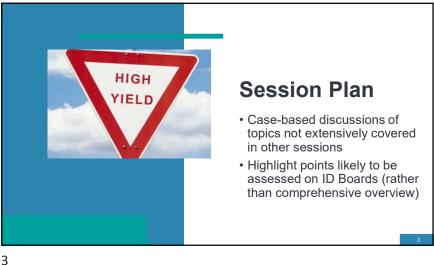
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Disclosures of Financial Relationships with **Relevant Commercial Interests** None

2 1



### **Question #1**

4

- A 51-year-old male with past medical history significant for insulin dependent diabetes presents with a sixmonth history of progressive arthralgias, abdominal pain, diarrhea, weight loss, and low-grade fevers.
- Work up thus far:
  - Negative blood cultures x 2
  - > Negative Rheumatoid factor
  - > Normal metabolic panels
  - > Mild normocytic anemia

Speaker: Stacey Rose, MD

### **Question #1**

Which of the following tests will most likely yield the diagnosis?

- A. Anti-streptolysin O Antibody
- B. Anti-nuclear Antibody
- C. Stool ova and parasite
- D. Duodenal biopsy

)

Caused by Trophyrema whipplei (gram variable bacterium, difficult to cultivate)

 More common in middle aged, Caucasian men

 Diagnosis often delayed due to indolent clinical presentation

 Most commonly diagnosed via duodenal biopsy, stained with PAS

 PCR increasingly used

Periodic acid-Schiff-diastase (PAS-D)-stained duodenal biopsy specimens with PAS-D-positive granules in the foamy macrophages (arrows).

# Whipple's: Clinical Presentations TABLE 1 Clinical manifestations of Tropheryma whipplei infectiona Classic Whipple's disease (% incidence) Chronic localized infectionsb Acute infectionsb Weight loss (79–99) Endocarditis Gastroenteritis (63–85) Abdominal pain (23–60) Arthritis (20–83) Reurological symptoms (6–63) Dolimans RAV, Bod CHE, Lacle MM. Kustere JG. 2017. Clinical manifestations, breatment, and diagnosis of Tropheryma whippple infections. Clin Microbiol Rev 30:529–555

Whipple's Endocarditis - Increasingly Diagnosed Consider in patients Increase in reported with arthralgias plus cases of T. whipplei "culture negative" endocarditis with endocarditis molecular diagnostics T. whipplei PCR from blood added to Duke's criteria (2023) for diagnosis of endocarditis Total published cases Cases from this article

Speaker: Stacey Rose, MD

#### Whipple's: Treatment

No gold standard

#### Options:

 Ceftriaxone or meropenem plus prolonged trimethoprim-sulfamethoxazole (~1 year)

OR

· Doxycycline plus hydroxychloroquine (12-18 mos)

Clinical manifestations, treatment, and diagnosis of Tropheryma whipplei infections. Clin Microbiol Rev 2017 Whipple's disease and Tropheryma whipplet infections: from bench to bedside. Lancet Infect Dis. 2022 Principles and Practice of Infectious Diseases, 9° ed



Symptoms improve, but relapse is common without prolonged treatment / suppression

10

#### **Question #2**

- A 20-year-old female schoolteacher presents with a 1-week history of fever and pain / swelling in knees, elbows and wrists. She notes that the pain moves from joint to joint.
- She reports being ill ~3 weeks prior with sore throat and headache which resolved without specific treatment.
- · She has no rash or lymphadenopathy.
- · She denies travel. She is sexually active with one male partner, using barrier protection (condoms).
- · Labs are notable for elevated ESR and CRP and + ASO and Anti-DNase B titers; pregnancy and HIV tests (4th generation Ag/Ab) are negative.

### **Question #2**

Which of the following is the best explanation for her symptoms?

- A. Acute HIV infection
- B. Mononucleosis due to Epstein Barr Virus
- C. Acute rheumatic fever
- D. Lemierre's syndrome

11 12

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· Cause: Trophyrema Whipplei

· Epidemiology: middle aged, Caucasian males

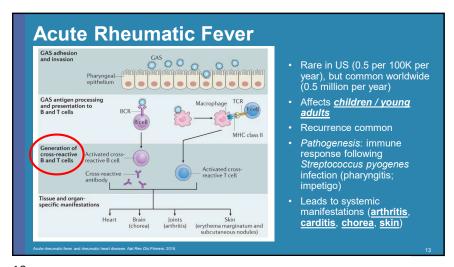
• Clinical presentation: classic - arthralgia, diarrhea, weight loss

- · Localized infection e.g., endocarditis (increasingly recognized)
- Diagnosis with duodenal biopsy (PAS stain; foamy macrophages)
  - or PCR of infected tissue or blood
- Prolonged treatment needed to prevent relapse

# Whipple's Disease

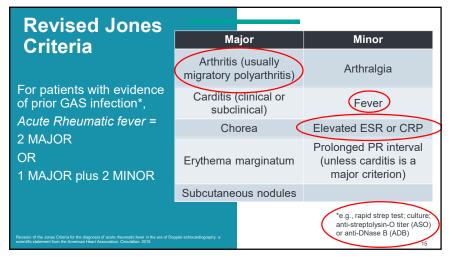
**Take Home Points** 

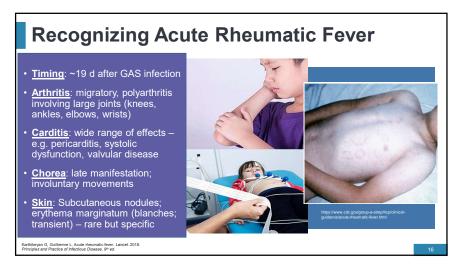
Speaker: Stacey Rose, MD



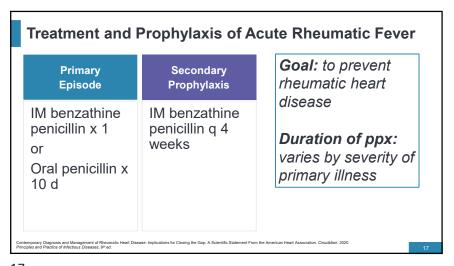
**Revised Jones** Major Minor Criteria Arthritis (usually Arthralgia migratory polyarthritis) For patients with evidence Carditis (clinical or of prior GAS infection\*, Fever subclinical) Acute Rheumatic fever = Chorea Elevated ESR or CRP 2 MAJOR Prolonged PR interval OR Erythema marginatum (unless carditis is a major criterion) 1 MAJOR plus 2 MINOR Subcutaneous nodules \*e.g., rapid strep test; culture; anti-streptolysin-O titer (ASO) or anti-DNase B (ADB)

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Speaker: Stacey Rose, MD



CATEGORY

Rheumatic fever with carditis and residual heart disease (persistent valvular disease")

Rheumatic fever with carditis but no residual heart disease (no valvular disease)

Rheumatic fever with carditis but no residual heart disease (no valvular disease)

Rheumatic fever without carditis

Syr or until age 21 yr, whichever is longer

Duration of Secondary Prophylaxis Following

Duration of Secondary Prophylaxis Following
Acute Rheumatic Fever:

<u>Longest if Carditis and Residual Valvular Disease</u>

ntemporary Diagnosis and Management of Rheumatic Heart Disease: Implications for Closing the Gap: A Scientific Statement From the American Heart Association. Circulation. 2020

17



- · Cause: immune dysregulation following S. pyogenes infection
- · Epidemiology: children / young adults; rare in US
- Clinical presentation: ~3 weeks following GAS infection
  - <u>Major</u>: migratory polyarthritis, carditis, chorea, subcutaneous nodules, erythema marginatum
  - Minor: fever, arthralgia, elevated ESR/CRP; PR prolongation
- Diagnosis based on <u>Jones criteria</u> = 2 major OR 1 major + 2 minor (plus e/o prior GAS infection e.g. ASO titer)
- Treatment and secondary ppx with <u>IM Penicillin</u>; duration based on carditis (10 yr or to age 40 if carditis + residual valvular disease)

#### **Acute Rheumatic Fever**

**Take Home Points** 

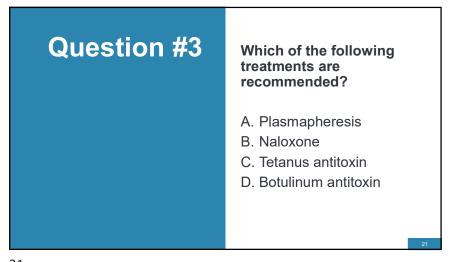
**Question #3** 

18

- A 34-year-old male with a history of injection drug use presents to the emergency room with two days of blurry vision and difficulty swallowing. He is also beginning to feel weak in his arm muscles.
- On examination, vital signs are normal, but the patient is noted to have ptosis and sluggish pupillary responses as well as slurred speech.

19 20

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Caused by \*Clostridium botulinum (gram positive, strict anaerobe with subterminal spore; found in soil)

Toxins prevent release of acetylcholine in neuromuscular junction

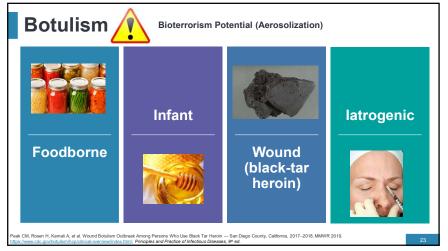
Leads to flaccid paralysis of motor and autonomic nerves, beginning with the cranial nerves (descending weakness)

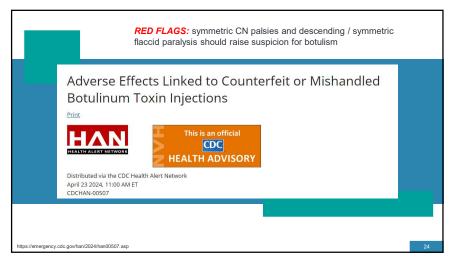
DX: culture or detection of toxin

\*other neurotoxin producing species of Clostridium: C. butyricum, or C. baratii

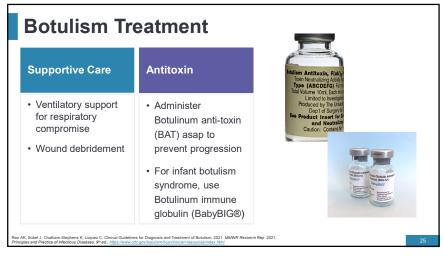
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21 22





Speaker: Stacey Rose, MD



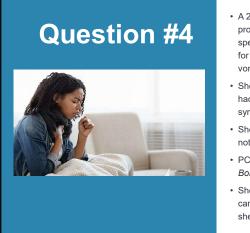
Cause: <u>Clostridium botulinum toxin</u> impedes acetylcholine release from neuromuscular junction

- Epidemiology: <u>food-borne</u> (home-canned veggies, fruits, fish); <u>infant</u> (honey); <u>wound</u> (black-tar heroin); <u>iatrogenic</u> (rare)
- Clinical features: <u>symmetric, descending flaccid paralysis</u>, starting with <u>cranial nerves</u> (ptosis, blurry vision, slurred speech)
- · Diagnosis: clinical; confirmed by culture or detection of toxin
- Treatment: antitoxin & supportive care; wound debridement

#### **Botulism**

**Take Home Points** 

25 26



- A 23-year-old female presents with a nonproductive cough for 2 weeks. She describes spells during which she coughs repeatedly for several minutes. On two occasions she vomited after coughing.
- She reports episodes of sweating but has had no fever or other constitutional symptoms
- She has tried several cough medicines, but nothing seems to help.
- PCR respiratory panel was positive for Bordatella pertussis.
- She works as a nurse in a pediatric intensive care unit and would like guidance for when she can return to work.

Question #4

https://www.youtube.com/watch?v=31tnXPlhA7w (NEJMvideo)

28

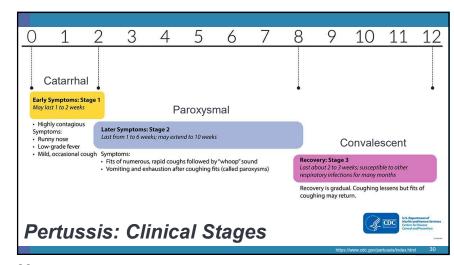
# Which of the following would you recommend for this patient?

- A. Azithromycin, with return to work after 5 days
- B. Azithromycin, with return to work after first dose
- C. No treatment, with return to work after 5 days
- D. No treatment; can return to work immediately

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29 30

**Pertussis** Clinical case criteria (in absence of alternate dx): • Cough illness lasting ≥2 weeks, with at least one Diagnosis of the following: Requires > Paroxysms of coughing; OR Clinical > Inspiratory whoop; OR > Post-tussive vomiting; OR Suspicion > Apnea (with or without cyanosis) Polymerase chain reaction (PCR) is most sensitive and specific · Nasopharyngeal swab / aspirate · Best if sent within first 3 weeks of illness measurement and purmane-seminane accuse the committee of the committee of



Speaker: Stacey Rose, MD





Symptomatic infection: exclude from work for 21 days from onset of cough OR until 5 days after the start of effective antimicrobial therapy



**Exposure**: regardless of vaccination status, administer post-exposure prophylaxis OR exclude from work for 21 days (if HCW interacts with persons at increased risk of complications)

33

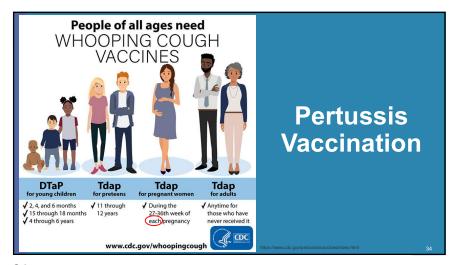


35

- Epidemiology: infants > adolescents
- · High risk for severe disease: infants, pregnant women, lung disease
- Clinical presentation: cough lasting 2+ weeks plus paroxysmal cough, inspiratory whoop, post-tussive vomiting or apnea
- · Diagnosis: clinical; PCR
- Treat with macrolide within 3 wks of onset (6 wks if high risk)
- Post-exposure prophylaxis: (within 3 wks of exposure) for household contacts / high risk / HCW likely to interact with high-risk patients
- · Symptomatic HCW can return to work after 5 d of effective treatment or 21 d after cough onset

# Bordetella pertussis

**Take Home Points** 



34

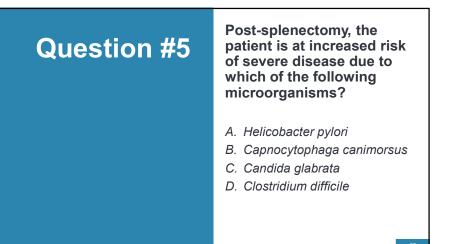
36





• A 34-year-old motorcyclist is involved in a severe motor vehicle accident. resulting in laceration of the spleen and requiring splenectomy.

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Why: reduced clearance of encapsulated organisms; impaired humoral immunity

On the boards, look for...

Streptococcus pneumonia

Hemophilus influenza type B

Neisseria meningitidis

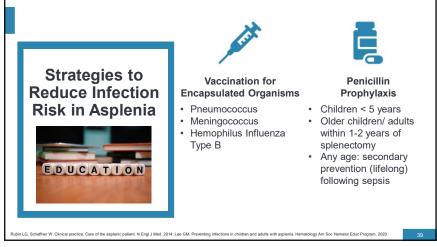
Capnocytophaga canimorsus (dog bite)

Babesia microti (tick borne)

Bordetella holmesii

Salmonella typhi

37



Increased risk for infection with encapsulated organisms (and others)...
 S. pneumoniae; N. meningitidis; HIB; Capnocytophaga; Babesia; Salmonella typhi
 Reduce risk of infection via:
 Immunizations
 PCN ppx if < 5 yrs old; recent splenectomy; h/o sepsis

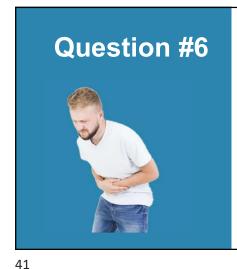
Infection in Asplenia

Take Home Points

40

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- A 19-year-old male with no past medical history presents with acute onset of pain that started in the periumbilical region and moved to the lower region.
- Physical exam is notable for point tenderness in the right lower quadrant.
- · Appendicitis is diagnosed based on clinical findings and imaging results, with no evidence of periappendiceal abscess.
- · The patient wants to avoid surgery if at all possible.

42

### **Question #6**

You note that antibiotic therapy for uncomplicated appendicitis has become accepted practice by some physicians and offer to counsel him regarding risks and benefits.

Which of the following is a recognized disadvantage of this approach, when compared to immediate surgery?

- A. Risk of *C. difficile* within 30
- B. Risk of bowel obstruction in 1
- C. 20% risk of intra-abdominal abscess within 30 days
- D. 30-50% risk of subsequent appendectomy within 4 years



In several studies, non-operative management (antibiotics alone) was "non-inferior" to operative management for acute, uncomplicated appendicitis

#### Features that should prompt **OPERATIVE** management:

- Appendicolith (+/-)
- Perforation
- Abscess
- · Suspicion of tumor
- · Peritonitis
- · Serious systemic illness

**Risks and Benefits** 30-50% of patients initially managed with antibiotics required appendectomy within 5 years Long term follow up suggests overall equivalent patient satisfaction For the ID Boards:

43 44

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know when to recommend surgery

Speaker: Stacey Rose, MD



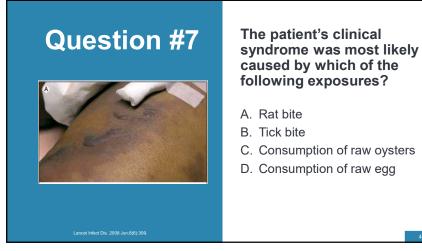
- Non-operative management of acute appendicitis may be considered if <u>uncomplicated</u>
  - <u>Features which should prompt immediate surgery:</u> perforation; abscess; suspected tumor; peritonitis; systemic illness
- · Up to 50% will require subsequent appendectomy
- ID board potential recognize when an operation is NEEDED

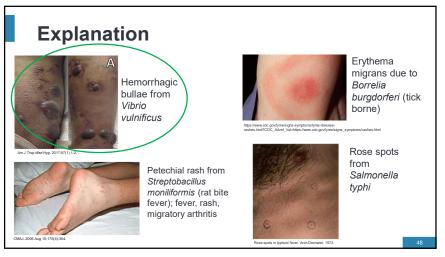
# **Appendicitis**

**Take Home Points** 

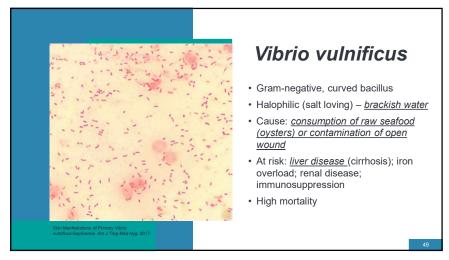
• A 44-year-old male with a history of cirrhosis due to Hepatitis B and alcoholism presents with fever, lethargy and leg swelling. On exam, he is febrile, hypotensive and tachycardic. Skin exam is as pictured.

45 46





Speaker: Stacey Rose, MD



Clinical · Abrupt onset · Fever, hypotension **Presentation** • Rapidly progressive skin lesions: and erythema → hemorrhagic bullae **Treatment**  Bacteremia common · Treatment: > 3rd generation cephalosporin plus doxycycline OR fluoroquinolone > Debridement (for necrotizing fasciitis)

50 49



51

- Epidemiology: consumption of raw oysters; contamination of wound (organism lives in warm, brackish water)
- At risk: liver disease, iron overload states (also chronic kidney disease; diabetes or other immune suppression)
- · Clinical presentation: rapidly progressive skin lesions with hemorrhagic bullae; fever, hypotension, sepsis
- · Diagnosis: clinical; blood cultures usually positive
- Treatment: 3<sup>rd</sup> generation cephalosporin plus doxycycline or fluoroquinolone; debridement

#### Vibrio Vulnificus

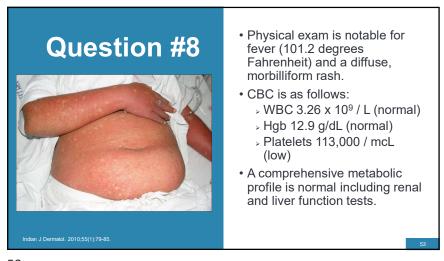
**Take Home Points** 

#### **Question #8**

52

- A 38-year-old female travels to Bangladesh for a friend's (outdoor) wedding.
- She has never traveled to this region. In preparation for the trip, she received Typhoid vaccine and was started on malaria prophylaxis with doxycycline.
- Five days after returning home, she develops fever, headache and diffuse muscle and joint pain.
- Over the next few days, a <u>rash</u> develops beginning on the dorsum of her hands and feet with spread to her arms, legs and torso.
- · She presents to urgent care for evaluation.

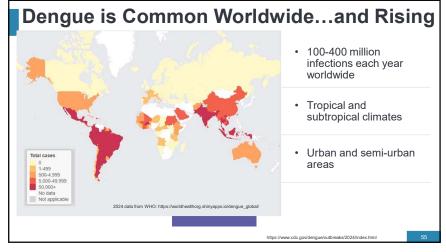
Speaker: Stacey Rose, MD

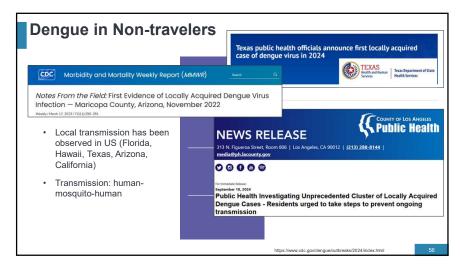


Which of the following tests is most likely to yield the diagnosis?

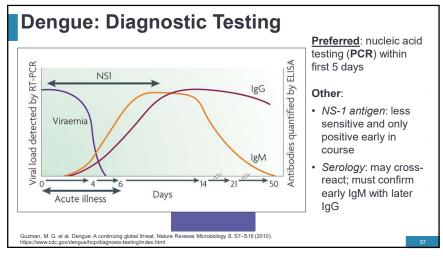
A. Dengue real-time PCR
B. Blood culture
C. Lyme enzyme immunoassay (EIA)
D. Malaria rapid diagnostic test (RDT)

53 54





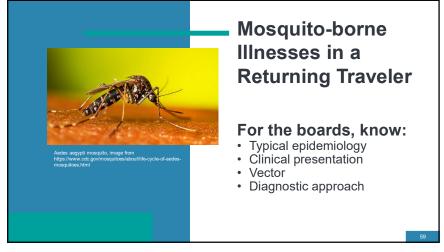
Speaker: Stacey Rose, MD



Symptoms typically improve in 1-2 weeks
May progress to severe Dengue (as rash and fever disappear)
Risk increased if prior infection (with another serovar)
Signs of severe dengue:

Hypotension / shock
Hemorrhage (mucosal / GI bleeding)

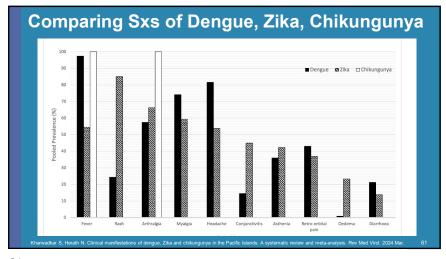
57 58



	Epidemiology	Vector	Clinical Features
Chikungunya	Africa, the Americas, Asia, Europe, islands in Indian and Pacific Oceans; prominent outbreak Caribbean 2013	Aedes aegypti (A. albopticus in Europe)	Fever and <b>joint pain</b> ; rash less common. Symptoms may last months.
Dengue	Worldwide in tropics / subtropics 4 serotypes; infection with a 2 <sup>nd</sup> serotype → severe illness	Aedes aegypti (or A. albopticus)	Fever, headache, rash, muscle and joint pain Severe: shock / hemorrhage
Zika	Prominent in Americas ~2017, then more widespread (Caribbean, Africa, India)	Aedes aegypti Also sexual transmission; maternal-fetal infection	Often asx; fever; rash (starts on face); conjunctivitis Fetal anomalies (microcephaly, blindness)

59 60

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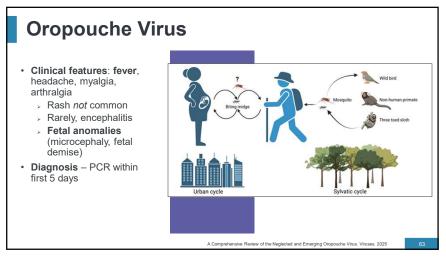
(Not So) New and Notable:
Oroupouche Virus

Orthobunyavirus genus

Transmitted by
Culicoides paraensis
(midge) and possibly
mosquitos

Typically, in South and
Central America → more
recently Cuba,
Dominican Republic, US
(returned travelers)

61



Malaria

• Epidemiology: worldwide, tropics and subtropics
• Vector: Anopheles mosquito
• Symptoms: Fever, headache, N/V, diarrhea; severe: anemia, jaundice, splenomegaly, neurologic
• Species-specific features

https://www.cdc.gov/malaria/diagnosis\_treatment/diagnosic\_tools.html

Speaker: Stacey Rose, MD



#### Malaria

- Epidemiology: worldwide, tropics and subtropics
- · Vector: Anopheles mosquito
- Symptoms: Fever, headache, N/V, diarrhea; severe: anemia, jaundice, splenomegaly, neurologic
- Species-specific features
- Microscopy (blood smear); RDT if microscopy not available

Important Updates on Locally Acquired Malaria Cases Identified in Florida, Texas, and Maryland This is an official **HEALTH UPDATE** Distributed via the CDC Health Alert Network August 28, 2023, 2:15 PM ET CDCHAN-00496 The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Update to share new information with clinicians, public health authorities, and the public about locally acquired malaria cases identified in the United States. On August 18, 2023, a single case of locally acquired malaria was reported in Maryland 🔀 in the National Capital Region. This case was caused by the Plasmodium falciparum (P. falciparum) species and is unrelated to the cases involving local transmission of Plasmodium vivax (P. vivax) malaria in Florida and Texas described in the HAN Health Advisory 494 issued on June 26, 2023. As an update to that report, to date, Florida has identified seven cases and Texas has identified one case of locally acquired P. vivax malaria, but there have been no reports of ocal transmission of malaria in Florida or Texas since mid-July 2023

65 66



Vector borne illnesses have overlapping features; look for keywords

- · Dengue, Zika, Chikungunya all spread via Aedes mosquitos
  - Dengue: headache, rash, "bone-break" pain, low platelets; infxn w/ 2nd serotype → severe dengue
  - · Zika: may be asx; rash / conjunctivitis common; birth defects
  - Chikungunya: prominent joint pain; may become chronic
- Diagnosis:
  - PCR if < 7 d
- · Serology if > 7 d but beware cross-reactivity
- Oropouche: midge; S. America; fever, birth defects; Diagnosis: PCR
- Malaria: Anopheles mosquito; fever, anemia, species-specific presentations (P. falciparum - severe; P. vivax / ovale - relapsing)
  - · Diagnosis: blood smear or rapid detection test (RDT)

## **Vector-borne Illnesses in a Returning Traveler**

Take Home Points



Speaker: Stacey Rose, MD



Kitchen Sink Summary - 2

#### Botulism:

- Due to *C. botulinum* toxin
- Food; infant; wound (black-tar heroin); iatrogenic
- Descending flaccid paralysis (starts with cranial nerves)
- Antitoxin / supportive care



#### Pertussis:

- Clinical diagnosis:
   2+ weeks of cough
  plus paroxysms,
  inspiratory whoop,
  post-tussive
  emesis, apnea
- Macrolide if within 3 weeks of onset or as PEP for contacts at risk of severe disease

70

69 70

#### Kitchen Sink Summary - 3 **Appendicitis** Increased risk of infection with Non operative encapsulated organisms management may be If prompt says asplenia, think. reasonable for uncomplicated cases Identify features that H. Influenzae type B should prompt surgery: Capnocytophaga Salmonella typhi Prevent infection with Abscess » Suspicion of tumor immunizations and

Kitchen Sink Summary - 4

#### Vibrio vulnificus:

- Liver disease at risk
- Exposure to raw seafood or contaminated wound (brackish water)
- Rapidly progressive, hemorrhagic bullae / sepsis
- Fluoroquinolone, ceftriaxone, debridement



Vector-borne illnesses in returning traveler

Chikungunya, Dengue, Zika all spread via <u>Aedes</u> mosquitos and can present with <u>fever</u> plus...

- Chikungunya joint pain
- <u>Dengue</u> headache, rash, muscle and joint pain; higher risk of severe / hemorrhagic Dengue with 2<sup>nd</sup> infection
- <u>Zika</u> rash, conjunctivitis; fetal anomalies; sexual transmission
- PCR if < 7 d; serology cross-reacts

Oropouche: midge; S. America; fever, birth defects; DX: PCR

Malaria: Anopheles mosquito; fever, anemia; species-specific presentations; DX: smear or RDT

72

71 72

PCN prophylaxis (if < 5 yrs old;

recent splenectomy; prior

episode of sepsis)

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Peritonitis

Systemic illness

Speaker: Stacey Rose, MD

