



Photo Opportunity I: Photos and Questions to Test Your Board Preparation

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Disclosures of Financial Relationships with Relevant Commercial Interests

- None

 **INFECTIOUS DISEASE IMAGES**
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A Joint Project of the Massachusetts General Hospital Infectious Diseases Division and Microbiology Lab

- Cases are from an educational web-site:
www.idimages.org

I acknowledge the contributors to the site for their case submissions and images.

Question #1

A woman in her forties presented with 6 days of fatigue, fevers and chills. She also had severe headache and myalgias.

Epidemiologic History

- Patient was single and not sexually active.
- Hiked in New Hampshire. Denied known tick bites. Dog; no other animal exposures.

Physical Examination

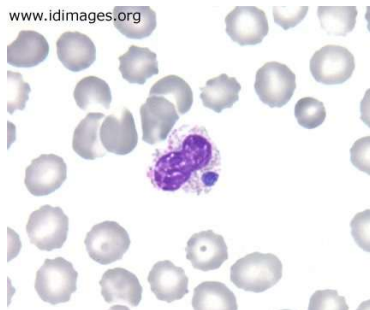
- Appeared well. T 103.5, BP 104/50, HR 122, RR 18
- No rash or adenopathy. Remainder of exam normal.

Question #1

Studies

- WBC 2.3 (51% P, 29% bands, 14% L, 4% atypical lymphocytes)
- Hct 39%
- Platelets 24.
- Chemistries, including liver enzymes, normal.
- Blood cultures negative.
- CXR: normal

Neutrophil with additional finding



Contributed by Anne Kasmar, M.D.

Question #1

What is the diagnosis?

- A. Meningococcemia
- B. Anaplasmosis
- C. Histoplasmosis
- D. Babesiosis
- E. "Spotless" Rocky Mountain Spotted Fever (RMSF)

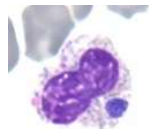
Neutrophil with additional finding



Contributed by Anne Kasmar, M.D.

Diagnosis and Follow-up

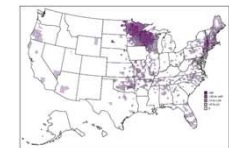
- Peripheral blood smear showed morulae inside neutrophils, consistent with anaplasmosis.



- Diagnosis confirmed with PCR testing.
- She was treated with doxycycline; symptoms completely resolved.

Anaplasmosis

- New England, north central states and West Coast.
- *Anaplasma phagocytophilum* transmitted by tick *Ixodes scapularis*.
- Sx: fevers, chills, myalgias, headache. Rash <10%.
- Labs: leukopenia, thrombocytopenia, elevated transaminases.
- Dx: visualization of intraleukocytic bacteria (morulae) on blood smear (20-80% of cases); serology (paired); serum PCR
- Treatment: doxycycline



Rule out coinfection with Lyme, Babesia (same vector)

Lyme



Babesia



Differential diagnosis

- **Meningococcemia:** no meningeal signs or rash to suggest acute meningococcemia; no arthritis/tenosynovitis/rash to suggest chronic meningococcemia
- **Histoplasmosis:** patient not immunosuppressed, which predisposes to disseminated histo; CXR not abnormal (infiltrates often present in histo)
- **Babesia:** ring-forms in red cells, not white cells
- **Rocky Mountain Spotted Fever:** would not explain morulae in neutrophils. RMSF (and human monocytotropic ehrlichiosis) more common in southeast, south central US

Question #2

Previously healthy man in his seventies presented with 2 weeks of fever, headaches, myalgias and 5 days of nonproductive cough, dyspnea, fevers

Epidemiologic history

- Lives in Southern California in mountain wilderness
- Leaves vehicle outside with windows down; cleans dashboard and upholstery
- No domestic pets; surrounded by rodents, deer, sheep, raccoons
- Prior to symptoms, he had visited local zoo; no direct animal contact
- No other travel history outside US; no known sick contacts

Contributed by Dr. Dave Patel

Question #2

Physical Examination

- Mild respiratory distress
- BP 141/80. HR 94. 98 °F, RR 20, O₂ 93% on 6 L oxygen (nasal canula)
- Respiratory exam: rhonchi at lung bases. Exam otherwise normal

Studies

- WBC 19.3; 10% atypical lymphocytes; no eosinophilia
- Hemoglobin 18.4 g/dL. Hematocrit 52.6%. Platelets 102,000
- Chlamydia pneumoniae, Mycoplasma, HIV-1/2, Coxiella serologies negative
- *Legionella pneumophila* urine antigen were negative
- Respiratory viral panel negative

Question #2



Chest X-ray demonstrating ground-glass opacities in upper and lower lobes consistent with pneumonia.



Chest CT: Hazy ground glass densities in lower lobes bilaterally with bilateral pleural effusions.

Question #2

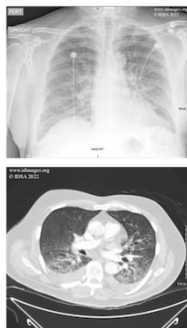
Clinical Course Prior to Diagnosis

- Patient admitted with diagnosis of community-acquired pneumonia.
- Started on azithromycin and ceftriaxone.
- He was initially requiring minimal supplemental oxygen, however, respiratory status worsened requiring high flow nasal canula at 20 L with fractional inspired oxygen of 80% saturation (FiO2%) during initial course of hospitalization.

Question #2

What is the diagnosis?

- A. Coccidioidomycosis
- B. Legionella pneumonia
- C. Hantavirus Cardiopulmonary Syndrome
- D. Leptospirosis Pulmonary Hemorrhage Syndrome
- E. Tularemia



Follow-up

- Hantavirus IgG and IgM serologies were positive.
- Patient improved and his symptoms resolved.

Hantavirus Cardiopulmonary Syndrome (HCPS): Clues

- Most cases in southwestern US; first recognized in Four Corners region
- Transmitted by rodent reservoir, often in rural settings
- Febrile illness, bilateral interstitial infiltrates, and respiratory compromise requiring oxygen within 72 hours of hospitalization
- Cardiopulmonary phase characterized by capillary leak, hemoconcentration (elevated hemoglobin/hematocrit), shock, pulmonary edema
- Diagnostic test: serologic assays

Question #3

- A man in his fifties presented with diarrhea, nausea, and vomiting of three days' duration
- Recently discharged from another hospital where he had received a one-week course of iv steroids for back pain
- **Past medical history:** spinal stenosis. Medication: prednisone
- **Social history:** Immigrated to US from Caribbean two decades ago; returned to visit one year ago
- **Physical Exam:** Temp 98.6. Mild epigastric tenderness. Remainder of exam normal

Question #3

Labs: WBC 12,000 (neutrophils 43%, bands 38%, lymphocytes 10%). Creatinine 1.8

Clinical course:

- Patient received iv fluids because of concern for acute gastroenteritis and dehydration
- On hospital day 3, developed lethargy and fever (temp 102.4)
- Shortly thereafter, developed respiratory failure. *Klebsiella* isolated from blood cultures (4/4 bottles) and cerebrospinal fluid

Question #3

Abdominal CT:
colonic wall inflammation



What is the diagnosis?

- A. Amebic infection
- B. Strongyloides hyperinfection syndrome
- C. Ascariasis
- D. Fascioliasis
- E. Colon cancer

Gram stain of sputum



Iodine stain of stool



Strongyloides Hyperinfection Syndrome

- May occur during immunosuppression, even short courses of steroids
- Accelerated autoinfection
- Larval migration in GI tract, lungs, skin and, at times, other organs
- Migration of filariform larva associated with entry of enteric bacteria (e.g., gram-negative sepsis, meningitis)
- Peripheral eosinophilia absent

Different Patient Larva currens: Cutaneous Strongyloidiasis

- Serpiginous urticarial rash caused by the dermal migration of filariform larvae
- Rash may move rapidly: 5-10 cm per hour



Question #4

- Man in his 20s presented with nine days of vomiting, diarrhea, fever, headaches.
- Lived on farm with goats, chickens, guinea pigs, turkeys, cats, dogs.
- Exam: Appeared acutely ill. T104.4°F. Exam otherwise normal.
- Studies: AST 111, ALT 79, Alkaline Phosphatase 146

Contributed by Paul M. Jost, M.D.

Question #4



Liver biopsy

What is the diagnosis?

- A. Coxiella
- B. Cryptococcus
- C. Histoplasma
- D. Cyclospora
- E. Bartonella

Contributed by Paul M. Jost, M.D.

Coxiella and “doughnut” granulomas

- *Coxiella burnetii* (agent of Q fever): exposure to infected ruminants (parturient goats, cattle, sheep).
- Transmission usually occurs by inhalation.
- Acute disease: fever, pneumonia and/or hepatitis.
- “Doughnut” granuloma (dense fibrin ring, central lipid vacuole) characteristic of Q fever
- May also be seen in Hodgkin's disease, EBV and Cytomegalovirus infections, drug hypersensitivity

Question #5

- 30-year-old woman with HIV (CD4 cell count 20, not on therapy) presented with gradual onset of word-finding difficulties, expressive aphasia and right upper extremity weakness over 4 weeks
- **Social history:** She lived in New England. No recent travel or known insect bites. Not sexually active.

Contributed by Wendy Yeh, M.D.

Question #5

- **Physical exam:** On exam, she was afebrile. She had oral thrush. She had difficulty naming objects and right-sided weakness.
- **Studies:** WBC count of 2.2 (44% P, 45% L)

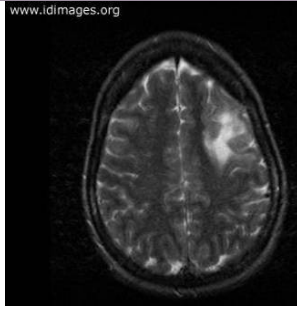


MRI: Abnormal T2 signal involving white matter, left fronto-parietal region. No enhancement, edema, mass effect

Question #5

What is the most likely diagnosis?

- A. An arbovirus
- B. A polyomavirus
- C. A herpes virus
- D. A spirochete
- E. A dematiaceous fungus

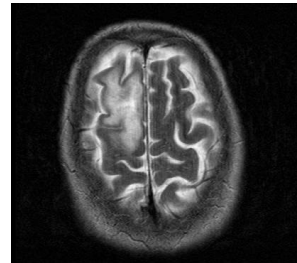
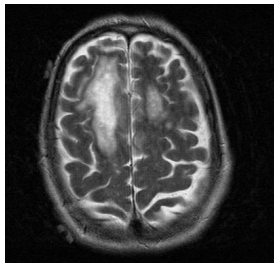


MRI: Abnormal T2 signal involving white matter, left fronto-parietal region. No enhancement, edema, mass effect

Progressive Multifocal Leukoencephalopathy

- CSF JC virus positive
- Demyelinating disease of central nervous system caused by reactivation of JC virus, a polyoma virus
- Immunocompromised hosts (heme malignancy; HIV, natalizumab, rituximab)
- Rapidly progressive focal neurologic deficits, usually due to cerebral white matter disease
- Rx: reversal of immunodeficiency. In people with HIV: antiretroviral therapy

PML



Contributed by Vince Marconi, M.D.

Differential Diagnosis

- **Arbovirus, such as West Nile Virus:** Unlikely because of no confusion, headache, meningeal signs, paralysis.
- **Herpes virus, such as HSV:** temporal lobe.
- **Spirochetal infection, such as syphilis:** central nervous system gumma or stroke-like syndrome (meningovascular disease).
- **Dematiaceous fungus:** no risk factors (e.g., adjacent paranasal sinus infection, penetrating trauma); lack of enhancement of brain lesion on imaging.

Question #6

- 63 yo M with history of renal transplant developed multiple erythematous, raised, pruritic lesions on his thighs over the course of several weeks.
- **Past medical history:** ESRD due to post-streptococcal glomerulonephritis, s/p cadaveric renal transplant ; HCV infection.
- **Meds:** prednisone 15 mg qd; azathioprine 150 mg qd
- **Social history:** Healthy cat at home. Lived in rural Maryland near farm animals and frequently saw deer in his yard. Avid gardener but recalled no recent puncture wounds. Several tick bites in past year.
- **Travel history:** Mexico 2 yrs ago.

Contributed by Raj Gandhi, M.D.

Question #6

Physical exam: T: 36.8. Multiple erythematous nodules on both lower extremities. Lesions were tender and non-fluctuant, some with a central necrotic area. There was no discharge. The remainder of exam normal.



Question #6

Studies

- WBC 3.3; Hematocrit 26%; Platelets 118,000
- BUN 59 mg/dL, Creatinine 2.1 mg/dL
- AST 70; Alkaline Phosphatase 321.
- CXR: normal
- Blood Cultures: no growth

Contributed by Raj Gandhi, M.D.

Question #6

What is the diagnosis?

- A. Cryoglobulinemic vasculitis related to HCV infection
- B. Nocardiosis
- C. Nontuberculous mycobacteria
- D. Cutaneous aspergillus
- E. Botryomycosis



Contributed by Raj Gandhi, M.D.

Diagnosis and Follow-up

- Patient underwent skin biopsy of a lesion on his lower extremity.
- Microscopic examination: abscess containing many polymorphonuclear leukocytes, scattered multinucleated giant cells.
- Special stains revealed acid-fast bacilli.
- Culture grew *Mycobacterium chelonae*.

M. chelonae

- Rapidly-growing mycobacteria
- Some strains grow best at 28-33°C
 - May account for its proclivity to cause cutaneous lesions on the extremities
- *M. chelonae* most commonly causes skin, bone and soft tissue infection
 - Disseminated cutaneous infection occurs in immunocompromised hosts, such as transplant patients and individuals on chronic steroids
 - Keratitis associated with contact lenses' wear and LASIK
 - Surgical site infection reported after cosmetic surgery, other invasive procedures

Question #7

- 50-year-old F was well until 7 days prior to admission when she noted "bite" on left thigh. Lesion enlarged over several days. Four days prior to admission, developed fatigue, arthralgias, myalgias, fever, headache. On admission (July), developed generalized rash on extremities, trunk, back.
- **SH:** Lived in New England. She had seen mouse in her basement. Denied sexual activity.
- **PE:** appeared well. T 100.5. No adenopathy. Lesion present on left thigh. Papular erythematous rash on extremities, back, chest.

Question #7

What does this patient most likely have?

- A. Varicella
- B. Mpox
- C. Cutaneous anthrax
- D. Rickettsialpox
- E. Lyme



Case contributed by Karen Thomas, M.D.
and Leena Gandhi, M.D., Ph.D

Rickettsialpox

- *Rickettsia akari*, member of spotted fever group of rickettsiae
- Transmitted to humans by mouse mite
- NYC outbreak in 1980s; high seroprevalence (16%) in people who inject drugs in Baltimore
- After bite of infected mite, *R. akari* proliferates resulting in papule, ulcerates to form eschar
- 3-7 days later, high fever, chills and headache.
- 2-3 days after onset of fever, generalized papulovesicular rash (not involving palms, soles)
- Diagnosis: serologic testing. Treatment: doxycycline

Rickettsialpox vs. Chickenpox

	Rickettsialpox	Chickenpox
Eschar	Yes	No
Lesions in crops	No	Yes
Number of lesions	Relatively sparse (20-40)	Many
Mature lesion	Papulovesicle	Vesicle

Rickettsialpox



Chickenpox



Question #8

- 55 yo M was admitted with nephrolithiasis and *E. coli* urosepsis.
 - Course was complicated by ARDS, requiring prolonged ventilatory support and a tracheostomy.
 - On hospital day 21, he developed a nosocomial MRSA pneumonia.
 - On hospital day 28, he developed new fever and rash.
- **Past medical history:** Hypertension. Atrial fibrillation
- Medications: vancomycin, nifedipine, digoxin, coumadin.

Contributor: John Beigel, M.D.

Question #8

- **Exam:** T 103.2. Erythematous areas in axillae, back, thigh. Bullae with yellow, serous, non-purulent fluid
- WBC 15.7 (84% P, 9% L, 3% M, 3% E). Bullous fluid cultures negative



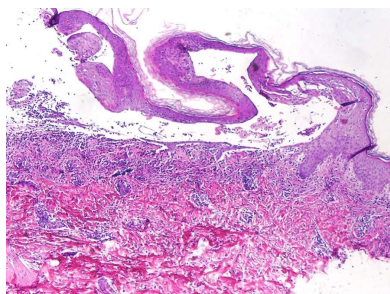
Question #8

What does this patient most likely have?

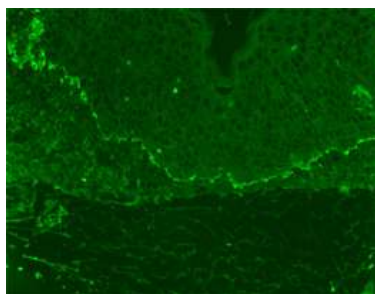
- A. Dermatitis herpetiformis
- B. Bullous pemphigoid
- C. Linear IgA bullous disease from vancomycin
- D. Herpes zoster
- E. Staphylococcal scalded skin syndrome



Contributor: John Beigel, M.D.



H & E: neutrophilic infiltrate at dermal-epidermal junction; sub-epidermal bulla



Immunofluorescence: IgA deposition, basement membrane, dermal-epidermal junction

Treatment/Follow Up

Vancomycin was discontinued, and the bullae gradually resolved after one week.

Linear IgA Bullous Disease

- Rare autoimmune subepidermal blistering disorder; usually idiopathic.
- Vesiculobullous eruption of the skin and MM
- Linear IgA deposition along the basement membrane zone
- Drug-induced LABD is most often due to iv vancomycin use.
- Generally resolves with discontinuation of vancomycin. May recur with rechallenge.

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Question #9

- 35-year-old man of Ethiopian descent cut his left thumb with a knife while slaughtering a lamb as part of Easter festivities. He washed the wound with water and applied lemon juice and alcohol. One week later, he developed swelling and tenderness and a fluctuant lesion at the site.
- Two weeks after the injury, he underwent incision and drainage; cultures grew *Staph. aureus* (oxacillin sensitive). Treated with cephalexin but did not improve.

Contributors: Drs. Isaac Bogoch, Rajesh Gandhi

Question #9

Physical exam

Afebrile; 2 x 2 x 2 cm firm lesion on his thumb, without discoloration, purulent discharge, fluctuance, or bleeding



Question #9

Labs:

- Creatinine and LFTs normal. Glucose 158. WBC 4.2 (normal differential)
- X-ray: fungating soft tissue lesion on dorsal aspect of distal thumb; no underlying bone or joint abnormality



Question #9

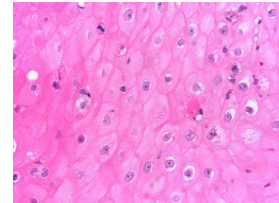
What is the diagnosis?

- A. Botryomycosis due to *S. aureus*
- B. Nocardia
- C. Brucella
- D. Orf
- E. Salmonella



Follow-up

- Lesion removed surgically
- Pathology: hyperkeratosis, epidermal necrosis, dermal infiltrate of mixed inflammatory cells; surface keratinocytes with eosinophilic inclusions
- PCR testing at CDC + for orf virus DNA



Appearance consistent with ecythma contagiosum

Orf (Contagious Ecthyma)

- Zoonotic infection caused by a dermatropic parapox virus (ds DNA) of goats and sheep
- Transmitted by contact with infected animal or fomites
 - Animal handlers; children after visiting petting zoos, livestock fairs
 - Clusters reported after Eid, other festivities involving lamb sacrifice (Passover, Easter)

Orf (Cont.)

- 3-7 d incubation period
- Macule or papule → nodule with red center, white halo and peripheral erythema → ulcerative lesion → regenerative papilloma
- Most resolve in 4-8 wk
- Human-to-human transmission has not been reported
- Protective immunity incomplete; persons can be infected multiple times

MMWR (April 13, 2012) highlighted 4 cases of orf associated with household meat processing or animal slaughter

- Bulla caused by orf virus infection after puncture by a bone of a recently slaughtered goat—PA, 2009
- Nodule caused by orf virus infection after contact with a lamb being sacrificed for a holiday — MA, 2010



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