Use of Antibiotics

Objectives:

- **not givin.**

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Resources: 435 team + Davidson + kumar + Recall questions step up to medicine.

- Editing file
- Feedback

Antibiotic use

Introduction:

Antibiotic: Chemical produced by a microorganism that kills or inhibits the growth of another microorganism.

Antimicrobial agent: Chemical that kills or inhibits the growth of microorganisms.

Important considerations when prescribing antibiotics: To avoid the abuse and misuse of the antibiotics which may lead to a severe damage to the body cells and vital organs.

1- Obtain accurate diagnosis of the infection, so you can't simply go to the pharmacy and expect the pharmacist to diagnose you! Nowadays, the ministry of health has imposing penalties for violators, so you can't buy an antibiotic without a prescription or just for a mild flu!

2- Empiric and definitive therapy.

3- Identifying opportunities to switch to narrow-spectrum.

4- Cost-effective (the cheapest) oral agents for the shortest duration necessary (don't give more than the duration needed!).

5- Understanding drug pharmacodynamics and efficacy at the site of infection, does the drug really reach the targeted site? for example, if the patient has meningitis, does the drug cross the blood brain barrier? and you also have to know: What is the best administration route? What is the best dose for this patient?

6- Host characteristics that influence antimicrobial activity: age, hepatic and renal functions, comorbidities.

7- Adverse effects of antimicrobial agents on the host.

1- Obtaining an Accurate Infectious Disease Diagnosis

- Determining the site of infection. by the symptoms, they are very suggestive and helpful to determine the site
- there are noninfectious causes of fever like malignancy or autoimmunes
- Defining the host (e.g., immunocompromised or immunocompetent)

- Establishing, when possible, a microbiological diagnosis especially for: Endocarditis, septic arthritis, meningitis. ceftriaxone for pneumococcal, penicillin for neisseria meningitidis
- Additional investigations to exclude noninfectious diagnoses.
- Microbiological diagnosis: Bacterial or fungal culture or Serologic testing.
- Frequently the "Most likely" microbiological etiology can be inferred from the clinical presentation:
- Cellulitis (streptococci or staphylococci) No need for positive culture, so I just have to be aware which antibiotic covers staph and strept and cost effective and with the least side effects, and the prescribe it to the patient.

- **Is An Antibiotic Indicated?**
- X-ray shows consolidation (pneumonia), either hospital or community acquired.
- Clinical diagnosis of bacterial infection, and CAP usually is caused either by streptococcus pneumoniae or by atypical organism such as: legionella, mycoplasma or chlamydia.
- Pneumonia (CAP) can also be treated empirically— Macrolide (to cover atypical organisms) or fluoroquinolone (to cover streptococcus) antibiotic—without performing specific diagnostic test.
- empirical treatment is a good decision here, microbiology will be confusing rather than helpful

- **Timing of Initiation of Antimicrobial Therapy:**

Urgent you may lose the patient if you didn't act quickly!	**Non-urgent**
1) Acute meningitis. 2) Septic shock, septicemia and circulating organisms leading to severe hypotension and death. 3) Febrile neutropenia. Empiric therapy should be initiated immediately after or concurrently with collection of diagnostic specimens.	Febrile and stable patient with fever for several days or months with no clue to diagnosis. In more stable clinical circumstances, hold antibiotics until appropriate specimens have been collected and submitted. Example: subacute bacterial endocarditis\ multiple sets of blood cultures.

What are the possible problems from a sputum sample?

1- It could have a false negative result.

2- It could be colonized with normal flora.

3- I can't always get a definitive diagnosis.

2- Empiric and definitive therapy

- Microbiological results do not become available before 24 to 72 hours.
- Empiric and guided by the clinical presentation.
- Inadequate therapy for infections in critically ill, hospitalized patients are associated with greater morbidity and mortality.
- Use broad-spectrum antimicrobial agents as initial empiric therapy.

• What organisms are likely to be responsible?

● **Based on:**

Hx & P.E. You might have a clue to DX.

● **Epidemiological data:**

Hospital-acquired (the patient has been in the hospital in the last few days: catheter, iatrogenic, implantation) vs. community-acquired, Prior antibiotic use (because broad spectrum antibiotics may kill the colonizing bacteria which reduces patient sensitivity to Abx, and that happens when your colonizing bacteria get exposed to abx and generate a 2nd generation which is resistant to the abx used).

● **Examples:**

1- Patient with dyspnoea and cough: Streptococcal pneumonia and atypical organism (kill of colonizers by aggressive or broad spectrum or abuse or misuse of the antibiotics makes pneumonia difficult to treat).

2- Patient with fever and urinary symptoms : E.coli the patients get the infection from themselves, it ascends from the genital tract to the urinary system through the urethra and it actually present normally in the bowel, so if your E-coli is exposed to too many Abx in the past treating a simple UTI will be a big problem due to abx resistance.

3- Patient with erythema over the right leg associated with pain and tenderness: Group A Streptococcus and Staphylococcus.

• Hospital-acquired infections:

Related to the presence of invasive devices and procedures:

A. Catheter related bacteremia: or central line

- Coagulase negative staph.

- Methicillin-resistant Staphylococcus aureus [MRSA] .

B. Catheter related UTI:

- Gram negative (eg, Pseudomonas aeruginosa).

Hospital acquired infection are usually more difficult to treat.

3- Identifying opportunities to switch to narrow-spectrum

Once:

1) Microbiology have identified the etiologic pathogen.

2) Antimicrobial susceptibility data are available.

⇒ Then every attempt should be made to narrow the antibiotic spectrum:

- It can reduces cost and toxicity.

- Prevent the emergence of antimicrobial resistance in the community.

- **Interpretation of Antimicrobial Susceptibility Testing Results:**
- Antimicrobial susceptibility testing measures the ability of a specific organism to grow in the presence of a particular drug in vitro:

  susceptible, resistant, or intermediate.
- Data are reported in the form of minimum inhibitory concentration (MIC):

The lowest concentration of an antibiotic that inhibits visible growth of a microorganism. We have to make sure that the abx dose exceeds the MIC so you can kill the organism.

- MIC 0.5 give vancomycin, MIC 2 give vancomycin with another antibiotics

Antimicrobial susceptibility testing:

Susceptible: indicates that the isolate is likely to be inhibited by the usually achievable concentration of a particular antimicrobial agent when the recommended dosage is used.

- Different antibiotics has different MIC.

- LIMITATION.

Bactericidal vs Bacteriostatic Therapy

Bactericidal	Bacteriostatic
Causes death and disruption of the bacterial cell. Drugs act on: 1. The cell wall: β-lactams. 2. Cell membrane: Daptomycin. 3. Bacterial DNA: Fluoroquinolones. Preferred in the case of serious infections such as endocarditis, pneumonia & meningitis to achieve rapid cure.	Inhibits bacterial replication without killing the organism. Act by inhibiting protein synthesis, such as: 1. Sulfonamides. 2. Tetracycline. 3. Macrolides.

Antimicrobial Combinations
Why to use it? Exhibits synergistic activity. **When?** It is used in the treatment of serious infections: A. Rapid killing is essential: Endocarditis caused by Enterococcus species with a combination of penicillin and gentamicin: bactericidal activity. B. Shorten the course: Endocarditis due to viridans group streptococci, A combination of penicillin or ceftriaxone with gentamicin for 2 weeks can be as effective as penicillin or ceftriaxone alone for 4 weeks) → Synergism (augmentation). C. Critically ill patient: Give empiric therapy for septic shock, blood cultures are reported to be growing gram-negative bacilli, it would be appropriate to provide initial therapy with 2 agents that have activity against gram-negative bacilli, particularly P aeruginosa. D. Polymicrobial Infections: Antimicrobial combinations, such as a third-generation cephalosporin or a fluoroquinolone plus metronidazole, can be used as a potential treatment option in these case.

4- Cost-effective oral agents for the shortest duration necessary

- Candidates for treatment of mild to moderate infections.
- Well-absorbed oral antimicrobial agents:

A. Pyelonephritis → Fluoroquinolones.

B. Community-acquired pneumonia → Augmentin and macrolides coverage.

- Bioavailability: The percentage of the oral dose that is available unchanged in the serum.

- Examples of antibiotics with excellent bioavailability are: Trimethoprim-sulfamethoxazole.

5- Understanding drug pharmacodynamics and efficacy at the site of infection

- The efficacy of antimicrobial agents depends on: their capacity to achieve concentration equal to or greater than the MIC (minimum inhibitory concentration) at the site of infection.
- Ocular fluid, CSF, abscess cavity, prostate, and bone are often much lower than serum levels, **For example:**

  A. First- and second- generation cephalosporins do not cross the blood-brain barrier, so you can't prescribe it in meningitis.

  B. Aminoglycosides: are less active in: 1- low-oxygen, 2- low-pH type of abscesses.

  C. Fluoroquinolones: achieve high concentrations in the prostate, preferred oral agents for the treatment of Prostatitis.

  D. Moxifloxacin: does not achieve significant urinary concentrations, therefore not suitable for treatment of UTIs, so a young women with UTI is given Fluoroquinolones (if not pregnant) or ciprofloxcine and not moxifloxacin.

6- Host characteristics that influence antimicrobial activity

- Host Factors to Be Considered in Selection of Antimicrobial Agents:

  1] Renal and Hepatic Function, because any impairment will lead to delayed clearance and drug accumulation and toxicity, or because the drug itself may be nephrotoxic and causes further damage and impairment to the kidneys and liver.

  2] Pregnancy and Lactation… Special considerations.. teratogenicity or otherwise toxic to the fetus:

drug	risk
Sulphonamides	A risk to develop kernicterus, especially preterm infants. The drug attache to the protein in the blood and detach the bilirubin, which make it cross the BBB causing severe damage.
Tetracycline	Staining of the teeth.
Fluoroquinolone	Cartilage damage to the fetus.
Thalidomide:	Phocomelia:

very effective antiemetic that was used to: - treat morning sickness - emesis in pregnant women.	The biggest man-made medical disaster ever, Over 10,000 children were born with a range of severe and debilitating malformations.

3] History of Allergy or Intolerance: - Penicillin and anaphylaxis.

4] Consider Special Host Factors: - Genetic e.g. G6PD (the patient may have hemolysis) - Renal function, - Liver function, - Drug interaction.

- **Assessment of Response to Treatment:** Whatever after this is just for reading

Response to treatment of an infection:

a. Clinical parameters.

- **improvement of symptoms and signs:** (eg,fever, tachycardia, or confusion).

b. laboratory values.

- **decreasing leukocyte count,** ii. radiologic decrease in the size of an abscess.

- **Antimicrobial Agents as Prophylactic:**

1. Presurgical Antimicrobial Prophylaxis:

- used to reduce the incidence of postoperative surgical site infections.

- A single dose of a cephalosporin (such as cefazolin) administered within 1 hour before the initial incision is appropriate for most surgical procedures.

2. Prevent Transmission of Communicable Pathogens to Susceptible Contacts:

- ciprofloxacin for close contacts of a patient with N.meningitidis.

3. Antimicrobial Prophylaxis Before Dental Procedures:

- Prosthetic valves, Rheumatic heart ⇒ to prevents Endocarditis.

- **Non Infectious Causes of fever:**

Some Examples: Adult onset Still disease | Drug induced fever | Fever associated with pulmonary embolism | Lymphoma.

- **Treatment of a Positive Clinical Culture in the Absence of Disease:**

Colonization without any associated manifestation of disease occurs frequently in certain populations:

⇒ Colonization of:

1- Old women with indwelling urinary catheter:

Active infection are absent (asymptomatic bacteriuria).

2- Endotracheal tubes in mechanically ventilated patients.

3- Chronic wounds.

- **The Appropriate Dose:**
- The lowest dose that is effective.
- Avoid sub-therapeutic doses.

Determined by	Modification Principles
1. Serious vs non-serious infections 2. Site of infection 3. Drug PK/PD properties 4. Other host factors (e.g. renal function … etc.)	1. Narrow vs broad spectrum agents. 2. Least toxic agent. 3. Cheaper.

- **New VS Current Antimicrobial Agent:**

Know:

- approved indications.
- advantages vs disadvantages.
- basic pharmacokinetics:
  - serum T ½.
  - activity at variou site.
- common adverse effects.

- **Criteria for Use of New Agent:**

- Antimicrobial activity is superior.
- Have a therapeutic advantage.
- Better pharmacokinetics:
  1. Site penetration
  2. Longer t ½
  3. Shorter duration
- Less toxic.
- Better tolerance.

- **The Four Moments of Antibiotic Decision-Making:**

1. Does my patient have an infection that requires antibiotics?
2. Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate?
3. A day or more has passed. Can I stop antibiotics? Can I narrow therapy or change from IV to oral therapy?
4. What duration of antibiotic therapy is needed for my patient's diagnosis?

- **Appropriate use of antimicrobial agents involves:**

- Obtaining an accurate diagnosis.
- Determining the need for and timing of antimicrobial therapy.
- Understanding how dosing affects the antimicrobial activities of different agents.
- Tailoring treatment to host characteristics.
- Sign for the narrowest spectrum and shortest duration of therapy, and: switching to oral agents as soon as possible.
- Non-antimicrobial interventions, such as abscess drainage, are equally or more important in some cases and should be pursued diligently in comprehensive infectious disease management.

Cases from the doctor

➢ **16 year old boy who presented with 3 days H/O high grade fever and severe headache.. examination revealed Temperature: 39 and patient has neck stiffness, otherwise fully conscious and has no neurological deficit:**

DDx: Acute viral or bacterial or fungal meningitis, and due to patient's age and symptoms duration it is most likely viral meningitis.

What is the most appropriate steps of approach:

A) Start combination of antibiotic and arrange for CSF study.

B) Arrange for urgent CT-scan brain.

C) Perform urgent LP and give the first dose of antibiotics.

D) perform urgent LP and if csf is abnormal, start RX.

…… A OR C ……

Patient was prescribed a dose of:

ceftriaxone and vancomycin and urgent LP is done.

We should give him 1st dose antibiotic before LP results come out, CT would be helpful unless we have an absolute contraindication to perform LP such as raised ICP (intracranial pressure), and meningitis can present with increased ICP, that's why most of the patient presents with headache. If a doctor performed a LP on a patient with high ICP, the patient may herniate and become quadriplegic and die within a week. And usually we are afraid from the pressure resulting from SOL (space occupying lesion) whether it is tumor, tuberculoma, bacterial abscess, etc.

How to know whether or not the patient has SOL?

1- Neurological deficit (homoplasia, hemiplegia). 2- Papilledema (eye examination). 3- Coma.

Result:

WBC: 1230 cells/mm…90% polymorph.. indicates bacterial infection RBC: NIL .. because its CSF

Gram stain: Gram positive intracellular diplococci (streptococcus pneumoniae).

- base skull is usually associated with staph

What you will do?

1- First dose antibiotic.

2- Send the patient for imaging study (CT scan) to rule out SOL.

3- If no SOL, perform a LP.

To continue the same antibiotics?

Yes or No.

Premature initiation of antimicrobial therapy…any harm?

1] Can suppress bacterial growth.

2] Preclude the opportunity to establish a microbiological diagnosis.

3] Require several weeks of directed antimicrobial therapy to achieve cure.

➢ A 23 years old man who has done a surgery at the base of the skull After trauma. Presented few days later with meningitis, CSF has revealed: WBC 1200 mainly polymorphs (bacterial), (If viral, it will have lymphocytes mainly), Culture: staph aureus (Hospital acquired, so it is aggressive gram negative!), usually gram -ve infections are related to hospital.

RX: Cefazolin it does not achieve therapeutic concentrations in the CSF.

Summary

<table>
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• Pneumonia (CAP)</td></tr>
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Examples:
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Questions

1. A35-year-old previously healthy man develops cough with purulent sputum over several days. On presentation to the emergency room, he is lethargic. Temperature is 39°C, pulse 110, and blood pressure 100/70. He has rales and dullness to percussion at the left base.There is no rash. Flexion of the patient's neck when supine results in spontaneous flexion of hip and knee. Neurologic examination is otherwise normal. There is no papilledema. A lumbar puncture is performed in the emergency room. The cerebrospinal fluid (CSF) shows 8000 leukocytes/µL, 90% of which are polys. Glucose is 30 mg/dL with a peripheral glucose of 80 mg/dL. CSF protein is elevated to 200 mg/dL. CSF Gram stain is pending. Which of the following is the correct treatment option?

a.Begin acyclovir for herpes simplex encephalitis.

b.Obtain emergency MRI scan before beginning treatment.

c.Begin ceftriaxone and vancomycin for pneumococcal meningitis.

d.Begin ceftriaxone, vancomycin, and ampicillin to cover both pneumococci and Listeria.

e.Begin high-dose penicillin for meningococcal meningitis.

2. A 59-year-old man undergoes coronary bypass surgery. He receives cefazolin prophylactically for 24 hours. On the ninth postoperative day, he develops a fever of 39.8°C with a heart rate of 115 beats/minute and a blood pressure of 105/65 mmHg. The surgical site is healing well with no redness or discharge. His white blood cell count is 14,000/mm3 and urinalysis reveals many white blood cells per high power field. Blood and urine cultures grow a non-lactose fermenting oxidase-positive gram-negative rod. Which of the following antibiotics is most appropriate to treat this infection?

a.Moxifloxacin.

b.Ceftriaxone.

c.Doripenem.

d.Trimethoprim-sulfamethoxazole.

e.Tigecycline.

3. You are a physician in charge of patients who reside in a nursing home. Several of the patients have developed influenza-like symptoms, and the community is in the midst of influenza A outbreak. None of the nursing home residents have received the influenza vaccine. Which course of action is most appropriate?

a.Give the influenza vaccine to all residents who do not have a contraindication to the vaccine (ie, allergy to eggs).

b.Give the influenza vaccine to all residents who do not have a contraindication to the vaccine;also give oseltamivir for 2 weeks to all residents.

c.Give amantadine alone to all residents.

d.Give azithromycin to all residents to prevent influenza-associated pneumonia.

e.Do not give any prophylactic regimen, but treat with oseltamivir if a clinical outbreak should occur.

4. A college wrestler develops cellulitis after abrading his skin during a match. He is afebrile and appears well, but the lateral aspect of his arm is red and swollen with a draining pustule. Gram stain of the pus shows gram-positive cocci in clusters.Which of the following statements is correct?

a.The patient will require hospital admission and treatment with vancomycin.

b.The organism will almost always be sensitive to oxacillin.

c.T he organism is likely to be sensitive to trimethoprim-sulfamethoxazole.

d.Community-acquired methicillin-resistant staphylococci have the same sensitivity pattern as hospital-acquired methicillin-resistant staphylococci.

e.T he infection is likely caused by streptococci.

5. An 18-year-old high school student presents to the emergency room with 1-day history of right knee pain, swelling, and redness. He is a quarterback in the school's football team.He remembers falling on the knee while practicing 2 days ago. The knee is tapped and 15 mL of cloudy fluid is sent for cell count, Gram stain, and culture. The Gram stain shows gram-positive cocci in clusters. Which of the following is the best course of action?

a.Start vancomycin and consult orthopedic surgery.

b.Consult orthopedic surgery.

c.Start linezolid awaiting culture results.

d.Start ceftriaxone.

e.Start telavancin and order magnetic resonance imaging of the knee.

6. A 62-year-old man presents to his new primary care physician for a first visit. The patient has not seen a doctor for more than 10 years. He has mild intermittent bronchial asthma. The patient is sexually active with a single long-term partner. He does not recall receiving any vaccines since childhood. Which of the following vaccines should be offered?

a. Pneumococcal, influenza, zoster, and tetanus-diphtheria-acellular pertussis.

b. Pneumococcal, influenza, zoster, and tetanus-diphtheria.

c. Pneumococcal, influenza, and human papilloma virus.

d. Pneumococcal, influenza, and tetanus-diphtheria-acellular pertussis.

e. Pneumococcal, influenza, and meningococcal.

7. Formation of essential components of bacterium cell wall is inhibited by:

A. Tetracycline.

B. Erythromycins.
C. Penicillin.
D. both A and B.

8. Susan H arrives at the emergency department with complaints of high fever, malaise, painful urination and severe flank pain. Lab tests indicate the presence of white blood cells and E.coli in her urine. A diagnosis of kidney infection (pyelonephritis) is made, and the decision is made to use a beta-lactam antibiotic that has both an appropriate antibacterial spectrum of activity, and good tissue penetration, yet is more resistant to beta-lactamases than narrow spectrum penicillins. The drug that best fits these characteristics is:

E. ceftriaxone
F. daptomycin
G. fosfomycin
H. nitrofurantoin
I. vancomycin

Answers:

1. **The answer is c.** This previously healthy male has developed acute bacterial meningitis as evident by meningeal irritation with a positive Brudzinski sign, and a CSF profile typical for bacterial meningitis (elevated white blood cell count, high percentage of polymorphonuclear leukocytes, elevated protein,and low glucose). The patient likely has concomitant pneumonia. This combination suggests pneumococcal infection. Because of the potential for beta-lactam resistance, the recommendation for therapy prior to availability of susceptibility data is ceftriaxone and vancomycin. Though herpes simplex can be seen in young healthy patients, the clinical picture and CSF profile are not consistent with this infection. The CSF in herpes simplex encephalitis shows a lymphocytic predominance and normal glucose. *Listeria monocytogenes* meningitis is a concern in immunocompromised and elderly patients. Gram stain would show gram-positive rods. *Neisseria meningitidis* is the second commonest cause of bacterial meningitis but rarely causes pneumonia (the portal of entry is the nasopharynx). Although penicillin G still kills the meningococcus, empiric therapy should cover all likely pathogens until Gram stain and culture results are available. Because the patient has no papilledema and no focal neurologic findings, treatment should not be delayed to obtain an MRI scan.

2. **The answer is c.** The patient has a healthcare–associated urinary tract infection complicated by gram-negative bacteremia. The complete identification of gram-negative rods might take 48 hours. Knowing the ability of the growing bacteria to ferment lactose might help in the early prediction of the likely pathogen at hand. Among lactose fermenting gram-negative rods, enterobacteriaceae like *E coli* are most common. Among non-lactose fermenting oxidase-positive gram-negative bacteria, *P.aeruginosa* is most common. Ceftriaxone, doripenem, and trimethoprim-sulfamethoxazole can be used to treat urinary tract infections while moxifloxacin and tigecycline do not achieve high enough concentration in urine to be used for this indication. Of the listed antibiotics, doripenem, which is a carbapenem beta-lactam antibiotic, is the only one with antipseudomonal activity. Antibiotics with antipseudomonal activity include certain penicillins (piperacillin/tazobactam and ticarcillin/clavulanate),cephalosporins(ceftazidime and cefepime),carbapenems(imipenem,meropenem, and doripenem),fluoroquinolones(ciprofloxacin and levofloxacin), and aminoglycosides (gentamicin,tobramycin, and amikacin).

3. **The answer is d.** The presentation strongly suggests vertebral osteomyelitis. MRI is sensitive and specific for the diagnosis of vertebral osteomyelitis and is the diagnostic procedure of choice. MRI will reveal the extent of contiguous disc and soft tissue involvement and will help assess for pending neurological compromise. The vertebrae are a common site for hematogenous osteomyelitis. Prior urinary tract infection is often the primary mechanism for bacteremia and vertebral seeding. Blood cultures at the time of presentation are positive in fewer than half of all cases. Treatment requires 6 to 8 weeks of antibiotics, but surgery is rarely required for cure.

4. **The answer is b**. (*Southwick,pp 401-402*.) HIV infection is usually diagnosed by the detection of HIV-specific antibodies using rapid HIV test or a conventional enzyme-linked immunosorbent assay (ELISA), which are highly sensitive tests, and confirmed by Western blot or indirect immunofluorescence assay, which are highly specific tests. Antibodies appear in few weeks after infection, sometimes after the development of acute HIV infection (acute retroviral syndrome).Clinicians should maintain a high level of suspicion for acute HIV infection in all patients who have a compatible clinical syndrome and who report recent high-risk behavior. When acute retroviral syndrome is a possibility, a plasma RNA polymerase chain reaction (PCR) should be used in conjunction with an HIV antibody test to diagnose acute HIV infection.Although HIV DNA testing is available, it offers no added advantages over the more readily available and FDA-approved HIV RNA testing. The patient's HIV serology (antibody testing) is negative, so repeating the serology testing by ELISA or ordering Western blot is not indicated at this point. It is appropriate to repeat the serology testing in 4 to 6 weeks.

5. **The answer is c.** The patient is an intravenous drug user who presents with fever, gram-positive bacteremia, a murmur, and evidence of systemic embolization—a picture consistent with infective endocarditis (IE). The positive blood cultures in this case are highly unlikely to represent contaminants. Ordering transesophageal echocardiogram (T EE) despite the negative transthoracic echocardiogram (T T E) is appropriate, given the former test's higher sensitivity. Repeating blood cultures 3 to 4 days after initial positive cultures and as needed thereafter is recommended to document clearance of bacteremia. In the case of gram-positive bacteremia, the duration of treatment is counted from the first negative blood culture. Placing long-term intravenous catheters like peripherally inserted central catheter (PICC) should be delayed, if possible, until the gram-positive bacteremia clears. It is not appropriate to treat IE with oral or bacteriostatic antibiotics. Once IE is confirmed, the patient at hand will require 6 weeks of IV antibiotics. There is nothing in the patient's presentation that is suggestive of osteomyelitis to require a bone scan.

6. **The answer is c.** Every positive culture requires interpretation. A positive culture could represent a pathogen, a colonizer, or a contaminant. he presence of symptoms and signs of infection in addition to supportive laboratory and radiologic data makes a cultivated micro be a pathogen.The patient has no symptoms or signs of infection and her urinalysis shows no pyuria. In this case, *C albicans is* a colonizer, and no antifungal therapy is indicated. Predisposing risk factors need to be eliminated to reduce the chances of colonization and to prevent a colonizer from becoming a pathogen. Removing a Foley catheter, controlling hyperglycemia and stopping broad-spectrum antibiotics,when feasible, represent some examples of risk factor elimination. Antifungal therapy (such as with fluconazole or amphotericin B) is inappropriate for fungal colonization alone.

7. **The answer is C.**

8. The answer is A. Ceftriaxone is a "3rd generation" cephalosporin that fits the characteristics described. Parenteral, broad spectrum beta-lactams such as ceftriaxone are the preferred antibiotics for initial empiric therapy of pyelonephritis caused by most pathogens (e.g. E. coli, Proteus, Klebsiella).