

Photo Opportunity 2021 (Dr. John Bennett)
Answers and Rationales

1. Pseudomonas aeruginosa (skin lesion)

The sharply delimited border of a rapidly expanding lesion in a febrile neutropenic patient should suggest ecthyma gangrenosum. Ecthyma gangrenosum is classically caused by *Pseudomonas aeruginosa* but can be caused by invasive molds, such as aspergillosis and mucormycosis or by a variety of other bacteria and molds. Infection can occur by inoculation or hematogenously. Ecthyma gangrenosum typically begin as painless red macules that quickly evolve into a sharply defined area of induration. These lesions progress from red to purple to black as necrosis of the skin evolves. Blisters may form on top, as seen here. Ecthyma lesions often can be seen to enlarge over as little as 12 hours. Culture of a punch biopsy or blood culture in hematogenous cases due to *Pseudomonas* is needed. For ecthyma gangrenosum due to a mold, histology, wet mount or culture of a skin punch biopsy is needed as blood cultures are negative. The other organisms listed do not cause the invasion and necrosis of deep dermal blood vessels that created the clinical picture of ecthyma gangrenosum.

2. Measles

Rash, conjunctivitis and cough should have tipped you to measles. The rash is completely unlike chickenpox and typhoid. Eleven days is a bit long for dengue and the rash in dengue is more purpuric. The patient didn't have rhinitis, that is, coryza, as many measles patients do and no Koplick spot was observed. The incubation period for measles, is 10-14 days so it's possible he got this in transit, such as in an airport. Measles is probably the most communicable and most preventable infection. If he was immunized, among the causes of breakthrough infections is fairly to keep the vaccine cold during all of its storage.

3. Colonic flora (actinomycosis of the liver)

A notable characteristic of actinomycosis is the ability over several weeks to form sinus tracts extending into contiguous tissue, in this case from the liver out through the abdominal wall. Appearance of a cluster of organisms, called a "grain", is another characteristic shared by only two other entities: mycetoma and botryomycosis. Mycetoma originates from inoculation into the skin from sites in nature, not extending out from the liver. Botryomycosis forms more loosely clustered clumps of organisms than in a grain and most common organism is *Staphylococcus aureus*.

4. Water (cryptosporidiosis)

The photomicrograph shows the parasite budding off from the surface of enterocytes, in which it was growing, and being shed into the intestinal lumen. *Cryptosporidium*, *Cyclospora* and *Cystoisospora* all

grow inside the intestinal epithelium and emerge as oocysts, to be excreted in the stool. Cryptosporium species are the smallest, 4 to 6 microns in diameter. Cyclospora are twice that size and cystoisospora even larger and football shaped. All three can be acquired by ingesting contaminated food or water but cryptosporidium is by far the most common and usually acquired from water. Cryptosporidium oocysts are quite hardy and resistant to killing by chlorine. Acid fast staining of stool has been used for identification but multiplexed nucleic acid panels are now available and detect cryptosporidium and Cyclospora.

5. Mosquito (Dengue)

When a traveler returns from a tropical area with fever and a rash within ten days of exposure, the differential should include dengue, chikungunya and zika, all acquired by mosquito bites. Of these, dengue is most common and is the most common cause of fever in travelers returning from every tropical region except sub-Saharan Africa. Dengue rash may be hard to see in dark-skinned patients, as this lady originally from Panama. Leukopenia is common and thrombocytopenia may occur, though wasn't present in this patient. Headache and muscle aches are common. For the other answers, short incubation periods could also be typhoid from humans or food, leptospirosis from animal urine and murine typhus from a rat flea would be less common exposures in this patient's visit to her urban family. However, *Aedes aegypti*, the usual mosquito vector, is well adapted to the urban environment and bites during the daytime.

6. Ocular palsy (cavernous sinus thrombosis)

Cavernous sinus thrombosis typically presents with ocular palsy because cranial nerves 3, 4 and 6 run through the sinus. Cranial nerves 8 (deafness) and 1 (smell) are not affected and the optic nerve (blindness) would not be affected without extension beyond the sinus.

7. Gram negative coccus (disseminated gonococcal infection)

Fever, a few scattered painless pustular skin lesions and tenosynovitis should make you think of disseminated gonococcal infection. Tenosynovitis (inflammation of the lining of the sheath that surrounds a tendon) as opposed to arthralgias or septic arthritis, is characteristic of disseminated GC. Often multiple tendons are simultaneously inflamed, especially the wrist, fingers, ankle, and toes. Since the patient was unconscious in a rat-infested alley, a spirochete in the blood would suggest rat bite fever due to *Spirillum minor*, but this organism is rarely seen in this hemisphere. A gram-negative rod could be rat bite fever due to *Streptobacillus moniliformis*, but this rarely grows in blood unless one uses special media and incubates for up to three weeks. A gram-negative coccus could be *Neisseria gonorrhoea* or meningitidis, either of which are possible in this setting, although GC is more likely than meningococcus. A gram-positive bacillus might be *Erysipelothrix* or *Listeria* or *Bacillus*, none of which fit the epidemiology or clinical situation. Growth in a blood culture at three days is not likely to be an endemic mycosis.

8. Enteric bacteria (bacterial liver abscess)

This is most likely a bacterial or amebic abscess, but amebic abscess was not offered as an option because amebic liver abscess is difficult to distinguish from bacterial abscesses. This lesion occurred within 3 weeks of exposure, assuming he acquired this on his travel, and thus it has become large quite quickly, unlike cysticercosis or echinococcosis, and is not cystic, like cysticercosis. He has fever and leukocytosis, unusual in cysticercosis or echinococcosis. Fasciola can present with a liver mass in the acute phase, but causes eosinophilia in this early stage, and the septated lesions would not be characteristic. Exposure history is weak for the listed parasitic infections, which were unlikely to occur in this traveler, based on geography and type of contaminated food that leads to infection. Echinococcus multilocularis only occurs in the northern hemisphere among people exposed to food contaminated by stool of wild canines, such as foxes and wolves. Fasciola hepatica infection is broadly distributed but occurs in people who ingest raw water plants, such as watercress. Paragonimus westermani infection is found in the Far East in people who ingest undercooked or pickled fresh water crustaceans such as crabs, and does not cause liver lesions.

9. Doxycycline (Rocky mountain spotted fever)

Development of a petechial rash on the fourth day is very consistent with Rocky Mountain Spotted fever, as is a severe headache, fever and myalgias. Treatment of this rickettsiosis is doxycycline, even in children. Meningococcal sepsis can cause a similar rash and severe headache but rash would have appeared earlier after the onset of severe headache.

10. Incubation on mycobacterial agar at 30°C (Mycobacterium marinum)

A chronic erythematous nodule on a skin surface exposed to brackish water or tropical fish tanks should suggest *Mycobacterium marinum* infection. *M. marinum* is difficult to see in biopsy so that diagnosis depends on culture. *M. marinum* grows poorly at the usual clinical laboratory incubator temperature of 35-37°C so should be cultured on any standard mycobacterial agar at 30°C. Iron is important for *Mycobacterium haemophilum* but not *M. marinum*. Fresh chocolate agar is recommended for *Bartonella henselae* culture. Sabouraud's agar is useful for sporotrichosis but not Mycobacteria. Sporotrichosis is acquired from thorny plants and not water. NNN medium is used for culturing Leishmania but there is no exposure history for that diagnosis.

11. Enterocytozoon bienersi

The tiny organisms within the cytoplasm are in the wrong location and of the wrong size for Cyclospora or Cryptosporidium but are the agents of microsporidiosis, an infection caused by species of Enterocytozoon and Encephalitozoon. There are 1200 species of microsporidia, all obligate intracellular parasites of vertebrates and invertebrates. However, none of the genus Microsporidium are known to infect humans, despite the name, microsporidiosis. Patients with AIDS are uniquely susceptible to

microsporidiosis with *E. bienewisi* being the most common agent and presenting as diarrhea and weight loss. There is no known effective therapy of *E. bienewisi* infection, other than restoring immune function with highly active antiretroviral therapy.

12. Vibrio (*Vibrio vulnificus*)

Vibrio species, usually *vulnificus*, can cause these rapidly spreading hemorrhagic lesions after ingestion of contaminated poorly cooked shellfish, raw oysters or exposure of skin wounds to brackish or salt water. *Vibrio vulnificus* and other *vibrio* species exist as free-living bacteria in marine environments. Shellfish ingestion is associated with this bacteremic syndrome in patients with cirrhosis or with various types of immunodeficiency. Incubation period is several days to a week. The illness begins as fever, followed by hypotension, followed by metastatic soft tissues lesions. There is no gastrointestinal manifestation. There is a very high fatality rate. Water exposure can cause cellulitis due to this organism even in healthy individuals.

13. Gram positive bacillus (*Arcanobacterium haemolyticum*)

When you see scarlet fever with a negative throat culture for *Streptococcus pyogenes*, think of this organism. *Arcanobacterium haemolyticum* causes a scarlet fever-like picture in young persons but without poststreptococcal sequelae. Illness is typically mild so that efficacy of macrolide therapy, which should be effective, is difficult to document. Growth of this diphtheroid-like organism is a little slower than *Streptococcus pyogenes*, often not being recognized until 48 to 72 hours after inoculation-many labs will not keep throat cultures this long. The negative throat culture for *Streptococcus pyogenes* of this patient with pharyngitis is against the diagnosis of scarlet fever. The rash also is atypical for scarlet fever, with no "strawberry tongue" and "circumoral pallor." The rash does not look like gonococcemia or meningococcal sepsis so Gram negative coccus is not a good choice.

14. Olecranon bursitis

When moving a joint is not very painful and there is inflammation near the joint, think of septic bursitis. Olecranon bursitis is distinguished from septic arthritis by not restricting range of motion. Localization to the olecranon bursa area is unlikely for cellulitis or gout. *Staph aureus* (MSSA or MRSA) causes 80% of septic bursitis, followed by aerobic streptococci. Patients have elevated leukocyte numbers in bursal fluid, but numbers may be modest (2000-20,000 cells/mm³). Treatment usually requires non surgical drainage with a needle in addition to a relatively short course of antibiotics (1 week often suffices although cases can require surgery and longer courses of antibiotics)

15. Lung (TB)

A lesion spanning two vertebral bodies and accompanied by a prevertebral fluid collection is vertebral osteomyelitis until proven otherwise. Vertebral osteomyelitis in this patient is more likely tuberculosis, acquired in India and now reactivating (Pott's disease). With all forms of extrapulmonary TB, it is not unusual to have a normal chest xray. We didn't do a chest CT on this man so I can't say if there was a small lesion we missed. If this were *Staphylococcus aureus*, which accounts for half the cases of vertebral osteomyelitis, the culture and Gram stain in this untreated patient should have been positive. *Brucella* is hard to detect but he has been out of the endemic area for 7 years. We are not given a probable source for bacteremia to originate. Actinomycosis from a gastrointestinal source is difficult to detect but the infection is rare.

16. Herpes simplex virus

Notice that this lesion has spread across the midline from one buttock to another. Herpes simplex is notable for spreading across the skin by inoculation, like happens in wrestlers and patients with eczema, who have inoculation lesions. This is unlike herpes zoster, which remains in a dermatome unless it spreads hematogenously. Ecthyma gangrenosum from *Pseudomonas* or *Rhizopus* would not spread across the buttocks. *Candida* can spread like this but is not this necrotic. If this patient had been taking acyclovir prophylaxis, this lesion would not have happened.

17. Mosquito (chikungunya)

Fever and rash in a traveler in the tropics has a wide differential but lingering arthralgias are highly suggestive of Chikungunya. Some other alpha viruses can cause polyarthralgia, such as O'nyong-nyong and Ross River but they are much less common than chikungunya. Zika, dengue and scrub typhus are not notable for arthralgia and parovirus B has arthralgias that are much less persistent.

18. Poorly cooked beef (toxoplasmosis)

The multiple brain abscesses found in this homeless man with advanced HIV infection could be many things but the biopsy shows a cyst of *Toxoplasma gondii*, full of bradyzoites. The sources of infection include exposure to stool of infected cats and ingestion of partially cooked meat. Although lamb is more often contains the infectious cysts, beef is more often eaten partially cooked, called beef "tartar" or as hamburgers with a partially cooked center.

And that's the end. Thanks for listening.