

## X. POLYMYXINS

The polymyxins are cation polypeptides that bind to phospholipids on the bacterial cell membrane of gram-negative bacteria. They have a detergent-like effect that disrupts cell membrane integrity, leading to leakage of cellular components and cell death. Polymyxins are concentration-dependent bactericidal agents with activity against most clinically important gram-negative bacteria, including *P. aeruginosa*, *E. coli*, *K. pneumoniae*, *Acinetobacter* spp., and *Enterobacter* spp. However, alterations in the cell membrane, lipid polysaccharides allow many species of *Proteus* and *Serratia* to be intrinsically resistant. Only two forms of polymyxin are in clinical use today, *polymyxin B* and *colistin (polymyxin E)*. *Polymyxin B* is available in parenteral, ophthalmic, otic, and topical preparations. *Colistin* is only available as a prodrug, *colistimethate sodium*, which is administered IV or inhaled via a nebulizer. The use of these drugs has been limited due to the increased risk of nephrotoxicity and neurotoxicity (for example, slurred speech, muscle weakness) when used systemically. However, with increasing gram-negative resistance, they are now commonly used as salvage therapy for patients with multidrug-resistant infections. Careful dosing and monitoring of adverse effects are important to maximize the safety and efficacy of these agents.

### Study Questions

Choose the ONE best answer.

29.1 A 45-year-old man presented to the hospital 3 days ago with severe cellulitis and a large abscess on his left leg. Incision and drainage were performed on the abscess, and cultures revealed methicillin-resistant *Staphylococcus aureus*. Which is the most appropriate treatment option for once-daily outpatient intravenous therapy in this patient?

- A. Ertapenem
- B. Ceftaroline
- C. Daptomycin
- D. Piperacillin/tazobactam

Correct answer = C. Daptomycin is approved for skin and skin structure infections caused by MRSA and is given once daily. A and D are incorrect because they do not cover MRSA. Ceftaroline covers MRSA, but it must be given twice daily.

29.2 Which of the following adverse effects is associated with daptomycin?

- A. Ototoxicity
- B. Red man syndrome
- C. QT<sub>c</sub> prolongation
- D. Rhabdomyolysis

Correct answer = D. Ototoxicity and red man syndrome are associated with vancomycin. QT<sub>c</sub> prolongation is associated with telavancin. Myalgias and rhabdomyolysis have been reported with daptomycin therapy and require patient education and monitoring.

29.3 A 72-year-old man is admitted to the hospital from a nursing home with severe pneumonia. He was discharged from the hospital 1 week ago after open heart surgery. The patient has no known allergies. Which of the following regimens is most appropriate for empiric coverage of methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* in this patient?

- A. Vancomycin + ceftipime + ciprofloxacin
- B. Vancomycin + ceftazolin + ciprofloxacin
- C. Telavancin + ceftipime + ciprofloxacin
- D. Daptomycin + ceftipime + ciprofloxacin

Correct answer = A. Vancomycin provides adequate coverage against MRSA, and ceftipime and ciprofloxacin provide adequate empiric coverage of *Pseudomonas*. B is incorrect because ceftazolin does not have activity against *Pseudomonas*. C is incorrect because telavancin should be avoided if possible with drugs that prolong the QT<sub>c</sub> interval, in this case ciprofloxacin. Daptomycin is inactivated by pulmonary surfactant and should not be used for pneumonia.

29.4 A 23-year-old man presents with acute appendicitis that ruptures shortly after admission. He is taken to the operating room for surgery, and postsurgical cultures reveal *Escherichia coli* and *Bacteroides fragilis*, susceptibilities pending. Which of the following provides adequate empiric coverage of these two pathogens?

- A. Cefepime
- B. Piperacillin/tazobactam
- C. Aztreonam
- D. Ceftaroline

Correct answer = B. While all of these agents cover most strains of *E. coli*, piperacillin/tazobactam is the only drug on this list that provides coverage against *Bacteroides* species.

29.5 A 68-year-old man presents from a nursing home with fever, increased urinary frequency and urgency, and mental status changes. He has a penicillin allergy of anaphylaxis. Which of the following  $\beta$ -lactams is the most appropriate choice for gram-negative coverage of this patient's urinary tract infection?

- A. Cefepime
- B. Ertapenem
- C. Aztreonam
- D. Ceftaroline

Correct answer = C. Based on the severity of the allergic reaction, aztreonam is the choice of all the  $\beta$ -lactams. Although cross-reactivity with cephalosporins and carbapenems is low, the risk rarely outweighs the benefit in these cases.

29.6 A 25-year-old man presents to the urgent care center with a painless sore on his genitals that started 2 weeks ago. He reports unprotected sex with a new partner about a month ago. A blood test confirms the patient has *Treponema pallidum*. Which is the drug of choice for the treatment of this patient's infection as a single dose?

- A. Benzathine penicillin G
- B. Ceftriaxone
- C. Aztreonam
- D. Vancomycin

Correct answer = A. A single treatment with penicillin is curative for primary and secondary syphilis. No antibiotic resistance has been reported, and it remains the drug of choice unless the patient has a severe allergic reaction.

29.7 A 20-year-old woman presents to the emergency room with headache, stiff neck, and fever for 2 days and is diagnosed with meningitis. Which is the best agent for the treatment of meningitis in this patient?

- A. Cefazolin
- B. Cefdinir
- C. Cefotaxime
- D. Cefuroxime axetil

Correct answer = C. Cefotaxime is the only drug on this list with adequate CSF penetration to treat meningitis. Cefdinir and cefuroxime axetil are only available orally, and cefazolin's CSF penetration and spectrum of coverage against *S. pneumoniae* are likely inadequate to treat meningitis.

29.8 Which of the following cephalosporins has activity against gram-negative anaerobic pathogens like *Bacteroides fragilis*?

- A. Cefoxitin
- B. Cefepime
- C. Ceftriaxone
- D. Cefazolin

Correct answer = A. The cephamycins (cefoxitin and cefotetan) are the only cephalosporins with in vitro activity against anaerobic gram-negative pathogens. Cefepime, ceftriaxone, and cefazolin have no appreciable activity against *Bacteroides fragilis*.

29.9 In which of the following cases would it be appropriate to use telavancin?

- A. A 29-year-old pregnant woman with ventilator-associated pneumonia
- B. A 76-year-old man with hospital-acquired pneumonia also receiving amiodarone for atrial fibrillation
- C. A 36-year-old man with cellulitis and abscess growing MRSA
- D. A 72-year-old woman with a diabetic foot infection growing MRSA who has moderate renal dysfunction

Correct answer = C. A is not a good option due to the potential of telavancin harming the fetus. Option B is not a good choice because the patient is on amiodarone, and telavancin can cause QT<sub>c</sub> prolongation. Option D is not an appropriate choice because the patient has baseline renal dysfunction and telavancin should be avoided unless benefit outweighs the risk. Option C is the best choice since telavancin is approved for skin and skin structure infections, and the patient has no apparent contraindication.

- 29.10 An 18-year-old woman presents to the urgent care clinic with symptoms of a urinary tract infection. Cultures reveal Enterococcus faecalis that is pan sensitive. Which of the following is an appropriate oral option to treat the urinary tract infection in this patient?
- A. *Cephalexin*
  - B. *Vancomycin*
  - C. *Cefdinir*
  - D. *Amoxicillin*

Correct answer = D. Option A and C are incorrect because enterococci are inherently resistant to all cephalosporins. Option B is incorrect because oral vancomycin is not absorbed and would not reach the urinary tract in sufficient quantities to treat a urinary tract infection. Option D is the best choice, as amoxicillin is well absorbed orally and concentrates in the urine.