

# Infectious Diseases Cases

2022 Montana ACP Chapter Annual Scientific Meeting  
September 15-17, 2022  
Providence St. Patrick Hospital

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# Disclosure

- ▶ Aaron Derry: none
- ▶ Dr. Claude Tonnerre: none



# Case 1: A 68 year-old female with left-sided weakness

- ▶ 68 yo female with a history of diastolic CHF, childhood rheumatic fever, mild mitral stenosis and mild aortic insufficiency
- ▶ Presenting with worsening LUE and LLE weakness
- ▶ No international travel, lives in Lake County



# Case 1 – 68 yo female with weakness

She has:

- A. CVA
- B. Neurosyphilis
- C. Cervical epidural abscess
- D. Toxoplasmosis
- E. Brain abscess
- F. Brain tumor
- G. Some kind of parasite eating her brain



# Case 1: A 68 year-old female with left-sided weakness

## HPI:

- ▶ Initial sxs ED 2/27 – L wrist swelling and pain. No weakness. L wrist sprain versus tendinitis, carpal tunnel syndrome. VSS
- ▶ 3/2 – PCP, normal exam, ? Hand tendinitis, Steroids rather than NSAIDs due to renal insufficiency. VSS
- ▶ 3/18 PCP – “persistent L hand numbness and tingling ... splint seems to help”, seemed to be in median nerve distribution, no TIA/CVA like sxs
- ▶ 3/25 EMG, “no evidence of carpal tunnel or ulnar nerve problems”, ordering MRI C spine
- ▶ 4/5 PCP: L cervical radiculopathy like sxs, L foot tingling, something like foot drop, no back or neck pain. Ordered MRI C spine and head CT



# Case 1: A 68 year-old female with left-sided weakness

- ▶ 4/6 – fall, seen by another provider, sent to ED and admitted
- ▶ VSS
- ▶ Normal exam except L sided weakness, 4/5 strength major muscle groups RUE, 3/5 L hip flexion, 4/5 knee flexion, foot dorsi/plantar flexion
- ▶ Labs normal (WBC 7.3, Hg 13.1, Plt 312 ... Cr 0.98, CO2 21 (gap 9) LFTs WNL
- ▶ MRI brain is abnormal...



# Case 1: A 68 year-old female with left-sided weakness





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What are you thinking now?

- ▶ A. CVA
  - ▶ B. Neurosyphilis
  - ▶ C. Cervical epidural abscess
  - ▶ D. Toxoplasmosis
  - ▶ E. Brain abscess
  - ▶ F. Brain tumor
  - ▶ G. Some kind of parasite eating her brain
- 
- ▶ A procedure was performed...



# Case 1: A 68 year-old female with left-sided weakness

- The **yellow circle** shows the scolex, or anterior head of the tapeworm.
- The **red circle** shows the hooks
- The **green circles** show suckers





# Case 1: A 68 year-old female with left-sided weakness

What are you thinking now?

- ▶ A. CVA
- ▶ B. Neurosyphilis
- ▶ C. Cervical epidural abscess
- ▶ D. Toxoplasmosis
- ▶ E. Brain abscess
- ▶ F. Brain tumor
- ▶ G. Some kind of parasite eating her brain



# Case 1: A 68 year-old female with left-sided weakness

- ▶ Subsequent hospital course
- ▶ Patient had resection of the lesion
- ▶ Pt was placed on steroids and anti-seizure medicine (taper after 6 months)
- ▶ Discharged to inpatient rehab
- ▶ Eye exam showed no ophthalmologic involvement
- ▶ Pt received 14 days of albendazole
- ▶ At follow up 4 months later, using an AFO for L leg, still with some plegia.



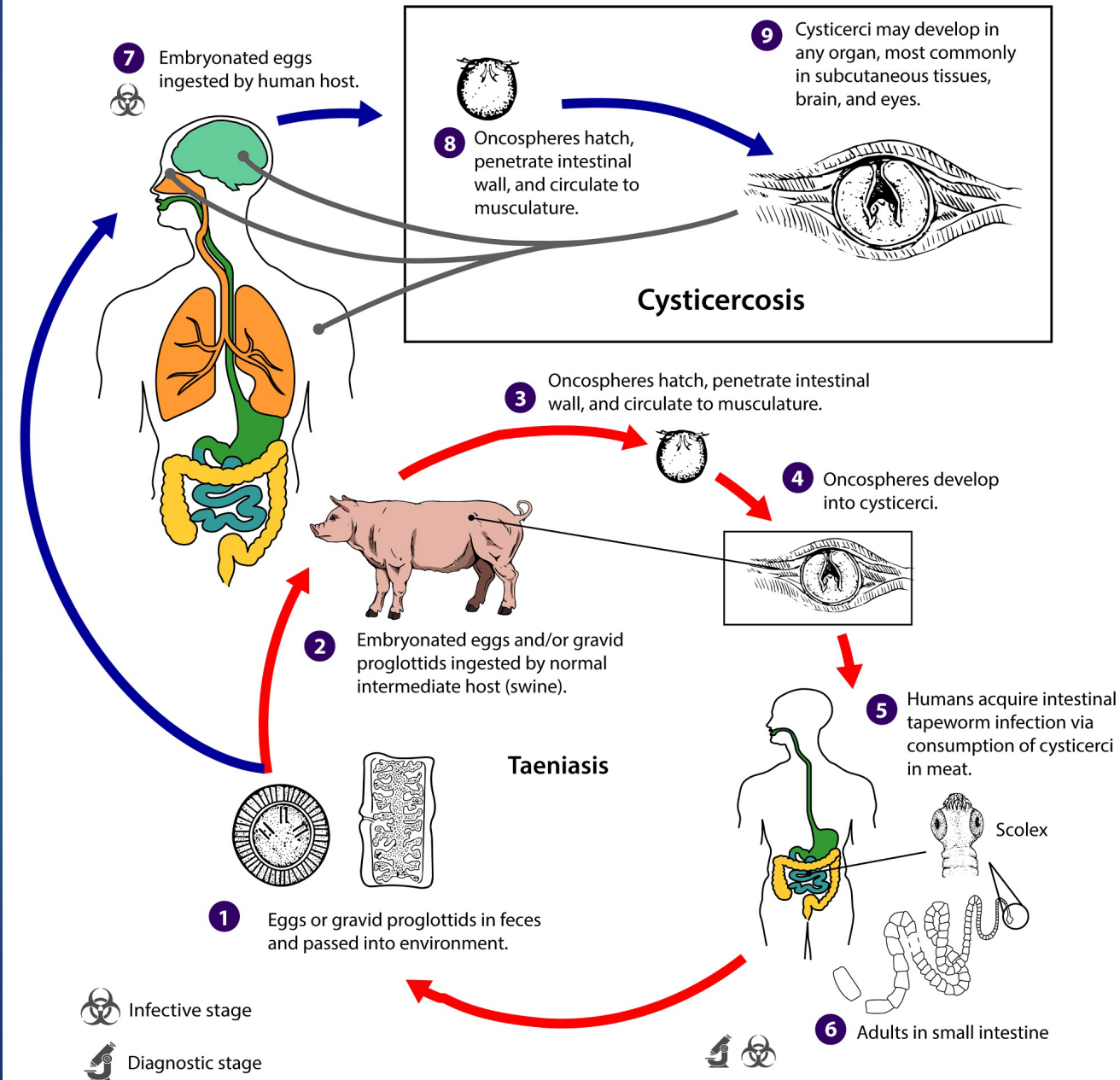
- ▶ From UpToDate:
- ▶ Endemic in Central and South America, sub Saharan Africa, India and Asia
- ▶ Highest prevalence in communities where pigs are raised and sanitation suboptimal.
- ▶ Seizure disorders in some communities as high as 3% with 30% of these with evidence of cysticercosis.
- ▶ *Taenia solium* can cause 2 distinct syndrome in humans:

1) Taeniasis (intestinal *Taenia* infection), which can come from undercooked pork (cysticerci in meat).

2) Cysticercosis, which is acquired by ingestion of embryonated eggs, (fecal -oral): a common misconception is that cysticercosis is acquired directly by eating pork. However, as the life cycle illustrates, ingestion of infected pork only causes adult tapeworm infestation (taeniasis); infected pork contains the larval cysts that develop into adult worms in the human intestine, but does not contain the eggs that cause cysticercosis



*Taenia solium*





# Cysticercosis

- ▶ Clinical manifestations and natural history (from UpToDate:
- ▶ Viable cysticerci are round, hypodense lesions (usually 5 to 20 mm in diameter) on computed tomography (CT). Viable cysticerci do not cause much inflammation in surrounding tissues and typically do not enhance after contrast administration.
- ▶ Cysticerci degenerate when attacked by the host immune response. The cyst wall increases in density and is often accompanied by edema and/or contrast enhancement; such findings reflect the host inflammatory response against the parasite and are frequently associated with seizures. In many cases, enhancing cysticerci retain features of viable cysticerci. When the cyst fluid begins to increase in density, the cysts are thought to no longer be viable.
- ▶ Nonviable cysticerci are solid, calcified nodular lesions (usually 2 to 4 mm in diameter; range 1 to 10 mm); they are usually nonenhancing but may be associated with perilesional edema in some cases. They are also associated with seizures.



# Cysticercosis

- ▶ Management (from UpToDate):
  - ▶ Manage ICP
  - ▶ Antiseizure medication in case of seizure
  - ▶ Combined antiparasitic and steroid therapy:
- ▶ Antiparasitic therapy is warranted for patients with viable and/or degenerating cysts in the brain parenchyma on neuroimaging. Administration of antiparasitic therapy and glucocorticoids depends on the number and characteristics of the cyst(s) on neuroimaging:
  - 1) Antiparasitic therapy is not indicated for patients with untreated hydrocephalus, cysticercal encephalitis, or calcified lesions only.
  - 2) For patients with one to two parenchymal cysts, we suggest treatment with albendazole rather than no antiparasitic therapy (**Grade 2A**).
  - 3) For patients with more than two parenchymal cysts, we suggest treatment with albendazole and praziquantel rather than monotherapy (**Grade 2C**).
- ▶ The duration of antiparasitic therapy is 10 to 14 days in most cases; patients with subarachnoid disease warrant an extended duration of antiparasitic therapy
- ▶ We recommend adjunctive administration of corticosteroids with antiparasitic therapy (**Grade 1C**). The optimal regimen is uncertain; commonly used regimens include prednisone (1 mg/kg per day) or dexamethasone (0.1 mg/kg per day) begun at least one day prior to antiparasitic therapy, continued for the duration of antiparasitic therapy, and followed by a rapid taper.



# Case 2: A 59 year-old male with pain all over and disseminated cutaneous lesions

## HPI:

- ▶ 59 yo male with renal transplant 11/3/2009 (polycystic kidney disease). First transplant 1989, then dialysis from 2001-2009.
- ▶ He was sent from vascular clinic “for evaluation of possible infected forearm hematoma. The patient has multiple medical problems, also including recent discovery of 3x3 cm LUL mass, fungating scalp lesion, and atrial fibrillation. He was hospitalized here in late April for angioedema blamed on his ACE inhibitor. Following that admission, he developed some redness and swelling to his right arm and was started on doxycycline for possible cellulitis a week after discharge”
- ▶ Mycophenolate 1 g bid, prednisone 7.5 mg daily, tacrolimus 0.5 mg bid, warfarin, spironolactone, labetalol, indapamide, clonidine, diltiazem, allopurinol



# Case 2: A 59 year-old male with pain all over and disseminated cutaneous lesions

## Exam

- ▶ Afebrile, tachycardic (irregular), normal respirations
- ▶ RUE old fistula proximally, forearm with large tender, fluctuant area, surrounding erythema, induration
- ▶ L wrist tender, limited ROM
- ▶ Large fungating mass on frontal scalp, minimal surrounding erythema
- ▶ 1 inch fluctuant area posterior L shoulder



# Case 2: A 59 year-old male with pain all over and disseminated cutaneous lesions

## Lab and imaging

- ▶ WBC 17.5 (88.7% neutrophils), Hg 14.5, Plt 172
- ▶ Lactate 2.4
- ▶ Na 126, K 5.8, Cr 2.52, Alb 2.9, LFTs WNL
- ▶ Scalp culture: 1+ GPCs in pairs and clusters on gram stain



L posterior thigh





# R frontal/temporal scalp





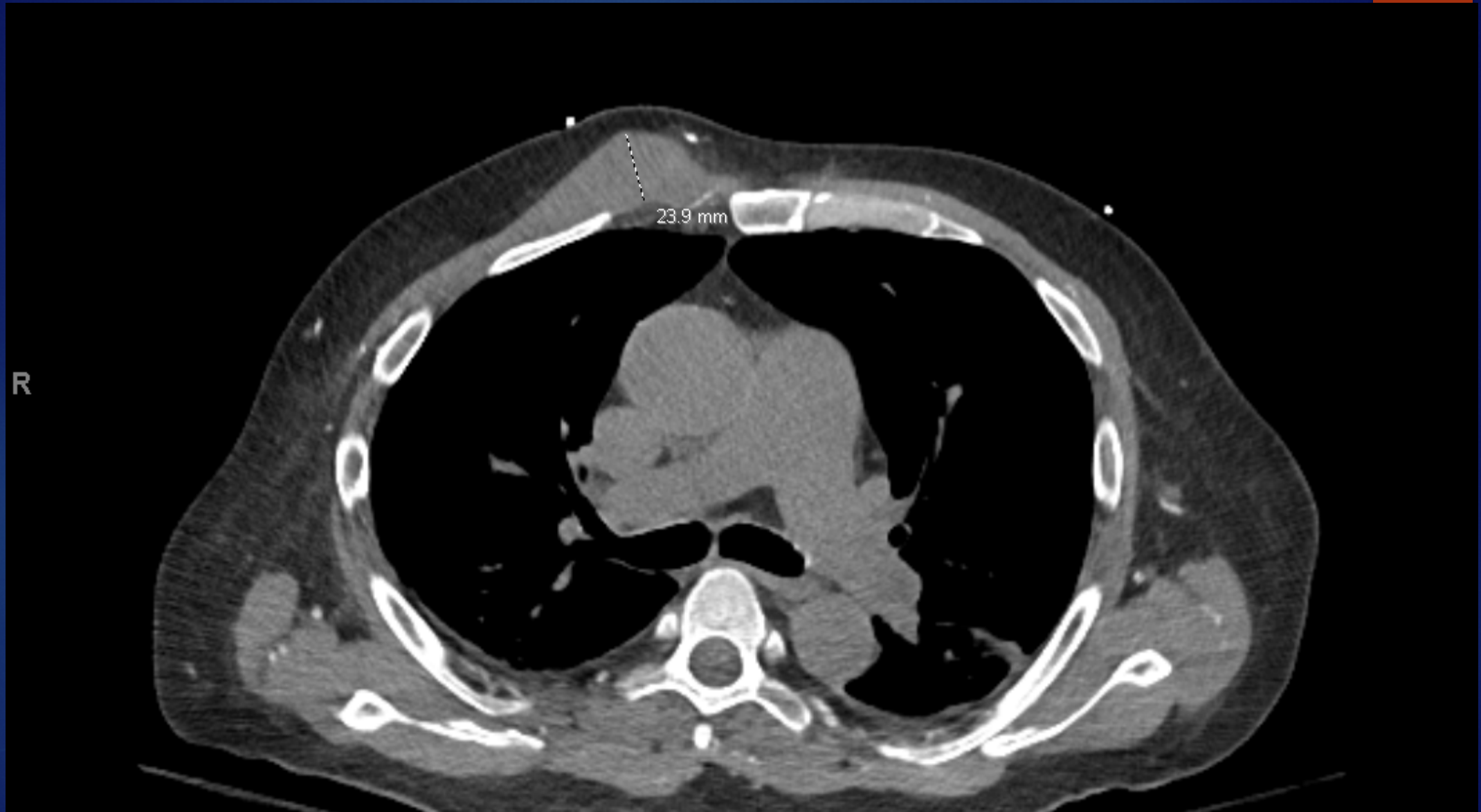
L forearm



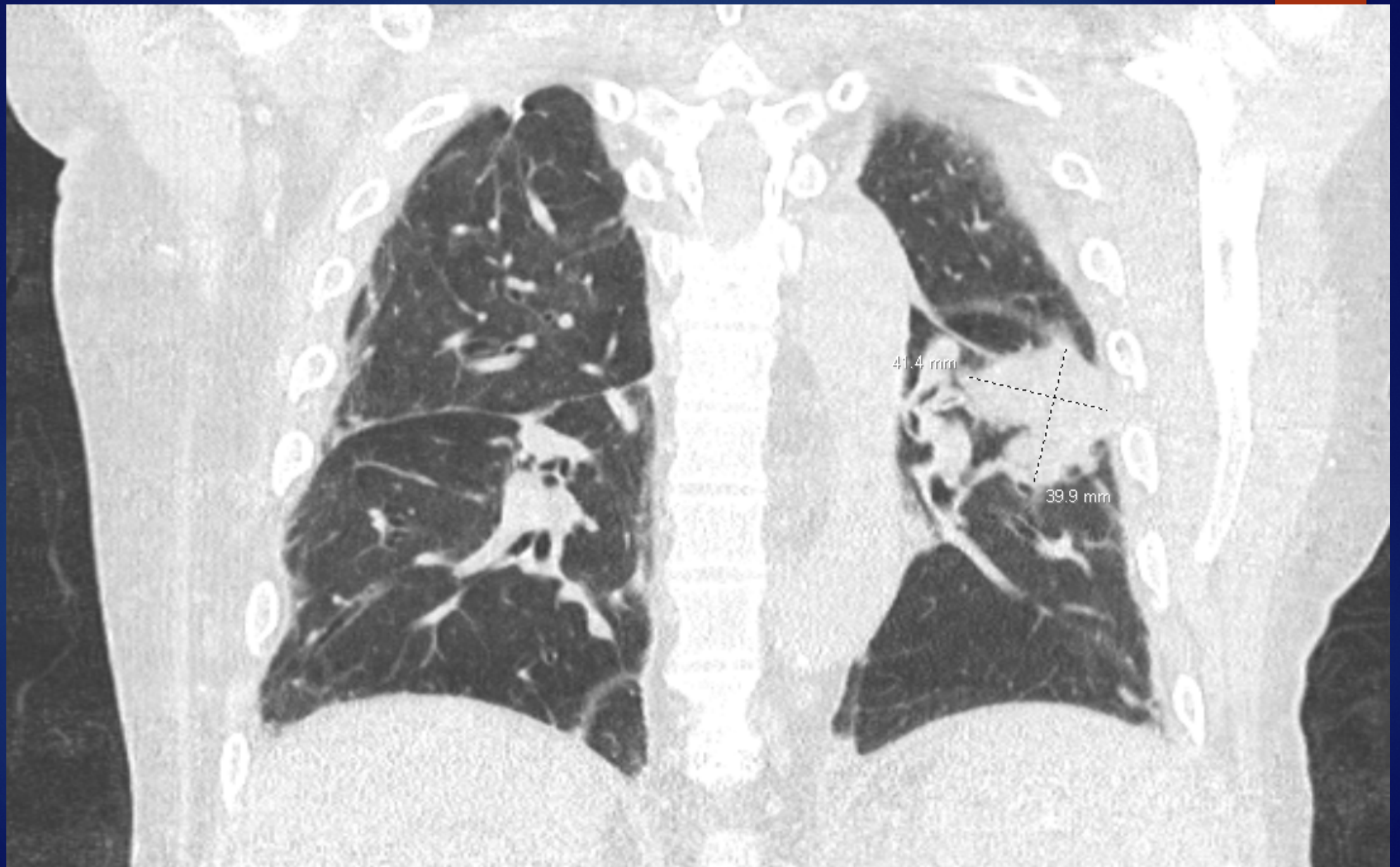
R forearm





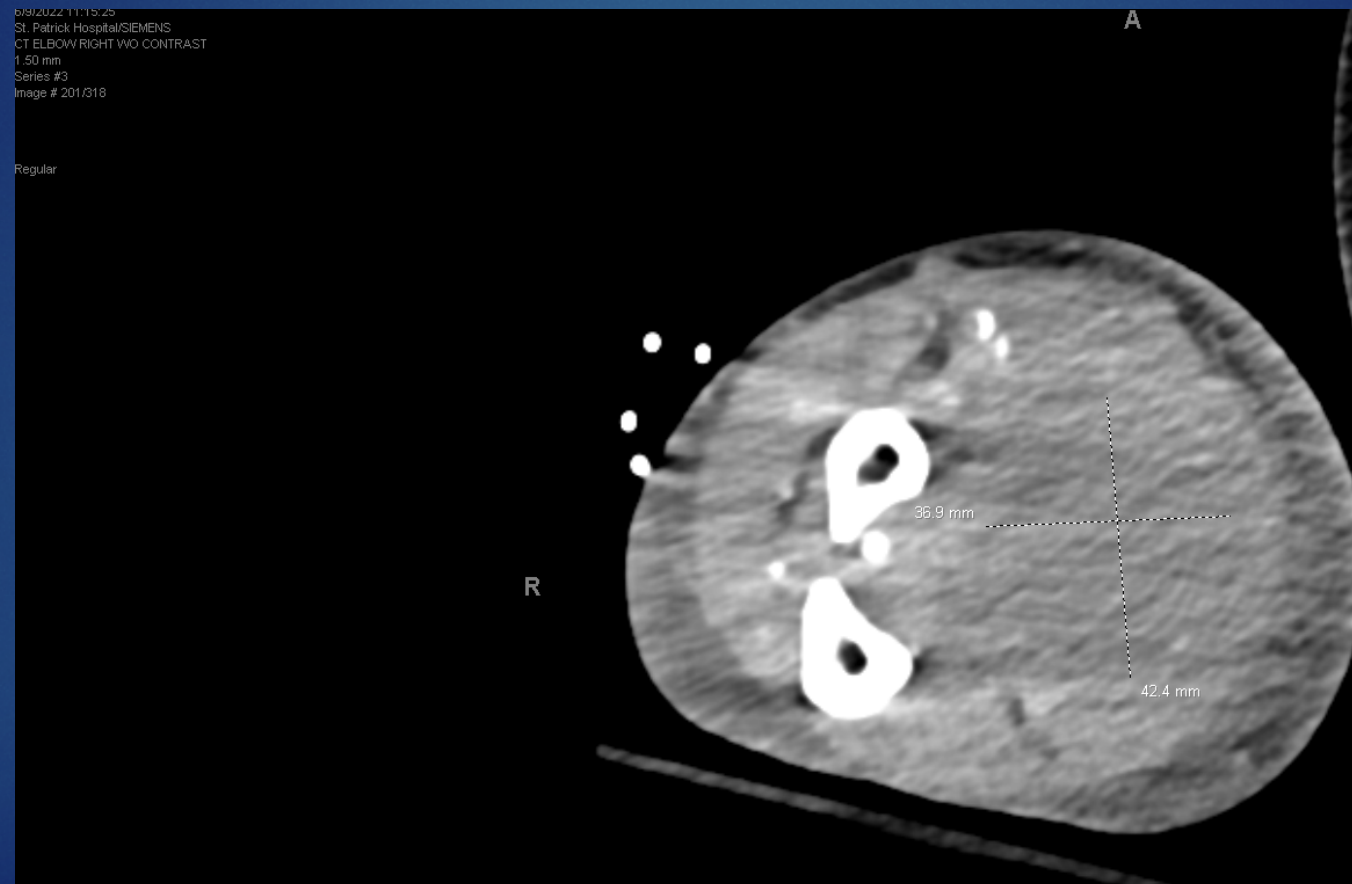








# R forearm





# R scalp lesion





# Case 2: A 59 year-old male with pain all over and disseminated cutaneous lesions

What is causing this?

- ▶ A) MSSA bacteremia with disseminated cutaneous abscesses
- ▶ B) Actinomyces abscesses
- ▶ C) Group B strep L sided endocarditis with peripheral stigmata
- ▶ D) Disseminated nocardia
- ▶ E) Disseminated rapid-growing Mycobacteria infection



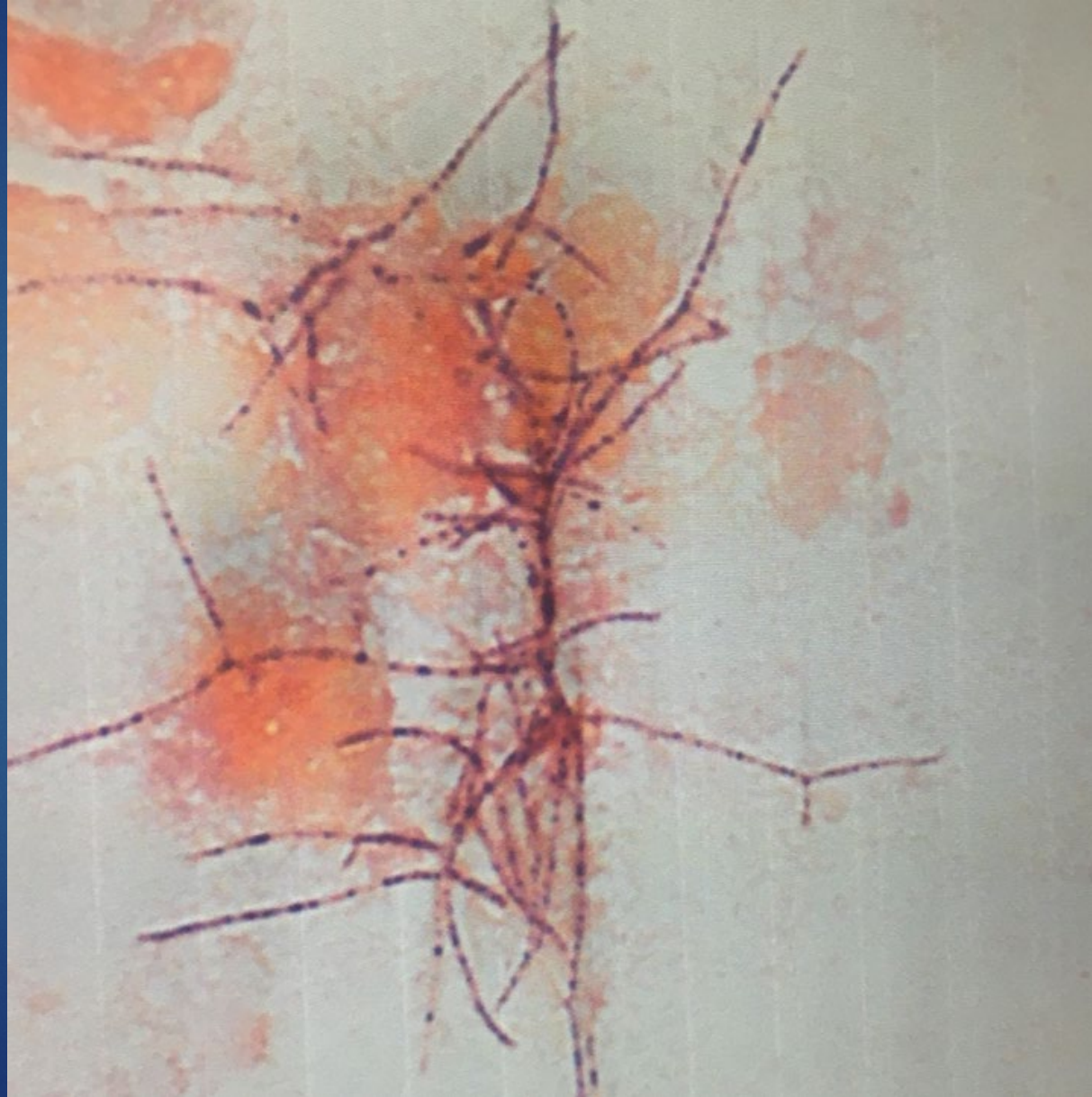
# Case 2: A 59 year-old male with pain all over and disseminated cutaneous lesions

Daytime micro over-read the gram stain: 1+ gram positive rods, branching, beaded filamentous rods

- ▶ 6/9: R arm with 3+ branching gram positive rods
- ▶ 6/10: R arm with branching gram positive rods
- ▶ 6/10: L shoulder: 2 + branching gram positive rods
- ▶ 6/13: L forearm 1 CFU cutibacterium acnes, 2+ branching gram positive rods



Gram stain  
from growth on  
aerobic plates





# Case 2: A 59 year-old male with pain all over and disseminated cutaneous lesions

What are you thinking now?

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# Nocardia

- ▶ Aerobic, Gram positive filamentous branching rods
- ▶ Found in soil rich in organic matter
- ▶ Usually acquired through inhalation or traumatic introduction
- ▶ Most commonly found in those with immune suppression but can be in hosts with normal immune systems



# Nocardia

- ▶ Sites of infection
  - ▶ Systemic (>2 sites involved) – 32% with 44 % with CNS involvement
  - ▶ Pulmonary only 39 %
  - ▶ CNS only 9%
  - ▶ Cutaneous/lymphocutaneous 8%
  - ▶ Single site extrapulmonary (eyes, bone) 12%
  
- ▶ From Clin Microbio Rev. 1994 Apr; 7 (2):213-64



## Brain MRI (DWI)

Brain MRI ordered due to high likelihood of CNS infection:

“4 mm focus of restricted diffusion and ring enhancement involving the high posterior left frontal lobe consistent with small brain abscess. “

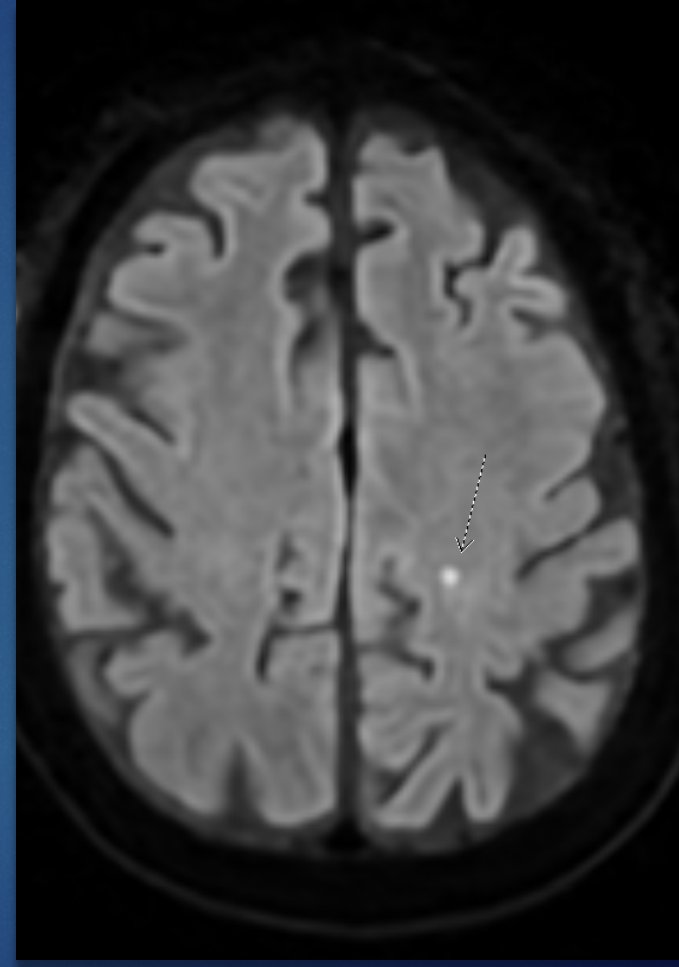




TABLE 1. Distribution of *Nocardia* spp. by the type of disease<sup>a</sup>

Species	No. of cases							Total
	Pulmonary (only)	Systemic + CNS <sup>b</sup>	CNS <sup>c</sup> only	Cutaneous + lymphocutaneous	Single site (extrapulmonary)			
					Eyes	Bone	Other	
<i>N. asteroides</i>	356	265 (113)	73	34	27	17	59	831
<i>N. brasiliensis</i>	8	20 (5)	3	43	0	2	7	83
<i>N. farcinica</i>	6	0 (0)	4	1	0	0	2	13
<i>N. otitidiscaviarum</i>	4	8 (5)	1	3	1	3	2	22
<i>N. transvalensis</i>	1	2 (2)	0	0	0	0	0	3
<i>Nocardia</i> spp.	37	39 (22)	10	1	1	4	6	98
Total	412	334	91	82	29	26	76	1,050



# Nocardia treatment

- ▶ Sulfonamides usually treatment of choice
- ▶ Minocycline, imipenem, ceftriaxone, linezolid also considered for empiric treatment
- ▶ Sensitivities are however quite variable, and final therapy should be based on actual results
- ▶ Typically 6 months of treatment or more



Source: Tissue

Body site: Cranium

Free Text Sources: Tissue

## Final Report

*Nocardia brasiliensis* / *Nocardia vulneris*

Identification by MALDI-TOF

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration.

This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

## Susceptibility Results

Organism: *Nocardia* species

Amikacin	Interpretation: SUSCEPTIBLE MIC (ug/mL): ≤0.5
Amoxicillin/Clavulanate	Interpretation: SUSCEPTIBLE MIC (ug/mL): 8/4
Ceftriaxone	Interpretation: SUSCEPTIBLE MIC (ug/mL): 8
Ciprofloxacin	Interpretation: RESISTANT MIC (ug/mL): 4
Clarithromycin	Interpretation: RESISTANT MIC (ug/mL): ≥32
Doxycycline	Interpretation: SUSCEPTIBLE MIC (ug/mL): 0.5
Imipenem	Interpretation: INTERMEDIATE MIC (ug/mL): 8
Linezolid	Interpretation: SUSCEPTIBLE MIC (ug/mL): 4



**Minocycline**

Interpretation: SUSCEPTIBLE  
MIC (ug/mL): 1

**Moxifloxacin**

Interpretation: SUSCEPTIBLE  
MIC (ug/mL): 0.5

**Tobramycin**

Interpretation: SUSCEPTIBLE  
MIC (ug/mL):  $\leq 2$

**Trimethoprim/sulfamethoxazole**

Interpretation: SUSCEPTIBLE  
MIC (ug/mL): 0.5/9.5



# Case 2: A 59 year-old male with pain all over and disseminated cutaneous lesions

- ▶ Pt had I and D of RUE mass as well as LUE mass
- ▶ Rx: Trim/sulfa 2 po tid, amox/clav 875 bid, CTX 2 g IV bid (DCd home 6/24). Also, tacrolimus 0.5 mg qd, mycophenolate stopped, pred 7.5
- ▶ 7/26: doing well, after 6 weeks of above, simplified to Trim/sulfa only
- ▶ 8/24: feeling better, MRI brain shows improvement, CT chest shows interval improvement, new “tree in bud” opacities, some rise in creatinine
- ▶ 9/7: admitted, ? CHF (has pending TAVR), some worsening of creatinine (2.2, best in last 6 months was 1.3). Switching off of trim/sulfa , starting doxycycline



# Case 2: A 59 year-old male with pain all over and disseminated cutaneous lesions





# Case 3: A 74-year-old lady with a skin lesion and enlarged lymph nodes

- ▶ The patient is a 74 y.o. lady with no specific past medical history.
- ▶ After a hike in the Bitterroot area, where she thinks she may have been bitten by an insect, she developed a lesion on the upper chest.
- ▶ A few days later, the lesion became inflamed and she started to notice enlarged lymph nodes at the base of the neck, as well as a fever up to 102.
- ▶ She was taking Advil and Tylenol. She was initially seen in the emergency room and prescribed cephalexin, but due to worsening symptoms, she was reassessed on July 27 and she was prescribed trim/sulfa .
- ▶ A culture was obtained, and she was switched to empirically ciprofloxacin



# Case 3: A 74-year-old lady with a skin lesion and enlarged lymph nodes

July 23:





# Case 3: A 74-year-old lady with a skin lesion and enlarged lymph nodes

July 27:





# Case 3: A 74-year-old lady with a skin lesion and enlarged lymph nodes

What are you thinking ?

- ▶ A) MRSA infection
- ▶ B) Tularemia
- ▶ C) Bartonella
- ▶ D) Y.pestis
- ▶ E) rapid-growing Mycobacteria infection



# Case 3: A 74-year-old lady with a skin lesion and enlarged lymph nodes

What are you thinking ?

- ▶ A) MRSA infection
- ▶ B) **Tularemia**
- ▶ C) Bartonella
- ▶ D) Y.pestis
- ▶ E) rapid-growing Mycobacteria infection



# Tularemia

- ▶ Aerobic gram-negative bacterium
- ▶ Several subspecies, but *F.tularensis* subspecies *tularensis* is the most common pathogen
- ▶ Found predominantly in the Northern hemisphere
- ▶ Many routes of transmission:
  - Arthropods (ticks, mosquitoes, horse flies, fleas, lice)
  - Percutaneous or mucosal exposure (bite, scratch, skinning)
  - Contaminated food and water
  - Airborne (lab precautions!!)



# Tularemia

► Clinical manifestations:

- Ulcer glandular/glandular tularemia: Combined, these are the most common presentation of tularemia in the United States. This is likely the same disease process, except that in glandular tularemia, the initial skin lesion may have been missed, or may have healed before the lymphadenopathy develops.
- Ocular tularemia: Rarely occurs in the setting of direct inoculation of the eye.
- Pharyngeal tularemia: rarely occurs in United States, seen in the setting of epidemics related to contaminated water for instance.
- Typhoidal tularemia: unusual presentation in the setting of immunosuppression or sick patients, without any focal findings. Can be secondary to any mode of acquisition of the disease.
- Pulmonary tularemia: either a primary infection after airborne acquisition, or could be secondary to dissemination from other forms. In some areas in the United States, this can represent up to a quarter of the cases. Of note, unless there is a clear exposure history, the possibility of a bite is an event should be considered



# Tularemia

- ▶ Diagnosis usually made by parents serologies or culture (although the yield is not very high). Molecular technique not yet readily available. Again, please warn the micro lab in case of suspicion of tularemia.
- ▶ Treatment options: Please see table below from Up-to-date

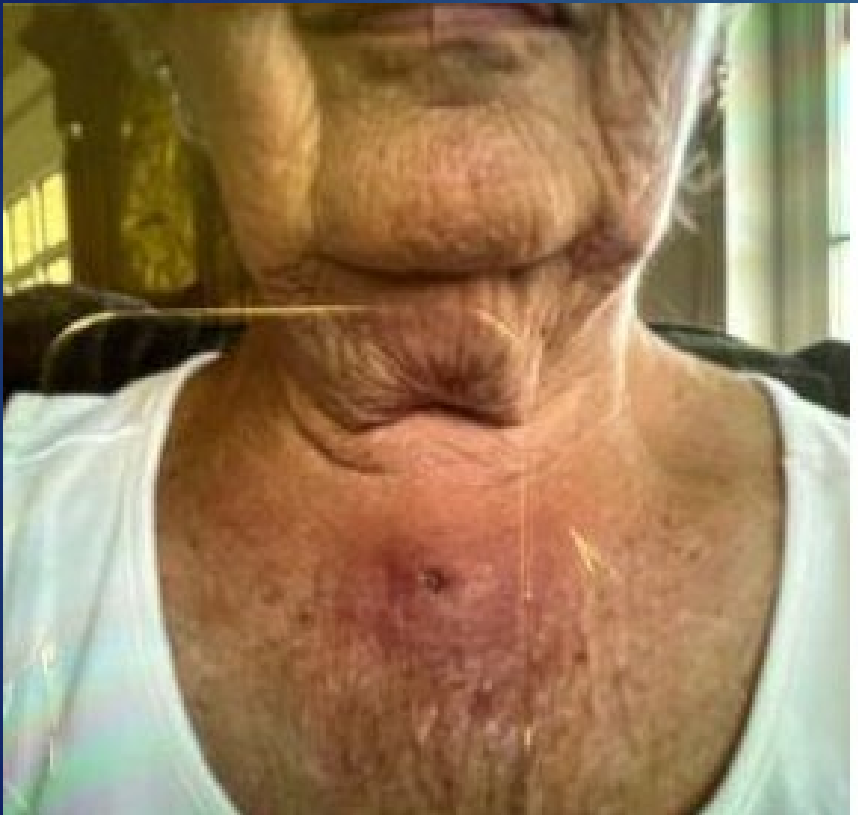
Antibiotics for treatment of tularemia

Drug	Adult dosing	Pediatric dosing
<b>Severe illness*</b>		
Streptomycin <sup>¶</sup>	10 mg/kg intramuscularly every 12 hours for 7 to 10 days (maximum daily dose 2 g)	30 to 40 mg/kg per day intramuscularly, in divided doses every 12 hours for 7 to 10 days (maximum daily dose 2 g) <sup>Δ</sup>
Gentamicin <sup>◇</sup>	5 mg/kg intramuscularly or intravenously daily, divided every 8 hours for 7 to 10 days	5 mg/kg intramuscularly or intravenously daily, divided every 8 or 12 hours for 7 to 10 days <sup>Δ</sup>
<b>Mild or moderate illness<sup>§</sup></b>		
Doxycycline	100 mg orally twice daily for 14 to 21 days <sup>‡</sup>	Doxycycline is not recommended for treatment of tularemia in children
Ciprofloxacin <sup>‡</sup>	500 to 750 mg orally twice daily for 10 to 14 days	20 to 40 mg/kg per day orally divided two doses for 10 to 14 days (maximum daily dose 1 g) <sup>§</sup>

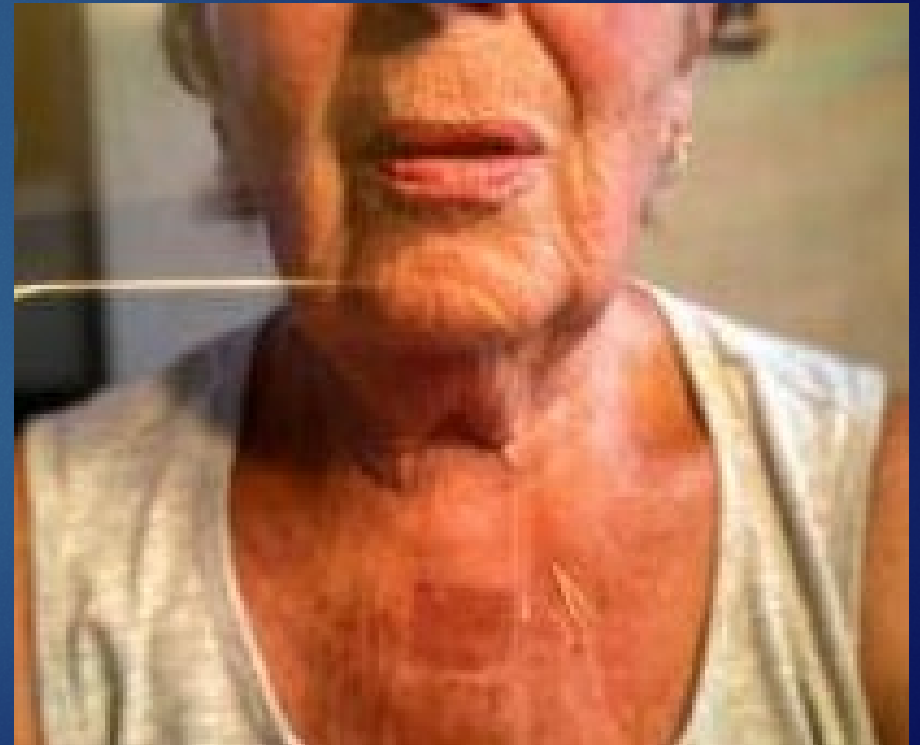


# Case 3: A 74-year-old lady with a skin lesion and enlarged lymph nodes

July 27:



August 8





# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

September 8 2020:

Patient is a 57 y.o. female who has a long history of Crohn's disease. The patient is on treatment with adalimumab. She reports a three-week history of progressive abdominal bloating and abdominal pain predominantly on the left side. The patient reports that her Crohn's disease is under good control currently. She denies any peripheral adenopathy. The patient did present to the emergency room. CT scan evaluation demonstrated moderate ascites with diffusely indurated mesentery and omentum. Thickening along the undersurface of the diaphragms is noted along with mild pathologic retroperitoneal and pericardial lymphadenopathy. No discrete mass was identified. The patient did undergo ultrasound paracentesis with removal of 600 cc of fluid. Pathology is pending although preliminary is nondiagnostic. The patient denies any fevers. She did receive some symptomatic relief from the paracentesis for reports increasing symptoms again.



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

September 28 2020:

Patient has ascites and thickened omentum with weight loss. Therefore there is definitely high concern that she has multiple peritoneal implants with a malignancy. We need a diagnosis to know what to do next. I have explained that to her and she understands. Case was also discussed with her oncologist Dr. Thomas.

Plan:

We will proceed with laparoscopy staying away from the left lower quadrant since she has previously had a colostomy. And then proceed with biopsy of any concerning material to get a diagnosis.



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

October 6 2020:

Procedure: Laparoscopy, conversion to laparotomy, Repair of Colotomy made by Trocar, Biopsy of Liver Capsule on Anterior superior Surface of Right Lobe of the Liver, Biopsy of Omentum, Biopsy of Peritoneum and Biopsy of Mesocolon Nodule

Pre-op Diagnosis: Failure to Thrive with Weight loss, Nausea, Thickened Omentum and Ascites

Post-op Diagnosis: same with nodular changes to surfaces, (Note: frozen section reveal no cancer and was suggestive of infection or inflammatory response)



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# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

October 7 2020:

She states that she is feeling better now that she has been placing antibiotics, **she endorses frequent travels to Brazil**, questionable allergy to clavulanic acid but tolerating cephalosporins well.

CT of the abdomen and pelvis from the 9/3/2020 showing multiple retroperitoneal and pericardial lymphadenopathies with ascitic fluid from the same day with results consistent with SBP. **Ascitic fluid cultures already showing GPC's.**

I have changed patient antibiotics, so far she is on ceftriaxone, Flagyl, vancomycin. Once we get more information will de-escalate antibiotics



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

October 8 2020:

## FINAL DIAGNOSIS

A. Liver, capsule, excisional biopsy:

- Liver parenchyma with surface **granulomatous inflammation** (see comment).

B. Omentum, excisional biopsy:

- Adipose tissue involved by **granulomatous inflammation**.

C. Peritoneum, biopsy:

- Fibrous tissue involved by **granulomatous inflammation**



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

October 8 2020:

## ADDENDUM

The granulomas are **noncaseating**. No foreign bodies are identified under polarized light. Broad spectrum AFB and fungal PCR analysis has been ordered, the results of which will be reported in an addendum. **Differential considerations are broad and include infectious organisms, postoperative granulomatous peritonitis, drug-induced and sarcoidosis, among others.**



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

CT abdomen September 3 2020:





# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

What are you thinking ?

- ▶ A) Crohn's disease flare
- ▶ B) Lymphoma
- ▶ C) Tuberculosis
- ▶ D) Histoplasmosis
- ▶ E) Cryptococcus



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

Positive Quantiferon, with a history of negative quantiferon in the past

November 18, 2021:

11/18/2020 2:08 PM - Edi, Lab Results In 771373

Specimen Information: Abdomen; Tissue

Component

AFB Smear Result

Negative

AFB Specimen Processing

Direct Inoculation

AFB CULTURE !

Positive

Comment:

Acid-fast bacilli have been detected in culture at 6 weeks; see AFB  
Organism ID by DNA probe

! AFB ID by DNA Probe

Component	1 yr ago
M. tuberculosis DNA	Positive !
M. avium Complex, DNA Probe	Negative
M. kansasii	Not Indicated
M. goodii	Not Indicated
Other	TNP



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

November 20 2020:

- Virtual visit, with initiation of standard 4 drug regimen: INH, Rifampin, Ethambutol and pyrazinamide

- January 13 2021:

*the genome.*

Misc AFB Susceptibility Testing2		Approved By: CB, CLSP
<u>Test Name</u>	<u>Abn. Flag   Test Result</u>	<u>Ref. Range/Units</u>
Specimen Source	Other; Abdomen	
Misc Susceptibility Testing	ID by DNA: <i>M. bovis</i> detected	
<i>M. bovis</i> is resistant to PZA and is a species in the <i>M. tuberculosis</i> complex.		



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites

January 13 2021:

- Pyrazinamide discontinued
- After initial 2months-regimen, patient completed another 10 months of INH and Rifampin
- Repeat CT showed resolution of inflammatory changes in abdomen



# Case 4: A 57-year-old lady with weight loss, thickened omentum and ascites



Full Length Article

## Detection of *Mycobacterium bovis* in artisanal cheese in the state of Pernambuco, Brazil

Results: Of the 107 samples analyzed, three (2.8%) were positive for *M. bovis* and their identities were confirmed by sequencing. This is perhaps the first report of the presence of *M. bovis* in artisanal cheese in the state of Pernambuco, Brazil.



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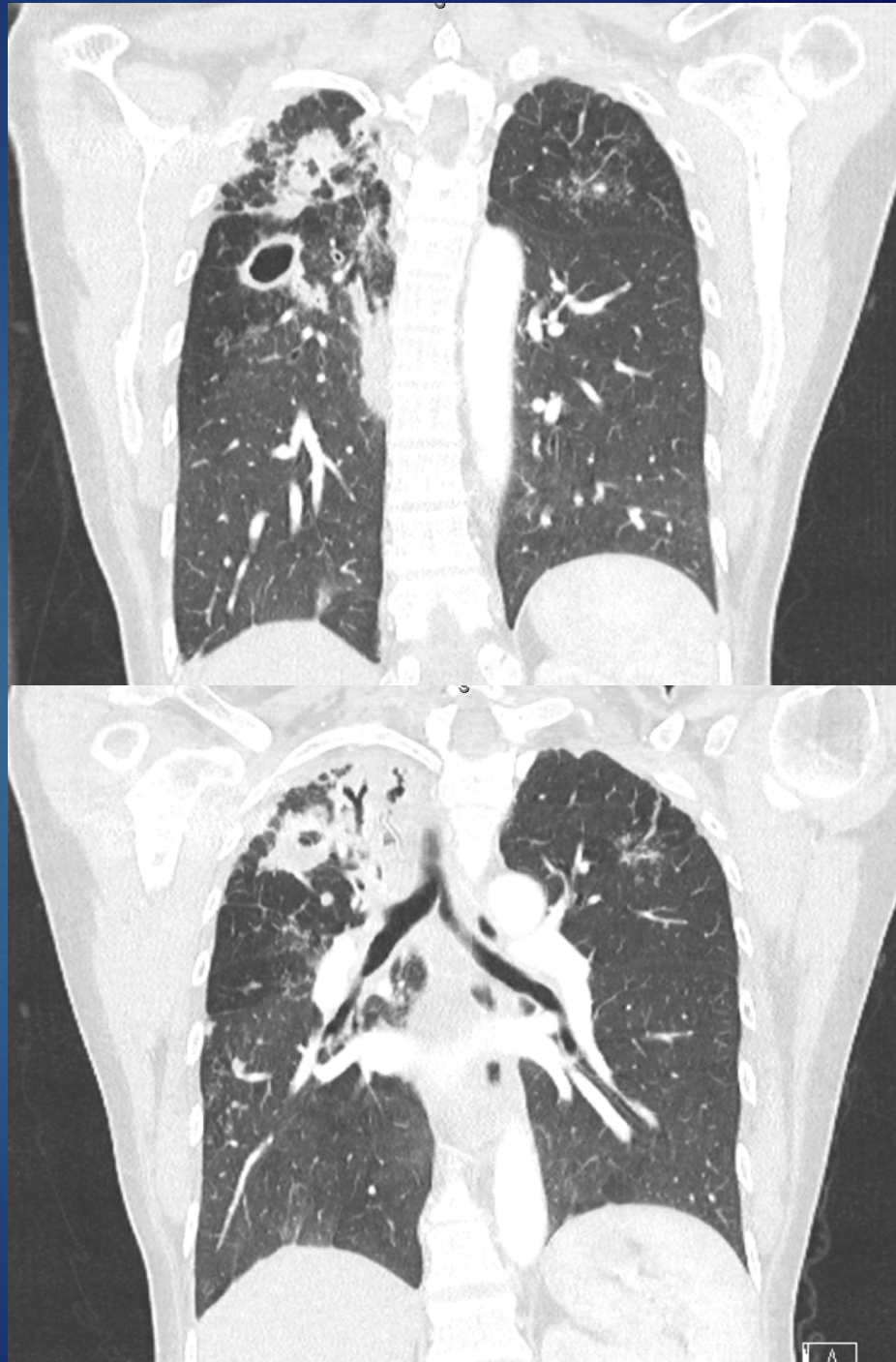
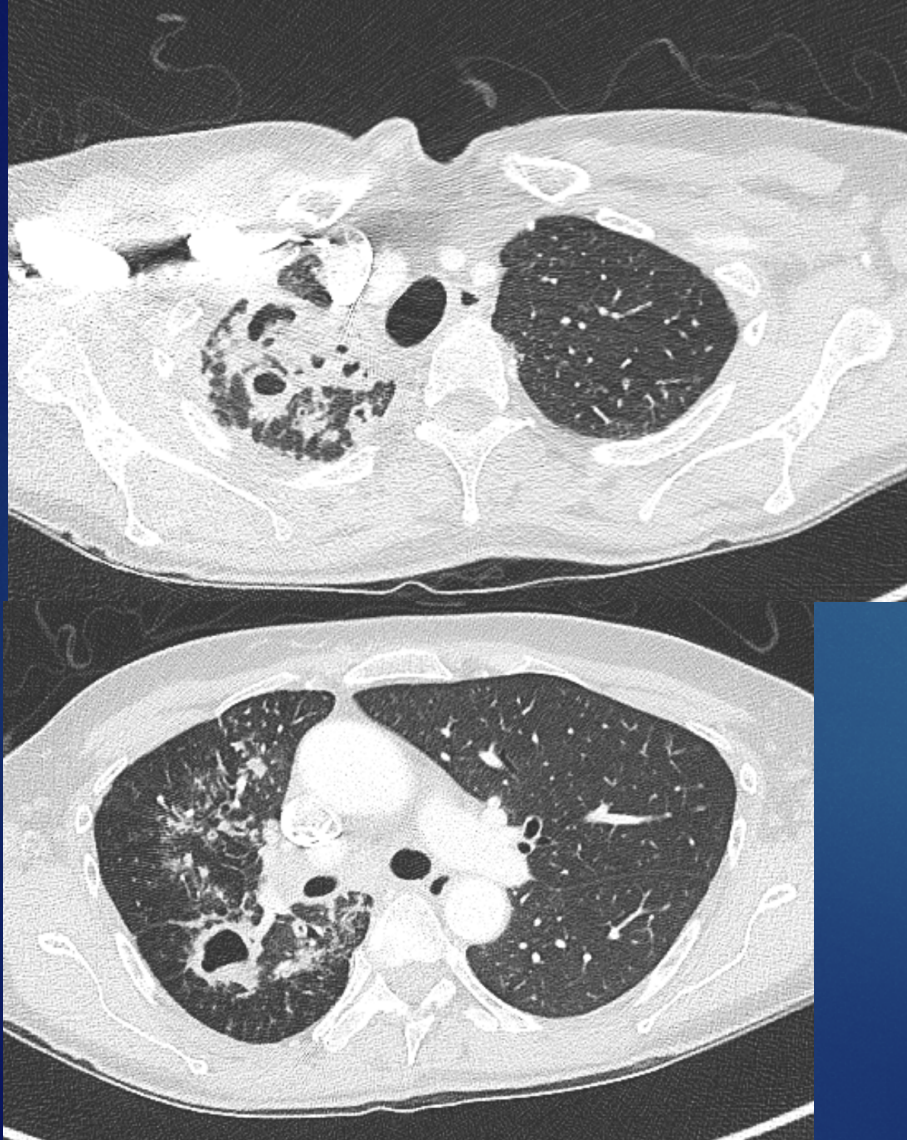
**Results:** Of the 107 samples analyzed, three (2.8%) were positive for *M. bovis* and their identities were confirmed by sequencing. This is perhaps the first report of the presence of *M. bovis* in artisanal cheese in the state of Pernambuco, Brazil.



Case 5: A 54-year-old lady from the former Soviet Union with unintentional weight loss, hemoptysis, night sweats, cavitory lung lesions on CT and 4+ AFB on a sputum smear...



# Case 5:





Case 5: A 54-year-old lady from the former Soviet Union with unintentional weight loss, hemoptysis, night sweats, cavitary lung lesions on CT and 4+ AFB on a sputum smear... What are you thinking ?

- ▶ A) Monoresistant TB
- ▶ B) Polyresistant TB
- ▶ C) Multidrug-resistant TB (MDR-TB)
- ▶ D) Pre-extensively drug resistant TB (pre-XDR-TB)
- ▶ E) Extensively drug resistant TB (XDR-TB)
- ▶ F) What?





Definitions for drug-resistant tuberculosis<sup>[1,2]</sup>

<b>Drug-resistant TB</b>	An isolate of <i>Mycobacterium tuberculosis</i> with resistance to one or more antituberculous drugs.
<b>Monoresistant TB</b>	An isolate of <i>M. tuberculosis</i> with resistance to a single antituberculous agent.
<b>Polyresistant TB</b>	An isolate of <i>M. tuberculosis</i> with resistance to more than one antituberculous agent; the isolate may be resistant to either isoniazid or rifampin but not both.
<b>Multidrug-resistant TB (MDR-TB)</b>	An isolate of <i>M. tuberculosis</i> with resistance to at least isoniazid and rifampin and possibly additional antituberculous agents.
<b>Pre-extensively drug-resistant TB (pre-XDR-TB)</b>	An isolate of <i>M. tuberculosis</i> with resistance to isoniazid and rifampin as well as a fluoroquinolone (levofloxacin or moxifloxacin) OR resistance to isoniazid, rifampin, and at least one second-line injectable agent (amikacin, capreomycin, kanamycin).
<b>Extensively drug-resistant TB (XDR-TB)</b>	An isolate of <i>M. tuberculosis</i> with resistance to isoniazid, rifampin, a fluoroquinolone (levofloxacin or moxifloxacin), and at least one second-line injectable agent (amikacin, capreomycin, kanamycin) OR resistance to isoniazid, rifampin, a fluoroquinolone, and either bedaquiline or linezolid.
<b>Primary drug resistance</b>	Drug resistance in a patient who has never received antituberculous therapy.
<b>Secondary drug resistance</b>	Development of resistance during or following antituberculous therapy in patients who had previously had drug-susceptible TB.

TB: tuberculosis.





**M. tuberculosis Nucleic Acid Amplification Test (NAAT)**

FINAL

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C2

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MTB DETECTED, Rifampin Resistance DETECTED

Identification and rifampin resistance determined by real-time polymerase chain reaction using the Cepheid GeneXpert system.

This test has been cleared by the U.S. Food and Drug Administration (FDA) for sputum and sputum sediment only. The test was also validated and its performance characteristics determined by Advanced Diagnostics Laboratories for bronchoalveolar lavage, urine and cerebrospinal fluid. These sources have not been cleared or approved by the FDA. This laboratory is certified

For additional information, including test methodology, please refer to the ADx Test Directory at [www.NJLabs.org](http://www.NJLabs.org)



Case 5: A 54-year-old lady from the former Soviet Union with unintentional weight loss, hemoptysis, night sweats, cavitary lung lesions on CT and 4+ AFB on a sputum smear...

Based on this information, you will start empiric treatment for

- ▶ A) Monoresistant TB
- ▶ B) Polyresistant TB
- ▶ C) Multidrug-resistant TB (MDR-TB)
- ▶ D) Pre-extensively drug resistant TB (pre-XDR-TB)
- ▶ E) Extensively drug resistant TB (XDR-TB)



# Case 5:

Based on this information, you will start empiric treatment for

- ▶ A) Monoresistant TB
- ▶ B) Polyresistant TB
- ▶ C) Multidrug-resistant TB (MDR-TB)
- ▶ D) Pre-extensively drug resistant TB (pre-XDR-TB)
- ▶ E) Extensively drug resistant TB (XDR-TB)

• **Rifampin** – Patients with rifampin monoresistance should be treated as for multidrug-resistant TB (MDR-TB), in accordance with World Health Organization guidelines [2-4]. Rifampin resistance is considered a surrogate for MDR-TB because rifampin monoresistance is rare [21,22].



RESEARCH SUMMARY

# Bedaquiline–Pretomanid–Linezolid Regimens for Drug-Resistant Tuberculosis

Conradie F et al. DOI: 10.1056/NEJMoa2119430

## CLINICAL PROBLEM

Bedaquiline–pretomanid–linezolid has had efficacy against highly drug-resistant tuberculosis, but the incidence of adverse events with the 1200-mg daily dose of linezolid has been high. Whether a different dose and duration of linezolid treatment might reduce adverse events while maintaining efficacy is unclear.

## CLINICAL TRIAL

**Design:** A dose-blind, randomized trial assessed the efficacy and safety of four regimens of linezolid as part of bedaquiline–pretomanid–linezolid treatment for highly drug-resistant tuberculosis.

**Intervention:** 181 participants (≥14 years of age in South Africa and the country of Georgia and ≥18 years of age in Russia and Moldova) with extensively drug-resistant (XDR) tuberculosis, pre-XDR tuberculosis, or rifampin-resistant tuberculosis that was not responsive to treatment or for which a second-line regimen had been discontinued owing to side effects were assigned to receive bedaquiline and pretomanid for 26 weeks, along with linezolid at one of two doses for either 26 weeks or 9 weeks. The primary end point was treatment failure or disease relapse (clinical or bacteriologic) at 26 weeks after completion of treatment. A favorable outcome was maintenance of negative culture status throughout follow-up in participants who had not had an unfavorable outcome previously.

## RESULTS

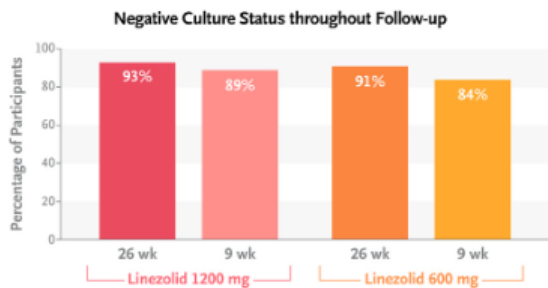
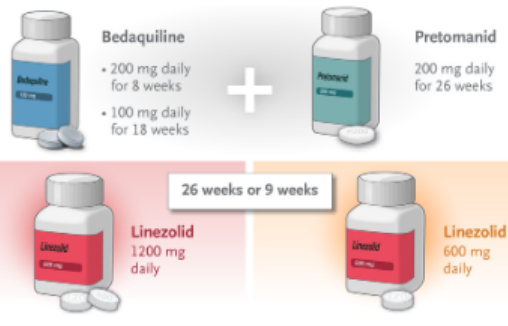
**Efficacy:** In the four treatment groups, the incidence of treatment failure or disease relapse (the primary end point) ranged from 7 to 16%; the incidence of a favorable outcome ranged from 84 to 93%.

**Safety:** Fewer linezolid dose modifications, peripheral neuropathy episodes, and myelosuppression events occurred with the lower dose of linezolid than with the higher dose. The higher dose had a poorer safety profile in the 26-week group than in the 9-week group; there was less difference between the two lower-dose groups.

## LIMITATIONS AND REMAINING QUESTIONS

- The small sample size limits the precision of estimates of efficacy.
- The trial was not powered for formal comparisons of efficacy among the treatment groups.

Links: [Full Article](#) | [NEJM Quick Take](#) | [Editorial](#)



## CONCLUSIONS

In patients with highly drug-resistant tuberculosis, 600 mg of linezolid for 26 weeks resulted in a more favorable risk-benefit profile than other dose–duration regimens tested.

## EDITORIAL

# Linezolid for Drug-Resistant Tuberculosis

Guy Thwaites, F.R.C.P., and Nhung V. Nguyen, M.D., Ph.D.

## Article

## Metrics

## 8 References

THE DEVELOPMENT OF A HIGHLY EFFECTIVE, ORAL, 6-MONTH REGIMEN FOR THE treatment of multidrug-resistant tuberculosis, which previously took 18 to 24 months to cure, is one of the defining achievements of the tuberculosis research community in this century.

The results of the Nix-TB study, which were published in the *Journal* in 2020,<sup>1</sup> showed that the combination of two new drugs, bedaquiline and pretomanid, with a repurposed oxazolidinone antibiotic agent, linezolid, given for 6 to 9 months to patients with drug-resistant or complicated multidrug-resistant tuberculosis, resulted in a favorable outcome in 98 of 109 patients (90%) at 6 months after the end of treatment. However, the efficacy of the regimen came at a cost — peripheral neuropathy developed in 88 patients (81%), and myelosuppression developed in 52 patients (48%). Both these conditions are well-recognized complications of prolonged linezolid treatment.

## ADVERTISEMENT





Questions?

No?

Thank you!