

9 - Zoonoses

Speaker: David M. Aronoff, MD



Zoonoses

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7/24/2024



• Disclosures of Financial Relationships with Relevant Commercial Interests

- None

Zoonoses: Important!

- Most recent epidemics & pandemics have been caused by zoonotic pathogens
- Emerging coronaviruses, hemorrhagic fever viruses, arboviruses, influenza A viruses & bacteria have caused recent major zoonotic epidemics



Case

A 38-year-old healthy man in western Canada, presented with 5-days of fever, chills, night sweats, diffuse myalgias, & arthralgias. Months earlier, he had killed a black bear & froze meat. 2 days before symptom onset, he & 4 household members ingested bear meat that had been thawed & cooked as meatballs. Three other household members also fell ill in the same time frame, but with milder symptoms. The meatballs had not been thoroughly cooked. 2 days after ingestion, the patient noted vague abdominal discomfort & nausea. 8 days after ingestion, he reported intense fever & chills, mild headache, severe prostration, myalgia in proximal limb muscles, transient abdominal pain, & pink-tinged urine. He denied vomiting, diarrhea, chest pain, shortness of breath, adenopathy, or rash. The fever lasted for 9 days total primarily at night.



Case

P/E: VS & exam findings normal

Labs: mildly increased WBC count ($10.4 \times 10^9/L$), with hypereosinophilia ($3.3 \times 10^9/L$; normal <0.50). AST = 61U/L (normal 15 to 45), creatine kinase (762 U/L; normal 55 to 170), & CRP (64.6 mg/L; normal <10).

Bilirubin, creatinine, & INR normal.

HIV screening & blood cultures at 5 days of incubation negative.

Trichinella serology on a sample 1 week after ingestion of bear meat was **negative**.



Question #1

Which of the following is the most likely infectious diagnosis?

- Acute trichinellosis from ingestion of viable *Trichinella* larvae
- Coxiella burnetii* infection (Q fever) from ingesting raw bear meat
- Bacteremic *Streptobacillus moniliformis* from inadvertent cutaneous inoculation while preparing bear meat
- Acute *Necator americanus* infection



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Answer #1

- Which of the following is the most likely infectious diagnosis?
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 - Acute *Necator americanus* infection

Case Continued

Given the clinical suspicion for *Trichinella* infection, empirical treatment with mebendazole (400 mg po TID) was initiated on day 12 of illness, for a total of 13 days

The diagnosis of acute trichinellosis was subsequently confirmed with repeat serological testing performed 6 weeks after having consumed the bear meat

Remember *Trichinella* organisms not killed by freezing or drying/curing. Cooking thoroughly is important






Table 1. Zoonotic pathogens causing recent epidemics








Zoonotic pathogen	Reservoir host/Vector	Disease (key syndromes)	Major recent epidemics
SARS-CoV	Likely bats	SARS (pneumonia)	Global (2002–2003)
MERS-CoV	Dromedary camels	MERS (pneumonia)	Saudi Arabia, South Korea (2012–2019)
SARS-CoV-2	Unknown	COVID-19 (pneumonia)	Global (2020–present)
Ebola virus	Likely bats	Ebola virus disease (haemorrhagic fever)	West Africa (2013–2016) DRC (2018–2020)
Lassa virus	Multimammate rat	Lassa fever (haemorrhagic fever)	Nigeria (2018)
Rift valley fever virus	Aedes and Culex mosquitoes	Rift valley fever (haemorrhagic fever)	East Africa (2006–2007)
Zika virus	Aedes mosquitoes	Zika virus disease (arthralgia/myalgia, rash)	Brazil, Americas (2015–2016)
Chikungunya virus	Aedes mosquitoes	Chikungunya fever (arthralgia/myalgia, rash)	Indian Ocean Islands, India (2004–2007)
Dengue virus	Aedes mosquitoes	Dengue fever (arthralgia/myalgia, rash, haemorrhage)	Americas (2010)
West Nile virus	Birds/Culex mosquitoes	West Nile disease (meningitis/encephalitis, paralysis)	United States (2002)
Influenza A viruses	Waterfowl, Poultry, Pigs	Influenza (pneumonia)	Global (2009)
Yersinia pestis	Rats/fleas	Plague (sepsis, pneumonia)	Madagascar (2017)
Brucella spp.	Cattle, sheep, goats	Brucellosis (undulant fever, endocarditis)	China (2020)
Coxiella burnetii	Cattle, sheep, goats	Q fever (pneumonia, hepatitis)	Netherlands (2007)

THERE ARE MANY

TABLE 1. Bacterial zoonoses by transmission mechanism and causative agent(s)

Transmission Mechanism	Causative Agent(s)
Bacterial zoonoses transmitted by direct contact with animals or infected animal materials	<i>Bacillus anthracis</i> <i>Brucella</i> spp. <i>Cat scratch disease</i> <i>Erysipelothrix rhusiopathiae</i> <i>Clavdia and meloidosis</i> <i>Leptospirosis</i> <i>Mycobacteriosis</i> <i>Q fever</i>
Bacterial zoonoses transmitted principally by animal bites or scratches	<i>Pasteurella multocida</i> and other spp. <i>Capnocytophaga canimorsus</i> <i>Brucella hemolytic</i> <i>Spirillum minus</i> and <i>Streptococcus moniliformis</i>
Vector-borne bacterial zoonoses	<i>Borrelia burgdorferi sensu lato</i> (incl. <i>Borrelia garinii</i> , <i>Borrelia afzelii</i>) <i>Borrelia recurrentis</i> , <i>Borrelia turicatae</i> , <i>Borrelia hispanica</i> , others <i>Yersinia pestis</i> <i>Francisella tularensis</i> Spotted fever and typhus group <i>Rickettsia</i> species <i>Ehrlichia chaffeensis</i> , <i>Anaplasma phagocytophilum</i> <i>Orientia tsutsugamushi</i>
Foodborne bacterial zoonoses and intoxications	<i>Salmonella enteritidis</i> <i>Campylobacter</i> spp. <i>Listeria monocytogenes</i> <i>Escherichia coli</i> STEC <i>Yersinia enterocolitica</i> <i>Clostridium perfringens</i> gastroenteritis <i>Bordetella pertussis</i> <i>Staphylococcus aureus</i>

- | | | |
|--|--|---|
|  <p>CATS</p> <ul style="list-style-type: none"> <i>Bartonella henselae</i> <i>Pasteurella multocida</i> <i>Yersinia pestis</i> <i>Francisella tularensis</i> |  <p>BIRDS</p> <ul style="list-style-type: none"> <i>Chlamydia psittaci</i> <i>Chlamydia</i> |  <p>FARM ANIMALS
(sheep, cows, horses, goats, chicken, etc)</p> <ul style="list-style-type: none"> <i>Bacillus anthracis</i> <i>Brucella</i> <i>Coxiella burnetii</i> <i>Campylobacter</i> <i>E. coli</i> (Shiga toxin*) <i>Erysipelothrix rhusiopathiae</i> Hepatitis E <i>Leptospira</i> <i>Parapoxviruses</i> (orf, etc) <i>Rhodococcus</i> <i>Salmonella</i> <i>Trichinella</i> |
|  <p>FISH</p> <ul style="list-style-type: none"> <i>Erysipelothrix rhusiopathiae</i> <i>Mycobacterium marinum</i> <i>Streptococcus iniae</i> <i>Vibrio</i> |  <p>DOGS</p> <ul style="list-style-type: none"> <i>Pasteurella multocida</i> <i>Capnocytophaga canimorsus</i> <i>Campylobacter</i> <i>Leptospira</i> <i>Staph. intermedius/pseudintermedius</i> | |

- | | | |
|--|---|--|
|  <p>LEECHES</p> <ul style="list-style-type: none"> <i>Aeromonas hydrophila</i> |  <p>RABBITS</p> <ul style="list-style-type: none"> <i>Francisella tularensis</i> |  <p>REPTILES</p> <ul style="list-style-type: none"> <i>Salmonella</i> |
|  <p>BEARS</p> <ul style="list-style-type: none"> <i>Trichinella spiralis</i> |  <p>RODENTS</p> <ul style="list-style-type: none"> <i>Leptospira</i> <i>Monkeypox</i> <i>Salmonella</i> <i>Spirillum minus</i> <i>Streptococcus moniliformis</i> <i>Yersinia pestis</i> |  <p>CAMELS</p> <ul style="list-style-type: none"> <i>MERS-CoV</i> |
|  <p>BATS</p> <ul style="list-style-type: none"> <i>Rabies</i> <i>Nipah virus</i> | | |

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Zoonoses: Various Routes of Infection

- **Direct contact with animal or animal tissue**
 - Cat scratch disease, anthrax, tularemia, brucellosis
- **Contact with insect vector**
 - Tularemia, plague
- **Intact skin contact with animal urine**
 - Leptospirosis
- **Ingestion of animal product**
 - Brucellosis, hepatitis E
- **Inhalation of animal product**
 - Q Fever



Case



PREVIEW QUESTION

25 yr male presented in July with painful right inguinal mass of one week's duration. He is otherwise well. Married. Monogamous. No hx penile or skin lesion. Fishing last week in Northern Virginia creek, hiked through wooded area. Picked ticks off legs & neck. Has kitten & dog. Exam: T37°C, 5 cm tender red mass in right midinguinal area, fixed to skin. Genitalia normal. Aspiration of soft center: 5 cc yellow pus. Gm stain neg. cephalexin 250 mg qid. One week later: mass unchanged. Culture neg. Syphilis FTA & HIV neg.

Question #2



PREVIEW QUESTION

Most likely dx:

- A. Bartonella henselae*
- B. Treponema pallidum*
- C. Haemophilus ducreyi*
- D. Francisella tularensis*
- E. Klebsiella (Calymmatobacterium) granulomatis*

Answer #2



PREVIEW QUESTION

Most likely dx:

- A. Bartonella henselae* *
- B. Treponema pallidum*
- C. Haemophilus ducreyi*
- D. Francisella tularensis*
- E. Klebsiella (Calymmatobacterium) granulomatis*

Purulent Inguinal Node

- *Bartonella henselae*: young cats
 - **Stellate abscess** on bx. **Warthin Starry** stain positive early
 - Dx: serology, PCR, or DFA on pus
- Tick borne tularemia ("glandular"): this case *could be* tularemia
 - Exposure to wild animals or their ticks
 - Gram stain, routine culture negative
 - Patient should be **systemically ill** (fevers, chills, malaise common)
 - **Uncommon**: 100-200 cases per year in the USA
- Chancroid: painful genital ulcer with adenopathy (can be purulent)
- No suppurative lymph nodes in syphilis or granuloma inguinale (*Klebsiella granulomatis*) (painless ulcers)




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Purulent Inguinal Node (continued)

- *Staphylococcus aureus*. Gram stain of pus & culture positive. Distal lesion may be present.
- Lymphogranuloma venereum (LGV)-
 - Sexually transmitted (no history in this case)
 - *Chlamydia trachomatis* L1-L3: genital lesion usually inapparent
 - Painful inguinal &/or femoral lymphadenopathy. "Groove sign"
 - Can form "Stellate abscesses" on bx
 - (+) Nucleic acid amplification test on urine, rectal swab, or wound



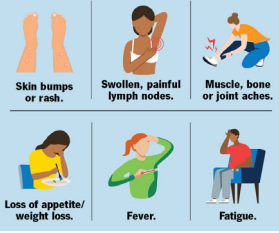
Groove sign

Cat Scratch Disease



- *B. henselae* causes most cases
- >13,000 cases in the USA per year³
- 80% <21 yrs old
- Clinical findings:
 - Acute suppurative lymphadenitis proximal to bite, scratch, lick of young cat
 - Fever, headache, poor appetite, & exhaustion
 - Cats have chronic bacteremia but seem healthy
- Cat fleas may transmit between cats & occasionally to humans

Symptoms of Cat Scratch Fever




Skin bumps or rash. Swollen, painful lymph nodes. Muscle, bone or joint aches. Loss of appetite/weight loss. Fever. Fatigue.

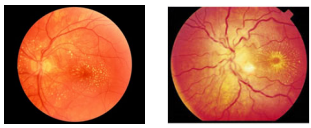
DIAGNOSIS

- Compatible clinical syndrome
- Fastidious, slow-growing
 - Hold 21 days
- Serology (but cross reactive with other *Bartonella* spp.)
- Molecular (PCR) on tissue/nodes

Cat Scratch Disease



- Papule or pustule often at inoculation site if sought
- Often self-limited
- Encephalitis, **stellate retinitis**, uveitis rare



Avk id #... - la trif#
sEfi- vt t #
~ aj· jafitafi

Cat Scratch Disease

Rx: 10% drain spontaneously
If not, node aspiration improves pain & helps exclude *Staph. aureus*

Treatment = AZITHROMYCIN x 5 d

(TMP/SMX, clarithromycin, ciprofloxacin or rifampin as alternatives)

Treat to prevent serious complications, since up to 14% of patients will have dissemination, with potential infection of the liver, spleen, eye, or CNS

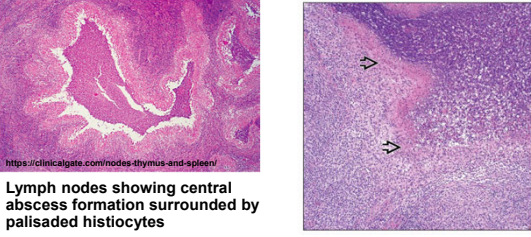
Warthin Starry Silver Stain



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Cat Scratch Lymphadenopathy
Stellate abscesses, necrotizing granulomas
 Necrotic area with neutrophils surrounded by **palisading histiocytes**



<https://clinicalgate.com/nodes-thymus-and-spleen/>
<https://basicmedicalkey.com/cat-scratch-disease/>

Lymph nodes showing central abscess formation surrounded by palisaded histiocytes

ANTHRAX

Cutaneous anthrax treated with doxycycline



At diagnosis 6 days later 4 weeks after diagnosis

ANTHRAX

- Skin (95%): pruritic papule on skin exposed to goat hair, animal hides. Small **vesicles around an ulcer**. +/- pain. **Edema**. Mild systemic symptoms.
- DX: *Aerobic*, encapsulated, sporulating **Gram positive** bacillus seen on smear, culture of vesicle fluid (alert the lab!)
- RX: Penicillin but "weaponized" strains resistant to multiple antibiotics
- Inhalation (5%), ingestion (<1%)
- Anthrax rare in USA

Edema
Vesicles
Necrotic ulcer



<http://www.pcds.org.uk/clinical-guidance/anthrax>
<https://www.ncbi.nlm.nih.gov/pubmed/10105696>

TULAREMIA

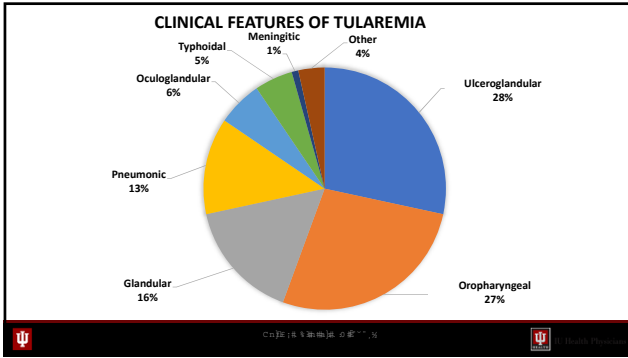


TULAREMIA

- Highly infectious gram-negative **coccobacillus** *Francisella tularensis*
- Vectors = **Ticks** (*Dermacentor variabilis* > *Amblyomma americanum*) & **Deerflies**
- Direct inoculation = rabbits, squirrels, muskrats, beavers, cats (bites)
- Hunters **skinning animals** (old days); farmers, veterinarians
- Red tender local lymph node inoculation site may form ulcer
- **Ulceroglandular** is the most common manifestation
- Risk of bioweaponization

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AN OUTBREAK OF PRIMARY PNEUMONIC TULAREMIA ON MARTHA'S VINEYARD

KATHERINE A. FELDMAN, D.V.M., M.P.H., RUSSELL E. ENSCORE, M.S., SARAH L. LATHROP, D.V.M., Ph.D., BELA T. MATYAS, M.D., M.P.H., MICHAEL MCGUILL, D.V.M., M.P.H., MARTIN E. SCHRIEFER, Ph.D., DONNA STILES-ENOS, R.N., DAVID T. DENNIS, M.D., M.P.H., LYLE R. PETERSEN, M.D., M.P.H., AND EDWARD B. HAYES, M.D.

ABSTRACT
Background In the summer of 2000, an outbreak of primary pneumonic tularemia occurred on Martha's Vineyard, Massachusetts. The only previously reported outbreak of pneumonic tularemia in the United States occurred on the island of Martha's Vineyard (1 to 21), infection with *F. tularensis* can result in various clinical presentations, depending on the route of inoculation, the dose of the inoculum, and the virulence of the organism. Primary pneumonic tularemia results from the inhalation of viable organisms.

TULAREMIA

- Incubation period: 3-5 days but up to 3 weeks
- DX: Serology; PCR
- Culture of *F. tularensis* is lab hazard. Notify the lab!
- Neg routine culture, needs chocolate agar or BCYE (like *Legionella*)
- RX: **gentamicin** (or streptomycin), **FQs**, **doxycycline**
- Prophylaxis (bioterrorism) doxycycline

Maugh & Gyuranecz. Lancet (2016)
Nelson CA, et al. CID (2024)

BCYE – buffered charcoal yeast extract



Glandular Tularemia

68-year-old with 1 wk fever then 2 mo progressive, painful swelling on R. side of neck

Exposure to a sick cat

Diagnosis made by + IgM (1:1280)

Improved with 4 wk doxycycline

jennifer cummings
@jenniferTVTweet

Two nights ago I gave a wild baby rabbit CPR w breaths after I took it from my Petey (cat). Today, I'm being admitted to the hospital with signs of "bunny fever" (Tularemia). I'm on 8L oxygen, a cocktail of very expensive antibiotics, anti-diuretics. Need light & love, please!

August, 2023

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SUPPLEMENT
Volume 78, Issue
Supplement_1, 15
February 2024
Tularemia: Update on
Treatment and Clinical
Findings

Volume 78, Issue Supplement_1
 15 February 2024





PLAGUE



www.plagueinfectiousdisease.com


PLAGUE

- *Yersinia pestis*
- Exists in the USA
 - Rodent flea bite
 - Prairie dogs, cats (outdoor/indoor)
- Fever, nausea & swollen, painful lymph nodes
- Sepsis, pneumonia-hematogenous or aerosol in crowded conditions

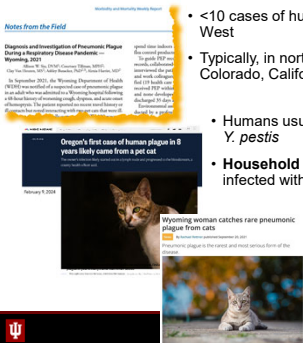



PLAGUE

- Gram negative coccobacillus
- **Bipolar-staining** bacilli
- **Safety pin** appearance
 - *Yersinia pestis*: lab hazard
- Treatment: **Streptomycin** >> doxy, cipro

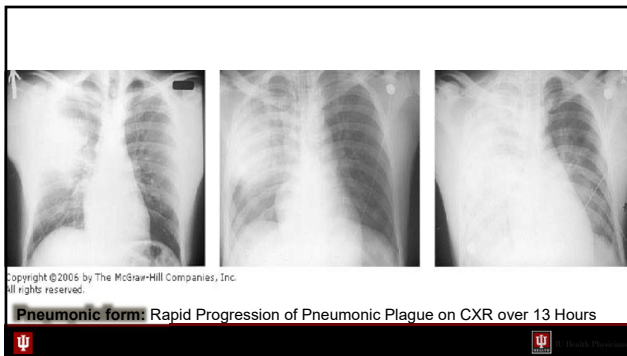
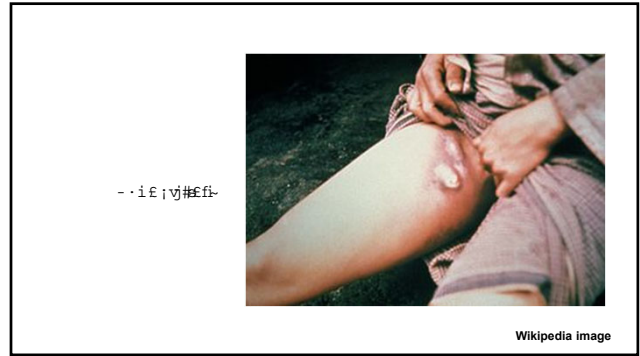
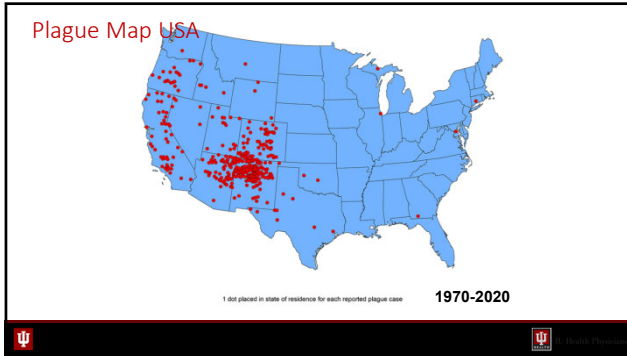


- <10 cases of human plague per year in USA, mostly rural West
- Typically, in northern New Mexico, northern Arizona, southern Colorado, California, southern Oregon & western Nevada
- Humans usually exposed from the **bites of fleas** carrying *Y. pestis*
- **Household pets can get infected** if they hunt rodents infected with plague or are bitten by an infected flea
- Pets can transfer the infection to humans via tissue or bodily fluids (e.g., respiratory droplets from cough or sneezes) or can carry home fleas that in turn bite humans



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Question #3

- 28 yr old male presents with temp 39°C, diffuse myalgia, headache, malaise. Returned 2 days ago from “Iron Man” race with running, biking, swimming in lake, climbing in Hawaii. Numerous mosquito bites. Exam: Conjunctival suffusion but no other localizing findings.
- WBC 14,500 with 80%PMN, no eos or bands. Platelets 210k.
- Bili 2.4, ALT 45, AST 52, Alk Phos 120, Cr 1.6. Hct 45%. BC neg. UA: normal

Most likely diagnosis:

- A. Malaria
- B. Dengue
- C. Ehrlichiosis
- D. Leptospirosis
- E. Zika

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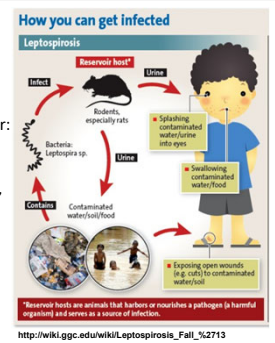
Answer #3

Most likely diagnosis:

- A. Malaria
- B. Dengue
- C. Ehrlichiosis
- D. Leptospirosis *
- E. Zika

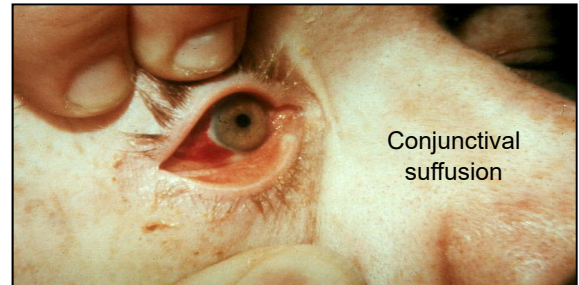
LEPTOSPIROSIS

- Spirochetes excreted in urine of infected host & able to survive in wet environment
- Exposed intact skin to animal urine in water: veterinarians, farmers, loggers, triathletes, white water rafting, trapping
- Urine from cows, pigs, dogs, raccoons, rats, mice.
 - Summer & early Fall



LEPTOSPIROSIS

- Fever, myalgia, headache (aseptic meningitis late in course)
- **Conjunctival suffusion**, +/- rash
- In severe cases: jaundice (Weil syndrome), azotemia, pulm. hemorrhage
 - Jaundice: *bilirubin is high out of proportion to transaminase elevation*
- Lab: serology by agglutination test, culture urine in Fletcher's medium
 - PCR & sequencing emerging
- Rx: **doxycycline** for outpatients, IV penicillin for inpatients
 - Jarisch-Herxheimer in first 2 hr



Question #4

A 41 year old car salesperson from Baltimore was admitted for a febrile illness & found to have *Brucella melitensis* in their blood culture. They had attended a dinner a month prior where some family members from Greece had brought food from home.

About two weeks prior to onset of fever, they had bought some lamb & beef at a farmer's market outside Baltimore.

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Question #4

The most likely source of the brucellosis was which of the following:

- A. Home made sausage from Greece
- B. Home made goat cheese from Greece
- C. Cole slaw from a Baltimore delicatessen
- D. Beef tartar, meat from the farmer's market
- E. Lamb kabobs, meat from the farmer's market

Answer #4

The most likely source of the brucellosis was which of the following:

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BRUCELLOSIS

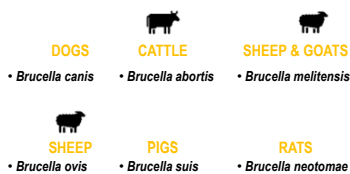
- Brucellosis is primarily transmitted through **direct contact** with infected animals or their bodily fluids, including vaginal discharges, aborted materials & semen
- Brucellosis can also be transmitted through the **ingestion** of raw or unpasteurized dairy products from infected animals, including milk & cheese (unpasteurized)
- Those who work closely with livestock, such as farmers, veterinarians & livestock handlers, are at a heightened risk

Qureshi KA, et al. *Ann Med* (2023)

BRUCELLOSIS

- An illness characterized by acute or insidious onset of fever & one or more of the following: fever, night sweats, arthralgia, headache, fatigue, anorexia, myalgia, weight loss, arthritis/spondylitis, meningitis, or focal organ involvement (endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly).
- Nodes, liver, spleen may be enlarged
- Rare in the US, with 80–120 cases reported annually; most of these are associated with *Brucella* exposures abroad

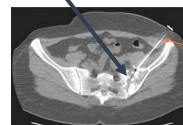
Animal Sources of *Brucella*



Qureshi KA, et al. *Ann Med* (2023)

BRUCELLOSIS

Later onset lesions in bone, liver
Epididymo-orchitis¹, endocarditis
sacroiliitis, tenosynovitis, meningitis



Biopsy
needle

Malodorous
perspiration

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BRUCELLOSIS (con't)

- WBC normal or low, anemia, plt can be low
- DX: Bone marrow/blood/tissue culture, serology, PCR
 - **LET THE LAB KNOW YOU ARE WORRIED ABOUT BRUCELLA**
(lab safety issue!)
- RX: Doxy plus rifampin or strep/gent
 - TMP-SMX in pregnant or young children

Qureshi KA, et al. *Ann Med* (2023)

Question #5

This common cause of acute hepatitis is acquired via fecal-oral transmission or from undercooked meats, especially pig/wild boar. It is particularly severe in pregnant patients, causing stillbirths & maternal mortality.

- A. Epstein Barr virus
- B. Cytomegalovirus
- C. Hepatitis E virus
- D. Hepatitis A virus

Answer #5

This common cause of acute hepatitis is acquired via fecal-oral transmission or from undercooked meats, especially pig/wild boar. It is particularly severe in pregnant patients, causing stillbirths & maternal mortality.

- A. Epstein Barr virus
- B. Cytomegalovirus
- C. **Hepatitis E virus ***
- D. Hepatitis A virus

Inhalation of animal products

Case

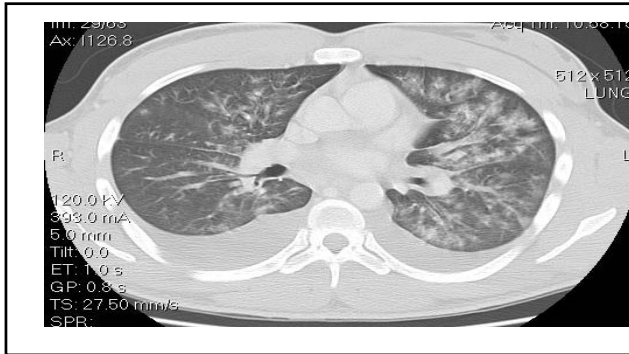
- A 22 year old previously healthy male contractor returned from Afghanistan one week prior to presentation. He had a three day history of fever, myalgia, arthralgia, mild headache & cough. He had vomited once & had mild midepigastic, nonradiating pain.
- The facility he was hired to guard was adjacent to the path that the local sheep & goat herders used on their way to market & he had purchased a wool rug from one of the locals. He remembers shaking it hard to get rid of the dust.
- He reported that some members of his guard unit also had flu-like illness from which they recovered without treatment.

Case

- Examination was normal except for a variable temperature up to 102°F
- WBC **3.3K**, platelets **121K**, creatinine 1.2, AST **144**, ALT **154**, alk phos 88, total bilirubin 0.6
- Admission chest Xray was normal
- Ceftriaxone was begun but the patient remained febrile & had the chest CT shown on the next slide

9 - Zoonoses

Speaker: David M. Aronoff, MD



Question #6

Which of the following is the most likely diagnosis?

- A. Brucellosis
- B. Anthrax
- C. Leptospirosis
- D. Q fever
- E. Visceral leishmaniasis

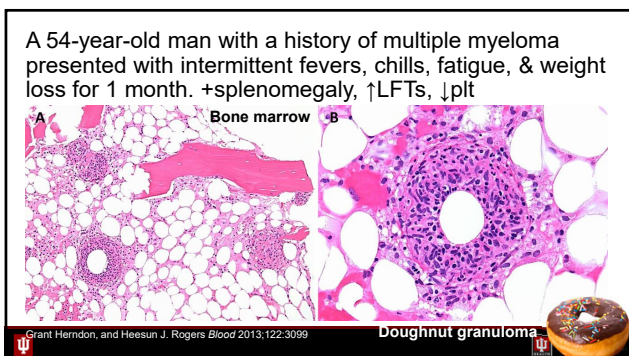
Answer #6

Which of the following is the most likely diagnosis?

- A. Brucellosis
- B. Anthrax
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- D. Q fever *
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Q FEVER

- *Coxiella burnetii*: tiny coccobacillus
 - Infects cows, sheep, goats, cats, etc.
- Spores survive in straw, manure, meat, *parturient tissue* for months.
 - Aerosol, ingest raw milk
- Acute pneumonia (in half cases), fever, headache, hepatosplenomegaly
- **Chronic endocarditis** on native or prosthetic valves
- **Granulomatous hepatitis**
 - Doughnut granulomas
- DX: serology, valve PCR; specific tissue stain; hard to culture
- RX: acute: Doxycycline or levofloxacin or azithromycin
- Chronic: doxycycline plus hydroxychloroquine



The End

Thank you!
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