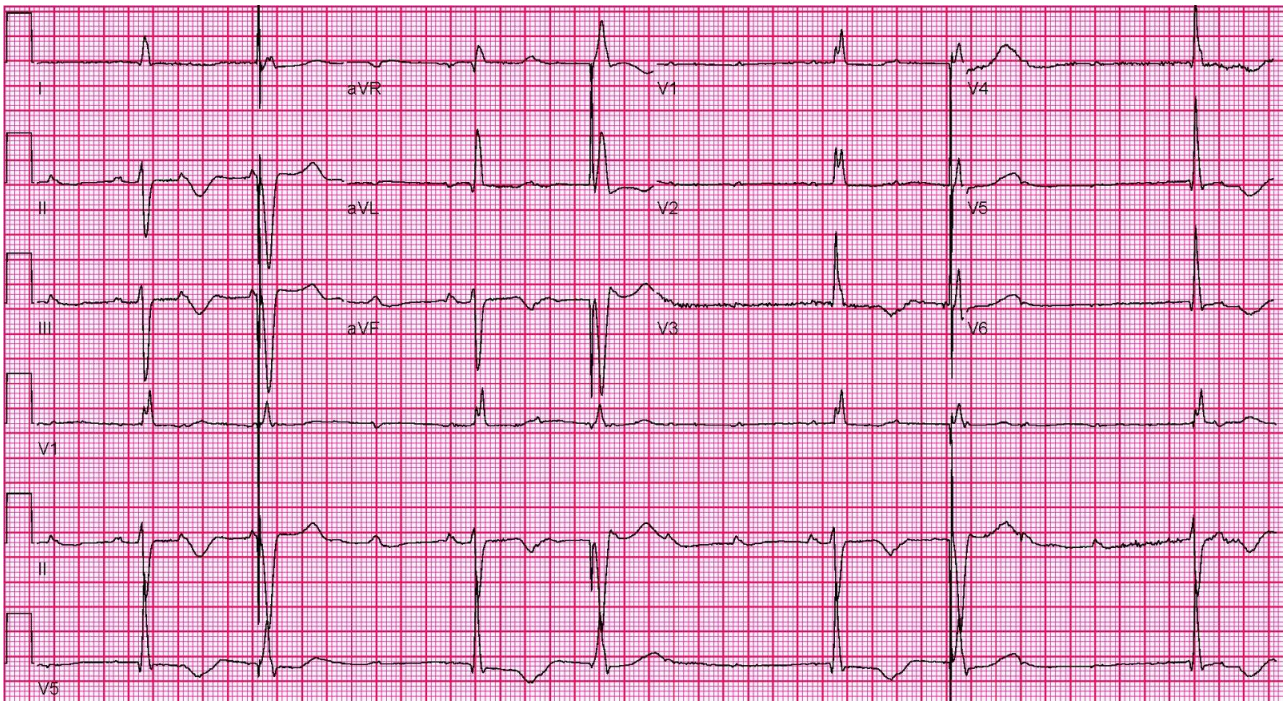
44. A 65-year-old man comes to the emergency department because of lightheadedness and fatigue for the past day. His medical history is significant for two prior myocardial infarctions and chronic hypertension. Daily medications include aspirin, nitroglycerin, atorvastatin, verapamil, spironolactone, enalapril, and hydrochlorothiazide. The patient's physician immediately orders an ECG, results of which are shown, and suspects an adverse drug reaction.



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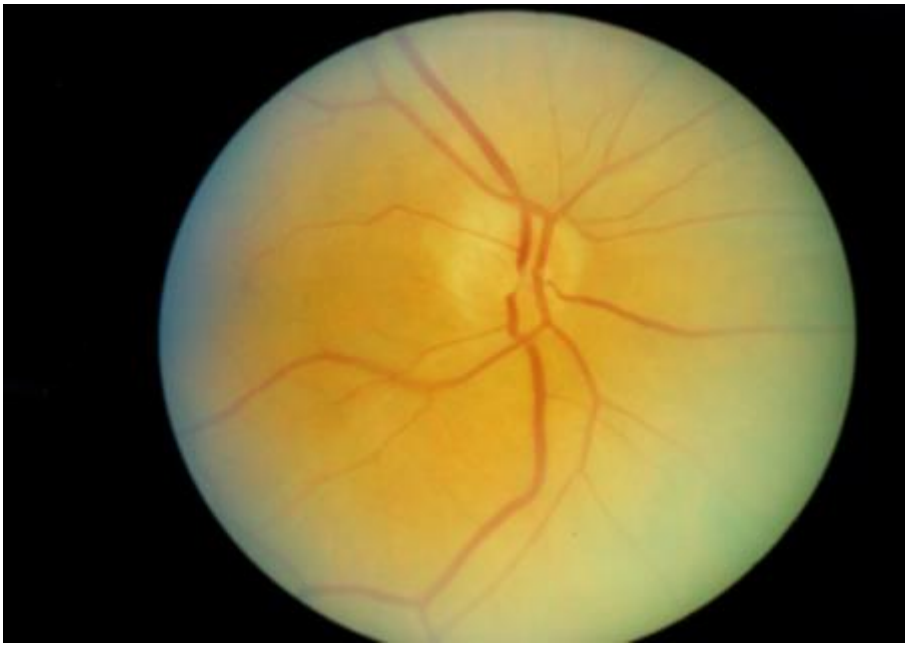
Which of the following pharmacological mechanisms is responsible for this patient's symptoms?

A. Activation of guanylyl cyclase
B. Inhibition of HMG CoA reductase
C. Inhibition of aldosterone receptor
D. Inhibition of angiotensin converting enzyme
E. Inhibition of cyclooxygenase
F. Inhibition of extracellular Ca2+ influx
G. Inhibition of the Na/Cl cotransporter

45. A 65-year-old woman visits her physician with what she thinks is the "flu." Her symptoms include headache, fatigue, and fever. The headache is constant, unilateral, and located in the frontotemporal region. The pain is not aggravated by light neck flexion or bright lights. She also reports pain on brushing her hair and while sleeping on just one side. She has had intermittent blurry vision. She has not experienced nausea, vomiting, or a rash, and there is no history of head trauma or headache syndromes. However, she has noted a 10-lb (4.5-kg) weight loss in the past 3 weeks. On physical examination, her temperature is 38.1°C (100.6°F), blood pressure is 120/70 mm Hg, and pulse is 90/min. She has a relative afferent pupillary defect in the eye on the same side as the headache. The fundus also is examined (see image).



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What treatment is most likely to be effective for this patient's condition?

A. Aspirin and intravenous immune globulin
B. Cyclophosphamide
C. Prednisone
D. Smoking cessation
E. Sumatriptan

46. A 68-year-old man comes to his primary care physician because of a 2-month history of fatigue. He has a history of poorly controlled hypertension refractory to various medical regimens, hyperlipidemia, type 2 diabetes mellitus, and a 55-pack-year smoking history. Current medications include atorvastatin, captopril, amlodipine, hydrochlorothiazide, and metformin. On auscultation of the heart, a delayed carotid upstroke as well as a crescendo–decrescendo murmur of the left lateral neck are noted. Vital signs are within the reference ranges. Laboratory studies show:

LDL: 198 mg/dL
HDL: 27 mg/dL
Triglycerides: 175 mg/dL
Glucose (fasting): 188 mg/dL

Doppler ultrasound studies of the neck show significant narrowing of the left carotid artery, with an estimated 16-fold decrease in blood flow. Resistance in which of the following vessels is most likely to be the highest in this patient?

A. Abdominal aorta
B. Femoral artery
C. Iliac artery
D. Left circumflex artery
E. Renal artery

47. A 9-year-old girl is brought to the emergency department with an arrhythmia that started while she was sitting in class. She was diagnosed at birth with a disorder that predisposes her to arrhythmias, but because her parents are not present, the hospital staff is unable to determine her medical history. Physical examination reveals no sternotomy scars. An ECG is obtained (see tracing). Which congenital cardiac abnormality does the patient most likely have?

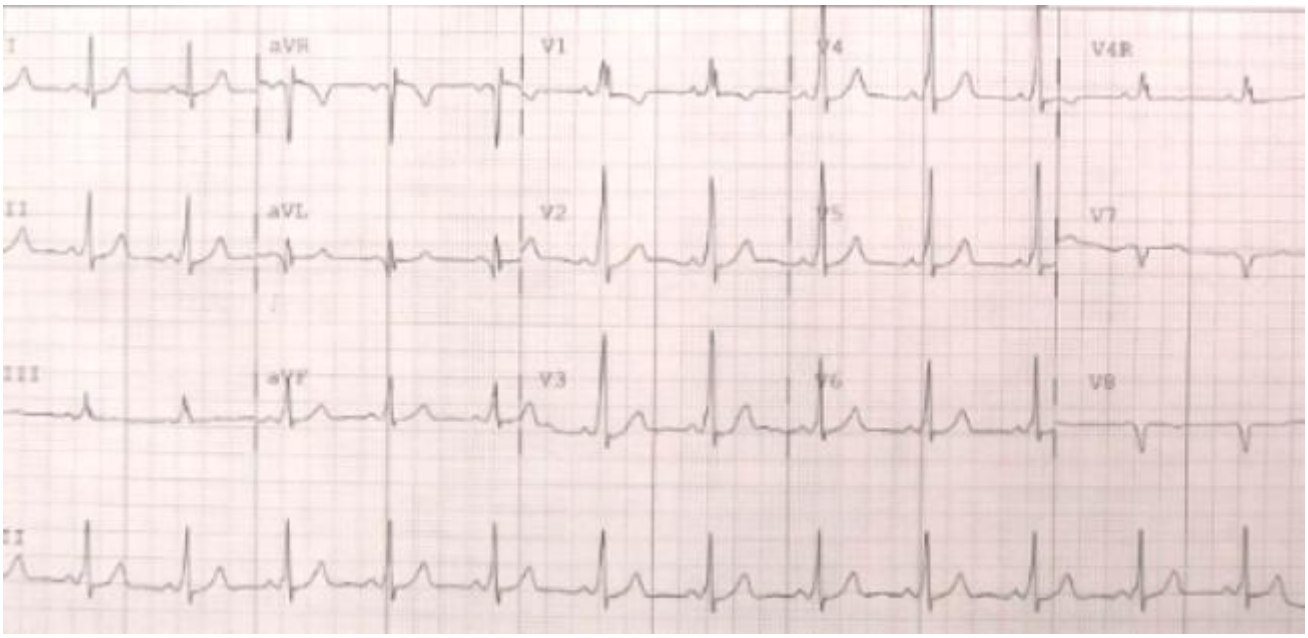
A. Accessory path between the atria and ventricles

B. Aorta arising from the right ventricle

C. Disordered myofibril hypertrophy

D. Left ventricle hypoplasia

E. Right ventricular hypertrophy with a ventricular septal defect



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48. A 62-year-old man is admitted to the hospital because of traumatic injuries sustained during a motor vehicle accident. He experiences extensive blood loss, requiring multiple transfusions. He has a central line and an indwelling urinary catheter. Several days later, his vital signs are as follows: temperature is 40.6°C (105°F); blood pressure is 60/30 mm Hg; pulse is 120/min; and oxygen saturation is 91% on room air. His breathing is rapid and shallow, and his arms and legs are warm to the touch. The patient is immediately given supplemental oxygen and a 2-L bolus of intravenous fluids, with no resulting change in blood pressure. On examination, an area of erythema and purulence surrounding the site of his central line is noted. Blood is drawn for culture. He is then admitted to the intensive care unit for further treatment.Which of the following best represents the relative molecular affinities of the drug that should be used to stabilize the patient's current condition?

A. $\alpha 1 > \alpha 2 > \beta 1$

B. $\alpha 1 = \alpha 2$ irreversibly

C. $\beta 1 > \beta 2 > \alpha$

D. Central α2-receptor
E. PDE-3 > PDE-5

49. A 62-year-old woman comes to her primary care physician because of weakness, fatigue, and progressive shortness of breath on exertion. She has also gained 10 lb over the past few weeks. The patient is a breast cancer survivor who had received radiation therapy. Physical examination reveals hepatomegaly, jugular venous distention that fails to subside on inspiration, and abdominal pain on palpation. The patient's temperature is 101.5°F (38.5°C) and blood pressure is 115/70 mm Hg. An echocardiogram shows a reduced bi-ventricular end diastolic volume. Which of the following is the most likely diagnosis?

A. Cardiac tamponade
B. Constrictive pericarditis
C. Dilated cardiomyopathy
D. Myocarditis
E. Systolic congestive heart failure

50. A 67-year-old man comes to the outpatient clinic with a chief complaint of progressive shortness of breath, particularly when he tries to lie flat. He reports needing to use four pillows at night to breathe comfortably. The patient is a retired chef who exercises infrequently and often travels to Africa and Asia with his wife. He has been drinking several glasses of whiskey every evening for the past 15 years but does not smoke or use illicit drugs. Physical examination reveals a laterally displaced and diffuse point of maximal impulse, an S3, pulmonary rales, hepatomegaly, and 2+ bilateral lower-extremity edema. X-ray of the chest shows a large, balloon-shaped heart. Given the presenting symptoms, what is the likely diagnosis?

A. Alcohol use disorder
B. Chagas disease
C. Hypertrophic cardiomyopathy
D. Radiation Exposure
E. Systemic sclerosis

51. A 2-year-old girl is brought to her pediatrician’s office for a well-child visit. The girls mother reports that the child is doing well. She is able to climb onto and down from furniture without help, knows the names of familiar people, and speaks sentences of two to four words. She is in the 70th percentile for height and weight. Physical examination is unremarkable except for a 2/6 heart murmur best heard in left upper sternal border with wide fixed split S2. Which of the following abnormalities explains the physical examination findings?

A. Aortic stenosis
B. Atrial septal defect
C. Mitral regurgitation

D. Patent ductus arteriosus
E. Transposition of great vessels
F. Ventricular septal defect

52. A 48-year-old woman with a history of hypercholesterolemia is referred to the cardiologist because of activity-induced chest pain. She describes the pain as a chest tightness that develops after walking several blocks, and goes away after several minutes of rest. In addition to arranging further testing, the physician gives the patient a tablet, and tells her to put it under her tongue when she has similar painful episodes. At low doses, which of the following best describes the primary mechanism(s) by which this medication alleviates the patient's symptoms?

A. Decreases afterload, decreases myocardial oxygen demands
B. Decreases plaque formation on coronary arteries
C. Decreases platelet activation in response to injury
D. Decreases preload, decreases myocardial oxygen demands
E. Increases afterload and decreases myocardial oxygen demands
F. Increases preload, decreases myocardial oxygen demands

53. An 85-year-old man with a history of congestive heart failure (CHF) and diabetes visits the emergency department, complaining of shortness of breath. In an effort to treat himself, he took calcium channel blockers that were prescribed for him a long time ago. Yet these treatments gave him no relief. Physical examination is significant for jugular venous distention, an S3 heart sound, and diffuse bilateral rales.

Which of the following drugs would be most effective in the immediate treatment of this patient?

A. Carvedilol
B. Digoxin
C. Furosemide
D. Metoprolol
E. Spironolactone

54. A 57-year-old man comes to the emergency department because of sudden-onset shortness of breath and crushing chest pain that radiates to his jaw and left arm. He also reports nausea and sweating. The pain started 4 hours ago while he was gardening. The pain is not positional and is not related to his breathing. For the past 3 months, he has been taking celecoxib daily for osteoarthritis. His temperature is 37.1°C (98.8°F), pulse is 89/min and regular, respirations are 20/min, and blood pressure is 110/80 mm Hg. The patient appears to be in considerable discomfort. He is sweating heavily and appears pale. Palpation of the chest wall does not elicit any tenderness. His lungs are clear to auscultation bilaterally. Cardiac auscultation reveals normal S_1 and S_2 sounds, and no arrhythmia is appreciated. ECG reveals ST-segment elevation in leads II, III,

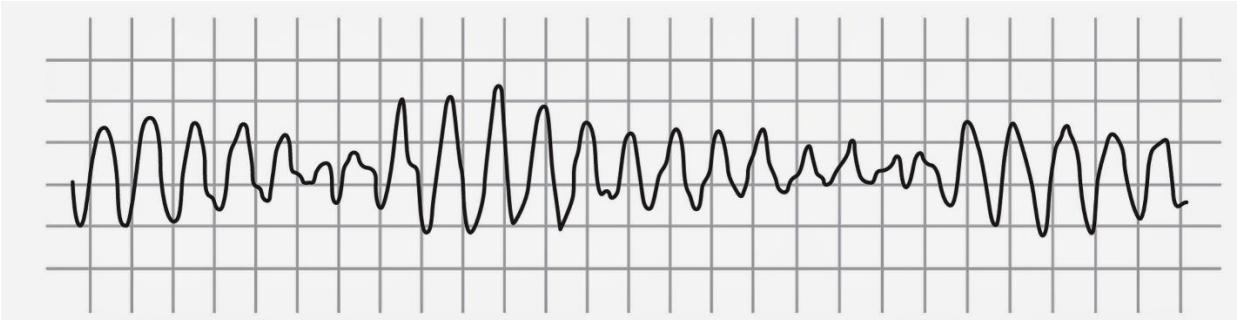
and aVF. Which set of effects of the patient's medication on prostanoid levels listed in the table most likely played a role in the development of his current condition?

Option	Prostaglandin I_2 (PGI_2)	Thromboxane A_2 (TXA_2)
A	↑	↓
B	↓	↓
C	↓	↑
D	No change	↓
E	↓	No change
F	No change	↑
G	↑	No change

55. A 28-year-old African-American man presents with fever, weight loss, diffuse myalgias, arthralgias, and abdominal pain. On examination, his blood pressure is 168/92 mm Hg, pulse is 83, and respiratory rate is 18. He has areas of ulceration and mottled purple discoloration on his lower extremities. His medical history is otherwise significant for hepatitis B infection. Laboratory tests reveal elevations in the white blood cell count, erythrocyte sedimentation rate, and C-reactive protein level. What histologic feature is commonly associated with this patient's disease process?

A. Caseating necrosis
B. Eosinophilic infiltrate
C. Fibrinoid necrosis
D. Granulomatous inflammation
E. Langhans giant cells

56. A 40-year-old man is brought to the emergency department because of a 5-hour history of heart palpitations. He has had no shortness of breath or dizziness. He has a history of Wolff-Parkinson-White syndrome and has had previous episodes of atrial fibrillation with rapid ventricular response. He takes no medications. He appears anxious. Blood pressure is 120/78 mm Hg and pulse is 158/min. An antiarrhythmic medication is administered. Results of an ECG performed after receiving the medication are shown.



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Which of the following medications was most likely administered?

A. Ibutilide
B. Lidocaine
C. Metoprolol
D. Mexiletine
E. Propafenone
F. Verapamil

57.A 21-year-old man comes for evaluation because of a 3-month history of occasional fainting episodes, palpitations, and lightheadedness. The patient was previously healthy and takes no medications. His family history is significant for several family members who died from sudden cardiac death before age 65. Temperature is 37° C (98.4° F), blood pressure is 123/75 mm Hg, pulse is 86/min, and respirations are 16/min. He is in not in acute distress. Physical examination shows no abnormalities. ECG shows normal sinus rhythm with a prolonged QT interval. Which of the following is the most likely diagnosis?

A. Brugada syndrome
B. Jervell and Lange-Nielsen syndrome
C. Mobitz type II atrioventricular block
D. Right bundle branch block
E. Romano-Ward syndrome
F. Wolff-Parkinson White syndrome

58. A 65-year-old man who is an inpatient in the cardiac care unit reports chest pain on inspiration. Pain is most severe when he is supine and is somewhat lessened when he sits up and leans forward. He was admitted to the hospital 2 days ago for myocardial infarction after he had experienced 6 hours of crushing substernal chest pain and was not treated with reperfusion or fibrinolytic therapy. Current medications include lisinopril, metoprolol, nitroglycerin, clopidogrel, and aspirin. On physical examination, temperature is 36.9° C (98.5° F), pulse is 66/min, respirations are 16/min, and blood pressure is 135/70 mm Hg. Oxygen saturation is 98% on room air. Lungs are clear on auscultation and S1/S2 are normal, but a faint rubbing noise is heard over the left side of the chest during systole and diastole. Troponin is positive, and CK-MB is not detectable. ECG shows Q waves in V3-V6 and ST elevations across all leads. Chest X-ray is normal.

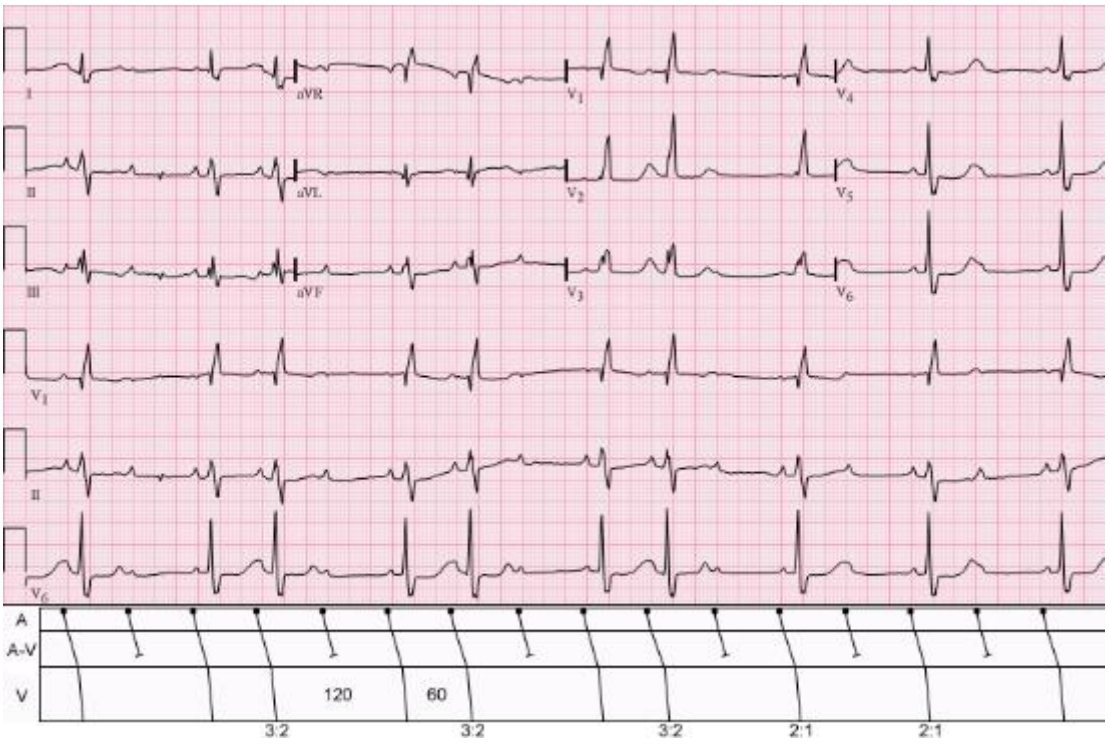
Which of the following is the most likely cause of this patient's chest pain?

A. Developing ischemia of cardiac myocardium
B. Pericardial inflammation due to necrotic myocardium
C. Pericardial inflammation secondary to autoantibodies against pericardial tissue
D. Pleural effusion
E. Pulmonary infarction
F. Ventricular wall rupture

59. A 52-year-old unresponsive man with a history of lung disease and coronary atherosclerosis is brought to the emergency department by emergency medical services. A stat ECG shows ventricular fibrillation. Electrical defibrillation is initiated but is unsuccessful. The emergency physician uses an antiarrhythmic drug to successfully treat the patient. The physician considers prescribing this antiarrhythmic drug for the patient on a long-term basis but is concerned about the side effects because of the patient's compromised pulmonary function. Which of the following is the primary mechanism of action of the antiarrhythmic that was most likely administered?

A. Accelerates depolarization in high-frequency depolarizing cells
B. Prolongs depolarization via sodium channel blockade
C. Prolongs the repolarization phase via potassium channel blockade
D. Reduces calcium influx in depolarizing cells
E. Reduces sympathetic stimulation of myocardial cells

60. A 28-year-old pregnant woman at 39 weeks' gestation is rushed to the hospital by her husband because she is in labor. Her medical history includes two previous pregnancies and one live birth. Her ECG shows normal sinus rhythm; her pulse is 80/min, and her blood pressure is 114/68 mm Hg. She elects to have epidural anesthesia for the delivery. Ten minutes after injection of the anesthetic, the woman reports palpitations and severe dizziness. Another ECG is obtained (see image). On investigation, her doctors discover that the resident pierced a vessel while inserting the epidural needle.



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Which of the following drugs was most likely administered for the procedure?

A. Accelerates depolarization in high-frequency depolarizing cells
B. Prolongs depolarization via sodium channel blockade

C. Prolongs the repolarization phase via potassium channel blockade
D. Reduces calcium influx in depolarizing cells
E. Reduces sympathetic stimulation of myocardial cells

61. A 58-year-old man is transported to the emergency department with the complaint of chest pain after eating a large steak dinner. During evaluation, he describes the chest pain as a constant heavy pressure that is localized to the area beneath his sternum. He has a history of coronary artery disease, hyperlipidemia, hypertension, and is obese by BMI. His current medication regimen includes simvastatin for his hyperlipidemia, and enalapril for hypertension prescribed during a visit to his primary care physician earlier in the week. The patient also states that he has new-onset erectile dysfunction and wonders if these symptoms are connected in any way. While discussing the man's condition with his wife, the patient begins coughing, and within 10 minutes he experiences nausea, shortness of breath, and diaphoresis.

Which of the following is the most likely cause of his symptoms?

A. Angina secondary to acute coronary syndrome
B. Autodigestion of the pancreas by pancreatic enzymes
C. Esophageal spasm due to consumption of large meal
D. Gastroesophageal reflux due to consumption of a large meal
E. Pulmonary embolism due to venous stasis

62. A 45-year-old woman is rushed to the emergency department by her husband. She started to experience palpitations, lightheadedness, and shortness of breath 1 hour ago. Her medical history is negative for any major illnesses, diagnoses, and hospitalizations. She does not take any medications. On admission, the patient's temperature is 37.6°C (99.7°F), pulse is 150/min, respiratory rate is 18/min, and blood pressure is 134/92 mm Hg. Her body mass index is 23.5 kg/m2. The attending physician immediately administers a drug that quickly terminates the patient's tachycardia and causes flushing, bronchospasm, and a significant drop in blood pressure. Which of the following medications was most likely administered?

A. Adenosine
B. Amiodarone
C. Ivabradine
D. Metoprolol
E. Procainamide

63. A 23-year-old man found unconscious with fresh needle tracks in his arm is brought to the emergency department by ambulance. The patient is resuscitated with naloxone and is admitted to the hospital. His temperature is 39° C (102.2° F). Upon examination, a "blowing" systolic heart murmur is heard that is loudest at the left lower sternal border. The murmur varies with respiration, becoming louder with inspiration.

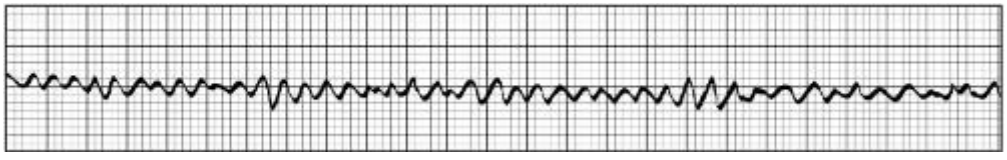
Additionally, the physician notes a prominent jugular venous pulse. Which of the following valvular abnormalities is most consistent with the murmur in this patient?

A. Aortic regurgitation
B. Aortic stenosis
C. Mitral regurgitation
D. Mitral stenosis
E. Tricuspid regurgitation
F. Tricuspid stenosis

64. A 72-year-old woman comes to her primary care physician because of a 2-month history of increasing shortness of breath on exertion and leg swelling. She has a long-standing history of rheumatoid arthritis. Current medications include azathioprine, prednisone, and occasional ibuprofen. She denies chest pain or any history of hypertension. She does not smoke cigarettes, and she has one glass of wine per week. Height is 172 cm (5 ft, 6 in), weight is 68 kg (150 lb), and BMI is 23. Her blood pressure is 118/72 mm Hg, pulse is 90/min, respiratory rate is 22/min, and oxygen saturation is 91% on room air. She has a prominent S4 heart sound on cardiac examination and bibasilar crackles on pulmonary auscultation. Jugular venous pressure (JVP) is 10 cm H_2O. Lower extremities show 2+ pitting edema bilaterally. Left ventricular ejection fraction is 60% according to echocardiogram. The patient is sent for additional diagnostic testing and the appropriate treatment is initiated. Which of the following is most likely responsible for this patient's clinical findings?

A. Concentric left ventricular hypertrophy
B. Dilated cardiomyopathy
C. Extracellular amyloid deposition
D. Ischemic heart disease
E. Myxomatous degeneration of mitral valve leaflets

65. An 87-year-old man suffered an acute ST-elevation myocardial infarction (STEMI) just a few minutes ago. He is subsequently treated with aspirin, metoprolol, and heparin. Immediately before being taken to the catheterization laboratory, the patient becomes unresponsive. He is placed on telemetry (see rhythm strip). The patient receives defibrillation, continuous CPR, and epinephrine, but he does not convert to sinus rhythm. He is given an additional agent while CPR, defibrillation, and epinephrine are continued.



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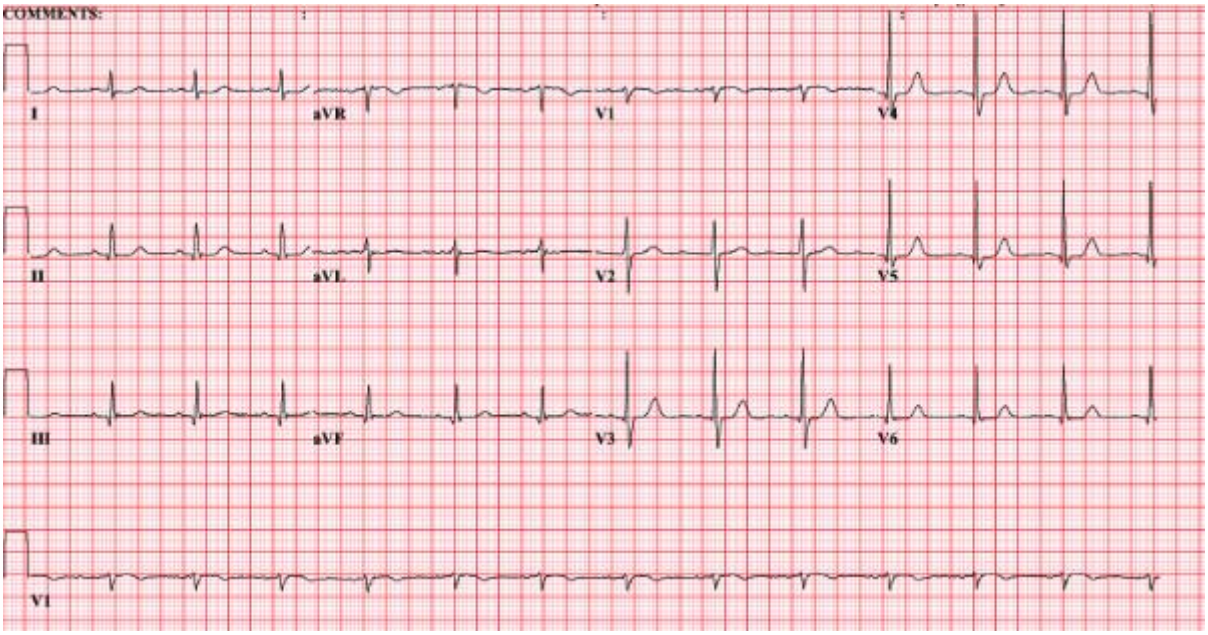
Which of the following potential adverse effects is associated with this additional agent

A. Bleeding
B. Increased post-MI mortality

C. Malar rash
D. Pulmonary fibrosis
E.Yellow-green vision

66. A 46-year-old man with a history of heart disease comes to the clinic for an annual check-up. He is concerned about long-term exposure to industrial chemicals, such as nitrates, because he works at an explosives factory. He reports that although he is in excellent health otherwise, he experiences headaches, dizziness, and palpitations every Monday. Physical examination is normal. An ECG is obtained (see image). His temperature is 37°C (98.6°F), respiratory rate is 14/min, and blood pressure is 122/85 mm Hg. Laboratory studies show:

Leukocyte count: 8000/mm^3
Hematocrit: 46%
Hemoglobin: 15 g/dL
Platelets: 310,000/mm^3
Na^+: 137 mEq/L
K^+: 3.5 mEq/L
Cl^-: 102 mEq/L
HCO_3^-: 24 mEq/L
Blood urea nitrogen: 12 mg/dL
Creatinine: 1.0 mg/dL



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Which of the following is the most likely serious complication that can occur as a result of his long-term exposure?

A. Anemia
B. Cardiac ischemia
C. Congestive heart failure
D. Dementia
E. Tuberculosis

ANSWERS MCQs IFOM

1. The correct is B. This patient, presenting with cramping leg pain upon exertion, elevated serum LDL and triglyceride concentrations, and low serum HDL concentrations, is most likely experiencing peripheral vascular disease. Such patients are typically treated with a lipid-lowering agent; statins (eg, atorvastatin) are first-line therapy. LDL transports cholesterol from the liver to peripheral tissues, while HDL transports cholesterol from the periphery back to the liver. High LDL and low HDL serum cholesterol concentrations both increase the risk of cardiovascular disease. The major cause of cardiovascular disease is atherosclerosis, which is a chronic inflammatory condition with immune competent cells in lesions producing mainly pro-inflammatory cytokines. However, as far as pharmacotherapy is concerned, lowering serum LDL concentrations is the only method proven to improve cardiovascular outcomes.Statins are particularly effective in lowering serum LDL cholesterol concentrations and have the added benefit of both increasing serum HDL cholesterol and decreasing triglyceride concentrations. As a result of their powerful LDL-lowering properties, they are the single most effective class of lipid-lowering drugs for preventing adverse cardiovascular outcomes and improving mortality in those with coronary artery disease. Statins work by competitively inhibiting HMG-CoA reductase, an enzyme required for the synthesis of cholesterol in the liver. This consequently causes an upregulation of liver LDL receptors and a subsequent increase in LDL uptake. The result is a marked decrease in circulating LDL and total cholesterol concentrations. Side effects include hepatotoxicity (for which liver function must be monitored) and myopathy (particularly when combined with a fibrate or niacin).

Unlike pharmacologic measures, lifestyle modifications that increase serum HDL concentrations do improve cardiovascular outcomes and should be encouraged in all patients with obstructive cardiovascular disease and dyslipidemia. These include smoking cessation, exercise, and dietary modification promoting weight loss.The other options are not the best answers.

Fibrates (eg, gemfibrozil) upregulate lipoprotein lipase and have profound triglyceride-lowering properties. They also activate peroxisome proliferator-activated receptor alpha (PPAR-α) to induce HDL synthesis. In patients with very high triglyceride concentrations, fibrates are used to prevent the development of pancreatitis. They are not first line for preventing adverse cardiovascular outcomes in peripheral vascular disease or cardiovascular disease.

Bile acid resins (eg, cholestyramine) prevent the intestinal reabsorption of bile acids, forcing the liver to use cholesterol in its replenishment. They are not as effective as statins in lowering LDL cholesterol.

Niacin inhibits lipolysis in adipose tissue, thereby reducing hepatic very-low-density lipoprotein (VLDL) synthesis. Niacin is most effective in raising HDL cholesterol,

which has not been proven to improve cardiovascular disease outcomes. Because of its side effect profile, niacin is generally used only in dyslipidemia that is refractory to treatment with other lipid-lowering agents.

Ezetimibe prevents cholesterol absorption at the small intestine brush border. It is inferior to statins both in lowering LDL cholesterol and preventing adverse cardiovascular outcomes, but it may be used in patients who have experienced adverse effects from statin therapy.

2. The correct is C. Thyroid dysfunction (both hypo and hyperthyrdoism) is a common manifestation of amiodarone toxicity. Amiodarone, an iodine-rich compound shares some structural characteristics with T4 (thyroxine) and may cause hypothyroidism by blocking conversion of T4 to T3. Fatigue, weight gain, and constipation are classic signs and symptoms of hypothyroidism. Notably, pulmonary toxicity is responsible for most deaths related to amiodarone therapy, with chronic interstitial pneumonitis being the most common form of pulmonary toxicity.Pulmonary fibrosis, hepatotoxicity, and bluish skin discoloration are other less common, classic manifestations of amiodarone toxicity. Amiodarone does not cause a shortened PR interval on ECG. Thyroid function, liver function, and pulmonary function should be monitored carefully in any patient receiving amiodarone therapy.

3. The correct is B. In this scenario, researchers are looking at determining relative risk of tobacco exposure and colon cancer development in a group of people with known tobacco exposure as compared to a group without such exposure. This is an example of a cohort study. Cohort studies can be prospective (follow the participants over time and determine rates of disease development) or retrospective (look into who developed disease—exposed versus unexposed). Retrospective cohort studies are much cheaper and faster to perform, but the researchers are not able to control confounding variables and bias as well as in prospective studies.Advantages of using cohort studies include clarity of temporal sequence (clearly indicate sequence between exposure and outcome), calculation of disease incidence and relative risk, investigation of rare exposures, and ability to decrease bias by careful selection criteria. Possible disadvantages of this study design include the long time of surveillance so they are not a great choice for diseases with long latency periods. The other answer options do not describe the type of study presented in this scenario. Case-control studies compare a group of people with a disease to a group of people without the same disease in order to identify factors that may contribute to a medical condition. They are used to calculate odds ratio. Cross-sectional studies examine frequency of disease and frequency of risk related factors assessed in the present time. They are used in calculating disease prevalence. Clinical trial is an experimental study comparing the effects of a treatment to other treatments and/or a placebo. The quality improves with studies that are randomized and controlled. In single blinded clinical trials, the information about the

test is masked for the participants, but the researchers are aware of which treatments the participants are receiving. In double blinding both patient and doctor are not aware whether patient is in experimental or control group thus eliminating the observer bias. Cross-over study is a longitudinal study in which subjects receive a sequence of different treatments or placebos. These studies are usually designed in such a way that participants receive the same number of treatments and participate for the same amount of time.

4. The correct is C. This patient, who is being treated for hypertension with captopril (an angiotensin-converting enzyme [ACE] inhibitor) is presenting with a dry cough, a known adverse effect of this drug class. ACE inhibitors increase bradykinin, a vasodilator that can cause respiratory symptoms such as cough and angioedema. For this reason, angiotensin II receptor blockers (ARBs) are first-line treatment of hypertension in patients with diabetes mellitus who are intolerant to ACE inhibitors. Although the hemodynamic effects of ARBs are similar to those of ACE inhibitors, they do not increase bradykinin and therefore do not cause cough or angioedema.The renin-angiotensin-aldosterone system (RAAS) can have profound effects on blood pressure through a variety of mechanisms. The RAAS pathway proceeds as follows:

Angiotensinogen (from the liver) is converted to angiotensin I by renin (secreted by renal juxtaglomerular cells).

Angiotensin I is subsequently converted to angiotensin II by ACE.

Angiotensin II exerts its effects on a number of tissues. This includes blood vessel receptors to promote vasoconstriction and adrenal cortical cells to secrete aldosterone, both of which ultimately lead to an increase in blood pressure.

ARBs (eg, losartan, candesartan, valsartan) act by blocking angiotensin II receptors. This inhibits the release of aldosterone, leading to volume contraction, as well as prevents constriction of the systemic vasculature. These mechanisms act to decrease blood pressure. Side effects include hyperkalemia and decreases in glomerular filtration rate. Additionally, ARBs are a known teratogen. They are first line in the treatment of hypertension, heart failure, and chronic kidney disease (eg, diabetic nephropathy) in those intolerant to ACE inhibitors.

ARBs reduce the complications of diabetes (eg, progression of kidney disease), and they are preferred agents for managing hypertension in patients with diabetes mellitus.

The other options are not the best answers:

ACE inhibitors (eg, captopril) prevent the conversion of angiotensin I to angiotensin II, leading to decreased circulating angiotensin II levels and subsequent decreases in aldosterone secretion and renal Na+ reabsorption. Renin and angiotensin I levels are increased.

Aldosterone receptor antagonists (eg, spironolactone, eplerenone) increase circulating renin, angiotensin I, angiotensin II, and aldosterone levels and decrease renal sodium

reabsorption. Aldosterone receptor antagonists improve mortality when used to treat heart failure and are first line in the treatment of hepatic ascites.

β1-receptor blockers inhibit the secretion of renin from juxtaglomerular cells, causing decreases in circulating renin levels, those of all downstream renin-angiotensin-aldosterone products, and subsequently renal Na+ reabsorption.

Aldosterone receptor agonists would decrease circulating renin, angiotensin I, angiotensin II, and aldosterone levels, while renal Na+ reabsorption would be increased.

5. The correct is A. This patient is young and is experiencing tachycardia. Any unexplained tachycardia is most likely caused by a pathologic mechanism. One of the more common forms of tachycardia in a young and otherwise healthy patient is paroxysmal supraventricular tachycardia (PSVT). Adenosine, when given in high-dose intravenous boluses, is extremely useful in abolishing atrioventricular (AV) nodal arrhythmias such as the PSVT demonstrated in this patient's ECG. The ECG shows an extremely fast regular heart rate (>150). It is clear that the electrical signal is originating above the ventricles because of the narrow QRS. However, the defining feature is that the P wave is obscured by the preceding T wave.

Adenosine works by hyperpolarizing AV node tissue, increasing conductance of potassium and reducing calcium current. As a result, the conduction through the AV node is markedly reduced. Adenosine's extremely short duration of action (15 seconds) also limits the occurrence of its adverse effects (ie, hypotension, flushing, chest pain, and dyspnea).

Amiodarone is a potassium channel blocker (class III), which will prolong the repolarization phase.

Flecainide is used when ventricular tachycardia progresses to ventricular fibrillation; it is also used for intractable supraventricular tachycardia.

Lidocaine, a class Ib antiarrhythmic, is used in the treatment of acute ventricular arrhythmias such as postmyocardial infarction arrhythmias.

Sotalol, a β-adrenergic-receptor blocker (class II) and a potassium channel blocker (class III), is used only for severe symptomatic arrhythmias.

6. The correct is D. This elderly man has shortness of breath and bilateral lower extremity edema that have increased over a six-month period. These signs and symptoms combined with his elevated brain natriuretic peptide (BNP) level and results of his EKG suggest that he has worsening congestive heart failurewith decreased ejection fraction. Sacubitril is found to decrease mortality and morbidity of patients with chronic heart failure with decreased ejection fraction. Sacubitril is a prodrug which gets activated to sacubitrilat via esterases. Sacubitrilat inhibits the enzyme neprilysin which degrades bradykinin (a potent vasodilator). In addition, neprilysin is responsible for degradation of atrial natriuretic peptide (ANP) and brain natriuretic

peptide (BNP). ANP and BNP decrease blood volume and blood pressure. ANP is released from atrial myocytes in response to increase in atrial volume and pressure. This peptide causes vasodilation and decreased reabsorption of sodium in the renal collecting tubules. ANP also promotes diuresis by vasodilation of afferent renal arterioles and vasoconstriction of efferent arterioles. BNP is released from ventricular myocytes in response to increased tension. It has similar action to ANP with longer half-life. BNP is used clinically to diagnose heart failure.

Sacubitril is combined with valsartan, an angiotensin receptor blocker (ARB) to block activation of the renin-angiotensin-aldosterone system (RAAS). This is an important mechanism in the treatment of congestive heart failure. In congestive heart failure, neurohormonal activation results in increased sympathetic response and RAAS activation.

The other answer choices are incorrect for the following reasons:

Antagonism of angiotensin II receptors describes the mechanism of action of ARBs. Valsartan, a member of this drug class, is part of the regimen recommended in the treatment of worsening congestive heart failure with decreased ejection fraction. However, sacubitril exerts its effect via a different mechanism.

Calcium channel blockers cause inhibition of calcium channels. These agents should not be used in the treatment of congestive heart failure with reduced ejection fraction, as they have variable degrees of negative inotropic activity and can cause hemodynamic deterioration with severe heart failure.

ACE inhibitors work by blocking angiotensin-converting enzyme. Although they may be prescribed for the treatment of congestive heart failure, they cannot be coadministered with sacubitril as both drugs inhibit the degradation of bradykinin, increasing the risk of angioedema.

Digoxin inhibits sodium/potassium ATPase

Beta-blockers act by blocking beta adrenergic receptors.

7. The correct is A. A cystic hygroma is an abnormal growth that usually appears on a baby's neck or head. It consists of one or more fluid-filled cysts and tends to grow larger over time. The growth is caused by an error in fetal development of lymphatic tissue, resulting in accumulation of lymph in sacs due to lymphatic congestion in the neck. There are two types of lymphatic malformations: macrocystic (large cysts) and microcystic (small cysts). Cystic hygromas are associated with other congenital anomalies such as nuchal lymphangioma, Down syndrome, Turner syndrome, and fetal hydrops. Cystic hygromas are commonly diagnosed by prenatal ultrasonography, or they may be discovered at birth or later in life. They can grow large and may affect breathing or swallowing and cause disfigurement of the body part they affect.

Cystic hygromas are treated with thin-needle aspiration of contents to decrease pressure on surrounding organs, especially if respiration or swallowing is

compromised. The definitive treatment consists of surgery or injection of sclerosing agents such as doxycycline, bleomycin, or pure ethanol.

This patient, in addition to a cystic hygroma, presents with findings suggestive of Turner syndrome: low-set ears and lymphedema of the hands and feet. Turner syndrome (45,X) is caused by the loss of one X chromosome. The signs and symptoms vary but include short stature, broad chest, webbed neck, swollen hands and feet seen at birth, low-set ears, and infertility. Turner syndrome is also associated with heart defects, horseshoe kidney, low thyroid hormone, and diabetes mellitus.

The other options are incorrect for the following reasons.

A hemangioma is a benign tumor derived from blood vessel cells and usually appears deep red. A thyroglossal duct cyst forms from a persistent thyroglossal duct and presents as a midline neck mass, which moves with tongue protrusion or swallowing. This patient has a posterior neck mass, which rules out a thyroglossal duct cyst.

A teratoma is a germ cell layer tumor. Most teratomas are found in an ovary or on the tailbone. Sebaceous cysts are mobile, smooth masses most commonly formed by keratin and are not usually seen in newborns.

Parotitis is an inflammation of the parotid glands, which presents as a lateral neck mass. Although infants may have parotitis, the swelling associated with parotitis is located on the lateral side of neck, posterior and medial to the ear.

8. The correct is B. This patient presents with a myocardial infarction (MI) that is treated with coronary angioplasty and antiplatelet therapy. Six days after the MI, he develops, tachycardia, hypotension, and loss of consciousness. These symptoms raise concern for left ventricular free-wall rupture. Five to 10 days after myocardial infarction (MI), mechanical weakening of the necrotic and inflamed myocardium can lead to rupture of the ventricular free wall, resulting in hemopericardium and cardiac tamponade. The physical manifestations of cardiac tamponade include distended neck veins, muffled or distant heart sounds, and pulsus paradoxus. As a result of this cardiac emergency, the patient becomes severely hypotensive because the blood in the pericardium restricts diastolic filling. Overall cardiac function is compromised, and cardiogenic shock occurs. Papillary muscle rupture occurs 4 to 7 days after acute MI, and leads to mitral regurgitation and pulmonary edema, Interventricular septum rupture would present with rapid hemodynamic compromise and cardiogenic shock, but typically follows inferior or anterior MI. Reinfarction is uncommon after coronary angiography, and usually does not present with rapidly progressive hypotension. Right ventricular free wall rupture is very unusual and would not follow a left circumflex artery MI.

9. The correct is C. Trimeric G proteins are composed of alpha, beta and gamma subunits. Upon activation, the alpha subunit dissociates from the beta and gamma subunits and mediates downstream events. This can involve increases in different

second messengers depending on the type of trimeric G protein involved. The Gαq subunit is part of a G-protein pathway that activates phospholipase C (PLC) after exchanging guanosine diphosphate (GDP) for guanosine triphosphate (GTP). As a result, PLC splits phosphatidylinositol bisphosphate (PIP2) into diacylglycerol (DAG) and inositol trisphosphate (IP3). As a result, protein kinase C is activated and calcium levels increase intracellularly resulting in muscle contraction.

The other options are incorrect for the following reasons:

Cyclic adenosine monophosphate (cAMP): Levels increase when Gs subunit and adenylate cyclase are activated; however, this drug activated Gq.

Cyclic guanosine monophosphate (cGMP): Levels increase when guanylyl cyclase is activated by mediators such as nitric oxide (NO); however, this drug activated Gq.

Nitric oxide: NO levels can increase cGMP, resulting in smooth muscle relaxation; however, this drug activated Gq.

Sodium: Drugs like digoxin can influence concentrations of sodium (Na+), potassium (K+), and calcium (Ca2+). However, digoxin binds to a Na+/K+ ATPase, not a G-protein.

Protein kinase A: PKA is activated by Gs and inhibited by Gi. It is not involved in the Gq pathway.

10. The correct is B. This patient presents with hypertension and new-onset atrial fibrillation. She has been given nadolol, a nonselective β-blocker. Nonselective β-blockers act by binding to β1- and β2-receptors. Thus they antagonize the effects of epinephrine and norepinephrine. The dominant adrenergic receptor type in the heart and juxtaglomerular cells of the kidneys is the β1-receptor. Stimulation of this receptor causes an increase in heart rate, contractility, and renin release. The dominant adrenergic receptor type in the vascular smooth muscle found in the walls of arteries and arterioles of the skeletal muscle vasculature is the β2-receptor, stimulation of which causes vasodilation, which in turn would act to decrease systemic vascular resistance (SVR). Blocking these receptors would cause decreased heart rate, contractility, and renin release and elevated SVR.

Because β2-blockade increases SVR, any answer with a decrease or no change as the effect on SVR is incorrect. β1-Blockade results in decreased heart rate, contractility, and renin release. So, any answer with an increase in heart rate, contractility, and/or renin release is incorrect.

11. The correct is B. The patient reports substernal chest pain radiating to the back, which is highly suggestive of aortic dissection. A new diastolic murmur in association with severe acute chest pain is a sign of acute aortic regurgitation. This is due to the dissection propagating proximal to the initial tear involving the aortic valve. Clinically, patients with this condition will have a wide pulse pressure, hypotension, and/or heart failure. Acute aortic valve regurgitation occurs in one-half to two-thirds of ascending

dissections and is most commonly heard along the right sternal border, unlike aortic regurgitation due to primary aortic valve disease, which is most commonly heard along the left sternal border. There are multiple causes for aortic dissections; however, the description of a tall, slender patient with long arms and fingers indicate Marfan syndrome as the most likely diagnosis.

Marfan syndrome is an autosomal dominant disorder involving the FBN1 gene mutation, located on chromosome 15, resulting in a defect in fibrillin-1 synthesis. Clinical features of this disorder include excessive linear growth of the long bones and joint laxity (except at the elbows where there is decreased extension), pectus carinatum (more specific) or pectus excavatum, arachnodactyly, ectopia lentis, and aortic root disease. Ectopia lentis is detected on slit-lamp examination after maximal dilatation of the pupil, in which the lens is usually displaced upward. Aortic root disease, leading to aneurysmal dilatation, aortic regurgitation, and dissection, is the main cause of mortality for patients with Marfan syndrome. On histology, the medial layer of the aortic root in patients with Marfan syndrome includes fragmentation of elastic lamellae, cystic medial necrosis, fibrosis, and loss of smooth muscle cells.

Atherosclerosis is associated with aortic dissection in patients over 70 years of age, which is not consistent with this young patient. Obliterative endarteritis of the vasa vasorum is associated with tertiary syphilis leading to aortic root dilatation and aortic regurgitation; it rarely leads to dissection. Multiple endocrine neoplasia type 2B patients have “Marfanoid habitus” but do not have ectopia lentis or aortic abnormalities. Ehlers-Danlos syndrome is a defect of type III collagen synthesis, which can lead to an ascending aortic aneurysm and dissection; however, this disease is not associated with tall stature and long arms and fingers.

12. The correct is C. This patient presents with fever, weight loss, myalgias, arthralgias, abdominal pain, hypertension, and elevations in the erythrocyte sedimentation rate, C-reactive protein level, and white blood cell count. Taken together, these findings are consistent with a diagnosis of polyarteritis nodosa (PAN), which is characterized by necrotizing immune complex inflammation of medium-sized, muscular arteries. No diagnostic serologic tests are specific for PAN. The diagnosis is usually made by the presence of the clinical symptoms described for this patient, results of physical exam (including skin findings, motor or sensory loss, and vascular exam abnormalities), hepatitis/rheumatologic test results, and sometimes biopsy or angiography findings.

Patients with classic PAN are negative for antineutrophil cytoplasmic antibodies and may have low titers of rheumatoid factor or antinuclear antibodies, both of which are nonspecific findings. In patients with PAN, appropriate serologic tests for active hepatitis B infection must be performed. Up to 30% of patients with PAN are positive for hepatitis B surface antigen. In patients with PAN, inflammation of the arterial wall

and surrounding connective tissue results from immune complex formation and deposition, leading to fibrinoid necrosis (indicated by the open arrow in the image).
Caseating necrosis is associated with tuberculosis infections. Eosinophilic infiltrate is a prominent feature in Churg-Strauss syndrome. Granulomatous infiltrate is evident in giant cell arteritis, and Langhans giant cells are associated with granulomatosis with polyangiitis. Onion skinning, seen with arteriolosclerosis, is linked to malignant hypertension.

13. The answer is D. This patient presents with a history of intellectual disability, seizures, and shortness of breath. He also has acne-like papules on his face, and an echocardiogram shows significant left ventricular outflow obstruction. Together, the history and findings suggest that the patient has tuberous sclerosis, a genetic condition (autosomal dominant) characterized by nodular proliferation of multinucleated atypical astrocytes. These form tubers, which are found throughout the cerebral cortex and periventricular areas. The classic triad of tuberous sclerosis, manifesting in only the most severe cases, consists of seizures, intellectual disability, and facial angiofibromas (also known as adenoma sebaceum). Half of patients with tuberous sclerosis will have a rhabdomyoma(see image), a primary tumor of cardiac muscle that, although benign, may compromise cardiac function. A rhabdomyoma may be found on an atrial or ventricular wall, causing outflow tract obstruction. Tuberous sclerosis is also notable for an association with angiomyolipomas of the kidney.
Dilated cardiomyopathy classically causes four-chamber dilation, often with coexisting hypertrophy, and eventually heart failure. Lipomas can create ball-valve obstructions and are most often located in the left ventricle, right atrium, or atrial septum. Myxomas are tumors usually found in the atria in adults. Transposition of the great vessels is a condition in which the pulmonary trunk arises from the left ventricle, and the aorta arises from the right ventricle.

14. The answer is D. This patient, who has diabetes and is a heavy smoker, comes to her physician with a report of chest pain on exertion. Her stage 2 hypertension and blood test results suggest coronary artery disease, for which the physician has prescribed a statin. Statins inhibit serum cholesterol levels by inhibiting hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase, which inhibits mevalonate and the synthesis of cholesterol further downstream. As a result, intracellular cholesterol is diminished while the LDL receptor is upregulated, which helps lower LDL cholesterol levels. This patient's concomitant use of a statin with a fibrate increases her risk of myopathy. Even when high doses of HMG-CoA reductase inhibitors are used alone, myopathy can be a side effect, so patients taking these medications are closely monitored. However, when given in combination with gemfibrozil (a lipid-lowering fibrate), the risk of myositis, myopathy, and rhabdomyolysis increases. As rhabdomyolysis occurs, myoglobin is released from the

broken-down muscle cells. Myoglobin is then filtered by the kidneys and can be present in the patient's urine (myoglobinuria). Metabolic acidosis, not metabolic alkalosis, is a rare side effect of statins. Transaminitis can occur with statins, but it would not be worsened by concomitant fibrate use. Statins have no known connection to hemoglobinuria or bilirubinuria.

15. The correct is C. This patient presents with a history of joint hyperflexibility and symptoms of hypotension, tachycardia, pulsus paradoxus, and jugular venous distention. This presentation suggests he most likely has Marfan syndrome. He is currently experiencing an aortic dissection that has led to cardiac tamponade. Cardiac tamponade is the result of fluid (often blood) accumulating in the potential space between the visceral and parietal pericardium. Because the fibrous layer of the pericardium is relatively inflexible and extra fluid is present in the space, the myocardium is prevented from fully expanding during diastole in cardiac tamponade. An echocardiogram often reveals right ventricular and/or right atrial collapse. This leads to severely decreased ventricular filling and decreased cardiac output. Cardiac tamponade often manifests with the Beck triad: hypotension, increased jugular venous pressure, and distant heart sounds. On an electrocardigram (ECG), the blood surrounding the heart can attenuate the recorded electrical signal. The ECG will show diffuse low-voltage QRS complexes and electrical alternans (see image). The amplitude of the QRS complex oscillates with each beat, which is thought to occur as the heart "swings" within the pericardial fluid.

Localized ST-segment elevations are characteristic of myocardial infarction (MI), which typically presents with crushing chest pain radiating to the arm. Diffuse ST-segment elevations with PR depressions would be seen in a patient with acute pericarditis. An S1Q3T3 pattern with right ventricular strain would be found in a patient with a pulmonary embolism. T-wave inversions are nonspecific ECG changes that can be a sign of subendocardial ischemia.

16. The correct is E. The patient's lipid profile, including elevated LDL and triglyceride levels, is diagnostic of hyperlipidemia. Statins are the gold standard for treatment of hyperlipidemia when a patient can tolerate their side effects. They have been proven to decrease morbidity and mortality rates associated with atherosclerosis. Statins competitively inhibit hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase, the enzyme that catalyzes the rate-limiting step in cholesterol synthesis, by obstructing part of the enzyme's active site. The subsequent decrease in intrahepatic cholesterol causes upregulation of hepatic LDL cholesterol receptors, ultimately lowering plasma LDL cholesterol levels. The Michaelis-Menten constant (Km) is the concentration of a substrate that brings about an initial velocity that is half the maximum velocity (Vmax) of the reaction. Because statins bind to the same binding site as the substrates of the enzyme, statins increase HMG-CoA reductase's apparent

Km. Well-known adverse effects of statin use include myalgia, myositis, and rhabdomyolysis.

Statins have no effect on the maximum velocity (Vmax) of the reaction because they reversibly bind to the same site as HMG-CoA and can be outcompeted in the presence of very high concentrations of HMG-CoA.

As for LDL, statins do not directly affect hepatic LDL receptor affinity for cholesterol (KD) or its activity. They indirectly increase the concentration of hepatic LDL receptors on the surface of hepatocytes, so they increase (not decrease) the Vmax of the reaction between LDL receptors and LDL cholesterol.

17. The correct is D. This patient presents with history of stable anginal symptoms, acute-onset chest pain, an elevated troponin level, and ST-segment changes on an ECG. Together the history, symptoms, and findings indicate a diagnosis of acute myocardial infarction (MI). The primary mechanism of acute MI involves acute plaque rupture with a background of atherosclerosis (see images). This promotes thrombogenesis and leads to coronary arterial thrombotic occlusion and obstruction of blood flow to the area of myocardium supplied by the artery.

The infarcted cardiomyocytes spill troponin into the bloodstream. Note that this patient has an inferior wall MI with ST-segment elevations. This is indicated by the ECG, which shows ischemic changes on leads II, III, and aVF.

Coronary artery dissection is associated with iatrogenic injury by catheter tips during invasive angiography or with the peripartum period in women. Coronary artery vasospasm, also called Prinzmetal angina, is less common than MI, especially in a patient with a history of stable angina. In a patient with thromboembolic disease, a thrombus travels through the bloodstream and causes occlusion of a blood vessel. It is associated with atrial septal defects and atrial fibrillation. Although this patient likely has coronary artery stenosis, it is a chronic process and not the direct cause of his acute symptoms.

18. The correct is B. Medications that inhibit the sodium-potassium-chloride cotransporter are the loop diuretics (eg, furosemide). Loop diuretics can be used in the treatment of patients with dilated cardiomyopathy. Dilated cardiomyopathy may progress to congestive heart failure (CHF), and acute exacerbations of CHF result in a fluid-overloaded state. A loop diuretic works to exogenously manipulate fluid balance. In the ascending limb of the loop of Henle, the sodium-potassium-chloride cotransporter reabsorbs sodium, chloride, and potassium. Inhibition of this cotransporter by loop diuretics causes an increased fractional excretion of sodium and diuresis. Loop diuretics reduce blood volume, which in turn leads to a reduction in venous return and a reduced preload. Loop diuretics are contraindicated for treatment of hypertrophic obstructive cardiomyopathy (HOCM) and hypokalemia. Although myocardial infarction (MI) may lead to congestive heart failure and pulmonary edema,

acute MI is not treated with loop diuretics. Unstable angina pectoris is treated with platelet inhibitors and nitroglycerin, not loop diuretics.

19. The correct is B. This researcher is determining the range of values within which the true mean of her study falls. This range is called the confidence interval and is typically set according to a specific Z score. A confidence interval of 95% will have a Z score of 1.96 and an alpha of 0.05 (type I error value of 5%). If the confidence interval for relative risk includes 1, H0 (null hypothesis) is not rejected. A standard deviation shows the variability that exists among a range of values that typically center around a mean. The median is represented by the center value in a numerical set, ordered from least to greatest. Standard error estimates the variability within a set of sample means around the true population mean. Variance helps to describe the variability within a population but does not draw any conclusions regarding the range within which the true mean can be found. A bimodal distribution is suggestive of two different populations plotted on one graph as the graph will have two means. Bimodal distributions will each have their own confidence interval.

20. The correct is C. This 17-year-old patient's history of an untreated illness and current production of frothy, dark urine should raise suspicion for glomerular disease. One common cause of postinfectious glomerulonephritis is infection with β-hemolytic streptococci, such as Streptococcus pyogenes. In addition to causing nephritic syndrome, S. pyogenes can also cause acute rheumatic fever if left untreated. Although rheumatic fever is a well-known cause of pancarditis, it can also induce Sydenham chorea, a restless, uncontrollable movement of the extremities. In its early stages, acute rheumatic fever can cause mitral regurgitation; however, this is not always the case. In later stages, stenosis can develop (mitral > aortic > tricuspid) as the valve orifice narrows. Such a condition is evidenced by the presence of a murmur and a possible arrhythmia. Poststreptococcal glomerulonephritis and acute rheumatic fever are immune-mediated type II hypersensitivity reactions, resulting in an M protein cross-reaction with host antigens (molecular mimicry). Although treatment with penicillin at the time of infection greatly reduces the risk of developing acute rheumatic fever, it does not prevent poststreptococcal glomerulonephritis sequelae. Juvenile Huntington disease involving a triple repeat expansion is responsible for 5%-10% of cases of Huntington disease. Subthalamic lesions may cause hemiballismus. An elevated blood ammonia concentration can cause encephalopathy. Substance abuse or intoxication may explain some of this patient's symptoms but is unlikely due to her other symptoms, the timeline, and the normal vital signs. A generalized seizure disorder can explain uncontrolled movements of the limbs but is unlikely due to normal findings on the neurologic exam and the symptoms of renal involvement.

21. The correct is A. A patient with osteoarthritis, hypertension, and diabetes presents to the emergency department with shortness of breath and chest pain that radiates down

both arms. A coronary angiogram reveals three blocked coronary arteries as the likely cause. The purpose of the question is to determine which of the given antibiotic choices is considered the best option to prevent infection at the vascular entry point for coronary angiography. First- and second-generation cephalosporins are favored for preventing surgical site infections, including cardiac procedures, due to their excellent activity against gram-positive bacteria, which are present on the skin and therefore more likely to be introduced into the surgical site. Given the options, the correct answer choice is cefazolin, a first-generation cephalosporin and the recommended antibiotic for surgical prophylactic treatment. It has a mechanism of action that inhibits cell wall biosynthesis by binding to penicillin-binding proteins. It is considered bactericidal because it kills the bacteria instead of simply inhibiting bacterial growth. Cefazolin is widely studied with proven efficacy, good duration of action, reasonable safety, low financial burden, and good spectrum of activity against the gram-positive organisms that are commonly encountered in surgical procedures. Common adverse reactions to cefazolin include injection site reactions (ie, pain, swelling, skin rash, hard lump), diarrhea, abdominal pain, stomach cramping, nausea, and vomiting. Vancomycin and clindamycin are alternatives to cephalosporins for patients allergic to β-lactams.

The other answer options are incorrect:

Ciprofloxacin has poor gram-positive antibiotic coverage.

Meropenem has antibiotic coverage that is too broad.

Vancomycin should be reserved for resistant staph infections.

Gentamicin has poor gram-positive antibiotic coverage.

22. The correct is C. This patient, who presents with fatigue, dyspnea, heart palpitations, and an irregularly irregular heartbeat, is likely suffering from atrial fibrillation. His history of hypertension, which is a common risk factor for the development of atrial fibrillation, further substantiates this diagnosis. Digoxin can be used to treat atrial fibrillation by decreasing conduction at the atrioventricular (AV) node and depressing the sinoatrial (SA) node. It acts to inhibit sodium potassium adenosine triphosphatase (Na+/K+ ATPase), most prominently in the myocardium. This action of digoxin also increases intracellular calcium in ventricular myocytes producing increased force of contraction.

The Frank-Starling effect is demonstrated by the cardiac function (cardiac output/red) curve on the above graph. The Frank-Starling effect describes the relationship between end-diastolic length of cardiac muscle fibers and force of contraction. Changes in contractility alter cardiac output for a given right atrial pressure (preload). Anything that increases inotropy will increase the slope of this curve. Anything that decreases inotropy will decrease the slope of this curve. These changes are shown with dashed red lines on the graph.

The venous return curve (teal) on the above graph illustrates how changes in circulating blood volume or venous tone affect right atrial pressures for a given cardiac output. Where the venous return curve intersects with the cardiac function curve determines an individual's cardiac output. Increases in venous return (eg, fluid infusion) will shift the x-intercept of this curve to the right (increased right atrial pressures). Decreases in in venous return (eg, acute hemorrhage) will shift the x-intercept of this curve to the left (decreased right atrial pressures).

Digoxin is a positive inotropic agent that increases cardiac contractility, thereby increasing cardiac output. On a cardiac function curve, this is reflected as an increase in cardiac output (due to increased slope of the cardiac output curve) with no change in the vascular function curve, as indicated by answer B.

Point C indicates a normal cardiac output and venous return in a healthy person. Increases in total peripheral resistance (e.g., phenylephrine) will cause a decrease in cardiac output and venous return for a given right atrial pressure, decreasing the slopes of both curves (point E). Decreases in total peripheral resistance (eg, arteriovenous shunts) will cause an increase in cardiac output and venous return for a given right atrial pressure, increasing the slopes of both curves (point A). A decrease in the slope of the cardiac function curve with no change in the venous return curve would reflect negative inotropy (eg, narcotic overdose) (point D).

23. The is correct B. This patient presents with split, fixed S2 sound and systolic murmur over left upper sternal border heard on heart auscultation, but is otherwise developmentally normal. These findings most likely point to atrial septal defect (ASD). Atrial septal defects are a group of congenital heart conditions which enable communication between atria due to a defect in the interatrial septum. During heart development, atria get first divided by septum primum, which grows downward and forms an opening at the lower end called ostium primum. The septum primum continues to grow downwards and eventually closes off ostium primum. During this process an opening in the upper part of septum primum forms creating ostium secundum. Ostium secundum provides a communication for blood between atria during fetal development. Eventually, a second wall of tissue or septum secundum forms over the ostium secundum, creating a passageway between septum secundum and ostium secundum. This passage is the foramen ovale. Foramen ovale stays open during fetal development and eventually closes soon after birth as pulmonary pressure drops. There are many types of atrial septal defects depending on which part of atrial septum becomes defective during development. Ostium secundum septal defect is the most common type and it can cause symptoms of exercise intolerance, palpitations, syncope, and easy fatigue. Complications of uncontrolled ostium secundum include pulmonary hypertension, right-sided heart failure, atrial fibrillation, stroke, and Eisenmenger syndrome. Patent foramen ovale has little hemodynamic consequence. It

is associated with migraine, paradoxical emboli, and decompression sickness. Ostium primum septal defect is seen in the lower portion of the septum at the level of the tricuspid and mitral valves. It is also known as endocardial cushion defect. It is associated with mitral and tricuspid valve defects as well as Down syndrome.

Atrial septal defects cause blood to flow from an area of higher pressure to an area of lower pressure, or in other words, left-to-right shunt. This extra volume causes overload of both the right atrium and right ventricle. This overload of the right ventricle eventually causes overload of the entire pulmonary vasculature, which contributes to the development of pulmonary hypertension. The right ventricle has to work extra hard to overcome higher pressures which over time can lead to right-sided heart failure. As the pressure in the right atrium increases it may rise to levels higher than the left ventricle and eventually result in right-to-left shunt (Eisenmenger syndrome). Upon auscultation of the heart there might be ejection systolic murmur which contributes to higher flow of blood over pulmonic valve. Fixed splitting of S2 is heard due to increased flow over the pulmonic valve keeping it open longer, regardless of inspiration. Once the ASD has been diagnosed, a determination of whether or not it has to be corrected surgically is made. If the ASD is not causing problems, the defect is simply monitored. If the ASD is causing atrial or ventricular enlargement, it is corrected surgically. Surgery is preferably done before significant pulmonary hypertension develops in addition to avoid paradoxical embolism

The other answer options are incorrect for the following reasons. Patent ductus arteriosus presents with a continuous machinery-like murmur in the left infraclavicular region. Mitral regurgitation causes a high-pitched holosystolic murmur best heard at the apex. Ventricular septal defect causes a pansystolic murmur over the lower sternal border. It might be associated with palpable thrill due to high pressure shunting of blood. Transposition of great vessels is usually diagnosed earlier in life as these patients appear cyanotic and short of breath with poor appetite and weight gain from fluid retention. Aortic stenosis is associated with a systolic crescendo-decrescendo murmur which radiates to carotids.

24. The correct is A. This patient presented with unexplained palpitations, tachycardia, and shortness of breath. These signs indicate that she should be evaluated for an arrhythmia, specifically supraventricular tachycardia. Often, this form of arrhythmia does not have any clear triggers.

Adenosine is a very short-acting drug that is useful in terminating certain forms of supraventricular tachycardia by hyperpolarizing the cell and decreasing atrioventricular (AV) node conduction. Adverse effects include flushing, hypotension, chest pain, bronchospasm, and a sense of impending doom.

The other options are not the best answers because they are not used to treat this patient’s condition. Ivabradine is used to treat stable angina in patients who cannot take

β-blockers. It works by inhibiting funny channels, thus prolonging phase IV of the cardiac action potential. Amiodarone is a class III antiarrhythmic. It mainly acts by decreasing K+ efflux, thus prolonging phase III. It is commonly used to treat atrial and ventricular tachycardia. Adverse effects include pulmonary fibrosis, hepatotoxicity, hypothyroidism, corneal deposits, and photosensitivity. Metoprolol is a class II antiarrhythmic. It decreases cAMP and Ca2+ currents, which subsequently decreases sinoatrial and AV node activity. Adverse effects include sexual dysfunction, bradycardia, and exacerbation of symptoms of chronic obstructive pulmonary disease. Procainamide is a class Ia antiarrhythmic. It is used to treat atrial and ventricular tachycardia by prolonging phase I of the cardiac action potential. Adverse effects include a lupus-like syndrome and torsades de pointes.

25. The correct is E. The arrow is pointing at phase 4 of the pacemaker action potential, which is characterized by the influx of Na+ ions into the myocytes. Norepinephrine exerts a positive chronotropic effect on the heart, thus increasing the slope of phase 4 and increasing heart rate. The slope of phase 4 is due to the funny current, or If, which is due to concurrent influx of Na+ and K+ ions. This funny current establishes the automaticity of the pacemaker cells, thereby determining heart rate. The automaticity occurs because when the membrane potential reaches -40 mV, the firing of an action potential is triggered. After a dose of norepinephrine, the If channels have an increased likelihood of opening and, therefore, increasing bion flux and heart rate. This may be visualized by an increased slope of phase 4. Acetylcholine and adenosine have the opposite effect on phase 4, decreasing the likelihood that the funny channels open and, therefore, decreasing heart rate. Cardiac myocyte action potential is characterized by 5 phases. Phase 0 is the rapid upstroke and depolarization (increase in membrane potential) characterized by opening of voltage-gated Na+ channels and Na+ influx. Phase 1 is the initial repolarization (when the resting membrane potential returns towards its pre-excitatory state) stage in which voltage-gated Na+ channels are inactivated and K+ efflux begins. Phase 2, known as the plateau, is due to the influx of Ca2+ ions, which balance K+ efflux. Phase 3 is the time of rapid repolarization and is due to massive K+ efflux. Phase 4 is the myocyte resting potential and is maintained due to high K+ permeability. The action potential of the SA node differs from that of cardiac myocytes in that phases 1 and 2 are absent. Phase 4 is due to the influx of Na+ and K+ ions (funny current) rather than K+ permeability. Phase 0 is due to entry of Ca2+ ions into the cell, and phase 3 is characterized by repolarization due to K+ efflux.

Distractor paragraph:

The other answer choices are incorrect:

- Increased conductance of Ca2+ could describe either phase 0 of the pacemaker action potential (which occurs after phase 4) or phase 2 of the myocardial action potential.

• K+ conductance is decreased in phase 0 of both the pacemaker and myocardial action potentials. K+ conductance would be increased, rather than decreased, in phase 3 of both the pacemaker and myocardial action potentials. In phase 4 of the pacemaker action potential, there is a slow inward current of K+.

Neither Cl- nor HCO3- significantly contributes to any of the pacemaker or myocardial action potential phases.

26. The correct is E. This patient presents with shortness of breath at rest, bilateral edema in his lower legs, and bilateral crackles in the lower lung fields. All of this is on a background of long-term untreated hypertension. He has congestive heart failure (CHF) secondary to untreated hypertension (HTN). CHF is a condition which develops as the heart loses the ability to sufficiently maintain blood flow throughout the body, either because of damage to the cardiac muscle or volume overload. Left-sided heart failure is caused by decreased ability of the left ventricle to pump blood to the systemic circuit, which causes a backup of blood into the pulmonary system, leading to symptoms of shortness of breath, especially when lying down, as seen in this patient. Right-sided heart failure is caused by decreased ability of the right ventricle to pump blood into the pulmonary circuit. The most common cause of right-sided heart failure is left-sided heart failure because the pulmonary circuit becomes congested. Right-sided heart failure causes backup of the venous system, leading to edema, commonly seen as swollen ankles, as seen in this patient. It also can be caused by coronary artery disease (CAD), atrial fibrillation, valvular heart disease, excess alcohol use, cardiomyopathy, smoking, amyloidosis, infections, myocardial infarction (MI), etc. All of these conditions cause cardiac remodeling over time and result in deficient cardiac output. The morphology of cardiac remodeling varies depending on the insulting agent. Ventricular hypertrophy and systolic dysfunction are seen in conditions of increased afterload such as HTN, aortic stenosis, or aortic insufficiency. Increased pressure causes cardiomyocytes to undergo hypertrophy by adding new sarcomeres in parallel. Activation of the renin-angiotensin-aldosterone system, due to decreased renal blood flow, increases the molecules responsible for cardiac remodeling, including angiotensin II, norepinephrine, and epinephrine. Regardless of the cause, if cardiac remodeling progresses, the heart muscle will lose its ability to produce adequate cardiac output (CO) and heart failure will ensue. Treatment of CHF is aimed at improving symptoms and decreasing further progression of disease. Lifestyle and dietary modifications are focused on decreasing fluid retention by reducing salt and free water intake. First-line therapy includes ACE inhibitors or angiotensin II receptor blockers (ARBs) and beta blockers. Isosorbide mononitrate and hydralazine can be used as an alternative to control blood pressure. Diuretics are widely used to help decrease fluid accumulation.

Decreased systemic vascular resistance is seen in patients with hypotension. This patient has chronic untreated hypertension. Acute damage and death of cardiomyocytes is seen in patients with myocardial infarction. If the MI is massive and if enough cardiac muscle is irreversibly damaged, CHF can result. The patient in the question has chronic fatigue and shortness of breath. He does not have any symptoms concerning for acute MI, and there is no history of a previous MI. Decreased pulmonary venous pressure, or pulmonary hypotension, would not be expected in this patient with CHF. Rather, the increased filling pressures in his left heart would expectedly lead to congestion and, therefore, increased pressure in the pulmonary veins. Decreased venous return results in blood backing up in the systemic vasculature and symptoms of vascular congestion seen in CHF. Although decreased venous return is seen in patients with CHF, it is not the underlying mechanism of disease.

27. The correct is B. This patient, who has a history of coronary artery disease, had an arteriovenous (AV) fistula created 5 years ago. Patients with underlying heart disease who undergo AV fistula construction for hemodialysis access are at risk of heart failure developing. The patient's presenting symptoms of progressive weakness, cough, and dyspnea on exertion are consistent with this diagnosis.

The construction of an AV fistula provides an easy access site for hemodialysis in patients with end-stage renal disease. They are also long-lasting and deliver a high rate of blood flow to the dialyzer. The effect of AV fistulas on the cardiovascular system is two-fold:

1. Shunting blood from the arterial to the venous system increases venous return to the heart, thereby increasing preload.
2. Bypassing the arterioles decreases total peripheral resistance of the systemic vasculature, thereby decreasing afterload.

The combination of increased preload and decreased afterload on the heart is an increase in cardiac output, which can eventually lead to high-output heart failure.

The left ventricular pressure-volume relationship can be represented by a pressure-volume loop. Increased preload would cause an increase in end-diastolic volume, which would be reflected as a rightward expansion of the pressure-volume loop. Decreased afterload would cause a decrease in left ventricular systolic ejection pressures, which would be reflected as a downward contraction of the pressure-volume loop. Both of these changes are shown by loop B.

The other answer choices are incorrect for the following reasons:

- Loop A shows a leftward expansion of the pressure-volume loop, which reflects increased contractility of the heart. Such a change could be seen with the administration of B1-agonists or digoxin.
- Loop C shows a rightward expansion of the pressure-volume loop, which reflects increased cardiac preload. Such a finding could be caused by anything that increases

venous return to the heart. However, it does not reflect the reduction in afterload that would also accompany an AV fistula.

- Loop D reflects a normal pressure-volume loop.
- Loop E reflects an increase in afterload with subsequent reduction in stroke volume. Such a change could be caused by anything that increases total peripheral resistance of the systemic vasculature. Afterload would be decreased, not increased, with an AV fistula.

28. The correct is E. This patient is found unconscious with needle tracks in his arm, and is resuscitated with naloxone in the emergency room. He is admitted to the hospital and on examination, he is found to have a systolic "blowing" murmur. The murmur is loudest at the left lower sternal border and increases with inspiration. These findings suggest he has tricuspid regurgitation or leakage of blood backwards through the tricuspid valve. While tricuspid regurgitation may be caused by right ventricular dilatation, the tricuspid valve is also the most common site of infective endocarditis in intravenous drug users. In these patients, infected venous blood (most often with S. aureus) returns to the right side of the heart, and seeds the tricuspid valve. Other valves may also be damaged, typically after tricuspid valve damage has occurred. The arrow in the echocardiograph indicates a vegetation on the tricuspid valve. Aortic regurgitation is a diastolic murmur associated with head bobbing and visibly pounding pulses. Aortic stenosis is a systolic murmur that is most often due to calcification secondary to the aging process. Mitral stenosis is a diastolic murmur, often seen in rheumatic fever, and is characterized by an opening snap. Mitral regurgitation radiates to the axilla, and does not increase with inspiration. Tricuspid stenosis is a rare condition characterized by a diastolic murmur.

29. The correct is E. The patient is a young man with occasional palpitations and syncope episodes. His family history is significant for several family members who died from a sudden cardiac death which is indicative of a congenital heart defect. ECG shows long QT interval concerning for congenital long QT syndrome. There are very few causes for sudden cardiac death in young patients. Another common cause is hypertrophic obstructive cardiomyopathy which does not fit in the clinical presentation of this clinical vignette. The QT interval is measured from the start of the Q wave to the end of the T wave and corresponds to the time when the ventricles start to contract to the time when they finish relaxing. An abnormally long or abnormally short QT interval is associated with cardiac arrythmias and death. Congenital long QT syndrome is a group of inherited disorders of myocardial repolarization typically because of a defect in ion channel. People with these conditions have an increased risk of sudden cardiac death because of the development of torsades de pointes. Romano-Ward and Jervell and Lange-Nielsen are two syndromes of congenital long QT syndrome. Romano-Ward syndrome has pure cardiac phenotype and has autosomal dominant

inheritance. It is caused by mutations in ANK2 gene causing disruption in ion channels and electrical currents in cardiac myocytes. Clinical symptoms include syncope, seizures, development of torsades de pointes and sudden cardiac death. Diagnosis is based on family history of sudden cardiac death, ECG findings, and exercise test. Treatment is aimed at decreasing the incidence of cardiac arrhythmias by using β-blockers and heart ganglion blocks.

The other options are incorrect for the following reasons:

- Jervell and Lange-Nielsen syndrome is an autosomal recessive disorder with associated sensorineural hearing loss.
- Brugada syndrome presents with EKG findings of pseudo-right bundle branch block and ST elevation in V1-V3. It is most commonly found in Asian males.
- Wolff-Parkinson-White syndrome is a type of ventricular preexcitation syndrome characterized by the presence of an abnormal fast accessory conduction pathway from atria to ventricle which bypasses the rate-controlling AV node. Ventricles start to depolarize earlier, which is evidenced on ECG by the presence of delta waves, widened QRS complex, and short PR interval.
- Mobitz type II AV block is characterized by intermittently nonconducted P waves not associated with PR interval lengthening or shortening. There is usually a fixed number of non-conducted P waves for every successfully conducted QRS.
- A right bundle branch block (RBBB) is characterized by a delay in depolarization of the right ventricle, resulting in a widened QRS complex. Characteristic ECG findings include terminal R wave in lead V1 (called R prime) and prolonged S wave in leads I and V6.

30. The correct is D. This patient was a restrained passenger in a high-speed motor vehicle collision involving rapid deceleration. She has dyspnea and severe chest and back pain and a widened mediastinum seen on chest x-ray. This presentation is concerning for traumatic aortic rupture.

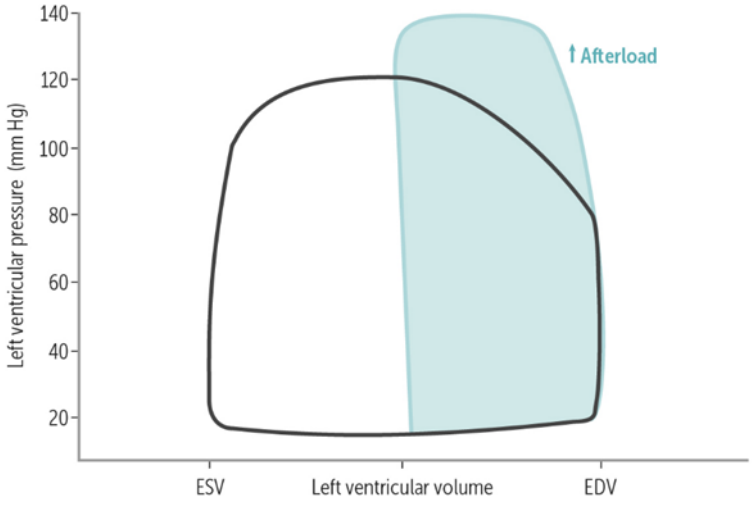
Rapid deceleration injuries, such as those involving high-speed motor vehicle collisions, are associated with a significant risk of traumatic aortic rupture due to shearing forces. During such injuries, a portion of the aorta is torn, resulting in profuse bleeding due to the extremely high pressures within the aorta. Shock can develop rapidly and is associated with a high mortality rate. Presenting symptoms of traumatic aortic rupture include severe tearing pain in the chest and/or back, dyspnea, hoarseness, and dysphagia. Aortic ruptures may also be contained at initial presentation, such that individuals are not hemorrhaging profusely. Such patients are likely to have elevated blood pressure in the upper extremities with perhaps decreased blood pressure in the lower extremities.

The aortic isthmus, which is located just distal to the left subclavian artery, is particularly vulnerable to tearing and is the most common site of traumatic aortic

rupture. The vulnerability of the isthmus is caused by its relative immobility, which makes it susceptible to the shearing forces that occur during rapid deceleration. The isthmus is particularly immobile because it is tethered to the pulmonary artery by the ligamentum arteriosum.

Although the other answer choices are possible sites of traumatic aortic rupture, they are far less common than rupture at the aortic isthmus because of their relatively increased mobility. The ascending aorta (A) and aortic arch(B) are the next most common locations of aortic rupture in blunt trauma. However, rupture at the level of the aortic isthmus is still five times more common. The origin of the left subclavian artery (C) is located just proximal to the aortic isthmus. However, its lack of tethering makes it more mobile and therefore unlikely to rupture. Of all the answer choices, the descending aorta (E) is the most mobile and therefore least likely to rupture.

31. The correct is E. This patient has a systolic murmur with ejection click, which is most indicative of aortic stenosis. The ejection click occurs due to a stiff, calcified valve opening with very high pressures. With a calcified vessel, there is delayed closure of the aortic valve, with very high pressure and turbulent flow through the stenotic valve. The location of the murmur and radiation to the neck are classic for aortic stenosis. This outflow obstruction leads to a prolonged left ventricular (LV) systole, as demonstrated in the diagram. As a compensatory mechanism to normalize LV wall stress, LV wall thickness increases by parallel replication of sarcomeres, producing concentric hypertrophy. Increased LV mass and increased systolic pressure lead to delayed closure of the aortic valve.



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32. The correct is B. This patient's current symptoms (fatigue, fever, weight gain secondary to edema and dyspnea on exertion) and physical exam findings (right-sided heart failure) are common to many conditions associated with elevated right-sided pressure including but not limited to restrictive cardiomyopathy, constrictive

pericarditis, right-sided heart failure. However, the patient's history of radiation therapy and the presence of the Kussmaul sign (jugular venous distention that fails to subside on inspiration) support a diagnosis of constrictive pericarditis. In patients with breast cancer, radiation therapy can be used as adjuvant therapy after mastectomy or breast-conserving therapy. Application of radiation to the thorax is associated with thickening of the pericardium. If severe enough, the thickened pericardium restricts the myocardium, leading to less space for blood to fill. Clinically, cardiac tamponade and constrictive pericarditis have similar presentations, although cardiac tamponade typically presents more acutely and with hemodynamic instability.

The other diagnoses are less likely for a patient like this one.

- A patient with cardiac tamponade would have an acute presentation with worsening vital signs.
- In a patient with dilated cardiomyopathy, dilated chambers would be seen on an echocardiogram.
- A patient with myocarditis would not typically present with the Kussmaul sign.
- A patient with systolic congestive heart failure would not present a reduced bi-ventricular end diastolic volume.

33. The correct is A. This patient presents with intermittent chest pain that is worse when he is in a supine position and severe enough to cause him to believe he is having a heart attack. However, his lack of cardiac risk factors and the lab results showing negative troponins make a diagnosis of myocardial infarction unlikely. Given the absence of respiratory symptoms, the negative cardiac enzymes, and lack of specific ECG changes (including ST elevation/depression, T-wave inversion, or development of Q waves), the most likely diagnosis for this patient is a noncardiac disease such as gastroesophageal reflux disease (GERD). GERD is caused by decreased lower esophageal sphincter tone and classically manifests with chest pain after meals that is worse when the patient is lying down. As seen in this patient, it may often present with a dry cough (but normal chest x-ray) and patients may report a metallic taste. It is the most frequent cause of esophageal-based chest pain and is the leading cause of unexplained noncardiac chest pain.

Although any patient presenting to the emergency department with chest pain should be monitored for cardiac causes, the other answer options are less likely to cause this patient's symptoms.

- Stable angina typically presents with chest pain on exertion that is relieved by rest, but it is not positional in nature.
- Myocardial infarction would be indicated by elevated troponins after 6 hours.
- Chest pain from pericarditis improves with leaning forward, and a friction rub would be heard during the cardiac exam.

• Chest pain from a pulmonary embolism is not positional and would present with respiratory symptoms.

34. The correct is F. For a pacemaker action potential, phase 0 upstroke is caused by the opening of voltage-gated calcium channels, allowing an influx of calcium. Phase 3 downstroke is caused by inactivation of calcium channels and activation of potassium channels, causing an efflux of potassium. Phase 4 (funny current) is caused by a mixed sodium/potassium inward current and T-type calcium channels which contributes to further depolarization, accounting for the automaticity of SA and atrioventricular (AV) nodes.

Verapamil is a calcium channel blocker. Calcium channel blockers have the greatest effect on phase 0 relative to other phases. Non-dihydropyridine (DHP) calcium channel blockers (eg, verapamil) also depress conduction through the AV node.

• Adenosine is an antidysrhythmic that hyperpolarizes the cell via potassium channels and inhibits L-type calcium channels. It will not significantly affect the calcium flow.

• Atropine is a muscarinic antagonist that increases heart rate but does not affect the inotropic balance of the cardiac cycle.

• Nifedipine is a DHP calcium channel blocker. DHP calcium channel blockers are potent vasodilators but do not have as significant an effect on the pacemaker action potential as do non-DHP calcium channel blockers.

• Procainamide is a sodium and potassium channel blocker and does not affect calcium flow.

• Propranolol is a β-blocker that increases the refractory period by slowing the conduction through the SA and AV nodes. It does not affect calcium flow in phase 0.

Phases of the pacemaker action potential		
Phase	**Movement**	**Channels**
0 = upstroke	Ca^{2+} influx	L-type, voltage-gated Ca^{2+} channels
3 = rapid repolarization	K^+ efflux	Opening of voltage-gated and Ca^{2+}-dependent K^+ channels, closure of voltage-gated Ca^{2+} channels
4 = slow diastolic depolarization	Membrane potential spontaneously depolarizes as Na^+ conductance increases (I_f), inward Ca^{2+} movement begins	ACh-sensitive K^+ channels, f-channels, T-type Ca^{2+} channels

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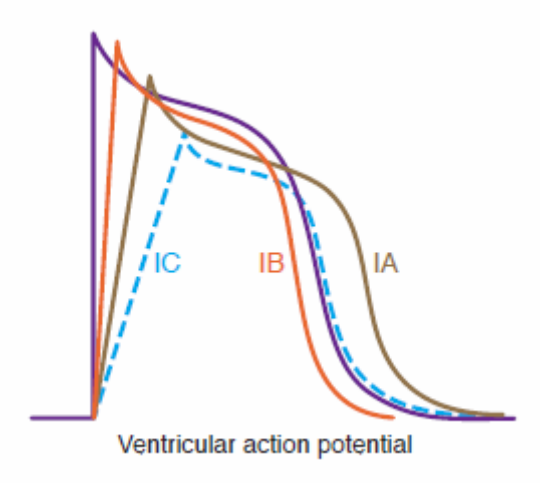
35. The correct is B. This patient is in ventricular fibrillation, which can be treated with a class 1B antiarrhythmic drug, such as lidocaine or mexiletine. Different class I drugs can affect the absolute refractory period (ARP). A class IA drug will prolong the ARP because it increases the action potential (AP) duration. A class IB drug will decrease the AP and therefore decrease the ARP. A class IC drug will not change the ARP. Regardless of ARP action, all class I drugs decrease the slope of phase 0.

Lidocaine, a class IB antiarrhythmic, is indicated in the treatment of ventricular fibrillation, particularly if a patient has a contraindication for amiodarone (such as hyperthyroidism). Adverse effects of class IB antiarrhythmics include central nervous system stimulation/depression and cardiovascular depression.

- Quinidine is a class IA antiarrhythmic and increases the AP duration.
- Propafenone is a class IC antiarrhythmic and does not affect the ARP.
- Sotalol is a class III antiarrhythmic that blocks the potassium channels. It increases the AP duration, refractory period, and QT interval.
- Diltiazem is a class IV antiarrhythmic that blocks calcium channels, resulting in a decreased conduction velocity and increased refractory period and PR interval.



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36. The correct is D. Blood flow through an artery is related to the difference in pressure between two points as well as the resistance to forward flow, and can be calculated using the following formula:

Flow (Q)= P1-P2/ R

Where P1-P2=pressure gradient across two points, R=resistance

Poiseuille's equation describes the resistance to flow as follows:

Resistance (R)= $\eta L/\pi r4$

where r=radius, η=viscosity of blood, and L=length of the artery

Combing the above two equations allows for the calculation of flow with changes in the radius of a vessel. It is important to note that value for the radius is raised to the fourth power. This is a powerful concept, as reducing the length of the radius by a factor of 2 will lead to a 16-fold increase in the resistance if all other factors remain constant (ie, viscosity, length, pressure gradient). This is demonstrated as follows:

R=(1/r4)=(1/(½)4)=16. Plugging this into the equation for blood flow shows that the value will decrease by a factor of 16.

Of note, the coronary arteries (eg, left circumflex artery) are the narrowest of the answer choices and are thus more predisposed to the effects of atherosclerotic plaque formation. Vessel radius is the greatest determinant of resistance to blood flow since even a small reduction in diameter causes a drastic increase in resistance. The clinical implications are two-fold:

Narrower vessels are inherently more susceptible to the adverse consequences of an atherosclerotic plaque.

The radius of vessels changes dynamically as a result of vascular smooth muscle contraction and relaxation, so other variables may transform a benign obstruction into a clinically apparent one. For example, administering a high dose of phenylephrine, an a1-adrenergic agonist, can cause marked vasoconstriction leading to decreased vessel radius and, in turn, an increased risk of adverse effects in atherosclerotic vessels due to a further reduction in lumen caliber.

This patient has significant risk factors for the development of coronary artery disease (eg, smoking, hyperlipidemia, diabetes mellitus, carotid artery stenosis), and his fatigue is likely of cardiac origin as a result of decreased perfusion of the myocardium. The decreased perfusion leads to impaired myocardial contractility, causing anginal-type pain with exertion.

The other answer choices are incorrect:

Stenotic lesions of the iliac artery may lead to symptoms of leg pain when walking.

The radius of the abdominal aorta is significantly larger than that of the carotid. Although this vessel may develop atherosclerosis, the clinical presentation in this case points to the coronary arteries as the source of disease.

Although atherosclerotic lesions of the renal artery are a common cause of secondary hypertension, the typical presentation is a patient with refractory hypertension as well as a systolic–diastolic bruit auscultated over the abdomen.

Atherosclerosis of the femoral artery may lead to peripheral vascular disease, causing decreased perfusion of the lower extremities. Patients present with leg/buttock claudication on exertion, as well as decreased hair, shiny skin, and weak/absent peripheral pulses.

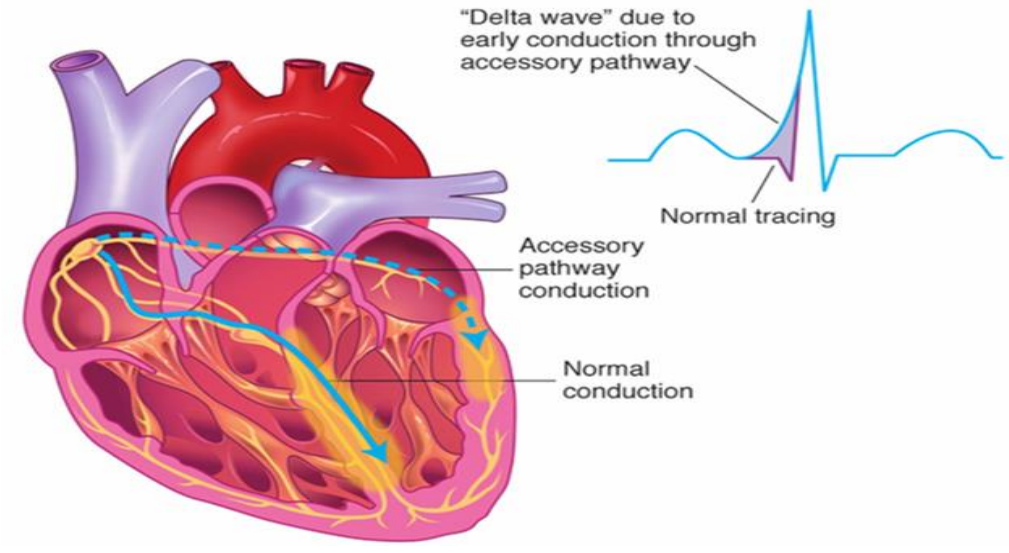
37. The correct is E. In a young man with a family history of heart disease complaining of syncope and palpitations, structural heart disease, such as hypertrophic obstructive cardiomyopathy or conduction disorders, such as Wolff-Parkinson White syndrome, should be high on the differential. Given this patient’s benign cardiac physical examination, hypertrophic obstructive cardiomyopathy is less likely.

This patient's ECG points toward a diagnosis of Wolff-Parkinson-White syndrome. Wolff-Parkinson-White syndrome is caused by an accessory conduction pathway

through the bundle of Kent. This leads to conduction of the electrical signal to the ventricles before the signal can be conducted through the atrioventricular (AV) node. The early ventricular depolarization is seen on the ECG as the delta wave and leads to a widened QRS complex. This occurs because the AV node signal reaches the ventricles later and depolarization is prolonged.

This early ventricular depolarization leads to systolic contraction of the ventricle earlier than is physiologically normal. As a result, decreased filling time of the ventricles during diastole occurs. This decreased filling time then causes decreased preload to be pumped during systole.

- Changes in conduction across the AV node would cause a prolonged or shortened PR interval but would not cause the characteristic changes seen on this patient's ECG.
- Increased conduction across the AV node would lead to an increase in heart rate, since conduction through the AV node is typically the slowest step of the cardiac cycle. It would not lead to the characteristic ECG changes shown.
- Inherited defects of myocyte ion channels are the cause of congenital long QT syndromes that may lead to sudden cardiac death in young patients. However, such defects would not lead to the characteristic ECG changes shown.
- Increased sympathetic tone would lead to an increase in heart rate, causing sinus tachycardia. It would not lead to the characteristic ECG changes shown.
- Delay of conduction across the AV node is the cause of AV block, which would lead to a prolonged PR interval, not a shortened one as seen on this patient's ECG.



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38. The correct is A. This patient is showing signs of progressive coronary artery disease with chest pain associated with activity (stable angina). Metoprolol, a β-blocker, is often used to treat this condition but has a negative chronotropic effect on the heart rate (HR).

As a class, β-blockers also have a negative inotropic effect, decreasing contractility. However, this should not be confused with stroke volume (SV). Remember that cardiac output (CO) = HR × SV. β-Blockers decrease HR, but even so, CO decreases by less than 10% due to a proportionally greater increase in SV (SV = end-diastolic volume [EDV] – end-systolic volume [ESV]).

The decrease in HR allows for increased diastolic filling, thus increasing EDV and preload. SV is intrinsically controlled by preload (the degree to which the ventricles are stretched before contracting, related to the Starling curve). The mean arterial pressure (MAP) is the average systemic blood pressure over a cardiac cycle and is determined by the CO, systemic vascular resistance (SVR), and central venous pressure (CVP). In practice, the contribution of CVP (which is a few millimeters of mercury) is generally ignored. MAP = CO × SVR. Since CO is decreased only slightly, the MAP will slightly decrease.

39. The correct is D. This patient presents with hypotension and secondary tachycardia. He also has signs of infection including fever, flushed skin, leukocytosis, and an elevated lactate level. Together, these signs and symptoms are highly suggestive of sepsis. When a patient is unresponsive to fluid resuscitation, the diagnosis of septic shock can be made. Sepsis occurs when blood vessels dilate and increase their capillary permeability, leading to hypotension as seen in this patient.

Goals in the treatment of sepsis include volume resuscitation, if the patient is responsive. Pharmacologic therapies are used to constrict the vessels to restore adequate perfusion to the essential organs. Sympathetic α1-stimulation of the veins causes venoconstriction, resulting in decreased venous compliance (another term for venous pooling). As a result, venous return to the heart is increased. This would in turn increase the preload and arterial pressure.

Stimulation of the α1-receptors on arteries and arterioles leads to vasoconstriction and increased total peripheral resistance. As a result, blood pressure increases. Treatment with a pressor, such as norepinephrine, will raise blood pressure.

- Activation of the renin-angiotensin-aldosterone system could increase arterial pressure by increasing fluid retention but would not occur quickly enough to help this patient.
- Parasympathetic stimulation of the heart would result in a decreased heart rate and a corresponding decrease in arterial pressure.
- Vasopressin can constrict the vessels via smooth muscle contraction by acting on V1 receptors. It can also help retain fluid by acting on V2 receptors. However, the onset of action would be too slow.

Stimulation of β-2 receptors would lead to vasodilation and a decrease in blood pressure.

40. The correct is A. This immigrant patient with a history of frequent episodes of pharyngitis presents with dyspnea, hemoptysis, pulmonary crackles, and a diastolic murmur with an opening snap. This presentation is characteristic of mitral stenosis. Mitral stenosis elevates the left atrial pressure to provide necessary driving pressure to fill the left ventricle through the higher resistance mitral valve. Pulmonary edema (crackles on auscultation) occurs when the left atrial pressure exceeds 25 cm H2O and the reabsorption capacity of the lymphatics is exceeded. With many patients, but especially immigrant patients, mitral stenosis is a result of rheumatic fever, which can develop as a complication of inadequately treated strep throat. Prior streptococcus infection, such as may have been causing her frequent cases of pharyngitis, causes an autoimmune attack on mitral valve leaflets.

The graph depicts a pressure-volume loop, which is a demonstration of the relationship between left ventricular pressure and volume during systole and diastole. The individual events of the cardiac cycle are labeled on this loop. The various stages of the cardiac cycle are represented by particular intervals on the loop.

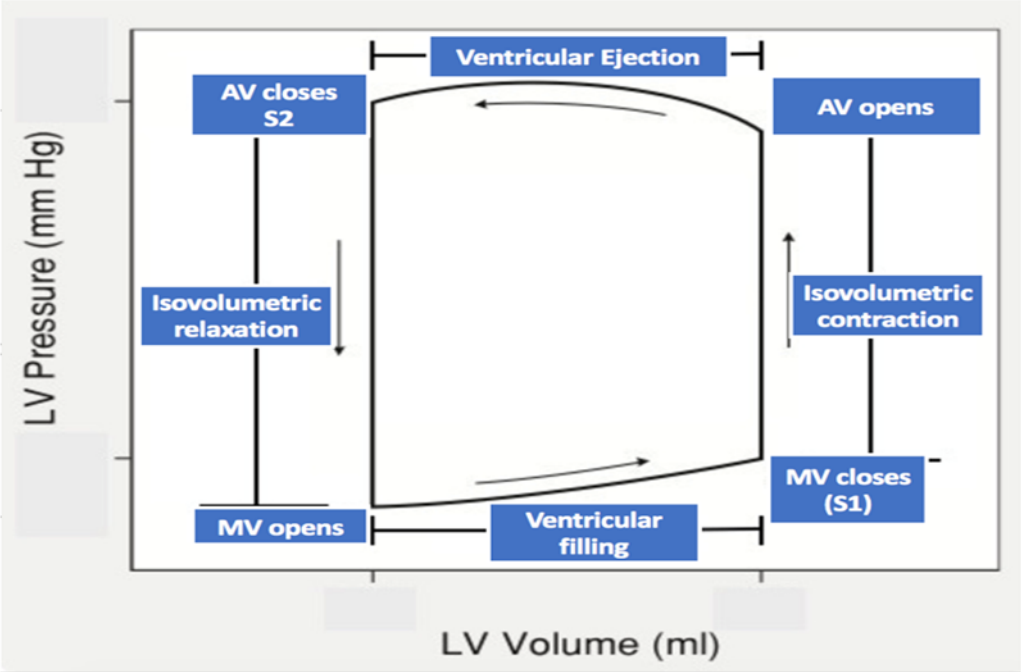
Systole is represented by intervals B → C and C → D. B → C represents isovolumetric contraction, which is characterized by active left ventricular contraction in the absence of any change in volume (ie, without any ventricular filling or ejection). It occurs after the mitral valve has closed (at point B) but before the aortic valve opens (at point C). The aortic valve opens when the pressure in the left ventricle has increased beyond the systemic diastolic pressure. C → D represents ventricular ejection, which occurs after the aortic valve opens and represents the time during the cardiac cycle when blood is actively ejected from the left ventricle. Ventricular ejection ends when the aortic valve closes (at point D).

Diastole is represented by intervals D → A and A → B. D→ A represents isovolumetric relaxation, which corresponds to the rapid decrease in left ventricular that occurs after the aortic valve closes (at point D) but before the mitral valve opens. As in isovolumetric contraction, no blood enters or leaves the ventricle at this time because both the mitral and aortic valves are closed. A → B represents ventricular filling, which begins when the ventricular pressure drops below the atrial pressure, causing the mitral valve to open and the ventricle to fill.

The patient in this question has an opening snap, which is characteristic of mitral stenosis. The opening snap sound results from the abrupt halt of the stiff, thickened mitral valve leaflets as they open during early diastole. The sound occurs when the mitral valve is at its maximum opening size, which occurs just after point A on the pressure-volume loop above. The more severe the thickening the earlier in diastole the opening snap occurs. As mitral stenosis progresses in intensity, the left atrial pressure increases because it requires higher pressure to force blood through an increasingly stenotic mitral valve. As a result, the opening snap occurs even earlier in diastole (even

more quickly after point A, closer to the S2 heart sound). The classic diastolic rumbling murmur that occurs after the opening snap in mitral stenosis results from the passage of turbulent blood flow through a stenotic mitral valve during ventricular filling.
The incorrect answers are wrong for the following reasons:

- Point B represents mitral valve closure and is the point at which the normal S1 heart sound can be heard. The mitral valve closes following ventricular filling when the pressure in the ventricle exceeds the pressure in the atrium.
- Point C represents aortic valve opening and the start of systolic ejection following a phase of isovolumetric contraction. Occasionally, aortic stenosis can present with an ejection click that can present at this time.
- Point D represents aortic valve closure and is the point at which the normal S2 heart sound can be heard. The aortic valve closes after systolic ejection when the pressure in the ventricles drops below aortic pressure.
- Point E represents the period of ventricular ejection during systole.



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41. The correct is B. This patient presenting with chest pain and dyspnea on exertion that quickly resolves with rest is likely experiencing stable angina. Echocardiography involves the induction of a transient change in regional function during stress. Positive stress echocardiography findings are suggestive of coronary artery disease, further substantiating this diagnosis. The next step in evaluation should be cardiac catheterization, which not only provides information about the hepatency of his coronary vessels via coronary angiography, but also provides hemodynamic measurements from the heart's chambers. Cardiac catheterization is the most precise method for establishing a definitive cardiac diagnosis.

During a cardiac catheterization procedure, a catheter with a balloon tip is progressively advanced from the superior vena cava through the right atrium, right ventricle, pulmonary artery, pulmonary artery wedge, and left heart chambers. Periodic pressure readings vary within each structure, and the location of the catheter at any given time may be inferred based on the range of pressures. Therefore, progressive advancement of the catheter through physiologically normal cardiac structures should yield the following notable changes in pressure readings:

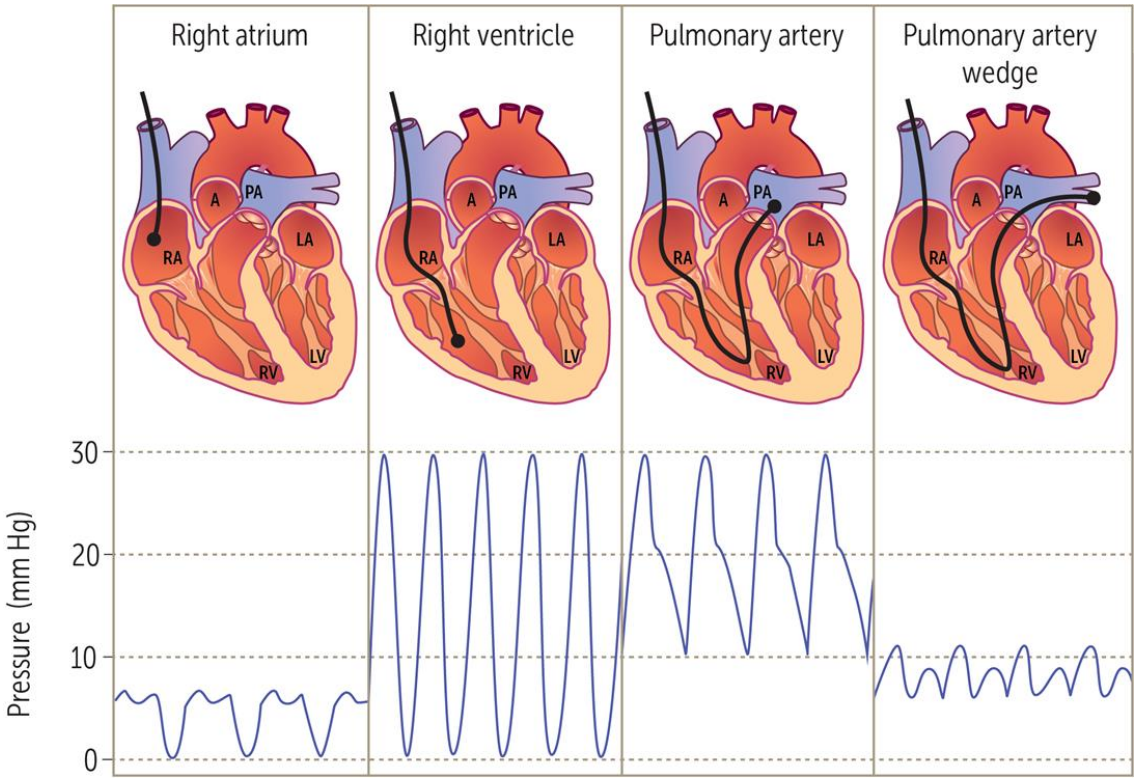
- Advancement of the catheter from the right atrium into the right ventricle will result in a dramatic increase in systolic pressure, and diastolic pressure will drop below that of the right atrium.
- Advancement of the catheter from the right ventricle into the pulmonary artery will yield no change in peak systolic pressure, while diastolic pressure will be increased.
- Advancement of the catheter from the pulmonary artery to the pulmonary artery wedge will provide the pulmonary capillary wedge pressure (PCWP), an approximation of the left atrial pressure, which will be the same as the pulmonary artery diastolic pressure.

Once during this patient's cardiac catheterization, the catheter recorded a pressure reading of 9-25 mm Hg. Upon advancement of the catheter, the pressure range subsequently became 9-12 mm Hg. These values are consistent with an initial reading in the pulmonary artery (normal: 4-30 mm Hg), with the catheter then being advanced to the pulmonary capillary wedge (a much smaller range, 4-12 mm Hg).

The other choices are not the best answers.

- The right atrium has a normal mean pressure range of 1-8 mm Hg.
- The right ventricle has a normal pressure range of 1-30 mm Hg.
- The mean pulmonary artery wedge pressure is normally 4-12 mm Hg and identical to that of the pulmonary artery diastolic pressure.

The left ventricle would normally have a dramatically higher peak systolic pressure (>90 m)



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42. The correct is B. This patient presents with red-yellow papules on her left arm, which are characteristic eruptive xanthomas of hypertriglyceridemia. Her increased triglyceride level confirms this diagnosis. In the case of hypertriglyceridemia greater than 886 mg/dl with a concomitant risk of pancreatitis, treatment with a fibrate is recommended in order to decrease triglyceride levels more dramatically and reduce the risk of recurrent pancreatitis. While fibrates are used to lower the triglyceride level they also carry a relative risk of 1.7 for cholesterol gallstones. Although fibrates can decrease LDL and increase HDL levels, again their most significant effect is a dramatic decrease in triglycerides. Fibrates activate peroxisome proliferator-activated receptor α to decrease expression of 7-α-hydroxylase, which catalyzes the rate-limiting step of bile acid synthesis. This increases cholesterol content in bile and can lead to supersaturation and, eventually, cholesterol gallstones. Elevations in liver enzymes from hepatotoxicity and myositis are also possible adverse effects. Decreased absorption of fat-soluble vitamins is an adverse effect of bile acid resins. Cardiac arrhythmia is a serious side effect of niacin (vitamin B3) use. Hypothyroidism can cause hypercholesterolemia, but it is not a common side effect of fibrates. Edema of ankles and legs is a side effect of thiazolidinediones, which are used to treat type 2 diabetes. This patient has hypertriglyceridemia, not type 2 diabetes.

43. The correct is A. This patient presents with untreated urinary tract infection (UTI), low urinary output, and costovertebral tenderness. These symptoms plus her vital sign changes and metabolic panel are consistent with pyelonephritis that has progressed to sepsis and acute kidney injury. The acute kidney injury (AKI) is a result of an ascending UTI that has most likely reached the kidney.The patient's highly elevated

blood urea nitrogen and creatinine, along with her report of recent-onset oliguria, suggest AKI. AKI can make the kidneys unable to properly secrete potassium in the urine, leading to hyperkalemia. Untreated, hyperkalemia can lead to ECG changes, most notably peaked T waves (shown below). It is extremely important to treat hyperkalemia in the setting of acute renal failure in order to prevent ECG changes, which can lead to arrhythmias and even cardiac arrest. Thus, along with measuring serum potassium, an ECG must always be checked in a patient with AKI and/or hyperkalemia. Treatment of hyperkalemia involves calcium administration to stabilize cardiac membranes. Bicarbonate, albuterol, and insulin with glucose/dextrose are also advised to promote the shift of potassium intracellularly. Kayexalate is also often given to prevent GI absorption of additional potassium.

The following ECG changes are not usually seen in AKI or hyperkalemia:

- QT prolongation is a characteristic of hypocalcemia.
- ST depression may indicate ischemic changes.
- T-wave inversions
- U waves are associated with hypokalemia rather than hyperkalemia.

44. The answer is F. This patient presents with lightheadedness and fatigue, and he has a history of prior myocardial infarctions that have required daily medications. His symptoms and history are suggestive of cardiac conduction irregularities. An ECG performed in the emergency department shows independent P and QRS complexes, indicative of a third-degree AV block, likely due to an adverse effect of his medications. Drugs that cause AV blocks typically elongate the QT segment and may result in torsades de pointes. Verapamil decreases Ca2+ conduction during phase 0 of the nodal action potential, delaying atrial depolarization rates. Such a delay can lead to uncoordinated firing of AV and SA nodes leading to complex dissociation. Therefore, verapamil is the likely cause of this patient's AV block. As a result, it is commonly contraindicated in a situation of heart failure with reduced ejection fraction (HFrEF).

The other options are not the best answers because they are not associated with heart block. Cyclooxygenase (COX) inhibitors such as aspirin affect blood viscosity and inflammatory regulators.Hydrochlorothiazide inhibits the Na/Cl cotransporter in the distal convoluted tubule of the kidney. Spironolactone functions by inhibiting the aldosterone receptor. Enalapril functions as an angiotensin converting enzyme (ACE)-inhibitor. Nitroglycerin is converted to nitric oxide, which decreases preload and cardiac O2 demand by activating guanylyl cyclase. Atorvastatin functions to lower cholesterol levels by inhibiting HMG CoA reductase.

45. The answer is C. The patient presents with symptoms of low-grade fever, weight loss, and headache, and findings on physical exam include afferent pupillary defect and chalky white fundus. Together, these indicate that she has giant cell (temporal) arteritis, the most common form of vasculitis. Hematoxylin-eosin-stained preparation (see

image below) demonstrates degeneration of the internal elastic lamina and replacement by granulomatous inflammation. The temporal artery is most commonly affected, followed by other branches of the carotid artery (vertebral and ophthalmic arteries). Corticosteroids are quite effective for managing temporal arteritis. They must be administered quickly to prevent the serious complication of blindness. In the United States, approximately 15% of patients with temporal arteritis also have polymyalgia rheumatica. Aspirin and intravenous immune globulin would treat Kawasaki disease, which typically affects pediatric patients. Smoking cessation would be appropriate for Buerger disease, a condition that presents with claudication, usually of the digits. Cyclophosphamide would treat microscopic polyangiitis, a disease with lower respiratory tract, nervous system, and renal symptoms. Sumatriptan is a treatment for migraines.

46. The answer is D. Blood flow through an artery is related to the difference in pressure between two points as well as the resistance to forward flow, and can be calculated using the following formula:

Flow (Q)= P1-P2/R

Where P1-P2=pressure gradient across two points, R=resistance

Poiseuille's equation describes the resistance to flow as follows:

Resistance (R)= $\eta L/ \pi r4$

where r=radius, η=viscosity of blood, and L=length of the artery

Combing the above two equations allows for the calculation of flow with changes in the radius of a vessel. It is important to note that value for the radius is raised to the fourth power. This is a powerful concept, as reducing the length of the radius by a factor of 2 will lead to a 16-fold increase in the resistance if all other factors remain constant (ie, viscosity, length, pressure gradient). This is demonstrated as follows: R=(1/r4)=(1/(½)4)=16. Plugging this into the equation for blood flow shows that the value will decrease by a factor of 16. Of note, the coronary arteries (eg, left circumflex artery) are the narrowest of the answer choices and are thus more predisposed to the effects of atherosclerotic plaque formation. Vessel radius is the greatest determinant of resistance to blood flow since even a small reduction in diameter causes a drastic increase in resistance. The clinical implications are two-fold:

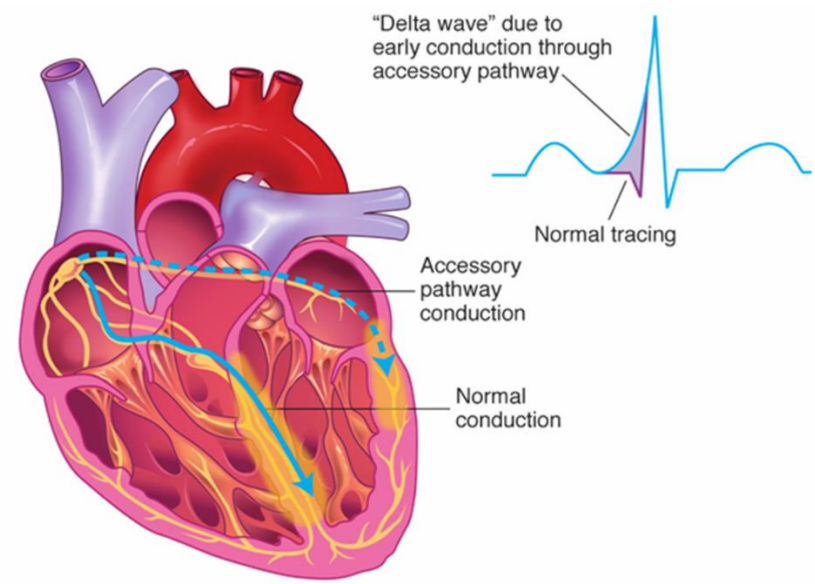
1. Narrower vessels are inherently more susceptible to the adverse consequences of an atherosclerotic plaque.
2. The radius of vessels changes dynamically as a result of vascular smooth muscle contraction and relaxation, so other variables may transform a benign obstruction into a clinically apparent one. For example, administering a high dose of phenylephrine, an a1-adrenergic agonist, can cause marked vasoconstriction leading to decreased vessel radius and, in turn, an increased risk of adverse effects in atherosclerotic vessels due to a further reduction in lumen caliber.

This patient has significant risk factors for the development of coronary artery disease (eg, smoking, hyperlipidemia, diabetes mellitus, carotid artery stenosis), and his fatigue is likely of cardiac origin as a result of decreased perfusion of the myocardium. The decreased perfusion leads to impaired myocardial contractility, causing anginal-type pain with exertion.

The other answer choices are incorrect:

- Stenotic lesions of the iliac artery may lead to symptoms of leg pain when walking.
- The radius of the abdominal aorta is significantly larger than that of the carotid. Although this vessel may develop atherosclerosis, the clinical presentation in this case points to the coronary arteries as the source of disease.
- Although atherosclerotic lesions of the renal artery are a common cause of secondary hypertension, the typical presentation is a patient with refractory hypertension as well as a systolic–diastolic bruit auscultated over the abdomen.
- Atherosclerosis of the femoral artery may lead to peripheral vascular disease, causing decreased perfusion of the lower extremities. Patients present with leg/buttock claudication on exertion, as well as decreased hair, shiny skin, and weak/absent peripheral pulses.

47. The answer is A. The patient presents with an arrhythmia, and her history indicates she was diagnosed at birth with a disorder that predisposes her to arrhythmias. It is likely that she has Wolff-Parkinson-White (WPW) syndrome, as indicated by the ECG and her symptoms. WPW is characterized by an atrioventricular (AV) accessory tract that bypasses the AV node and goes straight from the atrium to the ventricle (see figure below). Characteristic ECG findings of WPW syndrome include short PR intervals, long QRS intervals, and an up-sloping “delta wave” of the early QRS complex. A common arrhythmia is atrioventricular reciprocating tachycardia (AVRT). Transposition of the great arteries, characterized by an aorta arising from the right ventricle, and hypoplastic left heart syndrome, characterized by left ventricle hypoplasia, would not cause arrhythmia and syncope. Hypertrophic obstructive cardiomyopathy, characterized by disordered myofibril hypertrophy, typically presents with syncope or even sudden death during exertion in adolescence. Tetralogy of Fallot may cause ventricular tachycardia, but would generally have been surgically corrected if recognized at a young age.



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48. The answer is A. aThis patient is brought to the hospital after extensive blood loss and requires multiple transfusions. Several days after placement of a central line, he exhibits pyrexia and profound hypotension with warm peripheral extremities. These findings suggest that the patient is in septic shock, seemingly as a result of a central line infection that has led to bacteremia. The treatment for shock caused by sepsis is intravenous fluids and vasopressors, such as norepinephrine. Norepinephrine has affinity for the following adrenergic receptors, listed in decreasing affinity: α1 > α2 > β1. The most troubling problem in this patient with septic shock is the hypotension, so a pressor must be used.

None of the following answer choices represent the relative molecular affinities of the drug that will significantly increase this patient's blood pressure:

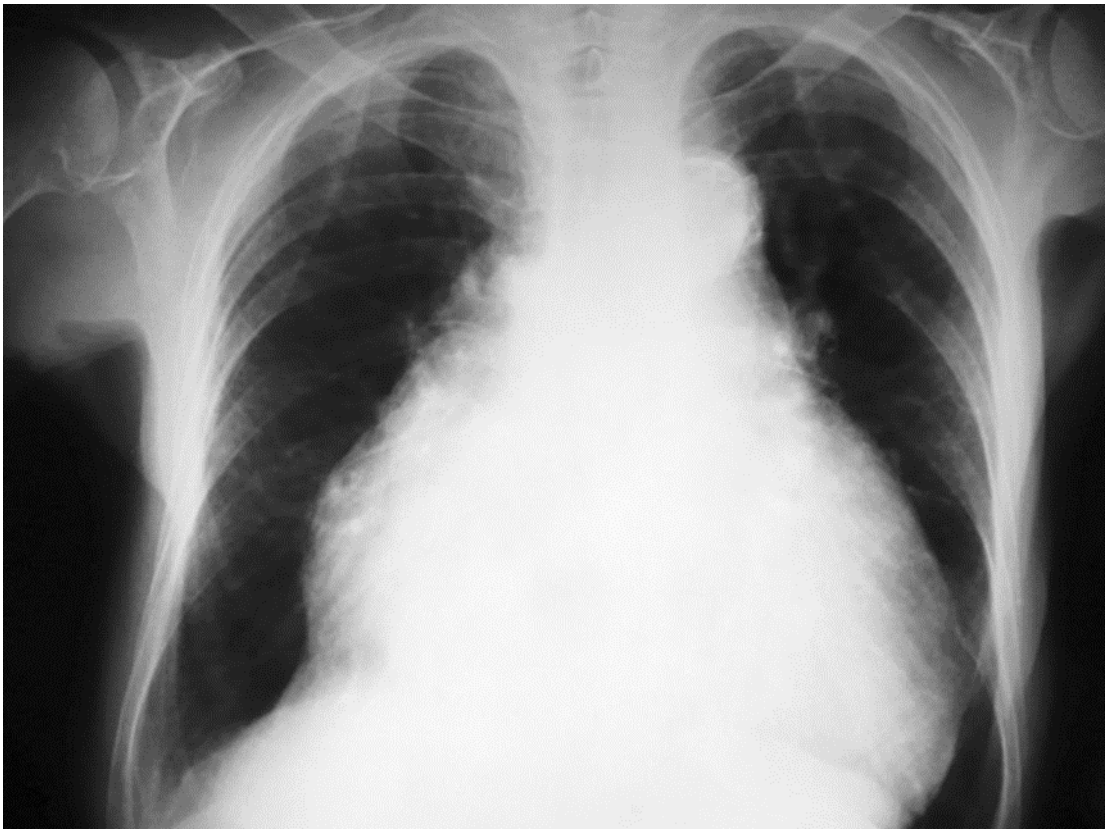
- Central α2-receptor: Clonidine is a selective central α2-receptor agonist used to treat hypertension. In this patient with hypotension, an antihypertensive drug would be contraindicated.
- β1 > β2 > α: Dobutamine is a sympathomimetic drug that is specific to β1-adrenergic receptors. The physiologic effects of dobutamine include increasing heart rate and contractility, which would be useful in the management of cardiogenic shock, rather than septic shock as seen in this patient. Because of its limited α1-adrenergic receptor activity, dobutamine would not induce sufficient vasoconstriction.
- PDE-3 > PDE-5:Milrinone, with affinity for phosphodiesterase 3 inhibition, is an inotropic agent used on a short-term basis in the management of cardiogenic shock. This patient is experiencing hypotension secondary to septic shock, which is primarily due to a massive, systemic vasodilation, rather than poor cardiac output.
- α1 = α2 irreversibly: Phenoxybenzamine is a nonselective irreversible α-blocker. It is typically used to decrease, not increase, blood pressure in patients with sympathetic crisis (pheochromocytoma). This patient is experiencing hypotension secondary to septic shock, so phenoxybenzamine would be contraindicated.

49. The answer is B. This patient's current symptoms (fatigue, fever, weight gain secondary to edema and dyspnea on exertion) and physical exam findings (right-sided heart failure) are common to many conditions associated with elevated right-sided pressure including but not limited to restrictive cardiomyopathy, constrictive pericarditis, right-sided heart failure. However, the patient's history of radiation therapy and the presence of the Kussmaul sign (jugular venous distention that fails to subside on inspiration) support a diagnosis of constrictive pericarditis. In patients with breast cancer, radiation therapy can be used as adjuvant therapy after mastectomy or breast-conserving therapy. Application of radiation to the thorax is associated with thickening of the pericardium. If severe enough, the thickened pericardium restricts the myocardium, leading to less space for blood to fill. Clinically, cardiac tamponade and constrictive pericarditis have similar presentations, although cardiac tamponade typically presents more acutely and with hemodynamic instability.

The other diagnoses are less likely for a patient like this one.

- A patient with cardiac tamponade would have an acute presentation with worsening vital signs.
- In a patient with dilated cardiomyopathy, dilated chambers would be seen on an echocardiogram.
- A patient with myocarditis would not typically present with the Kussmaul sign.
- A patient with systolic congestive heart failure would not present a reduced bi-ventricular end diastolic volume.

50. The answer is A. This patient presents with orthopnea, rales, hepatomegaly, and edema. These findings should immediately suggest heart failure. The displaced point of maximal impulse and a chest x-ray showing a large, balloon-shaped heart (like that shown in the image) indicates dilated cardiomyopathy. Dilated cardiomyopathy is a form of systolic heart failure. Dilated cardiomyopathy has several causes, which can be recalled with the mnemonic ABCCCD: Alcohol abuse, Beriberi, Coxsackie B myocarditis, chronic Cocaine use, Chagas disease, and Doxorubicin toxicity. Likewise, the mnemonic DCCCBA (Dilated Cardiac Complications Caused By Alcohol) may aid in remembering this specific cause of dilated cardiomyopathy. Hypertrophic cardiomyopathy is a genetic cardiovascular disease that is a common cause of sudden death in young athletes. Chagas disease is a parasitic infection transmitted by the reduviid bug, which is native to Latin America. Radiation therapy and systemic sclerosis both cause restrictive cardiomyopathy and diastolic heart failure, not dilated cardiomyopathy.



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51. The answer is B. This patient presents with split, fixed S2 sound and systolic murmur over left upper sternal border heard on heart auscultation, but is otherwise developmentally normal. These findings most likely point to atrial septal defect(ASD). Atrial septal defects are a group of congenital heart conditions which enable communication between atria due to a defect in the interatrial septum. During heart development, atria get first divided by septum primum, which grows downward and forms an opening at the lower end called ostium primum. The septum primum continues to grow downwards and eventually closes off ostium primum. During this process an opening in the upper part of septum primum forms creating ostium secundum. Ostium secundum provides a communication for blood between atria during fetal development. Eventually, a second wall of tissue or septum secundum forms over the ostium secundum, creating a passageway between septum secundum and ostium secundum. This passage is the foramen ovale. Foramen ovale stays open during fetal development and eventually closes soon after birth as pulmonary pressure drops. There are many types of atrial septal defects depending on which part of atrial septum becomes defective during development. Ostium secundum septal defect is the most common type and it can cause symptoms of exercise intolerance, palpitations, syncope, and easy fatigue. Complications of uncontrolled ostium secundum include pulmonary hypertension, right-sided heart failure, atrial fibrillation, stroke, and Eisenmenger syndrome. Patent foramen ovale has little hemodynamic consequence. It is associated with migraine, paradoxical emboli, and decompression sickness. Ostium primum septal defect is seen in the lower portion of the septum at the level of the

tricuspid and mitral valves. It is also known as endocardial cushion defect. It is associated with mitral and tricuspid valve defects as well as Down syndrome. Atrial septal defects cause blood to flow from an area of higher pressure to an area of lower pressure, or in other words, left-to-right shunt. This extra volume causes overload of both the right atrium and right ventricle. This overload of the right ventricle eventually causes overload of the entire pulmonary vasculature, which contributes to the development of pulmonary hypertension. The right ventricle has to work extra hard to overcome higher pressures which over time can lead to right-sided heart failure. As the pressure in the right atrium increases it may rise to levels higher than the left ventricle and eventually result in right-to-left shunt (Eisenmenger syndrome). Upon auscultation of the heart there might be ejection systolic murmur which contributes to higher flow of blood over pulmonic valve. Fixed splitting of S2 is heard due to increased flow over the pulmonic valve keeping it open longer, regardless of inspiration. Once the ASD has been diagnosed, a determination of whether or not it has to be corrected surgically is made. If the ASD is not causing problems, the defect is simply monitored. If the ASD is causing atrial or ventricular enlargement, it is corrected surgically. Surgery is preferably done before significant pulmonary hypertension develops in addition to avoid paradoxical embolism. The other answer options are incorrect for the following reasons. Patent ductus arteriosus presents with a continuous machinery-like murmur in the left infraclavicular region. Mitral regurgitation causes a high-pitched holosystolic murmur best heard at the apex. Ventricular septal defect causes a pansystolic murmur over the lower sternal border. It might be associated with palpable thrill due to high pressure shunting of blood. Transposition of great vessels is usually diagnosed earlier in life as these patients appear cyanotic and short of breath with poor appetite and weight gain from fluid retention. Aortic stenosis is associated with a systolic crescendo-decrescendo murmur which radiates to carotids.

52. The answer is D. This patient presents with a history of smoking, hypercholesterolemia and activity-induced chest pain. The patient's symptoms are consistent with stable angina pectoris. In stable angina pectoris, chest pain is brought on by situations that increase myocardial oxygen demands, such as exercise, cold, or emotional stress. However, the pain is usually relieved by rest. This patient's stable angina is most likely due to a fixed atheromatous plaque in one or more of her coronary vessels. The coronary blood flow through atherosclerotic vessels in stable angina is usually sufficient to meet the demands of the heart at rest. Yet during exertion, blood flow through the coronary vessels is not sufficient. The result is ischemia and chest pain. Sublingual nitroglycerin tablets are a mainstay of both diagnosis and treatment for angina pectoris. The nitroglycerin tablets work through the action of nitric oxide on the vascular smooth muscle, causing vasodilation via a cGMP-dependent mechanism.

At low doses, the organic nitrates affect veins more than arterioles, and the increased compliance of the veins decreases the venous return to the heart. As a result, preload decreases, and myocardial oxygen demand is reduced to a level that can be met by the narrowed coronary vessels. Nitroglycerin also dilates the coronary arterioles directly, and this increased coronary blood flow may be of particular importance in cases of angina due to coronary vasospasm. At higher doses the organic nitrates cause widespread arteriolar dilation in addition to venous dilation, which can decrease afterload by reducing blood pressure. However, higher doses can also lead to hypotension and reflex tachycardia. Dilation of the facial and meningeal arterioles can also cause flushing and headache. Decreasing platelet response does not affect hemodynamics, and is not affected. Similarly, a decrease in plaque formation will not treat the patient's existing angina pectoris. Nitroglycerin is primarily responsible for decreasing preload, not increasing it. Hydralazine, but not nitroglycerin, reduces afterload. Lastly, increasing afterload would cause more strain on the heart.

53. The answer is C. This patient presents with a medical history of heart failure, bilateral pulmonary rales, an S3 heart sound, and jugular venous distention. Together, these indicate an exacerbation of congestive heart failure (CHF) with secondary flash pulmonary edema. This patient tried to treat himself with calcium channel blockers, which have a negative inotropic effect on the myocardial cells and can delay conduction through the atrioventricular node. Thus they can further exacerbate CHF and lead to flash (sudden) pulmonary edema. Loop diuretics such as furosemide act rapidly and significantly relax smooth muscle in the pulmonary vessels. For these reasons, furosemide is used as first-line therapy to achieve diuresis in patients with pulmonary edema due to CHF exacerbations. Carvedilol, digoxin, metoprolol, and spironolactone are used in the treatment of CHF. However, in the acute setting of a patient with shortness of breath due to pulmonary edema, these medications are not appropriate.

54. The answer is E. This patient presents with crushing chest pain that radiates to the jaw and left arm and is not modified by position, breathing, or palpation of the chest wall. He is also experiencing diaphoresis and nausea. An ECG reveals ST-segment elevation in leads II, III, and aVF. His overall presentation is consistent with an inferior myocardial infarction, most commonly caused by an acute thrombus in a coronary artery. This patient is also taking a cyclooxygenase isoform 2 (COX-2) inhibitor (celecoxib) for osteoarthritis. COX-2 inhibitors preferentially reduce antithrombotic and vasodilating prostaglandin I2(PGI2) production in the vascular endothelium, resulting in vasoconstriction. They have little effect on thromboxane (TXA2) levels. TXA2, produced by activated platelets via the COX-1 enzyme, induces platelet aggregation and vasoconstriction. Selective inhibition of COX-2 resulting in reduction in PGI2 levels leads to coronary vasoconstriction and thrombus formation because of

unopposed TXA2 action. These conditions make the patient more susceptible to developing an acute coronary syndrome. COX-2 inhibitors do not cause any changes in TXA2 levels. Therefore any answer with anything other than "no change" for TXA2is incorrect, as seen in options A, B, C, D, and F. COX-2 inhibitors decrease the production of PGI2; thus any answer with nything other than "decreased" for PGI2 is incorrect, as seen in options A, D, F, and G.

55. The answer is C. This patient presents with fever, weight loss, myalgias, arthralgias, abdominal pain, hypertension, and elevations in the erythrocyte sedimentation rate, C-reactive protein level, and white blood cell count. Taken together, these findings are consistent with a diagnosis of polyarteritis nodosa (PAN), which is characterized by necrotizing immune complex inflammation of medium-sized, muscular arteries. No diagnostic serologic tests are specific for PAN. The diagnosis is usually made by the presence of the clinical symptoms described for this patient, results of physical exam (including skin findings, motor or sensory loss, and vascular exam abnormalities), hepatitis/rheumatologic test results, and sometimes biopsy or angiography findings.

Patients with classic PAN are negative for antineutrophil cytoplasmic antibodies and may have low titers of rheumatoid factor or antinuclear antibodies, both of which are nonspecific findings. In patients with PAN, appropriate serologic tests for active hepatitis B infection must be performed. Up to 30% of patients with PAN are positive for hepatitis B surface antigen. In patients with PAN, inflammation of the arterial wall and surrounding connective tissue results from immune complex formation and deposition, leading to fibrinoid necrosis (indicated by the open arrow in the image).

Caseating necrosis is associated with tuberculosis infections. Eosinophilic infiltrate is a prominent feature in Churg-Strauss syndrome. Granulomatous infiltrate is evident in giant cell arteritis, and Langhans giant cells are associated with granulomatosis with polyangiitis. Onion skinning, seen with arteriolosclerosis, is linked to malignant hypertension.

56. The answer is A. This patient with Wolff-Parkinson-White (WPW) has an acute history of heart palpitations. WPW syndrome is characterized by the presence of a fast accessory conduction pathway from atria to ventricle also known as bundle of Kent. The presence of this accessory pathway allows electrical signals to bypass the rate controlling atrioventricular (AV) node and cause ventricles to partially depolarize early. This partial depolarization causes the widening of QRS complex with characteristic delta wave. Patients with WPW syndrome can experience complications of atrial fibrillation with rapid ventricular response such as described in the question stem. Atrial fibrillation can be treated with different classes of antiarrhythmic agents such as beta-blockers, calcium channel blockers, or digoxin.

Class III antiarrhythmic agents are commonly used for treatment of atrial fibrillation with rapid ventricular rate in WPW syndrome. Class III antiarrhythmics work by blocking potassium channels, thereby prolonging repolarization. The resultant prolongation of the action potential duration and refractory period prevents reentrant arrhythmias. These agents have the ability to prolong the QT interval and can result in the development of polymorphic ventricular tachycardia. Class III antiarrhythmics include amiodarone, sotalol, ibutilide, and dofetilide. They are used for the treatment of supraventricular tachycardias, such as atrial fibrillation and atrial flutter. Amiodarone and sotalol can also be used to treat ventricular tachycardias. Ibutilide is an agent of choice for use in WPW syndrome. Ibutilide can cause prolongation of the QT interval leading to torsades de pointes. The patient in the question stem experienced torsades after treatment. Ibutilide is the most likely agent out of the answer choices to produce this finding.

The other options are incorrect for the following reasons:

Class I antiarrhythmic agents interfere with sodium channels. Class I agents are divided into three groups based on their effect on the action potential length. Class Ia agents (quinidine, procainamide, and disopyramide) lengthen the action potential and have an intermediate effect on phase 0. They are used to treat patients with ventricular arrhythmias and paroxysmal atrial fibrillation. Procainamide can be used in patients with WPW.

Class Ib agents (lidocaine, phenytoin, mexiletine, and tocainide) have a fast association/dissociation with sodium channels. They shorten the action potential duration and are used to treat patients with ventricular tachycardia. Class Ic agents (propafenone, flecainide, encainide) have a slow association/dissociation with sodium channels. They have the strongest effect on phase 0 of action potential but no effect on duration of action potential.

Class II agents (carvedilol, esmolol, timolol, metoprolol, atenolol, nebivolol, propranolol) are beta blockers. They work by blocking catecholamines at the beta-1 adrenergic receptors. They decrease sympathetic input to the heart which decreases intracellular cAMP and reduce calcium flux. They are especially useful in controlling supraventricular tachycardias by decreasing conduction through the AV node.

Class IV agents (verapamil, diltiazem) work by blocking non-dihydropyridine calcium channels. They shorten phase two of the cardiac action potential, decrease conduction through the AV node, and reduce contractility of the heart muscle. Class V agents (adenosine, digoxin, magnesium sulfate) have various mechanisms of action. They are used to treat supraventricular arrhythmias. Magnesium sulfate is used in the treatment of torsades de pointes.

57. The answer is E. The patient is a young man with occasional palpitations and syncope episodes. His family history is significant for several family members who

died from a sudden cardiac death which is indicative of a congenital heart defect. ECG shows long QT interval concerning for congenital long QT syndrome. There are very few causes for sudden cardiac death in young patients. Another common cause is hypertrophic obstructive cardiomyopathy which does not fit in the clinical presentation of this clinical vignette.

The QT interval is measured from the start of the Q wave to the end of the T wave and corresponds to the time when the ventricles start to contract to the time when they finish relaxing. An abnormally long or abnormally short QT interval is associated with cardiac arrythmias and death. Congenital long QT syndrome is a group of inherited disorders of myocardial repolarization typically because of a defect in ion channel. People with these conditions have an increased risk of sudden cardiac death because of the development of torsades de pointes. Romano-Ward and Jervell and Lange-Nielsen are two syndromes of congenital long QT syndrome. Romano-Ward syndrome has pure cardiac phenotype and has autosomal dominant inheritance. It is caused by mutations in ANK2 gene causing disruption in ion channels and electrical currents in cardiac myocytes. Clinical symptoms include syncope, seizures, development of torsades de pointes and sudden cardiac death. Diagnosis is based on family history of sudden cardiac death, ECG findings, and exercise test. Treatment is aimed at decreasing the incidence of cardiac arrhythmias by using β-blockers and heart ganglion blocks.

The other options are incorrect for the following reasons:

- Jervell and Lange-Nielsen syndrome is an autosomal recessive disorder with associated sensorineural hearing loss.
- Brugada syndrome presents with EKG findings of pseudo-right bundle branch block and ST elevation in V1-V3. It is most commonly found in Asian males.
- Wolff-Parkinson-White syndrome is a type of ventricular preexcitation syndrome characterized by the presence of an abnormal fast accessory conduction pathway from atria to ventricle which bypasses the rate-controlling AV node. Ventricles start to depolarize earlier, which is evidenced on ECG by the presence of delta waves, widened QRS complex, and short PR interval.
- Mobitz type II AV block is characterized by intermittently nonconducted P waves not associated with PR interval lengthening or shortening. There is usually a fixed number of non-conducted P waves for every successfully conducted QRS.
- A right bundle branch block (RBBB) is characterized by a delay in depolarization of the right ventricle, resulting in a widened QRS complex. Characteristic ECG findings include terminal R wave in lead V1 (called R prime) and prolonged S wave in leads I and V6.

58. The answer is B. This patient is a 65-year-old man who has new-onset pleuritic chest pain 2 days after myocardial infarction (MI) that was not treated with reperfusion. On physical examination, he has a friction rub, and an ECG shows widespread ST

elevations. Presentation is concerning for early infarct-associated pericarditis, one of several potential post-MI complications.

Three major types of pericardial complications can occur in patients following an MI:

1. early infarct-associated pericarditis
2. pericardial effusion
3. post-cardiac injury (Dressler) syndrome

Early infarct-associated pericarditis is caused by inflammation of the pericardium, which is caused by pericardial inflammation due to necrotic myocardium. It occurs most commonly 1-4 days after transmural MI when neutrophils are invading the entire necrotic myocardial wall. It is thought that this inflammation in the myocardial wall can extend to the pericardium, leading to pericarditis. Patients who have transmural MIs that were not treated with revascularization (PCI) or fibrinolysis (tPA) are most likely to experience early infarct-associated pericarditis, and since the PCI/reperfusion era, the incidence of peri-infarct pericarditis has decreased dramatically. Pericarditis can be associated with chest pain exacerbated by supine posture, a friction rub, and diffuse ST elevations and PR depressions on ECG. Although recommended in patients with viral or autoimmune pericarditis, treatment with routine anti-inflammatory therapy beyond daily aspirin (eg, NSAIDs) is generally avoided in patients with early infarct-associated pericarditis.

Pericardial effusion is a pericardial complication that is also more common after transmural MI and can occur secondary to fibrinous pericarditis or myocardial wall rupture with subsequent hemopericardium. Myocardial wall rupture occurs when the myocardial wall is at its weakest, which is usually 4-7 days post-MI when macrophages are invading and clearing the debris of dead tissue.

Dressler syndrome, or post-cardiac injury syndrome, presents with symptoms of pericarditis starting weeks to months after MI. Initial injury to the myocardial wall as part of the MI is thought to expose cardiac antigens to the body's immune system and stimulate an immune response. Immune complexes deposit onto pericardium, pleura, and lungs and elicit an inflammatory response.

The other options are not the best answers for the following reasons.

Pericardial inflammation secondary to autoantibodies against pericardial tissue is the likely cause of Dressler syndrome (post-cardiac injury syndrome), which typically occurs weeks to months after MI, not 2-3 days post-MI. If this patient had active ischemia indicative of repeat MI or angina, he would likely have substernal nonpleuritic, nonpositional chest pain, and there would be regional, not widespread, ST elevations on ECG. It is important to recognize that troponin may still be elevated several days after infarction because of the protein's prolonged half-life.

Ventricular wall rupture occurs 5-14 days after transmural MI and is associated with hemodynamic instability and possible tamponade presentation, not pleuritic chest pain and widespread ST elevations.

Pulmonary infarction can occur secondary to pulmonary embolism and can lead to pleuritic chest pain. However, this chest pain is unlikely to be associated with widespread ST elevations on ECG, and the patient would most likely present with dyspnea, hypoxia, and/or sinus tachycardia.

Pleural effusion can occur in association with MI. In the setting of reduced ejection fraction after myocardial injury, pulmonary venous hypertension can develop, which leads to the development of transudative pleural effusion. Pleural effusion would likely be seen on chest x-ray and would be unlikely to present with widespread ST elevations on ECG and positional pleuritic chest pain.

The most common causes of pericarditis are 1) viral (presenting with fever, leukocytosis) and 2) idiopathic. Other causes of pericarditis include bacterial, uremic, metastatic, post-MI, and autoimmune. This patient's lack of upper respiratory symptoms and status after untreated MI make post-infarct pericarditis more likely.

59. The answer is C. This unresponsive man with lung disease and coronary atherosclerosis is experiencing ventricular fibrillation that is unresponsive to electrical defibrillation but is successfully treated with an antiarrhythmic drug. Based on his presentation with shock-refractory ventricular fibrillation, this patient most likely received amiodarone, which has the primary mechanism of action of prolonging the repolarization phase via potassium channel blockade.

Amiodarone is known to have side effects of pulmonary fibrosis, hepatotoxicity, and hypothyroidism or hyperthyroidism. Amiodarone is primarily a class III antiarrhythmic agent, although it exhibits actions of all the other classes of antiarrhythmic agents. Repolarization of depolarized cells is slowed by class III antiarrhythmic agents. Class III antiarrhythmics block the potassium current responsible for the repolarization of cardiac cells. These agents prolong the duration of the action potential without altering phase 0 of depolarization or the resting membrane potential. All class III drugs have the potential to induce arrhythmias. There is also a decreased incidence of torsades de pointes with amiodarone compared with the other class III antiarrhythmic drugs.

A drug that accelerates depolarization in high-frequency depolarizing cells would increase membrane responsiveness, inducing further arrhythmias. A drug that prolongs depolarization via sodium channel blockade is considered a class I antiarrhythmic, and use of a class I antiarrhythmic would not be a cause of concern for a patient with a history of lung disease. Calcium channel blockers are typically used for rate control in patients with atrial fibrillation and would not be a cause of concern for a patient with a history of lung disease. β-Blockers reduce sympathetic stimulation of myocardial cells and are not typically used to treat shock-refractory ventricular fibrillation.

60. The answer is B. This patient, who is in labor at 39 weeks gestation, elects to have epidural anesthetic during the birth. After injection, she presents with cardiotoxic symptoms, including palpitations and dizziness. One of the most common local anesthetics used in delivery is bupivacaine. Bupivacaine is a long-acting amide-based local anesthetic that blocks voltage-gated sodium channels and prevents depolarization. The mechanism of action of bupivacaine allows greater cardiotoxicity than other drugs in this class. It can produce arrhythmias and hypotension if administered intravenously.

Her new ECG after bupivacaine administration shows dropped beats with a constant PR interval. These indicate that the patient has a second-degree heart block consistent with Mobitz type II. A Mobitz type II heart block is another cardiotoxic effect of bupivacaine when given intravenously.

The following drugs do not have the cardiotoxic effects seen in this patient when appropriate doses are used:

- Fentanyl is an opioid that functions by activating opioid receptors, and its use is associated with increased risk of neonatal respiratory depression during delivery. Fentanyl is typically used for sedation during endoscopy or oral surgery.
- Midazolam is a benzodiazepine used as preoperative sedation or for induction of general anesthesia.
- Morphine is an opioid that mainly binds and activates μ-opioid receptors. Its use is associated with increased risk of neonatal respiratory depression and withdrawal. Morphine is used for acute and chronic pain, but not during delivery.
- Baclofen is a skeletal muscle depressant used for spasticity, and works by activating the GABA-B receptor. It is primarily used for treating patients with spastic movement disorders.

61. The answer is A. The patient's symptoms of intense chest pain, nausea, shortness of breath, and diaphoresis suggest angina secondary to acute coronary syndrome, most likely myocardial ischemia. His history of coronary artery disease, hyperlipidemia, and obesity predispose him to rupture of cholesterol plaques, which can lead to coronary artery occlusion, which manifests as myocardial ischemia. Autodigestion of the pancreas by pancreatic enzymes may present similarly to myocardial ischemia, but would not acutely be associated with shortness of breath or diaphoresis. Esophageal spasm is associated with a consistent recurrence of symptoms occurring exclusively following meals and would not be accompanied by shortness of breath or diaphoresis or chest pressure. Gastroesophageal reflux often is mistaken for cardiac pathology (ie, "heartburn"); however, it can be differentiated by an absence of crushing pain and shortness of breath. Although pulmonary emboli may mimic this patient's presentation, he had no inciting event. While unprovoked deep vein thromboses (DVTs) and emboli

do occur, on an exam they should only be suspected in the presence of congenital clotting disorders.

62. The answer is A. This patient presented with unexplained palpitations, tachycardia, and shortness of breath. These signs indicate that she should be evaluated for an arrhythmia, specifically supraventricular tachycardia. Often, this form of arrhythmia does not have any clear triggers. Adenosine is a very short-acting drug that is useful in terminating certain forms of supraventricular tachycardia by hyperpolarizing the cell and decreasing atrioventricular (AV) node conduction. Adverse effects include flushing, hypotension, chest pain, bronchospasm, and a sense of impending doom. The other options are not the best answers because they are not used to treat this patient's condition. Ivabradine is used to treat stable angina in patients who cannot take β-blockers. It works by inhibiting funny channels, thus prolonging phase IV of the cardiac action potential. Amiodarone is a class III antiarrhythmic. It mainly acts by decreasing K+ efflux, thus prolonging phase III. It is commonly used to treat atrial and ventricular tachycardia. Adverse effects include pulmonary fibrosis, hepatotoxicity, hypothyroidism, corneal deposits, and photosensitivity. Metoprolol is a class II antiarrhythmic. It decreases cAMP and Ca2+ currents, which subsequently decreases sinoatrial and AV node activity. Adverse effects include sexual dysfunction, bradycardia, and exacerbation of symptoms of chronic obstructive pulmonary disease. Procainamide is a class Ia antiarrhythmic. It is used to treat atrial and ventricular tachycardia by prolonging phase I of the cardiac action potential. Adverse effects include a lupus-like syndrome and torsades de pointes.

63. The answer is E. This patient is found unconscious with needle tracks in his arm, and is resuscitated with naloxone in the emergency room. He is admitted to the hospital and on examination, he is found to have a systolic "blowing" murmur. The murmur is loudest at the left lower sternal border and increases with inspiration. These findings suggest he has tricuspid regurgitation or leakage of blood backwards through the tricuspid valve. While tricuspid regurgitation may be caused by right ventricular dilatation, the tricuspid valve is also the most common site of infective endocarditis in intravenous drug users. In these patients, infected venous blood (most often with S. aureus) returns to the right side of the heart, and seeds the tricuspid valve. Other valves may also be damaged, typically after tricuspid valve damage has occurred. The arrow in the echocardiograph indicates a vegetation on the tricuspid valve. Aortic regurgitation is a diastolic murmur associated with head bobbing and visibly pounding pulses. Aortic stenosis is a systolic murmur that is most often due to calcification secondary to the aging process. Mitral stenosis is a diastolic murmur, often seen in rheumatic fever, and is characterized by an opening snap. Mitral regurgitation radiates to the axilla, and does not increase with inspiration. Tricuspid stenosis is a rare condition characterized by a diastolic murmur.

64. The answer is C. This patient is a 72-year-old woman with long-standing rheumatoid arthritis (RA) who presents with insidious-onset exertional dyspnea and is found to have an S4 heart sound in the setting of jugular venous distension, pulmonary crackles, peripheral edema, and a normal ejection fraction. Presentation is suggestive of diastolic heart failure. In the context of this patient's long-standing RA and absence of hypertension, presentation is most likely secondary to SAA amyloidosis and associated restrictive cardiomyopathy.

Diastolic heart failure presents with symptoms of dyspnea, fatigue, jugular venous distention, pulmonary congestion, and peripheral edema in the setting of normal left ventricular ejection fraction (55%-70%). Diastolic heart failure is associated with increased LV diastolic pressures and impaired LV diastolic filling, which usually occurs secondary to conditions that decrease ventricular wall compliance. Therefore, patients commonly have an S4 heart sound, which occurs secondary to vibrations that are generated as the atrial kick tries to pump blood into a non-compliant ventricle.

The most common causes of diastolic heart failure include hypertensive heart disease, restrictive cardiomyopathy, and valvular heart disease, among others. This patient, who has no history of hypertension and no murmurs suggestive of valvular disease on examination, therefore most likely has restrictive cardiomyopathy. Restrictive cardiomyopathy can be caused by endomyocardial fibrosis, amyloidosis, sarcoidosis, hemochromatosis, chemotherapy exposure, or radiation exposure.

Cardiac amyloidosis is the most common form of restrictive cardiomyopathy in the United States and can lead to diastolic dysfunction, rhythm disturbances, and even ischemia. It presents rarely in patients with chronic inflammatory disease (such as RA or IBD) when fragments of serum amyloid A (SAA) protein, an acute-phase reactant, are deposited in the heart tissue. Cardiac amyloidosis can also occur in the setting of primary AL amyloidosis, TTR amyloidosis, and other forms of amyloidosis. Patients with systemic amyloidosis due to SAA or AL amyloidosis may also present with nephrotic syndrome, hepatomegaly, enlarged tongue, early satiety, or other symptoms. Diagnosis of cardiac amyloidosis is confirmed either through endomyocardial biopsy demonstrating amyloid deposits, or through biopsy of other tissues (abdominal fat pad, rectum) demonstrating amyloid deposits in patients with characteristic cardiac findings.

The incorrect answers are wrong for the following reasons:

- Myxomatous degeneration of the mitral valve leaflets is characteristic of mitral valve prolapse, or MVP, which, when severe, can lead to mitral regurgitation, LV volume eccentric hypertrophy, and systolic, not diastolic, heart failure. The patient would present with systolic murmur best heard at the apex as well as a possible S3 on cardiac examination.

• Ischemic heart disease (for example, as occurs in individuals with repeated myocardial infarctions) is typically associated with a dilated, scarred ventricle and systolic, not diastolic, dysfunction. In addition, this patient has no chest pain or history of myocardial infarction.

• Heart muscle can hypertrophy in response to stress via either concentric or eccentric hypertrophy. Concentric left ventricular hypertrophy (LVH) is characterized by the addition of sarcomeres (contractile units of cardiac myocytes) in parallel that leads to thickening of the wall and a decreased ventricular lumen size. It can lead to diastolic heart failure due to reduced compliance of the hypertrophic ventricle. Common causes of concentric LVH include causes of LV pressure overload such as chronic systemic hypertension, aortic stenosis, and aortic coarctation. As in concentric LVH, this patient's ventricular wall thickness is likely increased, but this increased wall thickness is due to the deposition of insoluble, fibrous misfolded proteins (amyloid) rather than the addition of sarcomeres in parallel. In contrast to concentric LVH, eccentric hypertrophy is characterized by the addition of sarcomeres in series, which increases LV lumen diameter and allows the heart to contract in greater force (via the Starling mechanism). Eccentric hypertrophy is caused by states associated with volume overload such as pregnancy and endurance athletics or in states of volume overload associated with mitral valve prolapse, dilated cardiomyopathy, or other disorders.

• Dilated cardiomyopathy can be caused by a variety of conditions, including excessive alcohol intake, ischemic heart disease, and myocarditis. Examination is associated with a pathologic S3 heart sound, and the patient typically has systolic heart failure with reduced LV ejection fraction.

65. The answer is D. This patient presents with an acute STEMI. Testing reveals ventricular fibrillation, an irregular ventricular rhythm without any distinct QRS complexes, ST segments, or T waves. Ventricular fibrillation is an important cause of sudden cardiac death, as well as death within the first 24 hours of an acute MI. If defibrillation fails to convert to sinus rhythm, epinephrine is given followed by amiodarone, according to the advanced cardiovascular life support (ACLS) protocol.

Amiodarone can cause pulmonary fibrosis (see image). Additional complications of amiodarone treatment can include hypotension, thyroid dysfunction (both hypothyroidism and hyperthyroidism), hepatotoxicity, and corneal deposits. Its use is also associated with other arrhythmias (namely, bradyarrhythmias and torsades de pointes). In patients taking amiodarone, remember to check pulmonary function, liver function, and thyroid function tests.

Increased post-MI mortality is associated with Class IC antiarrhythmics (flecainide and encainide). Yellow-green vision is a side effect of digoxin. Malar rash is a symptom of

drug-induced lupus, caused by procainamide, a type 1A antiarrhythmic. Bleeding is not a side effect of any antiarrhythmic drugs.

66. The answer is B. his patient has a history of heart disease and presents with headaches, dizziness, and palpitations, specifically every Monday. He has most likely been exposed to nitrates at his job. His symptoms are consistent with "Monday disease" due to prolonged nitrate exposure. In Monday disease, reflex tachycardia, dizziness, hypotension, flushing, and headache occur on Monday with re-exposure to nitrates. Although his ECG shows a normal heart rate of 80, it may have been taken at a time when he was not experiencing the tachycardia that is typical of this disease. Nitrates are common ingredients found in an explosives factory. Monday disease in an industrial exposure setting is the development of tolerance for the vasodilating action of nitrates during the work week and loss of tolerance over the weekend. Symptoms develop on Monday with re-exposure, due to loss of tolerance. The most severe consequence occurs when compensatory vasoconstriction is unopposed in critical areas such as the coronary vessels, leading to nonatherosclerotic-related cardiac ischemia. This coronary constriction is closely associated with abrupt cessation of exposure on Saturday morning. The patient does not present with symptoms of anemia, such as cyanosis or pallor of skin. Tuberculosis is commonly associated with exposure to silica dust, rather than nitrates. Congestive heart failure and dementia also are not associated with Monday disease.

CLINICAL CASES

1. A 58-year-old man comes to the physician complaining of occasional chest pain that occurs with strenuous activity. He is obese and has a history of hypertension and diabetes mellitus. During the physical examination, he admits to eating most of his meals at fast food restaurants. He also reports he has little time for exercise.

1.1 What is the most likely diagnosis?

Stable angina, characterized by chest pain with exertion, is often secondary to atherosclerosis. Stable angina is chest discomfort that occurs only during activity and resolves within several minutes of ceasing the activity. Patients with stable angina have minimal or no chest pain at rest. By contrast, unstable angina is defined as chest pain that changes or worsens. Unstable angina occurs at rest or increases in frequency, severity, or duration.

1.2 What risk factors increase a person's likelihood of developing this condition?

Hypertension, diabetes mellitus, advanced age, gender, and hyperlipidemia are major risk factors for atherosclerosis. Family history and smoking are also risk factors. Obesity and lack of exercise have not been definitively linked to increased risk of atherosclerosis.

1.3 What is the pathophysiology of this condition?

Endothelial injury resulting from various factors, including hyperlipidemia, smoking, and hypertension, can lead to monocytic and lipid infiltrates into the subendothelium (fatty streaks), release of growth factors leading to smooth muscle cell proliferation into the intima (proliferative plaque), and subsequent development of foam cells and complex atheromas with calcification and ischemia of the intima

1.4 What are the major forms of angina?

• Stable angina: Chest pain with exertion; responds to nitroglycerin.

• Unstable angina: Chest pain at rest secondary to thrombus in a branch. May not completely respond to

nitroglycerin; antithrombic agents and heparin may also be required.

• Prinzmetal angina: Chest pain at rest, secondary to coronary artery spasm. Treatment includes calcium channel blockers.

2. A 65-year-old woman with a 60-pack-year smoking history comes to her primary care physician with 3 months of shortness of breath and dry cough. Until recently, she was able to walk the four blocks to her local grocery store without shortness of breath; however, now she is able to walk only one block before having to stop and rest. She has been waking from sleep with difficulty breathing and feels uncomfortable lying flat in bed. Her physical examination is notable for crackles at the lung bases. There is no evidence of hepatosplenomegaly or jugular venous distention.

2.1 What is the most likely diagnosis?

Left heart failure (LHF) is evidenced by orthopnea, paroxysmal nocturnal dyspnea, dyspnea on exertion, and mild edema.

2.2 What are the common causes of this condition?

Hypertension, myocardial infarction, valvular heart disease, myocarditis, and cardiomyopathies are associated with the development of LHF.

2.3 What symptoms help differentiate right heart failure from left heart failure?

Right heart failure is characterized by compromised venous return. This can manifest as ascites, significant edema of the lower extremities, jugular venous distention, and hepatosplenomegaly secondary to liver and spleen congestion.

3. A 45-year-old man presents to his physician for a routine health maintenance visit. He reports that he has experienced intermittent heart palpitations. He denies any chest pain, dyspnea on exertion, or syncope. On physical examination, the patient is well appearing and in no distress. His blood pressure is 110/79 mm Hg. Auscultation of his chest while sitting reveals a late systolic click associated with a highpitched, late systolic murmur. The systolic click occurs closer to S1 with standing. His ECG is normal; a transesophageal echocardiogram shows a thin leaflike structure entering the inferior left atrium during
systole.

3.1 What is the most likely diagnosis?

Mitral valve prolapse (MVP), a condition found in 0.6%–2.4% of the population, is the most common valvular heart disease. Most cases are asymptomatic and discovered incidentally. However, left atrial enlargement may occur, resulting in occasional benign supraventricular arrhythmia that the patient perceives as palpitations. Men and women are affected equally. MVP is defined by the echocardiographic measurement of the superior displacement of one or both mitral leaflets into the left atrium (LA).

3.2 What is the pathogenesis of this condition?

MVP is multifactorial in origin with an autosomal dominant pattern of inheritance in some families. It can occur as a result of changes within the valvular tissue, geometric disparities between the left ventricle and mitral valve, and connective tissue disorders, such as Marfan syndrome (prevalence of 91%) and Ehlers- Danlos syndrome (6%).

3.3 What are the major complications of this condition?

MVP typically has a benign prognosis. A poorer prognosis is more likely in male, elderly patients with a systolic murmur, thickened and redundant mitral leaflets, or left atrial or ventricular hypertrophy. The most common complication is infective endocarditis as the mitral valve is partially damaged and therefore at increased risk for bacterial colonization. Other complications of MVP include severe mitral valve regurgitation, and cerebrovascular ischemic events. Risk stratification by clinical examination and echocardiography is necessary.

SECTION GASTROINTESTINAL SYSTEM
MCQs STEP 1

1. A 45-year-old woman presents with increasing fatigue, weakness, and tingling of her arms and legs. Physical examination finds numbness and loss of balance, position, and vibratory sense in both of her lower extremities. Histologic examination of a smear made from a bone marrow aspiration reveals asynchrony in red blood cell precursors between the maturation of their nuclei and their cytoplasm. Additional workup discovers achlorhydria, and a biopsy of the antrum of her stomach reveals chronic atrophic gastritis. Which of the following is the most likely diagnosis?

A. Fanconi anemia
B. Leukoerythroblastic anemia
C. Megaloblastic anemia
D. Myelophthisic anemia
E. Sideroblastic anemia

2. A 40-year-old female reports chronic gastritis. She tests positive for H. pylori. After a course of the appropiate antibiotic theraphy her symptoms subside. Which of the following is the most effective noninvasive test for the diagnosis of Helicobacter-associated gastric ulcers? a. Culture of stomach contents for H. pylori b. Detection of H. pylori antigen in stool c. Growth of H. pylori from a stomach biopsy d. Growth of H. pylori in the stool e. IgM antibodies to H. pylori

A. Culture of stomach contents for H. pylori
B. Detection of H. pylori antigen in stool
C. Growth of H. pylori from a stomach biopsy
D. Growth of H. pylori in the stool
E. IgM antibodies to H. pylori

3. A patient with peptic ulcer disease is taken off their medication because of undesirable side effects. As a result, the patient has rebound gastric acid hypersecretion. Which of the following drugs best accounts for the observed result?

A. An H1-receptor antagonist
B. A proton pump inhibitor
C. A cholinergic receptor antagonist
D. An antacid
E. A CCKB receptor antagonist

4. During the chewing of a bolus of food, but before swallowing, salivary secretion, gastric secretion, and pancreatic secretion are stimulated by which of the following neurocrine,endocrine,and paracrine mediators? Explain.

A. ACh, gastrin, histamine
B. ACh, CCK, nitric oxide
C. Nitric oxide, vasoactive intestinal polypeptide, histamine

D. Vasoactive intestinal polypeptide, gastrin, somatostatin
E. Nitric oxide, CCK, serotonin
5. A 31-year-old woman takes antacids with and after a meal so that gastric pH does not decrease below pH 6, for peptic ulcer disease. This agent will cause a greater than normal secretion of which of the following?
A. Gastrin
B. Secretin
C. Pancreatic bicarbonate
D. CCK
E. Somatostatin
6. Motility recordings in a patient with signs of bacterial overgrowth of the small intestine indicate an abnormal pattern of motility in the fasting state that is characterized by a lack of the normal periodic bursts of gastric and intestinal contractions. This patient is likely to demonstrate abnormal secretion of which of the following hormones?
A. CCK
B. Gastrin
C. Motilin
D. Secretin
E. Vasoactive intestinal polypeptide
7. A patient with alcoholic cirrhosis comes in vomiting blood. After stabilizing him with IV fluids, the next step should be administration of an agonist/analog of which of the following agents to inhibit gastric acid secretion and visceral blood flow?
A. Gastrin
B. Somatostatin
C. Histamine
D. Pepsin
E. Acetylcholine
8. A 56-year-old man presents with weight loss, cough, and diffuse chest pain. A chest x-ray reveals normal heart and lungs, but the radiologist detects a “bird’s beak” narrowing of the terminal esophagus, which is also seen with a barium swallow. Follow-up history indicates that the patient also has dysphagia and regurgitation. Manometry shows increased lower esophageal sphincter (LES) pressure with no relaxation upon swallowing, indicating a diagnosis of achalasia. Which of the following is the putative inhibitory neurotransmitter responsible for relaxation of gastrointestinal smooth muscle?
A. Dopamine
B. Vasoactive intestinal peptide
C. Somatostatin

D. Substance P
E. Acetylcholine
9. Which of the following nerves participate in sympathetic nervous regulation of the gastrointestinal tract
A. Lumbar spinal nerve
B. Trigeminal nerve
C. Vagus nerve
D. Axial spinal nerve
E. Sacral spinal nerve
10. Which of the following hormones is released by K cells
A. CKK
B. Gastrin
C. Secretin
D. GIP
E. Histamine
11. Which of the following is a function of GIP
A. Increase insulin secretion
B. Decrease insulin secretion
C. Increase glucagon secretion
D. Decrease glucagon secretion
E. Increase insulin sensitivity
12. A 42-year-old woman complains of a burning pain in the upper middle region of her abdomen. The pain usually occurs about 2 hours after a meal and frequently awakens her at night. Antacids can usually relieve the pain within a few minutes. An x-ray film reveals a typical duodenal ulcer identified as a discrete crater in the proximal portion of the duodenal bulb. Because the woman does not have a history of chronic use of aspirin or other nonsteroidal antiinflammatory drugs (NSAIDs), the bacterium Helicobacter pylori is assumed to be the major factor in the etiology of the ulcer. Which of the following is likely to be normal in this woman?
A. Basal acid output
B. Fasting serum gastrin
C. Gastrin response to a meal
D. Maximal acid output
E. Parietal cell mass
F. Pepsin secretion
13. A 43-year-old man with a recurrent history of ulcer disease associated with diarrhea and a strong family history of duodenal ulcer disease is suspected of having Zollinger-Ellison syndrome (gastrinoma). Secretin (1 U/kg) is given as a rapid intravenous

injection to test for gastrinoma. Which of the following results would support the existence of gastrinoma following secretin administration?
A. Gastrin release from antrum
B. Increased serum gastrin
C. Inhibition of gastric emptying
D. Inhibition of gastric secretion
E. Stimulation of pancreatic HCO_3^- secretion
14. 33-year-old man complains that his chest hurts when he eats, especially when he eats meat. An x-ray film shows a dilated esophagus, and achalasia is suspected. Esophageal manometry is used to confirm the diagnosis. Swallowing induced relaxation is reduced at which anatomic location in this man?
A. Lower esophageal sphincter
B. Lower esophagus
C. Middle esophagus
D. Pharynx
E. Upper esophageal sphincter
F. Upper esophagus
15. A 70-year-old woman undergoes a gastrectomy for Zollinger-Ellison syndrome. Her physician informs her that she will need to take intramuscular vitamin B12 shots for the rest of her life. Absence of which of the following cell types is responsible for this vitamin replacement requirement?
A. Chief cells
B. G cells
C. Goblet cells
D. Mucous neck cells
E. Parietal cells
16. A 42-year-old obese woman experiences episodic abdominal pain. She notes that the pain increases after the ingestion of a fatty meal. The action of which of the following hormones is responsible for the postprandial intensification of her symptoms?
A. Cholecystokinin (CCK)
B. Gastrin
C. Pepsin
D. Secretin
E. Somatostatin
17. Patients with functional dyspepsia (disturbed indigestion) and prominent nausea frequently experience spurts of excessive acid exposure to the upper duodenum. This results in pancreatic secretion, mainly through the action of which of the following substances?

A. Cholecystokinin
B. Gastrin
C. Glucagon
D. Secretin
E. Vasoactive intestinal polypeptide (vip)

18. A 30-year-old male seeks help because he lost weight and feels full after eating only a small amount of food. He is diagnosed with a delay in gastric emptying. Which of the following hormones has at physiological levels the strongest effect in inhibiting gastric emptying?
A. Cholecystokinin
B. Gastrin
C. Glucose-dependent insulinotropic peptide
D. Motilin
E. Pancreatic polypeptide

19. A 28-year-old, 166 cm (5.45 ft) tall woman, weighing 170 kg (375 lbs) successfully underwent biliopancreatic diversion surgery, in which a portion of her stomach was removed and the remaining portion of the stomach was connected to the lower portion of the small intestine (see Figure 2-18). What is her prevalence for peptic ulcer disease and for what reason?
A. It is higher due to inflammation caused by the surgical staples
B. It is higher due to the loss of secretin release
C. It is lower since chief cells were surgically resected
D. It is lower since g cells were surgically resected
E. It is unchanged since the surgery was successful

20. A 75-year-old male presented with a 6-month history of early satiety and with upper abdominal discomfort for many years. Physical examination revealed mild epigastric tenderness. Esophago-gastro-duodenoscopy showed a large, ulcerated mass in the upper stomach, which was found to be cancerous. Surgery resulting in the removal of the gastric fundus was performed. After successful surgery, the patient was advised to eat small portions and to drink small volumes because of which of the following?
A. Almost complete absence of gastric motility
B. Distorted emptying of liquids
C. Inadequate mixing of large food boluses
D. Lack of receptive relaxation in the stomach
E. Weaker and slower propulsion of food toward the pylorus

21. A patient with peptic ulcer disease is taken off their medication because of undesirable side effects. As a result, the patient has rebound gastric acid hypersecretion. Which of the following drugs best accounts for the observed result?
A. An H1-receptor antagonist

B. A proton pump inhibitor
C. A cholinergic receptor antagonist
D. An antacid
E. A CCKB receptor antagonist

22. A patient presents with Whipple's triad, including plasma glucose <60 mg/dL, symptomatic hypoglycemia, and improvement of symptoms with administration of glucose. CT of the abdomen shows enlargement of the islet cells suggestive of islet cell carcinoma. Which of the following is true regarding the islets of Langerhans?

A. They are found primarily in the head of the pancreas.
B. They constitute approximately 30% of the pancreatic weight.
C. They contain six distinct endocrine cell types.
D. They have a meager blood supply.
E. They secrete insulin and glucagon.

23. A woman presents with gallstones and no jaundice. She is prepared for exploratory surgery. The lesser omentum is incised close to its free edge, and the biliary tree is identified and freed by blunt dissection. The liquid contents of the gallbladder are aspirated with a syringe, the fundus incised, and the stones are removed. The entire duct system is carefully probed for stones, one of which is found to be obstructing a duct. In view of her symptoms, where is the most probable location of the obstruction?

A. The bile duct
B. The common hepatic duct
C. The cystic duct
D. Within the duodenal papilla proximal to the juncture with the pancreatic duct
E. Within the duodenal papilla distal to the juncture with the pancreatic duct

24. An 18-year-old female decides to get a tattoo for her birthday. Two months later she presents with a fever, right upper quadrant pain, nausea, vomiting, and jaundice. Which of the following lab values would most likely be found in a patient with infectious hepatitis?

A. An increase in plasma alkaline phosphatase
B. An increase in plasma bile acids
C. An increase in both direct and indirect plasma bilirubin
D. An increase in direct bilirubin, and a decrease in indirect bilirubin in the plasma
E. An decrease in both direct and indirect plasma bilirubin

25. A 63-year-old woman presents with diarrhea, abdominal pain, and flushing. The urinary excretion of the seratonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA) is elevated. Abdominal CT reveals a tumor in the terminal ileum. Surgical resection of the terminal ileum will most likely result in which of the following?

A. A decrease in absorption of amino acids
B. An increase in the water content of the feces

C. An increase in the concentration of bile acid in the enterohepatic circulation
D. A decrease in the fat content of the feces
E. An increase in the absorption of iron

26. A 40-year-old woman of fair complexion is admitted for evaluation of acute vomiting with abdominal pain. The episode began the night before after a fatty meal, and she has noted her stools are a peculiar grey white color. Abdominal examination is difficult because she is obese, but she exhibits acute tenderness in the right upper quadrant and has pain just below her left shoulder blade. Interference with which aspect of porphyrin metabolism best accounts for the white stools?

A. Sterile gut syndrome with defective bilirubin oxidation
B. Excess oxidation of bilirubin to urobilinogen
C. Heme synthesis defect causing increased bilirubin clearance
D. Bile duct excretion of bilirubin with oxidation to stercobilin
E. Excess reabsorption of urobilinogen with excess Urobilin

27. A 16-year-old type 1 diabetic is noncompliant with his required insulin therapy and develops hyperglycemia after eating several pieces of hard candy. The release of which of the following intestinal hormones would most likely be stimulated?

A. Gastric inhibitory peptide (GIP)
B. Gastrin
C. Motilin
D. Secretin
E. Somatostatin
F. Substance P
G. Vasoactive intestinal polypeptide (VIP)

28. A 57-year-old woman with a 30-year history of alcoholism and liver disease visits her physician complaining of abdominal swelling and shortness of breath. The physician determines that she has severe ascites. Which of the following factors contributes to the accumulation of fluid in the abdominal cavity?

A. Decreased plasma epinephrine and norepinephrine
B. Decreased plasma volume
C. Increased hepatic lymph flow
D. Increased hydrostatic pressure in splanchnic capillary beds
E. Increased natriuresis
F. Increased plasma albumin concentration
G. Increased plasma oncotic pressure

29. A 20-year-old woman admits herself to the emergency room with a yellow discoloration of the whites of her eyes. She says that she does not drink and that she has not experienced any changes in her stool. Her liver enzyme profile and direct serum

bilirubin levels are normal, while total bilirubin is elevated. What is the most likely cause for her jaundice?
A. Defect in hepatocytes
B. Defect in kupffer cells
C. Gallstones
D. Hemolysis
E. Tumor obstructing bile duct
30. A 54-year-old insulin-dependent diabetic notes that her insulin requirements have gone up dramatically in the past year (from 50 U to nearly 200 U of recombinant human insulin) and her blood glucose is still poorly controlled. A possible explanation for the worsening of her diabetes includes which of the following?
A. A high titer of anti-insulin antibodies
B. An improved diet
C. An improved exercise program
D. Progression of macrovascular disease
E. Weight loss
31. Exogenous peripherally injected insulin differs from endogenously secreted insulin in a number of aspects, including which of the following
A. Achieves a higher concentration in the periphery than in the liver, contrary to endogenous insulin
B. Contains c-peptide, which is missing from secreted endogenous insulin
C. Is able to bypass insulin resistance observed with endogenous insulin
D. Is always extracted from animal sources and, therefore, is less effective due to sequence differences and anti-insulin antibodies
E. Is in the form of proinsulin, whereas endogenous insulin has had c-peptide removed
32. An 18-year-old woman presented with 1 week of history of fever and malaise. She had mild jaundice and elevated temperature. Hemoglobin was 13.8 g/dL, leukocyte count 13 ×109per liter. Serum bilirubin was elevated (42 mmol/L) and contained 95% unconjugated bilirubin. Liver enzyme tests were normal. Which of the following is the most likely cause of these signs and symptoms?
A. Alcohol poisoning
B. Decreased glucuronyl transferase
C. Increased lactate dehydrogenase (ldh)
D. Excessive hemolysis
E. Obstruction of bile flow
33. A 37-year-old obese man presents with signs and symptoms of hyperglycemia. After appropriate workup, he is diagnosed as having type II diabetes mellitus, which is due in part to insulin resistance. Laboratory evaluation of his serum also finds hypertriglyceridemia, which is due to his diabetes. The most common type of

secondary hyperlipidemia associated with diabetes mellitus is characterized by elevated serum levels of which one of the following substances?
A. Chylomicrons
B. High-density lipoproteins
C. Intermediate-density lipoproteins
D. Low-density lipoproteins
E. Very-low-density lipoproteins
34. An apathetic male infant in an underdeveloped country is found to have peripheral edema, a “moon” face, and an enlarged, fatty liver. Which of the following is the basic defect causing this change in the liver?
A. Decreased protein intake leads to decreased lipoproteins
B. Decreased caloric intake leads to hypoalbuminemia
C. Decreased carbohydrate intake leads to hypoglycemia
D. Decreased fluid intake leads to hypernatremia
E. Decreased fat absorption leads to hypovitaminosis
35. A 47-year-old woman with hypermenorrhea develops an irondeficiency anemia requiring iron supplements. Which of the following statements is correct regarding iron digestion and absorption?
A. About 100 mg of iron is absorbed per day
B. Iron is absorbed rapidly from the small intestine
C. Iron is transported in the blood bound to transferrin
D. In general, iron must be oxidized from the ferrous to the ferric state for efficient absorption
E. Iron is transported into enterocytes by a ferroportin transporter on
the apical membrane
36. A middle-aged man presents with congestive heart failure with elevated liver enzymes. His skin has a grayish pigmentation. The levels of liver enzymes are higher than those usually seen in congestive heart failure, suggesting an inflammatory process (hepatitis) with scarring (cirrhosis) of the liver. A liver biopsy discloses a marked increase in iron storage. In humans, molecular iron (Fe) is which of the following?
A. Stored primarily in the spleen
B. Stored in combination with ferritin
C. Excreted in the urine as Fe^{2+}
D. Absorbed in the intestine by albumin
E. Absorbed in the ferric (Fe^{3+}) form
37. A 55-year-old man presents with increasing fatigue, weakness, anorexia, and jaundice over the past several months. Physical examination finds mild ascites and gynecomastia. A liver biopsy reveals regenerative nodules of hepatocytes surrounded

by fibrosis, as seen in the picture below. Which of the following is the source of the excess collagen deposited in these fibrotic bands?
A. Hepatocytes
B. Kupffer cells
C. Ito cells (Hepatic stellate cells (here HSC), also known as perisinusoidal cells or Ito cells (earlier lipocytes or fat-storing cells))
D. Endothelial cells
E. Bile duct epithelial cells
38. A 42-year-old obese woman experiences episodic abdominal pain. She notes that the pain increases after the ingestion of a fatty meal. The action of which of the following hormones is responsible for the postprandial intensification of her symptoms?
A. Cholecystokinin (CCK)
B. Gastrin
C. Pepsin
D. Secretin
E. Somatostatin

39. A young boy presents with failure to thrive. Biochemical analysis of a duodenal aspirate after a meal reveals a deficiency of enteropeptidase (enterokinase). The levels of which the following digestive enzymes would be affected?
A. Amylase
B. Colipase
C. Lactase
D. Pepsin
E. Trypsin
40. A 32-year-old man is on a high-protein, lowcarbohydrate diet because he has heard that this will help him build muscle. Which of the following peptides needs to be released to increase the secretion of pancreatic enzymes into the small intestine so that he can digest these types of meals?
A. Cholecystokinin
B. Gastrin
C. Motilin
D. Secretin
E. Somatostatin
41. A medical student is studying pancreatic function on a computer-simulated patient. The student is specifically trying to understand the insulin secretion pattern in the pancreatic cells. The student is presented with a list of substances that affect insulin secretion. She clicks on a substance and finds that it directly inhibits the patient's

insulin secretion. This response was most likely caused by which of the following substances?
A. Alpha2-adrenergic agonist
B. Beta2-adrenergic agonist
C. Cholecystokinin
D. Glucagon
E. Sugar water
F. Muscarinic agonists
42. A woman goes to a restaurant for a friend's birthday and eats a large meal. After the meal, a certain hormone is stimulated by acid entering her duodenum. This hormone inhibits stomach motility and stimulates bicarbonate secretion from the pancreas. Which of the following hormones is structurally related to the hormone in question?
A. Cholecystokinin
B. Gastrin
C. Glucagon
D. Somatostatin
E. Substance P
43. An 83-year-old woman with constipation is prescribed a high-fiber diet, which leads to an increased production of short-chain fatty acids (SCFAs). SCFA absorption occurs almost exclusively from which of the following segments of the GI tract?
A. Stomach
B. Duodenum
C. Jejunum
D. Ileum
E. Colon
44. A 47-year-old woman with hypermenorrhea develops an irondeficiency anemia requiring iron supplements. Which of the following statements is correct regarding iron digestion and absorption?
A. About 100 mg of iron is absorbed per day
B. Iron is absorbed rapidly from the small intestine
C. Iron is transported in the blood bound to transferrin
D. In general, iron must be oxidized from the ferrous to the ferric state for efficient absorption
E. Iron is transported into enterocytes by a ferroportin transporter on the apical membrane
45. A patient has vomiting and severe watery diarrhea after eating spoiled shellfish. Intravenous fluid and electrolyte replacement was started, and a stool specimen was

taken, which came back positive for Vibrio cholerae. Which of the following statements best describes water and electrolyte absorption in the GI tract?
A. Most water and electrolytes come from ingested fluids
B. The small intestine and colon have similar absorptive capacities
C. Osmotic equilibration of chyme occurs in the stomach
D. The majority of absorption occurs in the jejunum
E. Cholera toxin inhibits sodium-coupled nutrient transport
46. A multiparous mother brings in her second son, an 18-month-old active toddler, because she has noticed blood (sometimes red, one time "currant jelly")in his stools. Although the toddler is trying new foods, she doesn't think the blood is associated with anything in his diet. Your physical exam, including a digital rectal exam, is normal. You order an upper GI barium swallow with small bowel follow through and radiological report describes a 2-inchlong diverticulum, pointing toward the umbilicus, in the ileum, about 2 ft from the ileocecal valve. You explain to the mother that the blood is most likely from which of the following sources?
A. An appendix that must be removed
B. A Meckel's (ileal) diverticulum
C. Active diverticulitis
D. Internal hemorrhoids
E. A duodenal ulcer
47. A 63-year-old woman presents with diarrhea, abdominal pain, and flushing. The urinary excretion of the seratonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA) is elevated. Abdominal CT reveals a tumor in the terminal ileum. Surgical resection of the terminal ileum will most likely result in which of the following?
A. A decrease in absorption of amino acids
B. An increase in the water content of the feces
C. An increase in the concentration of bile acid in the enterohepatic circulation
D. A decrease in the fat content of the feces
E. An increase in the absorption of iron
48. A 50-year-old man comes in for a physical so he can attend a boy scout camp with one of his sons. You suggest a colonoscopy after he returns from camp. He agrees, but wants you to describe the procedure and potential risks and complications. You explain that the goal of a colonoscopy is to look at the entire length of the large intestine from the anus to the small intestine (ileocecal junction), observing polyps or diverticuli with a flexible fiber optic colonoscope inserted through the anus. There is a small risk of perforating the bowel especially when the colon takes a sudden turn or twists on itself at regions where it is intraperitoneal rather than attached to the posterior abdominal wall (retroperitoneal). Which of the following regions of the colon generally poses the

greatest risk for perforation because the bowel takes either a sudden change in direction or is suspended by a mesentery?
A. Rectum, sigmoid colon and descending colon
B. Sigmoid colon, descending colon and splenic flexure
C. Sigmoid colon, splenic flexure and descending colon
D. Sigmoid colon, splenic flexure and hepatic flexure
E. Descending colon, transverse colon and ascending colon
49. A 35-year-old man visits his family medicine physician complaining of bloating, a sense of urgency, cramping abdominal pain, meteorism, diarrhea with excessive flatulence several hours after ingestion of milk or dairy products. He says that he has always enjoyed milk and dairy products without any problems, but now eating them causes him abdominal distress. In this disorder, the area shown by the arrows would have a decrease in which of the following?
A. Specific disaccharidase activity
B. Glucose/galactose transporter activity
C. Passive diffusion of monosaccharides
D. Uptake of triglycerides by endocytosis
E. Active transport of glycerol
50. A 23-year-old woman complains of abdominal cramps and bloating that are relieved by defecation. Subsequent clinical evaluation reveals an increased maximal acid output, decreased serum calcium and iron concentrations, and microcytic anemia. Inflammation in which area of the GI tract best explains these findings?
A. Stomach
B. Duodenum
C. Jejunum
D. Ileum
E. Colon
51. A 39-year-old man presents with bloody diarrhea. Multiple stool examinations fail to reveal any ova or parasites. A barium examination of the patient's colon reveals a characteristic "string sign." A colonoscopy reveals the rectum and sigmoid portions of the colon to be unremarkable. A biopsy from the terminal ileum reveals numerous acute and chronic inflammatory cells within the lamina propria. Worsening of the patient's symptoms results in emergency resection of the distal small intestines. Gross examination of this resected bowel reveals deep, long mucosal fissures extending deep into the muscle wall. Several transmural fistulas are also found. Which of the following is the most likely diagnosis?
A. Ulcerative colitis
B. Lymphocytic colitis
C. Infectious colitis

D. Eosinophilic colitis
E. Crohn’s disease
52. An advertisement promotes energy bars containing fructose as an ideal food to take on extreme mountain-climbing expeditions. Which of the following statements concerning fructose absorption is true?
A. absorption of fructose into an intestinal epithelial cell is by facilitated transport and thus does not require energy
B. metabolism of fructose generates more energy than glucose
C. some fructose is already absorbed in the mouth and hence is the fastest way to get energy
D. the presence of fructose aids in absorption of vitamin A, C, and D
E. the presence of fructose inhibits reabsorption of glucose, which is then more readily available for muscle activity
53. A 14-year-old boy presents with weight loss and diarrhea. His tongue becomes sore and blistery after eating oatmeal or rye bread, which leads to the diagnosis of celiac disease. The boy and his parents are advised to be sensitive to symptoms of tetany and paresthesias, since they can occur as a consequence of malabsorption of which of the following?
A. Calcium
B. Carbohydrates
C. Fat
D. Iron
E. Water
54. Figure 2-8 shows the amounts of water ingested and secreted daily into the GI tract by a healthy individual. Since about 100 mL of water is excreted daily in the stool, which of the following volumes (in milliliter) best reflects the daily absorbed water in the indicated areas x, y, and z of the GI tract?
Saliva 1500 ml/day
Gastric secretions 2000 ml/day
Bile 500 ml/day
Intestinal secretions 1500 ml/day
Pancreatic juices 1500 ml/day
Total – 9000 ml/day
Ingest 2000 ml/day

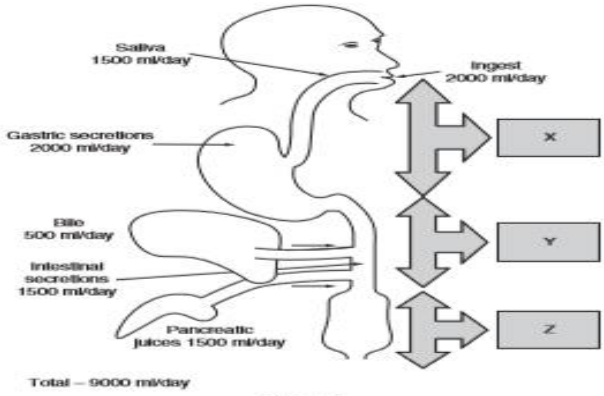

FIG. 2-8

	X	Y	Z
(A)	0	400	8500
(B)	0	8500	400
(C)	450	450	8000
(D)	450	8000	450
(E)	8000	450	450

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55. The parents bring a 5-month-old baby to the emergency room. It is their first child and they are insecure. The boy vomits frequently, seems to be constantly constipated, and has difficulties in defecation. A barium enema study reveals a region in the bowel that is collapsed and an enlarged colon above this area. Abiopsy from the part of the bowel 1 in above the anus is sent to the laboratory and histological analysis reveals the absence of ganglia in this tissue. What is the most likely diagnosis?

A. Cholecystitis

B. Gastroesophageal reflux disease

C. Hirschsprung disease

D. Polymyositis

E. Temporary problem with no treatment required

56. A patient presented with an acute abdomen including fever, marked abdominal distension, acidosis, and leukocytosis. Laparoscopy revealed that large parts of the small intestine were necrotic and as a consequence, the entire ileum of the patient was resected. It is expected that very soon after the surgery the patient will have considerable problems resulting from the malabsorption of which of the following?

A. Iron

B. Bile acids

C. Sodium

D. Vitamin b12

E. Protein

MCQs IFOM

1. A 35-year-old man is examined 2 days after he had abdominal surgery. He has been unable to eat during this time because of nausea. Bowel sounds are found to be hypoactive on physical examination. An abdominal x-ray film shows diffuse distention of the bowel without air-fluid levels, which is consistent with postoperative ileus. Further examination reveals decreased gastrointestinal motility and no slow waves on electric potential and force transducer recordings from gastrointestinal muscles over a period of 60 seconds. Which of the following is the underlying mechanism generating slow waves within the gastrointestinal tract?

A. Alternating contraction of circular and longitudinal muscle
B. Contraction of skeletal muscle
C. Depolarization and repolarization of smooth muscle cells
D. Hyperpolarization of smooth muscle cells
E. Increase in secretions of smooth muscle cells
F. Relaxation of smooth muscle cells

2. A 42-year-old man comes to the physician because of generalized itching. Physical examination reveals excoriations and yellowing of the skin but is otherwise normal. Laboratory tests show:

Total bilirubin: 2.7 mg/dL
Direct bilirubin: 0.4 mg/dL
Alkaline phosphatase (ALP): 305 U/L
Aspartate aminotransferase (AST): 76 U/L
Alanine aminotransferase (ALT): 80 U/L DN
Urine bilirubin: positive

Which of the following is the most likely mechanism underlying this patient's pruritus?

A. Absence of UDP-glucuronosyltransferase
B. Decreased levels of UDP-glucuronosyltransferase
C. Extravascular destruction of RBCs
D. Intrahepatic or extrahepatic interruption of bile flow
E. Intravascular destruction of RBCs

3. A 10-year-old boy is brought to the pediatrician because he has been vomiting every few hours for the past 2 days. He denies any recent travel or contact with sick persons. He has a history of asthma, which is well controlled with 1-2 puffs of salbutamol per day. His temperature is 98'F (36.7*C), blood pressure is 99/65 mm HE, pulse is 88/min, respiratory rate is 10/min, and oxygen saturation is 92% on room air. On examination, he appears lethargic and uncomfortable; however, no wheezing is appreciated on lung examination, and his abdomen is soft and nontender. Which of the sets of laboratory values shown in the tablewould most likely be found in the patient

Choice	pH	pCO_2	HCO^-_3

A	<7.4	Low	Low
B	<7.4	High	High
C	>7.4	Low	Low
D	>7.4	Low	High
E	>7.4	High	high

4. In a genetically modified mouse in which an existing gene has been replaced or disrupted with insertion of an artificial piece of DNA, researchers identified an inability to digest most macromolecules after finding excess protein and complex lipids in its stool. The mouse was found to be missing a protein in the cells lining the duodenum. The gene for which of the following enzymes is likely deficient in this mouse?

A. Amylase

B. Chymotrypsinogen

C. Enterokinase (enteropeptidase)

D. Lipase

E. Pepsin

5. A 3-week-old boy is brought to the emergency department by his parents after a 1-week history of nonbilious vomiting. His parents report that the child spits up after meals much more frequently than his older brother did at this age and that the vomiting sometimes seems forceful.

The section of the gastrointestinal tract affected in this condition typically playsa role in regulating which of the following parts of digestion?

A. Gastric acid production

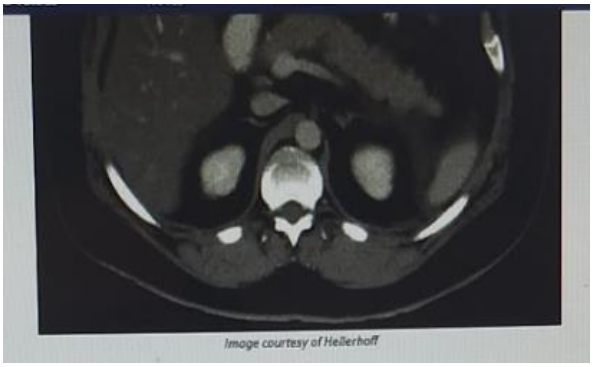
B. Gastric emptying

C. Prevention of food backflow into the esophagus

D. Propulsion of food into the stomach

E. Swallowing

6. A 44-year-old woman (gravida 2, para 2) come to the emergency department because of epigastric pain radiating into her back along with nausea and vomiting. Symptoms began 12 hours ago. Past medical history is significant for two normal spontaneous vaginal deliveries as well as recurrent episodes of right upper quadrant pain after eating. She has no medical problems and her only medication is combined oral contraceptive pills. Her temperature is 38°C (100.4°F), blood pressure is 90/60 mm Hg, pulse is 120/min, and respiratory rate is 28/min; oxygen saturation is 98% on room air. Her height is 174 cm (5' 8.5"), weight is 92 kg (202.8 Ib), and BMI is 30. On examination she appears ill and uncomfortable. Mucous membranes are dry and she has severe epigastric tendemess with voluntary guarding but no rebound. Lipase is 48 U/L, ALT is 130o U/L, AST is 95 UL, and beta-hCG is undetectable. A CT scan is shown.



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Formation of which of the following enzymes is the greatest contribution to this patient's symptoms

A. Amylase
B. Elastase
C. Enterokinase
D. Pepsinogen
E. Lactase
F. Trypsin

7. A 14-month-old boy is brought to the clinic by his parents. Earlier in the day after eating normally, he began to vomit intermittently. The parents report four to five previous episodes of vomiting, each of which was preceded by inconsolable crying and the child bringing his knees up toward his chest. Recently, they have noticed dark red stool. The mother's pregnancy and delivery were uncomplicated; the patient was previously healthy and has met developmental milestones. He has a temperature of 37.2'C (99.0° F), a pulse of 120 and a blood pressure of 110/70 mm Hg. On physical examination, a small amount of dark red blood is found in the rectal vault. He cries on palpation of the right lower quadrant of the abdomen. A typical development of which of the following structures is most likely responsible for his symptoms?

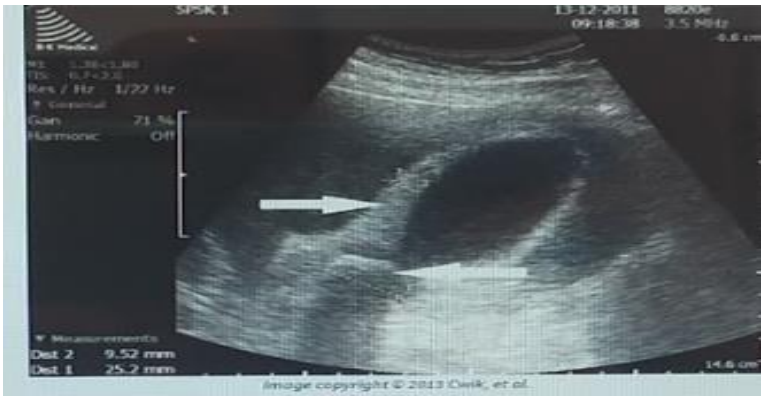
A. Anterior abdominal wall
B. Cecum
C. Foregut
D. Ventral and dorsal pancreatic buds
E. Vitelline duct

8. A 22-year-old woman presents with dyspnea on exertion (DOE), weakness, and fatigue. On physical examination, she has hair loss, spoon-shaped fingernails, and pale mucous membranes. She has a history of heavy menstrual bleeding. Laboratory tests reveal:

RBCs: 2 million/mm
Hb:6 g/dl
Mean corpuscular volume: 65 fL (normal: 80-100 fL)
Mean corpuscular hemoglobin: 24.0 pg (normal: 25.4-34.6 pg)
Ferritin:6 ng/mL (normal: 12-150 ng/ml)

Red cell distribution width: 17% (normal: 11.5-14.5%)
Malabsorption in what part of the gastrointestinal tract will produce this patient's laboratory test results?
A. Duodenum
B. Gastric fund us
C. Ileum
D. Jejunum
E. Sigmoid colon
9. A 43-years-old overweight woman presents to her doctor's office because of right upper quadrant abdominal pain. She has experienced similar episodes of this type of pain in the past and admits that it is worse after meals. Increased secretion of which of the following is responsible for this patient's postprandial pain?
A. Cholecystokinin
B. Gastrin
C. Pepsin
D. Somatostatin
E. Vasoactive intestinal peptide
10. A 27-year-old man with a history of Crohn disease comes to the emergency department because of abdominal pain and nausea. He localizes the pain to his right upper quadrant. He has had nausea and vomiting for the past 12 hours since this pain started. He states that he has had similar self -resolving episodes during the past 3 months. He endorses flatus and non-bloody regular stools. His Crohn disease was previously well controlled on infliximab, but because he recently lost health insurance, his last infusion was more than 3 months ago. On evaluation today, his temperature is 38 c (100.4" F), blood pressure is 106/70 mm HE. pulse is 110/min, and respiratory rate is 22/min. His abdomen is soft and tender in the right upper quadrant. No organomegaly is appreciated. There is no guarding or rebound. Results of laboratory studies are as follows:
WBC: 14.1x 10^9/L
RBC:3.81x10^12/L
HGB: 12.8 g/L
HCT: 399%
MCV: 91 fL
MCHC:35.3%
RDW: 11.3
Platelet: 450 x 10 9/L
Sodium: 140 mEq/L
Potassium: 3.9 mEq/L
Chloride 101 mEq/L

Bicarbonate: 24 mEq/L
BUN: 90 mg/dL
Creatinine: 2.3 mg/dL
Glucose: 18 mg/dL
Amylase: 20 U/L
Lipase: 23 U/L



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Which of the following is most likely responsible for this patient's current condition?
A. Ascending infection of the biliary tree
B. Hemolysis resulting in increased bilirubin formation
C. Impaired reabsorption of bile acids
D. Passage between the small bowel and the gallbladder
E. Perforation of bowel due to transmural inflammation
F. Scarring of the small bowel causing obstruction

11. A 34-year-old man comes to his primary care physician for his yearly well-patient physical examination. He reports that he "may have developed some reflux lately." He also states that when he eats certain foods, or has a meal too close to bedtime, he experiences a burning sensation below his sternum and a sour taste in his mouth. His medical history is significant for obesity, hypertension, and hyperlipidemia. He takes lisinopril and simvastatin and reports taking an "occasional" over-the-counter ranitidine for his gastrointestinal symptoms,typically with near complete resolution of the symptoms. His physician advises him to continue the use of this medication, as needed. He is also encouraged to lose some weight with diet and exercise. The patient is instructed to return if ranitidine is no longer sufficient to control his symptoms.

Which of the following describes the mechanism of action of the medication this patient is taking for his gastroesophageal reflux disease (GERD) ?
A. It binds to and activates the prostaglandin receptor.
B. It binds to and inhibits a G_s coupled receptor.
C. It binds to and inhibits activation of the somatostatin receptor.
D. It binds to and inhibits the H+/K+ ATPase of parietal cells.
E. It binds to the M receptor.

12. A 25-year old man with refractony schizophrenia begins taking clozapine. At a 1-month follow up visit, his serum clozapine is at a therapeutic level, but he complains of bilateral pain in his cheeks immediately anterior to his ears, as well as pain on swallowing. On further questioning, he also says he has produced more saliva lately than usual. On examination, he is found to be afebrile. Compared with normal saliva, which of the following would not increase in concentration in this patient's saliva?
A. Amylase
B. Bicarbonate
C. Chloride
D. Potassium
E. Sodium
13. A 53-year old man comes to the community health clinic with a report of fatigue and a feeling of being "unwell." His temperature is 37c (98.6°F), pulse is 96/min, respirations are 20/min, and blood pressure is 128/74 mm Hg. His lungs are clear to auscultation bilaterally. Although his abdomen is distended, the remainder of his body habitus appears cachectic. Examination of his legs reveals pitting edema of 2+. The patient's chart reveals that he has recently been involved in several motor vehicle colisions and cited for driving under the influence (DUI).
Laboratory test results include:
Leukocyte count: 8000/mm
Hemoglobin: 11 g/dL
Hematocrit: 359%
Aspartate aminotransferase: 120 U/L
Alanine aminotransferase: 50 U/L
Alkaline phosphatase: 80 U/L
What is the major physiologic mechanism for this patien’s findings:
A. Constriction of arterioles
B. Decrease production of serum proteins
C.Increasd permeability of capillaries
D.Increased permeability of glomeruli
E. Lymphatic blockage
14. A 35-year-old woman with a history of rheumatoid arthritis comes to see her primary care physician fora medication review. The doctor notices that she is at risk for peptic ulcer disease (PUD) and decides to prescribe her a medication that is likely to help prevent it. This medication, however, is known to be contraindicated in pregnancy. Therefore before writing the prescription, the doctor confirms that the patient is not pregnant and that she understands the risks were she to become pregnant while taking the medication. What is the mechanism of action of the drug the doctor most likely prescribed?

A. Acts as a prostaglandin agonist
B. Acts as a prostaglandin antagonist
C. Acts as a proton pump inhibitor
D. Acts as a somatostatin analog
E. Acts as an H2 receptor antagonist

15. A 40-year-old man comes to the emergency department with right upper quadrant pain and fever. During the abdominal examination, the patient is instructed to breathe out while the examiner applies gentle pressure on his right upper quadrant below the costal margin at the midclavicular line. The patient is then instructed to breathe in. At this point, he winces and abruptly stops his inhalation.

What is the next step in treating this patient?

A. Abdominal CT scan
B. Emergent cholecystectomy
C. Intraoperative cholangiogram
D. Right upper quadrant (RUQ) ultrasound
E. Supportive management with IV fluids

16. An 8-yearold boy is brought to the emergency department by his parents after 18 hours of severe vomiting, which began after he ate reheated leftover Chinese takeout. Vital signs are as follows:

Temp: 98.4°F (36.9°C)
Blood pressure: 100/55 mm Hg
Pulse: 125/min
Respiratory rate: 8/min

Findings on physical examination are notable for skin tenting and mild abdominal discomfort. Arterial blood gas analysis reveals a pH of 7.48, HCO2 level of 35 mEq/L, partial carbon dioxide pressure (Pco_2) of 48 mm Hg, and partial pressure of oxygen (P_{O2}) of 82 mm Hg.

What is the type of acid-base disturbance occurring in this patient:

A. Metabolic alkalosis and metabolic acidosis
B. Metabolic alkalosis and respiratory acidosis
C. Metabolic alkalosis and respiratory alkalosis
D. Metabolic alkalosis with respiratory compensation
E. Respiratory alkalosis
F. Respiratory alkalosis with metabolic compensation

17. An overweight 37-year-old woman presents to her physician because of severe right upper quadrant pain that began after she ate dinner. Her temperature is 100.5°F (38.1"C), blood pressure is 135/85 mm Hg, and pulse is 99. Urine B-human chorionic gonadotropin is negative. Laboratory tests reveal:

Serum total bilirubin level: 0.8 mg/dL

Serum aspartate aminotransferase level: 18 U/L
Serum alanine aminotransferase level: 20 U/L
Leukocyte count: 15,000 cells/uL
Ultrasonography of the right upper quadrant is performed.
What is the ultrasound image likely to show?
A. Adhesions along the hepatic flexure
B. Engorgement of the splenic vessels
C. Formation of a fistula between the gallbladder and small intestine
D. Obstructing mass at the head of the pancreas
E. Obstruction of the common bile duct by a gallstone
F. Wall thickening of the gallbladder
18. A 65-year-old woman presents to her primary care physician reporting symptoms of general muscle weakness, lightheadedness, recent weight loss of 10 Ib (4.5 kg), and diarrhea. She reports a sensation of "pins and needles" in her feet. She has decreased sensation to pinprick in her toes bilaterally, as well as a positive Romberg sign. She has a history of hypothyroidism.
This patient is most likely deficient in a substance produced by which of the following types of cells?
A. Chief cells
B. G cells
C. I cells
D. Mucus cells
E. Parietal cells
19. A 22-year-old college student presents to the emergency department with sudden-onset severe epigastric pain that radiates to the back. He has a history of heavy alcohol abuse, and lab tests show a markedly elevated amylase level. The organ involved in this patient's pathology plays a key role in normal gastrointestinal physiology. Under normal physiologic conditions, the organ is stimulated by a hormone that increases the secretion of bicarbonate.
Which of the following will increase release of this hormone?
A. Acid and fatty acids in the duodenal lumen
B. Fasting state
C. Increased stomach distention
D. The presence of fatty acids, amino acids, and oral glucose in the duodenum and jejunum
E.Vagal stimulation
20. A 45-year-old woman presents to her primary care physician with a 2 day history of intermittent abdominal pain, nausea, gas, and vomiting. She reports that her symptoms became worse after eating a hamburger and french fries at a barbecue

yesterday afternoon. She has a 15- pack-year history of cigarette smoking and typical alcohol consumption of two drinks every other weekend. Her vital signs include:
Pulse: 82/min
Blood pressure: 136/84 mm Hg
Respiratory rate: 16/min
The patient is obese. On examination, her heart has a regular rate and rhythm. Her lungs are clear to auscultation bilaterally. Her abdomen is soft but tender to palpation in the right upper quadrant. She reports a family history of hepatocellular carcinoma. Considering the gastrointestinal hormone that is triggering her abdominal pain, which of the following is another of its actions?
A. Decreased insulin release
B. Increased gastric acid secretion
C. Increased gastrointestinal motility
D. Increased insulin release
E. Increased pancreatic enzyme secretion

ANSWERS MCQs STEP 1

1. C
2. B
3. B
4. A
5. A
6. C
7. B
8. B
9. A
10. D
11. A
12. The correct answer is B. The fasting serum gastrin is normal in patients with duodenal ulcer (DU); however, the gastrin response to a meal (choice C) is increased. The increase in serum gastrin following a meal occurs, in part, because acid suppresses gastrin release less effectively in DU patients compared with controls. DU patients have an increase in parietal cell mass (choice E), which may be caused by the trophic (growth promoting) effects of gastrin. Patients with DU have an increased basal acid output (choice A) that totally disappears following eradication of the H. pylori infection. However, the increase in maximal acid output (choice D), which occurs in response to IV gastrin, can remain following eradication of the H. pylori infection and is likely to result from the increased parietal cell mass. The secretion of pepsin (choice F) is usually doubled in DU patients.
13. The correct answer is B. Gastrinomas are gastrin-secreting tumors usually present in the pancreas. Patients with gastrinoma have high serum gastrin levels, which lead to hypersecretion of gastric acid and consequent duodenal and jejunal ulcers. Injection of secretin is the most specific and easiest test for gastrinoma. Secretin inhibits antral release of gastrin (choice A), but it stimulates release of gastrin from gastrin tumors (gastrinoma) in almost all patients. A doubling of serum gastrin 5 to 10 minutes after administration of secretin (1 U/kg), coupled with acid hypersecretion and increased basal serum gastrin, strongly indicates the presence of gastrinoma. Secretin can inhibit gastric emptying (choice C), inhibit gastric secretion (choice D), and stimulate pancreatic HCO_3^- secretion (choice E), but these effects are not diagnostic for gastrinoma.
14. The correct answer is A. Achalasia is a disorder of esophageal motility that affects the lower esophageal sphincter (LES) and lower two-thirds of the esophageal body. The LES remains tonically contracted and does not relax as food moves down the esophagus. Relaxation is via the release of vasoactive intestinal peptide (VIP) from nerve endings. Therefore, food cannot move easily from the esophagus into the

stomach. The distal esophagus often becomes greatly dilated. Patients with achalasia most commonly complain of dysphagia (difficulty swallowing), chest pain, and regurgitation. During swallowing, the bolus of food is propelled through the pharynx (choice D) by peristaltic contractions. These contractions, along with relaxation of the upper esophageal sphincter (choice E), propel the bolus of food into the esophagus. Relaxation of the upper esophageal sphincter occurs normally in patients with achalasia. The upper, middle, and lower esophagus (choices B, C, and F) propel the bolus toward the stomach by coordinated contractions of the muscle layers.

15. The correct answer is E. The parietal cells of the stomach produce intrinsic factor, a glycoprotein that binds vitamin B12 in the lumen of the stomach and facilitates its absorption in the terminal ileum. Patients without a stomach and those with pernicious anemia (autoimmune destruction of parietal cells) require B12 replacement therapy. Recall that B12 deficiency will lead to megaloblastic anemia and the USMLE-favorite picture of a blood smear with hypersegmented neutrophils. Note that parietal cells also synthesize and secrete HCl. Chief cells (choice A) are responsible for secreting pepsinogen, the precursor to pepsin. G cells (choice B) secrete gastrin, which stimulates secretion of acid by the parietal cells found in the body and fundus of the stomach. Zollinger-Ellison syndrome is caused by a pancreatic or duodenal tumor that secretes gastrin (a gastrinoma). It is characterized by the development of severe peptic ulcer disease. Goblet cells (choice C) are part of the mucosa of the small intestine, not the stomach. They produce glycoproteins (mucins) that protect and lubricate the lining of the intestine. Mucous neck cells (choice D) secrete mucus and are located in the necks of the gastric glands.

16. The correct answer is A. This woman has a risk profile (female, fat, forties) and symptomatology consistent with gallstones (cholelithiasis). As would be expected, contraction of the gallbladder following a fatty meal often exacerbates the pain caused by gallstones. Cholecystokinin (CCK) is the hormone responsible for stimulation of gallbladder contraction; the release of CCK is stimulated by dietary fat. It is produced in I cells of the duodenum and jejunum. In addition to gallbladder contraction, CCK also stimulates pancreatic enzyme secretion and decreases the rate of gastric emptying. Gastrin (choice B) is produced by the G cells of the antrum and duodenum. Gastrin stimulates the secretion of HCl from the parietal cells and pepsinogen from the chief cells of the stomach. Gastrin secretion is stimulated by gastric distention, digestive products (e.g., amino acids), and vagal discharge. Pepsin (choice C) is a protease produced by the chief cells of the stomach (as pepsinogen). It is involved in the digestion of proteins. Pepsinogen release is stimulated by vagal stimulation, gastrin, local acid production, secretin, CCK, and histamine. Secretin (choice D) is produced by the S cells of the duodenum. It is secreted primarily in response to acidification of the duodenal mucosa. Secretin stimulates the secretion of bicarbonate-containing fluid

from the pancreas and biliary ducts. This neutralization allows pancreatic enzymes to function. Secretin also inhibits gastric acid production and gastric emptying. Somatostatin (choice E) is produced by the D cells of the pancreatic islets and in the gastric and intestinal mucosa. Somatostatin is an inhibitory hormone; it inhibits most gastrointestinal hormones, gallbladder contraction, gastric acid and pepsinogen secretion, pancreatic and small intestinal fluid secretion, and both glucagon and insulin release.

17. The correct is D. The strongest stimulator for the release of secretin from cells in the upper small-intestinal mucosa is the contact with acidic chyme. Increased serum secretin levels stimulate water and alkali secretions from the pancreas and the hepatic ducts and inhibit gastrin release. The release of pancreatic enzymes is stimulated by cholecystokinin (choice A). The most potent stimulators for the release of cholecystokinin are not acid, but digestion products of fat and protein. Strong stimulators for gastrin secretion (choice B) are vagus nerve excitation, distention of the stomach, and protein digestion products. Gastrin then stimulates acid secretion and mucosal growth. The major effect of glucagon (choice C) is to increase blood glucose levels. Hence, it is secreted in response to hypoglycemia and protein digestion products, which are then used for gluconeogenesis. VIP (choice E) indeed stimulates intestinal and pancreatic secretion. However, it acts as neurotransmitter in the enteric nervous system and is mainly released by mechanical and neuronal stimulation.

18. The correct is A. The major control mechanism for gastric emptying involves duodenal gastric feedback, hormonal as well as neural. The major hormone involved in the inhibition of gastric emptying is cholecystokinin (CCK), which is released by fat and protein digestion products. Gastrin (choice B) stimulates hydrochloric acid secretion and exerts a trophic effect on the gastric and intestinal mucosa. When the gastrin concentration is elevated to supraphysiologic levels, various other actions can be demonstrated including inhibition of gastric emptying. However, the physiologic importance of these actions is uncertain. Glucose-dependent insulinotropic peptide (GIP, choice C) is released from the intestinal mucosa by acid, fat, or hyperosmolarity and acts to some extent by inhibiting stomach functions including gastric motility. Although this function gave GIPits initial name (gastric inhibitory peptide), GIP's action as an enterogastrone is now controversial. The major physiologic action of GIP is to cause insulin release. Motilin (choice D) stimulates gastric motor activity, especially during the interdigestive phase, when it regulates contractions that serve to empty the GI residual contents. Pancreatic polypeptide (choice E) is a negative feedback regulator for pancreatic enzymes and bicarbonate secretion. It is considered to be a candidate hormone since it satisfies some, but not all of the criteria for hormonal status.

19. The correct is D. Peptic ulcers refer to areas of the stomach or duodenal lining which became eroded by stomach acid. Stomach acid is produced by parietal cells which are stimulated by gastrin. Since gastrin-secreting G cells are primarily found in the gastric glands of the distal stomach (gastric antrum), the surgically removed stomach portion, the patient's prevalence for peptic ulcer disease is lower after the surgery, and not unchanged as stated in choice E. However, the surgery is a dramatic event and increases the risk for many GI problems, including symptoms resulting from nutritional deficiencies. Hence, the surgery is only used for morbidly obese people (the patient's body mass index is above 50), who had no success with diet and medication. Inflammation potentially triggered by the surgical staples (choice A) might trigger prostaglandin release which has a protective function of the stomach lining. Although secretin (choice B) is known to suppress gastric acid release by inhibiting gastrin release, the lower number of G cells after surgery does not make this a good choice. Chief cells (choice C) are primarily present in the proximal stomach, the portion that remains after surgery.

20. The correct is D. The receptive relaxation reflex is a feature of the orad stomach, composed of the fundus and upper stomach body. Without food, the orad stomach shows low frequency, sustained contractions that are responsible for generating a basal pressure within the stomach. When food enters the stomach, a reflex is initiated, which allows gastric accommodation of large increases in volume with only small increases in intragastric pressure. The tonic contractions of the orad stomach also contribute to some extent to gastric emptying (choice B), since they generate a pressure gradient from the stomach to the intestine. However, neural and hormonal components play a more important role in regulating gastric emptying, which makes this not the best choice. Since the lower stomach is not affected by the surgery, characteristic motility patterns of the distal stomach remain (choice A). Features of the distal stomach include strong peristaltic waves of contractions, which cause the mixing of the chyme with digestive secretions (choice C), the grinding of the particles to a small size, and the propulsion through the gastroduodenal junction (choice E). All these motility patterns would still be a feature of the remaining stomach

21. The answer is B. Withdrawal from long-term use of proton pump inhibitors prescribed for peptic ulcer disease may be associated with rebound gastric hypersecretion. Pharmacological suppression of gastric acid secretion can occur when the administered drug binds to a receptor present on the parietal cell or when it antagonizes the hydrogen-potassium-ATPase pump responsible for the active secretion of hydrogen ion into the gastric lumen. At the present time, the most effective antisecretory compounds work by blocking the histamine type-2 (H2) receptor present on the parietal cell or by inhibition of the hydrogen pumps. The latter are the most potent and long-acting, thus increasing the probability of increasing serum gastrin.

22. E

23. The answer is C. Obstruction of any portion of the biliary tree will produce symptoms of gallbladder obstruction. If the common hepatic duct (answer b) or bile duct (answer a) is occluded by stone or tumor, biliary stasis with accompanying jaundice occurs. In addition, blockage of the duodenal papilla (of Vater), distal to the juncture of the bile duct with the pancreatic duct (answer e),can lead to complicating pancreatitis. If only the cystic duct is obstructed, jaundice will not occur because bile may flow freely from the liver to the duodenum. Bile duct obstruction also may arise as a result of pressure exerted on the duct by an external mass, such as a tumor in the head of the pancreas. Answserdis not anatomically correct.

24. C

25. B

26. D

27. The correct answer is A. Gastric inhibitory peptide (GIP) is produced in the duodenal and jejunal mucosa by K cells and is released in response to intraluminal glucose and fatty acids. GIP is sometimes called "glucose-dependent insulinotropic" peptide because it stimulates pancreatic insulin secretion in the presence of hyperglycemia. Note that although GIP release would be stimulated, the hormone would not have a pronounced effect in this type 1 diabetic, whose pancreatic islet cells do not produce adequate amounts of insulin.

Gastrin (choice B) is synthesized and stored primarily in the G cells of the stomach and TG cells of the stomach and small intestine. The stimuli for gastrin secretion include increased vagal discharge, digestive products, calcium salts, and gastric distention. Gastrin stimulates HCl secretion by parietal cells, histamine release from enterochromaffin cells, pepsinogen secretion by chief cells, gastric blood flow, and contraction of gastric circular smooth muscle. It has a trophic effect on gastric and small-intestinal mucosa and the pancreas, increases lower esophageal sphincter (LES) tone, and is a weak stimulus for the secretion of pancreatic enzymes and bicarbonate.

Motilin (choice C) is produced in the M and enterochromaffin cells of the duodenum and jejunum. Secretion occurs during fasting. Motilin acts to regulate the migrating myoelectric complex (MMC).

Secretin (choice D) is synthesized and stored in the S cells of the mucosa of the upper intestine. Acidification of the duodenal mucosa and the presence of fat and protein degradation products in the duodenum stimulate its secretion. The main role of secretin is to stimulate bicarbonate secretion from the pancreas and liver.

Somatostatin (choice E) is synthesized and stored in the D cells of the pancreatic islets, in the gastric antrum, and throughout the intestine. It is also present in the hypothalamus. It inhibits the release of gastrin, cholecystokinin (CCK), and most other gastrointestinal hormones. In brief, it "shuts off" the gut. Somatostatin inhibits the

release of glucagon by pancreatic alpha cells, as well as the release of insulin by the pancreatic beta cells (of the islets of Langerhans).

Substance P (choice F) is synthesized in the enterochromaffin cells of the upper small intestine and colon and also in the CNS. The stimulus for release of the substance occurs through vagal efferent pathways. Substance P stimulates salivary flow and gastrointestinal motility and functions in the transmission of pain impulses in the nervous system.

Vasoactive intestinal polypeptide (VIP; choice G) is produced by cells in the parasympathetic ganglia of sphincters, the gallbladder, and the small intestine. Stimuli for its release include vagal stimulation and intestinal distention. VIP promotes water and electrolyte secretion by the jejunum, ileum, and colon (via cAMP), relaxation of the smooth muscle and sphincters, stimulation of pancreatic bicarbonate secretion, and intestinal dilatation. It inhibits the secretion of gastric acid and gastrin.

28. The correct answer is D. Ascites often occurs in patients with cirrhosis and other forms of severe liver disease and is usually noticed by the patient because of abdominal swelling. Shortness of breath may occur because the diaphragm is elevated when the accumulation of fluid becomes more pronounced. A number of factors contribute to accumulation of fluid in the abdominal cavity. Portal hypertension plays an important role in the production of ascites by raising capillary hydrostatic pressure within the splanchnic bed. Elevated serum levels of epinephrine and norepinephrine (compare with choice A), resulting from increased central sympathetic outflow, are found in patients with cirrhosis and ascites. The increased sympathetic output leads to decreased natriuresis (compare with choice E) by activation of the renin-angiotensin system and diminished sensitivity to atrial natriuretic peptide Hypoalbuminemia (compare with choice F) and reduced plasma oncotic pressure (compare with choice G) promote extravasation of fluid into the peritoneal cavity, thereby contributing to the development of ascites. Interstitial fluid often weeps freely from the surface of the cirrhotic liver because of distortion and obstruction of hepatic lymphatics (compare with choice C). This interstitial fluid has a high protein concentration because the endothelial lining of the hepatic sinusoids is discontinuous. The entry of protein-rich interstitial fluid into the peritoneal cavity may account for the high protein concentration present in the ascitic fluid of some patients.

29. The correct is D. Rupture of large numbers of red blood cells can result in jaundice in the absence of any liver disease. The capacity of the liver to clear released heme metabolites such as bilirubin is temporarily exceeded. Since the liver will not perform its normal function to conjugate bilirubin before excretion in bile and urine, unconjugated bilirubin backs up in serum. This is the reason for the increase in total bilirubin, while conjugated bilirubin, also called direct bilirubin, is not affected. Direct bilirubin would be elevated with most defects of liver cells (choice A)and with

obstruction of bile flow by gallstones (choice C) or by a tumor (choice E). All these would most likely also affect bile formation and consequently absorption of dietary fat and fat-soluble vitamins, with the consequence of developing oily, fatty stool. Kupffer cells (choice B) are macrophages within the liver and don't play a role in the production of bilirubin.

30. The correct is A. The patient clearly has an increase in her state of insulin resistance. Given the magnitude of her increased insulin requirements, she most likely developed a high titer of antiinsulin antibodies that are preventing the injected insulin from lowering blood glucose effectively. Agood choice of lifestyle, including an improved diet (choice B), an improved exercise program (choice C), or weight loss (choice E) each are shown to beneficially affect her insulin requirements. Progression of macrovascular disease (choice D) is largely irrelevant to her insulin requirements, except to the extent that it might decrease her ability to exercise.

31. The correct is A. The concentration of exogenous insulin is higher at the site of injection in the periphery, compared to its concentration in the liver. On the other hand, endogenous insulin is higher concentrated in the liver than in the periphery. Insulin is normally secreted by the endocrine pancreas into the portal venous drainage. Thus, it passes through the liver before being seen by the periphery. Acertain fraction of insulin is extracted by the liver; so that the concentration of insulin seen by the liver is normally higher than that seen by the periphery. This discrepancy between exogenous and endogenous insulin might contribute to the problems experienced by diabetics such as hypertension and cardiovascular disease. Injected insulin is missing C-peptide (choice B), while endogenous insulin is cosecreted with C-peptide, the physiologic functions of which remain unknown. Injected insulin is biologically active and not in the proinsulin form (choice E). Exogenous insulin generally used today in the United States is recombinant human insulin, not from animal sources (choice D). The problem of developing anti-insulin antibodies is now rarer since the injected insulin is not from animals. Insulin resistance (choice C) is generally due to receptor downregulation or desensitization, or anti-insulin antibodies. Tissues become equally resistant to both the body's own (endogenous) and administered (exogenous) insulin.

32. The correct is B. Glucuronyl transferase is the enzyme that conjugates bilirubin in the liver, after which it is excreted in bile or urine. Ahereditary defect in glucuronyl transferase concentration, or activity, is called Gilbert syndrome. It may lead to mild jaundice and general discomfort with typical onset in childhood or early adulthood. Alcohol poisoning (choice A) leads to liver damage, and an elevation of conjugated bilirubin. Abnormalities of liver enzyme tests would be expected. Lactate dehydrogenase (choice C) catalyzes the conversion of lactate to pyruvate as part of cellular energy production. Since many cells including red blood cells are rich in LDH, increased serum LDH levels could point toward excessive hemolysis, but would not be

a cause for it. Although hemolysis that exceeds the capacity of the liver to clear bilirubin from serum (choice D) would lead to increased unconjugated bilirubin, it is not the best choice due to the woman's normal hemoglobin (12–16 g/dL for females). Obstruction of bile flow (choice E) leads to backup of largely conjugated bilirubin in the blood stream.

33. The answer is E. Increased serum lipids (hyperlipidemia) may be a primary genetic defect or may be secondary to another disorder, such as diabetes mellitus, alcoholism, the nephrotic syndrome, or hypothyroidism. Secondary hypertriglyceridemia in patients with diabetes mellitus usually occurs secondary to increased blood levels of VLDL. The reason for this is that with decreased levels of insulin with diabetes mellitus there is increased mobilization of free fatty acids from adipose tissue (increased lipolysis). This increases delivery of free fatty acids to the liver, which increases production and secretion of VLDL by the liver. This is a type IV hyperlipidemia pattern. Ethanol can also produce a type IV pattern due to increased VLDL. This is because ethanol also increases lipolysis of adipose tissue, which increases delivery of free fatty acids to the liver. Ethanol also increases the esterification of fatty acid to triglycerides in the liver and inhibits the release of lipoproteins from the liver.

34. The answer is A. Protein-energy malnutrition (PEM) in underdeveloped countries leads to a spectrum of symptoms from kwashiorkor at one end to marasmus at the other. Marasmus, caused by a lack of caloric intake (i.e., starvation), leads to generalized wasting, stunted growth, atrophy of muscles, and loss of subcutaneous fat. There is no edema or hepatic enlargement. These children are alert, not apathetic, and are ravenous. In contrast, children with kwashiorkor, which is characterized by a lack of protein despite adequate caloric intake, have peripheral edema, a "moon" face, and an enlarged, fatty liver. The peripheral edema is caused by decreased albumin and sodium retention, while the fatty liver is caused by decreased synthesis of the lipoproteins necessary for the normal mobilization of lipids from liver cells. Additionally, these children have "flaky paint" areas of skin and abnormal pigmented streaks in their hair ("flag sign"). In children with marasmus, the skin is inelastic due to loss of subcutaneous fat. In either severe kwashiorkor or marasmus, thymic atrophy may result in the reduction in number and function of circulating T cells. B cell function (i.e., immunoglobulin production) is also depressed, so that these children are highly vulnerable to infections.

35. The answer is C. Iron is transported in the blood bound to the bglobulin, transferrin. Excess iron is stored in all cells, but especially in hepatocytes where it combines with apoferritin. The stored form is called ferritin. The rate of iron absorption is extremely slow, with a maximum of only a few milligrams per day. Iron is absorbed primarily in the ferrous form. Therefore, ferrous iron compounds, rather than ferric compounds, are effective in treating iron deficiency.

36. The answer is B. Ferrous iron (Fe2+) is the form absorbed in the intestine by ferritin, transported in plasma by transferrin, and stored in the liver in combination with ferritin or as hemosiderin. There is no known excretory pathway for iron, either in the ferric or ferrous form. For this reason, excessive iron uptake over a period of many years may cause hemochromatosis (235200), the likely diagnosis for this man. This is a condition of extensive hemosiderin deposition in the liver, myocardium, pancreas, and adrenals. The resulting symptoms include liver cirrhosis, congestive heart failure, diabetes mellitus, and changes in skin pigmentation.

37. The answer is C. Cirrhosis refers to fibrosis of the liver that involves both central veins and portal triads. This fibrosis is the result of liver cell necrosis and regenerative hepatic nodules. These nodules consist of hyperplastic hepatocytes with enlarged, atypical nuclei, irregular hepatic plates, and distorted vasculature. There is distortion of the normal lobular architecture. These changes diffusely involve the entire liver; they are not focal. It is thought that the fibrosis is the result of fibril-forming collagens that are released by Ito cells, which are fat-containing lipocytes found within the space of Disse of the liver. They normally participate in the metabolism and storage of vitamin A, but they can secrete collagen in the fibrotic (cirrhotic) liver. Normally types I and III collagens (interstitial types) are found in the portal areas and occasionally in the space of Disse or around central veins. In cirrhosis, types I and III collagens are deposited throughout the hepatic lobule. These Ito cells are initiated by unknown factors and then are further stimulated by such factors as plateletderived growth factor and transforming growth factor-beta to secrete collagen. In contrast to Ito cells, endothelial cells normally line the sinusoids and demarcate the extrasinusoidal space of Disse. Attached to the endothelial cells are the phagocytic Kupffer cells, which are part of the monocyte-phagocyte system. Bile ducts, and thus the epithelial cells that form them, are found in the portal triads of the liver.

38. The correct answer is A. This woman has a risk profile (female, fat, forties) and symptomatology consistent with gallstones (cholelithiasis). As would be expected, contraction of the gallbladder following a fatty meal often exacerbates the pain caused by gallstones. Cholecystokinin (CCK) is the hormone responsible for stimulation of gallbladder contraction; the release of CCK is stimulated by dietary fat. It is produced in I cells of the duodenum and jejunum. In addition to gallbladder contraction, CCK also stimulates pancreatic enzyme secretion and decreases the rate of gastric emptying.

Gastrin (choice B) is produced by the G cells of the antrum and duodenum. Gastrin stimulates the secretion of HCl from the parietal cells and pepsinogen from the chief cells of the stomach. Gastrin secretion is stimulated by gastric distention, digestive products (e.g., amino acids), and vagal discharge.

Pepsin (choice C) is a protease produced by the chief cells of the stomach (as pepsinogen). It is involved in the digestion of proteins. Pepsinogen release is stimulated by vagal stimulation, gastrin, local acid production, secretin, CCK, and histamine.
Secretin (choice D) is produced by the S cells of the duodenum. It is secreted primarily in response to acidification of the duodenal mucosa. Secretin stimulates the secretion of bicarbonate-containing fluid from the pancreas and biliary ducts. This neutralization allows pancreatic enzymes to function. Secretin also inhibits gastric acid production and gastric emptying.
Somatostatin (choice E) is produced by the D cells of the pancreatic islets and in the gastric and intestinal mucosa. Somatostatin is an inhibitory hormone; it inhibits most gastrointestinal hormones, gallbladder contraction, gastric acid and pepsinogen secretion, pancreatic and small intestinal fluid secretion, and both glucagon and insulin release.

39. The correct answer is E. Enteropeptidase, formerly called enterokinase, activates trypsinogen by limited proteolytic digestion to give trypsin. Trypsin is itself capable of activating trypsinogen, which produces a positive feedback effect. Trypsin also activates chymotrypsinogen (and several other proteolytic enzymes), so deficiency of enteropeptidase results in a severe deficiency of enzymes that digest protein.
Amylase (choice A) aids in the breakdown of starches to oligosaccharides, maltose, and maltotriose.
Colipase (choice B), along with other lipases, functions to digest fats.
Lactase (choice C) is a brush-border disaccharidase that hydrolyzes the bond between galactose and glucose in lactose.
Pepsin (choice D) is a proteolytic enzyme secreted in an inactive form (pepsinogen) by the chief cells of the stomach. Pepsinogen is activated by stomach acid, and so is not dependent on enteropeptidase. Pepsin alone will not replace the activities of other proteolytic enzymes, partly because food does not remain in the stomach for an extended period of time.

40. The correct answer A. Release of cholecystokinin is stimulated by the presence of peptides, amino acids, or fatty acids in the small intestine. Cholecystokinin acts on the pancreas to stimulate secretion of pancreatic enzymes that aid in the digestion of these compounds.
Gastrin (choice B) secretion, which is stimulated by the presence of peptides or amino acids in the lumen of the stomach, produces an increase in gastric H+ secretion.
Motilin (choice C) is a hormone that regulates the migrating myoelectric complex, a series of contractions that occur during fasting, clearing the stomach and small intestine of any residual food. Secretin (choice D) secretion, which is stimulated by the presence of H+ and fatty acids in the duodenum, causes an increase in pancreatic and biliary HCO^{-}_{3} release and a decrease in gastric H+ release.

Somatostatin (choice E) secretion, which is stimulated by the presence of H+ in the lumen, results in decreased release of all gastrointestinal hormones and decreased H+ secretion in the stomach.

41. The correct answer is A. Alpha2-receptor agonists directly inhibit pancreatic insulin secretion.

Beta2-adrenergic agonists (choice B) stimulate insulin secretion.

Cholecystokinin (choice C) is a hormone that causes not only gallbladder contraction, but also insulin secretion from the pancreas.

Pancreatic glucagon release (choice D) acts as a paracrine stimulus for insulin secretion.

Sugar water (choice E) is a stimulus for the secretion of insulin from the pancreas.

Muscarinic activity (choice F) in the gastrointestinal tract enhances secretion of insulin from the pancreas.

42. The correct answer is C. The hormone in question is secretin. Acid entering the duodenum stimulates its secretion by the S cells in the duodenal lining. It inhibits stomach motility and stimulates bicarbonate secretion from the pancreas. Glucagon, secretin, and vasoactive peptide (VIP) are all structurally related.

Cholecystokinin (choice A) and gastrin (choice B) form another family of related hormones.

Neither somatostatin (choice D) nor substance P (choice E) are structurally related to secretin. In addition to their role in the gastrointestinal system, both hormones are also present in the brain.

43. The answer is E. The colon is the major site for the generation and absorption of short-chain fatty acids. They are products of bacterial metabolism of undigested complex carbohydrates derived from fruits and vegetables. In addition to exhibiting trophic effects on the colonic mucosa, they are believed to promote sodium absorption from the colon. The mechanism of action remains controversial.

44. The answer is C. Iron is transported in the blood bound to the bglobulin, transferrin. Excess iron is stored in all cells, but especially in hepatocytes where it combines with apoferritin. The stored form is called ferritin. The rate of iron absorption is extremely slow, with a maximum of only a few milligrams per day. Iron is absorbed primarily in the ferrous form. Therefore, ferrous iron compounds, rather than ferric compounds, are effective in treating iron deficiency.

45. The answer is D. Most water and electrolyte absorption occurs in the jejunum, with the duodenum serving primarily as the site of osmotic equilibration of chyme. Water absorption is passive and occurs as the direct result of active sodium absorption. The small intestine and colon absorb approximately 9 to 12 L of fluid per 24-hour period, most of which comes from gastrointestinal secretions. In contrast to the small

intestine, the colon has a limited capacity to absorb water (approximately 3 to 6 L per day); most water absorption in the colon occurs in the proximal colon.

46. The answer is B. Meckel's (ileal) diverticuli are the most common congenital abnormality of the digestive system. They are a remnant of the herniation and rotation of the midgut and at times the diverticulum remains attached to the umbilicus by a connective tissue stalk, as is mostly likely the case here. The diverticulum generally extends 2 inches from the ileum; about 2 ft from the ileocecal valve and usually manifests itself by bleeding prior to the first 2 years of life. There may be two types of ectopic tissue present in the diverticulum: either acid secreting epithelium (stomach; detected with radioactive technetium injected into the venous blood stream which then accumulates within the diverticulum) or pancreatic epithelium. (The rule of "2" helps remind you of the characteristics of Meckel's diverticulum.) The appendix (answer a) is a diverticulum off the cecum, not the ileum. Diverticuli (answer c) can cause blood in the stool but would be extremely rare in a toddler. Internal hemorrhoids (answer d) would generally be detected in a rectal exam, especially in a toddler and is not associated with "currant jelly" stools. The blood would more likely be black if a duodenal ulcer (answer e) were present, which would also be very rare in a toddler.

47. The answer is B. Removal of the terminal ileum can lead to diarrhea and steatorrhea. The terminal ileum contains specialized cells responsible for the absorption of primary and secondary bile salts by active transport. Bile salts are necessary for adequate digestion and absorption of fat. In the absence of the terminal ileum there will be an increase in the amounts of bile acids and fatty acids delivered to the colon. Fats and bile salts in the colon increase the water content of the feces by promoting the influx (secretion) of water into the lumen of the colon. Amino acids are absorbed in the jejunum. Iron is primarily absorbed in the duodenum. Gastrointestinal neuroendocrine tumors are derived from the diffuse neuroendocrine system of the GI tract, which is composed of amine- and acid-producing cells with different hormonal profiles, depending on the site of origin. The tumors they produce are generally divided into carcinoid tumors (ectodermal stem cells) and pancreatic endocrine tumors. One third of all primary gut tumors are carcinoid. Carcinoid tumors are frequently classified according to their anatomic area of origin (foregut, midgut, hindgut). Small intestinal (midgut) carcinoid tumors arise from the argentaffin cells of the crypts of Lieberkühn in the terminal ileum, and have a high serotonin content. Small intestinal carcinoids are the most common cause of the carcinoid syndrome (classic triad: cutaneous flushing, diarrhea, bronchospasm, right heart valvular lesions), which is manifest when they metastasize, but only occurs in 5 to 10% of carcinoid tumors.

48. The answer is D. The colon normally has two regions where it is retroperitoneal: the ascending and descending colon. There are also two normal points of flexure: the hepatic (right) and splenic (left) flexures. Therefore, the sigmoid colon, splenic flexure,

and hepatic flexure are the regions where the gastroenterologist has the greatest difficulty passing the fiberoptic scope, and thus have the greatest risk of bowel perforation. Other answers (answers a, b, c, and e) are not correct.

49. The answer is A. The area shown in the photomicrograph is the glycocalyx (brush border consisting of microvilli) of the small intestinal epithelium. It is the location of the brush border enzymes including lactase. The patient in the scenario is suffering from lactase deficiency which often has an adult onset since lactase activity decreases after childhood. The absence of lactase or reduced lactase activity results in passage of undigested lactose into the colon. Colonic bacteria carry out fermentation of the lactose to organic acids and hydrogen. The bloating, cramping, and abdominal pain are due to the breakdown of lactose and production of the hydrogen gas. The microvilli are also the site of the glucose/galactose transporter (answers b and c). However, the glucose/galactose transporter is not the site of the deficiency in lactose intolerance. Other brush border enzymes include the other monosaccharidases and enterokinase, which is important for cleavage of pancreatic zymogens (e.g., trypsinogen) to their active form. Digestion of lipids occurs through the action of bile (from the liver and bile duct) and lipase (from the pancreas). Bile serves to emulsify the lipid to form micelles, whereas lipase breaks down the lipid from triglycerides to fatty acids, glycerol, and monoglycerides (answers d and e). Those three breakdown products diffuse freely across the microvilli to enter the apical portion of the enterocyte by passive diffusion. Triglycerides are resynthesized in the smooth endoplasmic reticulum. Proteins are synthesized in the RER and are combined with sugar and lipid portions in the Golgi to form glycoproteins and lipoproteins. Those two types of molecules form the coverings of the triglyceride cores of the chylomicra. The chylomicra are released at the basolateral membranes by exocytosis into the lacteals. From the lacteals, the chylomicra travel into the cisterna chyli and eventually into the venous system by way of the thoracic duct. Digestion of fat occurs to a greater extent in the duodenum and jejunum than in the ileum. Sugars are broken down by amylase in the oral cavity, with continued digestion by brush border monosaccharidases. Proteins are broken down by pepsinogen in the stomach with continued breakdown in the small intestine by the enzymes of the pancreatic juice (e.g., trypsin, chymotrypsin, and carboxypeptidases). The products of protein digestion are amino acids that are actively transported by transporters also located in the brush border.

50. The answer is B. Inflammation of the duodenum may lead to increased acid output, hypocalcemia, and microcytic anemia. Increased basal and maximal acid outputs may result from excessive stimulation of the parietal cell (e.g., hypergastrinemia) or reduced inhibitory feedback (i.e., reduced effect of enterogastrone and the enterogastric reflex). The latter may occur when the proximal small intestine is inflamed. Although calcium is absorbed along the entire length of the small intestine, it is absorbed primarily in the

duodenum. Similarly, iron is absorbed primarily in the duodenum. Microcytic anemia is the result of reduced stores of iron, the most common anemia. Glucose-6-phosphatase deficiency is the most common metabolic disorder of red blood cells, and is also associated with a microcytic anemia, as is a-thalassemia.

51. The answer is E. The two inflammatory bowel diseases (IBDs), Crohn's disease (CD) and ulcerative colitis (UC), are both chronic, relapsing inflammatory disorders of unknown etiology. They both may show very similar morphologic features and associations, such as mucosal inflammation, malignant transformation, and extragastrointestinal manifestations that include erythema nodosum (especially ulcerative colitis), arthritis, uveitis, pericholangitis (especially with ulcerative colitis, in which sclerosing pericholangitis may produce obstructive jaundice), and ankylosing spondylitis. CD is classically described as being a granulomatous disease, but granulomas are present in only 25 to 75% of cases. Therefore, the absence of granulomas does not rule out the diagnosis of CD. CD may involve any portion of the gastrointestinal tract and is characterized by focal (segmental) involvement with "skip lesions." Involvement of the intestines by CD is typically transmural inflammation, which leads to the formation of fistulas and sinuses. The deep inflammation produces deep longitudinal, serpiginous ulcers, which impart a "cobblestone" appearance to the mucosal surface of the colon. Additionally in Crohn's disease, the mesenteric fat wraps around the bowel surface, producing what is called "creeping fat," and the thickened wall narrows the lumen, producing a characteristic "string sign" on x-ray. This narrowing of the colon, which may produce intestinal obstruction, is grossly described as a "lead pipe" or "garden hose" colon. In contrast to CD, UC affects only the colon, and the disease involvement is continuous. The rectum is involved in all cases, and the inflammation extends proximally. Because UC involves the mucosa and submucosa, but not the wall, fistula formation and wall thickening are absent (but toxic megacolon may occur). Grossly, the mucosa displays diffuse hyperemia with numerous superficial ulcerations. The regenerating, nonulcerated mucosa appears as "pseudopolyps."

52. The correct is A. Carbohydrate absorption occurs at enterocytes of the upper region of small intestinal villi. Fructose absorption is via the facilitated transporters GLUT5 across the apical enterocyte membrane and GLUT2 across the basolateral enterocyte. Glucose and galactose on the other hand are transported into enterocytes on carriers in combination with a sodium ion. The energy for this secondary active transport is provided by the electrochemical sodium gradient that is created by Na/K-ATPases. Experimental conditions that collapse the sodium electrochemical gradient, hypoxia, or poisoning of the Na-KATPase by ouabain inhibit glucose, but not fructose absorption. Nevertheless, the physiological importance of "saving energy" under extreme conditions such as mountain climbing through the use of fructose as energy source is questionable. For instance, fructose absorption is much slower than

absorption of glucose and galactose. The statements in choices B, C, D, and E are incorrect.

53. The correct is A. In patients with celiac disease the protein gluten, which is found in bread, oats, and many other foods containing wheat, barley, or rye, triggers an autoimmune response that causes damage to the small intestine leading to widespread manifestations of malabsorption. Calcium is difficult to absorb, so patients frequently experience symptoms of hypocalcemia such as muscle cramping, tetanic contractions, numbness, and tingling sensations. For sensory and motor nerves, calcium is a critical second messenger involved in normal cell function, neural transmission, and cell membrane stability. The nerves respond to a lack of calcium with hyperexcitability. The inability to absorb nutrients such as carbohydrates (choice B) leads to weight loss as experienced by the boy. Fat malabsorption (choice C) is not uncommon in patients with celiac disease as a consequence of greatly diminished absorptive surface. It would manifest in steatorrhea. Iron (choice D), like calcium, is difficult to absorb and may lead to anemia. The general decrease in electrolyte absorption leads to decreased water absorption (choice E). The increased osmotic load in the GI lumen accounts for the boy's diarrhea.

54. The correct is B. The small intestine absorbs massive quantities of water. Anormal person takes in about 2 Lof fluid every day. Another 7 Lof fluid are received by the small intestine daily as secretions from salivary glands (1.5 L), stomach (2 L), pancreas (1.5 L), liver (0.5 L), and the small intestine itself (1.5 L). That results in a total of about 9 Lof fluid entering the GI tract daily. In a healthy person the duodenum, jejunum, and ileum absorb the bulk of the water that enters the GI tract, here 8500 mL. The colon absorbs most of the remaining fluid (400 mL), not the bulk of it (choice A) and excretes about 100 mL daily. There is generally no water absorption in the esophagus and stomach. Therefore, choices C, D, and E are incorrect.

55. The correct is C. Hirschsprung disease is a genetic disorder caused by the absence of enteric nerve cells in the wall of the sigmoid colon and/or rectum. The portion of the bowel wall without nerve ganglia (aganglionic) cannot relax in response to bowel content so that the stool builds up behind the obstruction. In some children the problems begin shortly after birth, other infants are not acutely ill, but develop chronic symptoms such as constipation or anemia. Cholecystitis (choice A), caused by inflammation of the gallbladder, gastroesophageal reflux disease GERD (choice B), and polymyositis (choice D), a disorder affecting esophageal skeletal muscle, do not affect the neuronal regulation of the large intestine. Hirschsprung disease is almost always treated by surgical removal of the affected bowel segment and then joining the healthy bowel segments (choice E). A GI motility disorder might improve on its own due to the ability of the enteric nervous system in healthy GI tract portions to learn new motility patterns. However, it takes a very long time and the success is not certain.

56. The correct is B. After a meal about 90 percent of the bile acids and bile salts are absorbed from the lower ileum by way of active transport. They are directed to the liver, from where they can be released again via bile into the intestine. This enterohepatic circulation of bile acids between intestine and liver is physiologically very important for normal absorption of fat and fatsoluble vitamins, and if distorted, will lead to GI and other symptoms. The quantity of iron in the body (choice A) is maintained by controlled absorption from the duodenum, not the ileum. Although sodium (choice C) is actively absorbed in the ileum, there are additional absorption mechanisms available in the jejunum and in the colon. For instance, in the jejunum, sodium is absorbed by cotransport coupled with sugars and neutral amino acids, and in the colon, there are active sodium transport mechanisms as well. Hence, no immediate sodium imbalance is expected. Although vitamin B12 (choice D), complexed with intrinsic factor, binds to a transmembrane receptor in the ileum for absorption, a large amount of vitamin B12 (up to 5 mg) is stored in the liver. This liver storage is thought to be sufficient for 3–6 years so that symptoms from vitamin B12 deficiency will be expected at a later time, but not soon after removal of the ileum. Protein digestion (choice E) occurs in the small intestine, with absorption of amino acids primarily in the jejunum and to a lesser extent in the ileum, and with dipeptide absorption at about equal rates in these two segments. Removal of the ileum will not immediately lead to problems due to protein malabsorption.

ANSWERS MCQs IFOM

1. The correct answer is C. As in most muscle, contraction of gastrointestinal (GI) smooth muscle cells can be initiated by electrical activity and results in excitation-contraction coupling. However, the slow, rhythmic electrical changes noted in Gl smooth muscle, referred to as slow waves, are generated by a unique mechanism involving the interstitial cells of Cajal (ICCs). Slow waves are precisely timed, rhythmic depolarizations and repolarizations of the muscularis propria of the stomach and intestines, independent of the presence or absence of stimulus. They move in an oral-to-anal direction and occur at a frequency specific to each organ, with the stomach having the lowest frequency (3 cycles per minute) and the duodenum of the small intestine having the highest frequency (12 cycles per minute). They represent the basal electric rhythm of gastric and intestinal motility, although they don’t always result in mechanical activation. Hormones and neurotransmitters released near the GI smooth muscle cells can modulate the amplitude of the slow waves. Not all slow waves induce action potentials and generate smooth muscle contraction. Depending on the slow-wave amplitude and smooth muscle excitability, an action potential (typically calcium-driven “spike” potentials) can be initiated if the hormones and neurotransmitters increase the slow-wave depolarization enough to reach threshold. Only when

contractile events occur at the peak of the depolarization, during a slow wave, does coordinated smooth muscle contraction occur to facilitate movement through the digestive tract.

The other answer options are not mechanisms responsible for slow waves.

- When slow waves are accompanied by action potentials, smooth muscle contraction, not skeletal muscle contraction, occurs.
- Slow waves do not cause hyperpolarization of smooth muscle cells. (The potential becomes more negative, moving further away from the threshold.)
- Slow waves do not play a role in secretions of smooth muscle cells.
- Relaxation of smooth muscle cells occurs after an action potential has been triggered to contract smooth muscles.
- Alternating contraction of circular and longitudinal muscle is consistent with peristalsis, which is responsible for the movement of food and material throughoutt the GI tract.

2. The correct is D. This patient presents with jaundice in the setting of elevated total and direct bilirubin along with elevated liver enzymes (ALP, AST, and ALT) released due to liver damage. The most likely cause is cholestasis due to intrahepatic or extrahepatic biliary obstruction. This is usually accompanied by pruritus because of elevated bilirubin. The best step in the evaluation of these patients is imaging with a right upper quadrant ultrasonography to look for biliary dilatation. Conjugated hyperbilirubinemia can be caused by anything which obstructs the flow of bile through the intrahepatic or extrahepatic bile ducts. This includes gallstones, cholangiocarcinoma, pancreatic or liver cancer, liver flukes, primary sclerosing cholangitis, and primary biliary cholangitis. See theillustration to understand conjugated versus unconjugated bilirubin in the liver. It is very important to understand that even though an elevated alkaline phosphatase may be a result of liver disease, it is necessary to rule out other causes of elevated alkaline phosphatase such as bone disease.Intravascular destruction of RBCs would cause an increase in total bilirubin but without bilirubin in the urine and without elevation of alkaline phosphatase and aminotransferase. With extravascular destruction of RBCs, unconjugated bilirubin would be elevated, but there would be no bilirubin in the urine and hepatic enzyme levels would be normal. Absence or decreased levels of UDP-glucuronosyltransferase leads to excess unconjugated bilirubin that cannot be excreted or recycled and is therefore not in the urine.

3. The correct answer is E. This patient presents with episodic vomiting and lethargy. A history of several episodes of vomiting, especially if profuse, should suggest a primary metabolic alkalosis caused by the loss of hydrochloric acid from the stomach. Metabolic alkalosis is characterized by a pH=7.4 and high HCO3-. In response to metabolic alkalosis, the respiratory system compensates by decreasing ventilation,

which increases the Pco2, thus lowering pH. The patient's arterial oxygen saturation of 92% is consistent with reduced ventilation and elevated Pco,. However, compensatory responses can never overcorrect for the primary acid-base disorder, so the overall pH would still be expected to be greater than 7.4. Other causes of metabolicalkalosis includé diuretic use, antacid use, and hyperaldosteronism.

A and B can immediately be ruled out because pH would be expected to increase in the setting of severe vomiting. C and D include elevated pH in the setting of decreased PCO2 suggesting a primary respiratory alkalosis.

4. The correct answer is C. In this gene knockout experiment, researchers identify a mouse that is unable to digest most macromolecules and has excess protein and fat in its stool. These findings indicate that the gene for enterokinase (enteropeptidase) is deficient. This protein is embedded in the intestinal mucosa and is responsible for activating trypsinogen into trypsin. The active trypsin then activates the rest of the pancreatic enzymes including lipase, chymotrypsin, and carboxypeptidase. These enzymes are essential to the breakdown of some fat and all proteins. Preventing the function of these enzymes by knocking-out enterokinase would reduce the amount of proteins and fats that could be absorbed in the small intestines leading to more fats and proteins in the stool, as seen in the experimental model. Although enterokinase is not a pancreatic enzyme itself, it is most important for subsequent activation of proenzymes from the pancreatic exocrine organ. Additionally, unlike peptidase, which is an enzyme that breaks down peptides into amino acids, enterokinase only works to activate zymogens and does not break down peptides itself. The other answer choices are incorrect för the following reasons.

Loss of amylase activity would lead to increased amounts of carbohydrates, not fat and protein.

Loss of chymotrypsinogen activity would lead to increased amounts of protein, but not fat, in the stool

Loss of lipase activity would increase the amount of fat, but not protein in the patient's stool.

Loss of pepsin activity (present in the stomach and activated by stomach acid) would increase the amount of protein seen in the stool but would have no appreciable effect on fat in the stool.

5. The correct is B. This patient presents with a history of classic pyloric stenosis, which involves the pyloric sphincter, which controls passage of gastric contents into the duodenal bulb. This condition is much more common in male than in female infants and usually develops between 3 and 5 weeks of age, and very rarely after 12 weeks. The patient presents with regurgitation and relentless projectile, nonbilious vomiting. On physicäl examination, visible peristalsis generally can be seen, and a mass (commonly described as "olive"-like) usually can be palpated in the epigastric region.

The normal role of the pylorus is to limit the rate of gastric emptying. This is accomplished by contracting in response to each peristaltic wave.

6. The correct answer is F. This patient is a middle-aged obese G2P2 female with a likely history of biliary colic (recurrent postprandial RUQ pain) with acute epigastric pain radiating to the backin the setting of fever, hypotension, tachycardia and elevated ALT, AST and lipase. CT scan shows a diffusely edematous pancreas with fat stranding. Overall, presentation is characteristic of gallstone pancreatitis. The diagnosis of pancreatitis requires two of the following three criteria: epigastric pain, elevated lipase thre times the upper limit of normal, and imaging findings consistent with pancreatitis. Therefore, even though this patient received a CT scan, it was not entirely necessary for diagnosis since she was experiencing the other two criteria as well. The classic demographics of individuals who are susceptible to gallstones include the "4 F's": Forty, Female, Fertile (multiparity), and Fat. Individuals with gallstones are at an increased risk of developing both cholecystitis and pancreatitis due to gallstone obstruction of the cystic duct and pancreatic ampulla, respectively. Acute pancreatitis is treated with volume expansion, pain control, and pancreatic rest, whereby patients are kept NPO until symptoms begin to resolve. Zymogens are enzymes that are excreted in an inactivated state, but which are activated by other enzymes once they reach their location of action. Pancreatic enzymes are zymogens that are activated in the small intestine. Trypsinogen is converted to trypsin by brush border enzymes such as enterokinase. Trypsin then converts the other pancreatic zymogens to active enzymes and digests dietary protein. In pancreatitis, trypsinogen becomes inappropriately converted to trypsin which activates the other zymogens. As these active enzymes do not have dietary components to digest, they start to autodigest the pancreas, which can lead to necrosis. Pancreatic autolysis results in the massive systemic inflammatory response and pain seen in pancreatitis.

The other enzymes listed are not directly involved in activating the enzymes of the pancreas to autodigest pancreatic tissue in the setting of pancreatitis. Enterokinase is a brush border enzyme that converts trypsinogen to trypsin. Lactase is a brush border enzyme that catalyzes the hydrolysis of the carbohydrate lactose to glucose and galactose. Pepsinogen is a zymogen secreted by the stomach that is converted to pepsin when exposed to gastric acid. It aids in digestion of proteins. Amylase is a pancreatic (and salivary) enzyme that digests carbohydrates. It is excreted in its active form and does not play a major role in autolytic digestion of the pancreas in pancreatitis. Elastase is stored in zymogen granules as proelastase prior to secretion by the pancreas. Proelastase is activated by trypsin and is a proteolytic enzyme. Though elastase may playa role in autolysis in pancreatitis, trypsin plays the most important role in autolytic activity in pancreatitis.

7. The correct is E. This young child is experiencing sudden-onset intermittent abdominal pain, dark red stool, and vomiting; these symptoms indicate intestinal obstruction, likely secondary to intussusception. One possible anatomical cause for this is Meckel diverticulum. Meckel diverticulum is a congenital outpouching of the small intestine that results from the failed closure of the vitelline (omphalomesenteric) duct. The most common presenting symptom is painless lower gastrointestinal bleeding, usually manifesting in the form of melena. This is due to the ectopic production of gastric acid by parietal cells in the diverticulum, causing damage to the surrounding small intestine mucosa. Meckel diverticulum is an important cause of intestin al obstruction in children under the age of 2 years. It can be a lead point for intussusception and should be considered in allyoung children with intussusception, particularty when it is recurent. Meckel diverticulum also predisposes patients to volvulus. Meckel diverticulum is found in about 29% of the population, but of these individuals, only 2%-46 willhave symptoms. There is a 2:1 male:female prevalence; it is located 2 feet from theileocecal valve and is 2 inches in length (think rule of 2's). It can be identified with the 99mTe pertechnetate scan, because the ectopic parietal cells of the diverticulum have an affinity for the radioisotope. Atypical anterior abdominal wall development would lead to gastroschisis or omphalocele, which would be found before orat birth. The cecum on its own is not a common location of atypical development. Atypical development of the foregut can cause tracheoesophageal fistulas. Symptoms of tracheoesophageal fistulas would be apparent at birth. Atypical development of the pancreatic ducts can result in pancreatic divisum or annular pancreas. Pancreatic divisum is rarely symptomatic but could manifest with pancreatitis, nausea, and vomiting. Annular pancreas is unlikely to first present with vomiting at the age of 14 months.

8. The correct answer is A. This patient with fatigue, pale mucous membranes, decreased mean corpuscular volume (MCV) (-80 1L) and increased red blood cell distribution has the classic signs and symptoms of microcytic anemia caused by iron deficiency anemia. Her history of heavy menstrual bleeding is the most likely cause of her symptoms. Iron is absorbed in the duodenum via two independent mechanisms. Heme-associated iron is taken up by a heme transporter in the luminal plasma membrane of the duodenal epithelial cells. Ferrous iron ions can also be taken up by the divalent metal transporter channel in the luminal plasma membrane. Thus a deficiency of absorption in the duodenum, which can be caused independently by resection or disease of the duodenum (Crohn disease), will also cause iron deficiency. See the table for further information on differentiating types of anemia.

The other answer choices refer to areas of the gastrointestinal tract that are not responsible for iron absorption. The gastric fundus is important in vitamin Bi2 deficiency. The ileum is the site of absorption of fat-soluble vitamins A, D, E, and K,

as well as vitamin B12. The jejunum is linked to folate absorption, and the sigmoid colon is most responsible for water absorption.

	Iron deficiency anemia	Anemia of Crohn disease	α-Thalassemia minor	β-Thalassemia minor
MCV	Decrease	Decrease or normal	decrease	decrease
RDW	Increase	normal	normal	normal
Serum Fe	decrease	decrease	normal	normal
TIBC	increase	decrease	normal	normal
Ferritin	decrease	Increase or normal	normal	normal
Hb electrophoresis	normal	normal	normal	Nincrease HBA2

9. The correct answer is A. The patient is overweight, female, in her 40s, and complains of pain in the upper right quadrant that generally gets worse after eating. This is a classic presentation of cholelithiasis, or gallstones. A common mnemonic to recall a typical patient scenario for gallstones is "Fat, Female, Fertile, Forty. Patients with cholelithiasis experience pain after meals as a result of the release of cholecystokinin (CCK) from the duodenum, which is stimulated by fatty acids and aminoacids. CCK causes the gallbladder to contract while the stone obstructs the cystic duct.

Gastrin is released by the G-cells of the stomach in response to proteins or peptides and does not have an effect on gallbladder contraction. Gastrin leads to increased secretion of gastric acid and low pH inhibits gastrin secretion, leading to a negative feedback loop. In Zollinger-Ellison syndrome (ZES), a gastrin-secreting tumor in the pancreas (gastrinoma) causes excessive gastric acid secretion in the stomach. ZES patients generally present with more severe symptoms, such as midepigastric pain due to gastric ulcers, steatorrhea, wheezing or hematemesis.

Pepsin is a proteolytic enzyme that is released by chief cells in the stomach under the influence of gastrin and vagus nerve stimulation. It does not cause gallbladder contraction and its secretion would not cause the symptoms seen here.

Somatostatin and vasoactive intestinal peptide both cause relaxation, rather than contraction of the gallbladder.

Somatostatin is released by the D-cells of the duodenum, pyloric antrum, and pancreatic islets. It reduces smooth muscle contractions and inhibits the release of both insulin and glucagon from the pancreas.

Vasoactive intestinal peptide induces smooth muscle relaxation in the lower esophageal sphincter, stomach, gallbladder, and stimulates secretion of water into

pancreatic juice and bile. It also inhibits gastric acid secretion and absorption from the intestinal lumen.

10. The correct answer is C. This patient with a history of recently uncontrolled Crohn disease presents with right upper quadrant pain, a low-grade fever, nausea, and vomiting. His laboratory findings are significant for leukocytosis, and his right upper quadrant ultrasound reveals thickening of the gallbladder wall and obstruction by a stone. This patient has acute cholecystitis, or inflammation of the gallbladder, caused by gallstones blocking the cystic duct. Crohn disease causes transmural skip lesions - alternating areas of transmural inflammation and normal tissue-throughout the gastrointestinal tract. These commonly affect the terminal ileum, which is an important location for bile acid reabsorption. Bile acids are produced in the liver and function to emulsify and eliminate fat. They are normally recycled in the body via enterohepatic circulation, which refers to the passive reabsorption of bile acids through the terminal ileum. Thus, if significant terminal ileum disease exists in Crohn's patients, there is decreased bile acid reabsorption and increased elimination in the stool. Eventually, the bile produced in the body contains less bile acid andlacks the ability to effectively liminate cholesterol, leading to the formation of cholesterol stones. Additional consequences of decreased bile acids include increased lipid binding to calcium in the gastrointestinal tract, which leads to the increased absorption of oxalate and increases the risk of calcium oxalate stones in the kidney.

The other answers are incorrect for the following reasons:

A bowel perforation due to transmural inflammation is an intestinal complication of Crohn disease, but would present with a more unstable patient (eg, hypotensive, tachycardic, severe abdominal pain)

Gallstone ileus is a passage between the small bowel and the gallbladder that a gallstone can enter and cause an obstruction in the small bowel. This would present with symptoms of bowel obstruction (absent stool, absent flatus, diffusely distended abdomen)

Transmural bowel scarring in patients with Crohn disease may lead to strictures (narrowed areas) in the bowel This would present with symptoms of bowel obstruction (absent stool, absent flatus, diffusely distended abdomen)

Although hemolysis resulting in increased bilirubin formation can create pigment stones that can obstruct the gallbladder and cause acute cholecystitis, this patient has no history of hemolysis. His history of recently uncontrolled Crohn disease is more suggestive of cholesterol stones created from decreased reabsorption of bile acid.

Ascending cholangitis (ascending infection of the biliary tree) would present with fever, jaundice, and abdominal pain and would progress to shock, altered mental status, and/or death. This patient's symptoms are not severe enough to consider this diagnosis.

11. The correct is B. Ranitidine belongs to the class of drugs termed H2 receptor antagonists. Other H, receptor antagonists include famotidine and cimetidine. They bind to H2 receptors on parietal cells to block the receptors interaction with histamine. H2 receptors are coupled via a Gs, regulatory protein to adenylate cyclase and stimulate cyclic adenosine monophosphate (CAMP) formation, meaning that Ha receptors are Gs-coupled receptors. Therefore blockage of H2 receptors means that Gs-coupled receptors have been inhibited, resulting in decreased downstream cAMP and acid production. The mechanism of G-protein-coupled receptors and their activation schemes are important to understand, and the activation pathway is summarized in the diagram.

Proton pump inhibitors such as omeprazole, pantoprazole, and lansoprazole bind to and inhibit the H+/K+ ATPase pump on parietal cells.

Anticholinergics such as atropine bind to the muscarinic Mg-receptor.

Prostaglandins bind to the prostaglandin receptor.

Somatostatin analogs such as octreotide bind to the somatostatin receptor.

12. The correct answer is D. The patient presents with bilateral pain in his cheeks in front of his ears, as wellas pain on swallowing and sialorhea. Based on the timing of this presentation after recent treatment with clozapine, this patient has drug-induced parotitis. Although parotitis is classically associated with mumps, this manifestation has become uncommon since the introduction of a vaccine in 1967. Other causes of parotitis include autoimmune conditions, bacterial infections, and drugs (including clozapine). Hypersalivation is a distressing and common side effect of clozapine, which occurs in about one quarter of patients. Although it is a poorly understood side effect, it may sometimes cause salivary gland swelling. In general, saliva secreted from ductal acini starts out isotonic to plasma. The diagram here illustrates that as saliva travels, the excretory ducts and the intercalated ducts reabsorb Na and Cl and secrete K and HCO. At higher rates of flow, as in the setting of parotitis, saliva has less time in contact with the ductal epithelium, reabsorbs less Na and CI, and secretes less K. As a result, the salivary K concentration essentially remains static as flow rate increases. However, HCO secretion increases independently by the action of secretagogues. In addition, at lower salivary flows, saliva in the mouth tends to be hypotonic and slightly acidic compared with plasma. At higher flow rates, saliva is nearly isotonic to plasma and becomes more basic.

An increase in salivary flow rate would result in a higher, not lower, concentration of amylase

Bicarbonate secretion is stimulated by high flow, so bicarbonate conçentration would therefore be increased.

Sodium and chloride levels would be elevated as a result of decreased duration of contact with reabsorbing epithelium.

13. The correct answer is B. The patient presents with fatigue and malaise (general feeling of discomfort/not feeling well). On examination, the patient is edematous, with a distended abdomen and pitting edema of the legs. Furthermore, his aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels are both elevated, resulting in a notable AST to ALT ratio of 2.4. These findings, along with the history of frequent motor vehicle collisions (attributed to alcohol use), make the patient's presentation consistent with alcoholic hepatitis. Alcoholic hepatitis on lab studies is evidenced by a ratio of AST to ALT 21.5 and a normal alkaline phosphatase level. (Elevation would be suggestive of biliary obstruction.) Classic clinical signs include metabolic encephalopathy, ascites, and edema. The mild anemia is the result of the suppressive effects of alcohol on the bone marrow.

Capillary fluid exchange can be described by using the Starling equation, which is summarized by the following formula Net fluid flow=Kf [Pc- Pi)-c(πc- πi)], where Kf (capillary permeability to fluid) and c (capillary permeability to protein) are Constants.

Pc (capillary hydrostatic pressure) pushes fluid out of the capillary.

Pi(interstitial fluid hydrostatic pressure) pushes fluid into the capillary.

πc (plasma colloid oncotic pressure) pulls fluid into the capillary.

Pi (interstitial fluid colloid oncotic pressure) pulls fluid out of the capillary.

A positive net fluid flow indicates that fluid will move out of the capillary, and a negative net fluid flow indicates that fluid will move into the capillary. The major mechanism contributing to edema in this patient's disease is the decreased production of serum proteins (eg, albumin) by the liver damaged by chronic alcohol use. A decrease in serum proteins indicates decreased πc (capillary oncotic pressure), resulting in a loss of fluid from the capillaries into the interstitium.

Constriction of arterioles would decrease capillary pressure (Pc) and not lead to edema.

Capillary permeability would increase edema (increased Kf), but this patient lacks any evident cause of inflammation that would produce it.

Permeability of glomeruli may lead to protein loss and thus decreased πc, but this patient has no known kidney disease. Also, alcohol exerts its primary effects on the liver rather than the kidneys.

Lymphatic blockage may also increase edema by increasing interstitial fluid colloid osmotic pressure (increased πi), but this patient has no identifiable source of lymphatic blockage.

14. The correct answer is A. This patient has a history of rheumatoid arthritis and is likely to be taking nonsteroidal anti-inflammatory drugs (NSAIDs) regularly. NSAIDs reversibly inhibit both COX-1 and COX-2 enzymes, leading to a reduction in the production of prostaglandins by the gastric mucosa. These prostaglandins usually act to maintain the protective barrier and to decrease acid secretion, and so their down regulation by NSAIDs leaves the gastric mucosa vulnerable to damage. Of the

medications used to reverse ulcer vulnerability misoprostol is the most harmful in pregnancy and is therefore the medication that was most likely prescribed in light of this doctor's warnings.

Misoprostol is a prostaglandin E1 analog that acts as an agonist at the prostaglandin receptors on parietal cells. This, in turn, results in increased mucus and bicarbonate secretion and decreased acid secretion. Misoprostol may be used to prevent NSAID-induced ulcers when a patient needs to continue NSAID use, despite the gastrointestinal adverse effects. Another clinical use for misoprostol is in medically induced abortions, in which it is used in combination with mifepristone, a progesterone antagonist that causes the uterine lining to shed. Misoprostol, an analog of a prostaglandin in the E series (eg, PGE, PGE,) causes the uterus to contract, in addition to protecting the gastricnmucosa.

The other mechanisms of action listed are not associated with the drug prescribed by the physician for this patient.

Octreotide is a somatostatin analog, which decreases the production of stomach acid through in hibition of gastrin.

Ranitidine is an example of an H, blocker, which inhibits acid secretion at the histamine receptor.

NSAIDs are typically prostaglandin din antagonists, which inhibit gastriç acid and histamine production.

Omeprazole is a proton pump inhibitor, which is preferred for treating peptic ulcer disease. It is not contraindicated during pregnancy.

15. The correct answer is D. The patient presents with fever, right upper quadrant (RU) pain, and a positive Murphy sign (inspiratory arrest on palpation), which suggest acute cholecystitis. In acute cholecystitis, gallstones obstruct the cystic duct, leading to contraction of the gallbladder against resistance. With every contraction, the patient feels pain that can radiate to the right scapular region. Inflammation may follow, leading to thickening of the gallbladder wall and systemic symptoms including fever. In this patient, the examiner elicits the Murphy sign by palpating the RUQ at the midclavicular line to contact the gallbladder as the patient inspires.

The next step to diagnosing acute cholecystitis is a RUQ ultrasound, like that shown here. During this test, ultrasound imaging is first used to detect the exact location of the gallbladder. Murphy sign is then elicited by using the ultrasound probe to apply pressure to the gallbladder at the point of maximum tenderness. This patient will likely undergo elective cholecystectomy.

Emergent cholecystectomy is not indicated for acute cholecystitis until the diagnosis has been confirmed. Although abdominal CT can show acute cholecystitis, it is not the ideal mode of imaging, owing to cost and unnecessary radiation exposure. IV fluids and supportive treatment do not provide diagnostic information and should not be

initiated until after obtaining a RUQ ultrasound. Intraoperative cholangiogram is usualy done as a part of cholecystectomy and has no role in management of acute cholecystitis.

16. The correct answer is D. This patient is presenting with alkalosis (normal arterial pH is 7.35-7.45). The HCO3 level is substantially elevated (11 mEg/l above normal), which suggests that the patient is experiencing metabolic alkalosis. This alkalosis is caused by the patient's recent history of severe vomiting. The vomiting causes a loss of hydrochloric acid from the stomach.

Parietal cells of the stomach secrete new acid at the same time new bicarbonate enters the blood. The resulting alkalosis inhibits alveolar ventilation, which triggers arespiratory compensation (best explained by the Henderson-Hasselbalch equation). Through hypoventilation, the Pco_2 rises and generates carbonic acid, which aids in lowering and normalizing the pH. This expected Pco_2, can be quantified with the following formula:

(Expected P_{CO2} = (0.7 x HCO_3)+20 +5)

The patient's Pco_2 is 48, which is within the predicted range (39.5-49.5). It is necessary to know when to use the Winters formula and to distinguish acidosis from alkalosis. This patient does not have metabolic acidosis, and so the Winters formula is not applicable.

Here is what would be expected if the patient were experiencing the other acid-base disturbances listed:

Metabolic alkalosis and metabolic acidosis: If a metabolic acidosis were occurring simultaneously (such as in ketoacidosis or diarrhea) with this patient's metabolic alkalosis, the HCO_3 level would be closer to normal because the two processes would have opposing effects on HCO_3 levels and effectively cancel each other out.

Metabolic alkalosis and respiratory acidosis: If a simultaneous respiratory acidosis were occurring in addition to the patient's metabolic alkalosis, the Pco_2 would be even higher than anticipated.

Metabolic alkalosis and respiratory alkalosis: If a simultaneous respiratory alkalosis were occurring, the P_{C02} would be normal (meaning there is a failure of respiratory compensatory mechanisms) or it would be decreased.

Respiratory alkalosis: This condition normally results from increased respiration or hyperventilation, which increases the blood pH. This patient's Pco_2 is > 40 mm Hg. Metabolic compensation occurs to lower the blood HCO_3 levels by having the kidneys excrete more HCO_3.

17. The correct answer is F. This patient's presentation is most consistent with acute cholecystitis, which usually presents in patients with the "4 Fs": Fat, Female, Fertile, and Forty years old. These patients usualy have severe and constant right upper

quadrant pain as opposed to episodic pain, which is associated with biliary colic and gallstones without any inflammation.

Patients may also have a low grade fever, leukocytosis, and slight elevations in transaminase levels. Elevations in bilirubin and alkaline phosphatase concentrations are not common in uncomplicated cholecystitis, because the biliary obstruction is limited to the gallbladder. Inflammation of the gallbladder may also lead to diaphragmatic irritation, resulting in referred pain that radiates to the right upper shoulder or back. The Murphy sign is considered present or positive if the patient has increased pain or suddenly halts inspiration because of pain (inspiratory arrest).

Acute cholecystitis occurs when the cystic duct becomes acutely blocked by a gallstone, leading to retrograde inflammation of the gallbladder mucosa. Results of liver function tests are usually normal, but occasionally, enzyme levels may be slightly elevated. Sensitive findings include the presence of cholelithasis and a positive Murphy sign as confirmed by ultrasound. As shown in the image, signs of inflammation such as gallbladder wall thickening (e3 mm) are important secondary findings that confim the diagnosis; the presence of gallstones supports the diagnosis but is not diagnostic. Gallbladder wall distention and pericholecystic fluid are not highlighted in the image, but these findings are also significant.

It is important to remember that cholecystitis involves blockage of the cystic duct, whereas choledocholithiasis is an obstruction of the common bile duct (and would manifest with higher elevations in liver enzyme levels). Choledocholithiasis is especially dangerous because it often progresses to ascending cholangitis, which is an infection of the biliary tract.

Adhesions of the hepatic flexure would not present with fever, and subsequent ultrasound findings would not reveal gallbladder wall thickening or pericholecystic fluid.

Splenic vessel engorgement is more likely to lead to left upper quadrant discomfort and pain, rather than the right upper quadrant pain that is seen with acute cholecystitis.

Formation of a fistula between the gallbladder and small intestine indicates a gllstone ileus and would present with signs of small bowel obstruction.

Obstruction of the common bile duct by a gallstone is indicative of choledocholithiasis.

An obstructive mass at the head of the pancreas is more likely to result in painless jaundice, rather than right upper quadrant pain. Itis less likely that a patient would have an accompanying leukocytosis.

18. The correct answer is E. This patient describes symptoms of anemia (weakness, light-headedness) with some gastrointestinal effects (weight loss, diarrhea), which should raise suspicion for pernicious anemia. If a complete blood count were provided, this would be confirmed by low hematocrit and hemoglobin, as well as an elevated mean corpuscular volume to indicate that this is a macrocytic anemia. Additionally, a

blood smear would show hypersegmented neutrophils, consistent with a megaloblastic anemia. Megaloblastic anemia occurs when
DNA synthesis is inhibited during red blood cell production, which can occur in vitamin B12 and/or folate deficiency.
This patient is also experiencing neurologic symptoms consistent with peripheral neuropathy such as paresthesia (eg, "pins and needles" sensation, decreased sensation to pinprick at distal extremities) and positive Romberg sign (caused by diminished proprioception). Although both vitamin B12 and folate deficiencies cause macrocytic anemia, only vitamin B12 deficiency causes neurologic deficits.
Finally, this patient also has a history of hypothyroidism. The most common cause of hypothyroidism is Hashimoto thyroiditis, which is often associated with other autoimmune conditions, such as pernicious anemia. In pernicious anemia, an autoimmune process causes destruction of parietal cells, leading to decreased production of intrinsic factor, which is required for vitamin B12 absorption.
Chief cells secrete pepsinogens, which aid in protein digestion. This patient does not have signs of protein malnutrition.
G cells secrete gastrin, which increases gastric acid secretion and growth of protective gastric mucosa. This patient does not have signs of increased susceptibility to infection due to increased pH in the stomach.
I cells secrete cholecystokinin, which increases pancreatic secretions and gallbladder contraction, among other roles. Deficiency would impair fat digestion. Although this patient has weight loss and diarrhea, the other symptoms are better explained by pernicious anemia.
Mucus cells secrete mucus and bicarbonate to prevent damage to the lining of the stomach. This patient does not have signs of gastric ulcers.
19. The correct answer is A. This young man presenting with acute-onset epigastric pain that is radiating to the back has a history of alcoholism. Classically, this clinical picture is consistent with an episode of pancreatitis, which is most commonly caused by gallstones and alcohol. The amylase level is elevated during an episode of acute pancreatitis. Thus the organ of interest is the pancreas.
The hormone secretin acts on pancreatic duct cells to stimulate bicarbonate secretion, which facilitates functioning of pancreatic enzymes by neutralizing gastric acid. Secretin is released by duodenal S cells in response to increased acid and fatty acids in the lumen of the duodenum.
A fasting state increases release of motilin (from the small intestine) and ghrelin (from the stomach). Stomach distention and vagal stimulation increase release of gastrin (from the antrum of the stomach and duodenum). Fatty acids, amino acids, and oral glucose reaching the duodenum and jejunum increase release of glucose-dependent

insulinotropic peptide (GIP) from duodenal and jejunal K cells. None of these hormones increase bicarbonate secretion from the pancreas.

20. The correct answer is E. This patient's symptoms of intermittent abdominal pain in the right upper quadrant, exacerbated by a fatty meal, are classicfor cholelithiasis. Cholelithiasis commonly presents with intermittent right upper quadrant pain that worsens after a meal, nausea and vomiting, and restlessness resulting from the pain. Furthermore, the patient population in which cholelithiasis is most commonly diagnosed is represented by the 4 F's: Female, Fat, Fertile, and Forty. When fats from a fatty meal arrive at the duodenum, cholecystokinin (CCK) is released from duodenal and jejunal I cells. CCK causes the gallbladder to contract, which increases bile release to emulsity the fat in the meal. In cholelithiasis, CCK causes the gallbladder to contract against a cystic duct that is blocked by a gallstone, inducing crampy abdominal pain. Other functions of CCK include increased pancreatic enzyme secretion and inhibition of gastric emptying . CCK does not directly affect insulin release, gastric acid secretion, or gastrointestinal motility:

Somatostatin decreases insulin release while gastric inhibitory peptide (GIP) increases insulin release.

Gastric acid secretion is increased by the hormone gastrin.

Gastrointeestinal motility is increased by motilin.

CLINICAL CASES

1. A 32-year-old obese man, Gordon, visits his GP complaining of a 3-week history of occasional epigastric pain which is associated with heartburn. He smokes 20 cigarettes a day and drinks half a bottle of wine most nights.

1.1 What is the most likely diagnosis?

Reflux oesophagitis. The main symptoms of this disorder include odynophagia (painful swallowing) dysphagia due to oesophageal dysmotility and chest pain. There are several factors predisposing to the development of reflux oesophagitis: obesity, alcohol intake, caffeine intake, smoking, large meals – especially late at night, medications such as nitrates, calcium antagonists, anticholinergics , hiatus hernia

1.2 What will you initially advise or prescribe for him?

Antacids or PPI

2. A 43-year-old man presents to the physician's clinic with complaints of epigastric pain. After a thorough workup, the patient is diagnosed with peptic ulcer disease. He is started on a medication that inhibits the "proton pump" of the stomach. A 43-year-old man with peptic ulcer disease is prescribed a proton pump inhibitor

2.1 What is the "proton pump" that is referred to above?

Proton pump: H+-K+-ATPase (adenosine triphosphatase) pump.

2.2 What type of cell membrane transport would this medication be blocking?

Type of cell membrane transport: Primary active transport

2.3 What are four other types of transport across a cell membrane?

Other types of transport: Simple diffusion, restricted diffusion, facilitated diffusion, secondary active transport (cotransport and countertransport [exchange]).

3. A 34-year-old man presents to his primary care physician with the complaint of increased difficulty swallowing both solid and liquid foods. He notices that he sometimes has more difficulty when he is under stress. He often has chest pain and regurgitation and reports difficulty with belching. After a thorough examination, he is diagnosed with achalasia (disorder of the lower esophageal sphincter).

3.1 What part of the gastrointestinal (GI) tract is composed of striated muscle and smooth muscle?

Striated and smooth muscles in GI tract: Striated muscle found in pharynx, upper third of the esophagus, and external anal sphincter. Smooth muscle found in all areas in between, including the LES.

3.2 What factors are responsible for the tonic contraction of the lower esophageal sphincter (LES) between swallows?

Tone of the LES: Inherent to the LES smooth muscle and augmented by cholinergic nerves

3.3 What are the major neurotransmitters responsible for regulating contraction and relaxation of the LES.

Neurotransmitters in LES:Acetylcholine (ACh), vasoactive intestinal peptide (VIP), nitric oxide (NO), adenosine triphosphate (ATP).

4. A 52-year-old gentleman comes to your office with a history of intermittent difficulty swallowing solid food. His symptoms have been present for the past 5 years. He points to his supraclavicular notch when describing where the food feels stuck, although he is able to chew his food and transfer it into his posterior pharynx without difficulty. He does not choke or cough while eating. Drinking water will usually relieve his symptoms, although on several occasions he has self-induced vomiting. His symptoms are slightly worse now than they were several years ago, which prompted today's visit.

4.1 Would you classify his dysphagia as esophageal or oropharyngeal?

Dysphagia can be classified as either oropharyngeal or esophageal.1 These are distinct processes that require different evaluation and management. Oropharyngeal (or transfer) dysphagia occurs from disorders that affect the oropharyngeal area, typically from neurologic or myogenic abnormalities as well as oropharyngeal tumors. Oropharyngeal dysphagia is caused by disorders affecting swallowing function above the level of the esophagus, and esophageal dysphagia is caused by disorders affecting the body of the esophagus. Difficulty initiating a swallow and swallowing associated with coughing, choking, or nasal regurgitation suggest an oropharyngeal etiology. Esophageal dysphagia occurs from disorders of the esophagus and is most commonly due to mechanical obstruction or altered motility of the esophagus. A detailed history can distinguish between the 2 types of dysphagia and with further evaluation can establish the diagnosis in 80% to 85% of cases.

5. 55-year-old man presents to his physician complaining of burning chest pain that typically occurs after eating and radiates to the neck. Occasionally, the pain and a slight cough awaken him from sleep. He also complains of difficulty swallowing, particularly solid foods. The patient has had these symptoms for several years, but they seem to be worsening

5.1 What is the most likely diagnosis?

Gastroesophageal reflux disease (GERD), complicated by Barrett esophagus

5.2 What are the expected findings on endoscopy?

Endoscopy reveals an upward shift of the gastroesophageal junction (Z line) due the metaplasia of esophageal nonkeratinized squamous epithelium to gastric columnar epithelium in the setting of recurrent acid exposure.

5.3 What are the common treatments for uncomplicated cases of this condition?

Proton pump inhibitor (PPI) trial. Testing for Helicobacter pylori is appropriate in patients not responsive to ppIs. treatment with triple therapy (PPI, amoxicillin, clarithromycin) is used in H pylori–positive cases. Lifestyle modifications including elevation of the head of the bed, dietary restrictions, and weight loss are often used in conjunction with medical therapy.

6. A 66-year-old woman presents to her physician with left lower quadrant pain; a 3-week history of nausea, vomiting, and diarrhea; and an unintentional 15.9-kg (35-lb) weight loss over the past month. Her medical history is complicated by type 2 diabetes,

hypertension, breast cancer, erosive esophagitis, and chronic peptic ulcer disease. She takes several medications, including a β-blocker. CT of the abdomen reveals a 5 × 5-cm mass in the head of the pancreas. Relevant laboratory findings are as follows: Gastric pH: < 2.0 Gastrin: 1500 pg/mL (normal: < 90 pg/mL) Hematocrit: 26% Basal gastric acid output: > 15 mEq/h (normal: < 15 mEq/h)

6.1 What is the most likely diagnosis?

Gastrinoma, a gastrin-secreting, non–β islet cell tumor of the pancreas or duodenum. these tumors cause gastric hypersecretion of hydrochloric acid, which results in disseminated gastrointestinal ulcers.

6.2 What test can further support the diagnosis?

The secretin stimulation test elicits increased gastrin secretion by the cells in a gastrinoma, whereas normal gastric G cells are inhibited by secretin. the test therefore differentiates between the presence of a gastrinoma and other causes of hypergastrinemia.

6.3 What are the two most common neuroendocrine tumors?

Gastrinoma (two-thirds are malignant) and insulinoma (usually benign) are the most common neuroendocrine tumors.

6.4 What are the signs and symptoms of this condition?

Increased fasting gastrin level. Ulcers in unusual locations such as the proximal jejunum. Gastroesophageal reflux disease. Nausea/vomiting. epigastric pain. Weight loss.

6.5 With what syndromes is this condition commonly associated?

Zollinger-Ellison (ZE) syndrome is characterized by a classical triad of symptoms: increased gastric acid secretion, peptic ulcer disease, and diarrhea.

6.6 What is the appropriate treatment for this condition?

Surgical treatment involves resection of the tumor, surrounding pancreatic tissue, regional lymph nodes, and other structures in cases of metastasis (60%).

7. A 65-year-old immigrant woman from Japan presents with fatigue, weight loss, early satiety, and a gnawing stomach pain. She has been seen by multiple physicians, all of whom diagnosed her with peptic ulcer disease and treated her with antacids. However, the pain has not improved for 8 months. She has lost 16 kg (35 lb) and now complains of painful intercourse (dyspareunia) and painful defecation (dyschezia).

7.1 What is the most likely diagnosis?

Gastric cancer. Because of symptoms similar to peptic ulcer disease and gastritis, gastric cancer is frequently misdiagnosed. hence, patients are typically diagnosed at a late stage and prognosis is therefore poor (5% survival at 5 years).

7.2 What risk factors are associated with this condition?

Infection with Helicobacter pylori. Chronic gastritis. Smoking. Diets high in nitrosamines (ie, smoked, cured, or pickled foods) commonly found in east asia, the

andes, Scandinavia, and eastern europe. Pernicious anemia and type a blood (associated with gastritis). Family history. Previous gastric surgery.

8. A 37-year-old woman with a 20-year history of Crohn disease presents to her primary care physician complaining of fatigue. Physical examination reveals tachycardia (heart rate: 106/min), pale conjunctivae, angular cheilitis, and a beefy red tongue. Relevant laboratory findings include a hematocrit of 21% and an elevated mean corpuscular volume.

8.1 What is the most likely diagnosis?

Vitamin B12 deficiency.

8.2 What are the possible causes of this patient's condition?

The most common cause of vitamin B12 deficiency is pernicious anemia, an autoimmune disorder in which intrinsic factor–producing gastric parietal cells are destroyed. Intrinsic factor is necessary for vitamin B12 absorption. Other causes include malabsorption (eg, celiac sprue, enteritis, or Diphyllobothrium latum infection) and absence of the terminal ileum (as in Crohn disease or surgical resection). Vitamin B12 deficiency is rarely due to insufficient dietary intake. however, after several years, strict vegetarians are at risk, because the nutrient is found only in animal products.

8.3 What other vitamin deficiency can cause megaloblastic anemia?

Folic acid deficiency. although there is an elevated level of serum homocysteine as in vitamin B12 deficiency, accumulation of methylmalonic acid and neurologic symptoms are not associated with folic acid deficiency.

9. A 35-year-old woman presents to her physician complaining of several days of severe, gnawing epigastric pain. The pain is worse between meals and is somewhat relieved with milk, food, and antacids. She has had three peptic ulcers in the past 2 years. The pain is occasionally accompanied by diarrhea. She denies bloody stools or hematuria and does not use alcohol or tobacco. Upper endoscopy reveals prominent gastric folds and an erosion in the first portion of the duodenum. The patient's fasting gastrin level is 700 pg/dL.

9.1 What is the most likely diagnosis?

A history of recurrent peptic ulcers suggests Zollinger-ellison (Ze) syndrome, in which there is hypersecretion of gastrin from a gastrinoma, resulting in high gastric acid output.

9.2 What are the common risk factors for peptic ulcer disease?

Helicobacter pylori infection. Nonsteroidal anti-inflammatory drugs. Smoking.

9.3 With what endocrine disorder is this condition associated?

Approximately 20% of patients with Ze syndrome also have multiple endocrine neoplasia type I (Wermer syndrome). Such patients will also have parathyroid adenomas, resulting in hyperparathyroidism, and/or anterior pituitary tumors.

9.4 How is secretion of gastric acid normally regulated?

Gastric acid is secreted by parietal cells of the stomach in response to gastrin, acetylcholine (vagal input), and histamine . acid secretion is inhibited by somatostatin.

9.5 What is the pathophysiology of this patient's diarrhea?

The voluminous acid secretion overwhelms the buffering capacity of pancreatic bicarbonate. thus, pancreatic enzymes are inactivated in this acidic environment, impeding digestion. excess acid also interferes with the emulsification of fats, leading to steatorrhea.

9.6 What are the appropriate treatments for this condition?

Surgical treatment involves resection of the gastrinoma (typically at the head of pancreas). Medical treatment uses proton pump inhibitors to suppress gastric acid secretion.

10. A 26-year-old man presents to A&E with malaise, anorexia, vomiting and abdominal pain. On examination he looks unwell and has a high temperature of 38.7°C. He is jaundiced and is tender in his RUQ of the abdomen and has tattoos on his arms.

10.1 What may be the cause of his jaundice?

This is a common symptom of liver disease and is caused by the accumulation of bilirubin in the tissues

10.2 What questions do you specifically want to ask about in the history?

Recent travel abroad; IV drug abuse; Tattoos; Excess alcohol; High risk sexual activity; Healthcare professional; Farm sewage worker; Water sports; Any recent medications e.g. antibiotics (flucloxacillin, coamoxiclav) excess paracetamol, etc. He tells you that he has never used any IV drugs but that he is keen on muscle building and has taken a course of steroids two months ago. He smokes 20 cigarettes a day and binge drinks.

10.3 What blood tests will you do and which of these are useful in assessing liver synthetic function?

Albumin, INR, prothrombin time, the level of bilirubin, AST, ALT, GGT.

10.4 What other investigations would you consider performing?

USS abdomen; Liver screen; Hepatitis serology – specifically Hepatitis A,B,C;

Iron studies ; Autoantibodies – specifically ANA, SMA, AMA, LKM. His USS abdomen shows hepatomegaly with changes consistent with cirrhosis.

10.5 What are the causes of cirrhosis?

Hepatitis ; Alcohol; Non-alcoholic fatty liver disease; Autoimmune hepatitis; Primary biliary cirrhosis; Wilson disease; Alpha 1 antitrypsin deifiency Drug induced (eg, methotrexate, amiodarone); Haemochromatosis.

11. A 50-year-old HIV-positive man presents to his primary care physician with a 1-day history of nausea and vomiting. He also has severe epigastric pain radiating to the back. Review of the patient's medical history reveals that he is taking the reverse

transcriptase inhibitor didanosine. Laboratory testing reveals an amylase level five times higher than normal and a lipase level six times higher than normal.

11.1 What is the most likely diagnosis?

Acute pancreatitis.

11.2 What are the common causes of this condition?

Acute pancreatitis occurs when pancreatic enzymes (trypsinogen, chymotrypsinogen, and phospholipase a) are activated in pancreatic tissue rather than in the lumen of the intestine, resulting in the autodigestion of pancreatic tissue. the most common causes are Gallstones (leading to common bile duct obstruction) and EtOh. Other causes include Trauma, Steroids, Mumps, Autoimmune diseases, Scorpion stings, Hyperlipidemia, and certain Drugs, including antiretrovirals (mnemonic: GET SMASHeD).

11.3 What are the top three conditions to consider in the differential diagnosis?

Cholelithiasis refers to the presence of gallstones in the gallbladder that can obstruct the cystic duct. This obstruction can lead to biliary colic (short-term waxing-and-waning pain associated with the ingestion of fatty food) or cholecystitis (more prolonged, constant pain due to inflammation of the gallbladder). Intestinal obstruction often presents with abdominal pain, nausea, and vomiting but also with changes in bowel habits. Acute coronary syndrome should be considered in patients 50 years of age or older with abdominal pain and associated risk factors. In this patient, the significantly elevated amylase and lipase levels are sensitive and specific for acute pancreatitis

11.4 What is the appropriate treatment for this condition?

Most cases (85%–90%) are self-limited and resolve within 4–7 days of the start of treatment. typical treatment for acute pancreatitis includes avoiding oral intake, aggressive intravenous fluid resuscitation, pain control, and possibly nasogastric tube placement to decrease gastric secretions in the stomach. antibiotics are not recommended in uncomplicated pancreatitis but may be of use in severe, necrotizing pancreatitis.

12. A 42-year-old man presents to his doctor for a checkup after several years without medical care. His medical history is significant for extensive smoking, alcohol, and intravenous drug abuse. On review of systems, the patient reports bleeding gums and increased bruising. Physical examination reveals an overweight white male who appears older than his stated age, mild gynecomastia, palmar erythema, and pitting edema of the lower extremities. Abdominal examination reveals shifting dullness. Relevant laboratory findings are as follows: WBC count: 3200/mm3 Hematocrit: 28% Platelets: 90,000/mm3 Blood urea nitrogen (BUN): 36 mg/dL Creatinine (Cr): 1.5 mg/dL Albumin: 3.3 g/dL Partial thromboplastin time (PTT): 40 seconds Prothrombin

time (PT): 14 seconds Alanine aminotransferase (ALT): 60 U/L Aspartate aminotransferase (AST): 100 U/L

12.1 What is the most likely diagnosis?

Alcoholic cirrhosis of the liver. the ascites, palmar erythema, and gynecomastia all suggest liver failure. the moderately elevated transaminase levels suggest a chronic process (too many hepatocytes have already died to cause the dramatic rise seen in an acute process). Further indicators of chronicity include decreased albumin, elevated pt and ptt, thrombocytopenia, and decreased hematocrit. an aSt level higher than aLt level suggests an alcoholic, rather than viral, etiology (mnemonic: toASTed).

12.2 What are the causes of this patient's gynecomastia and bleeding gums?

The liver normally degrades estrogen. In liver failure, circulating serum levels of estrogen are higher, explaining the gynecomastia and palmer erythema. Bleeding gums are likely due to thrombocytopenia secondary to splenic sequestration and decreased platelet proliferation factor secreted by the damaged liver.

12.3 How does ascites form?

Ascites (an abnormal accumulation of serous fluid in the abdominal cavity) is caused by increased intrahepatic sinusoidal pressure secondary to intrahepatic obstruction within the cirrhotic liver, decreased degradation of aldosterone by the liver leading to sodium and water retention, and decreased plasma osmotic pressure due to decreased hepatic production of albumin. physical signs of ascites include shifting dullness, bulging flanks, and a fluid wave.

12.4 What do the laboratory findings reveal about renal function?

Elevated BUN and Cr levels (BUN: Cr ratio > 20) suggest prerenal failure. the kidneys are not perfused appropriately because of decreased intravascular volume (due to ascites). prolonged intravascular volume depletion in the setting of end-stage liver disease can cause intense renal vasoconstriction and renal failure unresponsive to volume loading; known as hepatorenal syndrome.

13. A 25-year-old woman presents to her physician with a 3-day history of crampy abdominal pain that started in the epigastrium. She also reports nausea, low-grade fever, and loss of appetite. She denies changes in urination or bowel habits, dysuria, or recent sick contacts. Her last menstrual period was 2 weeks ago. Relevant laboratory findings are as follows: WBC count: 13,000/mm3 β-Human chorionic gonadotropin (β-hCG): Negative Urinalysis: Negative for blood, WBCs, leukocyte esterase, and protein.What is the most likely diagnosis? Appendicitis.

13.1 What other conditions should be considered in the differential diagnosis of a 25-year-old female with abdominal pain?

Genitourinary: ruptured Graafian follicle, ectopic pregnancy (unlikely with a negative β-hCG), pelvic inflammatory disease, and ovarian torsion (usually moderate to severe pain of acute onset). **Gastrointestinal:** Crohn disease (can initially present

without changes in bowel habits), peptic ulcer disease, Yersinia enterocolitica infection (known as the great mimicker of appendicitis). **Renal:** Urinary tract infections usually present with increased frequency of urination, dysuria, and abnormal urinalysis. Cystitis can present with abdominal pain and pyelonephritis with classic flank pain.

13.2 What is the pathophysiology of this condition?

Obstruction is often implicated as the cause of appendicitis but is not required for disease progression. the appendiceal lumen may become obstructed by a fecalith, mucosal secretions, lymphoid hyperplasia or an infectious process resulting in a distended appendix, elevated intraluminal pressure, and subsequent arterial insufficiency and tissue death.

13.3 What is the appropriate treatment for this condition?

Surgery is the preferred treatment, along with supportive intravenous fluids and empiric antibiotics (in case of rupture). The gold standard for diagnosis is Ct scan of the abdomen with contrast;

14. An 18-year-old man presents with a 2-year history of abdominal pain and increasingly frequent bloody diarrhea. He has unintentionally lost 5.4 kg (12 lb) over 6 months and now complains of joint and lower back pain. He reports that several relatives have had similar complaints, and recently his 40-year-old uncle was diagnosed with colon cancer. Physical examination reveals diffuse voluntary guarding, no rebound tenderness, no masses, and no rectal fistulas. Colonoscopy reveals inflamed mucosa with friable pseudopolyps from the rectum to the splenic flexure.

14.1 What is the most likely diagnosis?

An inflammatory bowel disease. In this case, ulcerative colitis (UC) is more likely than Crohn disease (CD) because of the genetic component, associated joint/lower back pain, and gross appearance.

14.2 How can these two conditions be differentiated from one another?

Features of UC: bimodal age distribution, possibly autoimmune in origin, males > females, involvement of the rectum in all cases, continuous lesions confined to the mucosa, friable mucosal pseudopolyps on gross morphology and crypt abscesses and ulcers on microscopic morphology, no strictures or fistulas, but possibly a “lead pipe” colon without haustra and colon shortening.

Features of CD: involvement of the entire gastrointestinal tract, including the mouth (oral ulcers) and anus (bloody diarrhea or constipation), distal ileum is often affected, transmural inflammation and thickening (“string sign” on x-ray), cobblestone mucosa, skip lesions, and creeping fat, frequently causes strictures, fistulas, and perianal disease.

2.3 What extraintestinal manifestations are possible in this patient?

Extraintestinal manifestations in UC relate to its association with HLA-B27: ankylosing spondylitis, reactive arthritis (ie, arthritis, uveitis, urethritis), primary sclerosing cholangitis, and pyoderma gangrenosum. patients with primary sclerosing cholangitis have an even greater risk of colorectal cancer (CrC).

SECTION URINARY SYSTEM
MCQs STEP 1

1. Given these data below, what is the net filtration pressure at the glomerulus. Glomerular hydrostatic pressure = 44 mm HgBowman's capsule hydrostatic pressure = 9 mm HgOsmotic pressure of plasma = 28 mm HgOsmotic pressure of tubular fluid = 0

A. −5 mm Hg
B. 7 mm Hg
C. 25 mm Hg
D. 63 mm Hg
E. 81 mm Hg

2. As part of an experimental study, a volunteer agrees to have 10 g mannitol injected intravenously. After sufficient time for quilibration, blood is drawn, and the concentration of mannitol in the plasma is found to be 65 mg/100 mL. Urinalysis reveals that 10% of the mannitol had been excreted into the urine during this time period. What is the approximate extracellular fluid volume of this volunteer?

A. 10 L
B. 14 L
C. 22 L
D. 30 L
E. 42 L

3. A researcher is studying the substance para-aminohippuric acid (PAH) and its interaction with the kidneys. She injects a volunteer with the substance. She finds that which of the following can be determined by calculating the clearance of PAH?

A. Extracellular fluid (ECF) volume
B. Effective renal plasma flow (ERPF)
C. Glomerular filtration rate (GFR)
D. Plasma volume
E. Total body water (TBW)

4. A substance that is filtered, but not secreted or reabsorbed (substance X), is infused into a volunteer until a steady state plasma level of 0.1 mg/mL is achieved. The subject then empties his bladder and waits 1 hour, at which time he urinates again. The volume of urine in the second specimen is 60 mL, and the concentration of substance X is 10 mg/mL. What is the glomerular filtration rate (GFR) in this individual?

A. 30 mL/min
B. 60 mL/min
C. 100 mL/min
D. 300 mL/min
E. 600 mL/min

5. A 32-year-old man visits the physician for a periodic health maintenance examination. He has no complaints at this time. He is 170 cm (5 ft 7 in) tall and weighs 75 kg (165 lb). Physical examination is unremarkable. In this patient, the volumes of total body water, intracellular fluid, and extracellular fluid are, respectively,

A. 40 L, 30 L, 10 L
B. 45 L, 30 L, 15 L
C. 45 L, 35 L, 10 L
D. 50 L, 25 L, 25 L
E. 50 L, 35 L, 15 L

6. The following data were collected from a normal patient before and after an intervention. Assume that plasma osmolarity and glomerular filtration rate remain constant.

	Before	After
Urine osmolarity (mOsm/L)	900	250
Urine flow rate (mL/min)	0.65	2.3
Fractional clearance of sodium	1%	1 %
Osmolar clearance (mL/min)	2.0	2.0

The intervention that would best account for the observed changes is

A. Administration of furosemide
B. Administration of hydrochlorothiazide
C. Administration of lithium
D. A high dietary intake of potassium
E. A transfusion of 2 l isotonic saline

7. In a normal patient, if renal vascular resistance is decreased to 50% of its initial value, with no change in renal artery or renal vein pressure, which of the following combinations of changes will occur?

	Renal Blood Flow	Renal Artery $[O_2]$	Renal O_2 Use
(A)	double	increase	no change
(B)	double	no change	increase
(C)	increase 50%	decrease	increase
(D)	increase 50%	increase	no change
(E)	decrease 50%	no change	decrease

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8. A normal volunteer consents to an IV infusion of p-aminohippuric acid (PAH). After a short time, the plasma PAH is 0.02 mg/mL, the concentration of PAH in urine is 13 mg/mL, and the urine flow is 1.0 mL/min. What is the effective renal plasma flow (ERPF)?

A. 0.26 mL/min
B. 26 mL/min
C. 65 mL/min
D. 260 mL/min
E. 650 mL/min

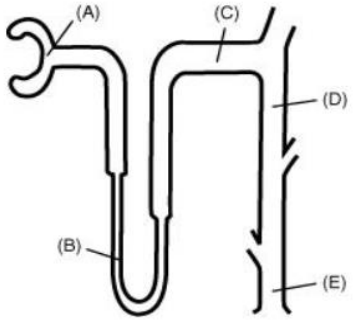
9. A 28-year-old man decides to donate a kidney to his brother, who is in chronic renal failure, after HLA typing suggests that he would be a suitable donor. He is admitted to the hospital, and his right kidney is removed and transplanted into his brother. Which of the following indices would be expected to be decreased in the donor after full recovery from the operation?

A. Creatinine clearance
B. Creatinine production
C. Daily excretion of sodium
D. Plasma creatinine concentration
E. Renal excretion of creatinine

10. In a study of renal function, the urine flow rate of an experimental animal is 2.0 mL/min, the glomerular filtration rate is 100 mL/min, and renal plasma flow is 500 mL/min. During this time, substance X is infused, and a steady state is achieved. The afferent arteriolar concentration of X is 100 mg/dL, the efferent arteriolar concentration is 120 mg/dL, and the renal vein concentration is 102 mg/dL. From these data, you can conclude that X is

A. Freely filtered and reabsorbed
B. Freely filtered and secreted
C. Freely filtered, but neither reabsorbed nor secreted
D. Not filtered, but secreted
E. Not filtered or secreted

11. A research physiologist decides to use a marker to measure the volume of total body water in a volunteer medical student. Which of the following substances would he most likely use?
A. Tritium
B. Cresyl violet
C. Evans blue
D. 131I-albumin
E. Inulin
12. A 67-year-old woman goes to her primary care physician because of muscle weakness, frequent urination, and increased thirst. On examination, her blood pressure is 180/90 mm Hg. On prior visits she has been normotensive. Laboratory studies show that she is hypernatremic and hypokalemic. A CT scan of the abdomen shows a nodule on her left adrenal gland. What is the most likely mechanism for her disorder?
A. Decreased glomerular capillary filtration coefficient
B. Excessive tubular sodium reabsorption
C. Increased renal secretion of renin
D. Increased renal vascular resistance
E. Patchy renal damage.
13. A 23-year-old man with diabetes mellitus has a glomerular filtration rate (GFR) significantly greater that normal, especially when he consumes excessive amounts of sweets. A decrease in which of the following parameters would tend to increase the glomerular capillary hydrostatic pressure?
A. Afferent arteriolar resistance
B. Bowman’s capsular hydrostatic pressure
C. Capillary filtration coefficient
D. Efferent arteriolar resistance
E. Plasma colloid osmotic pressure
14. To celebrate the end of the semester, a college student goes on an alcohol binge. She drinks day and night for 3 days straight. During this periode, her urinary flow rate increased from 1 to 10 mL/min. This increase in urinary flow rate will significantly increase the clearance of
A. Creatinine
B. Inulin
C. Penicillin
D. Phosphate
E. Urea
15. Under normal conditions virtually 100% of the filtered load of glucose is reabsorbed by the kidney tubules. Which part of the tubule shown below is expected to have the highest concentration of glucose under normal conditions?



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16. A previously well 12-year-old boy is brought to the Emergency Department with vomiting and severe abdominal cramps after a prolonged period of exercise. Elevated levels of serum creatinine and blood urea nitrogen suggest acute renal failure. Following treatment and recovery, his serum uric acid concentration (0.6 mg/dL) remains consistently below normal. To determine if his low serum uric acid level is related to renal dysfunction, uric acid clearance studies are conducted and the following data are obtained: Urine volume = 1 mL/min Urine uric acid = 36 mg/dL Which of the following is the patient's uric acid clearance?

A. 6 mL/min

B. 12 mL/min

C. 24 mL/min

D. 48 mL/min

E. 60 mL/min

17. Medical evaluation of a 55-year-old man finds the following laboratory data: increased hematocrit, increased RBC count, and increased serum erythropoietin. Which of the following abnormalities is most likely to be present in this individual?

A. Acute gastroenteritis

B. Pancreatic adenocarcinoma

C. Polycythemia rubra vera

D. Porphyria cutanea tarda

E. Renal cell carcinoma

18. Using laboratory micropuncture technique, blood plasma is collected from both the afferent arteriole and efferent arteriole of a renal cortical glomerulus. Which of the following has the lowest afferent/efferent arteriole concentration ratio?

A. Albumin

B. Chloride

C. Glucose

D. Potassium

E. Sodium

19. A patient with acute glomerulonephritis has a total plasma Ca2+ of 2.5 mmol/Land a GFR of 160 L/day. What is the estimated daily filtered load of calcium?

A. 64 mmol/day
B. 120 mmol/day
C. 240 mmol/day
D. 400 mmol/day
E. 800 mmol/day

20. Apatient with chronic renal insufficiency due to renal vascular disease has a net functional loss of nephrons. If we assume that production of urea and creatinine is constant and that the patient is in a steady state, a 50% decrease in the normal GFR will cause which of the following to occur?
A. Decrease plasma urea concentration
B. Greatly increase plasma na+
C. Increase the percent of filtered na+ excreted
D. Not affect plasma creatinine
E. Significantly decrease plasma k+

21. Which of the following is likely to cause a negative free-water clearance by the kidney?
A. Central diabetes insipidus
B. Demeclocycline, an inhibitor of the renal tubular actions of adh
C. Nephrogenic diabetes insipidus
D. Water deprivation
E. Water drinking

22. A25-year-old male athlete has just completed a long distance bicycle race during a hot, humid day. At the conclusion of the race, he provides a urine sample for testing. Assuming that his fluid intake during the race was zero, in what portion of the nephron shown in Figure 2-14 is the tubular fluid osmolality the lowest?

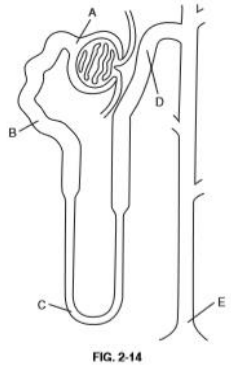

FIG. 2-14

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23. Which of the following persons will have a negative free-water clearance?
A. One who begins excreting large volumes of urine with an osmolality of 100 mosm/kg H_2O after severe head injury
B. One who drinks 2 lof distilled water in 30 minutes
C. One who is receiving lithium treatment for depression, and who develops polyuria that is unresponsive to administration adh

D. One with an oat cell carcinoma of the lung, who excretes urine with an osmolality of 1000 mosm/kg h2o
E. One with neurogenic diabetes insipidus
24. Which of the following conditions would likely be associated with decreased levels of circulating EPO?
A. Chronic alkalosis
B. Chronic renal failure
C. Emphysema
D. Pernicious anemia
E. Pulmonary fibrosis
25. Which of the following is a true statement regarding renal clearance of a substance?
A. Is measured in milligram per minute
B. Glucose is greater than that of insulin in the normal kidney
C. Insulin is zero
D. Pah remains constant regardless of the plasma level
E. Potassium clearance will increase after an injection of aldosterone
26. A 68-year-old postmenopausal female with a history of osteoprosis and essential hypertension is placed on the thiazide diuretic chlorothiazide, which has a beneficial action toward both conditions. Which letter in Figure 2-25 depicts the tubular location of epithelial cells containing a Na+/Cl−cotransport protein inhibited by thiazide diuretics?

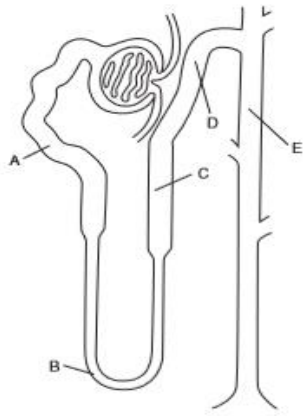

FIG. 2-25

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27. With respect to Figure 2-27, which of the following will decrease the GFR?

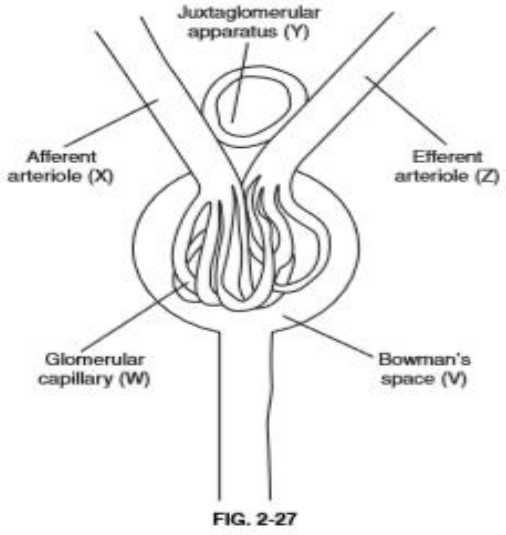

FIG. 2-27

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A. Decreased hydrostatic pressure in v
B. Decreased plasma protein concentration in w
C. Dilation of x
D. Dilation of z
E. Increased aldosterone secretion by y

28. A 23-year-old female has serum electrolytes tested as part of a routine physical. The laboratory results reveal a mild degree of hypokalemia. Which of the following will promote movement of extracellular potassium into the intracellular fluid compartment and cause hypokalemia?

A. Extracellular fluid hyperosmolality
B. Intravenous administration of a betaadrenergic blocker
C. Intravenous administration of insulin
D. Metabolic acidosis
E. Physical exercise

ANSWERS MCQs STEP 1

1. The correct answer is B. There is more than one way to think about this question. One way is to determine which of each of the descriptions corresponds to Pc, Pi, πc, and πi and then to use the Starling equation for net filtration pressure: (Pc − Pi) − (πc − πi). Perhaps faster and more intuitive is to just envision that the filtration pressure will be the difference between the forces pushing fluid out and the forces pulling fluid back into the glomerulus. The pushing forces are the hydrostatic pressure of the glomerulus (44 mm Hg) and the osmotic pressure of the tubular fluid (0). So the total pressure forcing fluid from the glomerulus into the tubular fluid is 44 mm Hg. The forces pulling the fluid back are the hydrostatic pressure of the Bowman's capsule (9 mm Hg) and the osmotic pressure of the plasma (28 mm Hg). The total pressure pushing the fluid back into the glomerulus is 9 + 28 = 37 mm Hg. The difference between the forces favoring filtration and those opposing it is therefore 44 − 37 = 7 mm Hg.

2. The correct answer is B. Volume = amount/concentration.

The amount of mannitol in the volunteer is equal to the amount injected minus the amount excreted: 10 g − 1 g = 9 g = 9000 mg. Therefore,

Volume= 9000 ÷ 65 mg/ 100 ml = 13.8 L

3. The correct answer is B. Volume = amount/concentration.

The amount of mannitol in the volunteer is equal to the amount injected minus the amount excreted: 10 g − 1 g = 9 g = 9000 mg. Therefore, ERPF= UPAH*V/ PPAH

At very high concentrations, the clearance of PAH would be less than ERPF and approaches GFR. The ECF volume (choice A) can be calculated by measuring the volume of distribution of solutes that move freely across capillary walls but cannot permeate cell membranes (e.g., inulin and mannitol).

GFR (choice C) is best calculated using a substance that is freely filtered at the glomerulus, not reabsorbed, and only minimally secreted into the urine. Creatinine fits the bill and is used clinically to measure the GFR (inulin also works and is used experimentally). Whereas the creatinine excretion exceeds filtration by 10 to 20% (because of the secretion), creatinine clearance is still a good approximation for GFR because the error due to secretion is balanced by an overestimation of plasma creatinine inherent in the measurement technique.

GRF= Ucreatine* V/ Pcreatine

The plasma volume (choice D) can be measured by measuring the volume of distribution of radioactively labeled serum albumin or of Evans blue dye (binds to albumin).

Total body water (TBW; choice E) can be measured by measuring the volume of distribution of tritium, deuterium, or antipyrine.

4. The correct answer is C. Because substance X is filtered, but not secreted or reabsorbed (like inulin), the clearance of substance X can be used to approximate GFR.
GRF= = Ux* V/ Px
GRF = (10 mg/ml)* (60 ml/hour)/ (0.1 mg/ml)= (10 mg/ml)* (1 ml/min)/ (0.1 mg/ml)=100 ml/min
5. The correct answer is B. Total body water (TBW) in liters equals approximately 60% of body weight in kilograms and therefore equals 45 L in a 75-kg person. Intracellular volume = 2/3 of TBW and is therefore 30 L in this case. Extracellular volume = 1/3 of TBW and is therefore 15 L in this case. Choices A, C, D, and E do not satisfy these condition
6. The correct answer is C. Lithium inhibits the action of antidiuretic hormone (ADH; vasopressin) on the V2 receptors in the collecting duct that regulate the permeability to water. Therefore, lithium administration will decrease water permeability in the collecting duct, which will increase urine flow rate and decrease urine osmolarity. Because ADH has minimal effects on sodium reabsorption in humans, the fractional clearance of sodium and the osmolar clearance are unaffected. (Osmolar clearance refers to the clearance of all particles, including sodium and anions, from the plasma per minute.)
Furosemide (choice A) inhibits the active reabsorption of sodium, potassium, and chloride in the thick ascending limb. This will deplete the medullary gradient, which could result in a slightly hypotonic urine, but furosemide will significantly increase the fractional clearance of sodium and hence the osmolar clearance.
Hydrochlorothiazide (choice B) inhibits the active reabsorption of sodium chloride from the distal convoluted tubule. Since the distal tubule is in the renal cortex, it will not inhibit the ability of the kidney to concentrate urine and therefore will not decrease the urine osmolarity so dramatically. It ill also increase the fractional clearance of sodium, and hence the osmolar clearance, but not as much as with furosemide.
High dietary intake of potassium (choice D) will increase plasma potassium levels, which will increase aldosterone secretion by direct action on the adrenal cortical cells. The aldosterone will decrease fractional clearance of sodium and will not increase urine flow rate.
Increased isotonic plasma volume (choice E) will increase atrial natriuretic factor (ANF), which will inhibit sodium reabsorption in the nephron and thus increase the fractional clearance of sodium as well as osmolar clearance.
7. The correct answer is B. Renal blood flow = (renal artery pressure − renal vein pressure)/renal vascular resistance (RVR). Therefore, if RVR is decreased to half its original value, with no pressure changes, renal blood flow must double (not increase 50%). Increased blood flow to the kidney and pressure in the glomerular capillaries increase renal oxygen use by increasing glomerular filtration rate, which increases the

filtered load of sodium and other solutes. Since active sodium reabsorption is load-dependent, increased tubular fluid sodium increases all active sodium reabsorption, which requires more ATP hydrolysis and synthesis (and hence more oxygen use). Renal artery oxygen concentration does not change, since it is dependent on normal lung function, not oxygen extraction by the kidney.

8. The correct answer is E. Approximately 90% of a small dose of PAH is cleared by the kidney in a single pass. If it were 100%, then the amount of PAH in urine (concentration times urine flow rate) divided by the amount of PAH in plasma would exactly equal the renal plasma flow. Because the extraction ratio (arterial-venous PAH concentration divided by arterial concentration) is 0.9 (90%) instead of 100%, physiologists speak of the quantity UPAHV/PPAH as the effective renal plasma flow, or ERPF. So, in this patient, we have (13 mg/mL × 1.0 mL/min)/0.02 mg/mL = 650 mL/min.

0.26 mL/min (choice A) can be obtained by multiplying 13 by 0.02 and dividing by 1. This value is far too low to be a normal ERPF, which is typically around 625 mL/min.

26 mL/min (choice B) is 100 times (13 × 0.02)/1. This value is far too low to be a normal ERPF, which is typically around 625 mL/min.

65 mL/min (choice C) might indicate that you set the ratio up correctly, but dropped a power of 10 in your calculations. This value is far too low to be a normal ERPF, which is typically around 625 mL/min.

260 mL/min (choice D) is 1000 times (13 3 0.02)/1, and is still too low to be a normal ERPF.

Timesaving note: If you remember that the ERPF is approximately 625 mL/min, you do not really need to calculate anything in this question. Choice E is the only reasonable answer.

9. The correct answer is A. Because creatinine is freely filtered by the glomerulus, but not secreted or reabsorbed to a significant extent, the renal clearance of creatinine is approximately equal to the glomerular filtration rate. In fact, creatinine clearance is commonly used to assess renal function in the clinical setting. When a kidney is removed, the total glomerular filtration rate decreases because 50% of the nephrons have been removed, which causes the creatinine clearance to decrease. In turn, the plasma creatinine concentration (choice D) increases until the rate of creatinine excretion by the kidneys (choice E) is equal to the rate of creatinine production by the body. Recall that creatinine excretion = GFR × plasma creatinine concentration. Therefore, creatinine excretion is normal when GFR is decreased following removal of a kidney because the plasma concentration of creatinine is elevated.

Creatinine is a waste product of metabolism. Creatinine production (choice B) is directly related to the muscle mass of an individual, but is independent of renal function.

The daily excretion of sodium (choice C) is unaffected by the removal of a kidney. The amount of sodium excreted each day by the remaining kidney exactly matches the amount of sodium entering the body in the diet.

10. The correct answer is E. If a substance is not filtered, its concentration in the efferent arteriole will be greater than the concentration in the afferent arteriole by an amount equal to the fraction of water filtered into the glomerulus. In this case, the filtration fraction (FF = glomerular filtration rate/renal plasma flow) = 100/500 = 20%, so efferent arteriolar concentration equals 120 mg/dL. All the filtered water except for that amount necessary to sustain urine flow is reabsorbed back into the peritubular capillaries, and so is present in the renal vein. In this case, the fractional excretion of water (= urine flow rate/glomerular filtration rate) = 2/100 = 2%, so renal vein concentration is 2% greater than afferent arteriolar concentration, giving a renal vein concentration of 102 mg/dL.

Note that answering this question did not require any calculations. The numbers are used in the discussion only to highlight the general concepts you should have recognized: the relationship between a substance's concentration in the afferent arteriole vs. the efferent arteriole provides information about filtration of the substance. The concentration of the substance in the afferent arteriole vs. the renal vein provides information about the secretion of that substance.

Filtration does not affect the concentration of freely filtered substances, so the afferent and efferent concentrations of any freely filtered substance will be the same (choices A, B, and C).

Secretion of a substance increases its excretion, which would decrease the renal vein concentration of the substance. Therefore, the renal vein concentration of a substance that is not filtered, but is secreted (to any significant degree), would be less than the afferent arteriolar concentration (choice D).

11. The correct answer is A. Antipyrine and tritium are both markers for total body water. Cresyl violet (choice B) is a histologic dye used to stain Nissl substance in neurons. It stains cell bodies.

Evans blue (choice C) is used to measure the plasma compartment.

131I-albumin (choice D) is used to measure the plasma compartment.

Inulin (choice E) is used to measure the extracellular fluid compartment.

12. The correct answer is B. This patient has symptoms of primary hyperaldosteronism caused by an adrenal adenoma. Symptoms for this are hypertension, muscle weakness, polyuria, polydipsia, edema, hypokalemia, hypernatremia, and metabolic alkalosis. The adrenal adenoma is secreting excess aldosterone, leading to increased sodium reabsorption and increased potassium secretion in the cortical collecting tubules. This increases intravascular volume, thus causing hypertension.

Choice A is incorrect because a decreased glomerular capillary filtration coefficient decreases GFR, leading to hypertension. This occurs in chronic glomerulonephritis due to inflammation and thickening of the glomerular capillary membranes. With an excess of aldosterone, renin amounts (choice C) are actually decreased due to negative feedback caused by excess aldosterone or by the excess extracellular fluid volume and increased arterial pressure. Increased renal vascular resistance (choice D) occurs when one renal artery is severely constricted. The ischemic tissue secretes large amounts of renin, leading to the formation of angiotensin II, which can cause hypertension. This patient does not have a disorder of the renal arteries.

Patchy renal damage (choice E) causes the damaged renal cells to secrete large amounts of renin, causing hypertension as described earlier. In this patient, the adrenal adenoma is not causing renal damage.

13. The correct answer is A. A decrease in the resistance of the afferent arteriole (i.e., arteriolar dilation) directly increases glomerular capillary hydrostatic pressure by lessening the drop in blood pressure that normally occurs along the vasculature proximal to the glomerulus. [Recall that the afferent arteriole is upstream from the glomerulus; the efferent arteriole is downstream from the glomerulus.] The glomerular capillary hydrostatic pressure is the determinant of glomerular filtration rate most subject to physiologic control. Bowman's capsular hydrostatic pressure (choice B) capillary filtration coefficient (choice C), and plasma colloid osmotic pressure (choice E) are important determinants of GFR, but they do not have any direct effect to increase or decrease the glomerular capillary hydrostatic pressure. A decrease in efferent arteriolar resistance (choice D) would tend to decrease the glomerular capillary hydrostatic pressure because the efferent arteriole is downstream from the glomerular capillaries.

14. The correct answer is E. Urine flow rate is controlled primarily by antidiuretic hormone (ADH), which regulates the amount of pure water retained in the urine. ADH also controls the reabsorption of urea in the papillary collecting duct. High urine flow rates indicate low ADH, which would increase urea clearance. In contrast, low urine flow rates indicate high ADH, which would result in a greater reabsorption of urea and a lower urea clearance. The concentration (and osmolarity) of all other solutes (choices A, B, C, and D) varies inversely with urine flow rate, resulting in no change in clearance. Recall that clearance = (urine concentration x urine flow rate)/ plasma concentration.

15. The correct answer is A. Glucose is freely filtered by the glomerular capillary membrane and totally reabsorbed in the proximal tubule under normal conditions. Therefore, the concentration of glucose is highest in the fluid leaving the Bowman capsule. The concentration of glucose is essentially zero in the thin descending limb of

loop of Henle (choice B), distal convoluted tubule (choice C), cortical collecting tubule (choice D), and medullary collecting tubule (choice E).

16. The answer is E. Clearance is a measure of how much plasma is totally cleared of a substance. It is calculated using the formula Clearance = Uuric acid × V/Puric acid = 36 mg/dL × 1 mL/min / 0.6 mg/dL = 60 mL/min.

The boy's hypouricemia is an inherited defect in the ability to reabsorb uric acid by the anion/urate exchangers on proximal tubule cells rather than an increased secretion of uric acid. Patients with hypouricemia sometimes develop exercise-induced acute renal failure. Although the mechanism is not known, some investigators suggest that uric acid has an important antioxidant role in the kidney and that the oxygen radicals produced during prolonged exercise are responsible for the acute renal failure in patients with low uric acid levels.

17. The answer is E. Polycythemia refers to an increased concentration of red blood cells (RBCs) in the peripheral blood. This is manifested by an increase in the red blood cell count, hemoglobin concentration, or hematocrit. The differential diagnosis of polycythemia includes primary polycythemia, which is due to a defect in myeloid stem cells (polycythemia rubra vera), and secondary polycythemia, which is caused by an increase in the production of erythropoietin (EPO). In patients with primary polycythemia, a myeloproliferative disorder, the red cell mass is increased but the levels of EPO are normal or decreased. That is, the abnormality is a primary defect in the red blood cells themselves. In contrast, with secondary polycythemia, the polycythemia is secondary to the increased EPO. This secondary increase in the EPO may be appropriate or inappropriate. Appropriate causes of increased EPO, in which the oxygen saturation of hemoglobin will be abnormal, include lung disease, cyanotic heart disease, living at high altitudes, or abnormal hemoglobins with increased oxygen affinity. Inappropriate causes of increased EPO include EPO-secreting tumors, such as renal cell carcinomas, hepatomas, or cerebellar hemangioblastomas. In contrast, pancreatic adenocarcinoma may be associated with migratory thrombophlebitis (Trousseau's sign). It is important to understand that an increase in red blood cell count, reported clinically as number of cells per microliter, is not the same thing as the RBC mass, which is a radioactive test that is reported in mL/kg. The RBC count and the RBC mass do not necessarily parallel each other. For example, a decreased plasma volume increases the RBC count but does not affect the RBC mass. An increased red blood cell concentration may be a relative polycythemia or an absolute polycythemia. A relative polycythemia is due to a decrease in the plasma volume (hemoconcentration), causes of which include prolonged vomiting or diarrhea (as seen with acute gastroenteritis), or the excessive use of diuretics. To summarize these clinical findings, an increased total red cell mass indicates an absolute polycythemia, increased serum EPO indicates a secondary polycythemia, and a normal oxygen

saturation of hemoglobin suggests an inappropriate secretion of EPO, such as seen with renal cell carcinoma.

18. The correct is A. The process of glomerular ultrafiltration creates a tubular fluid that is essentially protein free. Hence, as plasma passes from the afferent arteriole, through the glomerular capillaries to the efferent arteriole, the protein albumin concentration rises as approximately 20% of the fluid is filtered out, leaving the albumin behind, giving an afferent/efferent arteriole concentration ratio of approximately 0.8. By contrast, the glomerular capillary membrane is freely permeable to water and other small particles such as glucose (choice A), chloride (choice B), potassium (choice D), and sodium (choice E), so their concentrations do not change as approximately 20% of water and solute are filtered into Bowman's capsule, giving afferent/ efferent arteriole concentration ratios of 1.0.

19. The correct is C. About 40% of total plasma Ca^{2+} is bound to proteins and not filtered at the glomerular basement membrane. Therefore, the estimated daily filtered load is 1.5 mmol/L× 160 L/day = 240 mmol/day. The exact amount of free versus total Ca^{2+} depends on the blood pH: free Ca^{2+} increases during acidosis and decreases during alkalosis. None of the other choices (A, B, D, and E) reflect the correct renal calcium filtration load.

20. The correct is C. Both Na+ and K+ excretion are tightly regulated. Thus, as GFR decreases in disease, the percentage of filtered Na+ or K+ excreted increases to maintain a normal amount of Na+or K+ excretion (assuming Na+ and K+ intake remain the same). Substances like urea (choice A) (some reabsorption) and creatinine (choice D) (almost exclusively excreted by glomerular filtration) have no adaptive mechanisms to regulate plasma levels. Thus, a significant decrease in GFR results in significant increases in plasma creatinine and urea (assuming production of both substances remains constant). This is because the amount of substance x that is excreted ($Ux \cdot V$) equals the amount produced. Furthermore, $Ux \cdot V = GFR \cdot Px$. If GFR decreases, Px increases. Because of the increase in percent filtered Na+ and K+ that is excreted, an increase in plasma Na+(choice B) or a decrease in plasma K+(choice E) would not be expected with a GFR that is 50% of normal. Ux ÷urine concentration of x; Px ÷ plasma concentration of x; V ÷ urine volume.

21. The correct is D. Water deprivation will eventually increase extracellular fluid osmolality, which triggers release of ADH. ADH acts on the collecting duct to increase water reabsorption, thus making the excreted urine more concentrated via a negative free-water clearance. Choices B and C will reduce the sensitivity of the collecting duct to normal circulating ADH. Choices A and E will reduce the amount of ADH secreted by the posterior pituitary.

22. The correct is D. The bicycle racer is likely dehydrated from his exercise and ADH would be secreted by the posterior pituitary in response to increased extracellular

osmolality. The area of the nephron with the lowest osmolality will be the early distal tubule (choice D), a nephrondiluting segment. The fluid in Bowman's capsule (choice A) will be at the same osmolality as the plasma entering the glomerular capillaries. The fluid at the end of the proximal tubule (choice B) is isoosmotic with the Bowman's capsule fluid while the fluid in the thin descending loop of Henle (choice C) is greatly concentrated due to water reabsorption into the hyperosmotic medullary interstitium. The fluid at the end of the collecting duct (choice E) can be very concentrated or very dilute, but since ADH greatly increases water reabsorption in this segment, the fluid becomes very concentrated.

23. The correct is D. A negative free-water clearance occurs when the kidney is reabsorbing more water than it is excreting into the urine and is regulated by ADH. Choice D is correct because lung cancer can cause exogenous production of ADH, which will stimulate increased renal water reabsorption and thus a negative freewater clearance. Choice Ais incorrect because the decreased ADH secretion that may occur following a severe head injury will result in a positive free-water clearance. Choice B is incorrect because rapid intake of 2 L of water will inhibit ADH secretion and thus trigger a positive free-water clearance. Choice C is incorrect because the insensitivity to ADH that occurs during lithium treatment will increase water excretion and thus cause a positive free-water clearance. Choice E is incorrect because a person with neurogenic diabetes insipidus has a reduced secretion of ADH, which will cause reduced renal water reabsorption and thus a positive free-water clearance.

24. The correct is B. EPO is a glycoprotein produced primarily in the kidney, thus EPO levels tend to be depressed in chronic renal failure. EPO is a growth factor that stimulates the production of red blood cells. Its production by the kidney is triggered by low tissue oxygenation. Any condition that decreases the oxygen-carrying capacity of the blood (such as anemia, choice D) or that causes hypoxia by decreasing lung function (such as emphysema or pulmonary fibrosis, choices C and E) will produce elevated levels of circulating EPO. Alkalosis (choice A) increases hemoglobin's affinity for oxygen, making it more difficult for tissues to extract oxygen from the blood. In alkalosis, tissues thus tend to have lower oxygen content, with a resultant increase in circulating EPO levels.

25. The correct is E. Choice E is correct since the clearance of potassium is normally regulated by the action of aldosterone on the distal tubule exchange of sodium reabsorption with potassium secretion. Choice Ais incorrect because renal clearance represents the volume of plasma completely cleared of a substance per unit time, hence the units for renal clearance are milliliter per minute, and not milligram per minute. Choice B is incorrect because a normal kidney reabsorbs 100% of the filtered glucose, so glucose clearance is zero. By contrast, a significant amount of inulin is usually cleared by the kidney. Choice C is incorrect because although inulin is not secreted by

the tubule as is PAH, inulin is filtered but not reabsorbed and thus a normal kidney will clear approximately 20% of the inulin from the plasma. Choice D is incorrect because PAH is actively secreted by the proximal tubule. Above a certain plasma level, PAH secretion no longer can increase and thus clearance (calculated as the ratio of urine to plasma concentration multiplied by urine flow) will decline as plasma PAH concentration increases faster than urine PAH concentration.

26. The correct is D. The epithelial cells of the early portion of the distal tubule contain a Na+/Cl− cotransporter that is inhibited by thiazide diuretics which promote a diuresis and a natriuresis, and which secondarily, promote increased renal reabsorption of filtered calcium. Choices Aand B denote the proximal and thin loop of Henle segments, respectively; which do not have the properties of the early distal tubular segment. Likewise, choices C and E denote the thick ascending loop of Henle and the collecting duct, which also do not have the same properties as the early distal tubular segment.

27. The correct is D. These choices revolve around the Starling forces that directly regulate glomerular filtration. Choice D is correct and choice C is incorrect because glomerular capillary pressure is regulated by the ratio of upstream (afferent arteriole) and downstream (efferent arteriole) resistance to flow. Dilation of the afferent arteriole (choice C) will increase glomerular capillary pressure and increase filtration, whereas dilation of the efferent arteriole (choice D) will decrease the pressure and thus decrease filtration. Choice A is incorrect because Bowman's space pressure normally acts to oppose filtration, hence a decreased pressure will increase filtration. Choice B is incorrect because the osmotic pressure of the plasma proteins opposes filtration, so a decreased plasma protein concentration will predictably increase filtration. Choice E is incorrect, first of all because the juxtaglomerular apparatus does not secrete aldosterone, but instead secretes renin, which ultimately can trigger aldosterone secretion from the adrenal cortex via angiotensin II. Secondly, aldosterone is likely to trigger salt and water retention by an action on the distal nephron of the kidney, which is likely to alter the Starling forces in favor of increased glomerular filtration.

28. The correct is C. Among other actions, insulin is known to stimulate the uptake of potassium into cells of the body via stimulation of the Na+, K+ATPase. Choices A, B, D, and E, will either have the opposite action, or no effect.

CLINICAL CASES

1. A 37-year-old man visits his physician because he has noticed blood in his urine over the past week. He denies increased frequency or dysuria. He admits intermittent aching back pain over the past few months, which he attributes to sitting at his desk for long periods of time each day at work. Ultrasound shows massively enlarged kidneys bilaterally. The surface of the right kidney is studded with several well-circumscribed cysts, and the left kidney demonstrates similar lesions. His blood pressure is 148/84 mm Hg.

1.1 What is the most likely diagnosis?

Autosomal dominant polycystic kidney disease (aDpKD). aDpKD has a prevalence of approximately 1:1,000 and is the leading genetic cause of chronic renal failure. It is diagnosed with imaging.

2. A 70-year-old African-American man returns to his physician for his annual follow-up visit after prior diagnosis of monoclonal gammopathy of undetermined significance (MGUS). He reports he continues to have mild lower back pain and proximal extremity weakness and notes that he has had polydipsia and polyuria in the past several months. Physical examination is unremarkable. Urinalysis is notable for aminoaciduria, glucosuria, and phosphaturia. Relevant laboratory results are as follows: Sodium: 133 mEq/L Potassium: 3.3 mEq/L Chloride: 110 mEq/L Bicarbonate: 18 mEq/L Glucose: 85 mg/dL Calcium: 8.3 mg/dL Phosphate: 2.1 mg/dL Uric acid: 2.0 mg/dL

2.1 What is the most likely diagnosis?

This patient has likely developed Fanconi syndrome (FS), which is characterized by a generalized transport defect in the proximal tubules, thus representing a proximal (type II) renal tubular acidosis (RTA). FS is either acquired or inherited. It can be acquired as a rare complication of plasma cell dyscrasias, including multiple myeloma, MGUS, Waldenström macroglobulinemia, and primary amyloidosis. FS may also result from Sjögren syndrome, heavy metal poisoning, and drug reactions. If inherited, FS is mostly transmitted as an autosomal recessive trait. Although all of the urinalysis and laboratory findings support the diagnosis of FS, in a patient with MGUS and back pain, multiple myeloma should be on the differential.

2.2 What are the functions of the proximal convoluted tubules?

The proximal convoluted tubules are the “workhorses of the nephron” and reabsorb all glucose and amino acids and the majority of filtered sodium, potassium, phosphate, bicarbonate, and water. Ammonia is also secreted to buffer distally secreted H+.

2.3 What is the pathogenesis of this condition?

FS is characterized by multiple proximal tubular transport defects. the exact mechanism varies with the etiology of FS. In FS associated with monoclonal

gammopathies, kappa-type Bence Jones proteins have been found to be reabsorbed by proximal tubular cells. Subsequent failure to complete proteolysis of these light

2.4 What medication can mimic the presentation of this condition?

Acetazolamide works by inhibiting bicarbonate in the proximal tubule and thus can cause proximal rta.

2.5 What is glomerular filtration rate (GFR)?

The glomerulus filters plasma predominantly by molecular size and net charge. GFR measures the amount of plasma that is filtered into the Bowman's capsule from the glomerular capillaries within the glomeruli per unit time (milliliters per minute) and is a marker of renal function. Infusion of inulin is necessary for an accurate assessment of GFR because it is fully filtered but is not reabsorbed, secreted, metabolized, or produced endogenously. GFR, however, is more conveniently approximated by creatinine clearance (CCr), as represented by the formula: GFR = UCr × V/pCr = CCr (pCr, plasma concentration of creatine; UCr, urine concentration of creatine; V, volume of urine per unit time.) Since creatinine, unlike inulin, is secreted in the kidney, a creatinine-based GFr results in an overestimate of the true GFR. In FS, GFR is normal.

2.6 What is the mechanism of the observed hypokalemia?

The primary function of the kidneys is to preserve volume though the reabsorption of sodium and free water. In FS, there is an increased distal delivery of sodium due to the incompetent proximal tubules. the principal cells within the collecting ducts will compensate by increasing sodium reabsorption through an exchange for potassium. this results in potassium clearance rates that may be more than twice the GFr, indicating net tubular secretion. Metabolic acidosis secondary to defective proximal tubule bicarbonate reabsorption may also contribute to potassium loss, as cells tend to remove h+ from circulation through an exchange for potassium, thereby increasing the filtered load of potassium.

3. A 45-year-old man is brought to the emergency department by his mother after 2 days of worsening confusion, polyuria, polydipsia, and constipation. His past medical history is significant only for chronic osteomyelitis of the right arm secondary to a burn injury sustained in a house fire 5 years ago. Physical examination is unremarkable except for uniformly depressed deep tendon reflexes. The patient is also visibly uncomfortable and disoriented and is uncooperative during much of the examination. Electrocardiogram (EKG) reveals a QTc interval of 390 msec. Relevant laboratory findings are as follows: Serum calcium: 11.88 mEq/L Serum albumin: 1.45 mEq/L BUN: 21mg/dL Serum creatinine: 1.4 mg/dL Parathyroid hormone (PTH): 12 pg/mL Alkaline phosphatase: 980 U/L

3.1 What is the most likely diagnosis?

hypercalcemia. Symptoms include lethargy, hyporeflexia, confusion, depression, headaches, psychosis, bradycardia, a shortened Qt interval, nausea, vomiting,

constipation, muscle weakness, polyuria, polydipsia, and gastroduodenal ulcer disease (secondary to calcium-induced gastrin release).

3.2 How are ionized calcium and albumin used in the diagnosis of this condition?

Ionized calcium is the primary determinant of cellular and membrane activity. however, routine reporting of serum calcium levels includes calcium that is bound to proteins. approximately 45% of calcium circulates in the free or ionized form, and another 40% is bound to albumin (the remainder is bound to various anions). accurate assessment of calcium levels therefore requires the simultaneous measurement of albumin and serum calcium levels.

3.3 How does hypoalbuminemia affect this condition?

Hypoalbuminemia can decrease measured serum calcium levels independently of any net change in ionized calcium levels. For each decrease of 1.0 g/dL in serum albumin below the laboratory's reference normal value, 0.8 mg/dL should be added to the total calcium measured (the opposite is done in cases of hyperalbuminemia). Given the patient's hypoalbuminemia, the actual total serum calcium level is even greater than the already elevated total calcium observed.

3.4 What are the two most common causes of hypercalcemia?

Hyperparathyroidism (thus the importance of checking PTH levels) and malignancy are the leading causes of hypercalcemia.

3.5 What are the appropriate treatments for this condition?

Symptomatic hypercalcemia, as seen in this patient, should first be treated with a saline infusion to expedite renal calcium excretion. Furosemide may be initiated to promote calciuresis only after the patient is volume replete. Furosemide promotes natriuresis and increases calcium excretion. Bisphosphonates inhibit osteoclast activity and are also used to treat hypercalcemia. Given this patient's history of chronic osteomyelitis, suppressed PTH, and dramatically elevated alkaline phosphatase levels, there is a high clinical suspicion for underlying malignancy.

4. A 58-year-old man presents to the emergency department with a 1-week history of progressive weakness, fatigue, and shortness of breath on exertion. On physical examination, the man's heart rate is irregularly irregular, and his lung examination is notable for bilateral crackles that are most pronounced at the bases. X-ray of the chest demonstrates pulmonary edema. The patient is started on digoxin and furosemide. Three days later, he complains of light-headedness with progressive weakness. Laboratory values are significant for a serum sodium level of 142 mEq/L and a serum potassium level of 2.7 mEq/L. An EKG demonstrates torsades de pointes.

4.1 What is the most likely diagnosis? Hypokalemia.

What two main factors predisposed the patient to torsades de pointes?

The patient was started on digoxin to increase cardiac output and to treat the atrial fibrillation; furosemide was added to treat the pulmonary edema. However, furosemide

in the setting of congestive heart failure can lead to severe hypokalemia (serum potassium level < 2.5 meq/L). Hypokalemia has been shown to promote digitalis-induced arrhythmias, even when digitalis levels are in the therapeutic range. Digitalis toxicity can induce fatal arrhythmias.

4.2 What are the most common causes of this condition?

There are three broad etiologies of hypokalemia: decreased intake, increased losses, and increased translocation into cells. Decreased intake is a rare cause of hypokalemia. Increased losses can be: gastrointestinal, from diarrhea, laxative abuse, VIpomas, nasogastric suctioning, and/or vomiting; urinary, as from diuretic use, polyuria and other salt-wasting conditions, hyperaldosteronism, loss of gastric secretions, or metabolic acidosis; due to excessive sweating; increased translocation into cells occurs with hypothermia, alkalosis, increased insulin availability, and β-adrenergic activity.

4.3 How does alkalosis lead to this condition?

The Na+-K+-atpase pump keeps intracellular potassium levels much higher than the serum/extracellular level. However, in the setting of alkalosis, hydrogen ions leave cells to minimize ph change. In the process, hydrogen ions function in an apparent exchange for potassium that can lead to hypokalemia.

4.4 How is metabolic acidosis associated with this condition?

Metabolic acidosis causes an exchange of hydrogen ions into the cells for potassium ions into the plasma, leading to hyperkalemia. However, in the setting of metabolic acidosis (notably diabetic ketoacidosis), urinary potassium excretion is also increased. This leads to a situation in which potassium is being moved from the cells and then excreted in the urine. as a result, although the serum potassium level is normal or even high in metabolic acidosis, the total body stores are actually low. The hypokalemia often reveals itself once the acidosis is corrected.

4.5 What are the appropriate treatments for this condition?

Potassium can be repleted either directly (ie, with potassium chloride) or through the use of a potassiumsparing diuretic such as amiloride, spironolactone, or triamterene. amiloride is often the diuretic of choice, as it lacks the hormonal adverse effects of spironolactone (gynecomastia and amenorrhea).

5. An 86-year-old woman living in a nursing home is brought to the attention of the medical staff because of her lethargy. Relatives note that she has been unable to recognize family members in the past week. Her past medical history is notable for Alzheimer disease, osteoporosis, and hypertension. Her medications include memantine, donepezil, alendronate, and hydrochlorothiazide, the dose of which was recently increased. Physical examination reveals a blood pressure of 139/80 mm Hg. The patient is sleepy and oriented only to person. CT scan of the head is unremarkable. Laboratory testing is notable for a sodium concentration of 122 mEq/L and normal glucose levels, renal function, and hematocrit.

5.1 What is the most likely diagnosis?

Hyponatremia, which is commonly defined as a serum sodium concentration ≤ 135 meq/L. hyponatremia is more prevalent in the hospital setting or in nursing homes.

5.2 What are the common causes of this condition?

Most cases of hyponatremia can be thought of as arising from three general mechanisms: too much water, such as in the syndrome of inappropriate secretion of antidiuretic hormone (SIaDh), nephrotic syndrome, congestive heart failure, cirrhosis, or excessive fluids (iatrogenic or marathon runners); too little salt, such as in salt-wasting conditions (eg, aldosterone resistance or deficiency), diuretic abuse, dehydration, or vomiting; high serum osmolality, which most often occurs in the setting of hyperglycemia. this is a form of pseudohyponatremia where you correct for Na according to the glucose level.

5.3 What symptoms are typically associated with this condition?

The decreased osmolarity (for most cases of hyponatremia) causes an osmotic water shift that increases intracellular fluid volume. Clinical manifestations are typically neurologic in nature secondary to cerebral edema within the confines of the cranial vault. Nonspecific symptoms, such as malaise or nausea, are common. Headache, lethargy, confusion, and obtundation may appear as sodium levels fall further. Stupor, seizures, and coma can occur if progression is rapid or concentrations fall below 120 meq/L.

5.4 What is the pathogenesis of this condition in this particular patient?

This patient is likely suffering from diuretic-induced hyponatremia. Thiazides deplete serum sodium and potassium levels and stimulate aDh-mediated water retention. It should be noted, though, that loop diuretics are unlikely to cause hyponatremia, as the maximal urine concentrating ability, and thereby water retention, is reduced with the decrease in medullary interstitial tonicity. If hyponatremia develops over a period of days rather than acutely, the brain cells react to hyponatremia by secreting salts and, over time, organic osmolyte to prevent excess water entry and swelling. This may explain why no significant swelling can be seen on Ct scan of the head.

5.5 What other laboratory test will help identify the etiology of this condition in this patient?

Plasma osmolality, urine osmolality, fractional excretion of sodium, urine sodium concentration, and urine potassium concentration are helpful. If diuretics are responsible, as in this case, the plasma osmolality may be slightly low. Urine osmolality is elevated, as thiazides stimulate antidiuretic hormone (ADh). Urine sodium is elevated because of a thiazide-mediated decrease in reabsorption. However, some of the excess sodium delivered to the collecting duct is reabsorbed at the expense of potassium. Urine potassium therefore would also be elevated.

5.6 What is the most appropriate treatment for this condition?

Rapid correction of chronic hyponatremia can result in central pontine myelinolysis, a diffuse (not limited to the pons) demyelination syndrome. a rapid increase in serum osmolarity leads to brain cell shrinkage, and this is believed to result in demyelination. If hyponatremia occurs suddenly, over a few hours, then rapid correction is unlikely to cause demyelination as the brain will not have time to undergo compensatory measures as discussed above.

6. A 24-year-old woman presents to the emergency department with nausea, vomiting, tachypnea, sweating, and tinnitus. Her mother reports that she found an empty bottle of aspirin in the patient's bedroom. Physical examination reveals a temperature of 38.6°C (101.5°F), a heart rate of 100/min, a respiratory rate of 40/min, and altered mental status. Arterial blood gas is notable for a pH of 7.28, partial carbon dioxide pressure (Pco2) of 25 mm Hg, and bicarbonate of 17 mEq/L. Her anion gap is 22 mEq/L. Salicylate levels are pending. Intravenous fluids are initiated, and charcoal and sodium bicarbonate are administered orally. The patient is transferred to the intensive care unit for further stabilization.

6.1 What is the acid-base disturbance in this patient?

A mixed metabolic acidosis and respiratory alkalosis. the pH < 7.35 indicates acidemia. respiratory acidosis is unlikely given the below-normal pco2 and the high anion gap. In this setting the low bicarbonate indicates metabolic acidosis. Applying Winter's formula ($Pco_2 = (1.5 \times [HCO_3-]) + 8 \pm 2$), the appropriate respiratory compensation is pco2 = 1.5(17) + 8 = 33.5 ± 2. The "compensation" in this case is therefore excessive, suggesting an independent respiratory alkalotic process, which is consistent with a respiratory rate of 40/min.

6.2 What are the causes and two main types of metabolic acidosis?

Metabolic acidosis derives from the loss of bicarbonate or the retention of acid, leading to a non–anion gap acidosis in the former, and an anion gap acidosis in the latter. A non–anion gap acidosis is always the result of conditions that result in hyperchloremia (Cl– > 109 meq/L), such as renal tubular acidosis. The excess chloride suppresses bicarbonate reabsorption. Metabolic acidosis that is caused by retention of acid results in an anion gap metabolic acidosis because unmeasured acidic anions are retained. To recall the major causes of anion gap metabolic acidosis, the mnemonic MUD PILES is useful (Methanol, Uremia, Diabetic ketoacidosis, Paraldehyde or Phenformin, Iron tablets or Isoniazid, Lactic acidosis, Ethylene glycol, Salicylates.)

6.3 What are the causes of respiratory alkalosis?

Anything that stimulates the central respiratory drive and causes hyperventilation, such as cerebrovascular accidents or neurologic disease, can cause respiratory alkalosis. hypoxia, such as that caused by anemia, high altitudes, and pulmonary disease, can likewise increase respiratory rate and respiratory alkalosis. Other hyperventilatory

states such as mechanical overventilation or voluntary hyperventilation, such as in cases of anxiety, can also be causative.

6.4 How is anion gap calculated?

The equation $Na+ - (Cl- + HCO_3-)$ is typically used. K+ is typically not included because of its small contribution as a predominantly intracellular cation. a normal anion gap is 6–12 meq/L. the presence of unmeasured anions, such as salicylates, displaces and reduces serum bicarbonate, thereby producing an apparently larger gap.

6.5 What is the pathogenesis of this patient's condition?

Aspirin is hydrolyzed to salicylate once ingested. At toxic levels, salicylates cause a primary respiratory alkalosis by stimulating the medullary respiratory center to hyperventilate. Salicylates also stimulate skeletal muscle metabolism, increasing oxygen consumption and carbon dioxide production. This further stimulates hyperventilation. The metabolic acidosis component occurs because salicylates cause both lipolysis and uncoupling of oxidative phosphorylation, resulting in the production of organic acids, pyruvate, and ketones.

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