

Jawetz,

27th

Questions

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Spore forming. +ve

diarrhea. This disease is generally less severe than the classic form of pseudomembranous colitis. As many as 25% of cases of antibiotic-associated diarrhea are caused by *C difficile* infection. Other *Clostridium* species such as *C perfringens* and *C sordellii* have also been implicated. The latter two species are not associated with pseudomembranous colitis.

Concept Checks

- *Clostridium* species are large, spore-forming, anaerobic gram-positive rods that are found in the environment and in the gastrointestinal tracts of a large number of animals and humans.
- The clostridia are categorized by their ability to ferment carbohydrates and to digest proteins as well as by the toxins they produce.
- Toxins produced by pathogenic clostridia are responsible for a variety of serious diseases that include botulism, tetanus, and gas gangrene.
- *C botulinum* produces botulinum toxin, one of the most potent neurotoxins on the planet, responsible for botulism, a disease characterized by flaccid paralysis.
- *C tetani* also produces a neurotoxin, tetanospasmin, that blocks release of inhibitory neurotransmitters resulting in tetanus, a disease characterized by spastic paralysis.
- Other *Clostridium* species cause invasive wound infections (gangrene), septicemia, antibiotic-associated diarrhea, and food poisoning depending on the epidemiologic circumstances and the types of enzymes or toxins elaborated.

REVIEW QUESTIONS

1. A housewife who lives on a small farm is brought to the emergency department complaining of double vision and difficulty talking. Within the past 2 hours, she noted a dry mouth and generalized weakness. Last night she served home-canned green beans as part of the meal. She tasted the beans before they were boiled. None of the other family members are ill. On examination, there is symmetrical descending paralysis of the cranial nerves, upper extremities, and trunk. The correct diagnosis is which one of the following?
 - (A) Tetanus
 - (B) Strychnine poisoning
 - (C) Botulism
 - (D) Morphine overdose
 - (E) Ricin intoxication
2. Which one of the following is an important virulence factor of *Bacillus anthracis*?
 - (A) Protective antigen
 - (B) Lipopolysaccharide
 - (C) Pili
 - (D) A toxin that inhibits peptide chain elongation factor EF-2
 - (E) Lecithinase
3. A young man sustains major soft tissue injury and open fractures of his right leg after a motorcycle accident. One day later, he has a temperature of 38°C, increased heart rate, sweating, and restlessness. On examination, the leg is swollen and tense, with thin, dark serous fluid draining from the wounds. The skin of the leg is cool, pale, white, and shining. Crepitus can be felt in the leg. His hematocrit is 20% (~50% of normal), and his circulating hemoglobin is normal. His serum shows free hemoglobin. Which of the following microorganisms is the most likely cause of this infection?
 - (A) *Clostridium tetani*
 - (B) *Staphylococcus aureus*
 - (C) *Escherichia coli*
 - (D) *Bacillus anthracis*
 - (E) *Clostridium perfringens*
4. For the patient described in Question 3, which of the following is likely to be responsible for the hemolysis?
 - (A) Elongation factor
 - (B) Tetanospasmin
 - (C) Lecithinase
 - (D) Streptolysin O
 - (E) Toxin B
5. The reported incubation period for inhalational anthrax can be up to
 - (A) 2 days
 - (B) 10 days
 - (C) 3 weeks
 - (D) 6 weeks
 - (E) 6 months
6. A food commonly associated with *Bacillus cereus* food poisoning is
 - (A) Fried rice
 - (B) Baked potato
 - (C) Hot freshly steamed rice
 - (D) Green beans
 - (E) Honey
7. Tetanus toxin (tetanospasmin) diffuses to terminals of inhibitory cells in the spinal cord and brainstem and blocks which of the following?
 - (A) Release of acetylcholine
 - (B) Cleavage of SNARE proteins
 - (C) Release of inhibitory glycine and γ -aminobutyric acid
 - (D) Release of Protective Antigen
 - (E) Activation of acetylcholine esterase
8. A 45-year-old man who immigrated to the United States 5 years ago sustained a puncture injury to the lower part of his right leg when his rotary lawn mower threw a small stick into his leg. Six days later, he noticed spasms in the muscles of his right leg; on day 7, the spasms increased. Today—day 8—he had generalized muscle spasms, particularly noticeable in the muscles of his jaw. He was unable to open his jaw and came to the emergency department (ED). In the ED, you see a man who is alert and lying quietly in bed. A door slams down the hall, and suddenly he has general muscle spasm with arching of his back. The correct diagnosis is which of the following?
 - (A) Botulism
 - (B) Anthrax
 - (C) Gas gangrene
 - (D) Tetanus
 - (E) Toxic shock syndrome

9. Which of the following statements about tetanus and tetanus toxoid is correct?
- Tetanus toxin kills neurons.
 - Tetanus toxoid immunization has a 10% failure rate.
 - The mortality rate of generalized tetanus is less than 1%.
 - Double vision is commonly the first sign of tetanus.
 - Tetanus toxin acts on inhibitor interneuron synapses.
10. A 67-year-old man had surgery for a ruptured sigmoid colon diverticulum with an abscess. A repair was done, and the abscess was drained. He was treated with intravenous gentamicin and ampicillin. Ten days later and 4 days after being discharged from the hospital, the patient developed malaise, fever, and cramping abdominal pain. He had multiple episodes of diarrhea. His stool was positive for occult blood and the presence of polymorphonuclear cells. On sigmoidoscopy, the mucosa was erythematous and appeared to be inflamed, and there were many raised white to yellowish plaques 4–8 mm in diameter. Which of the following is the likely cause of the patient's problem?
- Staphylococcus aureus* enterotoxin
 - Bacillus cereus* toxin
 - Clostridium difficile* toxins
 - Clostridium perfringens* toxin
 - Enterohemorrhagic *Escherichia coli*
11. Infant botulinum has been associated with all of the following *Clostridium* species EXCEPT:
- Clostridium baratii*
 - Clostridium septicum*
 - Clostridium butyricum*
 - Clostridium botulinum*
12. Which of the following food items is most frequently associated with infant botulism?
- Corn syrup
 - Canned infant formula
 - Liquid multivitamins
 - Honey
 - Jarred baby food
13. All of the following are properties characteristic of *Bacillus anthracis* EXCEPT:
- Motility on wet mount examination
 - Medusa head colonies
 - Poly-D-glutamic acid capsule
 - In vitro susceptibility to penicillin
 - Absence of hemolysis on 5% sheep blood agar
14. Which of the following statements regarding vaccination for *Bacillus anthracis* is correct?
- It is routinely available for all citizens of the United States.
 - Recombinant vaccine trials have shown good safety and efficacy.
 - The current vaccine is well tolerated.
 - A single dose is adequate after exposure to spores.
 - Vaccination of animals is not useful.
15. All of the following statements regarding *Clostridium perfringens* are correct EXCEPT:
- It produces an enterotoxin.
 - It produces a double zone of β -hemolysis when grown on blood agar.
 - Some strains are aerotolerant.
 - It is the most common cause of antibiotic-associated diarrhea.
 - It can cause intravascular hemolysis.

Answers

- | | | | |
|------|------|-------|-------|
| 1. C | 5. D | 9. E | 13. A |
| 2. A | 6. A | 10. C | 14. B |
| 3. E | 7. C | 11. B | 15. D |
| 4. C | 8. D | 12. D | |

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NON - spore forming, aerobic, +ve

Concept Checks

- Several members of the large group of aerobic Actinomycetes are modified acid-fast positive, most commonly *Nocardia* and *R. equi*.
- *Nocardia* species are branching, beaded gram-positive rods found in soil and other environmental sources that cause systemic disease primarily in immunocompromised patients.
- *Nocardia* species are best identified after recovery on routine media by using molecular methods such as 16SrRNA gene or other gene target sequencing.
- Trimethoprim-sulfamethoxazole is the drug of choice for treatment of *Nocardia* infections. The use of other agents should be dictated by results of susceptibility testing.

ACTINOMYCETOMA

Mycetoma (Madura foot) is a localized, slowly progressive, chronic infection that begins in subcutaneous tissue and spreads to adjacent tissues. It is destructive and often painless. In many cases, the cause is a soil fungus (Eumycetoma) that has been implanted into the subcutaneous tissue by minor trauma. This form of mycetoma is discussed in Chapter 45. An actinomycetoma is a mycetoma caused by filamentous branching bacteria. The actinomycetoma granule is composed of tissue elements and gram-positive bacilli and bacillary chains or filaments (1 μm in diameter). The most common causes of actinomycetoma are *Actinomadura madurae*, *Streptomyces somaliensis*, *Actinomadura pelletieri*, *Nocardia asteroides*, and *N. brasiliensis*. These and other pathogenic actinomycetes are differentiated by biochemical tests, chromatographic analysis of cell wall components, and molecular techniques. Actinomycetomas respond well to various combinations of streptomycin, trimethoprim-sulfamethoxazole, and dapson if therapy is begun early before extensive damage has occurred. In advanced disease, amputation may be required.

Often students are confused by the terms “Actinomycetes” and “Actinomycosis.” The former have been described earlier; the latter is an infection caused by members of the anaerobic gram-positive genus *Actinomyces*. *Actinomyces* species and the disease actinomycosis are described in more detail in Chapter 21.

REVIEW QUESTIONS

1. Three months ago, a 53-year-old woman had surgery and chemotherapy for breast cancer. Four weeks ago, she developed a cough occasionally productive of purulent sputum. About 2 weeks ago, she noted a slight but progressive weakness of her left arm and leg. On chest examination, rales were heard over the left upper back when the patient breathed deeply. Neurologic examination confirmed weakness of the left arm and leg. Chest radiography showed a left upper lobe infiltrate. Contrast-enhanced computed tomography showed two lesions in the right hemisphere. Gram stain of a purulent sputum specimen showed branching gram-positive rods that were partially acid fast. Which of the following organisms is the cause of this patient's current illness?
 - (A) *Actinomyces israelii*
 - (B) *Corynebacterium pseudodiphtheriticum*
 - (C) *Aspergillus fumigatus*
 - (D) *Nocardia farcinica*
 - (E) *Erysipelothrix rhusiopathiae*
2. The drug of choice to treat this patient's infection (Question 1) is
 - (A) Penicillin G
 - (B) Trimethoprim-sulfamethoxazole
 - (C) Gentamicin
 - (D) Amphotericin B
 - (E) A third-generation cephalosporin
3. It is particularly difficult to differentiate *Erysipelothrix rhusiopathiae* from
 - (A) *Corynebacterium diphtheriae*
 - (B) *Bacillus cereus*
 - (C) *Actinomyces israelii*
 - (D) *Nocardia asteroides*
 - (E) *Lactobacillus* species
4. Movement of *Listeria monocytogenes* inside of host cells is caused by
 - (A) Inducing host cell actin polymerization
 - (B) The formation of pili (fimbriae) on the listeriae surface
 - (C) Pseudopod formation
 - (D) The motion of listeriae flagella
 - (E) Tumbling motility
5. An 8-year-old boy, who recently arrived in the United States, develops a severe sore throat. On examination, a grayish exudate (pseudomembrane) is seen over the tonsils and pharynx. The differential diagnosis of severe pharyngitis such as this includes group A streptococcal infection, Epstein-Barr virus (EBV) infection, *Neisseria gonorrhoeae* pharyngitis, and diphtheria. The cause of the boy's pharyngitis is most likely:
 - (A) A gram-negative bacillus
 - (B) A single-stranded positive-sense RNA virus
 - (C) A catalase-positive, gram-positive coccus that grows in clusters
 - (D) A club-shaped gram-positive bacillus
 - (E) A double-stranded RNA virus
6. The primary mechanism in the pathogenesis of the boy's disease (Question 5) is
 - (A) A net increase in intracellular cyclic adenosine monophosphate
 - (B) Action of pyrogenic exotoxin (a superantigen)
 - (C) Inactivation of acetylcholine esterase
 - (D) Action of enterotoxin A
 - (E) Inactivation of elongation factor 2
7. *Corynebacterium jeikeium* is
 - (A) Catalase negative
 - (B) Gram negative
 - (C) Often multidrug resistant
 - (D) Motile
 - (E) Common but clinically unimportant

8. Which of the following aerobic gram-positive bacilli is modified acid-fast positive?
- Nocardia brasiliensis*
 - Lactobacillus acidophilus*
 - Erysipelothrix rhusiopathiae*
 - Listeria monocytogenes*
9. Skin diphtheria as occurs in children in tropical areas typically
- Does not occur in children who have been immunized with diphtheria toxoid
 - Is clinically distinct from skin infections (pyoderma, impetigo) caused by *Streptococcus pyogenes* and *Staphylococcus aureus*
 - Is also common in northern latitudes
 - Results in protective antitoxin levels in most children by the time they are 6–8 years old
 - Yields toxin-mediated cardiomyopathy
10. A 45-year-old fisherman imbedded a fishhook into his right forefinger. He removed it and did not seek immediate medical therapy. Five days later, he noted fever, severe pain, and nodular-type swelling of the finger. He sought medical therapy. The violaceous nodule was aspirated, and after 48 hours of incubation, colonies of a gram-positive bacillus that caused greenish discoloration of the agar and formed long filaments in the broth culture were noted. The most likely cause of this infection is
- Lactobacillus acidophilus*
 - Erysipelothrix rhusiopathiae*
 - Listeria monocytogenes*
 - Rhodococcus equi*
 - Nocardia brasiliensis*
11. A biochemical reaction that is useful in the identification of the causative agent of the infection in Question 10 is
- Catalase positivity
 - Acid fastness using modified Kinyoun stain
 - Esculin hydrolysis
 - Tumbling motility
 - Production of H₂S
12. *Listeria monocytogenes* is frequently a foodborne pathogen because
- It can survive at 4°C.
 - It survives under conditions of low pH.
 - It survives in the presence of high salt concentrations.
 - All of the above are correct.
13. After recovery on laboratory media, the aerobic Actinomycetes are best identified by
- An automated system used in the laboratory
 - Classical biochemicals
 - Antigen detection tests such as an ELISA
 - Molecular methods such as 16SrRNA gene sequencing
14. Which of the following statements regarding *Rhodococcus equi* is correct?
- It is transmitted person to person.
 - It causes tuberculosis in cattle.
 - It is a rare cause of pulmonary infection in humans.
 - It produces a black pigment on sheep blood agar.
15. A hospitalized patient who had an indwelling urinary catheter develops fever, chills, suprapubic pain, and difficulty voiding 48 hours after the catheter is removed. His bladder appears

obstructed, and he has white blood cells and bacteria on a urinalysis. Cystoscopy reveals a large bladder stone, and the urine culture grows greater than 10,000 CFU/mL of a short, irregular gram-positive rod. The most likely organism causing this infection is

- Corynebacterium urealyticum*
- Nocardia brasiliensis*
- Actinomadura*
- Erysipelothrix rhusiopathiae*
- Lactobacillus acidophilus*

Answers

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|------|------|-------|-------|
| 1. D | 5. D | 9. D | 13. D |
| 2. B | 6. E | 10. B | 14. C |
| 3. E | 7. C | 11. E | 15. A |
| 4. A | 8. A | 12. D | |

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end

The staphylococci

carriage sites may diminish shedding of dangerous organisms. Rifampin coupled with a second oral antistaphylococcal drug sometimes provides long-term suppression and possibly cure of nasal carriage; this form of therapy is usually reserved for major problems of staphylococcal carriage because staphylococci can rapidly develop resistance to rifampin.

To diminish transmission within the hospital setting, high-risk patients, such as those in intensive care units and patients transferred from chronic care facilities where prevalence is high, are frequently surveyed for anterior nares colonization. Patients who test positive by culture or PCR are placed on contact precautions to minimize spread on the hands of health care workers. Health care workers should strictly adhere to infection control policies by wearing gloves and washing hands before and after patient contact.

Until relatively recently, MRSA was confined primarily to the hospital setting. Worldwide dissemination of a few distinct clones of CA-MRSA and now LA-MRSA has resulted in an increase in skin and soft tissue infections and necrotizing pneumonia, primarily in younger patients without known risk factors for MRSA acquisition. These strains appear to be more virulent. CA-MRSA isolates are characterized by the presence of PVL and the presence of staphylococcal cassette chromosome *mec* type IV (see discussion above under “Growth Characteristics”), which may explain the increased susceptibility to other antimicrobial agents compared with health care–associated MRSA strains.

CHAPTER SUMMARY

- Staphylococci are catalase-positive, gram-positive organisms that grow in clusters and are common inhabitants of the skin and mucous membranes of humans and animals.
- The pathogenic staphylococci, most importantly *S aureus*, hemolyze blood, coagulate plasma, and produce a variety of extracellular enzymes and toxins that make them virulent.
- *S aureus* has complex regulatory systems that respond to environmental stimuli to control the expression of its various virulence genes encoded on pathogenicity islands.
- *S aureus* causes a broad range of invasive and toxigenic diseases; CoNS are less virulent and more often associated with opportunistic infections (*S epidermidis*) or specific syndromes, such as *S saprophyticus* and urinary tract infections.
- Antimicrobial resistance among staphylococci can be quite extensive, encoded by a variety of mechanisms such as β -lactamase production and chromosomal *mecA*, *mecC*, and other resistance determinants.

REVIEW QUESTIONS

1. A 54-year-old woman develops a right shoulder abscess with a strain of *Staphylococcus aureus* that is resistant to nafcillin. She was treated with a 2-week course of intravenous vancomycin and improved. Three weeks later (week 5), the infection recurred, and she was given 2 more weeks of intravenous vancomycin and again improved. Four weeks later (week 11), the infection recurred and the patient was again started on intravenous vancomycin. The MICs for vancomycin for the *S aureus* isolates were as follows: initial isolate (day 1), 1 $\mu\text{g}/\text{mL}$; week 5, 2 $\mu\text{g}/\text{mL}$; and week 11, 8 $\mu\text{g}/\text{mL}$. The patient failed to improve with the third course of vancomycin, and alternative therapy was used. The mechanism that best explains the relative resistance of the patient’s strain of *S aureus* to vancomycin is
 - (A) Acquisition of the *vanA* gene from another microorganism
 - (B) Active transport of vancomycin out of the *Staphylococcus aureus* cell
 - (C) Action of β -lactamase
 - (D) Increased cell wall synthesis and alterations in the cell wall structure
 - (E) Phosphorylation and resultant inactivation of the vancomycin
2. An 11-year-old boy develops a mild fever and pain in his upper arm. A radiograph of his arm shows a lytic lesion (dissolution) in the upper part of the humerus with periosteal elevation over the lesion. The patient is taken to surgery, where the lesion is debrided (dead bone and pus removed). Culture from the lesion yields gram-positive cocci. A test shows that the organism is a *Staphylococcus* and not a *Streptococcus*. Based on this information, you know the organism is
 - (A) Susceptible to nafcillin
 - (B) β -Lactamase positive
 - (C) A producer of protein A
 - (D) Encapsulated
 - (E) Catalase positive
3. A 36-year-old male patient has an abscess with a strain of *Staphylococcus aureus* that is β -lactamase positive. This indicates that the organism is resistant to which of the following antibiotics?
 - (A) Penicillin G, ampicillin, and piperacillin
 - (B) Trimethoprim–sulfamethoxazole
 - (C) Erythromycin, clarithromycin, and azithromycin
 - (D) Vancomycin
 - (E) Cefazolin and ceftriaxone
4. Seven days ago, a 27-year-old medical student returned from Central America, where she had spent the summer working in a clinic for indigenous people. Four days ago, she developed an erythematous sunburn-like rash. She also has had headache, muscle aches, and abdominal cramps with diarrhea. Her blood pressure is 70/40 mm Hg. Pelvic examination shows she is having her menstrual period with a tampon in place; otherwise, the pelvic examination is normal. Her kidney function test (serum urea nitrogen and creatinine) results are abnormal, indicating mild renal failure. A blood smear for malaria is negative. Her illness is likely to be caused by which of the following?
 - (A) A toxin that results in greatly increased levels of intracellular cyclic adenosine monophosphate (cAMP)
 - (B) A toxin that degrades sphingomyelin
 - (C) A toxin that binds to the class II major histocompatibility complex (MHC) of an antigen-presenting cell and the V β region of a T cell
 - (D) A two-component toxin that forms pores in white blood cells and increases cation permeability
 - (E) A toxin that blocks elongation factor 2 (EF2)

5. Over a period of 3 weeks, a total of five newborns in the hospital nursery developed *Staphylococcus aureus* infections with *S aureus* bacteremia. The isolates all had the same colony morphology and hemolytic properties and identical antimicrobial susceptibility patterns, suggesting that they were the same. (Later molecular methods showed the isolates were identical.) Which of the following should be done now?
- Prophylactic treatment of all newborns with intravenous vancomycin
 - Protective isolation of all newborns
 - Closing the nursery and referring pregnant women to another hospital
 - Hiring all new staff for the hospital nursery
 - Culture using mannitol salt agar of the anterior nares of the physicians, nurses, and others who cared for the infected babies
6. The exfoliative toxins, TSST-1, and the enterotoxins are all superantigens. The genes for these toxins are
- Present in all strains of *Staphylococcus aureus*
 - Widely distributed on the staphylococcal chromosome
 - On both the staphylococcal chromosome (TSST-1 and exfoliative toxins) and on plasmids (enterotoxins)
 - On the staphylococcal chromosome in a pathogenicity island
 - On plasmids
7. A 16-year-old bone marrow transplant patient has a central venous line that has been in place for 2 weeks. He also has a urinary tract catheter, which has been in place for 2 weeks as well. He develops fever while his white blood cell count is very low and before the transplant has engrafted. Three blood cultures are done, and all grow *Staphylococcus epidermidis*. Which one of the following statements is correct?
- The *Staphylococcus epidermidis* organisms are likely to be susceptible to penicillin G.
 - The *Staphylococcus epidermidis* organisms are likely to be from the surface of the urinary tract catheter.
 - The *Staphylococcus epidermidis* organisms are likely to be resistant to vancomycin.
 - The *Staphylococcus epidermidis* organisms are likely to be from a skin source.
 - The *Staphylococcus epidermidis* organisms are likely to be in a biofilm on the central venous catheter surface.
8. A 65-year-old man develops an abscess on the back of his neck. Culture yields *Staphylococcus aureus*. The isolate is tested and found to be positive for the *mecA* gene, which means that
- The isolate is susceptible to vancomycin.
 - The isolate is resistant to vancomycin.
 - The isolate is susceptible to nafcillin.
 - The isolate is resistant to nafcillin
 - The isolate is susceptible to clindamycin.
 - The isolate is resistant to clindamycin.
9. Antimicrobial resistance has become a significant problem. Which one of the following is of major concern worldwide?
- Nafcillin resistance in *Staphylococcus aureus*
 - Penicillin resistance in *Streptococcus pneumoniae*
 - Penicillin resistance in *Neisseria gonorrhoeae*
 - Vancomycin resistance in *Staphylococcus aureus*
 - Tobramycin resistance in *Escherichia coli*
10. A group of six children younger than 8 years of age live in a semitropical country. Each of the children has several crusted weeping skin lesions of impetigo (pyoderma). The lesions are predominantly on the arms and faces. Which of the following microorganisms is a likely cause of the lesions?
- Escherichia coli*
 - Chlamydia trachomatis*
 - Staphylococcus aureus*
 - Streptococcus pneumoniae*
 - Bacillus anthracis*
11. Which of the following statements regarding the role of protein A in the pathogenesis of infections caused by *Staphylococcus aureus* is correct?
- It is responsible for the rash in toxic shock syndrome.
 - It converts hydrogen peroxide into water and oxygen.
 - It is a potent enterotoxin.
 - It is directly responsible for lysis of neutrophils.
 - It is a bacterial surface protein that binds to the Fc portion of IgG1.
12. Which of the following staphylococcal organisms produces coagulase and has been implicated in infections following a dog bite?
- Staphylococcus intermedius*
 - Staphylococcus epidermidis*
 - Staphylococcus saprophyticus*
 - Staphylococcus hominis*
 - Staphylococcus hemolyticus*
13. All of the following statements regarding Panton–Valentine leukocidin are correct *except*
- It is a two-component toxin.
 - It is commonly produced by community-associated MRSA strains.
 - It is an important virulence factor.
 - It is identical to one of the staphylococcal enterotoxins.
 - It forms pores in the membranes of white blood cells.
14. Which of the following statements best describes the function of the accessory gene regulator in *Staphylococcus aureus*?
- It regulates production of β -hemolysins.
 - It is influenced by environmental oxygen.
 - It controls the preferential expression of surface adhesins.
 - It is important in the control of autolysis.
15. All of the following are important infection control strategies in containing spread of MRSA in hospitals *except*
- Aggressive hand hygiene
 - Routine surveillance for nasal colonization among high-risk individuals
 - Contact isolation for patients who are colonized or infected with MRSA
 - Routine antimicrobial prophylaxis for all patients hospitalized for more than 48 hours
 - Aseptic management of skin lesions

Answers

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|------|------|-------|-------|
| 1. D | 5. E | 9. D | 13. D |
| 2. E | 6. D | 10. C | 14. C |
| 3. A | 7. E | 11. E | 15. D |
| 4. C | 8. D | 12. A | |

The streptococci

TABLE 14-2 Most Frequently Encountered Nonstreptococcal Catalase-Negative Gram-Positive Cocci and Coccobacilli

Genus ^a	Catalase	Gram Stain	Vancomycin Susceptibility	Comments
<i>Abiotrophia</i> ^b (nutritionally variant streptococcus)	Negative	Cocci in pairs, short chains	Susceptible	Normal microbiota of oral cavity; isolated from cases of endocarditis
<i>Aerococcus</i>	Negative to weakly positive	Cocci in tetrads and clusters	Susceptible	Environmental organisms occasionally isolated from blood, urine, or sterile sites
<i>Enterococcus faecalis</i> (and other enterococci)	D	None, α Rarely β	Some are resistant, mostly <i>Enterococcus faecium</i>	Abdominal abscess, urinary tract infection, endocarditis
<i>Gemella</i>	Negative	Cocci in pairs, tetrads, clusters, and short chains	Susceptible	Decolorize easily and may look gram negative; grow slowly (48 hours); part of normal human microbiota; occasionally isolated from blood and sterile sites
<i>Granulicatella</i> ^b (nutritionally variant streptococcus)	Negative	Cocci in chains, clusters	Susceptible	Normal microbiota of oral cavity; isolated from cases of endocarditis
<i>Leuconostoc</i>	Negative	Cocci in pairs and chains; coccobacilli, rods	Resistant	Environmental organisms; look like enterococci on blood agar; isolated from a wide variety of infections
<i>Pediococcus</i>	Negative	Cocci in pairs, tetrads, and clusters	Resistant	Present in food products and human stools; occasionally isolated from blood and abscesses
<i>Lactobacillus</i>	Negative	Coccobacilli, rods in pairs and chains	Resistant (90%)	Aerotolerant anaerobes generally classified as bacilli; normal vaginal flora; occasionally found in deep-seated infections

^aOther genera in which isolates from humans are rare or uncommon include, *Dolosicoccus*, *Dolosigranulum*, *Facklamia*, *Globicatella*, *Helcococcus*, *Ignavigranum*, *Lactococcus*, *Tetragenococcus*, *Vagococcus*, and *Weissella*.

^bRequire pyridoxal for growth.

- *S pneumoniae* is the major cause of community-acquired pneumonia but can also disseminate via the bloodstream to the central nervous system. Invasive disease is preventable through vaccination using either the 23-valent polysaccharide vaccine (adults) or the 13-valent conjugate vaccine (children). Drug resistance has become a problem in certain geographic regions.
- Enterococci are remarkable for the varieties of resistance determinants they have evolved that include β-lactam agents, glycopeptides, and aminoglycosides, among others. Newer agents such as linezolid and tedizolid are used for treatment of VRE infections. These organisms play a prominent role in health care-associated infections.

REVIEW QUESTIONS

1. A 48-year-old alcoholic man is admitted to a hospital because of stupor. He is unkempt and homeless and lives in an encampment with other homeless people, who called the authorities when he could not be easily aroused. His temperature is 38.5°C, and his blood pressure 125/80 mm Hg. He moans when attempts are made to arouse him. He has positive Kernig and Brudzinski signs, suggesting meningeal irritation. Physical examination and chest radiography show evidence of left lower lobe lung consolidation. An endotracheal aspirate yields rust-colored sputum. Examination of a Gram-stained sputum smear shows numerous polymorphonuclear cells and numerous gram-positive lancet-shaped diplococci. On lumbar puncture, the cerebrospinal fluid is cloudy and has a white blood cell count of 570/μL with 95% polymorphonuclear cells; Gram stain shows numerous gram-positive diplococci. Based on this information, the likely diagnosis is
 - (A) Pneumonia and meningitis caused by *Staphylococcus aureus*
 - (B) Pneumonia and meningitis caused by *Streptococcus pyogenes*
 - (C) Pneumonia and meningitis caused by *Streptococcus pneumoniae*
 - (D) Pneumonia and meningitis caused by *Enterococcus faecalis*
 - (E) Pneumonia and meningitis caused by *Neisseria meningitidis*
2. The patient in question 1 is started on antibiotic therapy to cover many possible microorganisms. Subsequently, culture of sputum and cerebrospinal fluid yields gram-positive diplococci

- with a minimum inhibitory concentration to penicillin G of greater than 2 µg/mL. The drug of choice for this patient until further susceptibility testing can be done is
- Penicillin G
 - Nafcillin
 - Trimethoprim–sulfamethoxazole
 - Gentamicin
 - Vancomycin
- This infection (question 1) might have been prevented by
 - Prophylactic intramuscular benzathine penicillin every 3 weeks
 - A 23-valent capsular polysaccharide vaccine
 - A vaccine against serogroups A, C, Y, and W135 capsular polysaccharide
 - A vaccine of polyribosylribitol capsular polysaccharide covalently linked to a protein
 - Oral penicillin twice daily
 - The pathogenesis of the organism causing the infection (question 1) includes which of the following?
 - Invasion of cells lining the alveoli and entry into the pulmonary venule circulation
 - Resistance to phagocytosis mediated by M proteins
 - Migration to mediastinal lymph nodes where hemorrhage occurs
 - Lysis of the phagocytic vacuole and release into the circulation
 - Inhibition of phagocytosis by a polysaccharide capsule
 - A 13-valent capsular polysaccharide protein conjugate vaccine for the pathogen in question 1 is recommended
 - For children up to age 18 years and for selected adults
 - Only on exposure to a patient with disease caused by the organism
 - For all children ages 2–23 months plus selected older children and adults with immunocompromising conditions
 - For children ages 24–72 months
 - For all age groups older than age 2 months
 - An 8-year-old boy develops a severe sore throat. On examination, a grayish-white exudate is seen on the tonsils and pharynx. The differential diagnosis includes group A streptococcal infection, Epstein-Barr virus infection, severe adenovirus infection, and diphtheria. (*Neisseria gonorrhoeae* pharyngitis would also be included, but the patient has not been sexually abused.) The cause of the boy's pharyngitis is most likely
 - A catalase-negative gram-positive coccus that grows in chains
 - A single-stranded positive-sense RNA virus
 - A catalase-positive gram-positive coccus that grows in clusters
 - A catalase-negative gram-positive bacillus
 - A double-stranded RNA virus
 - A primary mechanism responsible for the pathogenesis of the boy's disease (question 6) is
 - A net increase in intracellular cyclic adenosine monophosphate
 - Action of M protein
 - Action of IgA1 protease
 - Action of enterotoxin A
 - Inactivation of elongation factor 2
 - A 40-year-old woman develops severe headache and fever. Her neurologic examination findings are normal. A brain scan shows a ring-enhancing lesion of the left hemisphere. During surgery, a brain abscess is found. Culture of the abscess fluid grows an anaerobic gram-negative bacillus (*Fusobacterium nucleatum*) and a catalase-negative gram-positive coccus that on Gram stain is in pairs and chains. The organism is β-hemolytic and forms very small colonies (<0.5 mm in diameter). One person thought it smelled like butterscotch. It agglutinates with group F antisera. The organism most likely is
 - Streptococcus pyogenes* (group A)
 - Enterococcus faecalis* (group D)
 - Streptococcus agalactiae* (group B)
 - Streptococcus anginosus* group
 - Staphylococcus aureus*
 - Important methods for classifying and speciating streptococci are
 - Agglutination using antisera against the cell wall group-specific substance
 - Biochemical testing
 - Hemolytic properties (α-, β-, nonhemolytic)
 - Capsular swelling (quellung) reaction
 - All of the above
 - An 8-year-old girl develops Sydenham's chorea ("St. Vitus dance") with rapid uncoordinated facial tics and involuntary purposeless movements of her extremities, strongly suggestive of acute rheumatic fever. She has no other major manifestations of rheumatic fever (carditis, arthritis, subcutaneous nodules, skin rash). The patient's throat culture is negative for *Streptococcus pyogenes* (group A streptococci). However, she, her brother, and her mother all had sore throats 2 months ago. A test that if positive would indicate recent *S pyogenes* infections is
 - Antistreptolysin S antibody titer
 - Polymerase chain reaction for antibodies against M protein
 - ASO antibody titer
 - Esculin hydrolysis
 - Antihyaluronic acid antibody titer
 - All of the following statements regarding the hyaluronic acid capsule of *S pyogenes* are correct *except*
 - It is responsible for the mucoid appearance of the colonies in vitro.
 - It is antiphagocytic.
 - It binds to CD44 on human epithelial cells.
 - It is an important virulence factor.
 - A vaccine against the capsule is currently available.
 - Enterococci can be distinguished from nonenterococcal group D streptococci on the basis of which of the following characteristics?
 - γ-Hemolysis
 - Esculin hydrolysis
 - Growth in 6.5% NaCl
 - Growth in the presence of bile
 - Gram stain morphology
 - Which of the following statements regarding the *Streptococcus bovis* group is correct?
 - They possess Lancefield group D antigen.
 - Some strains are vancomycin resistant.
 - Infections caused by these organisms are benign.
 - All subspecies are PYR positive.
 - All subspecies are β-hemolytic.

14. Which of the following genera requires pyridoxal for growth?
- (A) *Aerococcus*
 (B) *Granulicatella*
 (C) *Enterococcus*
 (D) *Leuconostoc*
 (E) *Pediococcus*
15. Which of the following genera is typically resistant to vancomycin?
- (A) *Aerococcus*
 (B) *Gemella*
 (C) *Pediococcus*
 (D) *Streptococcus*
 (E) *Abiotrophia*

Answers

- | | | | |
|------|------|-------|-------|
| 1. C | 5. C | 9. E | 13. A |
| 2. E | 6. A | 10. C | 14. B |
| 3. B | 7. B | 11. E | 15. C |
| 4. E | 8. D | 12. C | |

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- Enterobacteriaceae express a variety of antigens that include somatic or O antigens (cell wall lipopolysaccharide), capsular or K antigens, and H or flagellar antigens. *Salmonella* express the Vi antigens. These antigens are virulence factors and can be used to serotype those organisms that possess them.
- Enterobacteriaceae cause a variety of human infections that can be broadly classified as either enteric diseases or extraintestinal infections such as urinary tract infections, bacteremia, and meningitis.
- Genera associated with enteric illnesses include *Salmonella*, *Shigella*, and diarrheagenic *E coli*, of which there are six types based on the mechanism of disease (eg, toxigenic or invasive or both).
- The most common extraintestinal infections caused by these organisms are urinary tract infections. *E coli* predominates, but the urea-positive organisms such as *Proteus* species can cause bladder and kidney stones.
- Enterobacteriaceae acquired in the hospital environment are often resistant to many antimicrobial agents usually mediated by plasmid-encoded resistance determinants.

REVIEW QUESTIONS

1. A 20-year-old college student goes to the student health center because of dysuria, frequency, and urgency on urination for 24 hours. She has recently become sexually active. On urinalysis, many polymorphonuclear cells are seen. The most likely organism responsible for these symptoms and signs is
 - (A) *Staphylococcus aureus*
 - (B) *Streptococcus agalactiae*
 - (C) *Gardnerella vaginalis*
 - (D) *Lactobacillus* species
 - (E) *Escherichia coli*
2. A 27-year-old woman is admitted to the hospital because of fever, with increasing anorexia, headache, weakness, and altered mental status of 2 days' duration. She works for an airline as a cabin attendant, flying between the Indian subcontinent and other places in Southeast Asia and the West Coast of the United States. Ten days before admission, she had a diarrheal illness that lasted for about 36 hours. She has been constipated for the past 3 days. Her temperature is 39°C, heart rate is 68 beats/min, blood pressure is 120/80 mm Hg, and respirations are 18 breaths/min. She knows who she is and where she is but does not know the date. She is picking at the bedclothes. Rose spots are seen on her trunk. The remainder of the physical examination is normal. Blood cultures are done, and an intravenous line is placed. The most likely cause of her illness is
 - (A) Enterotoxigenic *Escherichia coli* (ETEC)
 - (B) *Shigella sonnei*
 - (C) *Salmonella enterica* subspecies *enterica* serotype Typhimurium (*Salmonella* Typhimurium)
 - (D) *Salmonella enterica* subspecies *enterica* serotype Typhi (*Salmonella* Typhi)
 - (E) Enteroinvasive *Escherichia coli* (EIEC)
3. Blood cultures from the patient in question 2 grow a non-lactose-fermenting gram-negative bacillus. Which of the following is likely to be a constituent of this organism?
 - (A) O antigen 157, H antigen 7 (O157:H7)
 - (B) Vi antigen (capsule; virulence antigen)
 - (C) O antigen 139 (O139)
 - (D) Urease
 - (E) K1 (capsular type 1)
4. A 37-year-old woman with a history of urinary tract infections comes to the emergency department with burning on urination along with frequency and urgency. She says her urine smells like ammonia. The cause of her urinary tract infection is likely to be
 - (A) *Enterobacter aerogenes*
 - (B) *Proteus mirabilis*
 - (C) *Citrobacter freundii*
 - (D) *Escherichia coli*
 - (E) *Serratia marcescens*
5. An 18-year-old student has abdominal cramps and diarrhea. A selective agar plate is inoculated and grows suspicious gram-negative rods. Triple sugar iron agar is used to identify the isolates as salmonellae or shigellae. A result suggesting one of these two pathogens would be
 - (A) Production of urease
 - (B) Motility in the medium
 - (C) Inability to ferment lactose and sucrose
 - (D) Fermentation of glucose
 - (E) Production of gas in the medium
6. An uncommon serotype of *Salmonella enterica* subspecies *enterica* was found by laboratories in the health departments of adjacent states. The isolates were all from a small geographic area on either side of the border between the states, suggesting a common source for the isolates. (All of the isolates were from otherwise healthy young adults who smoked marijuana; the same *Salmonella* was isolated from a specimen of the marijuana.) By what method did the public health laboratories determine that these isolates were the same?
 - (A) Capsular (K antigen) typing
 - (B) O antigen and H antigen typing
 - (C) DNA sequencing
 - (D) Sugar fermentation pattern determination
 - (E) Decarboxylase reaction pattern determination
7. A 43-year-old man with diabetes has a 4-cm nonhealing foot ulcer. Culture of the ulcer yields *Staphylococcus aureus*, *Bacteroides fragilis*, and a gram-negative bacillus that swarms across the blood agar plate covering the entire surface of the agar after 36 hours. The gram-negative bacillus is a member of the genus
 - (A) *Escherichia*
 - (B) *Enterobacter*
 - (C) *Serratia*
 - (D) *Salmonella*
 - (E) *Proteus*
8. A 4-year-old boy from Kansas City who recently started attending preschool and after-school daycare is brought to his pediatrician for a diarrheal illness characterized by fever to 38.2°C, severe lower abdominal pain, and initially watery diarrhea. His mother became concerned because the stools are now blood tinged 24 hours into the illness, and the child appears quite ill. The mother reports that two other children who attend the same after-school daycare have recently had diarrheal disease, one of whom likewise had bloody stools. Which of the following is the most likely pathogen causing the illness in these children?
 - (A) O antigen 157, H antigen 7 (O157:H7)
 - (B) Vi antigen (capsule; virulence antigen)
 - (C) O antigen 139 (O139)
 - (D) Urease
 - (E) K1 (capsular type 1)

- (A) An enterotoxigenic strain of *Escherichia coli*
 (B) *Salmonella enterica* subspecies *enterica* serotype Typhi (*Salmonella* Typhi)
 (C) *Shigella sonnei*
 (D) *Edwardsiella tarda*
 (E) *Klebsiella oxytoca*
9. A 5-year-old girl attended a birthday party at a local fast food restaurant. About 48 hours later, she developed cramping abdominal pain and a low-grade fever and had five episodes of loose, bloody stools. She is taken to a local emergency department the next evening because the diarrhea has continued, and she now appears pale and lethargic. On presentation, she has a temperature of 38°C, and she is hypotensive and tachycardic. The abdominal examination reveals tenderness in the lower quadrants. Laboratory work is remarkable for a serum creatinine of 2.0 mg/dL, a serum hemoglobin of 8.0 mg/dL, thrombocytopenia, and evidence of hemolysis. What is the most likely pathogen causing this child's illness?
 (A) *Escherichia coli* O157:H7
 (B) *Salmonella enterica* subspecies *enterica* serotype Typhimurium
 (C) Enteropathogenic *Escherichia coli*
 (D) *Edwardsiella tarda*
 (E) *Plesiomonas shigelloides*
10. A 55-year-old homeless man with alcoholism presents with severe multilobar pneumonia. He requires intubation and mechanical ventilation. A Gram stain of his sputum reveals numerous polymorphonuclear leukocytes and gram-negative rods that appear to have a capsule. The organism is a lactose fermenter on MacConkey agar and is very mucoid. It is nonmotile and lysine decarboxylase positive. What is the most likely organism causing this man's illness?
 (A) *Serratia marcescens*
 (B) *Enterobacter aerogenes*
 (C) *Proteus mirabilis*
 (D) *Klebsiella pneumoniae*
 (E) *Morganella morganii*
11. Which of the following statements regarding O antigens is correct?
 (A) All Enterobacteriaceae possess identical O antigens.
 (B) They are found in the polysaccharide capsules of enteric bacteria.
 (C) They are covalently linked to a polysaccharide core.
 (D) They do not stimulate an immune response in the host.
 (E) They are not important in the pathogenesis of infection caused by enteric bacteria.
12. Which of the following test methods is the least sensitive procedure for diagnosis of colitis caused by Shiga toxin-producing *Escherichia coli*?
 (A) Culture on sorbitol MacConkey agar
 (B) Toxin testing using an enzyme immunoassay
 (C) Cell culture cytotoxin assay using Vero cells
 (D) Polymerase chain reaction for detection of the genes that encode Shiga toxin
13. An HIV-positive man recently traveled to the Caribbean for a 2-week vacation. He developed acute watery diarrhea and abdominal pain without fever during the second week of his vacation. Three weeks later, he is seen in clinic for persistent symptoms, and he is concerned because he is beginning to lose weight. Given this history, you suspect:
 (A) Enteroinvasive *Escherichia coli*
 (B) *Salmonella typhi*
 (C) Enteropathogenic *Escherichia coli*
 (D) *Shigella flexneri*
 (E) Enteroaggregative *Escherichia coli*
14. Heat-labile toxin of ETEC acts by which of the following mechanisms?
 (A) Attachment and effacement
 (B) Activation of adenylyl cyclase
 (C) Aggregative adherence
 (D) Ribosomal dysfunction
 (E) None of the above
15. A young woman presents with recurrent urinary tract infections caused by the same *Proteus mirabilis* strain. What is the major concern?
 (A) She does not take her medication.
 (B) She is pregnant because pregnant patients are more susceptible to UTIs.
 (C) She has a bladder or kidney stone.
 (D) Her partner is infected.
 (E) She has occult diabetes and should have a glucose tolerance test.

Answers

- | | | | |
|------|------|-------|-------|
| 1. E | 5. C | 9. A | 13. E |
| 2. D | 6. B | 10. D | 14. B |
| 3. B | 7. E | 11. C | 15. C |
| 4. B | 8. C | 12. A | |

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colonization in CF patients. In the United States, the Cystic Fibrosis Foundation (<http://www.cff.org>) supports a reference laboratory that uses phenotypic and genotypic methods to confirm the identity of organisms within the *B cepacia* complex. Susceptibility tests should be done on *B cepacia* complex isolates, although slow growth may make routine testing difficult. *B cepacia* complex isolates recovered from CF patients often are multidrug resistant. Trimethoprim-sulfamethoxazole, meropenem, and ciprofloxacin, or alternatively minocycline, are effective treatments.

STENOTROPHOMONAS MALTOPHILIA

S maltophilia is a free-living Gram-negative rod that is widely distributed in the environment. On blood agar, colonies have a lavender-green or gray color. The organism is generally oxidase negative, and positive for lysine decarboxylase, DNase, and oxidation of glucose and maltose (hence the name “maltophilia”).

S maltophilia is an increasingly important cause of hospital-acquired infections in patients who are receiving antimicrobial therapy and in immunocompromised patients. It has been isolated from many anatomic sites, including respiratory tract secretions, urine, wounds, and blood. The isolates are often part of mixed flora present in the specimens. When blood culture results are positive, it is commonly in association with use of indwelling plastic intravenous catheters.

S maltophilia is usually susceptible to trimethoprim-sulfamethoxazole and ticarcillin-clavulanic acid and resistant to other commonly used antimicrobials, including cephalosporins, aminoglycosides, imipenem, and the quinolones. The widespread use of the drugs to which *S maltophilia* is resistant plays an important role in the increased frequency with which it causes disease.

ACINETOBACTER

Acinetobacter species are aerobic, Gram-negative bacteria that are widely distributed in soil and water and can occasionally be cultured from skin, mucous membranes, secretions, and the hospital environment.

A baumannii is the species most commonly isolated. *Acinetobacter lwoffii* and other species are isolated occasionally. Some isolates have not received species names but are referred to as genomospecies. *Acinetobacter* are usually coccobacillary or coccal in appearance; they resemble neisseriae on smears, because diplococcal forms predominate in body fluids and on solid media. Rod-shaped forms also occur, and occasionally the bacteria appear to be Gram-positive. *Acinetobacter* grows well on most types of media used to culture specimens from patients. *Acinetobacter* recovered from patients with meningitis and bacteremia has been mistaken for *Neisseria meningitidis*; similarly, *Acinetobacter* recovered from the female genital tract has been mistaken

for *Neisseria gonorrhoeae*. However, the neisseriae produce oxidase, and *Acinetobacter* does not.

Acinetobacter often are commensals but occasionally cause nosocomial infection. *A baumannii* has been isolated from blood, sputum, skin, pleural fluid, and urine, usually in device-associated infections. *Acinetobacter* encountered in nosocomial pneumonias often originate in the water of room humidifiers or vaporizers. In patients with *Acinetobacter* bacteremias, intravenous catheters are almost always the source of infection. In patients with burns or with immune deficiencies, *Acinetobacter* act as opportunistic pathogens and can produce sepsis. *Acinetobacter* strains are often multidrug resistant, and therapy of infection can be difficult. In many cases, the only active agent may be colistin. Such multidrug-resistant strains are a common cause of serious wound infections among wounded servicemen in Iraq. Susceptibility testing should be done to help select the best antimicrobial drugs for therapy. The more susceptible *Acinetobacter* strains respond most commonly to gentamicin, amikacin, or tobramycin and to extended-spectrum penicillins or cephalosporins.

CHAPTER SUMMARY

- *P aeruginosa* is an oxidase-positive, frequently pigmented, Gram-negative, glucose-nonfermenting rod that elaborates enzymes, such as elastase, and other virulence factors that promote disease. This organism causes a broad range of infections from superficial skin disease, such as hot tub folliculitis, to gram-negative sepsis and ecthyma gangrenosum in neutropenic patients.
- *B pseudomallei* is found in the soil and water of Southeast Asia and northern Australia. Human infection with *B pseudomallei* can be acute, subacute, or chronic, and involves multiple organ systems. It is also considered a Category B agent of bioterrorism by the CDC.
- *B cepacia* complex are a group of closely related environmental organisms second only to *P aeruginosa* as a cause of morbidity and mortality in CF patients.
- *Acinetobacter* sp. and *S maltophilia* are two organisms frequently associated with hospital-acquired infections that are very drug resistant. In some cases, the only active agent for multidrug-resistant *Acinetobacter* is colistin.

REVIEW QUESTIONS

1. A sputum culture of a patient with cystic fibrosis grows *Pseudomonas aeruginosa* that forms very mucoid colonies. The implication of this observation is which one of the following?
 - (A) The *Pseudomonas aeruginosa* is highly susceptible to the aminoglycoside antimicrobial tobramycin.
 - (B) The *Pseudomonas aeruginosa* is infected with a pyocin (a bacteriocin).
 - (C) The colonies are mucoid because they have polysaccharide capsule of hyaluronic acid.

- (D) The exotoxin A gene has been disabled and the *Pseudomonas aeruginosa* is no longer able to block host cell protein synthesis.
- (E) The *Pseudomonas aeruginosa* has formed a biofilm in the patient's airway.
2. An environmental Gram-negative bacillus that is resistant to cephalosporins, aminoglycosides, and quinolones has become a very important nosocomial pathogen largely because it is selected by use of those antibiotics. This Gram-negative bacillus can take 2–3 days to grow and must be differentiated from *Burkholderia cepacia*. It is
- (A) *Pseudomonas aeruginosa*
 (B) *Acinetobacter baumannii*
 (C) *Alcaligenes xylosoxidans*
 (D) *Klebsiella pneumoniae*
 (E) *Stenotrophomonas maltophilia*
3. A 17-year-old girl with cystic fibrosis has a slight increase in her frequent cough and production of mucoid sputum. A sputum specimen is obtained and plated on routine culture media. The predominant growths are Gram-negative bacilli that form very mucoid colonies after 48 hours of incubation. These bacilli are oxidase positive, grow at 42°C, and have a grapelike odor. These Gram-negative bacilli are which of the following?
- (A) *Klebsiella pneumoniae*
 (B) *Pseudomonas aeruginosa*
 (C) *Staphylococcus aureus*
 (D) *Streptococcus pneumoniae*
 (E) *Burkholderia cepacia*
4. The sputum from a 26-year-old patient with cystic fibrosis is plated on a colistin-containing agar. After 72 hours of incubation, the colistin-containing agar grows Gram-negative bacilli that are oxidase positive but are otherwise difficult to identify. This microorganism is of major concern. It is sent to a reference laboratory so that molecular methods can be used to identify or rule out which of the following?
- (A) *Pseudomonas aeruginosa*
 (B) *Burkholderia cepacia*
 (C) *Haemophilus influenzae*
 (D) *Pseudomonas putida*
 (E) *Burkholderia pseudomallei*
5. *Acinetobacter* species:
- (A) Are only found in a hospital environment.
 (B) May appear as Gram-positive rods.
 (C) Can mimic the morphology of *Hemophilus* species in Gram stains of endocervical secretions.
 (D) Can be a significant cause of ventilator-associated pneumonia in intensive care unit patients.
 (E) Are susceptible to most antibiotics.
6. A 37-year-old firefighter sustains smoke inhalation and is hospitalized for ventilatory support. He has a severe cough and begins to expectorate purulent sputum. Gram stain of his sputum specimen shows numerous polymorphonuclear cells and numerous Gram-negative rods. Sputum culture grows numerous Gram-negative rods that are oxidase positive. They grow well at 42°C. On clear agar medium, they produce a green color in the agar. The agar where the green color is located fluoresces when exposed to ultraviolet light. The organism causing the patient's infection is
- (A) *Pseudomonas aeruginosa*
 (B) *Klebsiella pneumoniae*
 (C) *Escherichia coli*
 (D) *Burkholderia cepacia*
 (E) *Burkholderia pseudomallei*
7. The mechanism of action of exotoxin A of *Pseudomonas aeruginosa* is
- (A) To activate acetylcholine esterase
 (B) To block elongation factor 2
 (C) To form pores in white blood cells and increase cation permeability
 (D) To increase intracellular cyclic adenosine monophosphate
 (E) To split lecithin into phosphorylcholine and diacylglycerol
8. Patients deficient in these cells are at high risk for developing serious systemic infections with *Pseudomonas aeruginosa*:
- (A) Eosinophils
 (B) Neutrophils
 (C) Macrophages
 (D) Natural killer cells
 (E) CD4+ T cells
9. A marine wounded in Afghanistan returns to her home a paraplegic. Her past medical history included surgery to amputate both her legs below the knee and the placement of a suprapubic tube to repair damage to her bladder. She is now at the VA outpatient clinic with a recurrent urinary tract infection that has not responded to conventional antibiotic regimens for community-acquired cystitis. Her urine is positive for small, plump Gram-negative coccobacilli. When cultured, this organism does not ferment carbohydrates, does not hydrolyze urea, does not reduce nitrates, and does not make hydrogen sulfide. The organism most likely causing this marine's infection is:
- (A) *Klebsiella oxytoca*
 (B) *Escherichia coli*
 (C) *Staphylococcus saprophyticus*
 (D) *Proteus mirabilis*
 (E) *Acinetobacter baumannii*
10. A 70-year-old neutropenic patient was diagnosed with ecthyma gangrenosum 3 days after he developed a fever of 39°C. Blood cultures drawn the day his fever started grew out overnight a strictly aerobic, Gram-negative rod that was lactose negative and oxidase positive. Which of the following antibiotic regimens would be most appropriate for treating this patient?
- (A) Tobramycin + piperacillin/tazobactam
 (B) Vancomycin + metronidazole
 (C) Cefazolin
 (D) Tigecycline
 (E) Oxacillin

Answers

- | | | |
|------|------|-------|
| 1. E | 5. D | 9. E |
| 2. E | 6. A | 10. A |
| 3. B | 7. B | |
| 4. B | 8. B | |

end

tests in diagnosing active infection or after therapy is therefore limited.

E. Special Tests

Rapid tests to detect urease activity are widely used for presumptive identification of *H pylori* in specimens. Gastric biopsy material can be placed onto a urea-containing medium with a color indicator. If *H pylori* is present, the urease rapidly splits the urea (1–2 hours), and the resulting shift in pH yields a color change in the medium. In vivo tests for urease activity can be done also. In urea breath tests, ¹³C- or ¹⁴C-labeled urea is ingested by the patient. If *H pylori* is present, the urease activity generates labeled CO₂ that can be detected in the patient's exhaled breath.

Detection of *H pylori* antigen in stool specimens is appropriate as a test of cure for patients with known *H pylori* infection who have been treated.

Immunity

Patients infected with *H pylori* develop an IgM antibody response to the infection. Subsequently, IgG and IgA are produced, and these persist, both systemically and at the mucosa, in high titer in chronically infected persons. Early antimicrobial treatment of *H pylori* infection blunts the antibody response; such patients are thought to be subject to repeat infection.

Treatment

Triple therapy with metronidazole and either bismuth subsalicylate or bismuth subcitrate plus either amoxicillin or tetracycline for 14 days eradicates *H pylori* infection in 70–95% of patients. An acid-suppressing agent given for 4–6 weeks enhances ulcer healing. Proton pump inhibitors (PPIs) directly inhibit *H pylori* and appear to be potent urease inhibitors. The preferred initial therapy is 7–10 days of a PPI plus amoxicillin and clarithromycin or a quadruple regimen of a PPI metronidazole, tetracycline, and bismuth for 10 days.

Epidemiology and Control

H pylori is present on the gastric mucosa of fewer than 20% of persons younger than years 30 but increases in prevalence to 40–60% of persons age 60 years, including persons who are asymptomatic. In developing countries, the prevalence of infection may be 80% or higher in adults. Person-to-person transmission of *H pylori* is likely because intrafamilial clustering of infection occurs. Acute epidemics of gastritis suggest a common source for *H pylori*.

Concept Checks

- Campylobacters are oxidase positive, curved or spiral-shaped organisms that sometimes have a “gull’s wing” appearance. *C jejuni* is the major pathogen and is associated primarily with febrile diarrhea that may be bloody.

Contaminated food, primarily poultry, is the major vehicle for infection.

- *C jejuni* grows well at 42°C in a microaerophilic environment of 5% oxygen and 10% CO₂. Selective media that contain antibiotics are generally used to recover the organisms from stool.
- *Helicobacter* species are also curved or spiral-shaped pathogens. *H pylori* is associated with upper gastrointestinal diseases such as gastric and duodenal ulcers, gastric adenocarcinoma, and MALT lymphomas. The organism is urease positive, which protects it against gastric acidity. Diagnosis is made by a variety of methods including biopsy, urea breath tests, and stool antigen. Triple and quadruple antibiotic regimens that include PPIs are necessary for successful treatment.

REVIEW QUESTIONS

1. Long-term carriage and shedding is most likely to occur after gastrointestinal infection with which of the following species?
 - (A) *Escherichia coli* O157:H7
 - (B) *Shigella dysenteriae*
 - (C) *Vibrio cholerae*
 - (D) *Campylobacter jejuni*
 - (E) *Salmonella typhi*
2. A 63-year-old man visited his favorite oyster restaurant in a small town on the eastern shore of the Gulf Coast of Texas. He ate two dozen oysters. Two days later, he was admitted to the hospital because of an abrupt onset of chills, fever, and lightheadedness when he stood up. (In the emergency department [ED], his blood pressure was 60/40 mm Hg.) While in the ED, he developed erythematous skin lesions. These rapidly evolved into hemorrhagic bullae, which then formed ulcers. The man drank a six-pack of beer and one half-bottle of whisky each day. A microorganism of major concern for this patient is
 - (A) *Vibrio vulnificus*
 - (B) *Escherichia coli*
 - (C) *Salmonella typhi*
 - (D) *Clostridium perfringens*
 - (E) *Streptococcus pyogenes* (group A streptococci)
3. A family of four persons ate a meal that included undercooked chicken. Within 3 days, three members developed an illness characterized by fever, headache, myalgia, and malaise. Two of the patients had concomitant diarrhea and abdominal pain. The third person developed diarrhea after the systemic symptoms had cleared. Stool cultures grew *Campylobacter jejuni*. Which of the following culture conditions was most likely used to isolate *C jejuni*?
 - (A) Thiosulfate-citrate-bile-sucrose medium incubated at 37°C in 5% oxygen and 10% CO₂
 - (B) *Salmonella-Shigella* selective medium incubated at 37°C in ambient air
 - (C) MacConkey agar and Hektoen enteric agar incubated at 42°C in 5% oxygen and 10% CO₂
 - (D) 5% sheep blood agar incubated at 37°C in ambient air
 - (E) A medium containing vancomycin, polymyxin B, and trimethoprim incubated at 42°C in 5% oxygen and 10% CO₂

4. Bacteremia associated with a gastrointestinal infection is most likely to occur with which of the following?
- Salmonella typhi*
 - Vibrio cholerae*
 - Shigella boydii*
 - Vibrio parahaemolyticus*
 - Campylobacter jejuni*
5. During the El Niño years in the mid- to late 1990s, the waters of Puget Sound between Washington State and British Columbia warmed considerably. During this time, many people who ate clams and oysters from these waters became ill with a disease characterized by explosive diarrhea and moderately severe abdominal cramps. The diarrhea was usually watery, but in some patients, it was bloody. The diarrhea usually had an onset within 24 hours after eating the shellfish. Stool cultures typically yielded a pathogenic gram-negative bacillus. The microorganism of concern in this setting is
- Enterotoxigenic *Escherichia coli*
 - Vibrio cholerae*
 - Enterohemorrhagic *Escherichia coli*
 - Vibrio parahaemolyticus*
 - Shigella dysenteriae*
6. A patient presents to the emergency department with nonbloody diarrhea for 12 hours. The patient lives in Washington, DC, and has not recently traveled out of the area. Which one of the following is *unlikely* to be the cause of your patient's diarrhea?
- Salmonella typhimurium*
 - Campylobacter jejuni*
 - Shigella sonnei*
 - Vibrio cholerae*
 - Escherichia coli*
7. An 18-year-old woman in rural Bangladesh develops profuse (8 L/d) diarrhea. She has no symptoms other than the diarrhea and the manifestations of the fluid and electrolyte loss caused by the diarrhea. The most likely cause of her diarrhea is
- Campylobacter jejuni*
 - Enterotoxigenic *Escherichia coli*
 - Salmonella typhimurium*
 - Vibrio cholerae*
 - Shigella dysenteriae*
8. Age and geography are major factors in the prevalence of colonization by *Helicobacter pylori*. In developing countries, the prevalence of colonization may be greater than 80% in adults. In the United States, the prevalence of colonization with this microorganism in adults older than age 60 years is
- 1–2%
 - 5–10%
 - 15–20%
 - 40–60%
 - 80–95%
9. A 59-year-old man comes to the emergency department in the afternoon because of acute swelling and pain in his right leg. Earlier that morning, he had been working on a small sport fishing boat in an estuary on the Gulf Coast of Texas. While walking around the boat in shallow water, he scratched his leg, breaking the skin at the site of the current pain and swelling. He was not wearing boots. About 1 hour after the injury, the scratch became red and painful. Swelling developed. Within 3 hours, the leg below the knee had become markedly swollen.

The skin was red and tender. There was serous drainage from the wound, which had ulcerated and was now much enlarged. Near the wound, bullae were forming—the largest approximately 2.5 cm in diameter. The most likely cause of this medical emergency is

- Staphylococcus aureus*
 - Streptococcus pyogenes*
 - Clostridium perfringens*
 - Escherichia coli*
 - Vibrio vulnificus*
10. The *Vibrio cholerae* factor responsible for diarrhea is a toxin that
- Blocks EF-2
 - Yields increased intracellular levels of cAMP
 - Cleaves SNARE
 - Blocks EF-1-dependent binding of amino-acyl-tRNA to ribosomes
 - Cleaves VAMP
11. In September 1854, a severe epidemic of cholera occurred in the Soho/Golden Square area of London. Dr. John Snow, a father of epidemiology, studied the epidemic and helped stop it by which of the following actions?
- Banning the sale of apples at the local markets
 - Removing the handle of the Broad Street water pump
 - Stopping the sale of shellfish imported from Normandy
 - Pasteurizing milk
 - Promoted washing vegetables that were consumed raw
12. A 45-year-old man develops a gastric ulcer that can be visualized on a contrast medium-enhanced radiograph of his stomach. A biopsy specimen is taken from the gastric mucosa at the site of the ulcer. A presumptive diagnosis can be reached most rapidly by inoculating part of the specimen on which of the following?
- A medium used to detect urease incubated at 37°C
 - A medium containing vancomycin, polymyxin B, and trimethoprim incubated at 42°C
 - MacConkey agar medium incubated at 37°C
 - Thiosulfate-citrate-bile-sucrose medium incubated at 42°C
 - Blood agar medium incubated at 37°C

Answers

- | | | |
|------|------|-------|
| 1. E | 5. D | 9. E |
| 2. A | 6. D | 10. B |
| 3. E | 7. D | 11. B |
| 4. A | 8. D | 12. A |

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Concept Checks

- *F tularensis* is a faintly staining gram-negative coccobacillus that causes the zoonotic infection tularemia that can be mediated by vectors, such as ticks, through direct contact with animals or rarely through ingestion.
- There are three subspecies of *F tularensis*; subspecies *tularensis* (type A) is the most virulent and pathogenic for humans.
- There are several clinical manifestations of tularemia depending on the type of exposure; the glandular forms are well localized and associated with less mortality than the septicemic or inhalational forms of the disease.
- Diagnosis of tularemia can be made by recovery of the organism from appropriate clinical material and by serology.
- Agents that have been useful in treatment include streptomycin, gentamicin, tetracyclines, and fluoroquinolones. Because of its virulence, *F tularensis* is considered a potential agent of bioterrorism.

REVIEW QUESTIONS

1. A 68-year-old woman was seen in the clinic because she had felt feverish and had been experiencing increasing pain and swelling in her left knee during the past 3 weeks. Four years earlier, a prosthetic joint had been placed in her left knee. On examination, the knee was swollen, and fluid could be detected. An aspirate of the fluid was obtained. There were 15,000 polymorphonuclear cells/mL in the fluid. No organisms were seen on Gram stain. A routine culture was done. On the fourth day of incubation, colorless colonies smaller than 1 mm in diameter were seen on the blood and chocolate agar plates. The organism was a tiny gram-negative coccobacillus that was catalase positive and oxidase positive. A urea slant was inoculated and was positive for urease activity after overnight incubation. The patient was probably infected with which of the following microorganisms?
 - (A) *Haemophilus influenzae*
 - (B) *Haemophilus ducreyi*
 - (C) *Francisella tularensis*
 - (D) *Brucella species*
 - (E) *Staphylococcus aureus*
2. After the culture (Question 1) turned positive, additional history was obtained. Approximately 4 weeks before the onset of her knee pain, the patient had visited relatives in Israel and traveled to other countries in the Mediterranean area. She had a particular fondness for one food product that was the probable vehicle for her infection. The product most likely was
 - (A) Bananas
 - (B) Unpasteurized goat's cheese
 - (C) Rare hamburger
 - (D) Fresh orange juice
 - (E) Green tea
3. A 55-year-old game warden in Vermont found a dead muskrat on the bank of a stream. He picked up the animal, thinking it might have been illegally trapped or shot; it was not, and the game warden buried it. Four days later, he developed a 1.5-cm painful ulcer on the index finger of his right hand, a 1-cm ulcer on his right forehead, and pain in his right axilla. Physical examination also revealed right axillary lymphadenopathy. This patient is most likely infected with
 - (A) *Brucella species*
 - (B) *Rickettsia rickettsii*
 - (C) *Salmonella Typhi*
 - (D) *Haemophilus ducreyi*
 - (E) *Francisella tularensis*
4. An 18-month-old boy has been playing with a child who develops *Haemophilus influenzae* meningitis. The boy's parents consult his pediatrician, who says she is comfortable that the child will be fine because he has been fully immunized with the polyribitol ribose phosphate (PRP)-protein conjugate vaccine. For what reason is it necessary to immunize infants of 2 months to 2 years of age with polysaccharide-protein conjugate vaccines?
 - (A) The conjugate protein is diphtheria toxoid, and the goal is for the infant to develop simultaneous immunity to diphtheria.
 - (B) Infants 2 months to 2 years of age do not immunologically respond to polysaccharide vaccines that are not conjugated to a protein.
 - (C) The conjugate vaccine is designed for older children and adults as well as infants.
 - (D) Maternal (transplacental) antibodies against *Haemophilus influenzae* are gone from the infant's circulation by 2 months of age.
 - (E) None of the above.
5. An 11-year-old boy from Peru was referred to the Brain Tumor Institute. Three months earlier he had developed headaches and then slowly progressive right-sided weakness. A CT scan showed a mass lesion in the left hemisphere. He was thought to have a brain tumor. A lumbar puncture was not done because of concern about increased intracranial pressure and brain herniation through the tentorium cerebelli. During surgery, a mass lesion in the left hemisphere was found. Frozen sections of the tissue were done while the patient was in the operating room. Microscopy of the sections showed a granulomatous inflammatory reaction. No tumor was seen. Tissue was submitted for culture for *Mycobacterium tuberculosis*. Middlebrook 7H9 broth medium was used. Six days after the culture was set up, the automated machine detected that the culture result was positive. Results of an acid-fast stain and a Gram stain were both negative. Subcultures were done. Two days later, very small colonies were seen on the sheep blood agar plate. The organism was a tiny gram-negative coccobacillus that was catalase positive and oxidase positive. It showed urease activity after 2 hours of incubation on urea-containing medium. This child had infection with
 - (A) *Brucella species*
 - (B) *Mycobacterium tuberculosis*
 - (C) *Francisella tularensis*
 - (D) *Haemophilus influenzae*
 - (E) *Moraxella catarrhalis*
6. A 3-year-old child develops *Haemophilus influenzae* meningitis. Therapy is begun with cefotaxime. Why is this third-generation cephalosporin used rather than ampicillin?
 - (A) About 80% of *Haemophilus influenzae* organisms have modified penicillin-binding proteins that confer resistance to ampicillin.
 - (B) The drug of choice, trimethoprim-sulfamethoxazole, cannot be used because the child is allergic to sulfonamides.
 - (C) It is easier to administer intravenous cefotaxime than intravenous ampicillin.

- (D) There is concern that the child will rapidly develop a penicillin (ampicillin) allergy.
- (E) About 20% of *Haemophilus influenzae* organisms have a plasmid that encodes for β -lactamase.
7. A 55-year-old man with severe dental caries presented with 1 month of fever, malaise, and back pain and now presents with moderately severe shortness of breath. The examination reveals a febrile man who appears pale and dyspneic. Other physical findings include conjunctival petechiae, a grade III/VI systolic murmur, and an enlarged spleen. Blood cultures grow a pleomorphic gram-negative rod that is not hemolytic and that when tested is X and V factor negative. The most likely causative pathogen is
- (A) *Haemophilus influenzae*
 (B) *Haemophilus ducreyi*
 (C) *Aggregatibacter aphrophilus*
 (D) *Actinobacillus hominis*
 (E) *Haemophilus parainfluenzae*
8. All of the following statements regarding acellular pertussis vaccines are correct *except*
- (A) All formulations of the vaccine contain at least two antigens.
 (B) The acellular vaccine has replaced the whole cell vaccine in the childhood vaccine series.
 (C) All children should receive five doses of the vaccine before school entry.
 (D) The vaccine is approved only for young children and adolescents.
 (E) The vaccine is safer than and as immunogenic as whole-cell vaccines.
9. Which of the following subspecies of *Francisella tularensis* is the most virulent for humans?
- (A) *tularensis*
 (B) *holarctica*
 (C) *mediasiatica*
 (D) *novicida*
10. All of the following statements regarding the etiologic agent of chancroid are correct *except*
- (A) The organism is a small gram-negative rod.
 (B) The organism requires X factor but not V factor.
 (C) The organism grows well on standard chocolate agar.
 (D) On Gram stain of lesions, the organism occurs in strands.
 (E) The organism is susceptible to erythromycin.
11. A 3-month-old infant is brought to the pediatric emergency department in severe respiratory distress. The child appears dehydrated, and there is a prominent peripheral lymphocytosis. The chest radiograph reveals perihilar infiltrates. The child's grandmother, who watches the infant now that the mother has returned to work, has had a dry hacking cough for about 2 weeks. The most likely causative agent is
- (A) *Haemophilus influenzae* type b
 (B) *Bordetella pertussis*
 (C) *Streptococcus agalactiae*
 (D) *Chlamydia pneumoniae*
 (E) *Bordetella bronchiseptica*
12. In Question 11, the factor responsible for the profound lymphocytosis is
- (A) A hemagglutinin
 (B) A polysaccharide capsule
 (C) An A/B structured toxin
 (D) A heat-labile toxin
 (E) A neuraminidase
13. All of the following cause zoonotic infections *except*
- (A) *Francisella tularensis*
 (B) *Brucella melitensis*
 (C) *Bordetella pertussis*
 (D) *Bacillus anthracis*
 (E) *Leptospira interrogans*
14. Which of the following is not a recognized virulence factor of *Bordetella pertussis*?
- (A) Heat-labile toxin
 (B) Filamentous hemagglutinin
 (C) Tracheal cytotoxin
 (D) Pertussis toxin
 (E) Dermonecrotic toxin
15. Which of the following pathogens discussed in this chapter is on the select agent list?
- (A) *Haemophilus influenzae*
 (B) *Aggregatibacter aphrophilus*
 (C) *Bordetella pertussis*
 (D) *Francisella tularensis*
 (E) All of the above

Answers

- | | | | |
|------|------|-------|-------|
| 1. D | 5. A | 9. A | 13. C |
| 2. B | 6. E | 10. C | 14. A |
| 3. E | 7. C | 11. B | 15. D |
| 4. B | 8. D | 12. C | |

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in immunocompromised patients. *Yersinia* sepsis can be successfully treated with third-generation cephalosporins (possibly in combination with an aminoglycoside) or a fluoroquinolone (possibly in combination with another antimicrobial). In cases in which clinical manifestations strongly point to either appendicitis or mesenteric adenitis, surgical exploration has been the rule unless several simultaneous cases indicate that *Yersinia* infection is likely.

Prevention and Control

Contact with farm and domestic animals, their feces, or materials contaminated by them probably accounts for most human infections. Meat and dairy products have occasionally been indicated as sources of infection, and group outbreaks have been traced to contaminated food or drink. Conventional sanitary precautions are probably helpful. There are no specific preventive measures.

Concept Checks

- *Yersinia* species are zoonotic pathogens that cause disease in humans ranging from mild gastrointestinal infections to serious diseases with high mortality such as plague.
- *Y. pestis* is transmitted to humans usually through the bite of an infected flea, although inhalation is another potential route. *Y. pestis* possesses virulence factors transmitted by plasmids that allow it to survive in the gut of the flea and that contribute to severe clinical manifestations in humans.
- A bubo (an enlarged suppurative lymph node) forms close to the bite wound accompanied by fever and is the most common form of plague. From the localized lesion, the infection may disseminate causing the septicemic form of the disease.
- Treatment consists of supportive care and antibiotic treatment with streptomycin, gentamicin, doxycycline, or a fluoroquinolone antibiotic.
- *Y. enterocolitica* causes gastroenteritis or mesenteric lymphadenitis after ingestion of contaminated food or water.
- *Y. enterocolitica* can be recovered from the stool of infected patients using selective media called CIN agar incubated at room temperature.
- Treatment for gastroenteritis caused by *Y. enterocolitica* consists of trimethoprim-sulfamethoxazole, doxycycline, or a fluoroquinolone antibiotic.

PASTEURELLA MULTOCIDA

Pasteurellae are nonmotile, Gram-negative coccobacilli with a bipolar appearance on stained smears. They are aerobes or facultative anaerobes that grow readily on ordinary bacteriologic media at 37°C. They are all oxidase positive and catalase positive but diverge in other biochemical reactions.

P. multocida occurs worldwide in the respiratory and gastrointestinal tracts of many domestic and wild animals. It is perhaps the most common organism in human wounds inflicted by bites from cats and dogs. It is one of the common causes of hemorrhagic septicemia in a variety of animals, including rabbits, rats, horses, sheep, fowl, cats, and swine. It can also produce human infections in many systems and may at times be part of normal human microbiota.

Clinical Findings

The most common presentation is a history of animal bite followed within hours by an acute onset of redness, swelling, and pain. Regional lymphadenopathy is variable, and fever is often low grade. *Pasteurella* infections sometimes present as bacteremia or chronic respiratory infection without an evident connection with animals.

P. multocida is susceptible to most antibiotics. Penicillin G is considered the drug of choice for *P. multocida* infections resulting from animal bites. Tetracyclines and fluoroquinolones are alternative drugs.

REVIEW QUESTIONS

1. An 18-year-old male resident of Arizona came to the emergency department (ED) complaining of fever, pain in his left groin, and diarrhea for the past 2 days. On examination, he was afebrile, had a pulse rate of 126 beats/min, a respiratory rate of 20 breaths/min, and a blood pressure of 130/80 mm Hg. Left groin swelling and tenderness were noted. A groin muscle strain was diagnosed, attributed to a fall 2 days earlier. He was treated with nonsteroidal anti-inflammatory drugs and released. The next day, the patient reported feeling weak, had difficulty breathing, and collapsed while taking a shower. He was transported to a hospital ED and pronounced dead shortly after arrival. Cultures of blood samples obtained in the ED were positive for *Yersinia pestis*. An epidemiologic investigation indicated that the patient most likely became infected as a result of bites by *Y. pestis*-infected fleas while walking through a prairie dog colony (see Chapter 48). Which of the following statements about the pathogenesis of plague is correct?
 - (A) *Yersinia pestis* produces a coagulase when incubated at 28°C.
 - (B) There is no risk for pneumonia caused by person-to-person transmission of *Yersinia pestis*.
 - (C) *Yersinia pestis* organisms multiply in polymorphonuclear cells.
 - (D) After the bite of an infected flea, *Yersinia pestis* infection seldom, if ever, disseminates beyond the site of the flea bite and the regional lymph nodes.
 - (E) *Yersinia pestis* is transmitted to animals (and humans) in flea feces excreted when the flea is feeding.
2. The drug of choice to treat the patient in Question 1 would have been
 - (A) Ampicillin
 - (B) Cefotaxime
 - (C) Levofloxacin
 - (D) Erythromycin
 - (E) Streptomycin

3. *Yersinia pestis* entered North America through San Francisco in the 1890s, carried by rats on ships that had sailed from Hong Kong, where a plague epidemic occurred. The current reservoir for *Y. pestis* in the United States is
- Urban feral cats
 - Urban rats
 - Domestic cows
 - Coyotes
 - Rural wild rodents
4. Which of the following is generally not considered a potential agent of bioterrorism and biologic warfare?
- Yersinia pestis*
 - Botulinum toxin
 - Streptococcus pyogenes*
 - Brucella* species
 - Bacillus anthracis*
5. An 8-year-old boy was bitten by a stray cat. Two days later, the wound was red and swollen and drained purulent fluid. *Pasteurella multocida* was cultured from the wound. The drug of choice to treat this infection is
- Amikacin
 - Erythromycin
 - Gentamicin
 - Penicillin G
 - Clindamycin
6. Intimate contacts of patients with suspected plague pneumonia should receive which of the following agents as chemoprophylaxis?
- Gentamicin
 - Cefazolin
 - Rifampin
 - Penicillin
 - Doxycycline
7. In a patient who has the bubonic form of plague, all of the following specimens are acceptable for diagnosis *except*
- Stool culture on hektoen enteric agar
 - Blood culture using routine laboratory media
 - Culture of a lymph node aspirate on blood and MacConkey agars
 - Acute and convalescent serology
 - Immunohistochemical staining of lymph node tissue
8. All of the following statements regarding the pFra/pMT plasmid of *Yersinia pestis* are true *except*
- It encodes the capsular protein (fraction FI) that confers antiphagocytic properties.
 - It contains genes that yield plasminogen-activating protease that has temperature-dependent coagulase activity.
 - It contains genes that encode phospholipase D, which is required for organism survival in the flea midgut.
 - It is unique to *Yersinia pestis*.
 - It encodes factors that are important for survival in both the flea and the human.
9. All of the following statements regarding the epidemiology of infections caused by *Yersinia enterocolitica* are correct *except*
- Most human infections are caused by serotype O:1.
 - Humans acquire the infection from ingestion of food or drinks contaminated by animals or animal products.
 - Person-to-person spread is quite common.
 - A large inoculum is required to cause infection.
 - Infection is more prevalent in persons with histocompatibility antigen HLA-B27.
10. Optimum recovery of *Yersinia enterocolitica* from the stools of patients with gastroenteritis requires which of the following specialized media?
- Cefsulodin-irgasan-novobiocin agar
 - Xylose-lysine decarboxylase agar
 - Hektoen-enteric agar
 - Regan-Lowe medium
 - MacConkey agar
11. An organism suspected of being *Yersinia pestis* is recovered from a patient with sepsis. The isolate has bipolar staining and is catalase positive but is oxidase and urease negative and is nonmotile. At this point, what should be done?
- Nothing; the laboratory has confirmed the diagnosis.
 - Inoculate the isolate to an identification kit or automated system for confirmation.
 - Call the police because there is a possible bioterrorism event.
 - Send the isolate to the nearest public health laboratory for confirmation.
 - Send the isolate to the hospital across town for sequencing.

Answers

- | | | |
|------|------|-------|
| 1. A | 5. D | 9. C |
| 2. E | 6. E | 10. A |
| 3. E | 7. A | 11. D |
| 4. C | 8. B | |

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nasopharynx of 3–40% of persons and most often is found in children. Unlike the other neisseriae, it ferments lactose.

N sicca, *N subflava*, *N cinerea*, *Neisseria mucosa*, and *N flavescens* are also members of the normal microbiota of the respiratory tract, particularly the nasopharynx, and very rarely produce disease. *N cinerea* sometimes resembles *N gonorrhoeae* because of its morphology and positive hydroxyprolyl aminopeptidase reaction.

M catarrhalis was previously named *Branhamella catarrhalis* and before that *Neisseria catarrhalis*. It is a member of the normal microbiota in 40% to 50% of healthy school children. *M catarrhalis* causes bronchitis, pneumonia, sinusitis, otitis media, and conjunctivitis. It is also of concern as a cause of infection in immunocompromised patients. Most strains of *M catarrhalis* from clinically significant infections produce β -lactamase. *M catarrhalis* can be differentiated from the neisseriae by its lack of carbohydrate fermentation and by its production of DNase. It produces butyrate esterase, which forms the basis for rapid fluorometric tests for identification.

CHAPTER SUMMARY

- The genus *Neisseria* consists of two major pathogens, *N gonorrhoeae* and *N meningitidis*; both of them have elaborated factors that facilitate disease in otherwise healthy people. The remaining species constitute part of the normal human microbiota of the respiratory tract and may play a role in localized infections.
- Members of this genus are gram-negative diplococci that vary in their growth requirements. *N gonorrhoeae* is very fastidious, and selective enriched media containing antibiotics, amino acids, and so on are used to recover the organism in clinical cultures. The other species are less fastidious and grow on routine laboratory media.
- N gonorrhoeae* causes the sexually transmitted disease gonorrhea and is characterized by purulent cervicitis in women and purulent urethral discharge in men. Infants born to women infected at the time of delivery may develop purulent conjunctivitis.
- Diagnosis is made primarily by NAATs; treatment consists of intramuscular ceftriaxone plus an agent such as azithromycin or doxycycline to treat concomitant *Chlamydia* infections.
- N meningitidis* is the cause of endemic and epidemic meningitis. Its major virulence factor is the thick polysaccharide capsule. There are approximately 13 capsular types, of which the most common causes of disease are A, B, C, X, Y, and W-135.
- Meningococcal meningitis is a serious infection that carries a high morbidity and is often associated with sepsis because of its potent LOS. Penicillin is the drug of choice.
- Diagnosis is made by culturing the cerebrospinal fluid on chocolate agar incubated at 37°C in CO₂.
- Prevention consists of immunization with one of two conjugate vaccines (routinely recommended for children 11–12 years of age) or the polysaccharide vaccine.

REVIEW QUESTIONS

- The inhabitants of a group of small villages in rural sub-Saharan Africa experienced an epidemic of meningitis. Ten percent of the people died, most of them younger than the age of 15 years. The microorganism that most likely caused this epidemic was
 - Streptococcus agalactiae* (group B)
 - Escherichia coli* K1 (capsular type 1)
 - Haemophilus influenzae* serotype b
 - Neisseria meningitidis* serogroup A
 - West Nile virus
- A 9-year-old boy presented to the clinic with a urethral discharge for the past 24 hours. *Neisseria gonorrhoeae* was cultured from the specimen and found to be β -lactamase positive and resistant to high levels (≥ 32 $\mu\text{g/mL}$) of tetracycline. Which of the following statements about these antimicrobial resistance factors is correct?
 - β -lactamase production and high-level resistance to tetracycline are both mediated by genes on plasmids.
 - Whereas β -lactamase production is mediated by a gene on the bacterial chromosome, high-level tetracycline resistance is mediated by a gene on a plasmid.
 - Whereas β -lactamase production is mediated by a gene on a plasmid, high-level tetracycline resistance is mediated by a gene on the bacterial chromosome.
 - β -lactamase production and high-level resistance to tetracycline are both mediated by genes on the bacterial chromosome.
- A 6-year-old boy develops a fever and headache. He is taken to the emergency department, where he is noted to have a stiff neck, suggesting meningial irritation. A lumbar puncture is done, and culture of the cerebrospinal fluid grows *Neisseria meningitidis* serogroup B. Which of the following should be considered for his family (household) members?
 - No prophylaxis or other steps are necessary.
 - They should be given *Neisseria meningitidis* pilin vaccine.
 - They should be given *Neisseria meningitidis* serogroup B polysaccharide capsule vaccine.
 - They should be given rifampin prophylaxis.
 - They should be given sulfonamide prophylaxis.
- An 18-year-old woman who reports unprotected sex with a new partner 2 weeks previously develops fever and left lower quadrant abdominal pain with onset in association with her menstrual period. On pelvic examination in the emergency department, she has bilateral tenderness when the uterus is palpated. A mass 2–3 cm in diameter is felt on the left, suggestive of tubo-ovarian abscess. Subsequently, *Neisseria gonorrhoeae* is cultured from her endocervix. The diagnosis is gonococcal pelvic inflammatory disease. A common sequela of this infection is:
 - Cancer of the cervix
 - Urethral stricture
 - Uterine fibroid tumors
 - Infertility
 - Vaginal-rectal fistula
- A 38-year-old vice squad police officer comes to the emergency department with a chief complaint expressed as follows: “I have disseminated gonococcal infection again.” He is correct. Cultures of his urethra and knee fluid yield *Neisseria gonorrhoeae*.

- He has previously had five episodes of disseminated gonococcal infection. The patient should be evaluated for
- Selective IgA deficiency
 - A polymorphonuclear cell chemotactic defect
 - Deficiency of a late-acting complement component C5, C6, C7, or C8
 - Absent lymphocyte adenosine deaminase activity
 - Myeloperoxidase deficiency
- Which of the following individuals should routinely receive vaccination with the conjugate meningococcal vaccine?
 - A healthy young adolescent entering high school
 - A healthy child entering kindergarten
 - A 60-year-old man with insulin-dependent diabetes
 - A healthy 40-year-old technician who works in a cancer research laboratory
 - A 65-year-old woman with coronary artery disease
 - A 25-year-old sexually active woman presents with purulent vaginal discharge and dysuria 7 days after having unprotected sexual intercourse with a new partner. Of the choices below, what is the most sensitive diagnostic method for determining the likely etiologic agent?
 - Gram stain
 - An enzyme immunoassay
 - Bacterial culture on selective media
 - A nucleic acid amplification test
 - Serology
 - What is the currently recommended treatment for gonococcal urethritis in men who have sex with men in the United States?
 - Single dose of an oral fluoroquinolone
 - Seven days of oral doxycycline
 - Ceftriaxone given intramuscularly as a single dose
 - Spectinomycin given intramuscularly as a single dose
 - Seven days of oral amoxicillin
 - Which of the following cell components produced by *Neisseria gonorrhoeae* is responsible for attachment to host cells?
 - Lipooligosaccharide
 - Pili (fimbriae)
 - IgA1 protease
 - Outer membrane porin protein
 - Iron-binding protein
 - A 60-year-old man with severe chronic lung disease presents with fever, cough productive of purulent sputum, and worsening hypoxemia. A sputum sample is collected, and the specimen is sent promptly to the laboratory. Microscopic examination of a Gram stain reveals numerous polymorphonuclear leukocytes and predominately gram-negative diplococci that are both intracellular and extracellular. The organism grows well on 5% SBA and chocolate agar and is positive for butyrate esterase. What is the most likely organism causing this man's illness?
 - Neisseria gonorrhoeae*
 - Neisseria lactamica*
 - Moraxella catarrhalis*
 - Haemophilus influenzae*
 - Neisseria meningitidis*
 - One major advantage of the conjugate meningococcal vaccines compared with the polysaccharide vaccine is
 - Stimulation of mucosal secretory IgA
 - Fewer side effects
 - A T cell–dependent response to vaccine is induced
 - Inclusion of serogroup B
 - A 25-year-old woman presents with septic arthritis of the knee. The fluid aspirate grows a gram-negative diplococcus on chocolate agar after 48 hours of incubation. The isolate is oxidase positive and oxidizes glucose but not maltose, lactose, or sucrose. You suspect infection with:
 - Neisseria meningitidis*
 - Neisseria lactamica*
 - Moraxella catarrhalis*
 - Neisseria gonorrhoeae*
 - None of the above
 - All of the following are virulence factors associated with *N gonorrhoeae* except
 - Pili
 - Por
 - Lipooligosaccharide
 - Opa proteins
 - A thick polysaccharide capsule
 - The prevalence of gonococcal infections increased between 2009 and 2012.
 - True
 - False
 - A useful test to differentiate *Moraxella catarrhalis* from saprophytic neisseriae in respiratory samples is:
 - Butyrate esterase
 - Gram stain
 - Growth on 5% sheep blood agar
 - PYR
 - Oxidase

Answers

- | | | | |
|------|------|-------|-------|
| 1. D | 5. C | 9. B | 13. E |
| 2. A | 6. A | 10. C | 14. A |
| 3. D | 7. D | 11. C | 15. A |
| 4. D | 8. C | 12. D | |

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Anaerobic bacteria

CHAPTER SUMMARY

3. Gas in tissues (production of CO₂ and H₂)
4. Negative aerobic culture results

Diagnosis of anaerobic infection is made by anaerobic culture of properly obtained and transported specimens (see Chapter 47). Anaerobes grow most readily on complex media such as trypticase soy agar base, Schaedler's blood agar, brucella agar, brain–heart infusion agar, and others—each highly supplemented (eg, with hemin, vitamin K₁, blood). A selective complex medium containing kanamycin is used in parallel. Kanamycin (similar to all aminoglycosides) does not inhibit the growth of obligate anaerobes; thus, it permits them to proliferate without being overshadowed by rapidly growing facultative anaerobes. Cultures are incubated at 35–37°C in an anaerobic atmosphere containing CO₂.

Colony morphology, pigmentation, and fluorescence are helpful in identifying anaerobes. Biochemical activities and production of short-chain fatty acids as measured by gas-liquid chromatography are used for laboratory confirmation.

TREATMENT OF ANAEROBIC INFECTIONS

Treatment of mixed anaerobic infections is by surgical drainage (under most circumstances) plus antimicrobial therapy.

The *B fragilis* group of organisms found in abdominal and other infections universally produces β-lactamase, as do many of the *P bivia* and *P disiens* strains found in genital tract infections in women. Fortunately, these β-lactamases are inhibited by β-lactam–β-lactamase inhibitor combinations such as ampicillin–sulbactam. Therapy with antimicrobials (other than penicillin G) is necessary to treat infections with these organisms. At least two-thirds of the *P melaninogenica* strains from pulmonary and oropharyngeal infections also produce β-lactamase.

The most active drugs for treatment of anaerobic infections are clindamycin and metronidazole, although clindamycin resistance among the *B fragilis* group has increased in the past decade. Clindamycin is preferred for infections above the diaphragm. Relatively few anaerobes are resistant to clindamycin (*B fragilis* group excepted) and few, if any, are resistant to metronidazole. Alternative drugs include cefoxitin, cefotetan, some of the other newer cephalosporins, and piperacillin, but these drugs are not as active as clindamycin and metronidazole. The carbapenem antibiotics, ertapenem, imipenem, meropenem, and doripenem, have good activity against many anaerobes, and resistance is still uncommon. Tigecycline, has good in vitro activity against a variety of anaerobe species, including the *B fragilis* group. Penicillin G remains the drug of choice for treatment of anaerobic infections that do not involve β-lactamase–producing *Bacteroides* and *Prevotella* species.

- Anaerobic bacteria are organisms that do not grow in the presence of oxygen and require special handling to recover them from clinical material.
- Anaerobes constitute a substantial component of the normal human microbiota, yet some produce potent exotoxins that cause serious, life-threatening infections.
- Anaerobes are often implicated in mixed bacterial infections when an important mucosal barrier has been compromised such as in the case of trauma.
- *B fragilis* is one of the most frequently isolated gram-negative anaerobes from clinical material; it possesses a capsule capable of causing abscess formation.
- Treatment of anaerobic infections requires drainage of abscesses and antibiotics such as penicillin (for non-β-lactamase producers), clindamycin, cefoxitin, metronidazole, and the carbapenems.

REVIEW QUESTIONS

1. A 55-year-old man visits his physician complaining of a severe cough and production of purulent sputum. His breath has a very unpleasant fetid odor. Chest radiography shows a large amount of fluid in the left pleural space and a 5-cm lung cavity with an air-fluid level. A needle is inserted through the chest wall, and some of the fluid in the pleural space is removed; it is thick, yellow-gray in color, and malodorous. Which of the following organisms or sets of organisms are most likely to be cultured from the pleural fluid?
 - (A) *Bacteroides fragilis*, *Escherichia coli*, and enterococci
 - (B) *Prevotella bivia*, peptostreptococci, and *Staphylococcus epidermidis*
 - (C) *Prevotella melaninogenica*, *Fusobacterium* species, and viridans streptococci
 - (D) *Propionibacterium species*, peptostreptococci, and *Staphylococcus aureus*
 - (E) *Streptococcus pneumoniae*
2. An 18-year-old man develops fever with pain in the right lower quadrant of his abdomen. After initial evaluation, he is taken to the operating room. During surgery, a ruptured appendix with an abscess is found. *Bacteroides fragilis* is cultured from the abscess fluid. Which of the following factors promote abscess formation by *B fragilis*?
 - (A) Lipopolysaccharide
 - (B) Capsule
 - (C) Superoxide dismutase
 - (D) Pili
 - (E) Leukocidin toxin
3. Infections caused by *Bacteroides* species can be treated with all of the following antibiotics *except*
 - (A) Ampicillin–sulbactam
 - (B) Clindamycin
 - (C) Metronidazole
 - (D) Penicillin
 - (E) Cefoxitin

4. A 17-year-old high school senior develops infectious mononucleosis. About 2 weeks later, he develops a significantly higher fever, a worsening sore throat, an inability to swallow, and severe neck and chest pain. Upon admission, he has signs of sepsis and respiratory distress. What is the most likely organism causing this complication?
- (A) *Fusobacterium necrophorum*
 (B) *Bacteroides ovatus*
 (C) *Prevotella melaninogenica*
 (D) *Clostridium tetani*
 (E) *Actinomyces israelii*
5. The drug of choice for treatment of infections caused by *Actinomyces* species is
- (A) Tigecycline
 (B) Cefoxitin
 (C) Metronidazole
 (D) Imipenem
 (E) Penicillin
6. All of the following statements regarding anaerobes are true except
- (A) They possess the enzyme cytochrome oxidase
 (B) Many species are part of the normal human microbiota
 (C) They are often found along with aerobes in complicated infections
 (D) Special techniques are required to ensure their recovery from clinical specimens
 (E) Some species are more tolerant of exposure to oxygen than others
7. Lemierre's disease is a serious infection of the head and neck associated with which of the following anaerobes?
- (A) *Prevotella melaninogenica*
 (B) *Bacteroides thetaiotaomicron*
 (C) *Porphyromonas gingivalis*
 (D) *Peptococcus niger*
 (E) *Fusobacterium necrophorum*
8. Definitive identification of an anaerobe is likely best accomplished by
- (A) Colony morphology on anaerobic media
 (B) The presence of pigment
 (C) Susceptibility to a variety of antimicrobial disks
 (D) Cell wall fatty acid analysis using gas liquid chromatography
 (E) Gram stain morphology
9. A patient who has not maintained good dentition presents with induration and swelling of the mandibular area. On examination, you note purulent material draining from a small opening. The material appears yellowish, and there are some visible granules. You perform a Gram stain, and pleomorphic gram-positive rods with short branches are noted along with cells suggestive of acute and chronic inflammation. You suspect which of the following organisms?
- (A) *Bacteroides fragilis*
 (B) *Lactobacillus acidophilus*
 (C) *Clostridium perfringens*
 (D) *Actinomyces israelii*
 (E) *Staphylococcus aureus*

Answers

- | | | |
|------|------|------|
| 1. C | 4. A | 7. E |
| 2. B | 5. E | 8. D |
| 3. D | 6. A | 9. D |

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involvement is the small intestine and mesenteric lymph nodes, but any organ can be affected; most notably, musculo-skeletal, neurologic, cardiac, and ophthalmic manifestations are described. Histologically, there is a prominent macrophage infiltration and glycoprotein deposition. Characteristic vacuoles within the macrophage that stain with periodic acid-Schiff (PAS) stain (foamy macrophages) are pathognomonic of the disease. The intracellular and extracellular PAS-positive materials are bacilli. Historically, routine cultures of clinical specimens have been negative, but more recently the organism has been cultured in association with eukaryotic cells (human fibroblasts, deactivated peripheral blood monocytes). Before the organism was successfully cultured, PCR amplification of bacterial 16S ribosomal RNA allowed identification of a unique sequence from the bacteria in the lesions. Phylogenetic analysis has shown the organism is a gram-positive actinomycete not closely related to any known genus. The organism has been named *Tropheryma whippelii*. The diagnosis of Whipple disease is by PCR amplification of an appropriate specimen (bowel biopsy, brain biopsy, etc) for *T whippelii*.

REVIEW QUESTIONS

- Humans become infected with *Legionella pneumophila* by
 - Kissing a person who is a legionella carrier
 - Breathing aerosols from environmental water sources
 - Receiving a mosquito bite
 - Consuming undercooked pork
- An 11-year-old girl developed an acute onset of fever, chills, headache, vomiting, and severe migratory arthralgias (joint pain) and myalgias (muscle pain). Two days later, she developed a maculopapular rash over her palms, soles, and extremities. At the same time, her left knee became extremely painful and swollen. On examination, fluid was demonstrated in the knee. Further history disclosed that the patient had a pet rat. Culture of the fluid from her knee on 5% sheep blood agar showed 2-mm colonies after 3 days of incubation. Broth culture showed small puffball-like growth. Gram staining showed a gram-negative bacillus 0.5 μm wide and 1–4 μm long. Some extremely long forms (up to 150 μm) with beadlike chains, fusiform swellings, and large round bodies were seen. The microbiologist who observed the Gram-stained smear immediately knew the cause of the girl's infection to be
 - Pasteurella multocida*
 - Streptobacillus moniliformis*
 - Francisella tularensis*
 - Bartonella bacilliformis*
 - Yersinia pestis*
- A 70-year-old man presents with bilateral pneumonia. His *Legionella* urinary antigen test result is positive. Which of the following is the likely cause of his pneumonia?
 - Legionella pneumophila* serogroup 1
 - Legionella micdadei* serogroup 4
 - Legionella bozemanii* serogroup 2
 - Legionella longbeachae* serogroup 2
 - All of the above because the urinary antigen test is genus specific and not species or serotype specific.
- A 65-year-old man comes to the emergency department feeling feverish and “really tired.” He has a chronic cigarette cough, but this has dramatically increased in the past week and he has been producing whitish sputum. The previous day he had a temperature of 38°C and watery diarrhea. Physical examination reveals inspiratory and expiratory wheezes and rales over the right lower lung field. Chest radiography shows a patchy right lower lobe infiltrate. The differential diagnosis of this patient's disease is
 - Streptococcus pneumoniae* pneumonia
 - Legionella pneumophila* pneumonia
 - Haemophilus influenzae* pneumonia
 - Mycoplasma pneumoniae* pneumonia
 - All of the above
- Routine sputum cultures for the patient in Question 4 grow normal microbiota. Treatment with ampicillin for 2 days yields no improvement. A diagnosis of Legionnaires' disease is considered, and bronchoscopy is done to obtain bronchial alveolar lavage fluid and deep airway specimens. Which of the following would suggest a diagnosis of disease caused by *Legionella pneumophila* serotype 1?
 - Legionella urinary antigen assay
 - Direct fluorescent antibody on the bronchial alveolar lavage fluid
 - Culture of the bronchial alveolar lavage on charcoal yeast extract medium with antibiotics
 - Antibody assay on paired (acute phase and convalescent phase) sera
 - All of the above
- Charcoal is present in buffered charcoal yeast extract agar used to isolate *Legionella pneumophila* to
 - Provide the growth factors ordinarily provided by free-living amebas present in environmental water
 - Serve as a carbon source for the growth of *Legionella pneumophila*
 - Prevent hemolysis of the red blood cells in the medium
 - Provide a dark background
 - Act as a detoxifying agent
- A 23-year-old, otherwise healthy woman presents with a 3-day history of low-grade fever and headache. Examination reveals enlarged and slightly tender lymph nodes near her left elbow and in the left axilla. Approximately 2 weeks earlier, she had visited a friend whose cat had scratched her on the left arm; the site later developed a reddish papule. Which of the following statements about this disease is correct?
 - Characteristic histopathology in response to infection is acute, neutrophilic inflammation.
 - The diagnosis is based on a suggestive history and physical examination.
 - β -Lactam/ β -lactamase inhibitor combinations are the agents of choice for treatment.
 - The diagnosis is based on negative routine bacterial cultures of pus aspirated from involved lymph nodes.
 - The disease rapidly leads to sepsis even in immunocompetent people.
- Which of the following statements about bacillary angiomatosis is most correct?
 - It is caused by *Bartonella bacilliformis*.
 - It is typically confined to the skin.
 - The major differential diagnosis is Kaposi sarcoma.

- (D) The etiologic agent can be grown in 1–2 days in routine culture on sheep blood agar.
- (E) Dogs are the reservoir for the etiologic agent.
9. An important factor in the pathogenesis of Legionnaires' disease is that
- (A) *Legionella pneumophila* kills polymorphonuclear cells.
- (B) Alveolar macrophages phagocytose *Legionella pneumophila* using coiled pseudopods.
- (C) *Legionella pneumophila* invades pulmonary capillaries, leading to dissemination and systemic illness.
- (D) *Legionella pneumophila* induces alveolar macrophage phagosomes to fuse with lysosomes.
- (E) *Legionella pneumophila* outer surface protein A (OspA) is important for invasion of alveolar macrophages.
10. True statements regarding *Tropheryma whippelii* include all of the following *except*
- (A) It is easy to cultivate on chocolate agar after 3 days of incubation.
- (B) It is a gram-positive actinomycete.
- (C) It causes fever, abdominal pain, diarrhea, weight loss, and migratory polyarthralgia.
- (D) It stains with PAS.
11. All of the statements below regarding infections with *Legionella* are correct *except*
- (A) Hospitals that care for patients at risk for *Legionella* infections should know if their potable water systems contain *Legionella*.
- (B) Human-to-human transmission is the major mechanism of transmission of *Legionella* infection.
- (C) *Legionella* species can be visualized with Gram stain if carbolfuchsin is used for the counter stain.
- (D) The chest radiograph of a patient who has *Legionella* pneumonia is indistinguishable from that of patients with pneumonia caused by other pathogens.
- (E) A macrolide or quinolone are the drugs of first choice for treatment of *Legionella* infections.
12. Which of the following best represents the role of the Mip protein in *Legionella* pathogenesis?
- (A) It prevents phagosome–lysosome fusion.
- (B) It acts as a siderophore to capture iron.
- (C) It prevents phagocytosis.
- (D) It facilitates adherence to the macrophage and stimulates cellular invasion.
- (E) None of the above.
13. Pontiac fever is a severe form of pneumonia caused by *Legionella pneumophila* serotypes 1 and 6.
- (A) True
- (B) False
14. All of the following statements regarding *Streptobacillus moniliformis* are correct *except*
- (A) It is susceptible to penicillin.
- (B) It causes the disease rat-bite fever.
- (C) It causes Haverhill fever from ingestion of contaminated food.
- (D) The morphology of the organism is spiral shaped.
15. The diagnosis of Whipple's disease is best made by
- (A) Paired serum obtained 8 weeks apart
- (B) Prolonged culture on mycobacterial media
- (C) Nucleic acid amplification testing performed on tissue
- (D) Histopathology
- (E) None of the above

Answers

- | | | | |
|------|------|-------|-------|
| 1. B | 5. E | 9. B | 13. B |
| 2. B | 6. E | 10. A | 14. D |
| 3. A | 7. B | 11. B | 15. C |
| 4. E | 8. C | 12. D | |

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end

Mycobacteria

Concept Checks

- The NTM are a diverse group of organisms commonly found in the environment, and the group includes both saprophytes and human pathogens.
- The NTM can be further classified into the rapid growers (grow in < 7 days) and slow growers. Each group can be subdivided on the basis of pigment production.
- Members of MAC are among the most frequently isolated NTM. They are responsible for significant disease in patients with AIDS and others with chronic lung disease.
- *M kansasii* causes pulmonary infections that mimic tuberculosis. It responds to therapy with INH, RIF, and EMB.
- The rapid growers are diverse. *M fortuitum* complex, *M chelonae*, and *M abscessus* are the most prevalent. *M abscessus* causes the most severe disease and is often multidrug resistant.
- *M leprae* causes the disease leprosy. The organism is not cultivatable, so diagnosis is difficult. Treatment with dapson, RMP, and clofazimine is often prolonged for many years.

REVIEW QUESTIONS

1. A 60-year-old man has a 5-month history of progressive weakness and a weight loss of 13 kg along with intermittent fever, chills, and a chronic cough productive of yellow sputum, occasionally streaked with blood. A sputum specimen is obtained, and numerous acid-fast bacteria are seen on the smear. Culture of the sputum is positive for *M tuberculosis*. Which treatment regimen is most appropriate for initial therapy?
 - (A) Isoniazid and rifampin
 - (B) Sulfamethoxazole-trimethoprim and streptomycin
 - (C) Isoniazid, rifampin, pyrazinamide, and ethambutol
 - (D) Isoniazid, cycloserine, and ciprofloxacin
 - (E) Rifampin and streptomycin
2. If the patient's *M tuberculosis* isolate (question 1) proves to be resistant to isoniazid, the likely mechanism for resistance is
 - (A) β -Lactamase
 - (B) Mutations in the catalase-peroxidase gene
 - (C) Alterations in the β subunit of RNA polymerase
 - (D) Mutations in the DNA gyrase gene
 - (E) Mutations in the genes encoding the S12 protein and 16S rRNA
3. A 47-year-old woman presents with a 3-month history of progressive cough, weight loss, and fever. Chest radiography shows bilateral cavitory disease suggestive of tuberculosis. Sputum culture grows an acid-fast bacillus that is a photochromogen (makes an orange pigment when exposed to light). The organism most likely is
 - (A) *Mycobacterium tuberculosis*
 - (B) *Mycobacterium kansasii*
 - (C) *Mycobacterium gordonae*
 - (D) *Mycobacterium avium* complex
 - (E) *Mycobacterium fortuitum*
4. A 31-year-old Asian woman is admitted to the hospital with a 7-week history of increasing malaise, myalgia, nonproductive cough, and shortness of breath. She has daily fevers of 38–39°C and a recent 5-kg weight loss. She had a negative chest radiograph when she entered the United States 7 years ago. The patient's grandmother died of tuberculosis when the patient was an infant. A current chest radiograph is normal; results of other tests show a decreased hematocrit and liver function test abnormalities. Liver and bone marrow biopsies show granulomas with giant cells and acid-fast bacilli. She is probably infected with
 - (A) *Mycobacterium leprae*
 - (B) *Mycobacterium fortuitum*
 - (C) *Mycobacterium ulcerans*
 - (D) *Mycobacterium gordonae*
 - (E) *Mycobacterium tuberculosis*
5. It is very important that the patient in question 4 also be evaluated for
 - (A) HIV/AIDS
 - (B) Typhoid fever
 - (C) Liver abscess
 - (D) Lymphoma
 - (E) Malaria
6. Of concern regarding the patient in question 4 is that she could be infected with a *Mycobacterium* that is
 - (A) Susceptible only to isoniazid
 - (B) Resistant to streptomycin
 - (C) Resistant to clarithromycin
 - (D) Susceptible only to ciprofloxacin
 - (E) Resistant to isoniazid and rifampin
7. You observe a 40-year-old man begging on a street in a town in India. He has clawing of the fourth and fifth digits with loss of distal parts of the digits of both hands, strongly suggesting leprosy. The causative agent of this disease
 - (A) Is susceptible to isoniazid and rifampin
 - (B) Grows in parts of the body that are cooler than 37°C
 - (C) Can be cultured in the laboratory using Middlebrook 7H11 medium
 - (D) Is seen in high numbers in biopsies of tuberculoid leprosy lesions
 - (E) Commonly infects people in Texas because armadillos are hosts of *M leprae*
8. Which of the following statements about the purified protein derivative (PPD) and the tuberculin skin test is most correct?
 - (A) It is strongly recommended that medical and other health science students have PPD skin tests every 5 years.
 - (B) Persons immunized with BCG rarely, if ever, convert to positive PPD skin test results.
 - (C) The intradermal skin test is usually read 4 hours after being applied.
 - (D) A positive tuberculin test result indicates that an individual has been infected with *M tuberculosis* in the past and may continue to carry viable mycobacteria.
 - (E) A positive PPD skin test result implies that a person is immune to active tuberculosis.
9. A 72-year-old woman has an artificial hip joint placed because of degenerative joint disease. One week after the procedure, she has fever and joint pain. The hip is aspirated, and the fluid is submitted for routine culture and for culture for acid-fast

organisms. After 2 days of incubation, there is no growth on any of the media. After 4 days, however, bacilli are seen growing on the sheep blood agar plate, and similar-appearing acid-fast bacilli are growing on the culture for acid-fast bacteria. The patient is most likely infected with

- (A) *Mycobacterium tuberculosis*
 - (B) *Mycobacterium chelonae*
 - (C) *Mycobacterium leprae*
 - (D) *Mycobacterium kansasii*
 - (E) *Mycobacterium avium* complex
10. A 10-year-old child has a primary pulmonary *M tuberculosis* infection. Which of the following features of tuberculosis is most correct?
- (A) In primary tuberculosis, an active exudative lesion develops and rapidly spreads to lymphatics and regional lymph nodes.
 - (B) The exudative lesion of primary tuberculosis often heals slowly.
 - (C) If tuberculosis develops years later, it is a result of another exposure to *M tuberculosis*.
 - (D) In primary tuberculosis, all of the infecting *M tuberculosis* organisms are killed by the patient's immune response.
 - (E) In primary tuberculosis, the immune system is primed, but the PPD skin test result remains negative until there is a second exposure to *M tuberculosis*.
11. Which of the following statements regarding interferon- γ release assays (IGRAs) is correct?
- (A) They are useful for evaluating immunocompromised patients for active tuberculosis.
 - (B) They detect antigens present in all *Mycobacterium* species.
 - (C) They are not available yet for testing in the United States.
 - (D) They are performed using molecular probes that detect organism DNA.
 - (E) They are used as alternatives to the tuberculin skin test to evaluate for latent tuberculosis.
12. *M abscessus* most often causes pulmonary disease among which group of individuals?
- (A) Young children exposed to dirt
 - (B) African American smokers
 - (C) Elderly, nonsmoking white females
 - (D) Hispanic men who work outdoors
 - (E) Persons living in the Northwestern United States
13. A newly characterized rapidly growing *Mycobacterium* that has emerged as an important cause of central venous catheter associated infections is
- (A) *Mycobacterium phlei*
 - (B) *Mycobacterium mucogenicum*
 - (C) *Mycobacterium xenopi*
 - (D) *Mycobacterium smegmatis*
 - (E) *Mycobacterium terrae*
14. The definition of extensively drug-resistant (XDR) tuberculosis includes
- (A) Resistance to isoniazid
 - (B) Resistance to a fluoroquinolone
 - (C) Resistance to capreomycin, amikacin or kanamycin
 - (D) Resistance to rifampin
 - (E) All of the above

15. All of the following organisms are rapidly growing mycobacteria *except*

- (A) *Mycobacterium fortuitum*
- (B) *Mycobacterium abscessus*
- (C) *Mycobacterium mucogenicum*
- (D) *Mycobacterium nonchromogenicum*
- (E) *Mycobacterium chelonae*

Answers

- | | | |
|------|-------|-------|
| 1. C | 6. E | 11. E |
| 2. B | 7. B | 12. C |
| 3. B | 8. D | 13. B |
| 4. E | 9. B | 14. E |
| 5. A | 10. A | 15. D |

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end

Spirochetes, other spiral microorganisms

most likely to come in contact with water contaminated by rats (eg, miners, sewer workers, farmers, and fishermen) run the greatest risk of infection. Children acquire the infection from dogs more frequently than adults do. Control consists of preventing exposure to potentially contaminated water and reducing contamination by rodent control. Doxycycline, 200 mg orally once weekly during heavy exposure, is effective prophylaxis. Dogs can receive distemper–hepatitis–leptospirosis vaccinations.

REVIEW QUESTIONS

1. A 28-year-old woman who is 10 weeks pregnant presents to the obstetrics clinic for prenatal care. She has a history of treatment for syphilis 7 years previously. The results of serologic tests for syphilis are as follows: nontreponemal test, RPR, nonreactive; treponemal test (TP-PA), reactive. Which of the following statements is most correct?
 - (A) The mother's previous treatment for syphilis was effective.
 - (B) The baby is at high risk for congenital syphilis.
 - (C) The mother needs to be treated again for syphilis.
 - (D) The mother needs a lumbar puncture and a VDRL test of her CSF for neurosyphilis.
2. A 12-year-old Boy Scout went to summer camp for 2 weeks in late August at a site located just outside Mystic, Connecticut. When he returned home, his mother noticed a bull's-eye-shaped rash on the back of her son's left calf. Shortly after Labor Day, the boy developed a flulike illness that resolved after 4 days of bed rest. Three weeks later, the boy complained to his mother that his body hurt all over whenever he moved. This prompted a visit to the pediatrician, who ordered an infectious disease workup. What is the most likely source of the boy's infection?
 - (A) Respiratory transmission from another sick camper
 - (B) Ingestion of urine-contaminated water from a stream
 - (C) The bite of a mosquito harboring a parasite
 - (D) Ingestion of fecally contaminated food
 - (E) The bite of a spirochete-infected tick
3. Nontreponemal serological tests:
 - (A) Are useful in definitively identifying a *Treponema pallidum* infection.
 - (B) Measure antibodies against *Treponema pallidum*.
 - (C) Can be used to monitor antibiotic treatment of primary or secondary syphilis.
 - (D) Measure antibodies against lipids released from damaged cells.
 - (E) Are useful in diagnosing a disseminated gonococcal infection.
4. A 42-year-old woman went camping in the Sierra Nevada Mountains, where she slept for two nights in an abandoned log cabin. After the second night, a tick was found on her shoulder. Six days later, she developed fever to 38°C, which lasted for 4 days. Ten days later, she had another similar episode of fever. Examination of a blood smear stained with Wright stain showed spirochetes suggestive of *Borrelia* species. Which of the following statements about relapsing fever is correct?
 - (A) Each relapse is associated with an antigenically distinct variant.
 - (B) Blood smears should be made when the patient is afebrile.
 - (C) *Borreliae* do not pass transovarially from one generation to the next in ticks.
 - (D) The main reservoir for the *Borrelia* is deer.
 - (E) *Borrelia* is resistant to penicillin and tetracycline.
5. A 23-year-old man presented with a maculopapular rash over much of his trunk but not in his mouth or on his palms. Because secondary syphilis was considered in the differential diagnosis, a RPR test was done, and the result was positive at a 1:2 dilution. However, the TP-PA test result was negative. Which of the following diseases can be ruled out?
 - (A) Secondary syphilis
 - (B) Atypical measles
 - (C) Coxsackie virus infection
 - (D) Acute HIV 1 infection
 - (E) Allergic drug reaction
6. Which of the following animals is the source of *Leptospira interrogans*?
 - (A) Alligators
 - (B) Ducks
 - (C) Frogs
 - (D) Catfish
 - (E) Swine
7. A 27-year-old medical resident was admitted to the hospital because of sudden onset of fever to 39°C and headache. Two weeks previously, he had vacationed in rural Oregon, where he had frequently gone swimming in an irrigation canal that bordered land where cows were pastured. Blood tests done shortly after admission indicated renal function abnormality and elevated bilirubin and other liver function test results. Routine blood, urine, and CSF culture results were negative. Leptospirosis is suspected. Which of the following would be most likely to confirm this diagnosis?
 - (A) Testing acute and convalescent phase sera using the RPR test
 - (B) Culture of urine on human diploid fibroblast cells
 - (C) Testing serum by dark-field examination for the presence of leptospires
 - (D) Testing acute and convalescent phase sera for antileptospiral antibodies
 - (E) Culture of CSF on blood and chocolate agar
 - (F) Gram stain of CSF and blood
8. A 47-year-old man presents with slowly progressive arthritis in his knees. He enjoys hiking in the coastal areas of Northern California, where the prevalence of *Borrelia burgdorferi* in the *Ixodes* ticks is known to be 1–3% (considered low). The patient is concerned about Lyme disease. He never noticed a tick on his body and did not see an expanding red rash. The result of an EIA for Lyme borreliosis is positive. What should be done now?
 - (A) A biopsy specimen of the synovium of a knee joint should be examined for *Borrelia burgdorferi*.
 - (B) The patient should be given an antibiotic to treat Lyme disease.
 - (C) PCR on the patient's plasma should be done to detect *Borrelia burgdorferi*.
 - (D) A serum specimen should be submitted for immunoblot assay to detect antibodies reactive with *Borrelia burgdorferi* antigens.
 - (E) Culture of synovial fluid on blood and chocolate agar.

9. Which of the following organisms principally infects the liver and kidneys?
- Leptospira interrogans*
 - Staphylococcus aureus*
 - Escherichia coli*
 - Enterococcus faecalis*
 - Treponema pallidum*
10. All of the following statements regarding relapsing fever are correct *except*
- Epidemic disease carries a higher mortality rate than endemic disease.
 - Endemic disease in North America is caused by *Borrelia recurrentis*.
 - The recurrent febrile episodes are caused by antigenic variation among the spirochetes.
 - Penicillin is the drug of choice.
 - Crushing a tick could transmit the spirochetes.

Answers

- | | | |
|------|------|-------|
| 1. A | 5. A | 9. A |
| 2. E | 6. E | 10. B |
| 3. D | 7. D | |
| 4. A | 8. D | |

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end

M genitalium and *M pneumoniae* require a much longer incubation.

- *M pneumoniae* is an important cause of community-acquired pneumonia. Infection is insidious and often protracted. Diagnosis is best made clinically and confirmed by serology (fourfold rise in IgG or IgM) or by NAATs or both.
- The urogenital Mycoplasmas have been associated with nonchlamydial, nongonococcal urethritis in men (*U urealyticum*). Both *M hominis* and *U urealyticum* may cause postpartum fever and respiratory infections in premature infants. *M hominis* is more prevalent in women with bacterial vaginosis than in healthy women.
- *Mycoplasma* and *Ureaplasma* infections do not respond to β -lactam antibiotics. Tetracyclines, macrolides, and quinolones are the agents of choice.

REVIEW QUESTIONS

1. *Ureaplasma urealyticum* is so named because
 - (A) It thrives in the upper urinary tract.
 - (B) It requires urea as a growth substrate.
 - (C) It is a frequent cause of symptomatic urinary bladder infections in young women.
 - (D) It causes chronic urinary tract infections in premature babies born to mothers with ureaplasmas as part of the genital flora.
2. An 18-year-old sexually active woman develops left lower quadrant pain and fever. On pelvic examination, she has tenderness in the left adnexa, and a mass suggestive of a uterine tube abscess is palpated. The patient is diagnosed with pelvic inflammatory disease. Which of the following bacteria is considered to be a common cause of pelvic inflammatory disease?
 - (A) *Bacillus cereus*
 - (B) *Haemophilus influenzae*
 - (C) *Neisseria subflava*
 - (D) *Mycoplasma pneumoniae*
 - (E) *Chlamydia trachomatis*
3. Which of the following is important in the pathogenesis of mycoplasmal infections?
 - (A) The peptidoglycan in the mycoplasmal cell wall
 - (B) The presence of lacto-*N*-neotetraose with a terminal galactosamine as the host cell receptor
 - (C) The structures and the interactive proteins that mediate adhesion to host cells
 - (D) The absence of cilia on the surface of the host cells
 - (E) Growth in an anatomic site where anaerobic organisms thrive
4. A 25-year-old woman is referred to the sexually transmitted diseases clinic because of contact with a male partner with gonorrhea. The woman has had 15 male sex partners since becoming sexually active. The likelihood that she also has genital *Mycoplasma hominis* infection is
 - (A) 1%
 - (B) 5%
 - (C) 15%
 - (D) 40%
 - (E) 90%
5. A 25-year-old medical student has contact with a patient who has pneumonia with fever and cough. Four days later, the medical student develops fever and cough, and chest radiographs show consolidation of the right lower lobe. Routine bacterial sputum culture results are negative. Pneumonia caused by *Mycoplasma pneumoniae* is considered. All of the following are methods to confirm the clinical suspicion *except*
 - (A) PCR amplification of *Mycoplasma pneumoniae* DNA in sputum
 - (B) Culture of sputum for *Mycoplasma pneumoniae*
 - (C) Gram stain of sputum smear
 - (D) Culture of a lung aspirate for *Mycoplasma pneumoniae*
 - (E) Enzyme immunoassay test of acute and convalescent sera
6. Which type of test is most readily used to obtain laboratory confirmation of *Mycoplasma pneumoniae* infection?
 - (A) Culture in broth containing serum, glucose, and a penicillin (to inhibit other flora)
 - (B) PCR
 - (C) Electron microscopy
 - (D) EIA tests on acute and convalescent phase sera
7. A 13-year-old boy develops infection with *Mycoplasma pneumoniae*. What is the risk for infection in other members of his household?
 - (A) None; it is sexually transmitted
 - (B) 1–3%
 - (C) 10–15%
 - (D) 20–40%
 - (E) 50–90%
8. A 19-year-old man develops cough and fever. A chest radiograph shows consolidation of the left lower lobe. A diagnosis of pneumonia is made. Which of the following bacteria is a frequent cause of community-acquired pneumonia?
 - (A) *Legionella pneumophila*
 - (B) *Chlamydia pneumoniae*
 - (C) *Streptococcus pneumoniae*
 - (D) *Mycoplasma pneumoniae*
 - (E) *Klebsiella pneumoniae*
9. Initiation of infection by *Mycoplasma pneumoniae* begins with
 - (A) Elaboration of a polysaccharide capsule that inhibits phagocytosis
 - (B) Secretion of a potent exotoxin
 - (C) Endocytosis by ciliated respiratory epithelial cells
 - (D) Adherence to respiratory epithelial cells mediated by P1 adhesin
 - (E) Phagocytic uptake by alveolar macrophages
10. Infection with *Mycoplasma genitalium*:
 - (A) is not restricted to the genitourinary tract.
 - (B) results in inflammation causing urethritis in males and cervicitis in females.
 - (C) is best treated with a first-generation cephalosporin.
 - (D) is associated only with nongonococcal urethritis in males.
 - (E) is asymptomatic unless a co-infection with *Clamydya trachomatis* is present.

Answers

- | | | |
|------|------|-------|
| 1. B | 5. C | 9. D |
| 2. E | 6. D | 10. B |
| 3. C | 7. E | |
| 4. E | 8. E | |

end

REVIEW QUESTIONS

- Morulae (intracellular inclusions in leukocytes) are characteristic of which of the following diseases?
 - Malaria caused by *Plasmodium falciparum* infection but not *Plasmodium malariae* infection
 - Dengue
 - Babesia infection
 - Ehrlichiae infection
 - Loa loa
- Which of the following statements about epidemic typhus (*Rickettsia prowazekii* disease) is most correct?
 - The disease occurs primarily in sub-Saharan Africa.
 - It is transmitted by ticks.
 - Mice are the reservoir.
 - Historically, the disease occurs in times of prosperity.
 - Recrudescence can occur many years after the initial infection.
- The most useful drug to treat ehrlichiosis is
 - Doxycycline
 - Penicillin G
 - Trimethoprim–sulfamethoxazole
 - Gentamicin
 - Nitrofurantoin
- A disease characterized by malaise, headache, rigors, and fever developed in members of several families living in an unheated war-damaged house in an Eastern European country. Erythematous 2–6 mm macular red rashes appeared on the people's trunks and later on their extremities. Some of the people had coughs. One elderly person, although sick, was much less sick than other adults. The people huddled together to keep warm; body lice were common. Which of the following statements is most correct?
 - The disease that these people had is common in the Rocky Mountain states.
 - The elderly person may have had acute epidemic typhus many years ago and recrudescence typhus now.
 - Fleas from rodents in the house were spreading *Rickettsia typhi*.
 - The primary host of the body louse infecting the people is the rat.
 - Epidemic typhus can be prevented by a vaccine.
- Which of the following statements about Ehrlichiae and ehrlichiosis is most correct?
 - Dogs and mice are reservoirs.
 - Mosquitoes are the vectors.
 - Ampicillin is the treatment of choice.
 - Culture is a good method to confirm the diagnosis.
 - Ehrlichiae are typically found in lymphocytes.
- A group of urban teenagers visited a sheep ranch in a large Western state for a 2-week experience. While they were there, many of the pregnant ewes delivered lambs to the delight of the closely observing teenagers. About 10 days later, three of the teenagers developed flulike illnesses characterized by malaise, cough, and fever. One had an infiltrate on chest radiography, indicating pneumonia. The three teenagers had different doctors, but the physicians each drew a blood specimen and submitted it to the city health department for serologic testing. All three specimens were positive for Q fever. Public health investigators determined that all of the teenagers had been to the sheep ranch. When the investigators contacted the ranch, they were told that there was no Q fever there and that no one who lived at the ranch had been sick. The most likely explanation for the teenagers' illnesses and the lack of illness at the ranch is
 - There was no Q fever at the ranch, and it was acquired elsewhere.
 - The people at the ranch had been previously immunized against Q fever.
 - The teenagers acquired Q fever at the ranch, and the people who lived there had all previously had Q fever and were now immune to it.
 - The teenagers had other illnesses, and the positive Q fever serology result was unrelated.
 - The public health laboratory had errors in the Q fever serologic tests.
- A middle-aged sportsman, a resident of Oklahoma, took a hike through a rural wooded and brushy area near his home. The next morning, he noticed and removed a large (>1 cm) tick from his upper arm. About 1 week later, he experienced a gradual onset of fever and malaise. He now seeks medical attention because he is concerned about a possible infection transmitted by the tick. Which of the following diseases is most likely to be acquired from a tick?
 - Dengue
 - Rocky Mountain spotted fever
 - Typhus
 - Yellow fever
 - Malaria
- Which of the following drugs should *not* be used to treat Rocky Mountain spotted fever (*Rickettsia rickettsii* infection)?
 - Trimethoprim–sulfamethoxazole
 - Chloramphenicol
 - Doxycycline
- Which of the following should be used to prevent Rocky Mountain spotted fever (*Rickettsia rickettsii* infection)?
 - Attenuated *Rickettsia rickettsii* vaccine
 - Prophylactic doxycycline
 - Preventing tick bites by wearing protective clothing
 - Delousing with insecticide
- One week after deer hunting in a wooded area, a 33-year-old man developed fever to 39°C with headache and malaise. Over the subsequent 24 hours, he developed nausea, vomiting, abdominal pain, and diarrhea. On day 4, he developed a rash, initially around the wrists and ankles, which then progressively evolved, involving the arms, trunk, palms, and soles. Initially the rash was macular, but it quickly evolved into maculopapules, some with central petechiae. Rocky Mountain spotted fever caused by *Rickettsia rickettsii* was diagnosed. Which of the following statements about Rocky Mountain spotted fever is correct?
 - The vectors of *Rickettsia rickettsii* are ticks of the genus *Ixodes*.
 - A rash consistently appears by day 4 of illness.
 - Rickettsia rickettsii* forms inclusions in monocytes.
 - The patient's antibody response may not occur until after the second week of illness.
 - The highest incidence of this disease is in the Rocky Mountain states.

11. The recommended treatment for Q-fever endocarditis is
 - (A) Emergent surgery; antibiotics are not effective
 - (B) Levofloxacin monotherapy for 6 weeks
 - (C) 18 months of combination therapy with doxycycline and hydroxychloroquine
 - (D) Penicillin and gentamicin combination therapy using IgG titers to determine duration
12. *Coxiella burnetii* can be transmitted by milk when animals such as goats and cows are infected. The presently recommended conditions of “high-temperature, short-time” pasteurization are adequate to destroy viable *Coxiella* organisms.
 - (A) True
 - (B) False
13. The histopathological hallmark of infection caused by *Rickettsia rickettsiae* is
 - (A) Morulae within granulocytes
 - (B) Morulae within monocytes
 - (C) Granulomatous inflammation
 - (D) Intracellular vacuoles
 - (E) Perivascular lymphocytes
14. All of the following statements regarding Rickettsialpox are correct *except*
 - (A) The cause of the disease is *R akari*.
 - (B) Ticks of the genus *Amblyomma* are responsible for transmission.
 - (C) The disease is mild.
 - (D) Disease is more common in urban than rural areas.
15. Reasons why *C burnetii* could be a potential agent of bioterrorism include
 - (A) It is acquired by the inhalation.
 - (B) It is highly infectious.
 - (C) It can be difficult to treat depending on the phase of infection.
 - (D) Pneumonia may be severe.
 - (E) All of the above.

Answers

- | | | | |
|------|------|-------|-------|
| 1. D | 5. A | 9. C | 13. E |
| 2. E | 6. C | 10. D | 14. B |
| 3. A | 7. B | 11. C | 15. E |
| 4. B | 8. A | 12. A | |

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End

Chlamydia spp.

imported psittacine birds. Latent infections often flared up in these birds during transport and crowding, and sick birds excreted exceedingly large quantities of infectious agent. Control of bird shipment, quarantine, testing of imported birds for psittacosis infection, and prophylactic tetracyclines in bird feed have helped to control this source. Pigeons kept for racing or as pets or raised for squab meat have been important sources of infection. Pigeons populating buildings and thoroughfares in many cities, if infected, shed relatively small quantities of agent.

CHAPTER SUMMARY

- *Chlamydiae* are small organisms that multiply in the cytoplasm of their host cells using unique biphasic developmental cycles.
- The EB is the infectious particle that is environmentally stable. The RB is the metabolically active form that divides by binary fission within a membrane-bound vacuole.
- There are three species of *Chlamydia* that cause disease in humans: *C trachomatis*, *C pneumoniae*, and *C psittaci*.
- *C trachomatis* is responsible for sexually transmitted diseases that include cervicitis, pelvic inflammatory disease, urethritis, epididymitis, LGV, and proctitis, and when transmitted to infants of infected pregnant women, infant inclusion conjunctivitis and eosinophilic pneumonia.
- Diagnosis of *C trachomatis* urogenital infections is made most readily by NAATs; culture or DFA is required to diagnose pediatric syndromes. Treatment of infections caused by *C trachomatis* requires doxycycline or azithromycin.
- *C pneumoniae* causes a variety of upper and lower respiratory infections. Pharyngitis is common, and atypical pneumonia resembling that of *M pneumoniae* is responsible for approximately 5% of cases of community-acquired pneumonia.
- Serology using MIF is the most sensitive means of diagnosing *C pneumoniae*. NAATs are available in research and reference laboratories but vary in their performance. There is one FDA-approved commercial assay that detects *C pneumoniae*.
- *C psittaci* is acquired from contact with birds such as parrots, pigeons, and various domestic poultry.
- The disease psittacosis may be inapparent or mild, but severe pneumonia and sepsis associated with a high mortality rate have also been described.
- Diagnosis is made serologically; doxycycline is used for treatment.

REVIEW QUESTIONS

1. Which of the following statements about chlamydial antigens is correct?
 - (A) Chlamydiae have shared group or genus-specific antigens.
 - (B) There is no cross-reaction between *Chlamydia trachomatis* and *Chlamydia pneumoniae* antigens.
 - (C) All five serovars of *Chlamydia pneumoniae* cross-react with *Chlamydia psittaci*.
 - (D) One serovar of *Chlamydia trachomatis* causes eye infections, and the second serovar causes genital infections.
2. The following are part of the control of *Chlamydia psittaci* and psittacosis in birds *except*
 - (A) Quarantine of psittacine birds imported into the United States
 - (B) Only allowing sale of psittacine birds hatched in the United States
 - (C) Testing of birds for *C psittaci* infection
 - (D) Controlling the shipment of psittacine birds
 - (E) Putting tetracycline in the feed of psittacine birds
3. All of the following statements about perinatal *Chlamydia trachomatis* infections are correct *except*
 - (A) Between 15% and 40% of infants born to infected women develop inclusion conjunctivitis.
 - (B) Between 10% and 20% of infants born to infected women develop infant pneumonia.
 - (C) The incubation period for *Chlamydia trachomatis* inclusion conjunctivitis is 1–2 days.
 - (D) The incubation period for infant pneumonia is typically 2–12 weeks.
 - (E) Ocular prophylaxis with erythromycin or tetracycline for neonatal *Neisseria gonorrhoeae* infection is generally not effective against neonatal *Chlamydia trachomatis* infection.
 - (F) Infant pneumonia caused by *Chlamydia trachomatis* often presents with a staccato cough.
4. An adolescent girl came to the clinic because of a new and unusual vaginal discharge. She had recently become sexually active and had two new partners during the previous month. On pelvic examination, a purulent discharge was seen at the opening of her endocervical canal. Which of the following statements about this patient is most correct?
 - (A) A serologic test for syphilis is not indicated because her symptoms are not those of syphilis.
 - (B) A Gram stain of her endocervical specimen would show *Chlamydia trachomatis* inside polymorphonuclear cells.
 - (C) The differential diagnosis includes infection with *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or both.
 - (D) The endocervical specimen should be analyzed for herpes simplex.
 - (E) Initial treatment is with ampicillin.
5. The following statements about trachoma are correct *except*
 - (A) It follows chronic or recurrent eye infection with *Chlamydia trachomatis*.
 - (B) Millions of people worldwide have trachoma.
 - (C) Trachoma is readily prevented by a chlamydial vaccine.
 - (D) Progression of trachoma can be slowed by intermittent treatment with azithromycin.
 - (E) Trachoma involves scarring of the conjunctiva, eyelid deformities, and eyelash injury to the cornea.
6. Elimination of blinding trachoma involves all of the following *except*
 - (A) Periodic administration of azithromycin
 - (B) Face washing and hygiene
 - (C) Periodic culture screening of conjunctiva swab specimens for *Chlamydia trachomatis*

- (D) Environment improvements to sewage systems to decrease the number of flies
 (E) Surgery on deformed eyelids
7. Which one of the following statements about *Chlamydia pneumoniae* is most correct?
 (A) Transmission from person to person is by the airborne route.
 (B) It makes glycogen-rich inclusions that stain with iodine.
 (C) There are multiple serovars, including three that cause a systemic illness.
 (D) They are resistant to macrolides.
 (E) The reservoir is house cats.
8. The serovars of *Chlamydia trachomatis* generally can be divided into groups representing their clinical infections and anatomic site infected. Which of the following statements about the *C trachomatis* serovars is most correct?
 (A) There is no immunologic cross-reaction between *Chlamydia trachomatis* serovars A, B, Ba, and D and the *Chlamydia pneumoniae* serovar.
 (B) Serovars L1, L2, and L3 are associated with lymphogranuloma venereum.
 (C) The same *Chlamydia trachomatis* serovars are associated with blinding trachoma and sexually transmitted infections.
 (D) The antibody titer rise seen beginning around 6–8 years follows infections with *Chlamydia trachomatis* serovars D–K.
9. In the United States, it has long been known that the positive seroprevalence for *Chlamydia trachomatis* infection increases greatly during the primary school years (ages 6–10 years). A likely reason for this is
 (A) Frequent adenovirus infections
 (B) Increased incidence of infections with *Chlamydia trachomatis*
 (C) Cross-reactive antibodies with M protein of group A streptococci (*Streptococcus pyogenes*)
 (D) Children often have psittacosis
 (E) Frequent infections with *Chlamydia pneumoniae*
10. All of the following statements about lymphogranuloma venereum (LGV) are correct *except*
 (A) Chronic LGV proctitis can lead to rectal strictures and fistula formation.
 (B) The disease is more common in northern latitudes.
 (C) There may be marked systemic symptoms, including fever, nausea, vomiting, headache, and meningismus.
 (D) Chronic inflammation with LGV can lead to lymphatic obstruction.
 (E) Inguinal lymph nodes may become enlarged and matted, draining pus through the skin.
 (F) A few days or weeks after exposure, the disease manifests itself as a genital papule or vesicle.
11. Which of the following methods are considered the diagnostic tests of choice for urogenital infections caused by *Chlamydia trachomatis*?
 (A) Serology using complement fixation
 (B) Cell culture using cycloheximide containing McCoy cells
 (C) Direct fluorescent antibody testing on urethral and cervical specimens
 (D) Nucleic acid amplification methods
 (E) Enzyme immunoassays performed on genital tract specimens
12. Nucleic acid amplification tests that are currently available in the United States for diagnosing chlamydial infections are approved for testing all of the following specimens *except*
 (A) Self-collected vaginal swabs in women
 (B) First void urine samples obtained from men
 (C) Rectal swabs obtained from children 12 years of age or younger
 (D) Urethral swab samples obtained from adult men
 (E) Cervical swab samples obtained from adolescent girls
13. *Chlamydia pneumoniae* pneumonia most resembles infection caused which of the following organisms?
 (A) *Streptococcus pneumoniae*
 (B) *Mycoplasma pneumoniae*
 (C) *Haemophilus influenzae*
 (D) *Chlamydia trachomatis*
 (E) Rhinovirus
14. Inclusion conjunctivitis of the newborn
 (A) Is a mucopurulent conjunctivitis that occurs 7–12 days after delivery
 (B) Is caused by *Chlamydia psittaci*
 (C) Is a result of exposure to pet birds in the home
 (D) Is treated with systemic penicillin because it may progress to pneumonia
 (E) None of the above
15. The diagnostic method of choice for *Chlamydia trachomatis* pneumonia in the newborn is
 (A) A nucleic acid amplification test that targets the *ompA* gene
 (B) Culture of respiratory secretions in McCoy cells or other cell lines
 (C) Enzyme immunoassay testing of respiratory secretions
 (D) IgG antibodies detected by complement fixation

Answers

- | | | | |
|------|------|-------|-------|
| 1. A | 5. C | 9. E | 13. B |
| 2. B | 6. C | 10. B | 14. A |
| 3. C | 7. A | 11. D | 15. B |
| 4. C | 8. B | 12. C | |

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end

Anti
microbial

Chemotherapy

ethambutol is always given in combination with other anti-tuberculous drugs.

Ethambutol is usually given as a single oral daily dose. Hypersensitivity to ethambutol occurs infrequently. The most common side effects are visual disturbances, but these are rare at standard dosages: Reduction in visual acuity, optic neuritis, and perhaps retinal damage occur in some patients given high doses for several months. Most of these changes apparently regress when ethambutol is discontinued. However, periodic visual acuity testing is mandatory during treatment. With low doses, visual disturbances are very rare.

Rifamycins

Rifampin is a semisynthetic derivative of rifamycin, an antibiotic produced by *Streptomyces mediterranei*. It is active in vitro against some gram-positive and gram-negative cocci, some enteric bacteria, mycobacteria, chlamydiae, and poxviruses. Although many meningococci and mycobacteria are inhibited by less than 1 $\mu\text{g}/\text{mL}$, highly resistant mutants occur in all microbial populations in a frequency of 10^{-6} – 10^{-5} . The prolonged administration of rifampin as a single drug permits the emergence of these highly resistant mutants. There is no cross-resistance to other antimicrobial drugs.

Rifampin binds strongly to DNA-dependent RNA polymerase and thus inhibits RNA synthesis in bacteria. It blocks a late stage in the assembly of poxviruses. Rifampin penetrates phagocytic cells well and can kill intracellular organisms. Rifampin-resistant mutants exhibit an altered RNA polymerase.

Rifampin is well absorbed after oral administration, widely distributed in tissues, and excreted mainly through the liver and to a lesser extent into the urine.

In tuberculosis, a single oral dose is administered together with ethambutol, INH, or another antituberculous drug to delay the emergence of rifampin-resistant mycobacteria. A similar regimen may apply to non-tuberculous mycobacteria. In short-term treatment schedules for tuberculosis, rifampin is given orally, at first daily (together with INH), and then two or three times weekly for 6–9 months. However, no less than two doses weekly should be given to avoid a “flu syndrome” and anemia. Rifampin used in conjunction with a sulfone is effective in leprosy.

Oral rifampin can eliminate a majority of meningococci from carriers. Unfortunately, some highly resistant meningococcal strains are selected out by this procedure. Close contacts of children with *H influenzae* infections (eg, in the family or in daycare centers) can receive rifampin as prophylaxis. In urinary tract infections and chronic bronchitis, rifampin is not useful because resistance emerges promptly.

Rifampin imparts a harmless orange color to urine, sweat, and contact lenses. Occasional adverse effects include rashes, thrombocytopenia, light chain proteinuria, and impairment of liver function. Rifampin induces microsomal enzymes (eg, cytochrome P450).

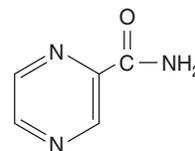
Rifabutin is a related antimycobacterial drug that is active in the prevention of infection caused by *M avium* complex.

Rifaximin is a derivative of rifampin that possesses an additional pyridoimidazole ring. It is a nonabsorbed oral agent useful in the treatment of traveler’s diarrhea and as salvage therapy for recurrent *C difficile* disease.

Rifapentine is used for the treatment of tuberculosis and because it is longer acting it is useful in regimens that are administered once or twice per week. Food increases the absorption.

Pyrazinamide

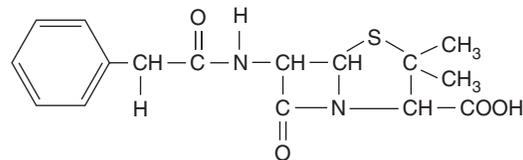
Pyrazinamide is related to nicotinamide. It is readily absorbed from the gastrointestinal tract and widely distributed in tissues. *M tuberculosis* readily develops resistance to pyrazinamide, but there is no cross-resistance with INH or other antituberculous drugs. The major adverse effects of pyrazinamide are hepatotoxicity (1–5%), nausea, vomiting, hypersensitivity, and hyperuricemia.



Pyrazinamide (PZA)

REVIEW QUESTIONS

- The antimicrobial agent whose structure is shown below is considered the drug of choice to treat infections caused by which one of the following microorganisms?



- Bacteroides fragilis*
 - Pseudomonas aeruginosa*
 - Herpes simplex virus
 - Streptococcus pyogenes* (group A streptococci)
 - Mycobacterium tuberculosis*
- Resistance of *Staphylococcus aureus* to the drug shown in Question 1 is caused by
 - The action of acetyltransferase
 - The action of β -lactamase
 - Substitution of the D-Ala-D-Ala dipeptide with the D-Ala-D-Lac dipeptide in the cell wall peptidoglycan
 - Decreased permeability of the bacterial cell wall to the drug
 - Staphylococcus aureus* being an intracellular pathogen
 - Streptococcus pneumoniae* resistance to the drug shown in Question 1 is caused by
 - The action of acetyltransferase
 - The action of β -lactamase
 - Substitution of the D-Ala-D-Ala dipeptide with D-Ala-D-Lac dipeptide in the cell wall peptidoglycan

- (D) Decreased permeability of the bacterial cell wall
 (E) Genetically modified binding proteins in the bacterial cell wall
4. All of the following statements about antimicrobial resistance of enterococci are correct *except*
- (A) Enterococci are resistant to sulfamethoxazole–trimethoprim *in vivo*.
 (B) Cephalosporins are not active against enterococci.
 (C) Resistance to the streptogramins (quinupristin–dalfopristin) has emerged.
 (D) Vancomycin-resistant enterococci are rare in Europe and the United States.
 (E) Vancomycin-resistant enterococci once consistently clonal are now heterogeneous.
5. A 20-year-old Asian woman, a recent immigrant to the United States, develops fever and a cough productive of blood-streaked sputum. She has lost 6 kg of body weight in the past 6 weeks. Her chest radiograph shows bilateral upper lobe infiltrates with cavities. Given the history and chest radiography findings, which of the following drug regimens would be the best appropriate initial therapy while awaiting culture results?
- (A) Isoniazid, rifampin, pyrazinamide, and ethambutol
 (B) Penicillin G and rifampin
 (C) Cefotaxime, clindamycin, and trimethoprim–sulfamethoxazole
 (D) Ampicillin–sulbactam
 (E) Vancomycin, gentamicin, and clindamycin
6. Aminoglycoside antibiotics typically cause which of the following adverse events?
- (A) They cause aplastic anemia.
 (B) They cause nonspecific stimulation of B cells.
 (C) They cause ototoxicity and nephrotoxicity.
 (D) They cause photosensitivity.
7. Which one of the following groups of antimicrobial agents acts on microorganisms by inhibiting protein synthesis?
- (A) Fluoroquinolones
 (B) Aminoglycosides
 (C) Penicillins
 (D) Glycopeptides (eg, vancomycin)
 (E) Polymyxins
8. There are many bacterial–antimicrobial resistance combinations. Which one of the following is of major international concern?
- (A) Sulfonamide resistance in *Neisseria meningitidis*
 (B) Penicillin G resistance in *Neisseria gonorrhoeae*
 (C) Ampicillin resistance in *Haemophilus influenzae*
 (D) Erythromycin resistance in *Streptococcus pyogenes* (group A streptococci)
 (E) Vancomycin resistance in *Staphylococcus aureus*
9. Which of the following factors is not generally considered when selecting initial antimicrobial therapy for an infection?
- (A) Age of the patient
 (B) Anatomic site of the infection (eg, meningitis or urinary tract infection)
 (C) Whether or not the patient is immunocompromised
 (D) Whether or not the patient has implanted devices in place (eg, artificial hip joint, artificial heart valve, urinary catheter)
 (E) Waiting for culture and susceptibility test results
10. All of the following agents have good activity against gram-positive organisms *except*
- (A) Daptomycin
 (B) Vancomycin
 (C) Aztreonam
 (D) Quinupristin–dalfopristin
 (E) Tigecycline
11. Tigecycline, a new glycolcycline antibiotic with good activity against a variety of pathogens, is best used for treatment of which of the following infections?
- (A) Meningitis
 (B) Intra-abdominal infections caused by mixed aerobic and anaerobic bacteria
 (C) Neonatal sepsis
 (D) Urethritis caused by *Chlamydia trachomatis*
 (E) As monootherapy for bacteremia caused by *Acinetobacter baumannii*
12. Which of the following carbapenem antibiotics has no activity against *Pseudomonas aeruginosa*?
- (A) Imipenem
 (B) Meropenem
 (C) Doripenem
 (D) Ertapenem
13. Which of the following agents would not be expected to demonstrate postantibiotic effect against gram-negative bacilli?
- (A) Imipenem
 (B) Ciprofloxacin
 (C) Gentamicin
 (D) Ampicillin
14. All of the following are common mechanisms of resistance to the penicillins *except*
- (A) Production of β -lactamases
 (B) Alterations in target receptors (PBPs)
 (C) Inability to activate autolytic enzymes
 (D) Failure to synthesize peptidoglycans
 (E) Methylation of ribosomal RNA
15. The drug of first choice for the treatment of serious anaerobic infections caused by *Bacteroides fragilis* is
- (A) Clindamycin
 (B) Ampicillin
 (C) Cefoxitin
 (D) Metronidazole
 (E) Amoxicillin–clavulanate

Answers

- | | | |
|------|-------|-------|
| 1. D | 6. C | 11. B |
| 2. B | 7. B | 12. D |
| 3. E | 8. E | 13. D |
| 4. D | 9. E | 14. E |
| 5. A | 10. C | 15. D |

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