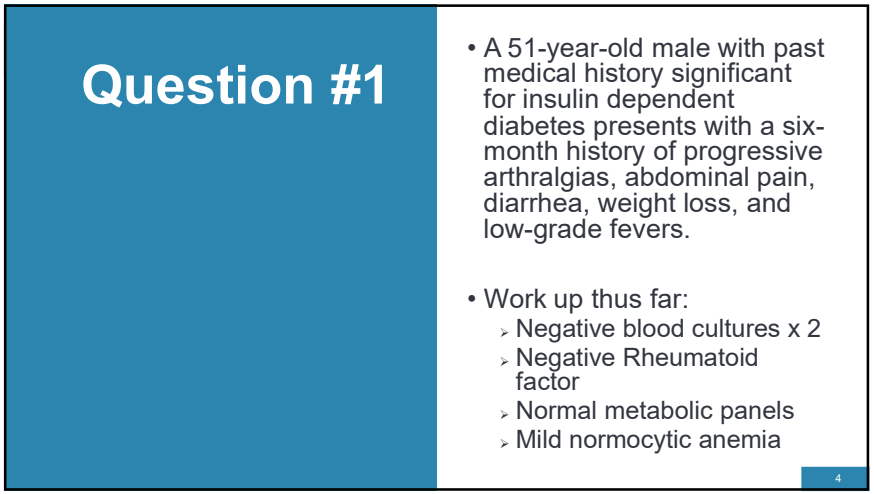
54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

1

2

3



4

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

5

5

Question #1

Diagnosis:
Whipple's disease

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

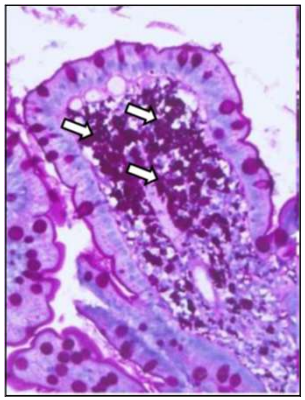
A. Anti-streptolysin O Antibody
B. Anti-nuclear Antibody
C. Stool ova and parasite
D. Duodenal biopsy

6

6

Whipple's Disease

- 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).

Dolmans RAV, Boel CHE, Lacle MM, Kusters JG. 2017. Clinical manifestations, treatment, and diagnosis of Tropheryma whipplei infections. Clin Microbiol Rev 30:529 –555.

7

7

Whipple's: Clinical Presentations

TABLE 1 Clinical manifestations of *Tropheryma whipplei* infection[a]

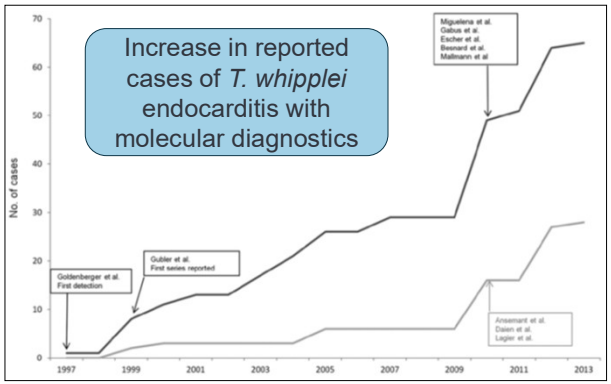
Classic Whipple's disease (% incidence)	Chronic localized infections[b]	Acute infections[b]
Weight loss (79–99)	Endocarditis	Gastroenteritis
Gastroenteritis (63–85)	Encephalitis	Pneumonia
Abdominal pain (23–60)		Bacteremia
Arthritis (20–83)		
Neurological symptoms (6–63)		

Dolmans RAV, Boel CHE, Lacle MM, Kusters JG. 2017. Clinical manifestations, treatment, and diagnosis of Tropheryma whipplei infections. Clin Microbiol Rev 30:529 –555.

8

8

Whipple's Endocarditis – Increasingly Diagnosed



- Consider in patients with arthralgias plus "culture negative" endocarditis
- *T. whipplei* PCR from blood added to Duke's criteria (2023) for diagnosis of endocarditis

Fenollar F, Célard M, Lagier JC, Lepidi H, Fournier PE, Raoult D. Tropheryma whipplei endocarditis. *Emerg Infect Dis*. 2013
Fowler VG, et al. The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria. *Clin Infect Dis*. 2023

9

9

Whipple's: Treatment

No gold standard

Options:

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

OR

- Doxycycline plus hydroxychloroquine (12-18 mos)

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

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

10

10

- 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

11

11

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.

12

12

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

Question #2

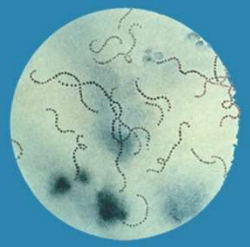
Which of the following is the best explanation for her symptoms?

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

13

13

Question #2



Streptococcus pyogenes (group A *Streptococcus*) on Gram stain.
Source: Public Health Image Library, CDC

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

14

14

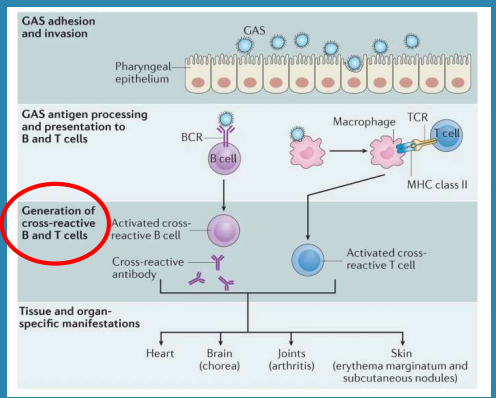
Explanation

- **Acute HIV** – joint symptoms not characteristic; HIV 4th gen testing should detect early infection
- **Mononucleosis due to EBV** – joint pains not characteristic; no mention of lymphadenopathy
- **Acute Rheumatic fever** – multisystem disease following group A strep; meets Jones criteria
- **Lemierre's** – septic thrombophlebitis of internal jugular vein following pharyngitis, typically caused by *Fusobacterium necrophorum*; joint pains not characteristic, no neck swelling

15

15

Acute Rheumatic Fever



Acute rheumatic fever and rheumatic heart disease. *Nat Rev Dis Primers.* 2016

- Rare in US (0.5 per 100K per year), but common worldwide (0.5 million per year)
- Affects ***children / young adults***
- Recurrence common
- *Pathogenesis*: immune response following *Streptococcus pyogenes* infection (pharyngitis; impetigo)
- Leads to systemic manifestations (**arthritis**, **carditis**, **chorea**, **skin**)

16

16

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

Revised Jones Criteria

For patients with evidence of prior GAS infection*,

Acute Rheumatic fever =

2 MAJOR

OR

1 MAJOR plus 2 MINOR

Major	Minor
Arthritis (usually migratory polyarthritis)	Arthralgia
Carditis (clinical or subclinical)	Fever
Chorea	Elevated ESR or CRP
Erythema marginatum	Prolonged PR interval (unless carditis is a major criterion)
Subcutaneous nodules	

*e.g., rapid strep test; culture; anti-streptolysin-O titer (ASO) or anti-DNase B (ADB)

Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015

17

17

Revised Jones Criteria

For patients with evidence of prior GAS infection*,

Acute Rheumatic fever =

2 MAJOR

OR

1 MAJOR plus 2 MINOR

Major	Minor
Arthritis (usually migratory polyarthritis)	Arthralgia
Carditis (clinical or subclinical)	Fever
Chorea	Elevated ESR or CRP
Erythema marginatum	Prolonged PR interval (unless carditis is a major criterion)
Subcutaneous nodules	

*e.g., rapid strep test; culture; anti-streptolysin-O titer (ASO) or anti-DNase B (ADB)

Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015

18

18

Recognizing Acute Rheumatic Fever

- **Timing**: ~19 d after GAS infection
- **Arthritis**: migratory, polyarthritis involving large joints (knees, ankles, elbows, wrists)
- **Carditis**: wide range of effects – e.g. pericarditis, systolic dysfunction, valvular disease
- **Chorea**: late manifestation; involuntary movements
- **Skin**: Subcutaneous nodules; erythema marginatum (blanches; transient) – rare but specific

https://www.cdc.gov/group-a-strep/hcp/clinical-guidance/acute-rheumatic-fever.html

Karthikeyan G, Guilherme L. Acute rheumatic fever. *Lancet*. 2018.
Principles and Practice of Infectious Disease, 9th ed.

19

19

Treatment and Prophylaxis of Acute Rheumatic Fever

Primary Episode	Secondary Prophylaxis
IM benzathine penicillin x 1 or Oral penicillin x 10 d	IM benzathine penicillin q 4 weeks

Goal: *to prevent rheumatic heart disease*

Duration of ppx: *varies by severity of primary illness*

Contemporary Diagnosis and Management of Rheumatic Heart Disease: Implications for Closing the Gap: A Scientific Statement From the American Heart Association. *Circulation*. 2020
Principles and Practice of Infectious Diseases, 9th ed.

20

20

CATEGORY	DURATION AFTER LAST ATTACK
Rheumatic fever with carditis and residual heart disease (persistent valvular disease[a])	10 yr or until age 40 yr, whichever is longer; sometimes lifelong prophylaxis (see text)
Rheumatic fever with carditis but no residual heart disease (no valvular disease[a])	10 yr or until age 21 yr, whichever is longer
Rheumatic fever without carditis	5 yr or until age 21 yr, whichever is longer

Duration of Secondary Prophylaxis Following Acute Rheumatic Fever:
Longest if Carditis and Residual Valvular Disease

Contemporary Diagnosis and Management of Rheumatic Heart Disease: Implications for Closing the Gap: A Scientific Statement From the American Heart Association. *Circulation*. 2020
Principles and Practice of Infectious Diseases, 9th ed.

21

21

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

Acute Rheumatic Fever

Take Home Points

22

22

Question #3

- 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.

23

23

Question #3

Which of the following treatments are recommended?

A. Plasmapheresis
B. Naloxone
C. Tetanus antitoxin
D. Botulinum antitoxin

24

24

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

Question #3

Which of the following treatments are recommended?

A. Plasmapheresis
B. Naloxone
C. Tetanus antitoxin
D. Botulinum antitoxin

25

25

Explanation

Tetanus: sardonic smile

Botulism: ptosis

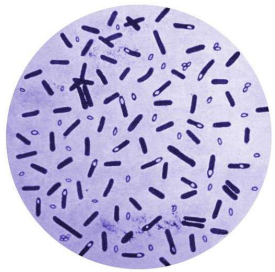
- Plasmapheresis – for Lambert-Eaton syndrome, immune attack of neuromuscular junction (chronic; associated with lung cancer)
- Naloxone – for opioid intoxication (respiratory suppression, *constricted* pupils)
- Tetanus antitoxin – for tetanus (rigid paralysis)
- Botulinum antitoxin – for botulism (flaccid paralysis)

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31137-7/fulltex
https://www.nejm.org/doi/pdf/10.1056%2FNEJMicm1003352

26

26

Botulism



https://phil.cdc.gov/details.aspx?pid=2107

- 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*

27

27

Botulism

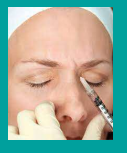
Bioterrorism Potential (Aerosolization)

Foodborne

Infant

Wound (black-tar heroin)

Iatrogenic



Peak CM, Rosen H, Kamali A, et al. Wound Botulism Outbreak Among Persons Who Use Black Tar Heroin — San Diego County, California, 2017–2018. MMWR 2019.
https://www.cdc.gov/botulism/hcp/clinical-overview/index.html; *Principles and Practice of Infectious Diseases, 9th ed.*

28

28

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

RED FLAGS: symmetric CN palsies and descending / symmetric flaccid paralysis should raise suspicion for botulism

Adverse Effects Linked to Counterfeit or Mishandled Botulinum Toxin Injections

Print

HAN HEALTH ALERT NETWORK

This is an official CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
April 23 2024, 11:00 AM ET
CDCHAN-00507

https://emergency.cdc.gov/han/2024/han00507.asp

29

29

Botulism Treatment

Supportive Care	Antitoxin
• Ventilatory support for respiratory compromise • Wound debridement	• Administer Botulinum anti-toxin (BAT) asap to prevent progression • For infant botulism syndrome, use Botulinum immune globulin (BabyBIG®)

Rao AK, Sobel J, Chatham-Stephens K, Luquez C. Clinical Guidelines for Diagnosis and Treatment of Botulism, 2021. *MMWR Recomm Rep.* 2021.
Principles and Practice of Infectious Diseases, 9th ed.; https://www.cdc.gov/botulism/hcp/clinician-resources/index.html

30

30

- Cause: *Clostridium botulinum* toxin impedes acetylcholine release from neuromuscular junction
- Epidemiology: food-borne (home-canned veggies, fruits, fish); infant (honey); wound (black-tar heroin); iatrogenic (rare)
- Clinical features: *symmetric, descending flaccid paralysis*, starting with *cranial nerves* (ptosis, blurry vision, slurred speech)
- Diagnosis: clinical; confirmed by culture or detection of toxin
- Treatment: *antitoxin* & supportive care; wound debridement

Botulism

Take Home Points

31

31

Question #4

- A 23-year-old female presents with a non-productive 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.

32

32

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

Question #4

https://www.youtube.com/watch?v=31tnXPIhA7w (NEJMvideo)

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

33

33

Question #4

https://www.youtube.com/watch?v=31tnXPIhA7w (NEJMvideo)

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

34

34

Whooping cough cases surge as vaccine rates fall

The U.S. has tallied 8,077 cases of whooping cough in 2025, compared with 3,847 cases in the same period last year, federal data shows.

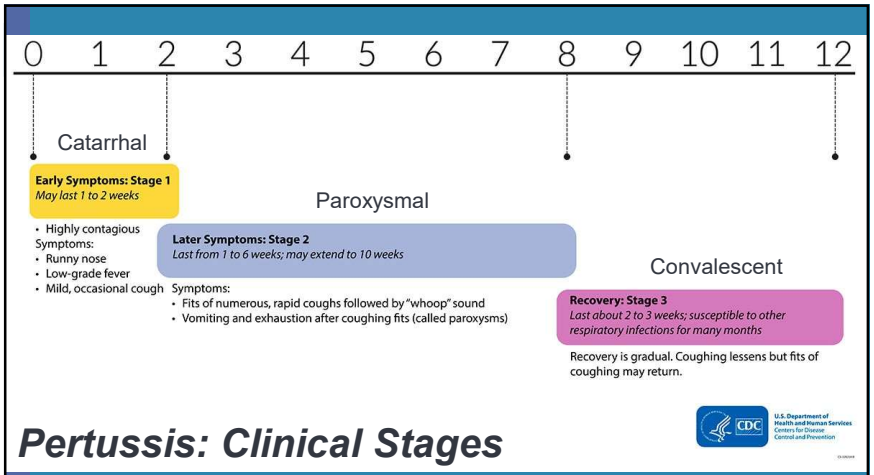
April 22, 2025

5 min

An infant receives a vaccination in Fayetteville, Georgia, in 2021. (Angie Wang/AP)

https://www.washingtonpost.com/health/2025/04/22/whooping-cough-pertussis-cases-rise/ 35

35



Pertussis: Clinical Stages

https://www.cdc.gov/pertussis/index.html 36

36

Pertussis Diagnosis – Requires Clinical Suspicion

Clinical case criteria (in absence of alternate dx):
- Cough illness lasting ≥2 weeks, with at least one of the following:
  - Paroxysms of coughing; **OR**
  - Inspiratory whoop; **OR**
  - Post-tussive vomiting; **OR**
  - 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

https://ndc.services.cdc.gov/case-definitions/pertussis-2020/; https://www.cdc.gov/pertussis/php/pcr-bestpractices/?CDC_AAref_Val=https://www.cdc.gov/pertussis/clinical/diagnostic-testing/diagnosis-pcr-bestpractices.html
Clinical evaluation and validation of laboratory methods for the diagnosis of Bordetella pertussis infection: Culture, polymerase chain reaction (PCR) and anti-pertussis toxin IgG serology (IgG-PT). *PLoS One*. 2018;
Evaluation of BioFire Respiratory Panel 2 plus for Detection of Bordetella pertussis in Nasopharyngeal Swab Specimens from Children with Clinically Suspected Pertussis. *Microbiol Spectr*. 2023

37

37

Treatment and Post Exposure Prophylaxis

- TREAT with macrolide (e.g. azithromycin) if within 3 weeks of onset
- Treat within 6 weeks of onset for infants or pregnant women

- POST EXPOSURE PROPHYLAXIS (PEP) given to household members and contacts at risk of severe infection (within 3 weeks of exposure)

https://www.cdc.gov/pertussis/index.html
Decker MD, Edwards KM. Pertussis (Whooping Cough). *J Infect Dis*. 2021.

38

38

Pertussis: Recommendations for Health Care Workers (HCW)

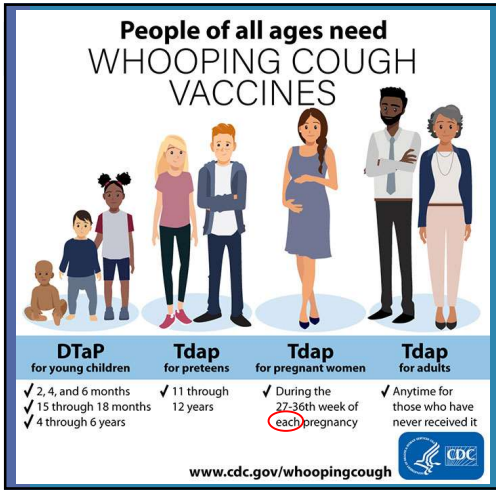
Symptomatic infection: exclude from work for 21 days from onset of cough OR until 5 days after the start of effective antimicrobial therapy

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)

Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC Guidelines. *MMWR Recomm Rep*. 2005.
https://www.cdc.gov/infection-control/hcp/healthcare-personnel-epidemiology-control/pertussis.html

39

39



Pertussis Vaccination

https://www.cdc.gov/pertussis/vaccines/index.html

40

40

- 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

41

41

Question #5

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

42

42

Question #5

Post-splenectomy, the patient is at increased risk of severe disease due to which of the following microorganisms?

A. Helicobacter pylori
B. Capnocytophaga canimorsus
C. Candida glabrata
D. Clostridium difficile

43

43

Question #5

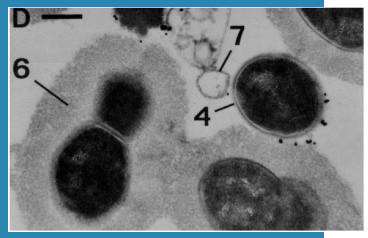
Post-splenectomy, the patient is at increased risk of severe disease due to which of the following microorganisms?

A. Helicobacter pylori
B. Capnocytophaga canimorsus
C. Candida glabrata
D. Clostridium difficile

44

44

Splenectomy and Infection Risk



Skov Sørensen et al. (1988) Infect Immun 56: 1890-1896

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*

Rubin LG, Schaffner W. Clinical practice. Care of the asplenic patient. N Engl J Med. 2014

45

45

Strategies to Reduce Infection Risk in Asplenia

Vaccination for Encapsulated Organisms

- Pneumococcus
- Meningococcus
- Hemophilus Influenza Type B

Penicillin Prophylaxis

- Children < 5 years
- Older children/ adults within 1-2 years of splenectomy
- Any age: secondary prevention (lifelong) following sepsis

Rubin LG, Schaffner W. Clinical practice. Care of the asplenic patient. N Engl J Med. 2014; Lee GM. Preventing infections in children and adults with asplenia. Hematology Am Soc Hematol Educ Program. 2020

46

46

- 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

47

47

Question #6

- 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.

48

48

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 <u>disadvantage</u> of this approach, when compared to immediate surgery?

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

49

49

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.

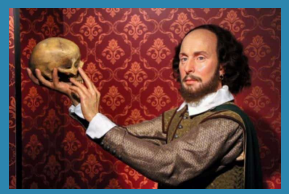
Which of the following is a recognized <u>disadvantage</u> of this approach, when compared to immediate surgery?

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

50

50

Appendicitis: to cut or not to cut…



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

CODA: N Engl J Med. 2020; APPAC: JAMA. 2018; Pediatr Surg Int. 2020

51

51

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:
know when to recommend surgery

Quality of Life and Patient Satisfaction at 7-Year Follow-up of Antibiotic Therapy vs Appendectomy for Uncomplicated Acute Appendicitis: A Secondary Analysis of a Randomized Clinical Trial. JAMA Surg. 2020

52

52

- Non-operative management of acute appendicitis may be considered if *uncomplicated*
  - Features which should prompt immediate surgery: 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

53

53

Question #7

- 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.

Lancet Infect Dis. 2008 Jun;8(6):399.

54

54

Question #7

Lancet Infect Dis. 2008 Jun;8(6):399.

The patient's clinical syndrome was most likely caused by which of the following exposures?

A. Rat bite
B. Tick bite
C. Consumption of raw oysters
D. Consumption of raw egg

55

55

Question #7

Diagnosis:
Vibrio vulnificus

The patient's clinical syndrome was most likely caused by which of the following exposures?

A. Rat bite
B. Tick bite
C. Consumption of raw oysters
D. Consumption of raw egg

56

56

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

Explanation

Hemorrhagic bullae from *Vibrio vulnificus*

Am J Trop Med Hyg. 2017;97(1):1-2.

Petechial rash from *Streptobacillus moniliformis* (rat bite fever); fever, rash, migratory arthritis

CMAJ. 2006 Aug 15;175(4):354.

Erythema migrans due to *Borrelia burgdorferi* (tick borne)

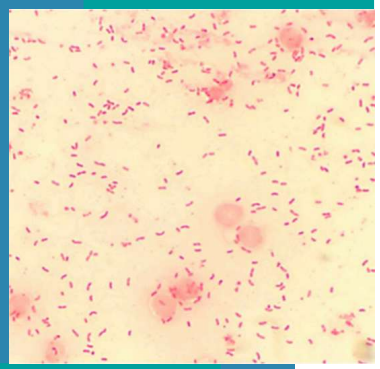
https://www.cdc.gov/lyme/signs-symptoms/lyme-disease-rashes.html?CDC_AAref_Val=https://www.cdc.gov/lyme/signs_symptoms/rashes.html

Rose spots from *Salmonella typhi*

Rose spots in typhoid fever. Arch Dermatol. 1972

57

57



Skin Manifestations of Primary *Vibrio vulnificus* Septicemia. *Am J Trop Med Hyg.* 2017.

Vibrio vulnificus

- Gram-negative, curved bacillus
- Halophilic (salt loving) – *brackish water*
- Cause: *consumption of raw seafood (oysters) or contamination of open wound*
- At risk: *liver disease* (cirrhosis); iron overload; renal disease; immunosuppression
- High mortality

58

58

Clinical Presentation and Treatment

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

Principles and Practice of Infectious Diseases, 9th ed.

59

59

- 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: 3rd generation cephalosporin plus doxycycline or fluoroquinolone; debridement

Vibrio Vulnificus

Take Home Points

60

60

Question #8

- 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 rash 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.

61

61

Question #8

Indian J Dermatol. 2010;55(1):79-85.

- Physical exam is notable for fever (101.2 degrees Fahrenheit) and a diffuse, morbilliform rash.
- CBC is as follows:
  - WBC 3.26 x 10^9 / L (normal)
  - Hgb 12.9 g/dL (normal)
  - Platelets 113,000 / mcL (low)
- A comprehensive metabolic profile is normal including renal and liver function tests.

62

62

Question #8

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)

63

63

Question #8

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)

64

64

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

Question #8 - Explained

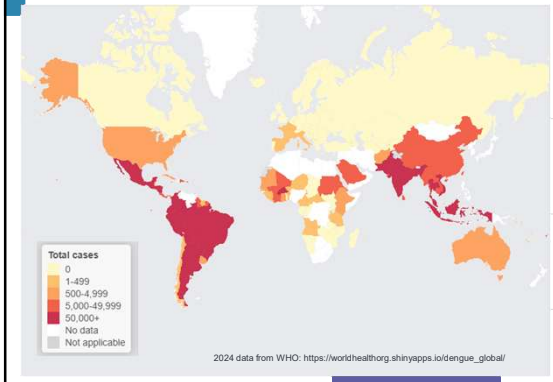
Fever, headache, body pain, rash and low platelets in a returning traveler

- **Dengue** – characteristic symptoms and epidemiology; PCR or NS1 antigen test recommended within first 7 days
- **Blood culture** – presumably looking for Typhoid fever, but rash is not characteristic and no gastrointestinal symptoms
- **Lyme** – wrong epidemiology (no known exposure to ticks) and rash not typical for Lyme; low platelets does not fit
- **Malaria** – RDT would be diagnostic, but no anemia and rash not typical with malaria; also was taking prophylaxis

65

65

Dengue is Common Worldwide…and Rising



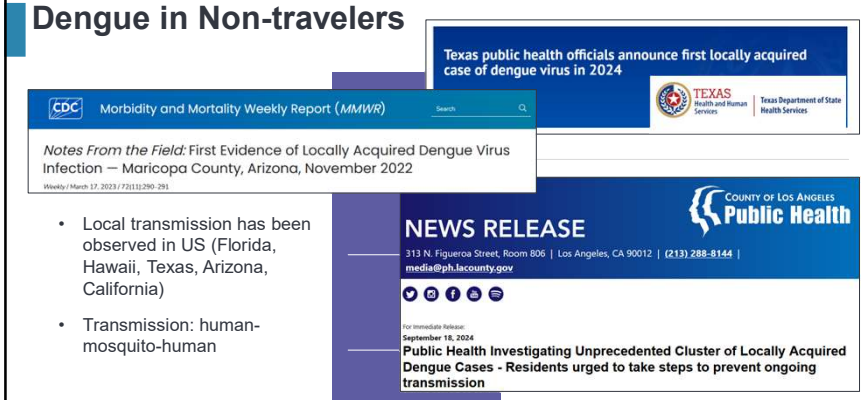
- 100-400 million infections each year worldwide
- Tropical and subtropical climates
- Urban and semi-urban areas

https://www.cdc.gov/dengue/outbreaks/2024/index.html

66

66

Dengue in Non-travelers



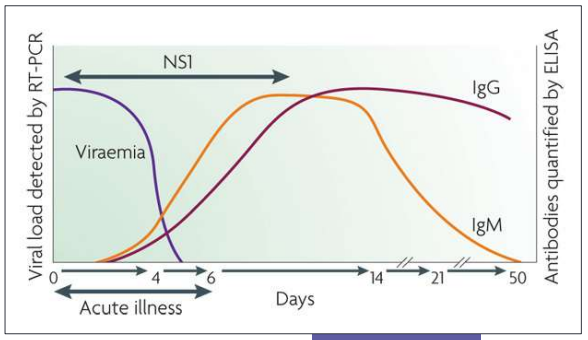
- Local transmission has been observed in US (Florida, Hawaii, Texas, Arizona, California)
- Transmission: human-mosquito-human

https://www.cdc.gov/dengue/outbreaks/2024/index.html

67

67

Dengue: Diagnostic Testing



Preferred: nucleic acid testing (**PCR**) within first 5 days

Other:

- *NS-1 antigen*: less sensitive and only positive early in course
- *Serology*: may cross-react; must confirm early IgM with later IgG

Guzman, M. G. et al. Dengue: A continuing global threat. Nature Reviews Microbiology 8, S7–S16 (2010).
https://www.cdc.gov/dengue/hcp/diagnosis-testing/index.html

68

68

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

Severe Dengue

- 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)

https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue
https://www.cdc.gov/dengue/hcp/clinical-signs/index.html

69

69

Mosquito-borne Illnesses in a Returning Traveler

Aedes aegypti mosquito, image from https://www.cdc.gov/mosquitoes/about/life-cycle-of-aedes-mosquitoes.html

For the boards, know:

- Typical epidemiology
- Clinical presentation
- Vector
- Diagnostic approach

70

70

Key Features of Mosquito-borne Illnesses

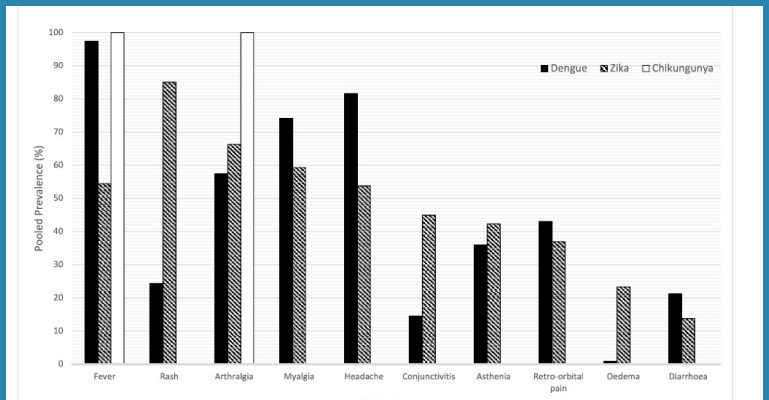
	Epidemiology	Vector	Clinical Features
Chikungunya	Africa, the Americas, Asia, Europe, islands in Indian and Pacific Oceans; prominent outbreak Caribbean 2013	***Aedes** aegypti* (*A. albopticus* in Europe)	Fever and **joint pain**; rash less common. Symptoms may last months.
Dengue	Worldwide in tropics / subtropics 4 serotypes; infection with a 2nd 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**)

CDC; PPID 9th edition

71

71

Comparing Sxs of Dengue, Zika, Chikungunya



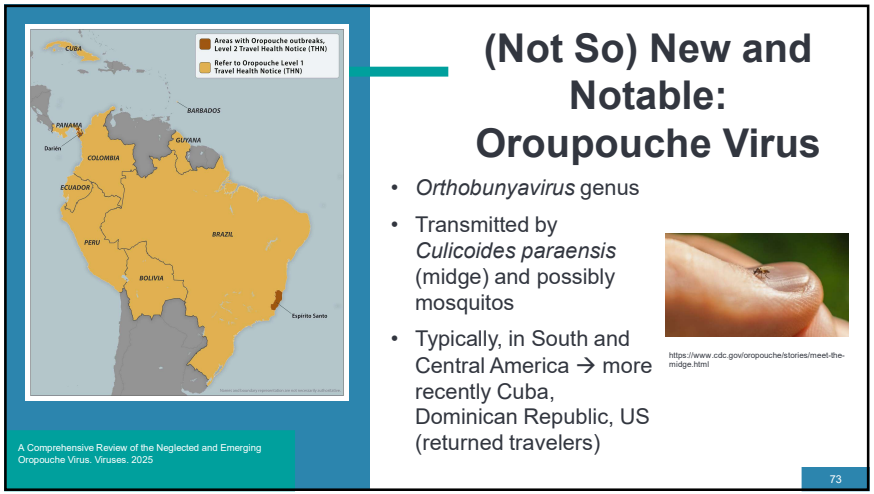
Kharwadkar S, Herath N. Clinical manifestations of dengue, Zika and chikungunya in the Pacific Islands: A systematic review and meta-analysis. Rev Med Virol. 2024 Mar.

72

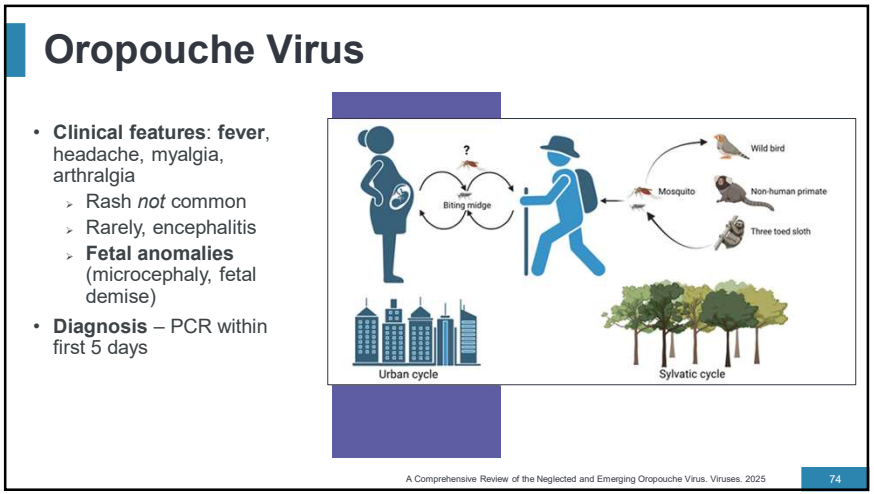
72

54 Kitchen Sink: Syndromes Not Covered Elsewhere

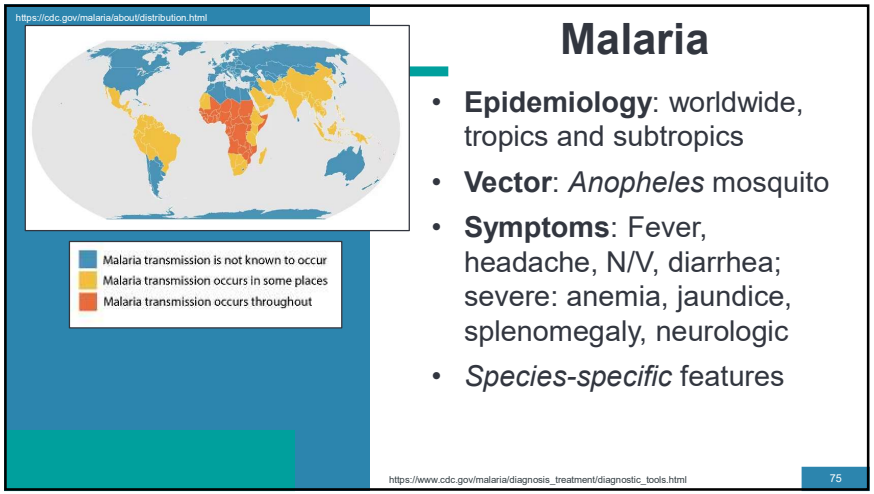
Speaker: Stacey Rose, MD



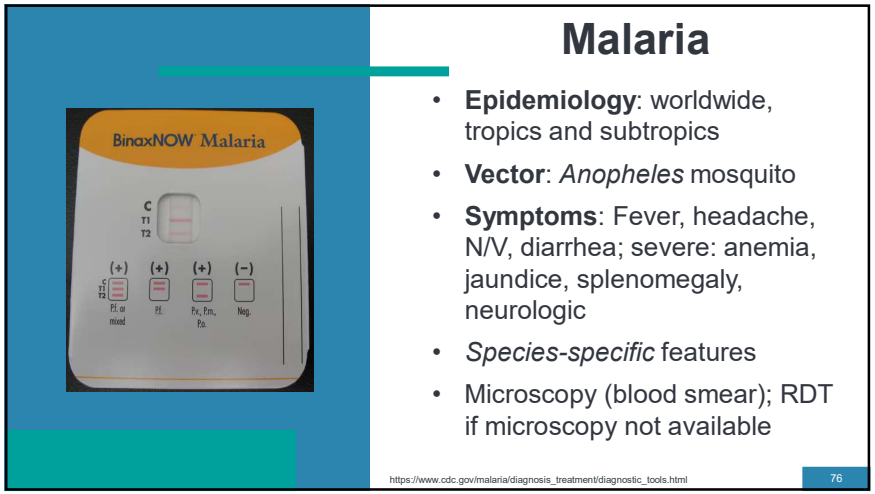
73



74



75



76

54 Kitchen Sink: Syndromes Not Covered Elsewhere

Speaker: Stacey Rose, MD

Important Updates on Locally Acquired Malaria Cases Identified in Florida, Texas, and Maryland

HAN HEALTH ALERT NETWORK

This is an official CDC HEALTH UPDATE

Distributed via the CDC Health Alert Network
August 28, 2023, 2:15 PM ET
CDCHAN-00496

Summary

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 local transmission of malaria in Florida or Texas since mid-July 2023.

https://emergency.cdc.gov/han/2023/han00496.asp#print 77

77

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

78

78

79

79

Kitchen Sink Summary - 1

Whipple's:

- Classic: arthralgia, diarrhea, weight loss
- Dx with duodenal bx (PAS+, foamy macrophages)
- Or PCR of tissue (heart valve for endocarditis)

Acute Rheumatic Fever:

- Kids / young adults with migratory polyarthritis, carditis, chorea, subcutaneous nodules, erythema marginatum following GAS pharyngitis
- Monthly IM penicillin prophylaxis for 10 years or to age 40 if carditis + residual valvular disease

https://www.cdc.gov/groupastrep/diseases-public/rheumatic-fever.html

80

80

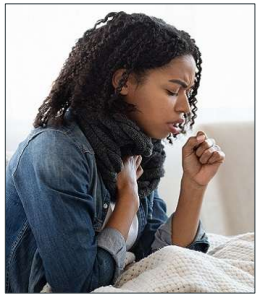
54 Kitchen Sink: Syndromes Not Covered Elsewhere

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

81

81

Kitchen Sink Summary - 3

Appendicitis

- Non operative management may be reasonable for uncomplicated cases
- Identify features that should prompt surgery:
  - Appendicolith +/-
  - perforation
  - Abscess
  - Suspicion of tumor
  - Peritonitis
  - Systemic illness

Asplenia

- Increased risk of infection with encapsulated organisms
- If prompt says asplenia, think…
  - *S. pneumoniae*
  - *N. meningitidis*
  - *H. Influenzae type B*
  - *Capnocytophaga*
  - *Babesia*
  - *Salmonella typhi*
- Prevent infection with immunizations and
- PCN prophylaxis (if < 5 yrs old; recent splenectomy; prior episode of sepsis)

82

82

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 Aedes mosquitos and can present with fever plus…

- Chikungunya – joint pain
- Dengue – headache, rash, muscle and joint pain; higher risk of severe / hemorrhagic Dengue with 2nd infection
- Zika – 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

83

83

Questions?

Stacey Rose, MD, FACP, FIDSA
srrose@bcm.edu

84