In January 2012, the Clinical and Laboratory Standards Institute (CLSI) changed the susceptibility breakpoints of piperacillin/tazobactam for *P. aeruginosa*. Before 2012, an isolate of *P. aeruginosa* was categorized as susceptible if the piperacillin/tazobactam MIC was 64 mcg/mL or less. Now, an isolate of *P. aeruginosa* will be categorized as susceptible if the piperacillin/tazobactam MIC is 16 mcg/mL or less. Therefore, isolates with MICs of 32 mcg/mL or 64 mcg/mL will no longer be categorized as susceptible. The prevalence of isolates with these MICs differs by institution. Because the susceptibility breakpoints have been lowered, the change in susceptibility may be because of these changes, but the only way to know is to look at the MIC distributions. Therefore, Answer Option C is correct. If the MIC distributions are similar to those in previous reporting periods, then the changes in susceptibility were caused by the lowering of the breakpoints. Answer Option A is incorrect because it would not be wise to initiate a restriction program before knowing the MIC distributions. A restriction program may not be needed if the MIC distributions are similar. Answer Option B is incorrect because it would not be prudent to do nothing and accept the change in susceptibility. Although susceptibility changes may be caused by clonal spread of a resistant pathogen, Answer Option D is incorrect because it may not be necessary if the MIC distributions are similar.


Correct answer is A: Discontinue his current antibacterial therapy, initiate colistin therapy, and ask the microbiology laboratory to confirm the presence of a carbapenemase using the modified Hodge test.

In 2010, the CLSI lowered the susceptibility breakpoints for the carbapenems to identify carbapenemase-producing Enterobacteriaceae. Given the MIC results in the patient case, the *Klebsiella pneumoniae* isolate phenotypically appears to be a carbapenem producer. Even though the MIC for imipenem is categorized as susceptible, the MIC for meropenem is intermediate, and clinical failures have been reported with these MIC values. In addition, there is a 2-fold variability with MIC testing, so the true imipenem MIC could be 2 mcg/mL. Given this information, it is prudent to begin therapy with an agent active against carbapenemase-producing Enterobacteriaceae; therefore, Answer Option A is correct. The modified Hodge test is highly sensitive and specific for carbapenemase production and can help direct therapy once the results are known. Answer Option B is incorrect because the organism is currently resistant to all the antibiotics the patient is...
receiving, and the patient is not improving clinically. Therapy must be adjusted promptly to decrease the likelihood of a poor clinical outcome. Answer Option C is controversial because imipenem is susceptible. However, because the patient is very ill, it is more prudent to begin colistin and await the results of the modified Hodge test before initiating carbapenem therapy. Isolates may produce carbapenemases, but the MICs may only be marginally increased. If carbapenemases are found, carbapenems should be used with caution, if at all, and certainly not as monotherapy. Answer Option D is incorrect because there are few to no data on the efficacy of high-dose cefepime in the treatment of carbapenemase-producing Enterobacteriaceae. High-dose cefepime may be an option if administered with another agent for synergistic activity, but the organism is resistant to all aminoglycosides.


3. Correct answer is D: Some Enterobacteriaceae isolates that produce extended-spectrum β-lactamases (ESBLs) have elevated MICs, but the MICs are less than 8 mcg/mL; therefore, the breakpoints are lowered to detect ESBL-producing Enterobacteriaceae.

Some isolates of Enterobacteriaceae produce ESBLs, causing an increase in the MIC compared with non-ESBL-producing strains, but the increase in MIC is not sufficient for these organisms to be categorized as resistant. Clinical failures have been reported, but the clinical data are limited. To phenotypically identify Enterobacteriaceae that may produce ESBLs, CLSI lowered the susceptibility breakpoints for ceftaxime, ceftriaxone, and ceftazidime, making Answer Option D correct. Answer Option A is incorrect because pharmacokinetic and pharmacodynamic modeling suggests adequate exposures of these agents for organisms with higher MICs. According to CLSI documents, data from animal studies were not used to modify the breakpoints, so Answer Option B is incorrect. Only limited clinical data are available to support lowering the breakpoints, so Answer Option C is incorrect.


4. Correct answer is C: The incidence of cefixime resistance is increasing in men who have sex with men; therefore, ceftriaxone 250 mg intramuscularly x 1 plus azithromycin 1 g orally x 1 is the preferred regimen.

According to the Centers for Disease Control and Prevention (CDC), the preferred treatment for urethral gonorrhea for all patients is ceftriaxone 250 mg intramuscularly x 1 plus azithromycin 1 g orally x 1, so Answer Option C is correct. Patients with gonorrhea have a high incidence of coinfection with Chlamydia trachomatis, so concomitant use of azithromycin is required. The incidence of fluoroquinolone-resistant Neisseria gonorrhoeae in men who have sex with men is still greater than 10%, so use of a fluoroquinolone is not recommended, making Answer Option A incorrect. Answer Option B is incorrect because the patient
also needs to receive therapy for potential coinfection with *C. trachomatis*. The incidence of resistance to cefixime is increasing, and the incidence of cefixime resistance in *N. gonorrhoeae* is highest in men who have sex with men. Therefore, Answer Option D is incorrect.

1. Centers for Disease Control and Prevention. Update to CDC’s sexually transmitted diseases treatment guidelines, 2010: oral cephalosporins no longer a recommended treatment for gonococcal infections. MMWR 2012;61:590-4. [Internet Link]

5. **Correct answer is B: Ceftaroline is very active against ceftriaxone-intermediate or ceftriaxone-resistant *Streptococcus pneumoniae*, and ceftaroline resistance in *S. pneumoniae* has not been reported in the United States.**

Ceftaroline is an advanced-generation cephalosporin with enhanced activity against gram-positive cocci including methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant *S. pneumoniae*. According to in vitro studies, pneumococcal isolates that are intermediate or resistant to ceftriaxone are susceptible to ceftaroline. In addition, CLSI recently changed the breakpoint of ceftaroline for *S. pneumoniae*. Isolates with a ceftaroline MIC of 0.5 mcg/mL or less will be categorized as susceptible. The highest MIC for *S. pneumoniae* isolates tested from the United States is 0.5 mcg/mL. As a result, all isolates of *S. pneumoniae* in the United States are susceptible to ceftaroline; therefore, Answer Option B is correct. Answer Option A is incorrect because the prevalence of pneumococcal isolates that are nonsusceptible ranges from 8% to 15% in the United States. Because no isolates of *S. pneumoniae* are resistant to ceftaroline, Answer Option C is incorrect. In a recent in vitro study, less than 80% of *S. pneumoniae* isolates tested were susceptible to meropenem, so Answer Option D is incorrect.


6. **Correct answer is B: Polymerase chain reaction (PCR)**

Polymerase chain reaction (Answer Option B) is the correct answer. A PCR detects specific sequences of DNA or RNA, which can be specific for a given pathogen or genetic material encoding for resistance. Answer Option A is incorrect because peptide nucleic acid fluorescence in situ hybridization (PNA FISH) can only provide rapid identification of specific bacterial and fungal pathogens. Answer Option C is incorrect because it is only currently available for identification of toxigenic *Clostridium difficile*; therefore, it is not useful for identification or susceptibility testing of bacterial or fungal pathogens. Answer Option D is incorrect because it can only provide rapid bacterial identification, and it is currently not approved for use in the United States.

7. **Correct answer is D:** The test will differentiate *S. aureus* from coagulase-negative staphylococci (CNS) after blood cultures are positive, but it cannot differentiate methicillin-susceptible *S. aureus* (MSSA) from MRSA.

The *S. aureus*/CNS PNA FISH test differentiates *S. aureus* from CNS, but it cannot differentiate MSSA from methicillin-resistant strains, so Answer Option D is correct. The test results are available in 90 minutes, so Answer Option A is incorrect. This PNA FISH test requires a positive blood culture, so Answer Options B and C are incorrect. In addition, the test cannot detect the *mecA* gene, which is another reason Answer Option B is incorrect.


8. **Correct answer is A:** The most likely bacterial pathogen is *P. aeruginosa*. Continue piperacillin/tazobactam and tobramycin and discontinue vancomycin.

The GNR Traffic Light PNA FISH assay differentiates *P. aeruginosa*, *K. pneumoniae*, and *Escherichia coli* within 1.5 hours after gram-negative bacilli are identified in positive blood cultures. The organism-specific fluorescence-labeled peptides turn green, yellow, and red for *E. coli*, *K. pneumoniae*, and *P. aeruginosa*, respectively. In this patient case, the test turned red, so the organism is most likely *P. aeruginosa*. Therefore, Answer Option A is correct. Because gram-positive cocci were not identified, there is no reason to continue vancomycin. Answer Option B is incorrect because *E. coli* would fluoresce green. Even if the test were green, switching therapy to ceftriaxone would depend on the prevalence of an ESBL- or carbapenemase-producing strain at the institution. Answer Option C is incorrect because of the color of the test, but the PNA FISH assay cannot determine ESBL production, even if the test is yellow and *K. pneumoniae* is the likely pathogen. Answer Option D is incorrect because the GNR Traffic Light assay does not detect *Acinetobacter baumannii*.

9. Correct answer is B: The fungal pathogen is either *Candida glabrata* or *Candida krusei*. Discontinue fluconazole and begin micafungin.

The Yeast Traffic Light PNA FISH assay can detect five *Candida* spp. from a positive blood culture. The test will fluoresce red if *C. glabrata* or *C. krusei* is present. A result of red fluorescence indicates probable resistance to fluconazole, and clinicians could interpret a red result to mean that fluconazole should be discontinued. Therefore, Answer Option B is correct because echinocandins have good activity for *C. glabrata* and *C. krusei* is an uncommon fungal pathogen, but the likelihood of encountering this pathogen depends on its prevalence within a given institution. Answer Option A is incorrect because *Candida albicans* or *Candida parapsilosis* will fluoresce green. A green result indicates likely susceptibility to fluconazole. Answer Option C is incorrect because *Aspergillus* is a mold, and the Yeast Traffic Light PNA FISH assay does not detect molds. Answer Option D is incorrect because *Candida tropicalis* will fluoresce yellow, indicating marginal susceptibility to fluconazole.


10. Correct answer is C: Clinical use of this assay decreases length of hospital stay and total hospital costs in patients with staphylococcal bacteremia after the test is implemented.

In a study by Bauer et al., implementation of the Xpert MRSA assay was associated with a faster time (1.7 days, p=0.002) to switch from vancomycin to cefazolin or nafcillin in patients with MSSA bacteremia, a shorter hospital stay (6.2 days shorter, p=0.07), and a reduction in hospital costs ($21,387 less, p=0.02). Therefore, Answer Option C is correct. The sensitivity and specificity of the test are greater than 98% for MSSA and MRSA, so Answer Option A is incorrect. In the study by Bauer et al., hospital mortality was 26% before the test was implemented and 18% after implementation, but the difference was not significant (p=0.33); therefore, Answer Option B is incorrect. The Xpert MRSA test uses PCR technology, so Answer Option D is incorrect.


11. Correct answer is C: Clinical use of the test results in a statistically significant decrease in 30-day mortality in patients with *Enterococcus faecium* bacteremia.

The *E. faecalis*/other enterococci (OE) PNA FISH assay can differentiate *E. faecalis* from other enterococcal species from positive blood cultures. In a study by Forrest et al., the 30-day mortality in patients with
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bacteremia caused by *E. faecium* was significantly lower after the PNA FISH assay was implemented compared with the mortality in patients with *E. faecium* bacteremia before the assay was implemented (26% vs. 45%, p=0.04). Therefore, Answer Option C is correct. The test cannot differentiate vancomycin-susceptible enterococci from vancomycin-resistant enterococci (VRE) strains, so Answer Option A is incorrect. However, because most *E. faecium* strains in the United States are resistant to vancomycin, identifying *E. faecium* from positive blood cultures allows clinicians to change drug therapy to an agent with activity against VRE strains (e.g., daptomycin, linezolid). Because the test can only be performed on positive blood cultures, Answer Option B is incorrect. Like all PNA FISH assays, the results are available in 90 minutes, so Answer Option D is incorrect.


12. Correct answer is A: For tests that identify drug resistance, susceptibility testing is still required because drug resistance may be caused by several mechanisms.

Most rapid molecular tests detect only prespecified pathogens. For example, the GNR Traffic Light PNA FISH assay will differentiate *E. coli*, *K. pneumoniae*, and *P. aeruginosa*, but it will not provide any data regarding the antimicrobial susceptibility of these pathogens. Tests that can identify specific resistance genes may be unable to detect other mechanisms of resistance present in an organism. Therefore, Answer Option A is correct because susceptibility testing will still be required to ensure the pathogen is susceptible. The test can be expensive (more than $100 per test), so Answer Option B is incorrect. Cost savings that come from the use of these tests are usually drug costs because therapy can be de-escalated, or cost savings can come from shorter hospital stays because appropriate therapy can be initiated sooner. Most rapid molecular tests specify only prespecified organisms; for example, a test may differentiate MSSA from methicillin-resistant strains but not identify gram-negative pathogens. Therefore, Answer Option C is incorrect. New technologies are being developed to identify the number of pathogens (Verigene by Nanosphere), but the test is not commonly used at this time. At present, most molecular tests require a positive blood culture before the test can be performed. Therefore, Answer Option D is incorrect.


13. Correct answer is B: The patient’s lack of exposure to the health care environment

Clindamycin susceptibility does not necessarily convey hospital-associated MRSA (HA-MRSA) versus community-associated MRSA (CA-MRSA) because some HA-MRSA can be susceptible to clindamycin, although not as frequently. The spider bite description, as well as the skin and soft tissue infection, is very common for CA-MRSA, but it is not compelling in determining community- versus hospital-associated
infections. This patient's lack of exposure to any health care environment is the most evident reason this is CA-MRSA, and it is consistent with the CDC's definition of CA-MRSA.


14. Correct answer is A: Trimethoprim/sulfamethoxazole 160/800 mg orally two times daily

Although MRSA is sensitive to clindamycin, the D-test is positive, indicating inducible resistance for clindamycin, which increases the chance of failure while on therapy. Although minocycline would be an alternative for the treatment of CA-MRSA, the dose would be 200 mg once, followed by 100 mg two times daily. Vancomycin and intravenous therapy are not needed at this time for this patient. Trimethoprim/sulfamethoxazole is very efficacious in the treatment of CA-MRSA and would be the best choice for this patient.


15. Correct answer is C: All intensive care unit (ICU) patients

Active MRSA surveillance has been shown to decrease MRSA rates and isolation in some studies. However, the cost savings is not very clear, especially when using the more expensive PCR screening. According to the literature, the recommendation for active surveillance would be in hospitals with a greater than 5% incidence of MRSA, and targeted patient populations of ICU or critically ill patients would be the first choice. Although no clear guidelines on continual surveillance exist, on the basis of this scenario and the literature, targeting ICU patients first would be the best choice.

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16. **Correct answer is A: Vancomycin 2 g intravenously once; then 1250 mg intravenously two times daily**

Vancomycin remains the first-line agent in the treatment of MRSA infections. Although some institutions are seeing an increase in their susceptibility profiles, vancomycin should be reliable in MRSA infections with MICs of 1.5 mcg/mL or less. In the 2009 vancomycin dosing guidelines, doses of 15 mg/kg of actual body weight are recommended, and in critically ill patients, it is recommended to initiate a loading dose of 20–30 mg/kg. Although daptomycin and tigecycline both have activity against MRSA and are as efficacious as vancomycin in MRSA infections, daptomycin would not be appropriate for pneumonia because of inactivation by surfactant, and tigecycline has shown unfavorable results in hospital-acquired pneumonia. Vancomycin remains the best choice.


17. **Correct answer is C: Serotonin syndrome**

Linezolid is a weak MAOI (monamine oxidase inhibitor) and should be used with caution in patients receiving concomitant therapy with selective serotonin reuptake inhibitors (SSRIs) such as sertraline because serotonin syndrome can occur. Serotonin syndrome is depicted by an increase in blood pressure, tachycardia, hyperthermia, and arthralgia/myalgia. Patients taking linezolid and SSRIs should be counseled on this risk.


18. **Correct answer is A: Switch to linezolid 600 mg orally two times daily.**

Discontinuing vancomycin therapy should be considered when patients do not respond to therapy, when adequate serum levels cannot be achieved, or if MIC is 2 mcg/mL or greater. With MICs greater than 1.5 mcg/mL, failures in vancomycin therapy have been observed, and targeting an AUC (area under the curve)/MIC greater than 400 is not very feasible. Daptomycin is effective against MRSA, but it should not be used for the treatment of pneumonia because of the effects on the drug by lung surfactant. Vancomycin should be discontinued and alternative therapy initiated for this patient.


19. Correct answer is D: Discontinue daptomycin and start linezolid 600 mg orally two times daily.

Daptomycin is associated with increases in creatine phosphokinase (CPK), associated arthralgia and myalgia, and rare cases of rhabdomyolysis. Daptomycin should be discontinued in anyone with unexplained arthralgia or myalgia while on therapy in conjunction with CPK level increases to greater than 1000 U/L and in patients with no symptoms but with CPK levels greater than 2000 U/L (10 times the upper limit of normal).


20. Correct answer is B: This patient, who has a VRE infection, should be placed in isolation, and antimicrobial treatment should be initiated.

Answer Option A is incorrect because the patient has a positive culture and is therefore not just colonized. Precautions for enterococci include barrier precautions such as a gown and gloves to enter the room. A stool screen is unnecessary because the patient is infected and has a positive urine culture for VRE.

21. Correct answer is A: Daptomycin

This agent is preferred because the patient is bacteremic and shows signs of urosepsis (fever and elevated white blood cell [WBC] count). Nitrofurantoin (Answer Option D) can be used for cystitis, and doxycycline (Answer Option B) should be reserved for cystitis and possibly upper urinary tract infection (UTI) without urosepsis. Linezolid (Answer Option C) should be avoided because the patient takes fluoxetine.

22. **Correct answer is D: Repeated courses of antimicrobials, urinary catheter, and prior colonization**

   The patient was transferred from home and did not have a solid-organ transplant or diabetes. He had received prior courses of antimicrobials, had been previously colonized, and has a urinary catheter.

23. **Correct answer is B: Daptomycin plus gentamicin**

   Because the isolate does not show high-level resistance to the aminoglycoside, it should be included in the regimen. Linezolid (Answer Option A) alone for enterococcal endocarditis should be used only when other options are not possible. Ampicillin plus ceftriaxone (Answer Option C) or quinupristin/dalfopristin plus ampicillin (Answer Option D) are appropriate options when the ampicillin MIC is less than 64.


24. **Correct answer is C: Nitrofurantoin**

   This patient has cystitis without systemic signs, so treatment is necessary, and nitrofurantoin is appropriate for this lower tract UTI. Daptomycin and tigecycline are both intravenous only and not necessary in this case.


25. **Correct answer is D: Linezolid**

   Linezolid penetrates the central nervous system well, and in a few cases, it has been shown to be successful in this setting. Tigecycline (Answer Option A) and doxycycline (Answer Option B) are bacteriostatic and should be used with caution in serious infections. Fosfomycin (Answer Option C) is only available orally and is used for lower UTIs.


26. **Correct answer is B: Discontinue clindamycin.**

   The first step in initiating therapy would be to discontinue the offending antimicrobial, if feasible. Given that this is day 13 of a 14-day course and the patient is responding, discontinuing clindamycin would be the most appropriate first step. All the choices would be appropriate doses to initiate for *C. difficile* therapy; however, according to the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) guidelines, metronidazole would be the first choice, with fidaxomicin a feasible, more expensive other choice. Vancomycin would be used first line in more severe cases.


27. **Correct answer is D: Do either cytotoxicity or PCR testing to confirm C. difficile infection (CDI).**

One way of testing for *C. difficile* toxins is a two-step method that uses EIA (enzyme immunoassay) detection of glutamate dehydrogenase (GDH) as initial screening and then uses the cell cytotoxicity assay or toxigenic culture as the confirmatory test for GDH-positive stool specimens only. In this case, GDH is positive, but toxins are negative, so a confirmatory second step is warranted by either cytotoxicity or PCR testing.


28. **Correct answer is A: Vancomycin 125 mg orally four times daily**

According to the SHEA/IDSA guidelines, a WBC count greater than 15,000 and a serum creatinine greater than 1.5 times the premorbid level would define CDI as severe. Based on the Zar et al. study, severe CDI is having more than 1 point of age older than 60 years, temperature greater than 38.3°C, albumin level less than 2.5 mg/dL, and/or WBC count greater than 15,000 cells/mm³. Therefore, by both methods, this patient meets the criteria of severe CDI, and treatment should begin with vancomycin 125 mg orally four times daily. Although fidaxomicin (Answer Option D) would be appropriate treatment, it was not FDA approved until after the guidelines were published.


29. **Correct answer is C: Discontinue previous therapy and initiate vancomycin 500 mg rectally four times daily plus metronidazole intravenously three times daily.**

The patient has developed severe, complicated CDI with hypotension, toxic megacolon, and ileus. Because of the ileus, oral therapy would have to be discontinued. For severe, complicated vancomycin, 500 mg rectally four times daily plus or minus metronidazole 500 mg intravenously three times daily should be initiated. Rifaximin (Answer Option D) is not FDA approved for CDI; studies have evaluated its utility in recurrent infections but not in severe, complicated infections. In addition, it is only available orally.


30. Correct answer is C: Metronidazole 500 mg orally three times daily for 10 days

For the first recurrent CDI, it is recommended to repeat the previous therapy for 10 more days; therefore, metronidazole 500 mg orally three times daily for 10 days would be the best option. Although fidaxomicin would be a good option and has been shown to decrease recurrent infections compared with vancomycin, the dose should be 200 mg twice daily.


31. Correct answer is C: Reinforce washing hands with soap and water with patients with *C. difficile*.

Probiotics may be helpful in repopulating normal gut flora and possibly binding toxins A and B, but they should not be given to patients in the ICU. Although decreasing or restricting certain antimicrobials such as cephalosporins may help with the incidence of CDI, prohibiting their use is not the most prudent measure. The role of proton pump inhibitors in CDI is controversial, although many studies have shown a correlation with their use and CDIs. One of the most important infection control measures in preventing the spread of CDI is to wash hands with soap and water. The alcohol hand sanitizers will not kill the *C. difficile* spores.

32. Correct answer is C: Audit and feedback

The program offers an evaluation of the risk of *Pseudomonas* infection and an audit of piperacillin/tazobactam use, together with feedback on the appropriateness of piperacillin/tazobactam in this patient. Answer Option A is incorrect because the program does not describe the need for prior authorization. The formulation is not restricted (Answer Option B). De-escalation (Answer Option D) generally describes programs in which therapy is changed upon some clinical situation. Had the program described an evaluation of *Pseudomonas* risk and substitution if certain criteria were not met, then a de-escalation program would have been an appropriate choice.


33. Correct answer is B: Dose optimization

The implementation of an extended infusion of piperacillin/tazobactam takes advantage of the pharmacodynamic properties of the β-lactam antibiotics, namely time-dependent pharmacodynamics, and thus would be considered a dose optimization strategy (Answer Option B). The dosage form is not converted to an oral formulation, making Answer Options A and C incorrect. Pathway implementation (Answer Option D) is incorrect because the program does not include a clinical pathway.


34. Correct answer is D: All of the above

Several outcomes could be measured with this type of intervention. Clinical outcomes such as length of stay (Answer Option A) and mortality (Answer Option C) could be compared with historical data to determine whether this intervention shortened or lengthened the patients’ hospital stay or resulted in improved mortality. Antimicrobial expenditures could be expected to be decreased by using fewer doses per day by extending the infusion time (Answer Option B). Depending on how the intervention is implemented and measured, several clinical and financial outcomes could be measured (Answer Option D; all of the above).

35. Correct answer is A: Antimicrobial expenditures per patient-day

Length of stay and mortality are more appropriate as clinical indicators for specific interventions, whereas antimicrobial expenditures signify the benefits of the overall program. Beardsley and colleagues reported annual savings ranging from $160,000 to $2.1 million or from $230,000 to $3.4 million, depending on the method of calculation, using antimicrobial expenditures per patient-day.

36. **Correct answer is A: Process measurement**

The article describes the degree of bundle implementation at different hospitals, which is considered a process measurement (Answer Option A). An outcome measurement (Answer Option B) might be hospital expenditures, length of stay, or clinical outcomes of particular infections. A policy statement like the one published in Infection Control & Hospital Epidemiology in 2012 describes recommendations for implementation.

1. SHEA, IDSA, PIDS. Policy statement on antimicrobial stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS). Infect Control Hosp Epidemiol 2012;33:322-7. [Medline]

37. **Correct answer is D: All of the above**

Several outcomes may be affected by the implementation of a bundle. Measuring several desirable outcomes such as the ones listed would be preferred.


38. **Correct answer is A: Monitor and direct antimicrobial use.**

Guidelines and pathways (Answer Option C) are secondary means to reach the goals of the program. The primary goal is not to decrease expenses (Answer Option B) or affect resistance (Answer Option D), although these may be downstream effects.


39. **Correct answer is A: Prior authorization**

This is a prior authorization program. An antimicrobial cannot be prescribed unless prior authorization is obtained.


40. **Correct answer is D: De-escalation**

Patients are de-escalated from intravenous to oral therapy. This could also be termed an *IV-to-oral* Oral *switch program*, but that was not one of the options listed.
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41. Correct answer is D: Audit and feedback

Audit and feedback is described as one of the core processes for an antimicrobial stewardship program. Guidelines, physician order entry, and decision support systems are supplemental strategies for improving antimicrobial use but are not considered core strategies.


42. Correct answer is D: Ertapenem will have minimal, if any, effect on the susceptibility of P. aeruginosa to the carbapenem class.

Ertapenem is a carbapenem antibiotic with negligible activity against P. aeruginosa, unlike imipenem, meropenem, and doripenem. Despite widespread concerns that ertapenem use could potentially select for carbapenem-resistant P. aeruginosa, several studies have failed to show a detrimental effect of ertapenem on the activity of the group 2 carbapenems on P. aeruginosa. In a review article, Nicolau et al. reviewed the results of 10 studies uniformly showing that ertapenem does not result in decreased susceptibility of P. aeruginosa to the other carbapenems. Therefore, Answer Option D is correct and Answer Option A is incorrect. In addition, Goldstein et al. observed an increase in imipenem susceptibility against P. aeruginosa after ertapenem was added to their hospital formulary. Answer Option B is incorrect because the prevalence of carbapenem-resistant Enterobacteriaceae has not been shown to increase after the addition of ertapenem to a hospital formulary. In a study by Graber et al., adding ertapenem to the hospital formulary resulted in increased susceptibility of P. aeruginosa to ciprofloxacin, so Answer Option C is incorrect.


43. Correct answer is A: Restriction of ciprofloxacin will result in a decrease in P. aeruginosa resistance to ciprofloxacin and antipseudomonal carbapenems.

Previous studies have shown that ciprofloxacin use is a risk factor for the development of carbapenem-resistant P. aeruginosa, and one study found fluoroquinolone use to be the only independent risk factor for imipenem-resistant P. aeruginosa. It is thought that fluoroquinolone exposure may select for mutations that up-regulate the MexEF-OprN efflux pump or reduce expression of the OprD porin. These mutations can result in resistance to both fluoroquinolones and group 2 carbapenems. Because a reduction in ciprofloxacin use also improves its susceptibility against P. aeruginosa, Answer Option A is correct. Restricting the use of...
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third-generation cephalosporins and subsequently using group 2 carbapenems would result in an increase in carbapenem-resistant *P. aeruginosa*, making Answer Option B incorrect. As mentioned earlier, restriction of one particular drug class may result in improved susceptibility to a different drug class, so Answer Option C is incorrect. In addition to increased susceptibility in *P. aeruginosa* after restriction of fluoroquinolones, improvements in patient outcomes, specifically reductions in mortality, have been described; thus, Answer Option D is incorrect.


44. Correct answer is C: Most evidence supporting prolonged infusion dosing regimens for β-lactams comes from Monte Carlo simulations and retrospective studies.

The pharmacodynamic parameter predicting clinical and microbiologic outcomes for the β-lactams is the length of time the free serum concentrations remain above the MIC for the pathogen (fT>MIC). Monte Carlo simulations and a few pharmacokinetic studies have shown that administering the dose of a β-lactam by prolonged infusion can increase the fT>MIC. In addition, a limited number of retrospective studies suggest that prolonging the infusion of a β-lactam improves clinical outcomes. Therefore, Answer Option C is correct. To date, no prospective, randomized clinical trials have shown better outcomes with prolonged infusions compared with standard infusions, so Answer Option A is incorrect. Prolonging the infusion of a β-lactam increases the fT>MIC, primarily for less susceptible bacterial strains with elevated MICs. If the MICs are low, standard infusion times will provide an adequate fT>MIC, making Answer Option B incorrect. Although clinical data are lacking, Monte Carlo simulations have shown that less drug may be administered when the β-lactam is administered by prolonged infusion, so Answer Option D is incorrect.


45. Correct answer is B: Antibiotic cycling has not been shown to significantly improve resistance rates, and several mathematical models predict higher frequencies with cycling; therefore, an antibiotic cycling protocol should not be implemented.

Despite the many studies that have been conducted, antibiotic cycling has not been shown to reduce resistance rates or improve susceptibility, but some studies have shown an increase in resistance with this practice. Mathematical modeling and published studies have shown that antibiotic cycling is inferior to treatment strategies where, at any given time, equal fractions of the patient population receive different antibiotics. Therefore, Answer Option B is correct. Answer Option A is incorrect because antibiotic cycling has not been shown to decrease resistance rates. Antibiotic cycling has been studied in rotating drugs at
different times (monthly, every 3 months, every 4 months), but none of the studies has shown improvements in susceptibility, so Answer Option C is incorrect. Answer Option D is incorrect because no studies have shown an improvement in susceptibility by using several drugs in the rotation.

1. Bergstrom CT, Lo M, Lipsitch M. Ecologic theory suggest that antibiotic cycling will not reduce antimicrobial resistance in hospitals. PNAS 2004;101:13285-90. [Medline]

46. Correct answer is D: Institute a stewardship program to promote antibiotic diversity and heterogeneity within the ICUs to ensure equal distribution of antibiotic use.

Studies published within the past 5 years have shown that antibiotic strategies promoting diversity and heterogeneous antibiotic use are effective in reducing the rates of gram-negative resistance, including ESKEPE pathogens. Therefore, Answer Option D is correct. These studies have calculated an AHI (antimicrobial heterogeneity index) for various dosing strategies, and changing empiric antibiotics in successive patients ensures mixing or heterogeneity of the antibiotics used. Resistance rates for gram-negative pathogens decreased when antibiotic use was heterogeneous, whereas resistance rates increased when antibiotic use was more homogeneous. Restriction of a single antibiotic class has been shown to improve resistance rates, but increased use of another agent results in development of resistance to that agent, so Answer Options A and B are incorrect. Adding an aminoglycoside to every patient may not be necessary, depending on the infection treated, and excessive use of aminoglycosides may lead to unnecessary toxicity, so Answer Option C is incorrect.


47. Correct answer is C: Begin piperacillin/tazobactam 6.75 g every 8 hours, infused over 4 hours, because the pharmacokinetics of piperacillin and tazobactam are altered in obesity.

Despite the increasing prevalence of obesity worldwide, the published studies evaluating the pharmacokinetics of antibiotics in obesity are few. Although the data have only been presented at scientific meetings and not published, the pharmacokinetics of several antibiotics have been studied in obesity. The pharmacokinetics of both piperacillin and tazobactam are altered in obesity. To achieve pharmacodynamic exposures similar to those in nonobese patients, the empiric dose of piperacillin/tazobactam should be increased in patients who are obese to ensure coverage for less susceptible pathogens, such as P. aeruginosa. Therefore, Answer Option C is correct. After the pathogen is identified and the results of susceptibility testing are known, the dose can be adjusted accordingly. The pharmacokinetics of meropenem and doripenem are not significantly altered to necessitate an increase in the doses of these drugs, so Answer Options A and B are incorrect. Pharmacokinetic data for cefepime are unavailable, so dosing recommendations in obesity are unavailable. However, a dose of 1 g every 12 hours is unlikely to be
adequate in ventilator-associated pneumonia, regardless of the patient’s body weight. Therefore, Answer Option D is incorrect.


48. Correct answer is A: Studies have shown a substantial increase in drug costs after an antimicrobial stewardship program is discontinued; therefore, the program should be continued.

A study by Standiford et al. describes antibiotic costs within a tertiary care academic medical center before the implementation of an antimicrobial stewardship program, during the program, and after discontinuation of the program. The program was discontinued after 7 years to shift resources to hire additional infectious diseases physicians to increase infectious diseases consults. After the program was discontinued, there was a significant increase in antibiotic costs equivalent to $2 million over 2 years. From these data, Answer Option A is correct and Answer Option B is incorrect. In addition, Beardsley et al. has shown continued financial benefits of a stewardship program for more than 10 years. Answer Option C is incorrect because no data suggest an established program can be continued with fewer staff and resources. Answer Option D is incorrect because there are no data evaluating the effect of discontinuing a stewardship program on changes in gram-negative resistance rates.