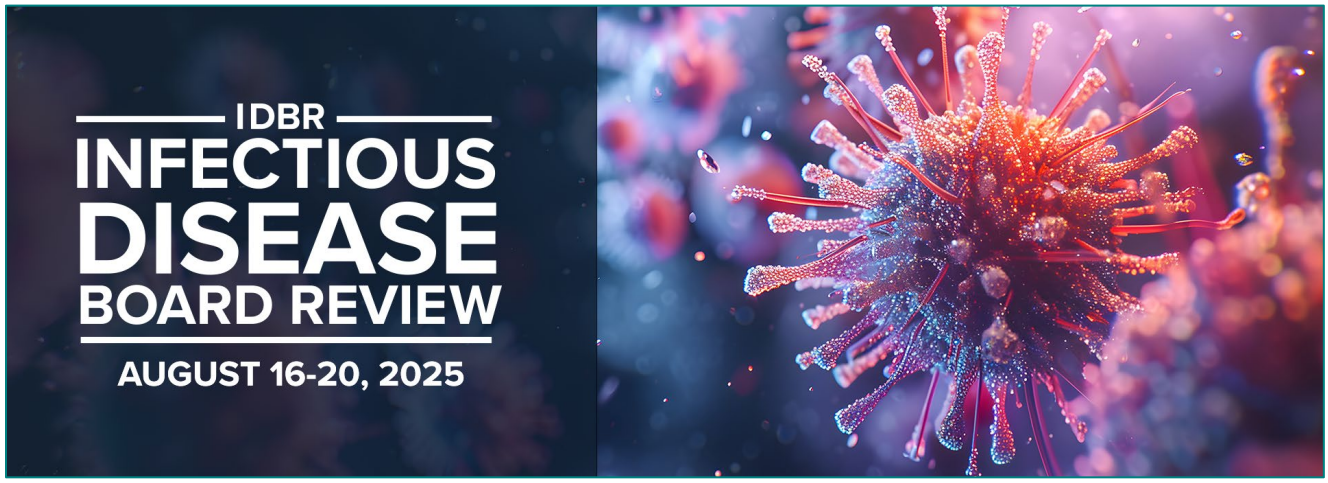


2025 IDBR Faculty Board Review Session Book

Course Directors:
John Bennett, MD
Henry Masur, MD

Course Co-Directors:
Barbara D. Alexander, MD, MHS
Paul Auwaerter, MD
David Gilbert, MD
Roy Gulick, MD, MPH
Robin Patel, MD
Andrew Pavia, MD
Richard Whitley, MD

Course Accredited by:

GW | Office of Continuing Education in the Health Professions

CONTENTS

SESSION 1 | SATURDAY, AUGUST 16, 2025

Session Moderator: Dr. Patel

Session Panelists: Drs. Black, Dhanireddy, Pavia, Saullo, and Tamma

Question #	Topic	Speaker
1	NDM Klebsiella	Patel
2	HIV Shingrix	Dhanireddy
3	Measles Rash	Pavia
4	MAC Rx in HSCT	Saullo
5	Pseudomonas DTR Rx	Tamma
6	Acinetobacter Rx	Patel
7	Follow-up Titers and Low CD4	Dhanireddy
8	Mpox diagnosis	Pavia
9	Cellulitis Rx Penicillin Allergy	Black
10	Ecthyma	Saullo
11	KPC Rx	Tamma
12	Vancomycin Dose	Black
13	Measles Vaccine HIV	Dhanireddy
14	Measles Prophylaxis	Pavia
15	Rilpivirine-Omeprazole	Black

This page left blank intentionally.

1 | NDM KLEBSIELLA | PATEL

A 62-year-old man is admitted to the hospital with fever, chills, and hypotension.

Blood cultures grow *Klebsiella pneumoniae*, which is found to be NDM (New Delhi metallo-β-lactamase) positive and resistant to all tested β-lactams, fluoroquinolones, and aminoglycosides. The patient has no known drug allergies.

Which of the following antibiotic regimens is most appropriate for targeted therapy of this patient's bacteremia?

A. Ceftazidime-avibactam plus aztreonam

B. Meropenem-vaborbactam

C. Sulbactam-durlobactam

D. Tigecycline plus ertapenem

Correct answer: Ceftazidime-avibactam plus aztreonam

Rationale

This question addresses the challenging scenario of treating a bloodstream infection caused by a *K. pneumoniae* producing the New Delhi metallo-β-lactamase (NDM). NDM is a carbapenemase that confers resistance to almost all β-lactam antibiotics, including carbapenems, and is often associated with resistance to multiple other antibiotic classes.

Ceftazidime-avibactam or meropenem-vaborbactam is effective against KPC (Klebsiella pneumoniae carbapenemase) producers but not against metallo-β-lactamases like NDM.

Ceftazidime-avibactam plus aztreonam is the best option.

Cefiderocol is a novel siderophore cephalosporin that has demonstrated activity against many carbapenemase-producing Enterobacterales, including those producing metallo-β-lactamases like NDM. It works by using the bacterial iron uptake system to enter the cell and is stable against hydrolysis by various β-lactamases, including NDM. In clinical trials and real-world studies, cefiderocol has shown efficacy in treating infections caused by carbapenem-resistant organisms, including those producing NDM. This was not offered as a choice here but is a reasonable but not preferred option.

Tigecycline is not recommended for bloodstream infections. Tigecycline achieves low serum concentrations and is not approved for the treatment of bacteremia.

Ertapenem would be ineffective against an NDM-producing organism.

2 | HIV SHINGRIX | DHANIREDDY

For a 25-year-old MSM with HIV infection (CD4 375cells/mm^3 with VL < 50 copies/uL), who received all recommended pediatric vaccines many years prior to his HIV diagnosis.

He had an episode of dermatomal herpes zoster when he was 19 years old but was not tested for HIV until several years later despite being at risk due to his sexual activity.

What would you recommend regarding zoster vaccine (Shingrix)?

A. As with HIV uninfected persons, he should receive zoster vaccine when he is age 65 years

B. He does not need zoster vaccine because of his prior episode of zoster

C. Zoster vaccine is contraindicated in any person with HIV

D. He should receive zoster vaccine (Shingrix) now

Correct answer: He should receive zoster vaccine (Shingrix) now

Rationale

Zoster Vaccine Recombinant, Adjuvanted (Shingrix) is approved by FDA for the prevention of herpes zoster in *immunologically normal* adults aged ≥50 years.

However, for *persons with HIV*, Shingrix is recommended for individuals age ≥18 years, regardless of a past episode of herpes zoster or receipt of attenuated ZVL (Zostavax).

This patient has a CD4 count >200 and is virologically suppressed. Thus, there is no reason to delay immunization.

If the patient were not virologically suppressed, to maximize immunologic response to the vaccine, providers can consider delaying vaccination until patient is virologically suppressed on ART and optimally has a CD4 count>200 cells/uL There is no risk in giving the vaccine to PWH with low CD4 counts since it is **not** a live virus vaccine, unlike vaccinia vaccine which is live.

3 | MEASLES RASH | PAVIA

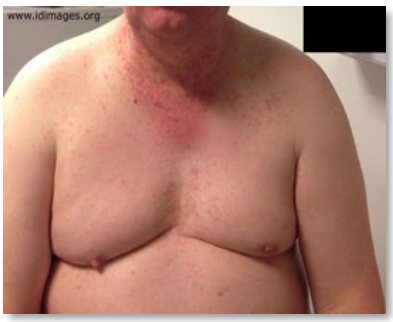
A 45-year-old businessman was well until five days before presentation when, in mid-spring, he developed a headache. Two days later, he developed a non-productive cough, throat discomfort and his eyes became watery and red.

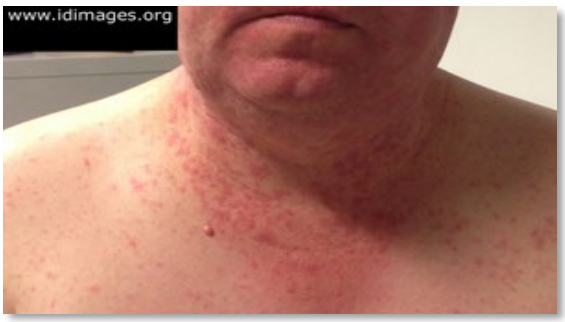
On his fifth day of illness, he developed a rash on face and then spread to his upper arms and chest.

He lived in the Midwest with his wife, teenagers, and dog. He was monogamous and denied illicit drug use. He travels throughout the US for work.

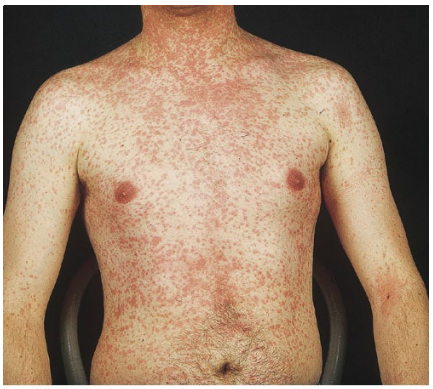
His temperature was 101 ºF. Physical exam showed a diffuse erythematous, blanching maculopapular rash on face, trunk and arms and conjunctival injection. The exam was otherwise normal.

Labs indicated WBC of 3300 cells per cubic mL, platelet count was normal.





Below is a picture of a rash in a different patient with the same diagnosis:



Which one of the following is the most likely diagnosis?

A. Syphilis

B. Scarlet fever

C. Parvovirus infection

D. Measles

E. Rocky mountain spotted fever

Correct answer: Measles

Rationale

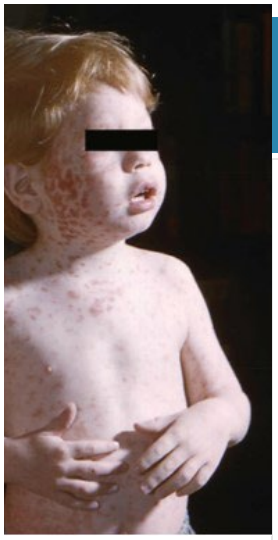
The patient was placed on airborne precautions and his testing for influenza was negative. His nasal specimen was positive for measles virus by direct fluorescent antibody (DFA). The measles IgM and IgG antibodies were also positive. His exposure was linked to being in the same airport as a person who had been diagnosed with measles of same genotype (imported case).

Measles is an acute febrile rash illness caused by an airborne virus; infected persons are contagious from several days before to several days after appearance of rash. The incubation period is 10-14 days from exposure. Prodromal symptoms include fever, cough, coryza, conjunctivitis. Koplik spots may appear toward the end of prodromal symptoms, just before the rash. As in this case, the rash typically begins on face, then spreads down the neck and body to involve the trunk and then extremities. Measles typically lasts 5-6 days, though complications such as pneumonia or encephalitis may occur.

Diagnosis: clinical; serum IgM; PCR on respiratory swab (or urine)

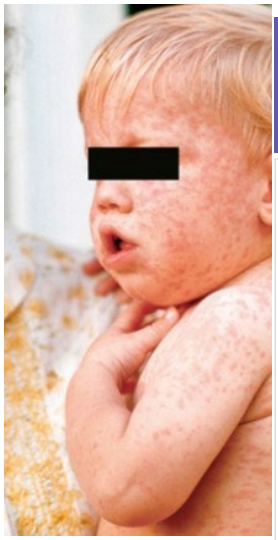
Post-exposure prophylaxis: vaccination (within 72 h) if not previously vaccinated or passive immune globulin (within 6 days) for those who are unable to receive the vaccine (e.g., pregnant; immunosuppression).

"German measles" (Rubella) vs. Measles (Rubeola)



German Measles (Rubella)

- Caused by RNA virus of *Togaviridae* family
- Often mild/ asymptomatic
- Viral prodrome → maculopapular rash which spreads from head to extremities, +/- arthritis
- Transmitted in utero (congenital rubella): deafness, cataracts, glaucoma, heart disease, cognitive defects



Measles (Rubeola)

- Caused by RNA virus of Paromyxovirus family
- Severe disease with complications including death
- Viral prodrome → cough / coryza / conjunctivitis, fever, Koplik spots → maculopapular rash which spreads from head to extremities

Secondary syphilis can present with a disseminated macular rash, but the pattern of spread described in this case is more characteristic of measles, and the patient has no known risk factors for a sexually transmitted illness.

Scarlet fever would be unlikely in an adult, and the characteristic rash is different (looks like sunburn, feels like sandpaper).

In adults, Parvovirus typically manifests as fever and joint pains. The characteristic "slapped cheeks" rash is more common in children, whereas adults can get a more generalized, pruritic rash.

The patient does not appear to have epidemiologic risk factors for Rocky Mountain spotted fever; also, the rash associated with RMSF classically has a centripetal spread, meaning it starts on the extremities and moves inward towards the trunk.

4 | MAC Rx in HSCT | Saullo

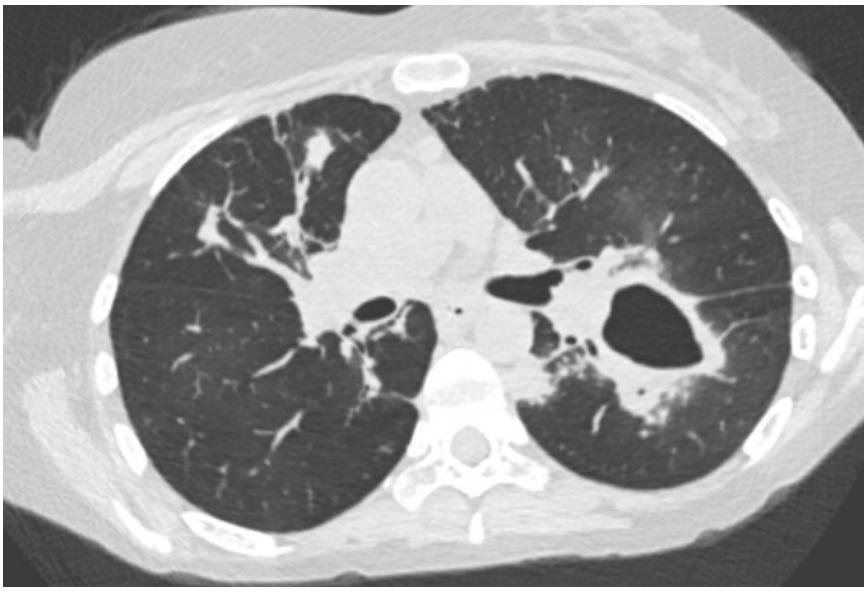
A 55-year-old female with underlying acute myelogenous leukemia underwent a matched unrelated donor allogeneic hematopoietic cell transplant (HCT) 12 months prior, complicated by chronic graft versus host disease (GVHD).

Systemic GVHD therapies have included steroids, ruxolitinib, sirolimus and more recently belumosudil. Her chronic GVHD in the past has involved her skin, gastrointestinal tract, and lungs.

The patient had been intermittently lost to follow-up and now presents with multiple months of worsening shortness of breath, cough, sputum production and low-grade fevers. She has discontinued all her medications.

Cross-sectional imaging of the chest (shown below) demonstrated progressing, multifocal pulmonary consolidation and cavitation. Expectorated sputum and bronchoalveolar lavage cultures demonstrate only *Mycobacterium avium* complex (MAC) and transbronchial biopsy demonstrates granulomatous inflammation with numerous acid-fast bacilli seen.

Antimicrobial susceptibility demonstrates macrolide and amikacin-susceptible MAC and the patient is started on oral azithromycin, ethambutol and rifabutin plus eight weeks of thrice weekly IV amikacin.



Assuming the patient tolerates her anti-MAC regimen, which of the following statements is most appropriate regarding the total duration of MAC therapy?

A. Azithromycin, ethambutol and rifabutin should be continued 4 weeks beyond cessation of the IV amikacin at 8 weeks, for a total of 12 weeks of total therapy

B. Azithromycin, ethambutol and rifabutin therapy should be continued for 6 months

C. Azithromycin, ethambutol and rifabutin should be continued for 6 months after conversion of respiratory cultures from positive to negative

D. Azithromycin, ethambutol and rifabutin should be continued for at least 12 months after conversion of respiratory cultures from positive to negative

E. None of the above statements are correct as this patient will not benefit from MAC treatment

Correct answer: Azithromycin, ethambutol and rifabutin should be continued for at least 12 months after conversion of respiratory cultures from positive to negative

Rationale

This patient meets diagnostic criteria for pulmonary MAC based on guidelines put forth by American Thoracic Society (ATS), European Respiratory Society (ERS), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and Infectious Diseases Society of America (IDSA) [Clin Infect Dis. 2020 Aug 14;71(4):e1-e36].

Diagnostic criteria for MAC include:

1. “Clinical” – the presence of pulmonary and systemic symptoms,
2. “Radiologic” – demonstration of nodular and cavitary lesions on computed tomography (CT) scan, and
3. “Microbiologic” – positive cultures growing MAC in both expectorated sputum and bronchial lavage, along with a transbronchial biopsy consistent with mycobacterial lung disease.

The patient's specific risks for MAC pulmonary disease include her lung graft-versus-host disease (GVHD) and the history of multiple immunosuppressive therapies.

Despite the cavity and chronic GVHD, treatment has a reasonable chance of success. As such, stating that treatment is not useful is incorrect.

In patients with MAC cavitary pulmonary disease, susceptibility-based treatment for macrolides and amikacin is indicated. The current recommendation for macrolide-susceptible MAC pulmonary disease it to utilize a treatment regimen with at least 3 drugs, with a macrolide (preferentially azithromycin) and ethambutol. Further, for patients with cavitary MAC pulmonary disease daily or thrice weekly intravenous amikacin should be considered for at least the initial 2 to 3 months. The rationale for combination therapy is to prevent the development of drug resistance, particularly macrolide resistance.

Another key aspect highlighted in this case is the duration of therapy. While the optimal duration of MAC-directed therapy remains uncertain, current guideline recommendations are to monitor sputum cultures regularly during treatment, and to extend therapy for at least 12 months after culture conversion is achieved. As such, the shorter durations suggested in options 1 through 3 are also incorrect.

5 | Pseudomonas DTR Rx | Tamma

A 24-year-old male with acute myelogenous leukemia (absolute neutrophil count =0 for the past 7 days) has the acute onset of fever, cough, shortness of breath and substantial hypoxemia. Chest Xray shows new multilobar pneumonia.

Pseudomonas aeruginosa is recovered from bronchoalveolar lavage and two blood cultures.

The antibiogram is as follows:

Antibiotic	MIC	Interpretation
Amikacin	> 8 µg/mL	R
Aztreonam	> 16 µg/mL	R
Cefepime	> 16 µg/mL	R
Ceftazidime	> 16 µg/mL	R
Ciprofloxacin	> 2 µg/mL	R
Colistin	2 µg/mL	I
Gentamicin	> 8 µg/mL	R
Meropenem	16 µg/mL	R
Piperacillin/tazobactam	> 64/4 µg/mL	R
Tobramycin	> 8 µg/mL	R

Which one of the following antibiotics is most <u>likely</u> to be active and clinically effective against DTR-P. aeruginosa infections?

A. **Ceftolozane-tazobactam**
B. Sulbactam-durlobactam
C. Meropenem-vaborbactam
D. Polymyxin/Colistin

Correct answer: Ceftolozane-tazobactam

<u>Rationale</u>

Polymyxins including colistin are not recommended for systemic therapy in most situations

- Penetration into pulmonary epithelial lining fluid is suboptimal
- Colistin is administered IV as inactive prodrug colistin methanesulfonate; slowly and incompletely converted to colistin
- Difficult to achieve adequate colistin plasma concentrations in patients with normal renal function
- Several reports of clinical failure and resistance emergence during polymyxin monotherapy
- Nephrotoxicity and neurotoxicity are often associated with such therapy

Beta Lactam drugs may have activity against the Pseudomonas aeruginosa isolated from this patient:

β-Lactam Agents	DTR-*P. aeruginosa*
Ceftolozane-tazobactam (2014)	
Ceftazidime-avibactam (2015)	
Meropenem-vaborbactam (2017)	
Cefiderocol (2019)	
Imipenem-cilastatin-relebactam (2020)	
Sulbactam-durlobactam (2023)	

Susceptibility to ceftolozane-tazobactam, ceftazidime-avibactam, and imipenem-cilastatin-relebactam ranges from 50-90%: these are preferred agents:

- Risk of emergence of resistance after a single treatment course is highest for ceftolozane-tazobactam or ceftazidime-avibactam treatment.
- Cefiderocol could be used but is considered a second line agent for Pseudomonas aeruginosa.
- Repeat antibiotic susceptibility testing if the patient has future P. aeruginosa infections.

6 | ACINETOBACTER RX | PATEL

A 39-year-old male has been in the ICU for weeks following a severe motor vehicle accident involving extensive burns and prolonged intubation.

He has been making progress with rehabilitation, afebrile with a tracheostomy but on no antibiotics for the prior 10 days, when he develops a new fever, hypoxemia and multifocal infiltrates.

The patient is started on vancomycin and cefepime.

Endotracheal aspirate and three blood cultures grow *Acinetobacter baumannii*.

What empiric therapy would you start pending susceptibility testing?

A. Ceftolozane-tazobactam

B. Meropenem-aztreonam

C. Colistin

D. Sulbactam-durlobactam

E. Meropenem-cilastatin-relebactam

Correct answer: Sulbactam-durlobactam

Rationale

This organism is a carbapenemase producing *Acinetobacter baumannii* (CRAB)

- Distinguishing colonization from infection can be difficult
- Commonly recovered from non-sterile sites (e.g., respiratory specimens, wounds)
- 98% of large global collection of *A. baumannii* isolates susceptible to sulbactam-durlobactam
- First choice: Sulbactam-Durlobactam (plus imipenem or meropenem)
- Second choice: High-dose Ampicillin-Sulbactam (plus an additional agent)
- Potential “additional agents” include polymyxin B or minocycline or cefiderocol

7 | FOLLOW-UP TITERS AND LOW CD4| DHANIREDDY

A 65-year-old patient with HIV infection (CD4 = 50 cells/uL and VL=300,00 copies/mm^3) comes to your clinic for evaluation and management. He recently immigrated to the US from Haiti.

The patient was never vaccinated in Haiti or subsequently.

His risk factor HIV is men-having-sex with men. He is frequently undomiciled.

As you make a list of vaccine(s) which you have decided to administer, which will need follow up titers to demonstrate serologic response?

A. Zoster vaccine

B. Pneumococcal and meningococcal vaccines

C. Mpox vaccine

D. Hepatitis A and Hepatitis B vaccines

E. RSV and Influenza vaccines

Correct answer: Hepatitis A and Hepatitis B vaccines

Rationale

Patients with "low" CD4 counts do not respond as well to vaccines as patients with CD4 counts higher than 200-350 cells/mm^3 but indicated vaccines should not be delayed pending CD4 increase in most situations.

This patient is undomiciled and thus likely has an on-going risk for HAV. In addition, it's wise to provide immunizations and other services while the patient can access care.

Post vaccine titers are indicated for patients after HBV vaccination, and after Hepatitis A vaccination if the PWH has a CD4 count<200/mm^3 at the time of immunization—this patient had a CD4 count of 50 cells/uL.

From the NIH IDSA HIVMA Guidelines: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/whats-new.

Hepatitis A

- People with HIV with CD4 count <200 cells/mm^3 who have ongoing risk for HAV should be immunized at entry to care and assessed for antibody response 1 to 2 months after completion of the series. If negative, revaccinate when their CD4 count is >200 cells/mm^3.
- For people with HIV with CD4 count <200 cells/mm^3 who do not have ongoing risk for HAV, waiting for a CD4 count >200 cells/mm^3 prior to immunization is an option.

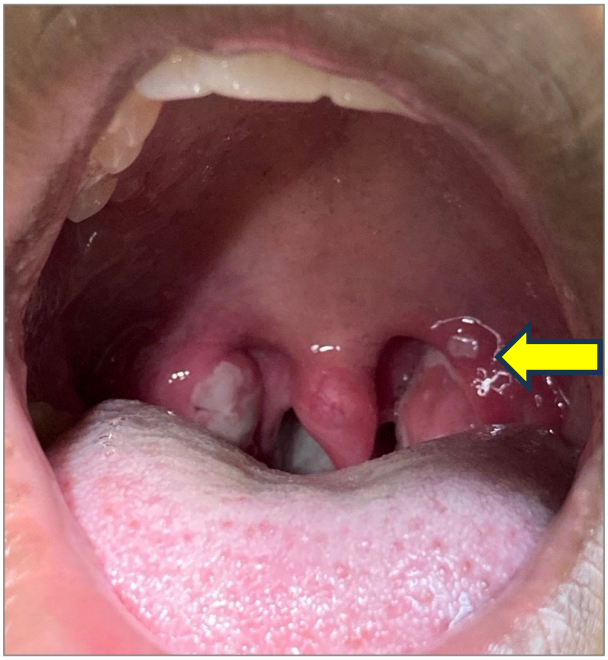
Hepatitis B

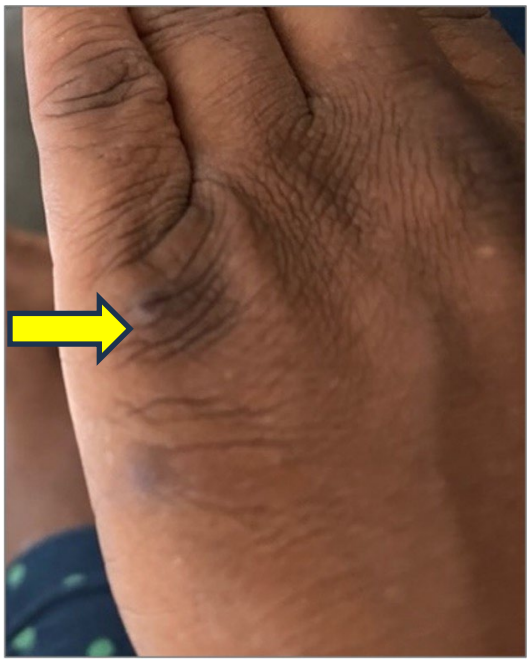
- Anti-HBs should be obtained 4 weeks after completion of the vaccine series to document response to HepB vaccination, defined as anti-HBs >10 mIU/ml.

8 | MPOX DIAGNOSIS | PAVIA

A 23-year-old man presented to the emergency department with 18 days of severe sore throat, not improving despite injection of ceftriaxone and a course of azithromycin given him in emergency room visits 2 and 14 days prior. Rapid strep tests on a throat swab had been negative at prior visits. In addition, four pustular lesions had appeared in the prior two days, scattered over his trunk and extremities. He felt feverish at night but had not taken his temperature. He lived in downtown Washinton DC, worked in retail, had sex with men and had no recent travel, medications, or illicit drugs. On exam, he had severe tonsilitis, temperature of 38.5C, prominent submental lymph nodes and four skin lesions like the one shown below. His routine labs were normal.

Figures of throat and hand:





Which of the following is most likely to be useful?

A. **Throat swab**
B. Rapid HIV test
C. Urine NAAT
D. Serology for syphilis
E. Blood culture

Correct answer: Throat swab

Rationale

A throat swab for Mpox DNA is indicated because of the suggestive skin lesion and the possibility of being infected by receptive oral sex. Notification of the health department and contact tracing for vaccine candidates would be useful. A skin biopsy could be diagnostic if throat swabbing is not available.

Throat swab for herpes simplex could be done but localization to the posterior oropharynx and this severity is unusual.

Throat swab or NAAT for gonorrhea and Chlamydia trachomatis seems of low utility because of the prior antibiotics and a presentation unusual for these infections.

9 | CELLULITIS RX PENICILLIN ALLERGY | BLACK

A 54-year-old man presents with a two-day history of increasing erythema, swelling, warmth, and mild tenderness in in the skin of his left lower leg.

No swelling, fluctuance, purulence, or bullae noted.

He has a mild fever (100.4°F) but no tachycardia, no respiratory distress. No chills, nausea, or vomiting. Denies any known injury, insect bite, or wound.

On exam, no infection of the interdigital spaces is seen.

No history of prior cellulitis or venous insufficiency. He takes no chronic medications.

Six months ago, he experienced itchy, raised, red welts on his arms within a few hours of beginning a course of amoxicillin for acute bacterial sinusitis.

Which of the following would be the best therapeutic approach?

A. **Cephalexin 500 mg po q6h (no skin testing)**
B. Penicillin skin testing. If no reaction, cephalexin 500 mg po q6h
C. Cephalexin skin testing. If no reaction, cephalexin 500 mg po q6h.
D. Clindamycin 300 mg po q8h
E. Doxycycline 100 mg po q12h

Correct answer: Cephalexin 500 mg po q6h (no skin testing)

Rationale

This is a case of nonpurulent lower extremity cellulitis in an otherwise healthy person. The most likely cause is Streptococcus pyogenes. Outpatient management with cephalexin or dicloxacillin is the usual recommendation…unless there are contraindications to these drugs.

His history with amoxicillin is suggestive of an immediate penicillin hypersensitivity (non-anaphylactic), rendering dicloxacillin a poor choice.

According to the 2022 allergy practice parameter update (J Allergy Clin Immunol 2022;150:1333-1393), a patient with penicillin hypersensitivity of any kind can be administered a structurally dissimilar cephalosporin without skin testing or additional precautions.

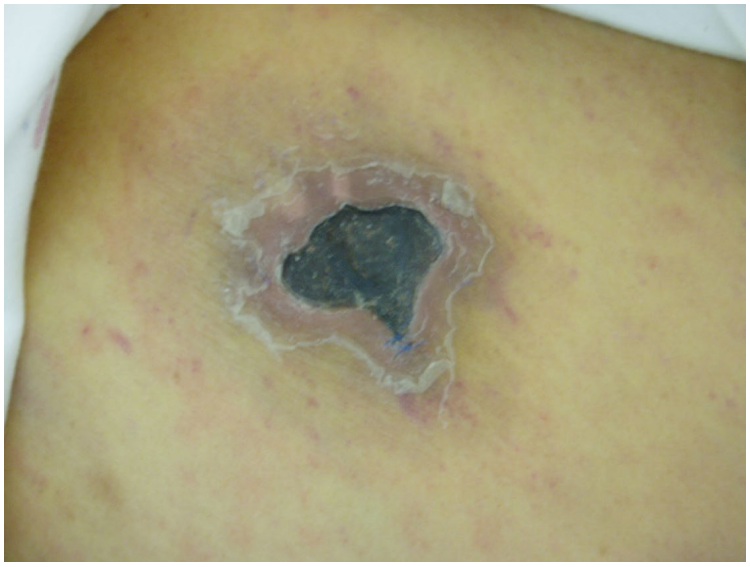
- Per the guideline:
    - "While penicillin skin testing has been the most carefully studied skin test reagent for drug allergy, we suggest penicillin skin testing primarily for patients with a history of anaphylaxis or a recent reaction suspected to be IgE-mediated (e.g., immediate onset urticaria). For most other patients with histories of penicillin allergy that are remote and benign, direct challenge without preceding skin testing is the preferred approach."
    - "Immediate allergic reactions to cephalosporins appear largely to be related to antigenic responses to the R1 group/side chains rather than the core beta-lactam portion of the molecule or R2 group/side chains."
    - Amoxicillin and cephalexin do not have identical R-1 side chains.

Clindamycin is a less attractive choice because of resistance concerns among streptococci and its unnecessary antianaerobic coverage, as well as its propensity to cause diarrhea.

Concerns with streptococcal resistance render doxycycline a similarly poor choice.

10 | ECTHYMA | SAULLO

A 69-year-old female was seen because the nurse noted a new skin lesion. The patient was hospitalized for fever, found due to Candia parapsilosis bacteremia, treated with caspofungin for the last three days. She was day 87 post allogeneic stem cell transplant with chronic graft versus host disease causing colitis, for which she was receiving prednisone 60 mg, sirolimus, daclizumab and rituximab. She was also receiving filgrastim for chronic neutropenia (WBC 11600. ANC 1000). One exam, she complained of fatigue and was not aware of six skin lesions on her extremities and abdomen. Vital signs were temp 37.4C, pulse 121, BP 106/67.



Which is the most likely cause of skin lesions?

A. **Ecthyma gangrenosum**
B. Pyoderma gangrenosum
C. Sweet syndrome
D. Disseminated herpes zoster
E. Nontuberculous mycobacteriosis

Correct answer: Ecthyma gangrenosum

Rationale

The necrotic center in a heavily immunosuppressed patient is the hallmark of ecthyma gangrenosum, caused by a mold or Gram-negative bacillus. A sharp margin of the necrotic area is from thrombosis of deep dermal blood vessels. The lesion can be single from local minor trauma or, as in this case, multiple

from a hematogenous source. Lesions start with a small red macule, usually painful, enlarging over hours to becoming red, then purple, then necrotic in the center. The patient's prednisone may have suppressed her fever and, together with profound illness, caused her to ignore the lesions. Although most patients are more neutropenic than this one, she was immunosuppressed by her GVHD and other medications. This patient's lesion was due to mucormycosis, for which the caspofungin was inactive.

Pyoderma gangrenosum is a single indolent ulcer, often in patients with inflammatory bowel disease. Sweet syndrome lesions are rarely necrotic in the center. Disseminated zoster would have multiple smaller lesions. Nontuberculous mycobacteriosis is more indolent, without necrotic centers.

11 | KPC Rx | Tamma

A 30-year-old female with a cardiac transplant at age 4 for a hypoplastic heart has had multiple cardiac procedures.

She presents to the Emergency Room with fever, rigors, and hypotension.

Cultures of blood and bronchoalveolar lavage grow *Klebsiella pneumoniae* with the following antibiogram.

Antibiotic	MIC	Interpretation
Amikacin	> 8 µg/mL	R
Aztreonam	> 16 µg/mL	R
Cefepime	> 16 µg/mL	R
Ceftazidime	> 16 µg/mL	R
Ciprofloxacin	> 2 µg/mL	R
Ertapenem	2 µg/mL	R
Gentamicin	> 8 µg/mL	R
Meropenem	8 µg/mL	R
Piperacillin/tazobactam	> 64 µg/mL	R
Tobramycin	> 8 µg/mL	R

Bla-kpc is present.

For this KPC producing organism, what would you recommend for treatment? (assuming NDM and OXA-48 are rare in your institution)

A. Ceftolozane-tazobactam
B. Meropenem-aztreonam
C. Meropenem-vaborbactam
D. Ceftazidime-gentamicin
E. Sulbactam-durlobactam

Correct answer: Meropenem-vaborbactam

Rationale

What is carbapenem resistant enterobacterales (CRE):

- Resistant to at least one carbapenem
    - ~50% of CRE have a carbapenemase gene
- Common carbapenemases:
    - Klebsiella pneumoniae carbapenemases (KPCs)
    - New Delhi metallo-β-lactamases (NDMs)
    - Oxacillinases (OXA-48-like)

β-Lactam Agents	KPCs	NDMs	OXA-48-like
Ceftazidime-avibactam (2015)			
Cefotolozane-tazobactam (2014)			
Meropenem-vaborbactam (2017)			
Cefiderocol (2019)			
Imipenem-cilastatin-relebactam (2020)			
Sulbactam-durlobactam (2023)			

KPC Producers

- Many Enterobacterales species; not unique to K. pneumoniae
- Treatment options
    - Preferred: Ceftazidime-avibactam, meropenem-vaborbactam, imipenem-cilastatin-relebactam
    - Alternative: Cefiderocol

NDM-Producing Enterobacterales

- 10% of carbapenemase-producing Enterobacterales in the United States=NDM
- Main risk factor: previous medical care in Indian subcontinent
- Treatment options
    - Preferred: Cefiderocol or ceftazidime-avibactam PLUS aztreonam (note that a new avibactam-aztreonam combination is coming onto the market and would usually also be active)

OXA-48-like-Producing Enterobacterales

- Rare in the United States (<5% of carbapenemase-producing Enterobacterales)
- Main risk factor: previous medical care in Indian subcontinent, Middle East, or Europe
- Treatment options
    - Preferred: Ceftazidime-avibactam or cefiderocol

What You Should Know About CREs

- Always perform susceptibility testing-resistance is hard to predict
- CRE: carbapenemase or non-carbapenemase-producing
- KPC: most common carbapenemase
- NDM: medical care in South Asia
- VIM, IMP, OXA-48-like carbapenemases—Less common

12 | VANCOMYCIN DOSE | BLACK

A 32-year-old man (injection drug user) with MRSA tricuspid valve endocarditis is prescribed six weeks of vancomycin. The hospital can perform vancomycin AUC_{24} monitoring as well as trough-only monitoring.

The patient is 5'11", 166 pounds (75 kg). Serum creatinine is 0.8 mg/dL. Estimated creatinine clearance (using the Cockcroft-Gault equation) is >120 mL/min.

A loading dose of vancomycin 2 gm IV (infused over 2 hours) is administered, followed by 1 gm IV (infused over 1 hour) q12h.

A peak and trough concentration are measured before and after the fourth maintenance dose. The peak is 21.2 µg/mL, trough is 8 µg/mL. His calculated AUC_{24} is 341 µg/mL x hr. The target AUC_{24} is 400-600 µg/mL x hr.

What would be the appropriate management approach?

A. Change vancomycin dose to 2 gm IV (infused over 2 hr) q12h

B. Change vancomycin dose to 1.5 gm IV (infused over 1.5 hr) q12h

C. The prescribed vancomycin dose is appropriate

D. Repeat the AUC_{24}, as the patient is not yet at steady state

E. AUC_{24} monitoring is inappropriate for this condition

Correct answer: Change vancomycin dose to 1.5 gm IV (infused over 1.5 hr) q12h

Rationale

For serious MRSA infections treated with vancomycin (such as infective endocarditis), AUC monitoring is preferred over trough-only monitoring (Am J Health Syst Pharm 2020;77:835). The target AUC is 400-600 µg/mL x hr.

His AUC24 is out of the therapeutic range. The key point is this: AUC24 is directly proportional to the total daily vancomycin dose (the number of divided doses does not matter). His AUC24 is 341 at 2 gm/day. Doubling his daily dose (i.e., 2 gm q12h) would double the AUC24 to 682 (supratherapeutic). 1.5 gm q12h (3 gm/day) would result in an AUC24 just over 500.

Two methods are used for calculating the AUC: Log-linear equations and Bayesian methodology. Log-linear equations are a simpler calculation, but a peak and trough concentration at steady state are required. The Bayesian calculation is possible with a single concentration (that does not have to be

drawn at steady state), and results are probably better. However, it requires complex and expensive computer software.

This patient's CrCl is >120 mL/min. This means his vancomycin half-life is about 6 hours. A peak and trough measured around the fourth dose are clearly at steady state. Therefore, AUC_{24} can be determined using either method.

13 | MEASLES VACCINE HIV | DHANIREDDY

One of your longstanding HIV patients comes to see you in HIV clinic. She excitedly reports that she just got a volunteer position in your hospital that will entail visiting patients with cancer to share her experiences as a cancer survivor. She is 72 years old, used to work as an insurance executive, survived an episode of breast cancer 20 years ago (managed with mastectomy, chemotherapy, and hormone therapy), and has well-controlled HIV (CD4 count 513, viral load <assay). She requests a copy of her immunization records to submit to the hospital so that she can begin her volunteer work.

You review her records and note that she has not been vaccinated against measles.

Which of the following would you do?

A. Provide her with a letter stating that she was born before 1957 and therefore does not need to get measles vaccine

B. Provide her with a letter stating that she has HIV and therefore measles vaccine is contraindicated

C. Provider her with a letter stating that she has a history of cancer and therefore measles vaccine is contraindicated

D. Provider her with a letter stating that has HIV and a history of cancer and therefore measles vaccine is contraindicated

E. Vaccinate her with MMR

Correct answer: Vaccinate her with MMR

Rationale

For the general public the following is considered evidence of immunity to measles:

- 1 dose measles vaccine administered after the patient's first birthday
- Laboratory evidence of immunity (measles IgG) or active infection (measles PCR or IgM in the appropriate clinical context)
- Birth before 1957

For people at higher risk for exposure (e.g., international travelers, post-secondary education, healthcare workers):

- 2 doses measles vaccine
- Laboratory evidence of immunity

The threshold for demonstrating evidence of immunity is higher for healthcare workers compared to the general public. They need to provide documentation of 2 doses of MMR or laboratory evidence of immunity. Birth before 1957 is not considered adequate evidence of immunity for healthcare workers. Because our patient will be working in healthcare she needs to meet this higher standard.

MMR is a live vaccine and therefore contraindicated in immunocompromised patients, but our patient does not fall into this category because her HIV is well-controlled, her cancer is remote, and she is not currently on immunosuppressive medications.

14 | MEASLES PROPHYLAXIS | PAVIA

A 58-year-old liver transplant recipient (transplant 3 months ago) on active immunosuppression (tacrolimus and prednisone) has a significant exposure to measles one day earlier.

He had a single dose of measles vaccine in the late 1960s.

Prior to transplant, he tested seronegative for measles IgG, but there wasn't enough time before Transplant to safely immunize him.

What do you recommend?

A. Acyclovir prophylaxis for two weeks

B. Ribavirin prophylaxis for two weeks

C. Intravenous immunoglobulin (IVIG) 500 mg/kg

D. Remdesivir for four weeks

Correct answer: Intravenous immunoglobulin (IVIG) 500 mg/kg

Rationale

Although we don't fully understand the protection of a single dose of measles vaccine over 50 years ago, we know that he is immunocompromised and was seronegative prior to Transplant.

CDC guidelines suggest he should receive IVIG within six days of exposure.

Acyclovir does not have efficacy against measles.

Remdesivir has shown some anti-measles activity in experimental animal models, but there's no data for use as prophylaxis.

15 | RILPIVIRINE-OMEPRAZOLE | BLACK

A patient with well controlled HIV (viral load less than 50 copies/ml) for the past year inquires about switching from dolutegravir-lamivudine-tenofovir (TDF) because he had read about bone loss with this regimen.

Changing to dolutegravir-rilpivirine would be relatively contraindicated if this patient had which of the following issues?

A. Taking atorvastatin

B. Positive HBV surface antibody positive

C. Taking omeprazole

D. Archived M84V mutation

E. Remote history of efavirenz use

Correct answer: Taking omeprazole

Rationale

Reducing gastric acid will decrease absorption of rilpivirine, making omeprazole contraindicated. There is no interaction of either dolutegravir or rilpivirine with atorvastatin. A positive serology for HBV core antibody, but not antibody to surface antigen, would be a contraindication for the switch because of the danger of HBV reactivation. A prior failure with another NNRTI, such as efavirenz, would raise concern about resistance to rilpivirine, but not simply use of the drug. An M84V mutation would affect lamivudine resistance but not rilpivirine.

SESSION 2 | SUNDAY, AUGUST 17, 2025

Session Moderator: Dr. Aronoff

Session Panelists: Drs. Boucher, Kotton, Mitre, Platts-Mills, and Thomas

Question #	Topic	Speaker
16	Mycoplasma Macrolide Resistance	Aronoff
17	Cellulitis Prophylaxis	Boucher
18	Letermovir Prophylaxis	Kotton
19	Diarrhea Rx	Platts-Mills
20	HCV Rx	Thomas
21	Post Artesunate Hemolysis	Mitre
22	Whipple's Dx	Aronoff
23	E. faecium in CNS	Boucher
24	CMV Encephalitis MRI	Kotton
25	STEC	Platts-Mills
26	Chronic Hepatitis E	Thomas
27	Loa loa	Mitre
28	C. diff Rx	Aronoff
29	Shigellosis	Platts-Mills
30	P. vivax Relapse	Mitre

This page left blank intentionally.

16 | MYCOPLASMA MACROLIDE RESISTANCE | ARONOFF

A previously healthy man is referred for poor response of his community-acquired pneumonia to azithromycin and ceftriaxone. He remains febrile on day 3 of hospitalization but is clinically stabile and not intubated. The admission respiratory panel had been positive only for *Mycoplasma pneumoniae* and negative for other respiratory viruses. Urine antigen for pneumococci and *Legionella* were negative and admission sputum culture had been reported as normal flora.

What might management include?

A. Change azithromycin to doxycycline

B. Change ceftriaxone to meropenem

C. Add vancomycin

D. Change ceftriaxone to ertapenem

E. Repeat NP swab for SARS-COv-2 (COVID-19)

Correct answer: Change azithromycin to doxycycline

Rationale

Resistance of *Mycoplasma pneumoniae* to macrolides such as azithromycin, while still uncommon, seems to be increasing and suggests that in this patient, who is likely infected with *M pneumoniae*, that doxycycline might be preferred to azithromycin. A fluoroquinolone could also be considered. Coverage of *Staphylococcus aureus* with vancomycin seems unnecessary in the absence of a positive culture and no evidence of prior predisposing influenza. Broadening coverage to a carbapenem is poor antibiotic stewardship in the absence of suggestive culture results. Repeating a PCR for COVID-19 is unlikely to be positive if the first test was a PCR and not the less sensitive antigen test.

17 | CELLULITIS PROPHYLAXIS | BOUCHER

A 60-yr old woman has had repeated episodes of erysipelas in her left arm after breast surgery and radiation for cancer had caused substantial lymphedema in that arm. She has inquired whether you might prescribe something she could take to prevent these infections. She has no history of drug allergies or intolerance.

Among the options you discuss with her might include taking which of these antibiotics prophylactically?

A. Trimethoprim-sulfamethoxazole

B. Penicillin V

C. Clindamycin

D. Amoxicillin-clavulanate

E. Erythromycin

Correct answer: Penicillin V

Rationale

Any decision about long-term prophylaxis has to consider efficacy, safety, cost and patient's preferences.

The most significant pathogen in recurrent erysipelas is Streptococcus species, particularly S. pyogenes (group A) and, less often, S. agalactiae (group B). These organisms remain susceptible to penicillin, and several clinical trials have shown a beneficial effect of penicillin V prophylaxis in preventing recurrent cellulitis.

Increasing resistance in streptococci to clindamycin and erythromycin, plus abdominal discomfort with erythromycin, makes these less attractive. Activity of trimethoprim-sulfamethoxazole against streptococci is controversial. Amoxicillin-clavulanate would be useful for staphylococcal soft tissue infection but that organism is less likely and the unnecessarily broad spectrum of amoxicillin-clavulanate is also undesirable.

18 | LETERMOVIR PROPHYLAXIS | KOTTON

Based on randomized controlled trials, Letermovir was approved by the U.S. FDA for prophylaxis of cytomegalovirus (CMV) in adult CMV-seropositive recipients [R+] of allogeneic hematopoietic stem cell transplants and adult CMV seronegative kidney transplant recipients from CMV R+ donors.

Compared with Valganciclovir, which of the following is true about Letermovir?

A. Is associated with a higher risk of leukopenia
B. Requires dose adjustment for renal impairment
C. Does not require dose adjustment when administered with cyclosporin
D. Is not active against other herpes viruses besides CMV, including herpes simplex virus (HSV) or varicella zoster virus (VZV)

Correct answer: Is not active against other herpes viruses besides CMV

Rationale

Letermovir is an antiviral active against CMV with a unique mechanism of action as an inhibitor of the CMV DNA terminase complex.

Letermovir is not associated with cross-resistance to other anti-CMV agents, however there is a concern for a low barrier to resistance, thus its use is limited to prophylaxis rather than treating patients with active high-level viremia.

Unlike valganciclovir, letermovir has potential drug interactions (moderate cytochrome P450 3A inhibitor) and does not have activity against HSV or VZV.

Letermovir also does not require dose adjustment for kidney impairment.

Among 589 adult CMV-seronegative kidney transplant recipients who received an organ from a CMV-seropositive donor, letermovir was noninferior to valganciclovir for prophylaxis of CMV disease over 52 weeks, with lower rates of leukopenia or neutropenia, supporting its use for this indication.

19 | DIARRHEA RX | PLATTS-MILLS

A 52-yr old man vacationing in Cancun, Mexico developed frequent watery stools (about 5/24 hours). This was interfering with his snorkeling and other vacation activities but not causing abdominal pain, fever or bloody diarrhea. He has only a few days of vacation left and wants his diarrhea to be over. He takes simvastatin and clopidogrel.

In addition to prescribing loperamide and/or bismuth subsalicylate, which of these other drugs might be reasonable to add?

A. Ciprofloxacin

B. Rifaximin

C. Rifampin

D. Azithromycin

E. Doxycycline

Correct answer: Rifaximin

Rationale

Rifaximin and rifamycin SV are poorly absorbed rifamycins that can be used for traveler's diarrhea and have no substantial drug-drug interactions, unlike rifampin, which has numerous interactions and is not indicated for traveler's diarrhea. Doxycycline is also not indicated for traveler's diarrhea and causes photosensitivity that would be a problem for this patient's outdoor activities. Ciprofloxacin and azithromycin are not recommended for mild traveler's diarrhea and interaction between azithromycin and simvastatin would make azithromycin less desirable.

20 | HCV RX | THOMAS

56-year-old man presents for treatment of HCV infection.

He has a history of type 2 diabetes mellitus, significant coronary disease, and HTN.

He is taking atorvastatin, metformin, and hydrochlorothiazide.

He is HIV negative, HBsAg negative. His HCV RNA is 3.2 log IU/ml. FIB-4 is 5.6 (high risk for advanced fibrosis).

Transient elastography 28 kPa (cirrhosis).

Creatine clearance is 84.

Ultrasound of RUQ is negative for HCC but shows ascites.

UGI shows several varices and the performing gastroenterologist says it is too early to list for transplant.

Which is the best option?

A. Glecaprevir and pibrentasvir for 8 weeks
B. Glecaprevir and pibrentasvir for 16 weeks
C. Sofosbuvir and velpatasvir for 12 weeks
D. Sofosbuvir and velpatasvir for 24 weeks
E. Sofosbuvir alone for 24 weeks

Correct answer: Sofosbuvir and velpatasvir for 24 weeks

Rationale

This patient has decompensated cirrhosis. In addition to co-management with a hepatologist or gastroenterologist, HCV treatment may be given but differs from persons without decompensation. Although very safe and effective with compensated cirrhosis, glecaprevir is contraindicated when there is decompensation such as is evident with ascites, varices, and/or hepatic encephalopathy.

The sofosbuvir velpatasvir options are either 12 weeks with low-dose ribavirin 600 mg/d OR 24 weeks without ribavirin. Here, the ribavirin option isn't offered but would be less optimal with severe coronary disease due to the risk of anemia.

There are no monotherapy options ever used to treat HCV.

It's not likely ID physicians would be expected to know how to interpret FIB-4 or Elastography results without looking those tests up!

Ref https://www.hcvguidelines.org/unique-populations/decompensated-cirrhosis

21 | POST-ARTESUNATE HEMOLYSIS | MITRE

A35-year-old Illinois resident, in prior good health, presented to the emergency room with high fever, beginning a week after returning from a 5-day meeting in Ghana. He was found to have severe falciparum malaria, with a parasitemia of 7% and treated with intravenous artesunate, transitioned on day 2 to artemether-lumefantrine to finish a three course. At discharge, his hemoglobin was 10 gm%, malaria smear negative for ring forms but contained a few gametocytes. A week later he returned to the emergency room with fatigue and dyspnea. Physical examination was normal, though with BP slightly low for him (100/50) and pulse 92. Hemoglobin was 4.9 gm%, reticulocytes 12%, haptoglobin undetectable, total bilirubin 1.4 gm/dl, and LDH 902 U/L. Rapid diagnostic test (RDT, BinaxNow) for malaria was negative.

What is the probable reason for this condition?

A. Post-artesunate hemolysis
B. Autoimmune hemolytic anemia
C. G6PD deficiency reaction to lumefantrine
D. Babesia coinfection
E. False negative RDT, relapsed malaria

Correct answer: Post-artesunate hemolysis

Rationale

Patients treated with intravenous artesunate for severe malaria can present after 1-2 weeks with severe hemolysis. Most patients are nonimmune travelers from a non-endemic area. The mechanism is unclear but may be splenic clearance of erythrocytes pitted by falciparum ring forms. Transfusion is often required. Autoimmune hemolytic anemia is possible but less likely in this previously healthy man. Lumefantrine does not hemolyze G6PD deficient erythrocytes. Hemolysis from relapse is unlikely in the absence of fever. False negative RDT can occur, particularly with nonfalciparum malaria. Rarely, P. falciparum may activate the aldolase band but not the HRP2 band on the BinaxNow test kit if the parasite has mutated the HRP2 gene. Babesiosis is not reported in Africa.

22 | WHIPPLE'S DX | ARONOFF

A 58-year-old male presents with a four-month history of migratory polyarthralgia and then develops intermittent low-grade fevers, weight loss (15 lb), fatigue and chronic diarrhea with greasy and foul-smelling stools.

He lacks risk factors for HIV infection.

He was born and resides in a farming community in central California and is employed as an accountant.

His history is only notable for hypertension and hyperlipidemia, for which he has received medications since his mid-40s.

On physical examination, he has diffuse abdominal tenderness, mild peripheral lymphadenopathy, and a skin exam wherein he appears tanned but has no recent sun exposure.

Laboratory testing reveals anemia, hypoalbuminemia, and elevated acute-phase reactants.

Which of the following tests would most likely lead to a diagnosis?

A. **Small bowel biopsy**
B. Serological testing for Celiac disease
C. Multiplex molecular panel for enteric pathogens
D. Stool ova and parasite collections x 3, including trichrome staining
E. Large bowel biopsy

Correct answer: Small bowel biopsy

Rationale

This case is representative of Whipple's disease due to the bacteria *Tropheryma whipplei*, a rare infection that classically causes a multisystem disease with prominent small bowel disease, malabsorptive features.

Clues that suggest Whipple's disease include joint symptoms heralding the GI manifestations and typical lymphadenopathy and fever. Skin darkening may occur due to vitamin D malabsorption, which induces

compensatory secondary hyperparathyroidism leading to enhanced melanocyte-stimulating hormone production. Normochromic normocytic anemia and hypoalbuminemia are commonly seen.

The small bowel biopsy is the gold standard approach to diagnosis wherein PAS-stained macrophages containing the organisms are seen, although PCR of the obtained tissue has higher sensitivity and specificity and should be pursued when microscopy is negative, and a high suspicion remains.

Multiplex molecular panels commercially available for gastrointestinal infections do **not** include testing for *T. whipplei*.

Celiac disease, an autoimmune disorder due to gluten intolerance, can mimic some features but does not cause lymphadenopathy, fever, or skin darkening. Screening for celiac disease can include antibody testing, although a small bowel biopsy is also the gold standard for this condition.

While stool ova and parasite studies with trichrome stain can detect parasites such as Cryptosporidium and Microsporidium, the features of this case, such as arthralgia, fever, and skin darkening, are inconsistent with these parasitic diseases.

Large bowel biopsies can help suggest diagnoses such as *C. difficile* (pseudomembranous colitis), viral (CMV or HSV), parasitic (*Entamoeba histolytica, Strongyloides stercoralis*) and fungal (*Histoplasma capsulatum*) infections, but are not helpful in diagnosis of Whipple's disease, where organisms are localized to the small bowel.

23 | E. FAECIUM IN CNS | BOUCHER

A 27-year-old man is referred by neurosurgery for assistance in management of a surgical complication. Nine days previously the patient had undergone endolymphatic decompression for his refractory Meniere's syndrome. Preoperative cefazolin had been given. The day following his left suboccipital craniotomy, CSF had been seen leaking from his operative wound. A lumbar drain was inserted, then removed 8 days later when CSF leakage had stopped. The following morning the patient awoke with headache and temperature of 101 °F. He was alert and oriented but had nuchal rigidity. Lumbar puncture found an opening pressure of 380 mm, a CSF WBC of 9,500/μL with 90% neutrophils, glucose less than 5 mg/dL and protein 151 mg/dL. Gram stain had Gram positive cocci in pairs and chains. Vancomycin, ceftazidime and metronidazole were begun. Head CT showed fluid in the left mastoid sinus but no other abnormalities. The next day the patient remained febrile, with a peripheral WBC of 14,200/μL. The microbiology laboratory said MALDI-TOF on early growth from the CSF indicated *Enterococcus faecium*.

What would be the most helpful change in his antibiotics?

A. Increase vancomycin from 2 to 4 gm/24 hr

B. Change ceftazidime and metronidazole to piperacillin-tazobactam

C. Change vancomycin to daptomycin

D. Change vancomycin to linezolid

E. Change vancomycin to dalbavancin

Correct answer: Change vancomycin to linezolid

Rationale

The principal concern is the likely antibiotic resistance of *Enterococcus faecium*. The organism is likely to be resistant to vancomycin (VRE), dalbavancin (and other lipoglycopeptide antibiotics). Resistance to piperacillin may also be present, not from a beta-lactamase reversed by tazobactam. Daptomycin is a reasonable consideration but its poor penetration into CSF is a concern in what appears to be an infection of CSF by a lumbar drain. The good penetration of linezolid into CSF and its usual activity against *E. faecium*, including VRE, makes is a reasonable choice for empirical therapy, pending susceptibility results. An additional challenge may be any foreign body, such a dural patch, that may have been left in the operative site. That is always a question worth asking the referring neurosurgeon.

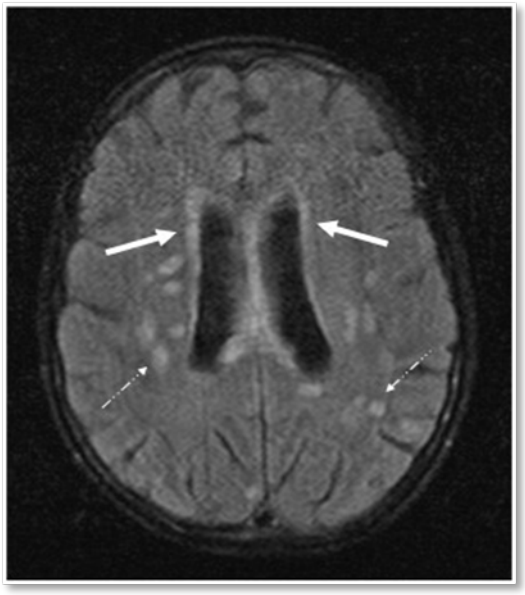
24 | CMV ENCEPHALITIS MRI | KOTTON

A 32-year-old female with HIV infection (VL = 100k, and a CD4 count below 10 cells/mm^3) has failed all available ART regimens.

Her mother brings her to the clinic because of confusion for 1-2 weeks. She is afebrile, oriented x 1, and slow to respond.

She has nystagmus and CN VI palsy on the right.

The contrast enhanced MRI image (shown below) is read as showing ventriculitis, i.e., inflammation of the ependymal lining of the lateral cerebral ventricles.



Which PCR of CSF would most likely provide the most likely diagnosis?

A. JC
B. EBV
C. CMV
D. HHV6
E. HHV8

Correct answer: CMV

Rationale

CMV Encephalitis should be considered when patients fit the following.

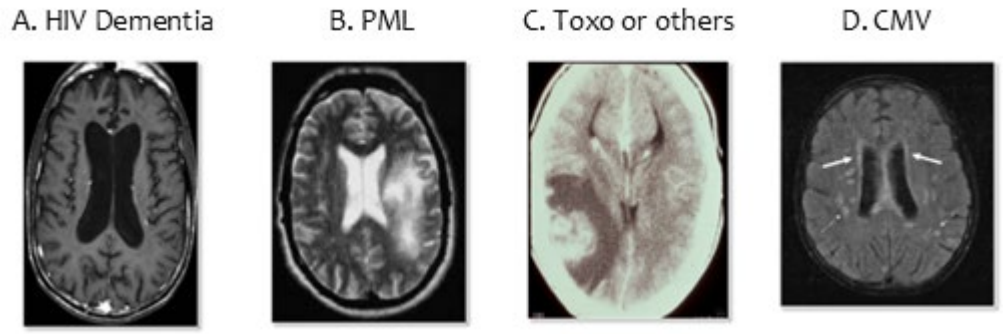
- Imaging
    - Periventricular Enhancement (shown in image above) or
        - Less common: Micronodular throughout CNS

    *Clinical and Laboratory Characteristics

    - Low CD4 (<50)
    - Rapid onset (days or weeks-unlike HIV dementia)
    - Focal CN findings or nystagmus
    - CSF pleocytosis sometimes with polys

Hopefully the exam will not expect you to be a neuroradiologist.

However, there are several patterns you should recognize especially but which should be considered with the appropriate clinical presentation:



A. Ventriculomegaly and cerebral atrophy, typical of HIV dementia
B. White matter lesions typical of JC encephalitis (progressive multifocal leukoencephalopathy)
C. Mass lesions typical of toxoplasma, lymphoma and many other fungal, mycobacterial and neoplastic processes
D. Ventricular enhancement, characteristic of CMV encephalitis

25 | STEC | PLATTS-MILLS

A 21year old undergraduate student is admitted to the hospital with 2 days of fever and diarrhea, with 12 bowel movements per day.

She presented after an episode of hematochezia. She denies travel outside of the US and no other students in her dorm are ill.

Physical exam is notable for fever to 38.7 C; other vital signs are within normal limits. The abdominal exam reveals diffuse tenderness but no rebound or peritoneal signs.

Labs are notable for a WBC of 15k, potassium of 2.4 and creatinine of 1.8.

Abdominal CT shows severe pancolitis most pronounced in the cecum and ascending colon.

A GI pathogen panel returns positive for Shiga-like toxin producing E. coli (STEC).

What is the most appropriate therapy for this patient?

A. Supportive care; discontinue antibiotics

B. Ciprofloxacin

C. Azithromycin

D. Piperacillin-tazobactam

E. Loperamide

Correct answer: Supportive care; discontinue antibiotics

Rationale

This patient has dysentery (bloody inflammatory diarrhea) due to Shiga-like toxin producing E coli (STEC), also known as enterohemorrhagic E coli (EHEC). Infection is typically food-borne and often associated with ingestion of contaminated beef. The most well-known STEC is E coli O157:H7 but other strains can cause an identical syndrome.

The IDSA guidelines on the management of diarrhea recommend that for immunocompetent adults with bloody diarrhea who are not septic, empiric antibiotics should be deferred. This is because for some infectious causes, antibiotics don't improve outcomes but can cause complications, as is the case with STEC. The use of antibiotics or anti-diarrheal agents such as loperamide in STEC infection increases the risk of the development of hemolytic uremic syndrome (HUS). HUS is a thrombotic microangiopathy characterized by thrombocytopenia, hemolytic anemia, and acute kidney injury. For this reason, antibiotics should be avoided for uncomplicated STEC gastroenteritis.

Appropriate management of STEC infection includes supportive care with hydration and electrolyte repletion. A notable exception is when there are clinical or radiographic findings concerning for acute abdomen or perforation, in which case antibiotics directed against enteric organisms, such as piperacillin-tazobactam, (and surgical consultation) are indicated. This patient did not have peritoneal signs or perforation, and therefore antibiotics could be safely deferred.

Ciprofloxacin is an appropriate treatment for traveler's diarrhea or for dysentery due to Shigella if the isolate is susceptible.

Azithromycin is recommended as therapy for *Campylobacter* gastroenteritis.

26 | CHRONIC HEPATITIS E | THOMAS

A 42-year-old man is referred for asymptomatic elevation of his liver function tests.

He underwent a living-related donor kidney transplantation 14 months earlier secondary to end-stage renal disease from uncontrolled hypertension (CMV D^-/R^-).

Six months after his transplant, his physicians noted an asymptomatic increase in aminotransferases, with aspartate aminotransferase (AST) 8 times the upper limit of normal (ULN), alanine aminotransferase (ALT) 6 x ULN, and gamma glutamyl transferase (GGT) 5 x ULN.

His total bilirubin was mildly elevated, and his alkaline phosphatase was normal.

The following were serologies were negative:

- Hepatitis A virus
- Hepatitis B virus (HBV) surface antigen
- Hepatitis C virus (HCV)
- Human immunodeficiency virus (HIV)- 1,2
- Epstein-Barr virus VCA IgM
- Herpes simplex virus 1 and 2 IgG
- Cytomegalovirus IgG

Also, negative or normal were:

- HBV DNA and HCV RNA were undetectable
- Liver autoimmunity panel was negative
- Abdominal ultrasound was normal

He denied alcohol consumption. He recently returned from living the past year in Germany and is an avid consumer of sausage.

His immunosuppressive regimen included tacrolimus, mycophenolate mofetil, and prednisolone.

His liver function tests have continued to be elevated over the past 9 months despite changes in his immunosuppressive regimen and antihypertensive medications.

His physical examination was unremarkable.

His BMI was 20 kg/m^2. No scleral icterus was noted, and no stigmata of cirrhosis were noted.

A liver biopsy demonstrated lobular hepatitis without fibrosis.

Which of the following entities is most likely responsible for his hepatitis?

A. Coxiella burnetii

B. Hepatitis D

C. Hepatitis E

D. Leptospira interrogans

E. Non-alcoholic hepatosteatosis

Correct answer: Hepatitis E

Rationale

The most likely etiology for his persistently elevated liver function tests is chronic hepatitis E infection.

There are multiple HEV genotypes that vary regionally and with regard to their zoonotic reservoirs.

Genotype 3 hepatitis E virus largely has been observed in Europe, where it is endemic in swine. Although illness is self-limited in previously health patients, some immunosuppressed patients, largely solid organ transplants to date, have become chronically infected and develop persistent hepatic function abnormalities and viremia. Cirrhosis can occur.

Oral ribavirin has been reported to reduce viremia. Eating undercooked pork has been identified as a risk factor for infection by genotype 3 HEV.

Genotypes 1 and 2 HEV are reported from Southeast Asia. Fatal infections have been reported in pregnant women.

The patient is not infected with Hepatitis B so cannot be infected with Hepatitis D.

While Coxiella may cause hepatitis, the patient has no other manifestations of Q fever, and the liver biopsy did not reveal any granulomas.

He has no other manifestations to suggest Weil's disease due to Leptospira.

The biopsy did not reveal evidence of hepatic steatosis.

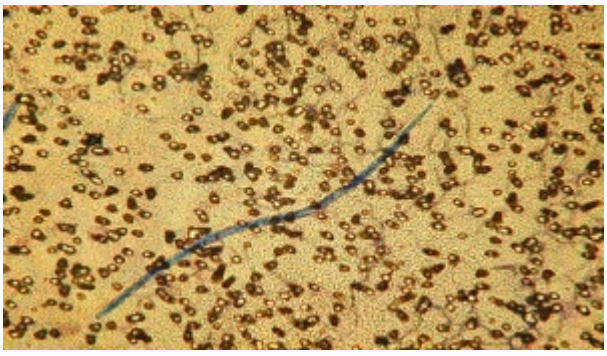
27 | LOA LOA | MITRE

A 29-year-old anthropologist presents with a chief complaint of recurrent soft tissue swellings.

He spends several months a year in tropical areas of Cameroon.

For the past three months he has noticed occasional focal swellings of his hands and forearms. These are about 4-6 cm in diameter, last for about a day and then spontaneously resolve.

Giemsa stain of a filtered daytime blood sample shows the following.



Which of the following should be assessed prior to initiating therapy?

A. Lumbar puncture

B. Quantitative microfilaria count

C. Stool exam for ova and parasites

D. Brain MRI

E. Glucose-6-phosphate dehydrogenase level

Correct answer: Quantitative microfilaria count

Rationale

The patient's symptoms are consistent with Calabar swellings due to Loa loa. This is further supported by the finding of microfilaria in a daytime blood sample. The treatment of choice for L. loa is diethylcarbamazine (DEC). However, DEC can cause significant adverse effects, including death from encephalitis and shock, in patients with very high circulating microfilaria levels (>2,500 microfilariae/ml). This is believed to be due to a severe inflammatory response against dying microfilariae. Thus, high L. loa microfilaria levels are a contraindication for DEC treatment.

In individuals with high levels of Loa loa microfilaremia the circulating level of microfilaria can be reduced with apheresis or albendazole prior to administration of DEC.

Antihistamines and corticosteroids have been used to limit post-treatment reactions, but do not prevent serious side effects such as encephalopathy.

28 | C. DIFF RX | ARONOFF

An 18-year-old male is admitted with diarrhea, fever, and abdominal pain. Six weeks previously, he was diagnosed with parotiditis, and prescribed clindamycin for 14 days.

Approximately 2 weeks later, he developed onset of frequent non-bloody liquid stools. *Clostridioides difficile* PCR and antigen returned positive, and he completed a 10-day course of oral fidaxomicin.

He initially improved, but 5 days before admission started having recurrent liquid stools, decreased appetite, diffuse abdominal pain, and fever prompting hospital admission.

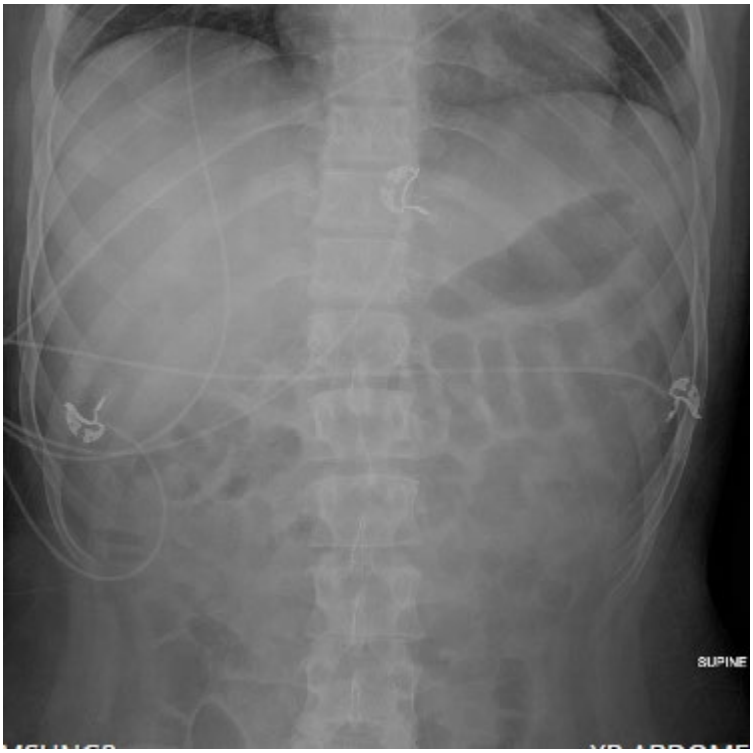
On exam he is a thin, uncomfortable appearing man. Temperature is 102.4 F, BP is 102/68, HR is 95 and O2 saturation is 98% on room air. Abdominal exam is notable for diffuse discomfort to palpation, but no peritoneal signs. Bowel sounds are hyperactive.

Labs include:

WBC=10.9, Cr=0.68

Stool C diff PCR and antigen are both positive.

Abdominal imaging shows dilated loops of bowel, but no evidence of ischemic colitis or megacolon:



What is the best treatment option for this patient?

A. Oral vancomycin and IV metronidazole
B. Fecal microbiota transplant
C. Oral vancomycin x 10 days followed by rifaximin for 20 days
D. Oral Metronidazole x 14 days
E. Fidaxomicin x 10 days

Correct answer: Fidaxomicin x 10 days

Rationale

This patient presents with first recurrence of *C difficile* infection (CDI). IDSA Guidelines published in 2021 have led to changes in the treatment of this disease. For patients with an initial (first) episode or first recurrence, recommended therapies are fidaxomicin or oral vancomycin, with a preference for fidaxomicin based on lower rates of subsequent recurrence.

Fidaxomicin treatment options include daily therapy for 10 days (initial infection or recurrence) or daily therapy for 5 days followed by every other day treatment for an additional 20 days (recurrent CDI). Adjunctive therapy with bezlotoxumab, a monoclonal antibody directed against *C difficile* toxin B, can also be given as adjunct therapy with either fidaxomicin or oral vancomycin, although this was not an option for this question.

The other options are not appropriate choices for a patient with non-fulminant **first** recurrence:

For patients with **fulminant disease** (sepsis, ileus, or megacolon) enteric therapy with oral vancomycin dosed at 500mg every 6 hours plus IV metronidazole is recommended. Vancomycin by enema has also been used. The patient in this question, while ill, does not meet criteria for either fulminant disease or even severe disease (WBC >15,000 cells/mL or creatinine >1.5mg/dL).

Fecal microbiota transplantation (FMT) plays an important role in re-establishing the colonic microbiome and is recommended in conjunction with antimicrobial treatment for patients who have had 3 or more episodes of CDI. Many experts recommend deferring FMT for acute CDI until after systemic antibiotics have been completed.

Oral vancomycin is an option for both the initial episode and for recurrences of CDI, though fidaxomicin is preferred because its use is associated with fewer recurrences, and it has a narrower spectrum of activity.

Oral metronidazole has been shown to be inferior to other options. It can be considered for patients with non-severe initial presentation of CDI when cost or availability preclude use of fidaxomicin or oral vancomycin; it has no role in treatment of no-fulminant recurrent disease.

29 | SHIGELLOSIS | PLATTS-MILLS

A 32-year-old man in Chicago had the sudden onset of diarrhea with blood and mucus in the stool, accompanied by abdominal cramps and low-grade fever. Two days later his spouse developed the same symptoms. Neither had recent travel and no unusual food exposures other than the patient had eaten salmon at a business lunch with friends two days before onset. He was not aware of any illness in his business associates.

Which of the following is the likely pathogen?

A. **Shigella sonnei**
B. Salmonella typhimurium
C. Enterohemorrhagic E. coli
D. Norovirus
E. Vibrio parahaemolyticus

Correct answer: Shigella sonnei

Rationale

Transmission to a household member is suggestive of a low inoculum infection, such as shigellosis, norovirus or giardiasis. This combined with the blood and mucus in the stool points towards shigellosis. The most common Shigella species in the USA is S. sonnei, transmitted by stool or contaminated food. Enterohemorrhagic E. coli can cause blood in the stool, but mucus and abdominal cramps are unusual. Vibrio parahaemolyticus causes watery diarrhea, often from a seafood source. The most prominent symptom of norovirus is vomiting, without blood or mucus in the stool. Salmonella is uncommonly transmitted between persons in the household and would not have blood and mucus in the stool.

30 | P. VIVAX RELAPSE | MITRE

A 34-year-old male construction worker from Los Angeles presents with fever and chills for the past two days. He had been healthy but while visiting his mother in Honduras had developed a fever and treated by a physician there for malaria with several days of a medicine he did not know. He had then been fine after returning two months ago. A rapid test in the emergency department is positive for malaria, not falciparum. A smear is sent to a reference laboratory for confirmation.

Which of the following is a probable explanation for this situation?

A. False positive rapid test

B. Infection acquired in Los Angeles

C. Drug resistant malaria

D. Relapse of P. vivax malaria

E. Relapse of P. ovale malaria

Correct answer: Relapse of P. vivax malaria

Rationale

Plasmodium vivax is the most common species of Plasmodium in Honduras and can relapse weeks or months after successful treatment if initial therapy is not followed by a course of primaquine or tafenoquine. The same potential for relapse is present with the two species of Plasmodium ovale, Plasmodium ovale curtisi or plasmodium ovale wallikeri, but neither is found in Central America, occurring in West Africa and Southeast Asia. False positive tests occur with any of the rapid malaria tests, more often with P. falciparum than P. vivax false positives, so that confirmation by smear is always necessary. However, false positives remain uncommon. Autochthonous malaria remains rare in Los Angeles. Drug resistance wouldn't explain the initial response.

This page left blank intentionally.

SESSION 3 | MONDAY, AUGUST 18, 2025

Session Moderator: Dr. Auwaerter

Session Panelists: Drs. Aronoff, Bell, Bennett, Dorman, Ghanem, and Klompas

Question #	Topic	Speaker
31	Borrelia hermsii	Auwaerter
32	H pylori Rx	Aronoff
33	Malignant Hyperthermia	Bell
34	TB Sent Home	Dorman
35	M genitalium Partner Rx	Ghanem
36	Measles Isolation	Klompas
37	Addison's Histo	Bennett
38	Lyme Serology	Auwaerter
39	H pylori Test of Cure	Aronoff
40	TB in Hospital	Dorman
41	Mpox Isolation	Ghanem
42	Candida auris Disposable Probes	Klompas
43	Staph Toxic Shock	Bennett
44	Rifampin and ART	Dorman
45	KPC Cluster	Klompas

This page left blank intentionally.

31 | BORRELIA HERMSII | AUWAERTER

A 42-year-old man from Northern California presents to the clinic with intermittent daily fever spikes as high as 104ºF, headache, and myalgias that lasted for about three days.

He felt well, but the following week he experienced these symptoms again, prompting him to see medical care.

He had been hiking in the forested mountains in the Sierra Nevadas and stayed in a restive cabin for several nights, two weeks before the onset of symptoms.

He reports some mosquito bites but no tick bites. However, he wondered about flea or chigger bites around his ankles where he noted some blood upon wakening one morning after sleeping in a bed in the cabin.

On exam, he had a temperature of 103ºF and associated rigor. His exam revealed no findings, such as a heart murmur, joint swelling or rash. However, laboratory findings revealed mild thrombocytopenia and elevated liver enzymes.

Which diagnostic approach would most likely confirm the pathogen causing his illness?

A. Acute and convalescent serology for *Babesia microti*

B. IgM and IgG for *Rickettsia rickettsii*

C. PCR for *Ehrlichia chaffeensis*

D. **Wright-stained blood smear**

E. Serology for *Borrelia burgdorferi*

Correct answer: Wright-stained blood smear

Rationale

Borrelia hermsii* is the agent of tickborne relapsing fever (TBRF), which is acquired following bites of *Ornithodoros soft ticks primarily acquired during warm temperatures at elevations of 2000-7000 ft. In the U.S. TBRF is acquired most frequently in the mountains of the Cascades, Sierra Nevadas, Rockies, and limestone caverns of Texas. The fever pattern of spikes separated by the relative absence of symptoms along with the history suggests hiking and staying in a mountain cabin are clues directing toward TBRF.

Soft ticks do not attach and engorge but rather bite frequently usually at night at several sites—hence may mimic mite or chigger bites. Diagnosis can be considered confirmed through a Wright-, Giemsa- or acridine orange-stained blood smear during a febrile episode showing spirochetemia. Spirochetemia is often at high concentrations (100-1000x that of Lyme disease) during febrile episodes and absent during afebrile days.

PCR is another alternative method of diagnosis, and the Centers for Disease Control also has serology for *B. hermsii* that could assist if acute and convalescent serology is secured. Borrelia *miyamotoi* can also cause spirochetemia and a similar illness.

B. miyamotoi relapsing fever has been described in causing human infection in California (carried by the *Ixodes pacificus* tick) but is more frequently encountered in New England, Mid-Atlantic and upper midwestern states. In both cases, doxycycline is the treatment of choice.

Babesia microti occurs in the upper Midwest, New England and mid-Atlantic states but has not been described as being acquired in California. A different babesia species, *Babesia duncani,* has rarely caused disease acquired in Pacific coastal states.

This illness is not characteristic of Rocky Mountain spotted fever (although 10% lack rash at presentation) and a single serology is insufficient to diagnose infection. Ehrlichia chaffeensis is transmitted by the Lone Star tick (*Amblyomma americanum)* and is rarely found in California, instead predominantly in Gulf, Southeastern and Eastern seaboard states.

Lyme disease does occur uncommonly in California, transmitted by the *Ixodes pacificus* tick, but typically presents with erythema migrans rather than a systemic illness with thrombocytopenia.

Colorado tick fever, a viral infection, can also have a relapsing course and would have been a reasonable diagnosis, though the afebrile interval is usually only a few days.

32 | H PYLORI RX | ARONOFF

A 50-year-old man presents with a 3-month history of epigastric pain, bloating, and nausea.

He reports worsening symptoms after meals but denies weight loss or gastrointestinal bleeding.

He has no history of NSAID or aspirin use.

A urea breath test is positive for *Helicobacter pylori* infection.

The patient has never been treated for H. pylori, and antibiotic susceptibility testing is not available.

Which of the following is the most appropriate first-line treatment?

A. Clarithromycin plus metronidazole

B. Levofloxacin plus metronidazole triple therapy

C. Bismuth subsalicylate, tetracycline and metronidazole

D. Amoxicillin and tetracycline

Correct answer: Bismuth subsalicylate, tetracycline and metronidazole quadruple therapy for 14 days

<u>Rationale</u>

Helicobacter pylori is the most common chronic bacterial infection worldwide, with a global prevalence exceeding 40%. It is a leading cause of peptic ulcer disease and gastric cancer. Treatment guidelines have evolved due to increasing antibiotic resistance, particularly against clarithromycin and levofloxacin.

- Preferred treatment for treatment-naive patients:
    - According to the 2024 ACG Clinical Guideline, bismuth quadruple therapy (BQT) for 14 days is the preferred first-line regimen when antibiotic susceptibility is unknown.
    - BQT includes:
        - PPI (standard dose, twice daily)
        - Bismuth subcitrate (120–300 mg) or subsalicylate (300 mg), four times daily

        - Tetracycline (500 mg), four times daily
        - Metronidazole (500 mg), three or four times daily
    - This regimen does not rely on clarithromycin, avoiding issues with macrolide resistance.
- Incorrect Answer Choices:
    - A) Clarithromycin-based triple therapy: Incorrect. Clarithromycin resistance rates exceed 30% in many regions, leading to poor eradication rates. This regimen should only be used if clarithromycin susceptibility is confirmed.
    - B) Levofloxacin triple therapy: Incorrect. *H. pylori* resistance to fluoroquinolones is high (>30%), and levofloxacin is not a recommended first-line treatment.
    - D) Amoxicillin plus metronidazole monotherapy: Incorrect. Amoxicillin resistance is common. Monotherapy is ineffective against H. pylori, as combination therapy is needed to prevent resistance and achieve eradication. Key Takeaways:
- Bismuth quadruple therapy for 14 days is the preferred first-line regimen when antibiotic susceptibility is unknown.
- Clarithromycin and levofloxacin-based regimens should be avoided unless antibiotic susceptibility is confirmed.
- All patients treated for *H. pylori* should undergo a test-of-cure at least 4 weeks after completing therapy.

33 | MALIGNANT HYPERTHERMIA | BELL

You are called to the PACU to see a 29-year-old man with a fever of 40°C who is 4 hours post-operative from an arthroscopic repair for a rotator cuff injury.

He is a healthy male with no underlying disease and was injured playing soccer. The patient is somnolent, flushed, diaphoretic, and rigid. His blood pressure was elevated from 150/80 to 180/100 twenty minutes ago. Now the BP is 110/60.

He is given one ampule of Narcan (naloxone) but does not respond.

Which of the following treatments would you suggest?

A. IVIG

B. High-dose corticosteroids

C. Dantrolene

D. Subcutaneous or IV epinephrine

E. High-dose ceftriaxone

Correct answer: Dantrolene

Rationale

This could be either an example of the neuroleptic malignant syndrome (NMS) or malignant hyperthermia, both of which should be treated with dantrolene. The clinical scenario is most consistent with malignant hyperthermia.

The malignant hyperthermia syndrome usually occurs in the operating room and is related to inhaled general anesthetics or a depolarizing paralytic agent (succinylcholine). The malignant hyperthermia syndrome occasionally occurs as late as 24 hours after the offending drug, so this patient with high fever and muscular rigidity could well have malignant hyperthermia. Malignant hyperthermia is inherited by an autosomal dominant mutation so think of this if a family history of reaction with anesthesia is provided.

Neuroleptic malignant syndrome is due to an idiosyncratic reaction to neuroleptics and certain antiemetics and is characterized by four features: mental status change, rigidity, fever, and dysautonomia. Extremities are described as “lead pipes.” Labile hypertension, arrhythmias, and elevated liver function tests and CPK, plus hypoxia are characteristic. Look for this in association with withdrawal or changes in anti-Parkinson medications where an NMS-like syndrome occurs from withdrawal of dopaminergic activity.

Look for these drugs:

Neuroleptic Agents

- Aripiprazole
- Chlorpromazine
- Clozapine
- Fluphenazine
- Haloperidol
- Olanzapine
- Perphenazine
- Quetiapine
- Risperidone
- Thioridazine
- Ziprasidone

Antiemetic agents

- Domperidone
- Droperidol
- Metoclopramide
- Prochlorperazine
- Promethazine

Certain overdoses can overlap with NMS, especially cocaine and ecstasy.

Treatment should include treating the muscle rigidity (benzodiazepines), hyperthermia (cooling blankets), arrhythmias, and hypertension. Drug therapy is dantrolene or bromocriptine, non-depolarizing paralytic agents, dopamine, and muscle relaxants.

This syndrome can be confused with Serotonin syndromes that are associated with serotonin uptake inhibitors. Patients often have nausea and vomiting as a prodrome and then are agitated and hyper-reflexive with myoclonus and ataxia.

The drugs associated with serotonin syndrome include:

- Cocaine
- Droperidol
- Ondansetron
- SSRIs (Citalopram, Paroxetine)
- Linezolid (usually in combination with SSRIs)
- Fentanyl

In a question or a patient if there is rigidity, think of NMS; if there is a prodrome of nausea and vomiting followed by hyperreflexia and tremor or clonus, think of serotonin syndrome. For the boards you should look for malignant hyperthermia, malignant neuroleptic syndrome, and serotonin syndrome (see table below).

	SEROTONIN SYNDROME	**NMS**	**MALIGNANT HYPERTHERMIA**
Onset	<1 day	1st dose to many weeks	In operating room up to 24 hours post
Neuromuscular Exam	Hyper-reactivity (tremor, clonus)	Muscular rigidity, bradyreflexia	Muscular rigidity, respiratory acidosis
Causative Drugs	Serotonin agonists	Antipsychotics	Inhaled anesthetics, succinylcholine
Treatment	Stop offending agent *Benzodiazepine, Cyproheptadine*	Stop offending agent *Bromocriptine, Dantrolene, Amantadine*	Stop offending agent, Dantrolene
Resolution	< 24 hours	Days to weeks	Days

Certain overdoses, especially cocaine and ecstasy, can be difficult to distinguish from NMS or MH. However, the clinical context should point you in the appropriate direction.

34 | TB SENT HOME | DORMAN

A 34-year-old man is admitted with 3 weeks of intermittent fevers, productive cough, and a 15lb weight loss. He was born in Guatemala but has been living in the US for the past 12 years.

He is married and has two kids, ages 6 and 8. All family members are healthy. Workup is significant for fever (temp 38.2 C), mild tachypnea (respiratory rate 24 breaths per minute), mild hypoxemia (oxygen saturation 93% on ambient air), and cavitary lesion in the right upper lobe.

HIV test is negative.

Sputum gram stain and culture are unrevealing.

Sputum AFB smear is negative but tuberculosis nucleic acid amplification on the sputum is positive.

He's started on empiric treatment with isoniazid, rifampin, pyrazinamide, and ethambutol.

When can this patient be discharged home?

A. **Immediately**
B. As soon as sputum cultures confirm drug susceptible tuberculosis
C. After symptom improvement and a minimum of one week of active treatment
D. After a minimum of two weeks of active treatment

Correct answer: Immediately

Rationale

Tuberculosis is routinely managed in ambulatory settings without needing to hospitalize patients. Our case patient was hospitalized before tuberculosis was diagnosed in order to expedite the workup of his concerning symptoms. He now had a compatible diagnosis, is on treatment that is likely active, and is clinically stable. As such he is stable for discharge with close follow-up to assure he is tolerating and responding to anti-tuberculous therapy.

Special considerations may apply to patients who are undomiciled, who live in congregate settings such as group homes or dormitories, or who have vulnerable family members at home (especially a newborn or someone with a compromised immune system). In such cases, consultation with the local health department is advised to come up with a plan.

This will usually entail finding a way to keep the patient away from congregate facilities or vulnerable persons until the patient is no longer contagious.

Of course, his family will need evaluation and close follow up.

Reference: Centers for Disease Control and Prevention. Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005. MMWR 2005;54(No. RR-17).

35 | M GENITALIUM PARTNER RX | GHANEM

A 32-year-old cis-gender woman is diagnosed with *M genitalium* cervicitis following a work-up for persistent cervicitis.

She presents for treatment with her male partner. The partner is asymptomatic. She is instructed to take doxycycline for one week, followed by moxifloxacin for one week.

What is the most appropriate next step when managing the partner?

A. No treatment

B. Treat with one week of doxycycline followed by 4 days of azithromycin

C. Treat with the same regimen as his partner

D. Perform a nucleic acid amplification test for *M genitalium* from a urine specimen

E. Perform a culture test for M genitalium from a urethral specimen

Correct answer: Perform a nucleic acid amplification test for *M genitalium* from a urine specimen

Rationale

When a patient is diagnosed and treated for *M genitalium*, the CDC recommends that their partners be tested for *M genitalium* and, if positive, treated.

This is different than the recommendation to treat all partners of index patients with early syphilis, gonorrhea, and chlamydia, irrespective of test positivity for those pathogens. The difference in recommendations is that treatment is prolonged, and failures are common with *M genitalium*. Thus, testing first can eliminate those who test negative. This seems like a question that the exams could easily pose.

However, The CDC recommends that partners who cannot or refuse to be tested for M genitalium be treated empirically with the same regimen used to treat the index patient.

The doxycycline + azithromycin regimen should only be used if macrolide susceptibility can be demonstrated. Culture takes weeks to months to grow *M genitalium*, and it is insensitive.

CDC Recommended Regimens if M. genitalium Resistance Testing is Available

- If macrolide sensitive: Doxycycline 100 mg orally 2 times/day for **7 days**, followed by azithromycin 1 g orally initial dose, **followed by** 500 mg orally once daily for **3 additional days** (2.5 g total)
- If macrolide resistant: Doxycycline 100 mg orally 2 times/day for **7 days followed by** moxifloxacin 400 mg orally once daily for **7 days**

Recommended Regimens if M. genitalium Resistance Testing is Not Available

- If M. genitalium is detected by an FDA-cleared NAAT: Doxycycline 100 mg orally 2 times/day for **7 days,** followed by moxifloxacin 400 mg orally once daily for **7 days**

https://www.cdc.gov/std/treatment-guidelines/mycoplasmagenitalium.htm

accessed 2/15/2025

36 | MEASLES ISOLATION | KLOMPAS

A 24-year-old woman presents to the emergency department with two days of high fever, profound fatigue, and cough. She was previously healthy and has lived in the US all of her life in an isolated religious community which did not immunize its children or adults.

Review of systems is notable for conjunctivitis and nasal congestion but no shortness of breath, abdominal pain, diarrhea, or rash.

She returned one week ago from a trip to Bosnia and Herzegovina with a church group. While abroad she did volunteer work in a school, went hiking in the mountains, stayed on a farm, helped to milk cows, and drank unpasteurized milk.

On exam she looks unwell, temperature is 103 degrees Fahrenheit, heart rate is 110 beats per minute, blood pressure is 100/70mm Hg, respiratory rate is 24 breaths per minute, oxygen saturation is 94% on ambient air.

Exam is notable for conjunctival infection but is otherwise normal. She has no rash.

Chest x-ray is normal. Nasopharyngeal swab is negative for influenza, RSV, and SARS-CoV-2 by PCR.

What precautions if any will you implement for this patient in the Emergency Department or in the hospital if she were to be admitted?

A. Airborne

B. Droplet

C. Contact

D. Contact + Droplet

E. Contact + Airborne

Correct answer: Airborne

Rationale

Measles is high on the differential diagnosis for this patient given her history of growing up in a community that did not believe in vaccines, and travel to a region with high endemic rates of measles and the clinical constellation of high fever, malaise, cough, and coryza.

The absence of rash does not rule out measles since the rash only comes 2-4 days after prodromal symptoms began.

The patient may have Koplik spots in her mouth, but these are often overlooked if not specifically sought out.

The appropriate precautions for measles are Airborne precautions.

This patient has never been vaccinated. She could have had measles as a child, but such information is not provided. She would logically be considered at risk for measles until more information was available.

Facts about measles:

- Incubation period: 11-12 days from exposure until first symptoms appear

- Prodrome: fever, cough, coryza, conjunctivitis, Koplik spots
- Rash: begins 2-4 days after the prodrome started, maculopapular, starts on head and face then spreads downward to the neck, trunk, legs, and feet
- Contagious period: 4 days before to 4 days after onset of rash
- Isolation: airborne
- Testing: throat or NP swab for PCR, serum for IgM
- Treatment: Vitamin A for patents overseas with poor nutritional status, an effect not shown in a USA study

37 | ADDISON'S HISTO | BENNETT

A 52-year-old household domestic worked in rural West Virginia presented with increasing malaise and fatigue, a 20-pound weight loss and a chronic labial ulcer. Physical examination was otherwise normal. The ulcer appeared a few weeks earlier, was only painful (stinging sensation) when urinating and not associated with regional adenopathy. She was not sexually active. The biopsy of the ulcer showed yeast forms consistent with Histoplasma. A urine antigen test was positive for histoplasmosis. She was started on itraconazole 200 mg twice daily. In the absence of health insurance, other tests were confined to routine blood work, which found a WBC 4,300 with a normal differential, hemoglobin of 10 gm%, normal serum creatinine and normal electrolytes except for an elevated potassium of 6.0 meq/l. Over the next month, her labial ulcer healed, her WBC rose to 5,400 and hemoglobin to 12 gm%. Blood chemistries were unchanged. Easy fatigability continued, she did not gain weight and was unable to return to work.

Which of the following would be the most useful next step in her workup?

A. 24-hour urine aldosterone

B. 8 am plasma cortisol

C. Trough itraconazole level

D. Plasma free T4

E. Stool occult blood

Correct answer: 8 am plasma cortisol

Rationale

The differential diagnosis is broad but a particular concern for patients with disseminated histoplasmosis is Addison's disease, a frequent and subtle complication, most commonly manifest as fatigue and anorexia. The best initial diagnostic test is an 8 am plasma cortisol. Serum potassium may be elevated from decreased adrenal cortical production of aldosterone.

Measuring urine aldosterone would not address the cause of hypoaldosteronism. A trough itraconazole is recommended because absorption is variable, but this patient's labial ulcer healed, and CBC improved. If her fatigue is due to hypothyroidism, the elevated potassium would not be explained. Fecal occult blood would make more sense if her hemoglobin had not been rising.

38 | LYME SEROLOGY | AUWAERTER

Which of the following statements regarding serological testing for Lyme disease (*Borrelia* burgdorferi) is correct?

A. **FDA-approved modified two-tier testing (MTTT, two EIA tests) offers better sensitivity if performed in the setting of erythema migrans than standard two-tier testing (STTT, one EIA followed by an immunoblot)**

B. PCR offers the best sensitivity compared to the CSF index (antibody-testing) for diagnosing neuroborreliosis

C. For clinicians awaiting test results, STTT typically yields positive test results faster than MTTT

D. Serologic cross-reactivity can yield false positive results when diagnosing Lyme disease in the setting of a co-infection with *Babesia microti*

E. Using MTTT or STTT can determine if a lesion that resembles erythema migrans is Southern Tick-Associated infection (STARI)

Correct answer: FDA-approved modified two-tier testing (MTTT, two EIA tests) offers better sensitivity if performed in the setting of erythema migrans than standard two-tier testing (STTT, one EIA followed by an immunoblot)

Rationale

MTTT testing offers better sensitivity in early Lyme disease and faster turnaround than STTT. MTTT uses two EIAs compared to STTT, which relies on a first-tier EIA followed by immunoblots (IgM and IgG) that are technically demanding and delay reporting. Research studies of erythema migrans (where serological testing is not recommended for people with likely exposure to ticks in an endemic region) have shown that MTTT outperforms STTT while performing similarly in later-stage cases of Lyme disease.

PCR does not reliably detect organisms in the CSF, whole blood or skin, due to paucibacillary infection and, therefore, is not routinely used except in synovial fluid analysis.

Although cross-reactivity between *B. burgdorferi* and *Anaplasma* phagocytophilum has been serologically described, this does not appear to be the case with the parasite *Babesia* spp.

The only method to conclusively prove STARI is if the offending tick is brought in for identification, proving it is a lone star tick (*Amblyomma americanum*). No pathogen has been found responsible for STARI, which is probably an enhanced reaction to the lone star tick's bite.

Even though MTTT offers better sensitivity than STTT in early Lyme disease (sensitivity 38-61% compared to 28-54% [Branda, CID 2018;66(7):1133-1139] e.g., erythema migrans) it is still insufficient to rule out *B. burgdorferi* infection compared to STARI.

39 | H PYLORI TEST OF CURE | ARONOFF

A 45-year-old male is diagnosed with *Helicobacter pylori* infection by endoscopy and antral gastric biopsy performed for weight loss and abdominal pain. There is a family history of gastric cancer. He is treated for 14 days with bismuth subsalicylate, metronidazole, a proton pump inhibitor, and tetracycline.

What would be best option to evaluate this patient regarding *Helicobacter* infection/disease after completing antibiotic therapy?

A. No further testing is necessary for one year

B. Perform the stool *Helicobacter pylori* antigen test 8 weeks after treatment

C. Perform the urea breath test 3 weeks after treatment

D. Repeat endoscopy, biopsy and rapid urease test (RUT) 6 weeks after treatment

Correct answer: Perform the stool *Helicobacter pylori* antigen test 8 weeks after treatment

Rationale

This patient should have test of cure (TOC) for *H. pylori* therapy to confirm eradication of the organism. The *H. pylori* stool antigen test performs with high sensitivity and specificity; is non-invasive; and is FDA-approved for TOC, making this the optimal approach.

The test should be performed at least 4 weeks after completion of bismuth or antibiotic treatment and at least 2 weeks of PPI therapy to avoid false negatives.

Both the urea breath test and endoscopy with rapid urease testing are acceptable alternatives. However, the urea breath test is dependent on live organisms. Three weeks after treatment is too soon to repeat this test as a false negative result may occur.

Given the recent endoscopy and biopsies, it is not necessary to again perform endoscopy to evaluate for gastric cancer, and it is not necessary to perform an invasive test to confirm cure of H. pylori infection.

40 | TB IN HOSPITAL | DORMAN

A 78-year-old woman is admitted to hospital with 2 months of progressive weakness, fatigue, shortness of breath, and 10 lb weight loss.

She has a history of non-Hodgkins lymphoma that was treated 20 years ago with radiation and chemotherapy.

Workup is notable for bilateral, patchy, upper lobe predominant infiltrates on chest CT.

Bronchoscopy gram stain and culture are unrevealing but AFB smear is positive and a tuberculosis nucleic acid amplification test is positive. She's placed on Airborne precautions, moved to an Airborne Infection Isolation Room (AIIR), and started on standard 4-drug anti-tuberculous therapy.

She has multiple complications unrelated to her tuberculosis and thus must stay on the rehabilitation service.

The team calls and asks when can she come off airborne precautions?

A. Immediately –she does not need isolation in the hospital

B. As soon as her symptoms are clearly improving

C. After a minimum of two weeks of active therapy

D. After at least three consecutive AFB smears collected ≥ 8 hours apart are negative

E. After a minimum 2 weeks active therapy, symptom improvement, and 3 negative sputum AFB smears

Correct answer: After a minimum 2 weeks active therapy, symptom improvement, and 3 negative sputum AFB smears

Rationale

CDC explains as follows:

- A patient who has drug-susceptible TB of the lung, airway, or larynx, who is on standard multidrug antituberculosis treatment, and who has had a substantial clinical and bacteriologic response to therapy (i.e., reduction in cough, resolution of fever, and progressively decreasing quantity of AFB on smear result) is probably no longer infectious.
- However, because culture and drug-susceptibility results are not usually known when isolation decisions are made, all patients with suspected TB disease should remain under airborne precautions while they are hospitalized until they have had three consecutive negative AFB sputum smear results, each collected in 8–24-hour intervals, with at least one being an early morning specimen; have received standard multidrug antituberculosis treatment (minimum of 2 weeks); and have demonstrated clinical improvement.

Reference: Centers for Disease Control and Prevention. Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005. MMWR 2005;54(No. RR-17): page 43.

41 | MPOX ISOLATION | GHANEM

A healthy 32-year-old man is admitted to the hospital following a motor vehicle accident.

Incidentally, he is noted to have multiple painful genital lesions and is diagnosed with Mpox. Many of his lesions have a scab. He is placed in a private room with standard Mpox precautions (contact, droplet, and airborne in this case).

From the infection control standpoint, which of the following statements best describes the optimal time to discontinue isolation?

A. He is currently no longer infectious and does not need isolation

B. When all lesions have a scab

C. When all scabs have fallen off

D. When all scabs have fallen off and re-epithelialization has occurred

E. He will remain infectious and require isolation for at least 12 weeks after onset of clinical manifestations of infection

Correct answer: He will no longer be infectious when all scabs have fallen off and re-epithelialization has occurred

Rationale

From the infection control standpoint, a person will no longer be infectious when all scabs have fallen off and re-epithelialization has occurred.

Keep in mind that Hospital Epidemiology/Infection Control at various hospitals may have different standards- and those should be followed.

Of note, the WHO recommends wearing condoms for 12 weeks after infection to minimize the risk of *sexual* transmission.

42 | CANDIDA AURIS DISPOSABLE PROBES| KLOMPAS

The surgical intensive care unit and the associated stepdown floor in which you work is struggling with an ongoing cluster of *Candida auris* infections.

Seven cases have been identified thus far.

The infection control team cohorts all the *Candida auris* patients into one section of the ICU, places known carriers on Contact Precautions, institutes weekly screening of all uninfected ICU and stepdown patients in order to detect and isolate newly colonized patients early, and institutes daily chlorhexidine baths for all patents.

Hand hygiene is closely monitored and encouraged.

Each patient bay is equipped with a dedicated stethoscope, blood pressure cuff, pulse oximeter, EKG leads, and glucometer.

The only equipment taken from patient to patient are axillary temperature probes that are fastidiously cleaned between each patient. Despite these measures additional cases are detected.

What are the best next steps to abort the cluster?

A. Cleaning each room twice daily with a quaternary ammonium compound

B. Administering prophylactic fluconazole to all patients

C. Switching to disposable temperature probes

D. Changing the curtains between patients' beds daily

E. Flushing all sink drains in patient rooms with bleach foam twice a week

Correct answer: Switching to disposable temperature probes

Rationale

Candida auris is an emerging pathogen that is resistant to many firstline antifungal treatments, firstline disinfecting agents, and that has a proclivity to persist in the hospital environment despite routine cleaning. It tends to be relatively resistant to quaternary ammonium compounds so cleaning with bleach is preferred.

Widespread use of fluconazole is a risk factor for promoting *Candida auris* colonization and spread. Hospital curtains between beds have indeed been found to be colonized with *C. auris* and other pathogens but other interventions focused on patients and the items that directly touch them are likely higher yield than changing curtains. Hospital sink drains are frequently colonized with MDR Gram negatives, and some hospitals do routinely clean them with bleach, but they have not been implicated in the spread of *C. auris* to date.

A cluster of *C. auris* infections in a neuroscience ICU in England was ultimately attributed to persistent colonization of axillary temperature probes despite routine cleaning hence best answer here is switching to disposable temperature probes.

43 | STAPH TOXIC SHOCK | BENNETT

A 64-year-old woman presented in the emergency room with fever, nausea, sore throat, muscle pain, headache and several loose stools over the past 24 hours. She had been in good health and was recovering well after functional endoscopic nasal surgery done 9 days ago for chronic sinusitis. She lived in downtown Chicago with her husband, a dog, a kitten and her 5-year-old granddaughter, who had been ill with a cough and low-grade fever. The patient had no recent travel and was taking no medications. On examination she had a temperature of 38.9C, pulse 109 and BP 86/45. She had a diffuse erythematous rash, particularly notable on her palms. Routine labs were notable for a creatinine of 3.1 mg/dl, WBC 14,900 and platelets of 112,000. She was given three liters of saline with little improvement in her blood pressure, admitted to intensive care and began requiring oxygen support.

What was the most likely pathogen?

A. Streptococcus pyogenes

B. Staphylococcus aureus

C. Capnocytophaga canimorsus

D. Bartonella henselae

E. COVID-19

Correct answer: Staphylococcus aureus

Rationale

Staphylococcal toxic shock is a well described complication of nasal surgery, attributed to Staphylococci infecting a paranasal sinus. Post operative nasal packing has been thought to contribute. Symptoms often appear a week or so after surgery but can be delayed. Hypotension, fever, renal failure, myalgias, abdominal pain, nausea, vomiting and diarrhea are common. Although recovery of Toxin 1-producing Staphylococcus aureus from nasal discharge is usual, sinus pain is not a feature. Antibiotic therapy may include not only an antistaphylococcal beta lactam but also one directed at toxin production, such as linezolid. Clindamycin may be useful, but macrolide resistance is a concern.

Streptococcus pyogenes can cause a similar syndrome, but an infected site is usually notable, often in soft tissue. Acute rheumatic fever can follow Streptococcus pyogenes infection but would not have hypotension.

Capnocytophaga sepsis could follow a bite from her dog, particularly if she had a history of splenectomy.

Bartonella henselae can occur in kitten owners but does not cause hypotension.

Adults can get multisystem inflammatory syndrome (MIS-A) 2-6 weeks after COVID-19, but the patient herself had no history of respiratory infection, such as was occurring in her granddaughter.

44 | RIFAMPIN AND ART| DORMAN

A patient with HIV initiated bictegravir/tenofovir alafenamide/emtricitabine (BIC/TAF/FTC) once daily. The patient's HIV viral load has declined from 1.3 million c/mL at ART initiation to 1000 c/mL after 6 months on antiretroviral therapy. The patient is also on rifampin and isoniazid plus pyridoxine for treatment of pulmonary tuberculosis.

What is the most likely cause for this patient's incomplete virologic response?

A. The patient had a high baseline HIV-1 RNA level and may require more time to achieve viral suppression

B. Drug-drug interaction between rifampin and tenofovir alafenamide

C. Drug-drug interaction between rifampin and bictegravir

D. High pill burden contributing to non-adherence

Correct answer: Drug-drug interaction between rifampin and bictegravir

Rationale

Bictegravir is **contraindicated** with rifamycins because CYP3A4 induction will significantly reduce bictegravir concentrations and can compromise efficacy of the antiretroviral regimen.

High baseline HIV viral load may lead to a longer time to achieving viral suppression but is not the most likely cause in this case. INSTI-based regimens are generally highly effective; if viral suppression is not achieved within 12 weeks, repeat genotypic resistance testing may be considered.

Although coadministration of tenofovir alafenamide (TAF) with rifamycins is not recommended in FDA labeling, coadministration may be considered per antiretroviral treatment guidelines that consider newer pharmacokinetic research.

High pill burden causing adherence challenges is a concern for people with HIV requiring complex treatment regimens for co-infections, such as tuberculosis, but it is not the most likely cause in this case.

45 | KPC CLUSTER | KLOMPAS

You are asked to investigate a cluster of hospital-onset carbapenem-resistant Enterobacterales (CRE) bloodstream infections. There have been 4 cases thus far, all with *Klebsiella pneumoniae*. Whole genome sequencing suggests the isolates are all closely related. You review the patients' histories:

- 37-year-old woman admitted with gallstone pancreatitis
- 62-year-old man admitted with hematemesis due to a duodenal ulcer and *H. pylori*
- 42-year-old woman admitted for endoscopic gastric bypass revision

- 17-year-old woman admitted with diarrhea, weight loss, and anemia.

What steps will you take next to identify the potential source of this cluster?

A. Identify any hospital staff that cared for all 4 patients; if so, work with occupational health to get these employees cultured (nails, axillae, groin, rectal swabs)

B. Review whether there was a common hospital food served to all 4 patients, if so, work with the hospital kitchen to requisition any remaining ingredients and culture

C. Check to see if all 4 patients were admitted to the same room or same unit: if so, culture the environment (bed rails, door handles, computer keyboards, etc.)

D. Establish whether all 4 patients were prescribed a common intravenous medication; if so, requisition the remaining lot from pharmacy and send for culture

E. Look whether all 4 patients had common procedures; if so, culture any devices used in all 4 procedures and review the hospital's disinfection process for these devices

Correct answer: Look whether all 4 patients had common procedures; if so, culture any devices used in all 4 procedures and review the hospital's disinfection process for these devices

Rationale

All 4 patients were admitted for gastrointestinal disorders that likely required endoscopy for evaluation and management. Duodenoscopes are classic sources for healthcare-associated clusters because their intricate components and narrow internal channels make them extremely difficult to reliably disinfect. If a duodenoscope gets colonized and is imperfectly disinfected between patients, then it can serve as a vector to transfer pathogens from one patient to another.

This cluster is less likely due to colonized staff members since sustained transmission to multiple patients is usually via healthcare workers' hands and these are more commonly colonized with gram positives rather than gram negatives. Contaminated food is less likely the source of the cluster because the patients presented with bloodstream infections rather than gastrointestinal syndromes. Environmental contamination is possible but less likely; the fact that all patients were admitted for gastrointestinal issues that required endoscopy is a more likely explanation than environmental contamination. Likewise, a contaminated intravenous medication is also possible given that patients developed bloodstream infections but again the fact that all patients were admitted for gastrointestinal issues that likely required endoscopy is a higher likelihood explanation for this cluster.

Clin Infect Dis 2017;64:894-901 and *Clin Infect Dis* 2017;65:1159-1166.

SESSION 4 | TUESDAY, AUGUST 19, 2025

Session Moderator: Dr. Gulick

Session Panelists: Drs. Bloch, Gandhi, Maldarelli, Masur, Saag, and Tunkel

Question #	Topic	Speaker
46	2-1-1 Prep	Gulick
47	Rheumatic Fever	Bloch
48	KS Lung Bx	Gandhi
49	Resistance Testing and DC Drugs	Maldarelli
50	Toxo Bactrim	Masur
51	MAC Proph	Saag
52	Powassan Encephalitis	Tunkel
53	PrEP and Women	Gulick
54	Tularemia	Bloch
55	Definition Viral Suppression	Gandhi
56	Rapid Initiation ART	Maldarelli
57	KS Skin Biopsy	Masur
58	Cabo-Rilpivirine Indications	Saag
59	Listeria Rhombencephalitis	Tunkel
60	ART Pregnancy	Maldarelli

This page left blank intentionally.

46 | 2-1-1 PrEP | Gulick

A 22-year-old man asks about HIV pre-exposure prophylaxis (PrEP) options. His friend takes "on-demand" PrEP and he asks your opinion.

What do you respond?

A. On-demand PrEP cannot be recommended because it is not FDA-approved

B. On-demand is not recommended in current guidelines

C. On-demand PrEP has only been studied with tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC)

D. On-demand PrEP has not been studied in men-who-have-sex-with-men (MSM)

Correct answer: On-demand PrEP has only been studied with tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC)

Rationale

While the strategy of on-demand PrEP is not FDA-approved, a number of clinical guidelines recommend it as an alternative strategy, including New York State, IAS-USA, and WHO.

On-demand PrEP is the strategy of taking 2 doses of TDF/FTC 2-24 hours before sex, 1 dose within 24 hours afterwards, and a final dose within 48 hours afterwards – the strategy has ONLY been studied in MSM (e.g., not heterosexual men, injection drug users or women).

- Daily PrEP is the FDA-approved use of a daily pill (Truvada or Descovy) (emtricitabine and tenofovir disoproxil fumarate-FTC-TDF or emtricitabine and tenofovir alafenamide-FTC - TAF) that combines two drugs to prevent HIV transmission. Many studies have shown that it can reduce the risk of HIV transmission by up to 99%. Studies have been done proving PrEP is effective for men, women, and transgender people, as well as preventing transmission through injection drug use. The United States Prevention Task Force has given PrEP Grade A status.
- The PrEP 2-1-1 dosing strategy has not been FDA approved but has been studied with Truvada (FTC/TDV) and shown to be an effective HIV prevention choice for MSM. PrEP 2-1-1 can prevent HIV transmission during anal sex. PrEP medication absorbs slower into vaginal tissue than anal tissue, so PrEP 2-1-1 is not an effective option for vaginal sex. PrEP 2-1-1 can be an option for people who have less frequent anal sex or for people who are unable or prefer not to take daily PrEP.

47 | Rheumatic Fever | Bloch

A 16-yr old male high school student from suburban Alexandria, Virginia presented with episodes during the past three months when he felt like his heart was "bursting from his chest" when he was doing push-ups in gym class. This went away promptly when he stopped exercising. He said it didn't feel like skipped beats and was not associated with chest pain or dyspnea.

He grew up in Iran, but his family has moved the USA four years previously. On exam, he was afebrile and appeared healthy.

A grade 3 systolic and diastolic murmur was heard at the left sternal border. Echocardiogram found mitral stenosis and regurgitation, with a thickened mitral valve without vegetations and an enlarged left atrium. EKG showed first degree heart block with a PR interval of 300 msec and no extrasystoles.

Routine chemistries and CBC were normal but CRP and ESR were elevated.

Which of these tests would be the most helpful in diagnosis?

A. Anticardiolipin IgG
B. Anti dsDNA
C. Anti Coxiella burnetii phase 2 IgG
D. Anti streptococcal DNase B
E. PCR on blood for Tropheryma whipplei

Correct answer: Antistreptococcal DNase B

Rationale

This youth appears to have rheumatic valvulitis as a sequela of acute rhematic fever. Rheumatic fever is rare in developed countries, and it is likely that his initial infection occurred internationally. His elevated inflammatory markers and first-degree heart block suggest recent reactivation from a streptococcal pharyngitis, but he does not meet the Jones Criteria for acute rheumatic fever. The revised Jones criteria require evidence of a preceding *S pyogenes* infection PLUS 2 major criteria or 1 major and 2 minor criteria:

Major:

- Arthritis
- Carditis
- Sydenham chorea
- Subcutaneous nodules
- Erythema marginatum

Minor:

- Polyarthralgia
- Fever
- Elevated inflammatory markers
- PR prolongation

A test for prior group A streptococcal infection such as antibody to streptococcal DNase B or antistreptolysin O (ASO) would support reactivation. A throat culture for streptococcal pharyngitis would also be appropriate. The tests for causes of endocarditis, such as marantic, Libman Sacks, Q fever or Whipple's endocarditis, are low yield in the absence of evidence for endocarditis.

Recognition of rheumatic heart disease is important to prevent progressive valvular destruction. A part of this youth's management may include antibiotic treatment to eradicate any current group A

streptococcal infection, monthly injections of benzathine penicillin G to prevent recurrence and treatment of breakthrough infection with another class of antibiotics.

48 | KS LUNG BX | GANDHI

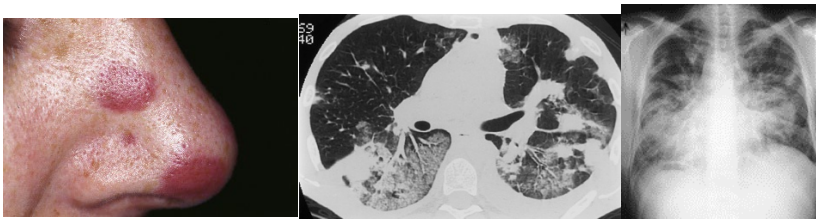
A 35-year-old woman presents to her primary care clinic with 6 weeks of cough, shortness of breath, and new skin lesions. She has no fever or weight loss. She is found to be HIV positive (CD4 count 150 cells/mm^3 and HIV viral load 500,000 copies/mL).

She has lived in Delaware all of her life, with no long-distance travel. She has no unusual pets or exposures although she does admit to commercial sex work over the past two decades.

On physical examination she has multiple purple-red skin lesions on her face, trunk and extremities.

Her PaO2 on room air is 95% and her routine blood count and chemistries are normal.

Her chest x-ray is strikingly abnormal, as is her chest CT scan which is read as showing reticular nodules, consolidation, and effusions consistent with Kaposi sarcoma.



https://phil.cdc.gov/Details.aspx?pid=6436

Serologic studies for cryptococcus and histoplasma are negative, and she is IGRA negative.

Induced sputum studies are negative for PCP (PCR), routine culture, and mycobacterial and fungal cultures at 7 days.

How would you evaluate the cause of the pulmonary and endobronchial lesions before starting treatment for Kaposi sarcoma?

A. **Bronchoalveolar lavage**
B. Transbronchial biopsy
C. Percutaneous needle biopsy of lung
D. Nothing further

Correct answer: Bronchoalveolar lavage

Rationale

This patient's pulmonary disease is not necessarily related to her HIV infection but given the subacute presentation and the slowly progressive skin lesions, an HIV related process seems likely.

With a low CD4 count, this patient could have a variety of opportunistic infections as a cause of her lung disease, even though she has no fever, weight loss, or other systemic symptoms or suspicious laboratory tests. With a 6-week history of cough, but no fever, this pulmonary process seems unlikely to be caused by a common community acquired respiratory virus or bacterium.

She should have evaluation for causes of lung disease that might be present in addition to her cutaneous Kaposi sarcoma. Bronchoalveolar lavage would be appropriate for the infectious etiologies. If seen in this case when bronchoscopy was performed, purple endobronchial lesions could be assumed to be KS, but…a second process in the lungs would certainly be possible.

In this case a BAL without tissue biopsy of the bronchus or lungs would be reasonable with close follow up.

The teaching points:

- BAL has a high yield for infectious causes of pulmonary disease in this setting but there is no cytologic test that is sensitive and specific for KS
- *Transbronchial biopsies or biopsies of endobronchial lesions when Kaposi sarcoma is being considered are not recommended because of the vascular nature of these tumors and risk of bleeding if biopsied*
- *Similarly, there is risk of bleeding with a percutaneous needle biopsy of the lung if these pulmonary lesions are KS*

For this patient, a skin biopsy for Kaposi sarcoma plus a negative BAL for the likely infectious agents would be appropriate to assume this patient has pulmonary KS, supplemented by the usual serologies, cultures and PCRs…but…it's conceivable that an infectious process could be missed, so close follow up is appropriate.

In this patient, chemotherapy in combination with ART should be administered since she has visceral involvement (also indicated for extensive and/or symptomatic KS skin lesions, extensive oral disease, tumor-associated edema and/or ulceration).

Liposomal doxorubicin and paclitaxel exhibit comparable response rates and progression-free survival, but liposomal doxorubicin exhibits less high-grade toxicity relative to paclitaxel.

49 | RESISTANCE TESTING AND DC DRUGS | MALDARELLI

A 21-year-old patient with HIV on bictegravir/tenofovir alafenamide/emtricitabine (BIC/TAF/FTC) and history of adherence challenges resulting in intermittent low-level viremia presents to clinic. When lab results return, viral load has increased to 34,000 c/mL. The patient admits to discontinuing therapy because "he feels fine". Genotypic resistance testing is ordered.

How soon after discontinuation of antiretroviral therapy should resistance testing ideally be performed in order to detect drug resistance mutations?

A. Within 4 weeks

B. Within 3 months

C. Within 6 months

D. Within 12-18 months

Correct answer: Within 4 weeks

Rationale

Ideally, HIV resistance testing should be completed while the patient is still taking the failing antiretroviral regimen. If antiretroviral treatment has been discontinued, resistance testing should be performed within 4 weeks. Testing after 4 weeks may still be useful; however, it is possible that drug resistance mutations may be missed as the virus reverts to wild type.

50 | TOXO BACTRIM | MASUR

A 50-year-old male has HIV (CD4=40 cells/uL and HIV viral load =600,000 copies/uL) has central nervous system toxoplasmosis documented by a compatible CT of the head and a positive CSF PCR for toxoplasma.

The patient also has cryptosporidiosis with 6 stools per day plus considerable nausea and thus has limited food intake.

The pharmacy cannot obtain sulfadiazine or pyrimethamine.

What would be the best option for toxoplasmosis therapy?

A. Atovaquone
B. Clindamycin plus Primaquine
C. Trimethoprim-Sulfamethoxazole
D. Azithromycin plus Doxycycline
E. Nitazoxanide

Correct answer: Trimethoprim sulfamethoxazole

Rationale

The classic treatment of choice for cerebral toxoplasmosis is sulfadiazine plus pyrimethamine, i.e., this is the best studied regimen. However, both drugs can be difficult to obtain, and pyrimethamine is often exorbitantly expensive.

Trimethoprim-sulfamethoxazole is probably as effective as sulfadiazine plus pyrimethamine although this combination is not as well studied as sulfadiazine-pyrimethamine. TMP-SMX has the advantage of being available IV or PO, while sulfadiazine and pyrimethamine are both exclusively available as oral preparations.

Clindamycin-pyrimethamine is a good option for CNS toxoplasmosis but the option here is clindamycin-primaquine, the regimen for PCP. Hopefully the exam will not try to confuse you like was done here by two regimens that look the same to the reader who is not careful!

Atovaquone has activity against toxoplasmosis but it likely not as effective as TMP-SMX or clindamycin-pyrimethamine. Moreover, it is poorly absorbed with a high fat diet. In a patient with nausea and diarrhea, atovaquone would be a poor choice for therapy.

Azithromycin has some activity as does doxycycline but neither one is a good choice.

Nitazoxanide has no activity again toxoplasmosis.

51 | MAC PROPH | SAAG

Which of the following is correct regarding primary prophylaxis for disseminated mycobacterium avium complex (MAC) disease?

A. Initiate primary prophylaxis if CD4 count is <50 cells/mm^3
B. Initiate primary prophylaxis if CD4 count is <100 cells/mm^3
C. Initiate primary prophylaxis if CD4 count is <200 cells/mm^3
D. Primary prophylaxis is not recommended for people with HIV who immediately initiate antiretroviral therapy

Correct answer: Primary prophylaxis is not recommended for people with HIV who immediately initiate antiretroviral therapy

Rationale

Primary prophylaxis for MAC is not needed when fully suppressive antiretroviral therapy is initiated but is recommended in people with HIV who have CD4 count <50 cells/mm^3 **and** are not receiving ART or remain viremic on ART (after ruling out disseminated MAC disease).

However, patients who are unable to take ART reliably are also unlikely to take MAC prophylaxis reliably.

52 | POWASSAN ENCEPHALITIS | TUNKEL

A 72-year-old male living in a rural area of Southern New York State was admitted to the hospital in June with a five-day history of nausea, vomiting, headache, fever, somnolence, and confusion.

On examination, he had a temperature of 39°C, was oriented only to the person, had weakness in the right lower extremity, a faint maculopapular rash on his upper chest and back, and a right facial droop.

Routine laboratory tests were normal. LP: showed 108 WBC/mm^3 with 31% PMN, protein 113 mg/dl, and glucose 67 mg/dl. IgM serology for West Nile Virus on the CSF and serum was negative, as was the PCR for herpes simplex and West Nile virus.

MRI showed diffuse hyperintensity in the left basal ganglia on T2 and FLAIR imaging. He became progressively obtunded, requiring intubation for airway protection.

According to his wife, he had been in good health and had returned two weeks before his illness from a camping trip with his family in a lake area in New Hampshire. She said her husband had been concerned about finding a few ticks on his body while camping but had removed them the day he thought he had acquired them.

Which of the following agents is the most likely cause of this illness?

A. Varicella Zoster virus
B. Herpes simplex virus
C. Zika virus
D. Powassan virus
E. Enterovirus D68

Correct answer: Powassan virus

Rationale

The diagnosis of acute encephalitis is suggested by a prodrome of only a few days, followed by progressive decline in mental status.

Although herpes simplex is one of the most common etiologies in a previously healthy patient, the combination of a negative PCR and no temporal lobe lesion on MRI is against that diagnosis. Varicella zoster virus would rarely cause encephalitis in a noncompromised patient.

Mosquito-borne encephalitis is possible in June, but only two were listed: Zika is not seen in the Northeast, and West Nile is excluded with the negative PCR and CSF IgM antibody test.

Enterovirus D68 is a rare, person-to-person transmitted virus that can cause flaccid paralysis in children under 5 years and a few immunocompromised adults.

Tick-borne encephalitis occurs in Europe due to a different virus, but in the USA, a closely related, tick-transmitted agent is the Powassan virus. First described in 1958, at least a hundred cases have been reported in the USA and Canada. Infection is transmitted by Ixodes ticks, mostly *I. cookei* in the Great Lakes area and *I. scapularis* in the Northeast. *I. scapularis* also transmits Lyme borreliosis, *Borrelia miyamotoi, Anaplasma phagocytophilum* and *Babesia microti*. Even transient tick attachment can transmit the Powassan virus in animal experiments, unlike Lyme disease.

Diagnosis of Powassan virus infection can be done by PCR of CSF early in infection or IgM serology on CSF later. Plaque reduction neutralization testing (PRNT) from reference laboratories can help distinguish Powassan infection from related flaviviruses, such as West Nile. No antiviral therapy is known to be effective.

53 | PrEP and Women | Gulick

Which of the following has demonstrated the greatest efficacy for HIV pre-exposure prophylaxis in women?

A. Daily tenofovir alafenamide/emtricitabine

B. On-demand tenofovir disoproxil fumarate/emtricitabine (2-1-1 dosing)

C. Monthly intramuscular cabotegravir

D. Every 2-month intramuscular cabotegravir

Correct answer: Every 2-month intramuscular cabotegravir

Rationale

Daily tenofovir alafenamide/emtricitabine is currently not recommended in this population due to lack of data, although this is an area of active research.

On-demand dosing of tenofovir disoproxil fumarate/emtricitabine (2-1-1 dosing) is not recommended due to lack of efficacy in this population. In women, injectable HIV pre-exposure prophylaxis treatments have been shown to be superior to oral tenofovir based HIV pre-exposure prophylaxis options.

Intramuscular cabotegravir may be used for HIV pre-exposure prophylaxis in people assigned female at birth who are at risk for HIV through receptive vaginal sex. Cabotegravir LA is administered into the gluteal muscle monthly for two months and then every two months thereafter. For those who are concerned about side effects, daily oral cabotegravir can be administered for a four-week lead-in period prior to initiating injections.

54 | TULAREMIA | BLOCH

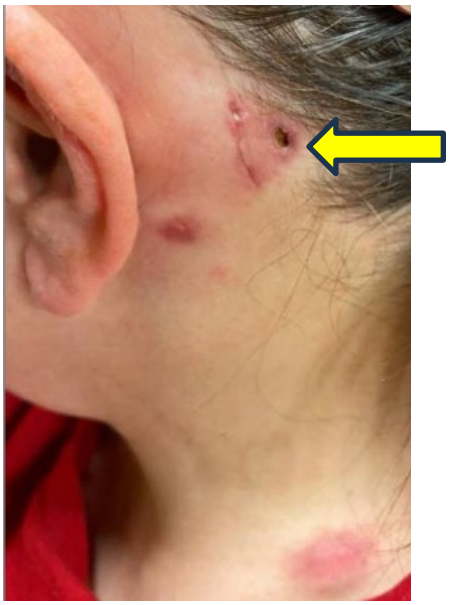
A 49-year-old previously healthy female is referred to the ID clinic with 1-month of left sided neck swelling.

Two weeks before the onset of symptoms, she found a tick embedded behind her left ear. She removed this without difficulty but developed an ulcerated area at the site of attachment (see arrow below).

Subsequently she developed left posterior auricular and posterior chain lymphadenopathy. A lymph node biopsy showed inflammatory changes with negative AFB and fungal stains. She denies fevers or sore throat but does endorse fatigue.

She lives in a suburb of Nashville and works as a publicist. She has a pet dog and two cats, all of whom are healthy. She is an avid gardener and notes both rabbits and deer have been eating the planted vegetables. She denies sick contacts.

Physical exam shows the lesions below:



Lab tests including CBC diff and CMP are both within normal limits.

What is the most likely cause of this patient's symptoms?

A. *Bartonella henselae*
B. Kikuchi syndrome
C. *Ehrlichia chaffeensis*
D. *Yersinia pestis*
E. *Francisella tularensis*

Correct answer: *Francisella tularensis*

Rationale

This patient has ulceroglandular tularemia related to the antecedent tick bite. Tularemia, also known as "rabbit fever," can be caused by exposure to infected animals but also may be spread through tick or deer fly bites. The most common clinical syndromes associated with tularemia are listed below:

- **Typhoidal:** Fever and sepsis without any localized findings.
- **Pneumonic:** The most serious form of disease, associated with pulmonary infiltrate. This can occur through inhalation (the classic example being inadvertent pulverization of a rabbit by a lawn mower, with aerosolization of body fluid) or through dissemination to the lungs following one of the other forms.
- **Ulceroglandular**: Often due to the bite of an infected tick or deer fly, with ulceration at the site of attachment and regional lymphadenopathy.
- **Pharyngeal:** Transmitted through ingestion of contaminated meat or water. This presents as sore throat associated with submandibular lymphadenopathy.
- **Oculoglandular:** This form develops through conjunctival exposure, with pre-auricular lymphadenopathy (also known as Parinaud's syndrome).
- **Glandular**: Similar to ulceroglandular, but without the ulceration.

Tularemia is a potential agent for bioterrorism and can pose a risk for the microbiology staff if there is inadvertent inhalation of bacteria. For this reason, the lab should be notified when there is suspicion for this organism. Diagnosis is through culture or serology. Treatment is with streptomycin or gentamicin, ciprofloxacin, or doxycycline.

Bartonella henselae causes cat scratch disease (CSD), which often presents with lymphadenopathy. While cat ownership puts this disease on the differential, involved lymph nodes are typically in a regional distribution from the scratch, most commonly in the axilla or groin. Ulceration does not occur at the site of injury.

Kikuchi's syndrome typically is seen in younger women, causes bilateral cervical lymphadenopathy, and is not associated with ulceration.

Ehrlichia chaffeensis causes ehrlichiosis, a tickborne infection endemic to the Southeast and South-Central US. Ehrlichiosis presents with fever, headache, and myalgias; eschars do not occur at the site of tick bite and lymphadenopathy is not present.

Yersinia pestis, the cause of plague, is spread by fleas, not ticks, and does not cause ulceration at the site of inoculation. Plague is rare in the US, with cases limited to rural areas in the West and Southwest.

55 | DEFINITION VIRAL SUPPRESSION | GANDHI

A person with HIV who takes antiretroviral therapy as prescribed and achieves and maintains viral suppression will not transmit HIV to their sex partners (Undetectable = Untransmittable).

Viral suppression in the context of treatment as prevention is defined by the Centers for Disease Control and Prevention as?

A. HIV-RNA level below the lower limit of detection of available assay

B. HIV-RNA level < 50 copies/mL

C. HIV-RNA level < 200 copies/mL

D. HIV-RNA level < 1000 copies/mL

Correct answer: HIV-RNA level < 200 copies/mL

Rationale

The CDC definition of viral suppression is HIV-RNA level < 200 copies/mL.

56 | RAPID INITIATION ART| MALDARELLI

A 24-year-old man newly diagnosed with HIV presents to care for rapid initiation of antiretroviral therapy. The patient previously received pre-exposure prophylaxis (PrEP) with intramuscular cabotegravir x 1 dose which was discontinued due to injection site reaction with subsequent use of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for PrEP. Baseline labs, including hepatitis B serologies and HIV resistance testing, are pending.

Which of the following is an appropriate choice for rapid ART initiation?

A. Bictegravir/Tenofovir Alafenamide/Emtricitabine

B. Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine

C. Dolutegravir/Lamivudine

D. Doravirine/Tenofovir Disoproxil Fumarate/Emtricitabine

Correct answer: Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine

Rationale

For rapid initiation of antiretroviral therapy, bictegravir, dolutegravir, or darunavir based three drug regimens (i.e., including tenofovir disoproxil fumarate or tenofovir alafenamide PLUS emtricitabine or lamivudine) are preferred regardless of previous use of TDF/FTC for PrEP. However, patients with exposure to intramuscular cabotegravir for PrEP should not be initiated on bictegravir or dolutegravir based therapy until integrase strand transfer inhibitor (INSTI) genotype results are available. In these cases, protease inhibitor-based therapy with darunavir/ritonavir or darunavir/cobicistat PLUS tenofovir disoproxil fumarate or tenofovir alafenamide PLUS emtricitabine or lamivudine is recommended.

57 | KS SKIN BIOPSY | MASUR

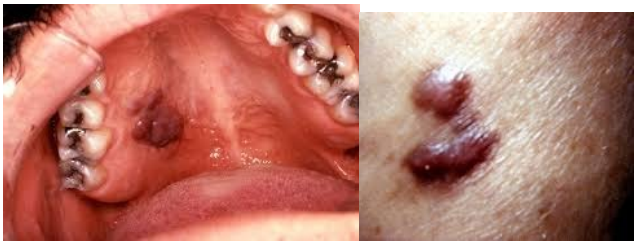
A 44-year-old male has noted about ten small skin and oral lesions appearing and growing slowly over several months. He feels well and has no other complaints. He is afebrile.

He admits to multiple same sex partners over the past 20 years. He was aware of his HIV diagnosis several years ago but had never wanted to pursue therapy.

His physical examination and chest Xray are normal other than the skin and mucosal lesions.

Laboratory values are remarkable for positive HIV serology, CD4 count 400 cells/mm^3, HIV viral load of 400,000 copies/mL. His routine hematology and chemistry blood work are normal.

Some of his lesions are shown below.



https://phil.cdc.gov/Details.aspx?pid=6436

What diagnostic test(s) should you order to establish the cause and determine the therapy of these skin and mucosal lesions?

A. Skin biopsy only

B. Skin and mucosal biopsies

C. Skin biopsy and HHV 8 serology

D. Skin biopsy, serum HHV 8 PCR, and serum HHV 8 serology

E. No further test: the diagnosis of Kaposi sarcoma can be made clinically in this case

Correct answer: Skin biopsy only

Rationale

This patient should have a biopsy of an easily accessible lesion to confirm a diagnosis of Kaposi sarcoma. If the skin biopsy is positive for KS, it is reasonable to assume the mucosal lesion is due to KS unless there is some specific reason to think it is something different. A KS diagnosis can be confused with Bacillary Angiomatosis, caused by Bartonella henselae. Patients with bacillary angiomatosis do not invariably have fever and systemic symptoms. KS diagnosis should be confirmed by immunohistochemical (IHC) staining of tumors with antibodies recognizing the HHV-8-encoded latency-associated nuclear antigen (LANA).

Initiating ART alone, without chemotherapy, can effectively treat limited cutaneous KS with no known visceral disease and is therefore recommended as initial therapy in most cases.

Chemotherapy, in combination with ART in people with HIV, should be administered in patients with extensive and/or symptomatic KS skin lesions, extensive oral disease, tumor-associated edema and/or ulceration, or any visceral involvement of KS.

Serologic testing for HHV-8 antibodies is not used for either diagnostic testing or routine screening for HHV-8-related illnesses and does not inform a decision about whether to treat or what treatment to use. The lack of a standardized role for HHV-8 serology is in part due to the poor sensitivity and specificity of the current assays.

Measurement of plasma HHV-8 is thought by some to be useful for diagnosis and monitoring of some HHV-8-related diseases but not Kaposi sarcoma. For patients with KICS (KSHV-Associated Inflammatory

Cytokine Syndrome), detection of HHV-8 in blood is part of the diagnostic criteriaHHV-8 DNA levels in the PBMCs are elevated in patients with active (Multicentric Castleman's Disease (MCD) and Primary Effusion Cell Lymphoma (PEL) An undetectable plasma HHV-8 DNA may exclude a diagnosis of MCD.

58 | CABO-RILPIVIRINE INDICATIONS| SAAG

A 36-year-old male with HIV, well controlled on antiretroviral therapy (TDF/FTC/DTG) for the last two years, presents to establish care at a new clinic.

He is requesting to switch to long-acting injectable therapy with Cabotegravir / Rilpivirine as a friend recently started this treatment with a high degree of satisfaction.

The patient's treatment history includes TDF/FTC/EFV which was discontinued due to poor tolerance and intermittent adherence; subsequent genotyping revealed a K103N mutation.

Other medical history includes methamphetamine use disorder (currently in remission) and depression (treated with escitalopram).

Recent labs are as follows:

- HIV viral load < 20 copies per mL
- CD4+ T cell count 452 cells per cubic mL
- RPR non-reactive
- Hepatitis B surface antibody negative
- Hepatitis B core IgG positive
- Hepatitis B surface antigen positive
- Hepatitis B DNA viral load < 10 IU / mL
- Hepatitis C IgG negative
- Complete blood count, basic metabolic panel and liver function testing are all within normal limits.

For this patient, which of the following would preclude switching to long-acting injectable therapy with cabotegravir /rilpivirine (LA CAB/RPV)?

A. History of treatment failure with TDF/FTC/EFV
B. K103N mutation
C. Current treatment with escitalopram
D. Positive Hepatitis B surface antigen
E. History of methamphetamine use disorder

Correct answer: Positive Hepatitis B surface antigen

Rationale

This patient's labs suggest that he has chronic hepatitis B infection (positive surface antigen, positive core IgG); the Hepatitis B viral load is suppressed because his HIV treatment regimen includes medications that are also active against Hepatitis B (TDF/FTC).

Switching to LA CAB/RPV – which does not have activity against Hepatitis B - could result in Hepatitis B reactivation and associated complications including liver failure and thus would **not** be recommended.

Neither treatment failure with TDF/FTC/EFV nor a K103 N mutation would preclude switching to cabotegravir/rilpivirine long-acting injectable therapy; rather, documented resistance to either cabotegravir or rilpivirine would be a contraindication.

When switching antiretroviral therapy, potential drug interactions should always be considered, but escitalopram does not interact with cabotegravir/rilpivirine long-acting injectable therapy and thus would not prohibit treatment initiation. Notably drug interactions to be aware of include medications which induce uridine diphosphate (UDP)-glucuronosyl transferase (UGT)1A1 and/or cytochrome P450 (CYP)3A enzymes, which may result in loss of virologic response, such as: anticonvulsants (carbamazepine, oxcarbazepine, phenobarbital, phenytoin); rifamycin-class antimicrobials; systemic steroids; and St. John's wort (herbal medication).

Finally, a history of substance use disorder is not a contraindication to cabotegravir/rilpivirine long-acting injectable therapy; in fact, there is some evidence to suggest that this agent is helpful in "safety net" populations including those with housing insecurity, mental illness, or substance use disorder.

In general, when considering replacing an oral antiretroviral therapy regimen with LA CAB/RPV, the following criteria apply:

- Sustained viral suppression for at least 3 months (although there is a growing body of literature about the success of using LA CAB/RPV as initial therapy)
- No history of documented or suspected resistance to either CAB or RPV
- No active HBV infection (unless also receiving TAF, TDF, or entecavir)
- Not pregnant or actively planning pregnancy
- Not receiving medications with significant drug interactions

Sources:

https://nida.nih.gov/news-events/news-releases/2023/02/long-acting-antiretroviral-therapy-suppresses-hiv-among-people-with-unstable-housing-mental-illnesses-substance-use

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/optimizing-antiretroviral-therapy

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212888s000lbl.pdf

59 | LISTERIA RHOMBENCEPHALITIS | TUNKEL

A 31-year-old woman is brought to the emergency department by her husband for fever and neurological symptoms.

She was completely well until 3 days earlier, when she felt nauseated and vomited twice. During the next two days she had fever, felt "achy," developed a headache, and continued to have nausea and vomiting. Upon awakening this morning, she complained of double vision, and her husband noted her eyes "weren't looking in the same place."

In the emergency room, she was found to have a temperature of 102.4°F. There was no rash. She had mild nuchal rigidity, right 6th cranial nerve palsy, and a sensory deficit over most of the left side of her body. Her gait was very unsteady. The rest of the exam was unremarkable. An MRI of the head demonstrated inflammation of the pons and medulla.

Which one of the following organisms is the most likely cause of her illness?

A. Streptococcus pneumoniae
B. Nocardia nova
C. Mycobacterium tuberculosis
D. Listeria monocytogenes
E. Cryptococcus neoformans

Correct answer: Listeria monocytogenes

Rationale

This patient has inflammation of the brainstem (rhombencephalitis).

Listeria monocytogenes can involve the meninges and/or the brain parenchyma, including the brainstem, producing meningitis, abscess, or encephalitis.

Listeria rhombencephalitis is a well-described syndrome that typically occurs in healthy adults (unlike other forms of listeriosis). The classic syndrome is a biphasic illness characterized by a prodrome of fever, headache, nausea, and vomiting lasting about 3-4 days, followed by the sudden onset of progressive, asymmetrical cranial nerve deficits, cerebellar signs, and hemiparesis or hemisensory deficits, with or without meningeal signs.

There is a long list of organisms (e.g., HSV, TB, Crypto) and non-infectious causes (paraneoplastic, multiple sclerosis, autoimmune) that are less common. Think of Listeria first among infections, but the board exam could also expect you to know about other causes of rhombencephalitis, especially anti-NMDAR encephalitis, an autoimmune encephalitis and a cause of brainstem encephalitis that is often associated with ovarian teratoma in young women and is diagnosed by serum and CSF antibodies!

Streptococcus pneumoniae causes meningeal infection and almost never produces parenchymal brain disease.

Nocardia infection of the CNS presents more indolently and involves the cortex, typically with abscess formation.

Parenchymal brain infection can occur with tuberculosis but usually has a slower progression and involves formation of tuberculomas in the cortex. Progression is too rapid for cryptococcosis.

60 | ART PREGNANCY | MALDARELLI

A woman with HIV, a history of multiple antiretroviral regimens, and prior virologic failures is currently well controlled on a regimen of dolutegravir (DTG) once daily plus darunavir/cobicistat/tenofovir alafenamide/emtricitabine (DRV/c/TAF/FTC) once daily. She is now pregnant and presents for follow up.

Which of the following statements is correct?

A. The patient is well controlled on the current regimen; continue standard treatment and monitoring measures

B. Tenofovir alafenamide is not recommended in pregnant individuals

C. Darunavir/cobicistat is not recommended in pregnant individuals

D. Darunavir/cobicistat dose should be increased from once daily to twice daily

Correct answer: Darunavir/cobicistat is not recommended in pregnant individuals

Rationale

Darunavir/cobicistat (DRV/c) is not recommended during pregnancy due to substantially lower exposures of darunavir and cobicistat during the second and third trimesters.

However, patients who are well controlled may continue DRV/c during pregnancy provided they receive more frequent viral load monitoring (every 1-2 months). Alternatively, the patient may be switched to darunavir/ritonavir. In pregnancy, darunavir/ritonavir should be dosed twice daily, although this leads to a much greater pill burden which would be a concern in patients with a history of adherence challenges.

Darunavir/cobicistat is not FDA-approved to be given twice daily due to the cobicistat component and lack of safety data. Both tenofovir alafenamide and tenofovir disoproxil fumarate are preferred NRTI options in pregnancy. In a pregnant patient with complex HIV history, expert consultation is advised.