THE UNIVERSITY OF ARIZONA
COLLEGE OF MEDICINE TUCSON
Pediatrics

Banner Children's
Diamond Children's
Medical Center

Unusual, challenging and surprising cases: a day in the life of an ID doc

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Disclosures

- I have no conflicts of interest to disclose
- There will be some discussion of off label use of medications

Learning Objectives

1. Recognize key findings that may point to an alternative diagnosis
2. Identify red flags that suggest severe infection
3. Describe infections that may be seen in Arizona
4. Describe the thought process of an ID doc

15 y/o boy with recurrent fevers

- For the last 6 weeks has cycling fever
  - Temp as high as 105 for a few days, then afebrile for a week, then recurs
  - Gets myalgias with fevers, but otherwise asymptomatic
  - Feels fairly well in between fevers
  - When you examine him during an afebrile period he has normal findings
  - What do you think he has?

Horses vs Zebras

- History often points you in the right direction
  - Timing, quality and circumstances of the fevers/symptoms
  - Exposures?
    - Geography
      - Including within the US and parts of AZ
    - Animals
    - Water
    - Vectors
    - Non pasteurized dairy products and fruit juices
    - Pica
    - Gardening, etc

Recurrent fevers?

- What is the family calling a fever?
- It's all about the timing
  - "Fever for months"
    - What is the longest time (in days) you have gone without a fever?
    - What is the longest time (in days) the fever has lasted?
  - Clockwork
  - Random
- What are the symptoms associated with fever?
  - Are there completely different syndromes or infections here?
  - Not uncommon to have URI, URI, OM, rash illness, diarrheal illness, URI
- Are other contacts experiencing similar symptoms?

Recurrent fevers?

- Red flags
  - MSK findings, altered mental status/meningismus, respiratory distress, petechial rash, lethargy, weight loss, milestones loss, etc
- Few infections cause truly relapsing fever
- Non-infectious etiologies
  - Periodic fever syndromes
  - Autoimmune diseases (ie Crohns)
  - Occasionally malignancy

Let’s get even more basic

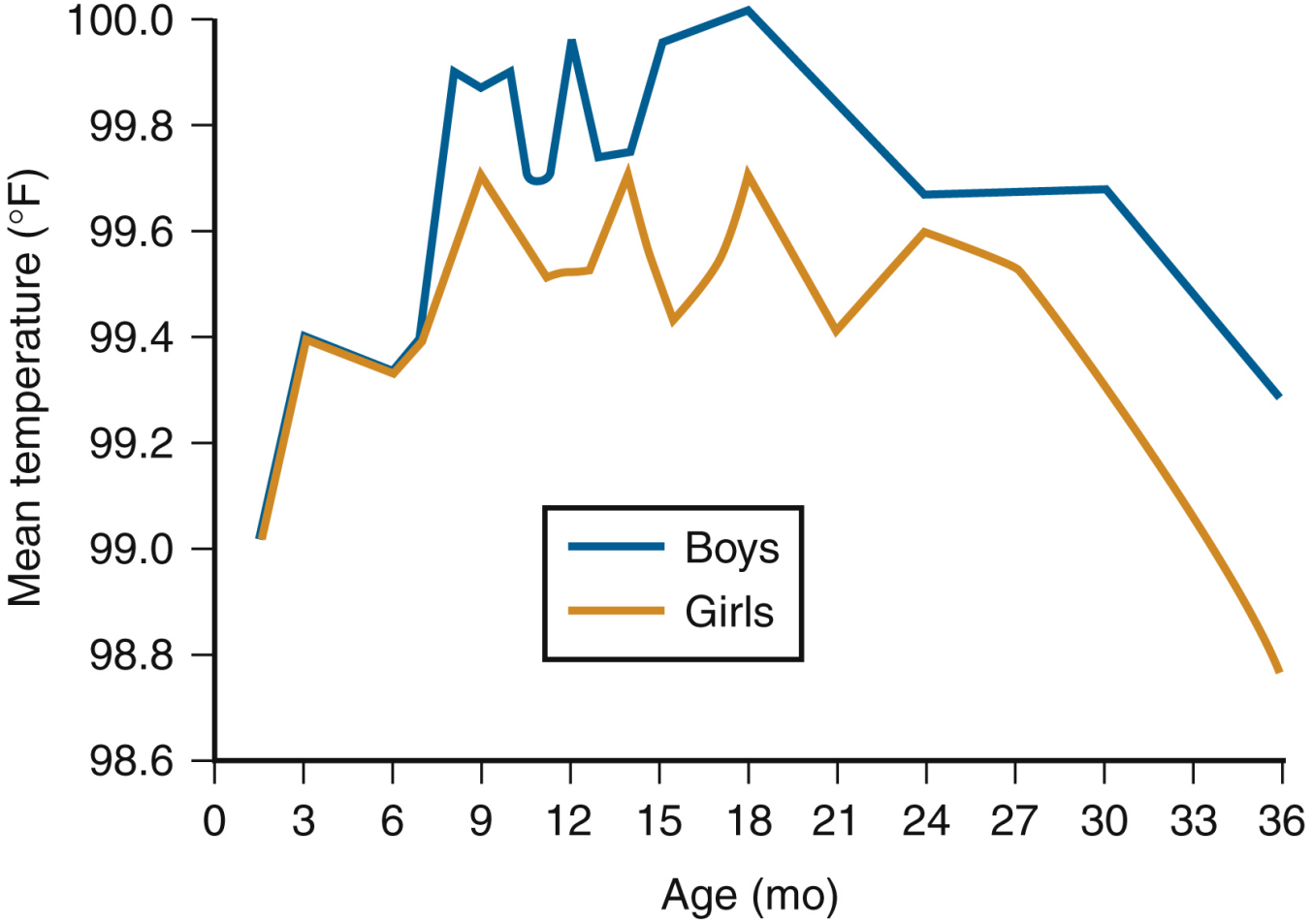
- What temperature constitutes a fever?
  - 100°F
  - 100.4°F
  - 101°F
  - 101.5°F
- Does where you measure matter?

98.6?

- Wunderlich: 1800's
  - Axillary measurements
  - Said to have made millions of measurements in 25,000 adults
  - Range 97.2-99.5
    - Nadir 2-8am, Zenith 4-9pm
    - Women tended to have slightly higher and more variable temps
    - May have variability based on race
  - Suggested that temps above 100.4 were always "suspicious" and "probably febrile"
- Mackowiak et al in 1980s, much fewer subjects
  - Oral temps in shigella vaccine trial
  - Mean was 98.2
    - Interesting since axillary temps tend to be lower than oral temps
- What about the "I run low" folks???

Feigin 2019; Mackowiak JAMA 1992

Mean rectal temperatures in young children in the 1930s



Long 2023

Tools of measurement

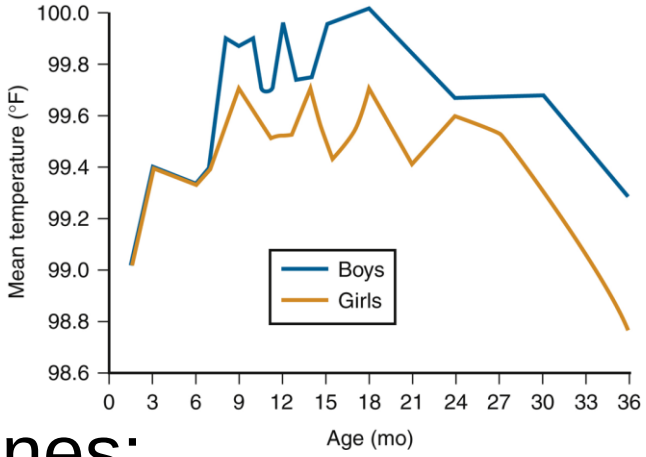
- Chemical thermometers
  - Mercury, alcohol
- Electronic thermometers
- Infrared
- All have their pros/cons

Where to measure

- Goal is to approximate core temperature with easy access
  - Gold standard is rectal
    - Can be higher than true core temp
  - TM, sublingual, temporal areas supplied by branches of carotid artery
- Hand on the forehead?
  - 33% PPV, 96% NPV
- Variance in temp by site, but also variability of the variability depending on the patient
    - Can’t just add or subtract degrees based on site

Back to what's a fever?

- Raise/lower the bar depending on what you are worried about
  - CDC H1N1 info: if you had a "fever of 100" you should be evaluated
  - Febrile infant: 100.4
  - Fever and neutropenia guidelines: 100.4 >1 hour or a single 101.0
  - Surgery rounds:101.5?

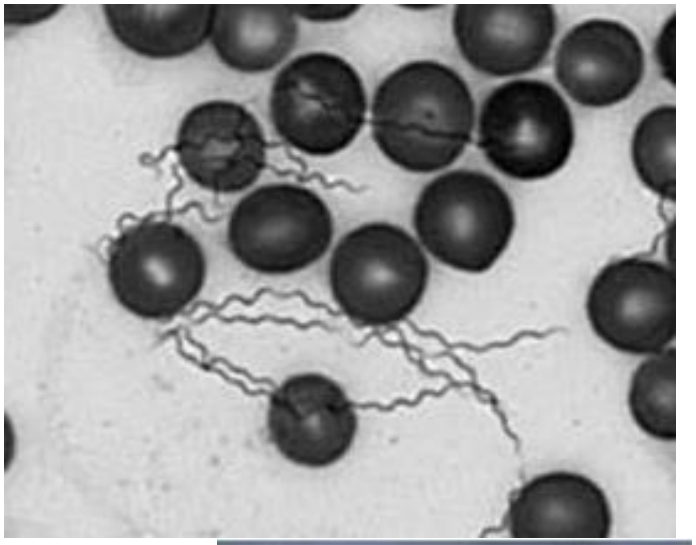


Back to our patient's story: additional details

- He stayed in a cabin in the mountains of NE Arizona just before the onset of his fevers
- Mouse droppings in the cabin
- His grandmother visited the same cabin 5 years prior and developed the same infection
- What's he have?

Borrellia hermsii:

- Tick Borne relapsing fevers
  - Borrelia spp
- Vector: soft ticks live in rodent nests
  - Often feed at night for up to 30 minutes
    - Painless and usually not noticed
- Classic scenario is someone who stayed in a rodent infested cabin in a mountainous area of the Western US
- Like most spirochetal illnesses it is treated with doxycycline



Our patient

- Got doxycycline and never had another fever
- CDC serology confirmed the infection
- His grandmother had spirochetes seen on her peripheral smear at presentation in the ED 5 years prior
  - Sepsis presentation but improved quickly with antibiotics

Recurrent fevers

- Usually various mild intermittent infections, sometimes with a bacterial infection mixed in
- True relapsing febrile infection rare
  - Borrelia spp relapsing fevers
  - Malaria
  - Spirillium minus (rat bite fever)
- Periodic fever syndromes
  - PFAPA and Hyper IgD tend to be fairly clockwork at 3-6 week intervals

Next case: chronic fevers

- 7 y/o with spastic CP, severe developmental delay, seizures, and fevers for 9 months.
  - Fevers are intermittent at times, other times persistent
    - Up to 102
  - Off and on cough, chest imaging shows infiltrates concerning for pneumonia
    - Has gotten various courses of antibiotics without change in symptoms or improvement on imaging
      - Penicillin, amox-clav, cephalexin, etc
  - Thrush on his tongue
  - Parents note he has lost 5 pounds in the last few weeks
  - Poor secretion control; fed orally with no known aspiration events

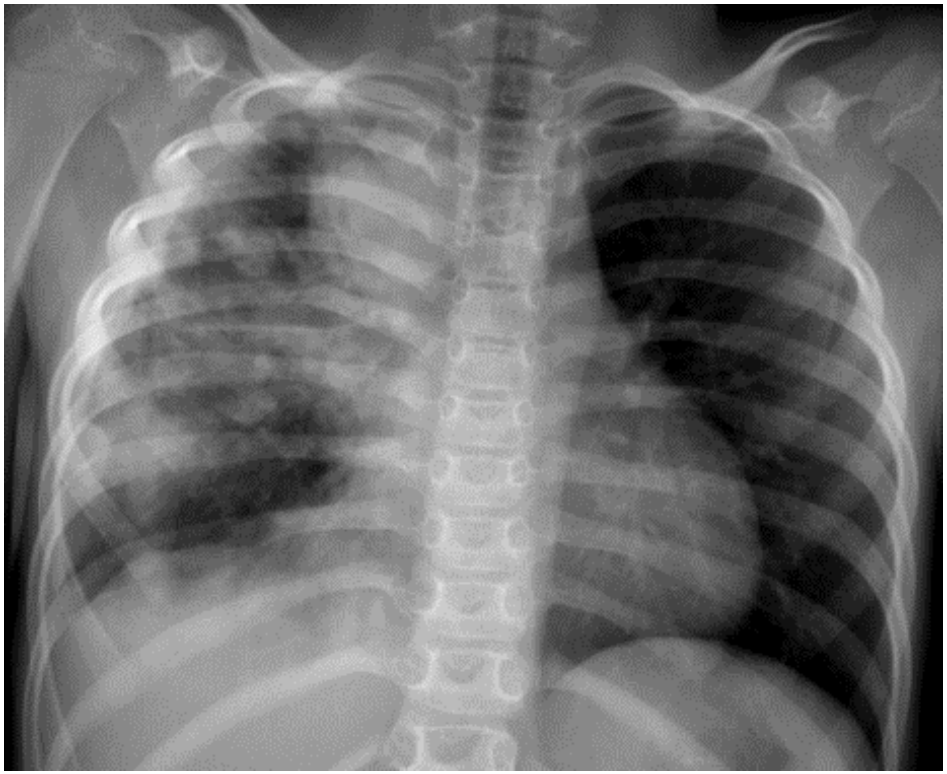
Exam

- Cachectic
- Contractures and hyperreflexia
- White plaque on the tongue
- Normal lung exam
- Otherwise nothing else on exam to suggest source of fever

- Labs: elevated ESR/CRP
- Blood cultures negative
- 2 negative Tspots

Red Flags?

- Cachexia/weight loss
- Persistence of fever/abnormal imaging despite antibiotics
- Elevated CRP
- Thrush?



- 7 y/o with spastic CP, dev delay, sz, wt loss, chronic fevers unresponsive to courses of antibiotics with abnormal CXR and CT scan findings
- What do you think he has?
  - Candida?
  - Resistant typical bacteria
  - Aspiration pneumonia
  - TB
  - Cocci
  - Autoimmune diseases?
  - Malignancy?

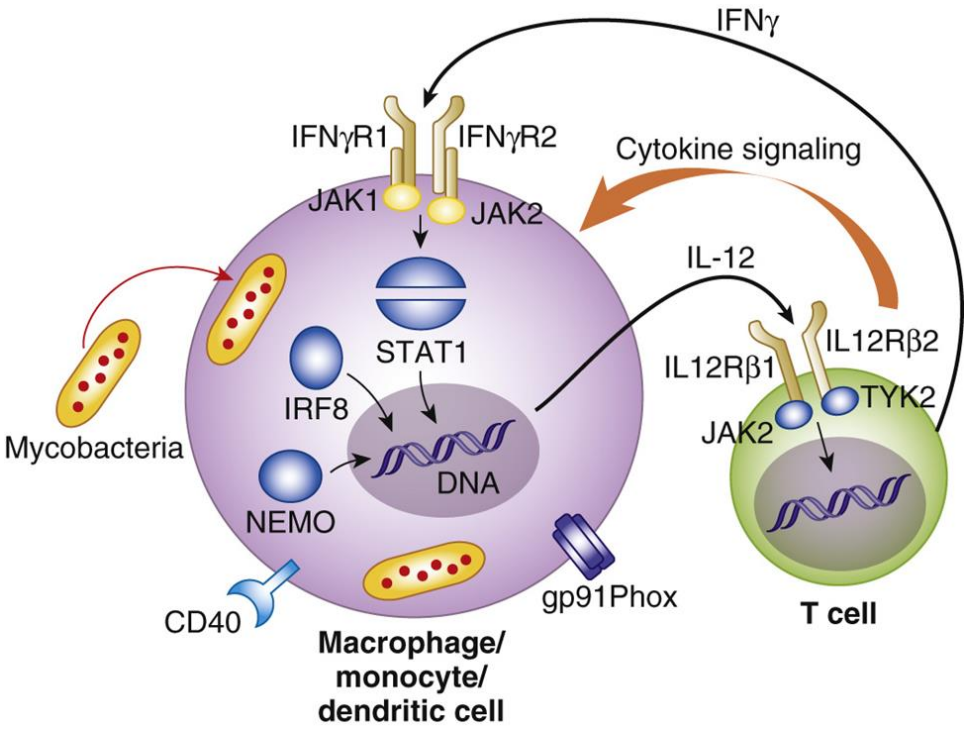
- Born in the US, UTD on vaccines
- Parents from Guatemala, asymptomatic
- No known TB exposures
- No animal exposures, travel or other concerning exposures
- No family history of autoimmune disease, immune deficiency, childhood malignancy

What we (I) did

- Treat him for aspiration pneumonia and see how he does
  - Some slight improvement at 1st but then still with fevers
- Bronch
  - Oops, cultures grew TB
    - And I exposed everyone in the bronch suite to TB

But he had a negative IGRA x2?

- Interferon gamma response assay
- Tspot, Quantiferon gold



Quantiferon Gold plus

- 3rd gen test
- ELISA
  - 4 vs 1 tube (same volume of blood: 4ml)
- Mix patient's blood with TB antigens (ESAT-6, CFP-10)
- Measure IFNγ response by CD4 and CD8 cells
  - CD8 more intracellular
    - May be more active in children, immune compromised
- Positive and negative control

https://www.qiagen.com/us/applications/tb-management/tb-testing/qft-plus/cd8-technology

Quant gold results example

Overall result	**Quantiferon-TB plus 4T**	**Positive**
Negative Control	Quantiferon (TM), NIL	1.58 IU/ml
Positive Control	Quantiferon (TM), Mitogen-NIL	6.94 IU/ml
CD4 response	Quantiferon-TB1-NIL	4.57 IU/ml
CD8 response	Quantiferon-TB2-NIL	5.19 IU/ml

Overall result	**Quantiferon-TB plus 4T**	**Indeterminate**
Negative Control	Quantiferon (TM), NIL	0.01 IU/ml
Positive Control	Quantiferon (TM), Mitogen-NIL	0.05 IU/ml
CD4 response	Quantiferon-TB1-NIL	0.00 IU/ml
CD8 response	Quantiferon-TB2-NIL	0.00 IU/ml

T-SPOT

- Similar principle of measuring IFNγ response to TB antigens
- Elispot

https://www.tspot.com/why-the-t-spot-tb-test/technology/

IGRAs

- Better sensitivity and specificity for TB compared to PPD
  - Latent TB: High ninety percentile
  - Active TB, likely much lower: around 80% sensitivity
- Results may be affected by immune deficiency, poor nutrition, etc
- Cross reacts with *M. kansasii*, *M. szulgai* and *M. marinum*
- Claim to fame: doesn't cross react with BCG
- OK per AAP for use in children ≥2 years of age
  - But better data for ≥4 years of age

The Problem with TB

- Estimated 2 billion people have TB infection (about 1 in 4 people)
  - 90% of those live in developing countries (40x higher rate compared to developed countries)
  - 1.6 million deaths/year due to TB
  - 15-20% of cases are children
  - Estimated 9 million children orphaned due to parental mortality from TB

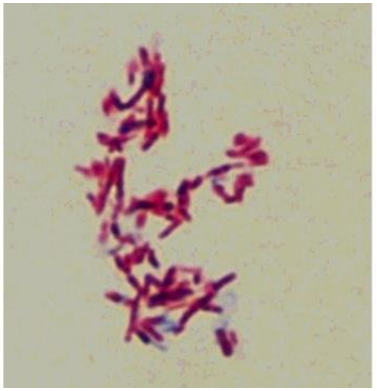
The Problem with TB

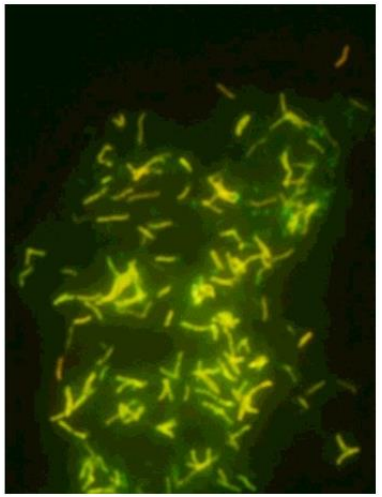
- United States (relatively low rate of TB: 3/100,000 population)
  - 67% of cases in foreign born individuals
    - 30-50% of recent immigrants infected prior to entry into the US
  - 6% of cases in children <15 years of age
    - Highest rates in <3 years of age which are most vulnerable to severe disease
  - Most children with TB acquired it from a close caregiver
- AZ: 154 cases in 2022, majority born in foreign country

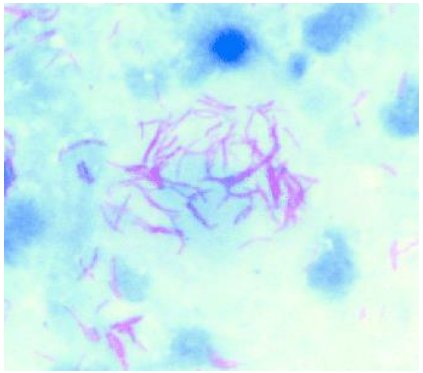
Feigin 2019; www.AZDHS.gov

The Bacterium

- Mycobacterium tuberculosis complex
  - M. tuberculosis, M. africanuum, M. bovis, M. canetti, M. microti
- Obligate aerobe
  - Often see upper lobe disease
- Slow grower (3-6 weeks on solid media, another 2 weeks for susceptibility results)
- Treatable with multidrug antibiotic regimen
  - Usually start out with 4 drugs, end up with 2
  - Problems with antibiotic resistance throughout the world







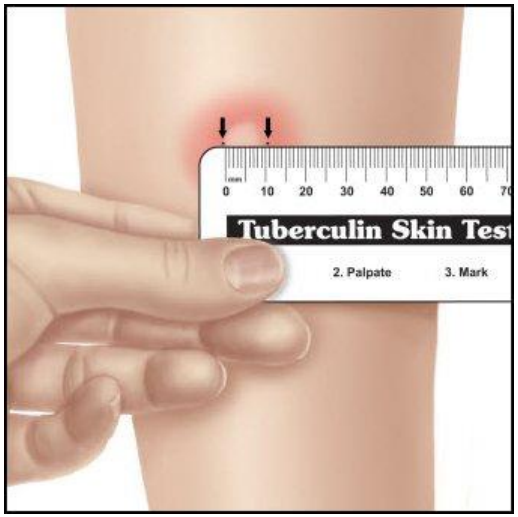
Feigin 2019; Caulfield JCTOMD 2016; Prasad ATMPH 2011

7 month old FTT

- OK until 2 months of age and hasn't been growing much since then
- Afebrile
- Abnormal CXR, hasn't responded to cefdinir
  - Don't forget the lateral
- PPD 7mm
  - Is this a positive PPD?

PPD

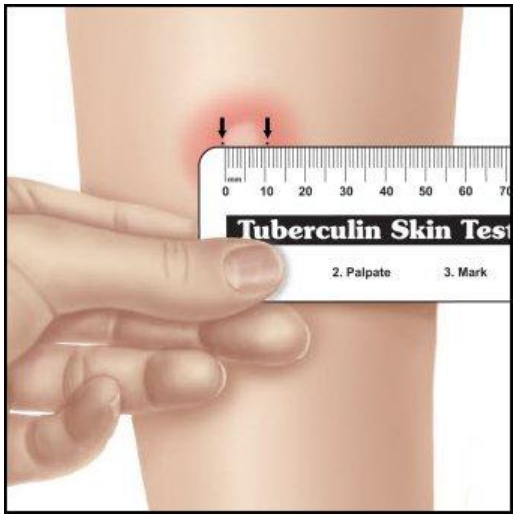
- Measure the induration perpendicular to the long axis of the arm
  - Note the mm so you can interpret in the right setting
  - Type IV hypersensitivity reaction
    - 48-72 hours
- Positive: sliding scale
  - Depends on risk factors
  - Document the mm induration



https://www.cdc.gov/tb/webcourses/course/chapter3/3_testing_for_tb_disease_and_ltbi_3_mantoux_tuberculin_skin_test_reading_the_tst_induration.html

PPD Sliding scale based on risk

- 5mm
  - Immunocompromised
  - Contact with contagious TB
  - Exam/CXR findings consistent with TB
- 10mm
  - ≤4 years old (CDC uses 5)
  - Born in or travel to endemic country
    - Travel usually 1 month or greater time in country
  - High risk diseases (DM, malnutrition, CRF, Hodgkin disease)
  - Living in or exposure to adults living in high-risk congregate settings
    - Prison, long term care facility, homeless shelter, etc
- 15mm
  - Everyone else



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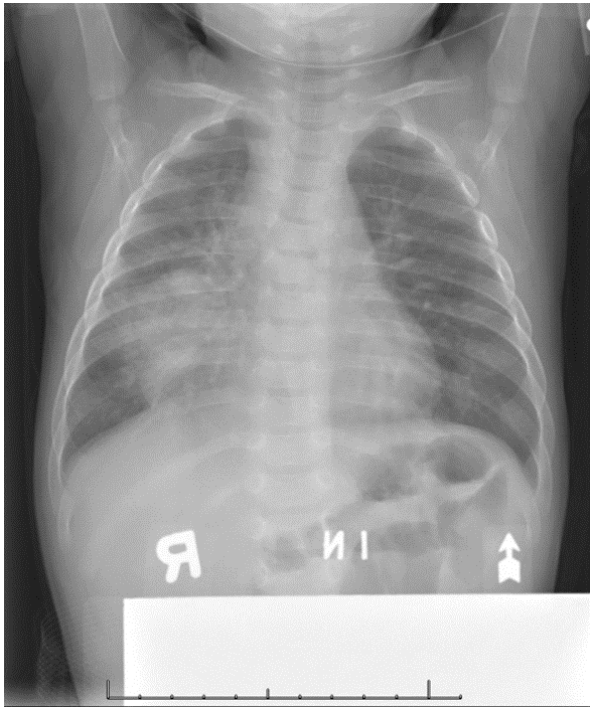
PPD

- Cross reacts with many other mycobacteria (including attenuated M. bovis in the BCG vaccine and many non tuberculous mycobacteria)
  - But should be interpreted irrespective of BCG vaccine history since majority of positive PPD in setting of BCG vaccine still have tuberculosis infection
- Sensitivity of 75-85% (much lower in HIV)
  - May not respond to the PPD until 3 weeks to 3 months after initial infection
  - May become anergic if not tested for a long time and have latent infection (2 step)
- Often misinterpreted by inexperienced providers
  - Measure the induration, not erythema

Back to our 7m old with TB

- Is he contagious?
- Does he need a negative pressure room?
- Probably not
- Children under the age of 10 tend not to be contagious
  - Tend not to have significant cough
    - Less force than older adolescents/adults
  - Fewer bacilli present in airways
  - Rarely smear positive
  - Exceptions: cavitary lesions, laryngeal involvement, congenital infection



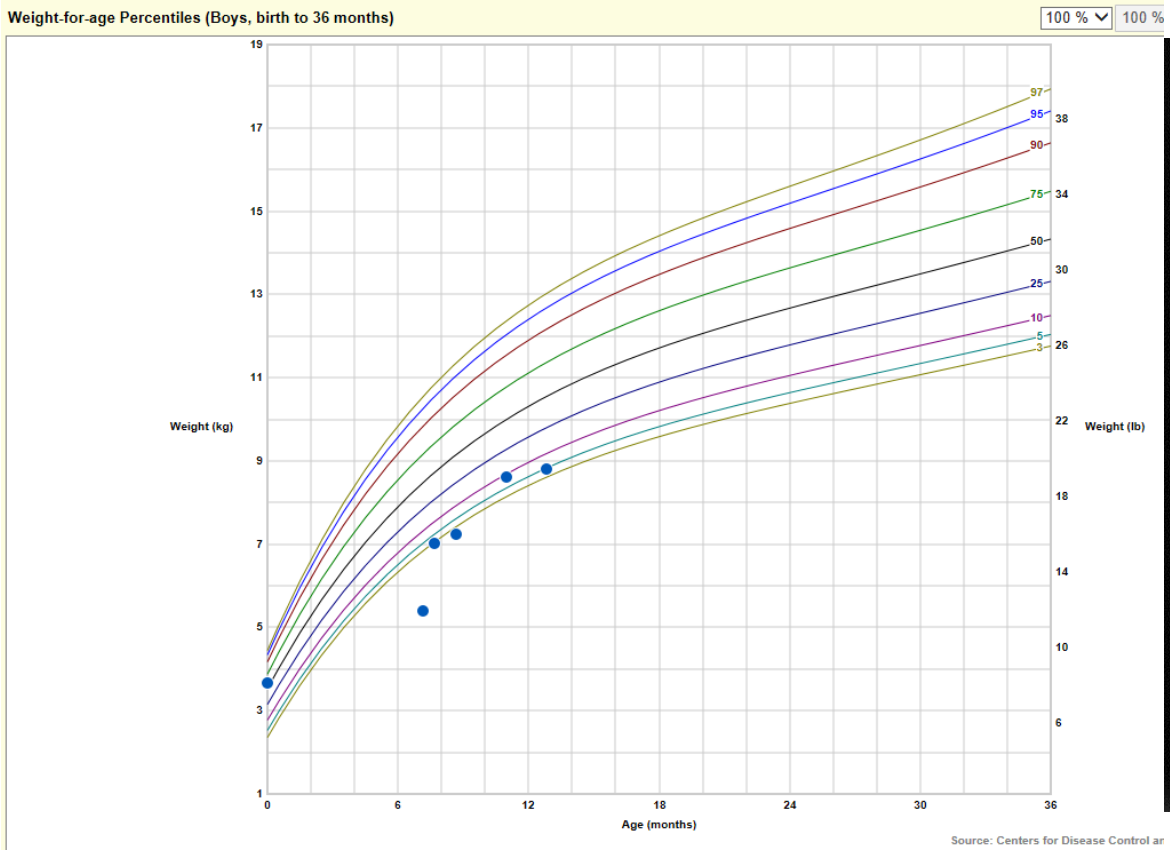
But….

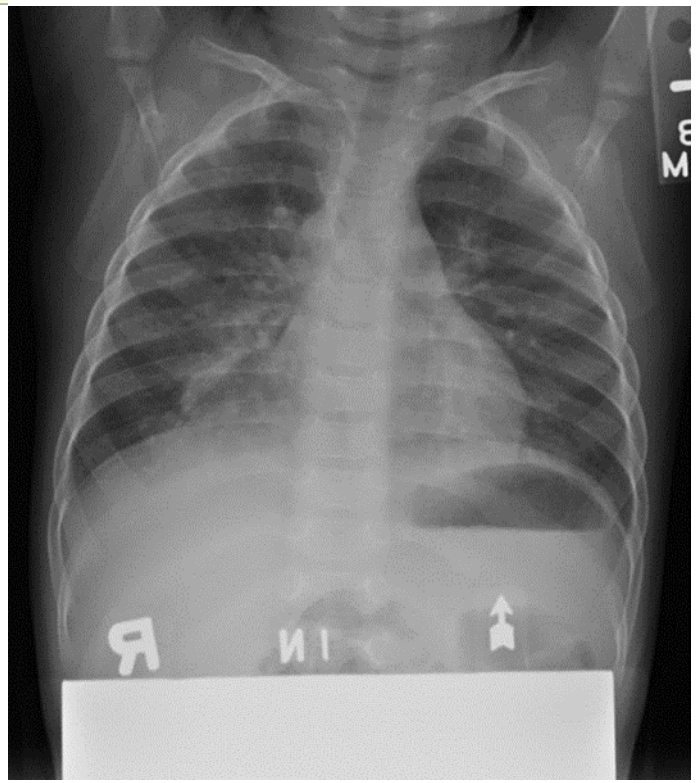
- Children are usually infected by an adult caregiver that is contagious and may be there at the medical visit
  - I tend to put young patients in negative pressure until things sorted out when active TB is present

His Caregivers

- Mom has cough with hemoptysis and is smear positive
  - Born in Bosnia but lived in the US since she was 3 (about 20 y/o now)
- Did mom just develop disease after prolonged “latent” infection?
  - Maybe, but on further questioning grandfather has a “smoker’s cough” with weight loss and CT showed he had cavitary TB

Our patient on 4 drug TB therapy





Another one

- 19 y/o adult with 4 months of cough, weight loss, night sweats and abnormal CXR
  - Smear positive
- Has a 12-month old at home
  - What do you want to know about this child?
  - What do you do about it?

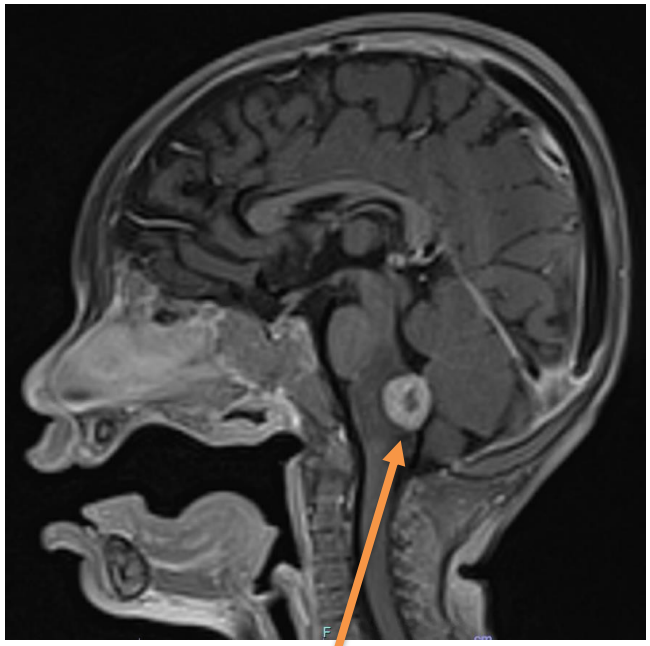
Young children

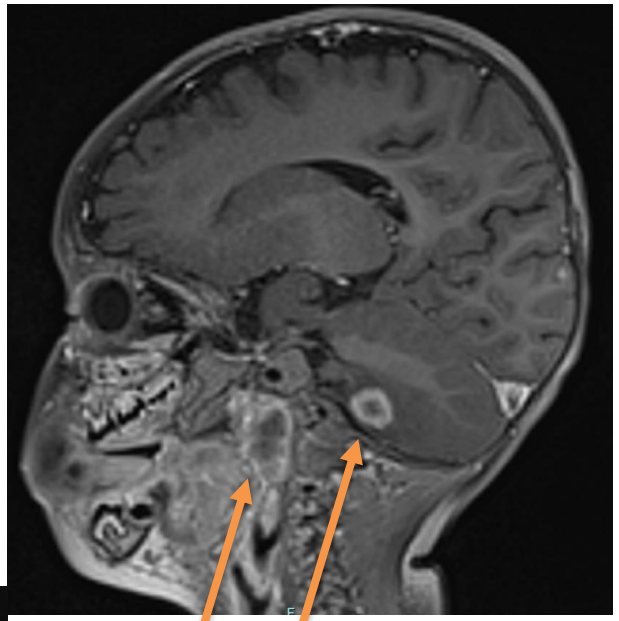
- High risk of severe disease
  - Often asymptomatic early on
- Get a work up
  - PPD plus CXR plus evaluation for symptoms and physical findings
- If PPD negative/normal exam/normal CXR
  - “Window prophylaxis” in contacts<5 years of age
    - Retest in 8-10 weeks
- If PPD positive or abn exam or abn CXR
  - Full work up
    - Gastric aspirates, LP, etc

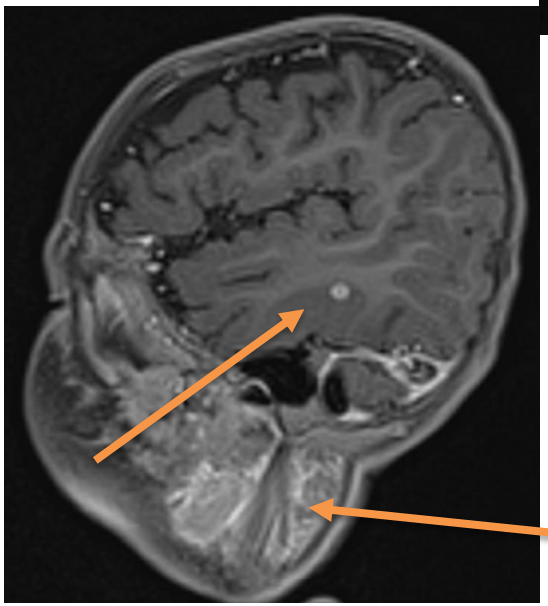
The 12-month old

- Cough and fever for weeks
- Cervical adenopathy
- Chest imaging shows necrotizing pneumonia
- Normal mental status

But….







12-month old

- Gastric aspirates eventually grew pan susceptible *M. tuberculosis*
- Did fine on steroids and multidrug treatment
- Mom positive quantiferon and neg CXR
  - Didn’t get treatment as recommended for her own latent infection
    - Returned a few months later with cough and pneumonia and grew TB from sputum samples
      - Responded well to therapy

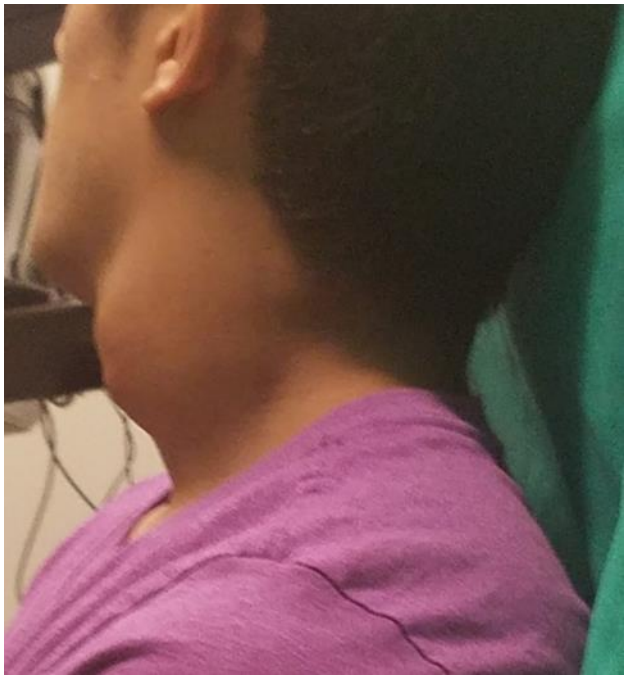
TB infection spectrum

- Exposure->infection->disease
- Untreated infection in Adults develops into disease 5-10% of the time throughout their lifetime (much higher in HIV patients)
  - Half of that risk occurs within 2-3 years of initial infection, but activation can occur at any time
  - Up to 40% of immune competent adults will develop serious, life-threatening forms of the disease
- Untreated infection in children
  - <1 y/o 50% annual risk of developing TB disease
  - <5 y/o 6-24% annual risk
  - 6-15 y/o 6-12% annual risk
- Treatment of latent infection decreases risk of developing disease by 90%

TB (“latent”) infection regimens

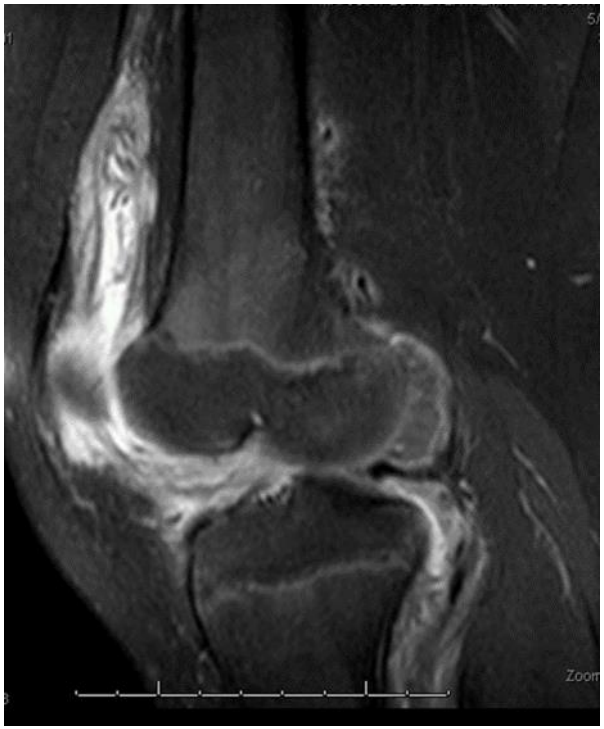
- INH x9 months
- Rifampin x4 months
- Weekly INH + Rifapentine x 12 weeks

Other TB fun



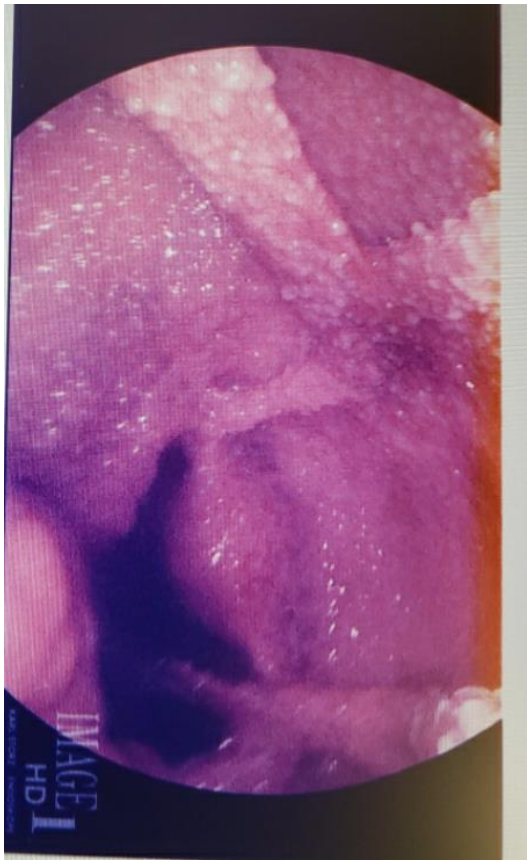
- Afebrile, negative CXR, positive quantiferon. Lived in India

Other TB fun



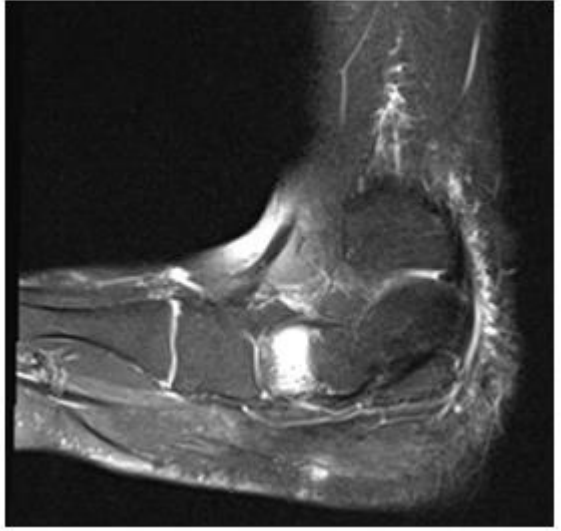
- Afebrile, negative CXR, PPD a couple of inches wide by 1 inch tall a week after placement. Born in China and recently visited for several weeks.

Other TB fun

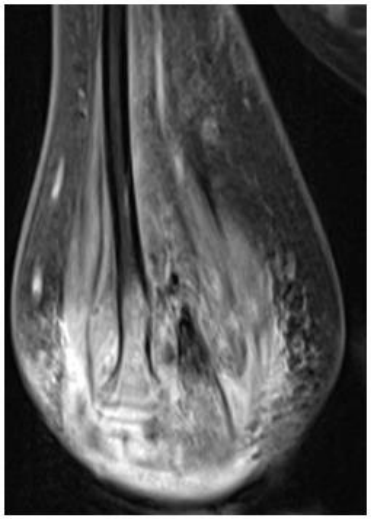


- Febrile, negative CXR, positive quantiferon, born in Vietnam and recently visited for several weeks.

Last TB case



- 16 y/o spastic CP, dev delay, Gtube feeds, multiple MSK findings
- Quantiferon positive
- AFB seen on I&D
- Patient and family born in US, no travel, no one with symptoms, no high risk exposures
- How did she get TB?



It's actually *Mycobacterium marinum*

- Environmental organism
  - Often associated with water
    - She would do water therapy at home
  - Tends to be an opportunist
- Cross reacts to cause a positive IGRA
  - Also see cross reactivity with M. szulgai and M. kansasii
- Know the limitations of your testing
- Did well with therapy
- Immune work up unrevealing

Heme/onc calls:

- 17 y/o boy with history of castleman's disease on immune suppression with new rash, chest pain and night sweats.
- On steroids (Pred 60mg/day) and recent course of rituximab for the Castleman's. Under fairly decent control but has chronic leg pain

- Skin lesions started a few weeks ago and a couple of new ones since then. Somewhat tender
  - Night sweats started about that time but no fever
- Few days of chest pain and non productive cough
  - Not hypoxic, not tachypneic

More history

- Goes back and forth between southern AZ and northern Mexico
- Went wading in a creek a month or so ago
- No injuries/trauma
- No drug use
- Sexually active with 3 female partners in his lifetime
  - Recent HIV screening test negative
- No known TB exposures
- No animals, no queso fresco, etc

Xray

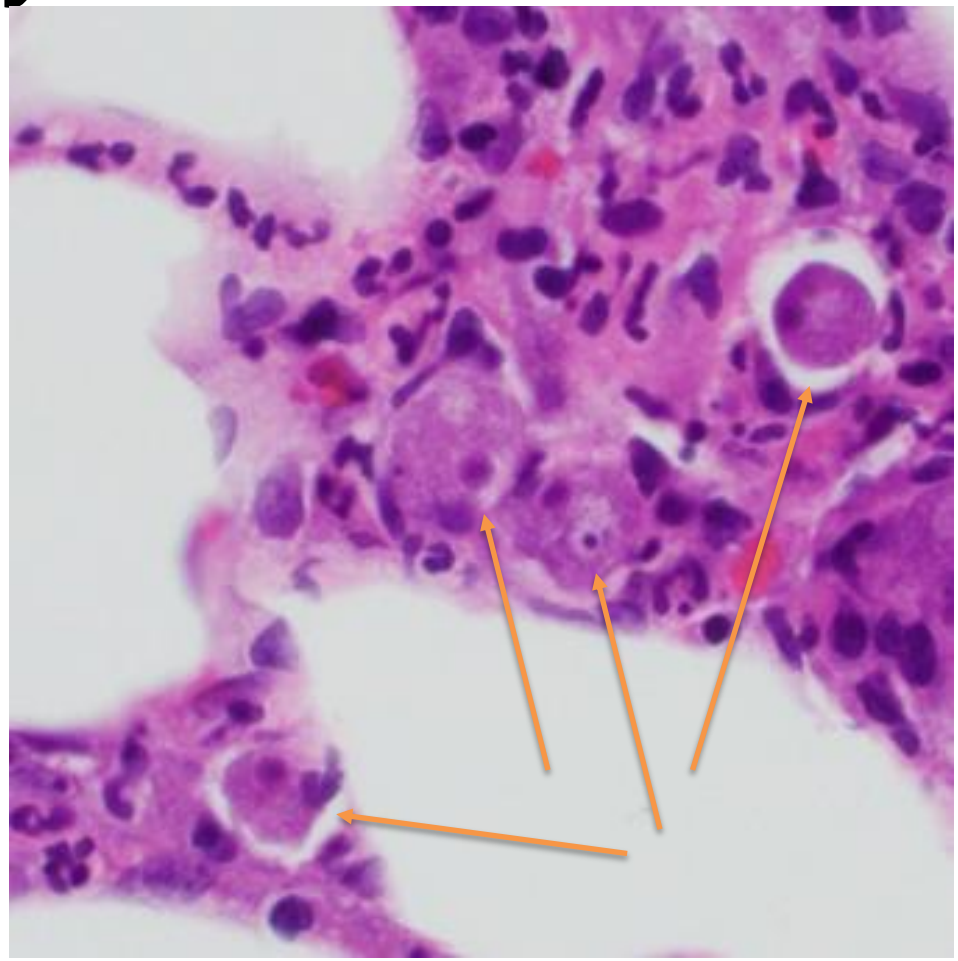
- What do you call this pattern?
  - Miliary
    - Lymphohematogenous spread
- What diseases do you think about?
  - TB, cocci, histo, blasto
    - Can cause cutaneous manifestations
      - My vote was for cocci
- Rule out HIV, syphilis (weird skin lesions)
- Consider non-infectious causes
  - Sarcoidosis, hypersensitivity pneumonitis, etc

But…

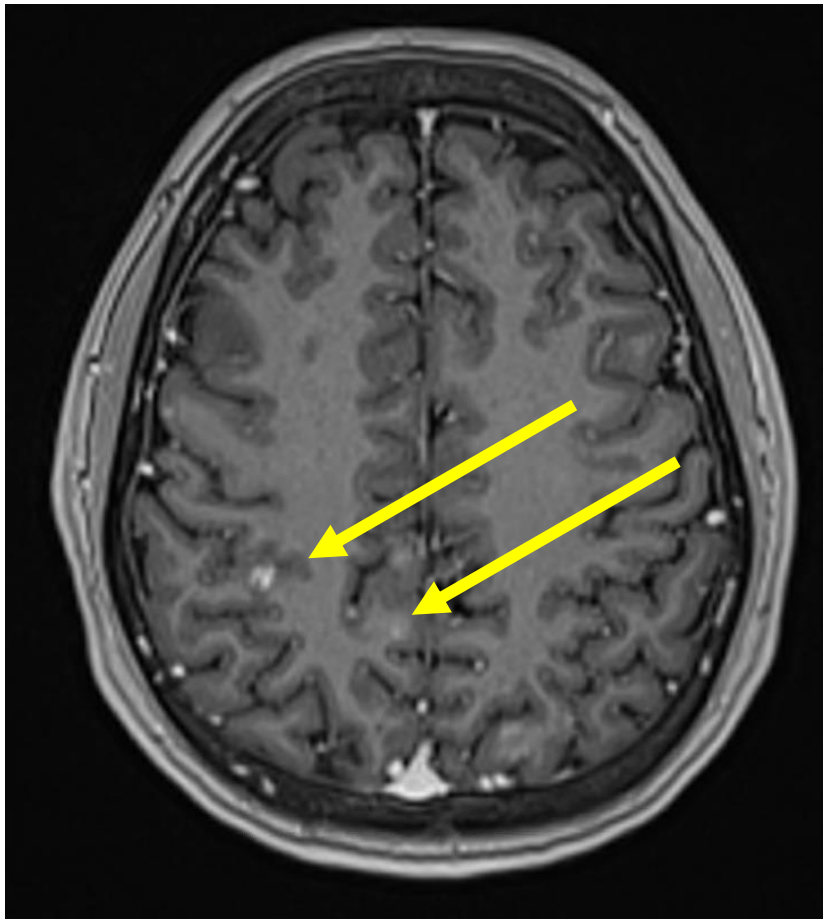
- Coccidioides serology negative
  - Does this rule out cocci infection?
    - EIA, IMDF, CF, antigen, culture
    - Can look for other things like eosinophilia
- Quantiferon negative
  - Remember also doesn't rule out infection
- Sputum samples: nothing on stain and cultures pending (may not going to get any growth for days-weeks)
- Where else can we look for the diagnosis in the meantime?
  - Some urgency in an immune compromised patient

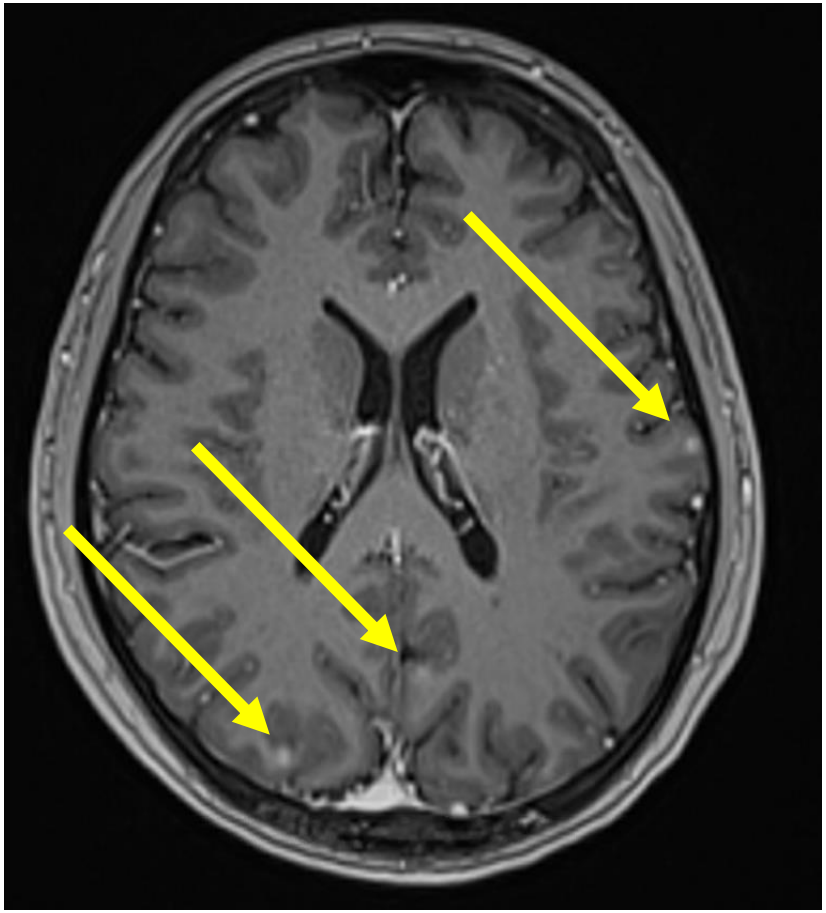
Skin biopsy: ameba?

- Well, that's not what we expected…
- Got additional imaging based on known natural history of this disease



Numerous lesions throughout brain, brainstem, but normal mental status





Balamuthia vs acanthamoeba

- Called CDC, suspected acanthamoeba based on distribution
- Started pentamidine, flucytosine, fluconazole, sulfadiazine, azithromycin
- Next day started miltefosine when got here
- Sent PCR of tissues to confirm
  - Positive for Balamuthia from skin and lung biopsy specimens. Negative from CSF sample

Course

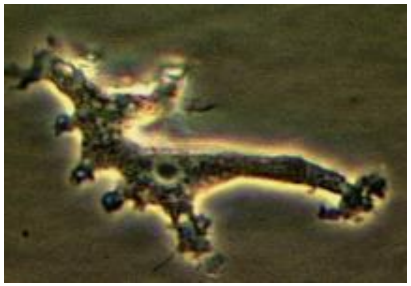
- Initially was stable, then developed progressive hypoxia, altered mental status and obtundation, respiratory failure
  - Later AKI likely due to adverse effects from his regimen
- Given known >90% mortality rate family decided not to escalate care and patient died a few days later

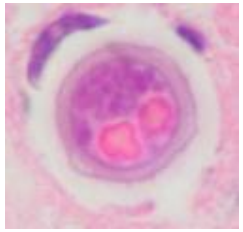
Free living ameba

- Naegleria
  - “Brain eating ameba”
  - Warm waters, thought to invade cribiform plate
    - Sometimes associated nasal irrigation
- Acanthamoeba
  - Granulomatous encephalitis and other organs, especially in immune compromised patients
  - Contact lens keratitis
- Balamuthia
  - Granulomatous encephalitis, can involve other organs
  - Can have skin and other findings
  - Can involve immune competent patients

Balamuthia mandrillaris

- Not recognized as a pathogen until the late 1980s when a pregnant mandrill at the San Diego zoo died from it
- Over 100 cases described in humans in the US since then
  - >90% mortality
  - 3 children in Southern AZ have contracted this illness and died in the last 15 years





15 y/o with fever and a rash

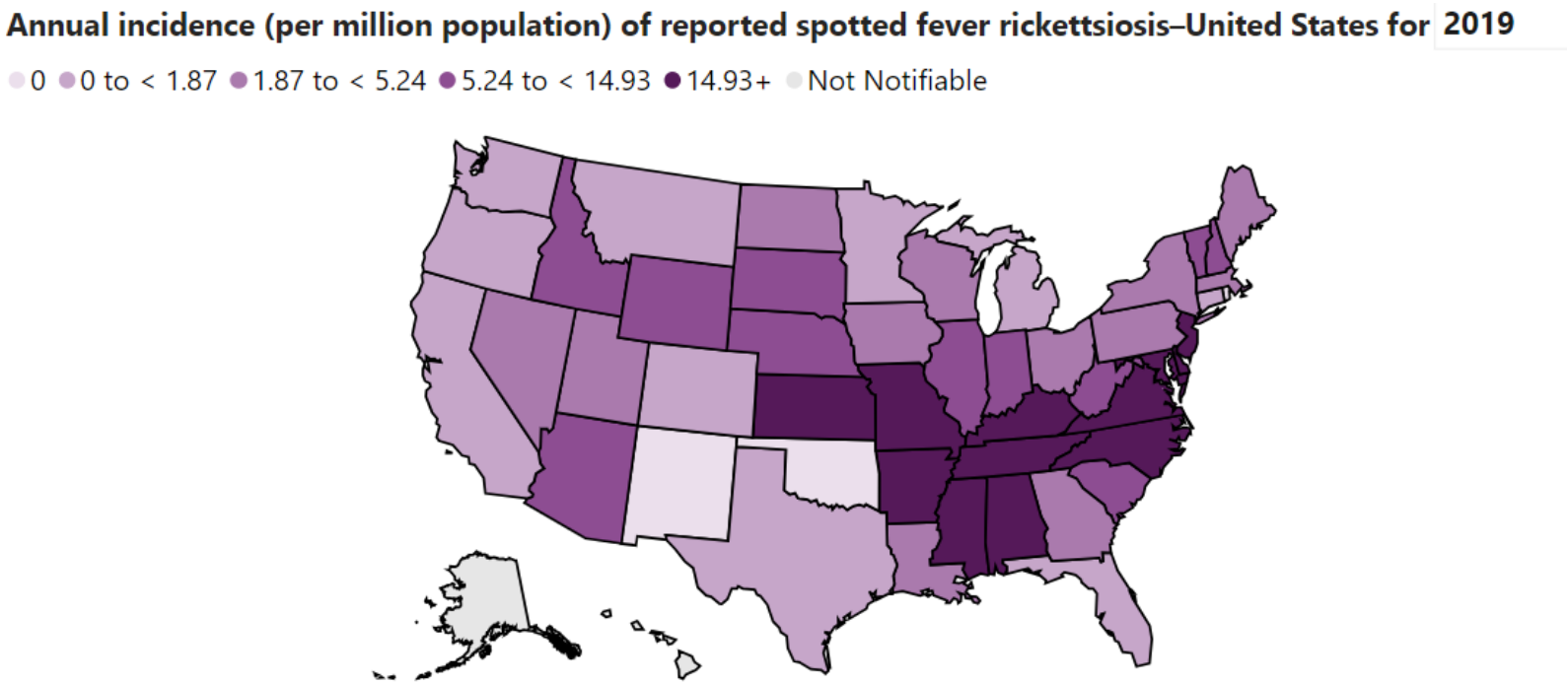
- Headache for a few days
- Fever for 5 days up to 103
- Started with red papules on arms and legs, now spreading to the trunk and now has petechiae
- Sodium is 128, platelets 90k
- From the Whiteriver area
- What does he have?

Classic RMSF

- Triad fever, headache, rash
  - But the full triad often isn't present, especially early on
  - Classic rash: peripheral, spreading centrally
    - Maculopapular, often becomes petechial
- Vasculitis that affects many organs of the body
- Can have hyponatremia and thrombocytopenia
- Many cases misdiagnosed at 1st visit
- Mortality of 20% if untreated
  - 5% if treated
  - Increased morbidity/mortality risk with each day delay in treatment
- Clinical diagnosis: serology often negative at presentation (and usually takes a few days to get results)

Feigin 2019;Traeger CID 2016

RMSF



- 470 cases reported in AZ since 2005
  - 5% mortality

https://www.cdc.gov/rmsf/stats/index.html

RMSF in AZ can be different

- Different tick
  - Rhipicephalus sanguineus
- Affects children more
  - More likely to be exposed to dogs/ticks
- Tends to cluster in Native American Reservations
- More common in communities with free-roaming dogs
- 67% without rash at presentation
  - 32% never developed a rash at all while ill
- 19% were afebrile
- 22% had CXR concerning for pneumonia

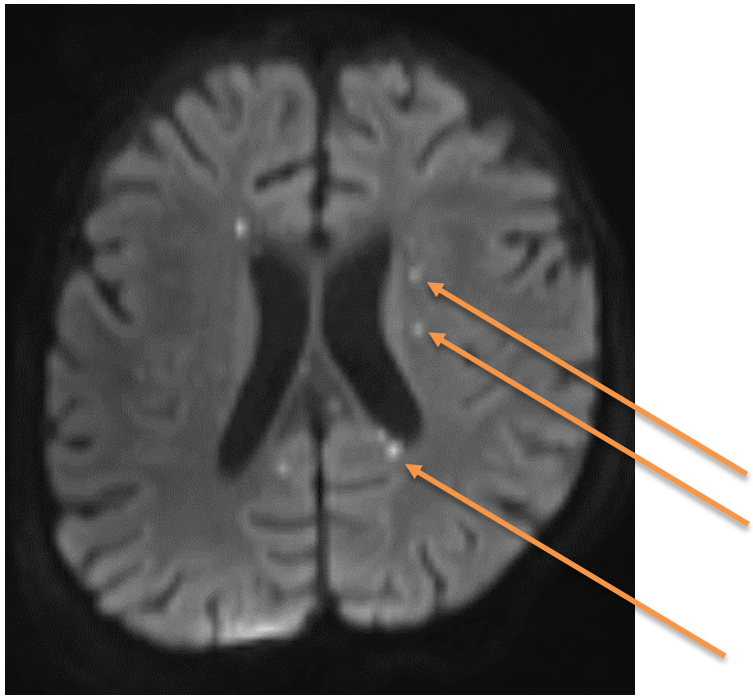
Traeger et al CID 2016

RMSF: Northern Mexico

- Similar characteristics to AZ
- Mortality rate higher at 33%
- Low rate of diagnosis at initial visit when most likely to have better outcome

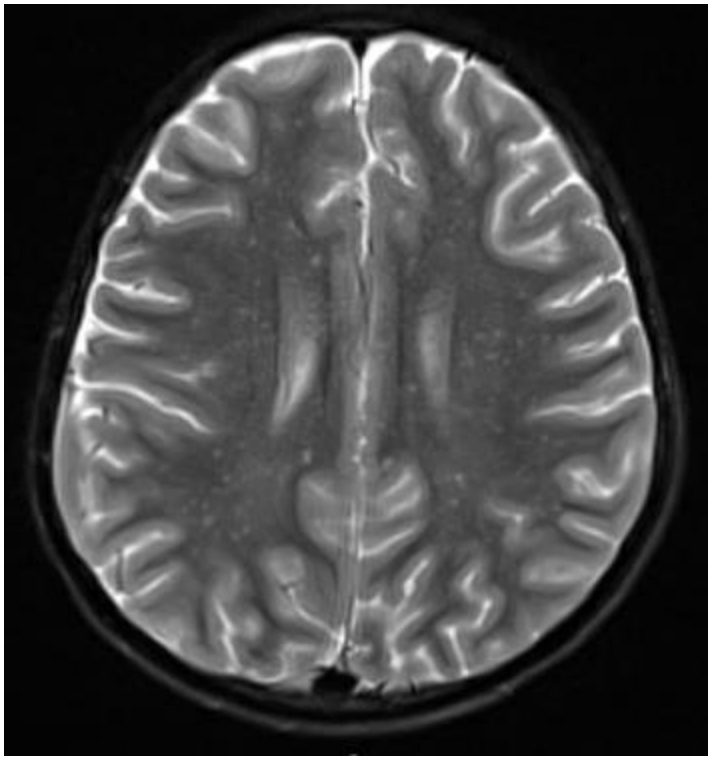
RMSF: It gets bad

- 14 month old missed diagnosis for about a week
  - Rash present for 5 days before onset of fever
    - Misdiagnosed and chickenpox and rubella
  - No known tick exposure
- AKI, retinal hemorrhages, myocarditis, digit necrosis, CNS infarcts, splenic infarcts
- Febrile for 2 weeks despite rx



RMSF: 3 y/o from Mexico

- 4 days of rash and fever
- Admitted with seizures



More RMSF

- 12 y/o with several days of fever, headache, petechial rash in AL
  - Had removed a tick several days before and went to the ED with onset of symptoms and notified the provider of the tick exposure
    - No Rx
  - Referred to heme/onc for petechiae
    - Recognized he had RMSF and admitted
  - Within hours became obtunded, developed ARDS requiring oscillator vent, developed abdominal compartment syndrome
  - Eventually recovered with rx

18 y/o with jaundice

- Southern AZ
- Fever to 104 and rash for a few days
  - Rash started on the chest/abdomen, was maculopapular
- Had some sore throat
- Has gotten various antibiotics in Mexico without improvement
- No concerning exposures
- Tbili 17, dbili 13, ALT 120, nl coags, Na 129
- WBC 38K (neutrophil predominant), PLT 60, nl H&H
- What's he got?

RMSF again

- Rash evolved to petechiae the next day
- Started on Doxycycline in addition to other broad spectrum abx to cover other possible bacteria
- Tbili, ALT, platelets, Na and WBC all slowly improved
  - Febrile for a week on treatment
- Remember that RMSF doesn't always follow the book. Don't be afraid to treat with doxy and assess response.
- Sometimes the answer is: "I think this patient has a doxycycline deficiency"
  - Safe to use in all ages

15 y/o male with fever and shoulder pain

- Goes to an urgent care on the day of onset of fever/pain
  - Had been lifting weights and playing basketball, no known injury
  - Temp is 101, normal heart rate, RR and O2 sats
  - Has some congestion and mild cough. Scattered crackles on pulm exam
  - Mild proximal biceps tenderness, but not red/swollen
  - WBC 21 (mostly neutrophils),
  - Mycoplasma IgM is positive
  - CXR and arm xray normal
- Prescribed azithro and home
- Any red flags?

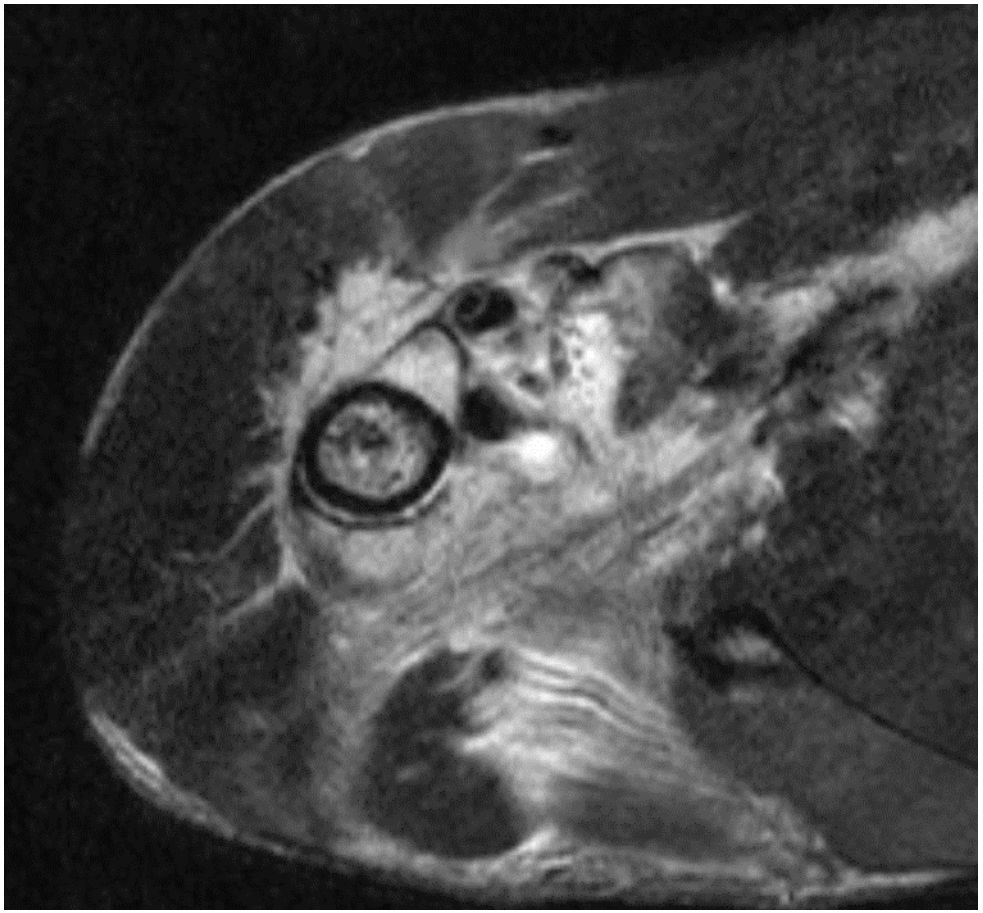
2 days later

- Fever is worsening to 104
- Arm pain is much worse
- Cough is improved
- Goes to another urgent care
  - Normal pulmonary exam
  - Biceps tender, warm
  - Noted positive mycoplasma, told to continue azithro and follow up as needed
- Any red flags here?

2 more days go by

- Still has fever to 104
- Arm pain much worse and now involves shoulder, upper arm and elbow.
- Elbow is swollen; elbow/arm/shoulder tender on exam
- CRP 30mg/dl
- MRI is done

MRI



Course

- Findings: osteomyelitis of the humerus, septic arthritis of the shoulder and elbow, myositis with soft tissue abscess
- I&D grew fusobacterium
- Slowly improved and regained function after antibiotics and I&D

What went wrong here?

- Early assessment wasn't off base
- Pay attention to the natural history of disease
  - Mycoplasma ab are tricky
    - IgM can be positive for 6 months and longer
  - Fever can be persistent with antibiotic treatment in mycoplasma pneumonia
    - But the cough was improving and MSK pain/swelling became more prominent
  - Consider superinfection or coinfection
- Why didn't the xray show osteomyelitis or septic arthritis?
  - Need >50% demineralization which doesn't usually occur for at least 2 weeks (if at all)

Bacterial MSK infection in children

- Pyomyositis, septic arthritis, osteomyelitis
- Usually hematogenously spread
  - Staph aureus, Group A strep, strep pneumo, salmonella, (kingella in young children)
    - Fusobacterium is quite rare
  - Rapid progression and death is possible
- Can see contiguous spread, traumatic/surgical complications less commonly

Bacterial MSK mimics

- Viral myositis
- Toxic synovitis
- Just happened to sprain an ankle while having a viral URI
  - But minor trauma often precedes septic arthritis/osteo

Don’t miss bacterial MSK infection

- Fever + focal MSK pain + abnormal focal exam = MRI
- Fever + focal MSK pain + elevated CRP = MRI
- U/S if joint, especially hip
- Tap the joint for diagnostics when indicated
- Get blood cultures
- Remember: Negative Xray isn’t good enough

18 y/o with skin lesions

- Few months ago started with a nodule continues to increase in size.
- Over next few months ulcerates and develops subcutaneous nodules on his arm
  - No improvement with various antibiotics
- No systemic symptoms
- Works with livestock in Southern AZ

What's on your differential?

- Cocci
- TB
- Mycobacterium marinum
- Nocardia
- Non infectious skin conditions
- Sporothrix

- Biopsy confirmed Sporothrix schenckii
- Treated with itraconazole and lesions resolved

2 other cases, similar stories

Sporothrix species

- Fungus that tends to be present in decaying plant matter
  - Minor injury leads to direct inoculation
  - Tends to be in more humid areas of the world
    - Only a few cases described in AZ
- Sphagnum moss: gardeners in the Midwest
    - Classic rose thorn injury boards question
- 1940's thousands of gold miners in the Transvaal infected, likely from rotting timbers
    - Outbreak improved when they sprayed the timbers with fungicide
- Various outbreaks around the world associated with hay
- All 3 of our patients handled hay

AAP Red Book

12 y/o boy with fever and thrombocytopenia in the Winter

- 1 week of fever, sore throat, mild intermittent non bloody diarrhea, NBNB emesis x4, temp up to 101
  - No cough/dyspnea/chest pain, rash, MSK pain/swelling, adenopathy
- FSGS diagnosed 9 months ago
  - Has been on 60mg of prednisone for months

Exam

- Afebrile at initial evaluation
- Tachycardic (103), II/VI SEM, good cap refill
- Mildly distended abdomen with liver edge palpable 1-2 cm below costal margin
- Stable pitting edema LE bilaterally
- o/w nothing major

Labs

- Normal WBC, H&H but platelets in the 77k range
- BUN and creatinine elevated above baseline

Red Flags?

- More of a combination rather than any one thing
  - Immune compromised state
  - Abnormal labs: low Plt, BUN/Cr above baseline
  - Physical exam findings: tachycardic though afebrile
    - Dehydration?

What's on your differential

- Bacteremia/sepsis (fevers, imm comp, low plt)
- GI pathology
  - GI bug, intraabdominal infection/abscess, etc
- Viral things
  - EBV, CMV, respiratory/GI viruses
- And much more…

Missing key history points

- Actually… he was born in Tanzania and lived his whole life in a refugee camp until 8 months ago when he emigrated legally to the US and has been in Tucson since then
  - Sometimes the travel history is obvious, other times not so much
    - Don’t forget to ask

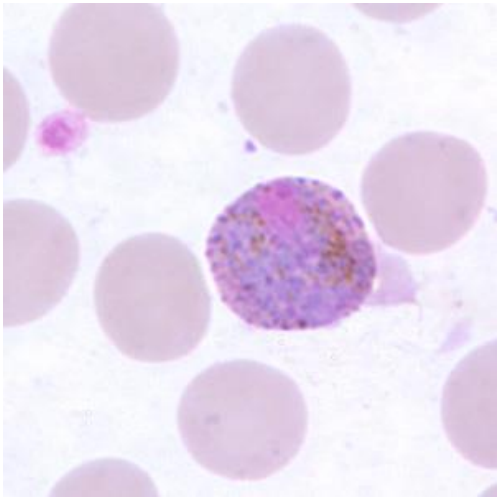
What do you add to your differential now?

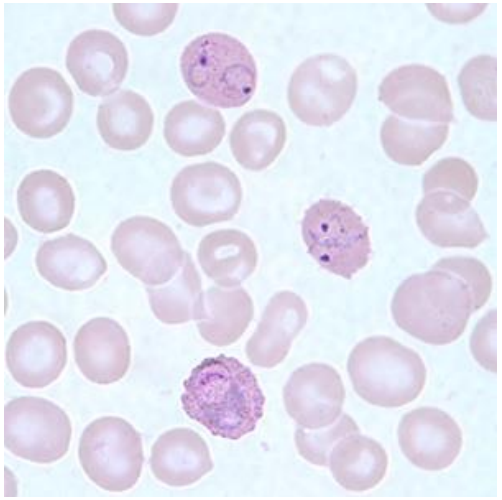
- TB
- HIV
- Malaria
- Typhoid
- More recent travel may add on other things

- Patients that emigrate legally, especially from Africa usually go through an evaluation process
  - Test for TB
  - Often empirically treat for malaria
  - Often empirically treat for intestinal parasites
  - No longer screen for HIV
- Our patient received these treatments prior leaving his country of origin

The lab calls…

- Ring forms and gametocytes in the smear consistent with malaria.
- How is this possible if he got treated for malaria 9 months ago and he hasn’t been symptomatic until now?





https://www.cdc.gov/dpdx/malaria/

Malaria

- Acute phase of fever within days to weeks of mosquito bite
  - Severe disease with rapid progression is possible, especially with *P. falciparum*
  - Rapid diagnosis and treatment is needed
- *P. ovale* and *P. vivax* often cause milder disease but produce hypnozoites that infect the liver and can reactivate months to years later
  - Can prevent by treating with primaquine if they don't have G6PD deficiency
- Many travelers don't take malaria prophylaxis
  - Visiting friends and relatives

Conclusion

- Zebras are rare
  - Good history and physical can often help you cut to the chase
- Rethink things when the typical course isn't being followed
- Red flags
  - Cytopenias
  - Prolonged fevers
  - MSK findings
  - Weight loss
  - Markedly elevated inflammatory markers

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