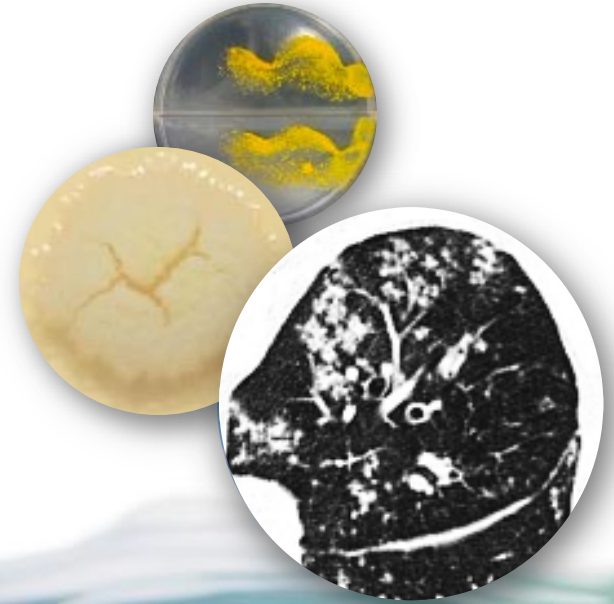


Non-Tuberculous Mycobacteria Case Reports

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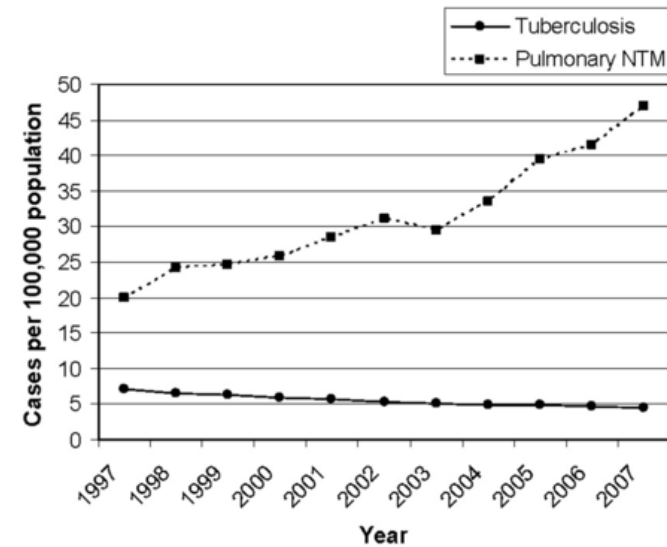
Overview

- Review of NTM
- Case 1
- Case 2



Non-Tuberculous Mycobacteria

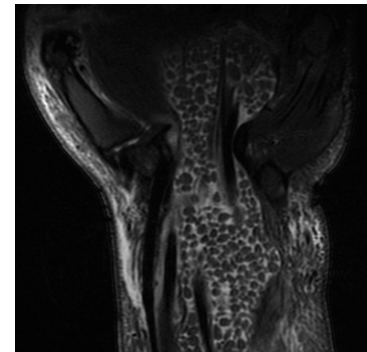
- Ubiquitous organisms
 - Found in soil and water
 - Need to correlate with clinical picture
- Opportunistic infection
 - Most patients are immune compromised or have preexisting damage
 - Prevalence increasing worldwide
- Advances in diagnostic technology and enhanced control of Tuberculosis has made it clear that other mycobacteria can cause similar disease



Adjemian *et al.* 2010 and CDC 2011.

Clinical Syndromes

- Progressive pulmonary disease
- Lymphadenitis
- Disseminated disease
- Skin and soft tissue infections



Non-Tuberculous Mycobacteria

- Over 125 different species
 - ~40% documented to cause disease in humans

Species names	This study [N, %]	[7] [N, %]	[12] [N, %]
<i>M. avium</i> complex	106 (62.2)	138 (42.1)	34 (29.0)
<i>M. avium</i>	68 (39.5)	62 (18.9)	10 (8.5)
<i>M. intracellulare</i> (type I, II)	39 (22.7)	76 (23.2)	24 (20.5)
<i>M. abscessus</i>	33 (19.2)	37 (11.3)	4 (3.4)
<i>M. fortuitum</i> complex	7 (4.1)	64 (19.5)*	1 (0.9)
<i>M. septicum</i>	5 (2.9)	-	-
<i>M. nonchromogenicum</i>	4 (2.3)	-	-
<i>M. asiaticum</i>	3 (1.7)	-	-
<i>M. mucogenicum</i>	3 (1.7)	3 (0.9)	-
<i>M. scrofulaceum</i>	3 (1.7)	-	-
<i>M. shimoidi</i>	2 (1.2)	-	-
<i>M. kansasii</i>	2 (1.2)	13 (4.0)	33 (28.2)
<i>M. gordonae</i>	1 (0.6)	33 (10.1)	31 (26.5)
<i>M. peregrinum</i>	1 (0.6)	*	2 (1.7)
<i>M. pulveris</i>	1 (0.6)	-	-
<i>M. terrae</i> complex	-	28 (8.5)	-
<i>M. chelonae</i>	-	7 (2.1)	-
<i>M. celatum</i>	-	2 (0.6)	-
Others	-	3 (1.2) [†]	12 (10.3) [‡]
Total	172 (100.0)	328 (100.0)	117 (100.0)

Runyon Classification

- Photochromogens
 - *M. marinum*
- Scotochromogens
 - *M. gordonae*
- Non-chromogens
 - *M. avium* complex
- Rapid growers (5-7 days)
 - *M. fortuitum*
 - *M. chelonae*
 - *M. abscessus*





Case 1

Recalcitrant

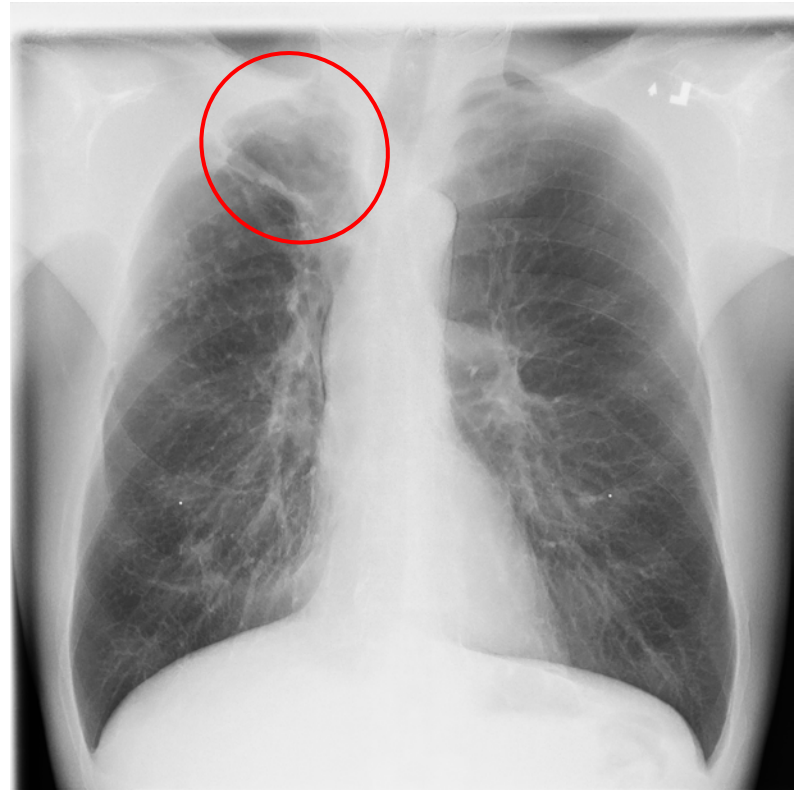
Patient History



- 52 year old man presents after a few months of productive cough and a 40 lb unintentional weight loss.
- Asthma and a 2.5 pack/day smoking history.
- Smoked since he was 14 and both parents died of lung cancer.
- No significant travel history, animal exposure, or sick contacts.
- No history of steroids use or other immune suppressants
- Otherwise healthy man with remote medical history of a knee surgery and back surgery more than 10 years prior.

On presentation

- Patient feels he is “drowning in phlegm”
- Blood seen in sputum on several occasions
- Does not improve on routine antibiotics
- Cavitory lesion seen on X-ray
- Despite a lack of exposure history he is presumed to have Tb



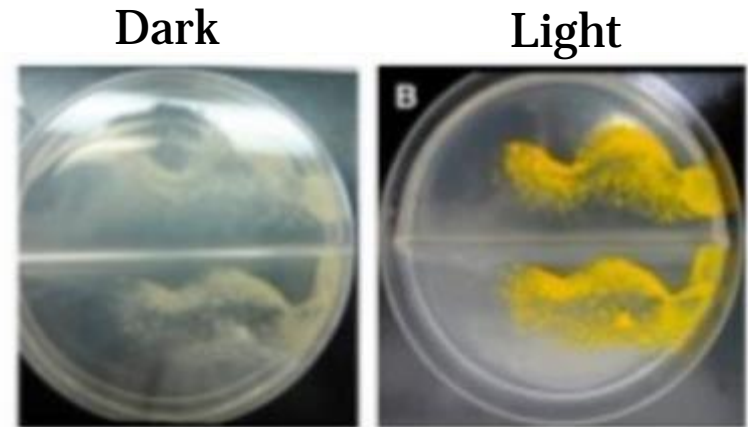
1-3 months since presentation



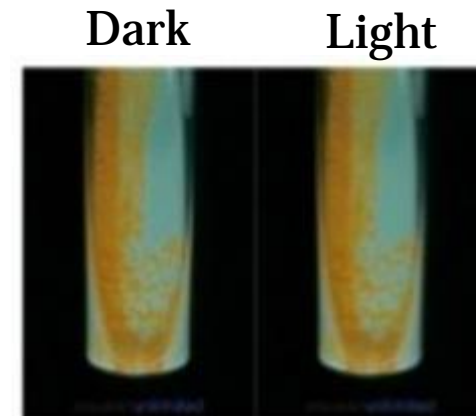
- He is started on RIPE therapy
 - Rifampin**
 - Isoniazid**
 - Pyrazinamide**
 - Ethambutol**
- Quantiferon Gold ordered and sputum cultures sent
 - Quantiferon Gold negative
 - Sputum smear positive for AFB
 - PCR negative for Tuberculosis
 - RIPE therapy stopped
- Sputum culture eventually identifies *Mycobacterium szulgai*
 - RIPE therapy restarted
- Referred to UW Hospital for management

Mycobacterium szulgai

- Unusual cause of disease
- Very rarely isolated from environmental sources
- Nearly always clinically relevant
- First described in 1972 by Marks and Jenkins and named after Dr. Szulga who developed the lipid identification method that helped to describe this pathogen.
- Colonies are slow growing 14-25 days
- Scotochromogen at 37 C and photochromogen at 25 C
 - Only Mycobacteria to do this
- Does not grow at 42 C



Photochromogen at 25 C



Scotochromogen at 37 C



Mycobacterium szulgai

- Often present like pulmonary Tuberculosis
- Seen in wounds less frequently
- Most common: upper lobe cavitation in older men with some kind of lung damage
- Generally susceptible however, they tend to be more resistant to isoniazid



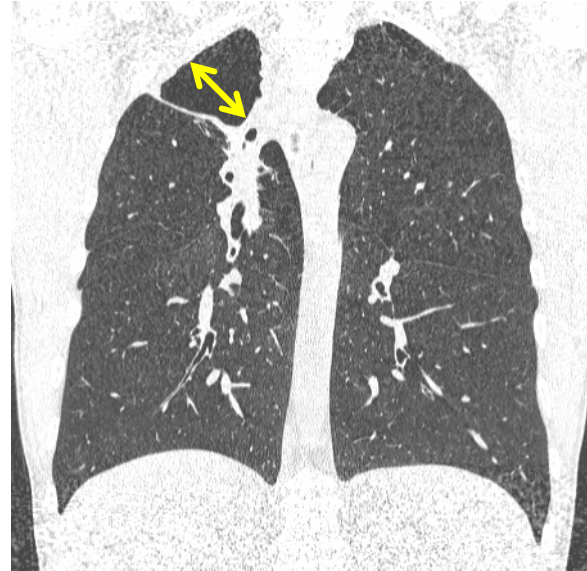
3 months from presentation

- Antimicrobial susceptibility testing is ordered
- Patient worked up for immune defects
 - Negative for HIV, normal T cell counts, no unusual illness as a child. No apparent immune defect
 - Damage from heavy smoking and asthma?
- Patient is highly encouraged to quit smoking and is given resources to assist with this.
- Patient instructed to continue antibiotics until susceptibilities return

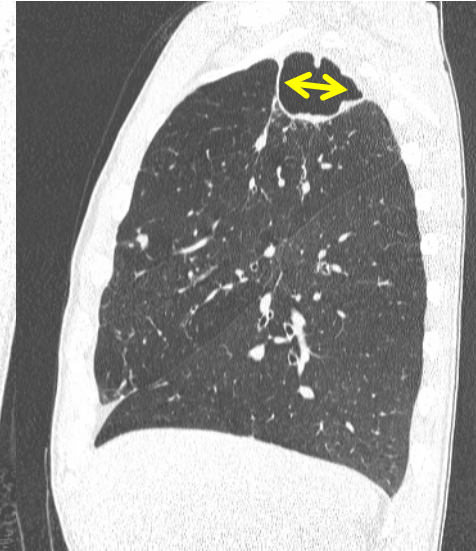
CT scan 3 months from presentation

- Large cavitory lesion on upper right lobe

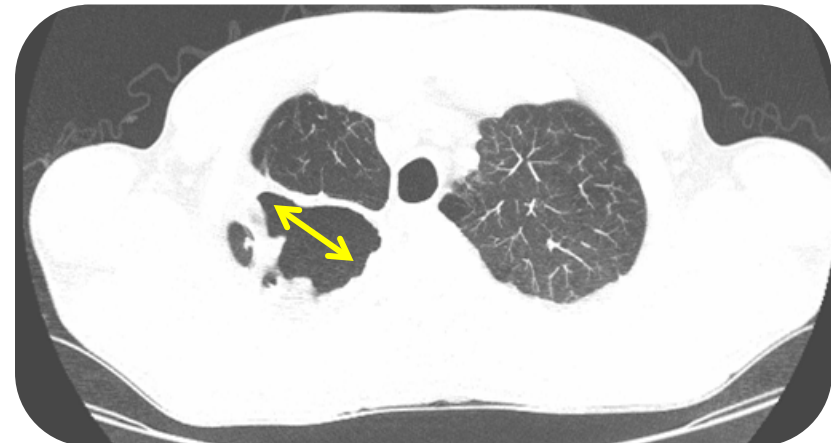
Front view



Side view



Bottom up view



Mycobacterium szulgai susceptibility testing

Drug	Results
Amikacin	Susceptible
Capreomycin	Susceptible
Ciprofloxacin	Susceptible
Clarithromycin	Susceptible
Cycloserine	Susceptible
Ethambutol	Susceptible
Ethionamide	Susceptible
Isoniazid low	Resistant
Isoniazid high	Susceptible
Kanamycin	Susceptible
PAS	Susceptible
Rifampin	Susceptible
Streptomycin low	Susceptible
Streptomycin high	Susceptible

Key

Susceptible

Intermediate

Resistant



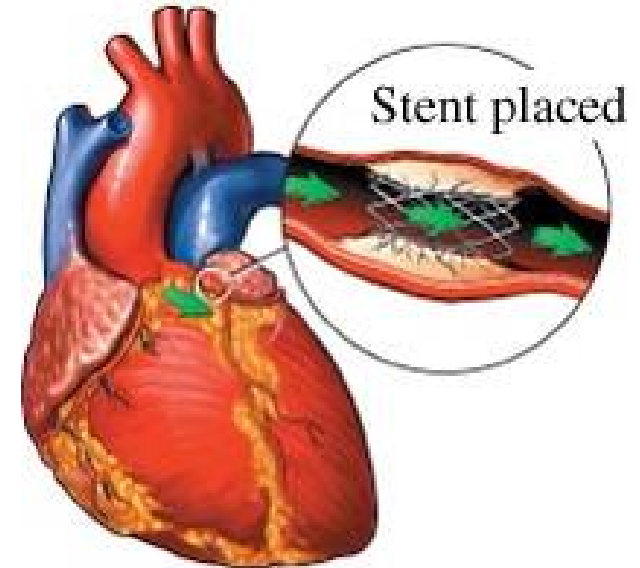
6 months from presentation

- Decreases smoking
- Feeling better
- Gaining weight
- Less phlegm
- Less hemoptyses

- Repeat sputum cultures remain positive for *M. szulgai*

1 year from presentation

- Patient has a heart attack
 - Has stent placement
 - Started on blood thinners
 - Diagnosed with coronary artery disease
- Repeat sputum cultures remain positive for *M. szulgai*
- Patient indicates he does not always take his antibiotics. Is not interested in changing his antibiotic regimen.



1 year from presentation

- Patient has resumed smoking 1.5-2.5 pack/day
- Endorses headaches and stomach pain
- Indicates poor compliance with antibiotics
- Persistent infection and increasing nodularity prompt discussion of lung lobe resection
- Due to blood thinners and recent heart attack surgery is declined
- Culture remain positive for *M. szulgai*
- New susceptibilities run



Mycobacterium szulgai Susceptibility Testing

Drug	At presentation	1 year later
Amikacin	Susceptible	Susceptible
Capreomycin	Susceptible	Susceptible
Ciprofloxacin	Susceptible	Intermediate
Clarithromycin	Susceptible	
Cycloserine	Susceptible	Susceptible
Ethambutol	Susceptible	Susceptible
Ethionamide	Susceptible	Susceptible
Isoniazid low	Resistant	Resistant
Isoniazid high	Susceptible	Intermediate
Kanamycin	Susceptible	Resistant
Levofloxacin		Susceptible
Linezolid		Susceptible
Moxifloxacin		Susceptible
Ofloxacin		Susceptible
PAS	Susceptible	Resistant
Rifampin	Susceptible	Susceptible
Streptomycin low	Susceptible	Resistant
Streptomycin high	Susceptible	Susceptible

Key

Susceptible

Intermediate

Resistant

Increased
resistance

1.5 years from presentation

- Patient is lost to follow-up for a few months
- Patient has trouble eating and has worsening GI discomfort.
 - Blames antibiotics and stops therapy
- For next 6 month he intermittently takes his antibiotics.
 - Off and on for about 4 days at a time when he feels bad
 - Stops again when he feels stomach discomfort

2 years

- Patient returns to the clinic
- Clinician stresses the importance of antibiotics
- Recommends changes to therapy to help with tolerance and circumvent new resistance patterns.
- Patient refuses to change his antibiotic regimen
- Surgery is discussed and declined by the patient
- Culture remains positive for *M. szulgai*
- New susceptibilities run

Mycobacterium szulgai Susceptibility Testing

Drug	At presentation	1 year later	2 years later
Amikacin	Susceptible	Susceptible	
Capreomycin	Susceptible	Susceptible	
Ciprofloxacin	Susceptible	Intermediate	Intermediate
Clarithromycin	Susceptible		
Cycloserine	Susceptible	Susceptible	
Ethambutol	Susceptible	Susceptible	
Ethionamide	Susceptible	Susceptible	
Isoniazid low	Resistant	Resistant	
Isoniazid high	Susceptible	Intermediate	
Kanamycin	Susceptible	Resistant	
Levofloxacin		Susceptible	Intermediate
Linezolid		Susceptible	Susceptible
Moxifloxacin		Susceptible	Susceptible
Ofloxacin		Susceptible	Resistant
PAS	Susceptible	Resistant	
Rifampin	Susceptible	Susceptible	
Streptomycin low	Susceptible	Resistant	
Streptomycin high	Susceptible	Susceptible	

Key

Susceptible

Intermediate

Resistant

Increased
resistance



2.25 years

- Patient indicates he stopped taking his antibiotics all together a few weeks back.
- He has stopped coming in for testing.
- States he understands that stopping treatment may lead to death
- Patient does not follow up with testing or clinic visits



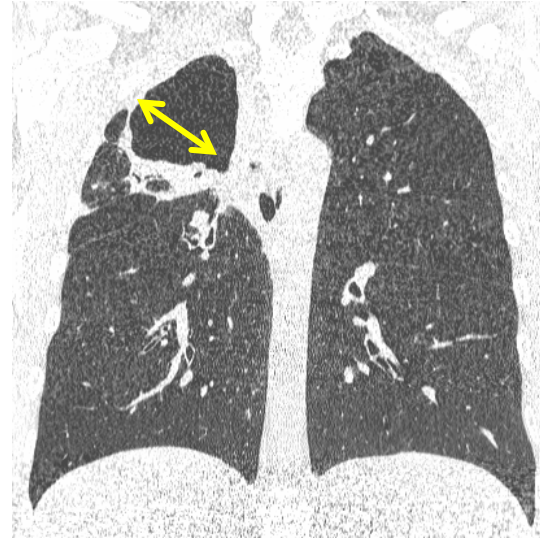
3 years from presentation

- Patient presents at ED with worsening symptoms
 - Cough
 - sputum production that is bloody
 - shortness of breath affecting his ability to work
 - Recent diagnosis of COPD and type 2 diabetes
 - Says he has not taken antibiotics for several months

Chest CT at 3 years from presentation

- Worsening cavitary lesion
- Several nodular frond-like opacities
- Patient says he is ready to try for a cure
- Restarts antibiotics
- New cultures grow *M. abscessus* **only**

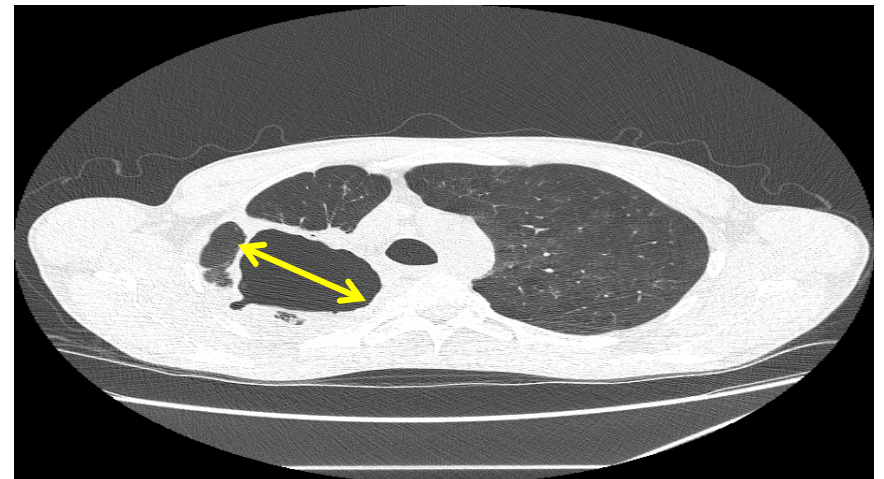
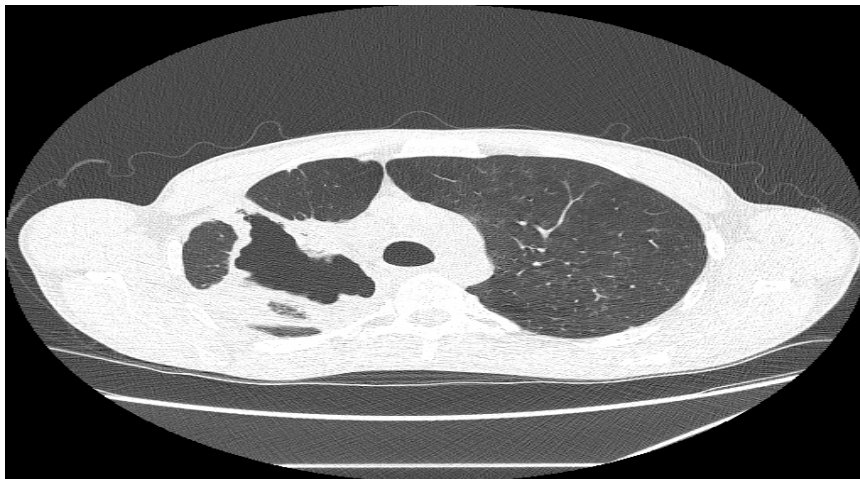
Front view



Side view



Bottom up view



M. abscessus

- Rapid grower (nonchromogenic)
 - Growth on blood agar on day 5
- *M. abscessus* complex
 - *abscessus* (common)
 - *massiliense* (common)
 - *bolletii* (rare)
- Second most common NTM after MAC
- First isolated from a knee abscess in 1952
- Usually causes skin and soft tissue or pulmonary infections
- Found in water and soil
- Generally hard to treat
 - One study showed only 58% cure after a year of therapy with combination of IV and oral antibiotics



Susceptibility testing

M. abscessus

Drug	Result
Amikacin	Susceptible
Augmentin	Resistant
Azithromycin	Susceptible
Cefoxitin	Susceptible
Ciprofloxacin	Resistant
Clarithromycin	Susceptible
Clofazimine	Susceptible
Doxycycline	Resistant
Imipenem	Intermediate
Kanamycin	Susceptible
Linezolid	Intermediate
Moxifloxacin	Resistant
Tigecycline	Susceptible
Tobramycin	Intermediate
Trimethoprim/sulfa	Resistant

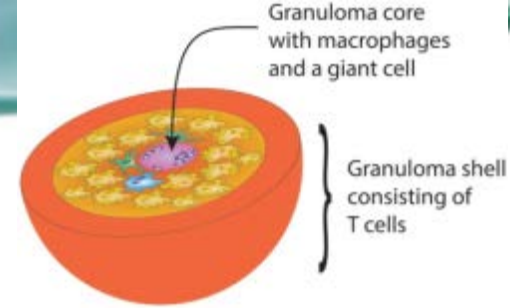
M. szulgai

Drug	1 year later
Amikacin	Susceptible
Capreomycin	Susceptible
Ciprofloxacin	Intermediate
Cycloserine	Susceptible
Ethambutol	Susceptible
Ethionamide	Susceptible
Isoniazid low	Resistant
Isoniazid high	Intermediate
Kanamycin	Resistant
Levofloxacin	Intermediate
Linezolid	Susceptible
Moxifloxacin	Susceptible
Ofloxacin	Resistant
PAS	Resistant
Rifampin	Susceptible
Streptomycin low	Resistant
Streptomycin high	Susceptible

3.5 years

- Chronic cough
 - 2-3 blood clots a day
- Recently quit his job due to chronic shortness of breath
- Quit smoking last month and has gained 10 lb
- Undergoes surgery: Right upper, middle lobes, and involved ribs resected
- Discharged home with a PICC line for IV antibiotics
 - Amikacin, Cefoxitin, Rifampin, Ethambutol, and Clarithromycin

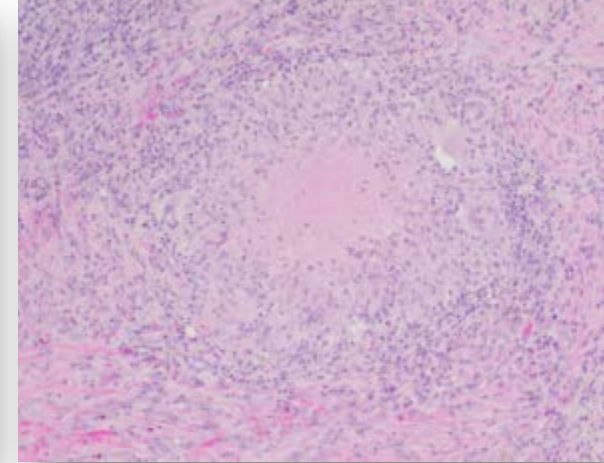
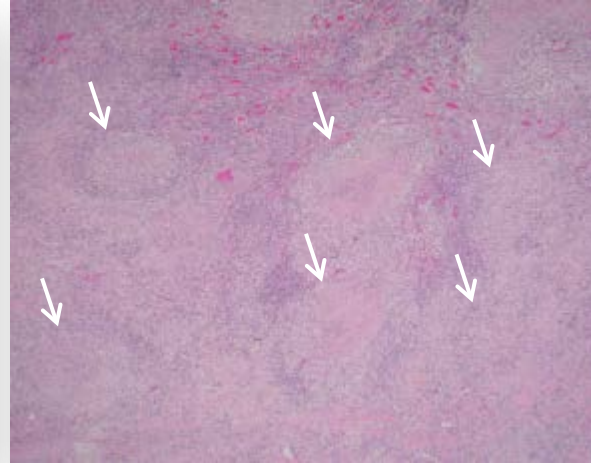
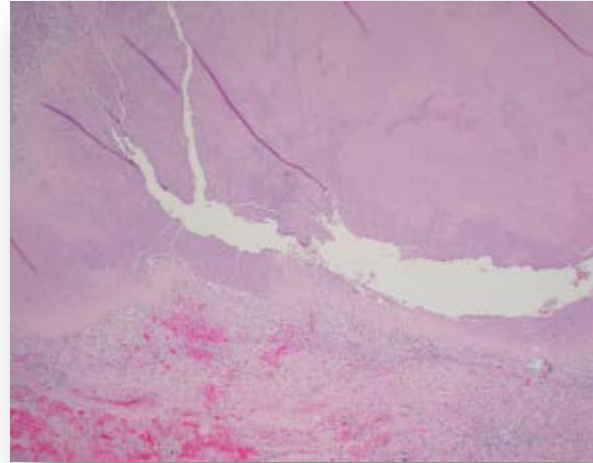
Pathology



40X

100X

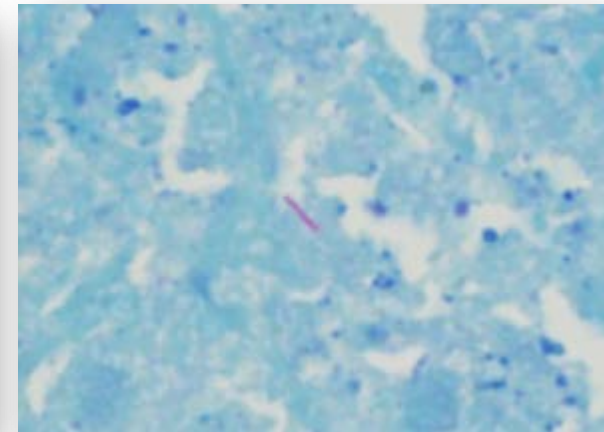
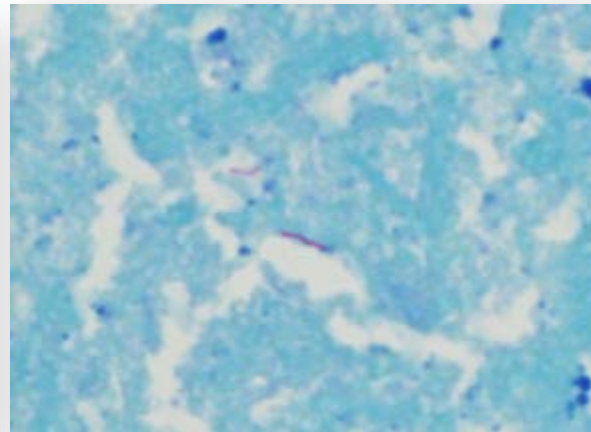
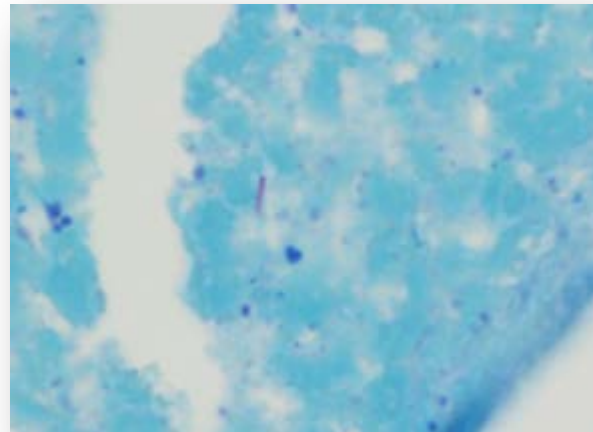
400X



1000X

1000X

1000X



M. abscessus susceptibility testing

Drug	1st	2nd
Amikacin	Susceptible	Susceptible
Augmentin	Resistant	Resistant
Azithromycin	Susceptible	Susceptible
Cefepime		Resistant
Cefotaxime		Resistant
Cefoxitin	Susceptible	Intermediate
Ceftriaxone		Resistant
Ciprofloxacin	Resistant	Resistant
Clarithromycin	Susceptible	Susceptible
Clofazimine	Susceptible	Susceptible
Doxycycline	Resistant	Resistant
Gentamicin		Intermediate
Imipenem	Intermediate	Intermediate
Kanamycin	Susceptible	Susceptible
Linezolid	Intermediate	Resistant
Moxifloxacin	Resistant	Resistant
Tigecycline	Susceptible	Susceptible
Tobramycin	Intermediate	Intermediate
Trimethoprim/sulfa	Resistant	Resistant

Key

Susceptible

Intermediate

Resistant

Increased
resistance

One month later (~3.5 years)

- In the next few weeks he feels worse
 - Fever, chills, vomiting
- Discontinue his all antibiotics including the IV
- The next day his chest wound opens and large amount of chunky, discolored, purulent material drains
- He then feels much better
 - Resumes oral antibiotics only
- On exam a large amount of thick purulent material is draining from his chest tube site
 - IV antibiotics restarted
 - Culture grows *M. abscessus*

3.5 years

- Chest wall thickening
- Emphysema
- “Tree and bud” opacities in remaining right lung

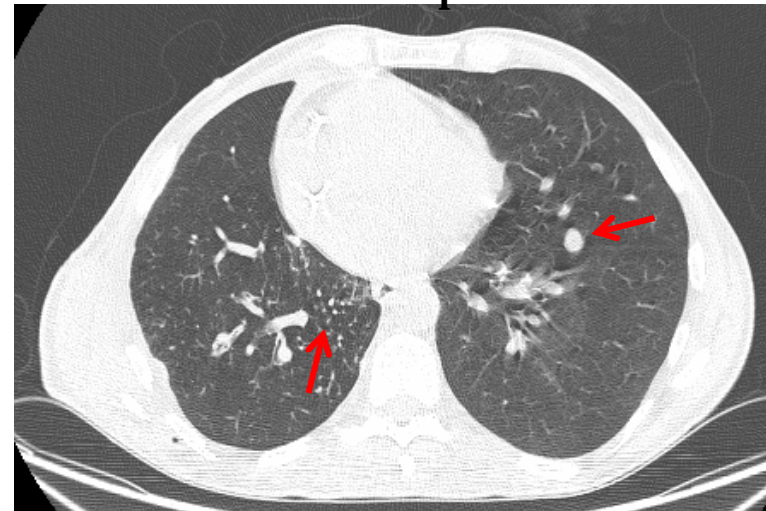
Front view



Side view



Bottom up view

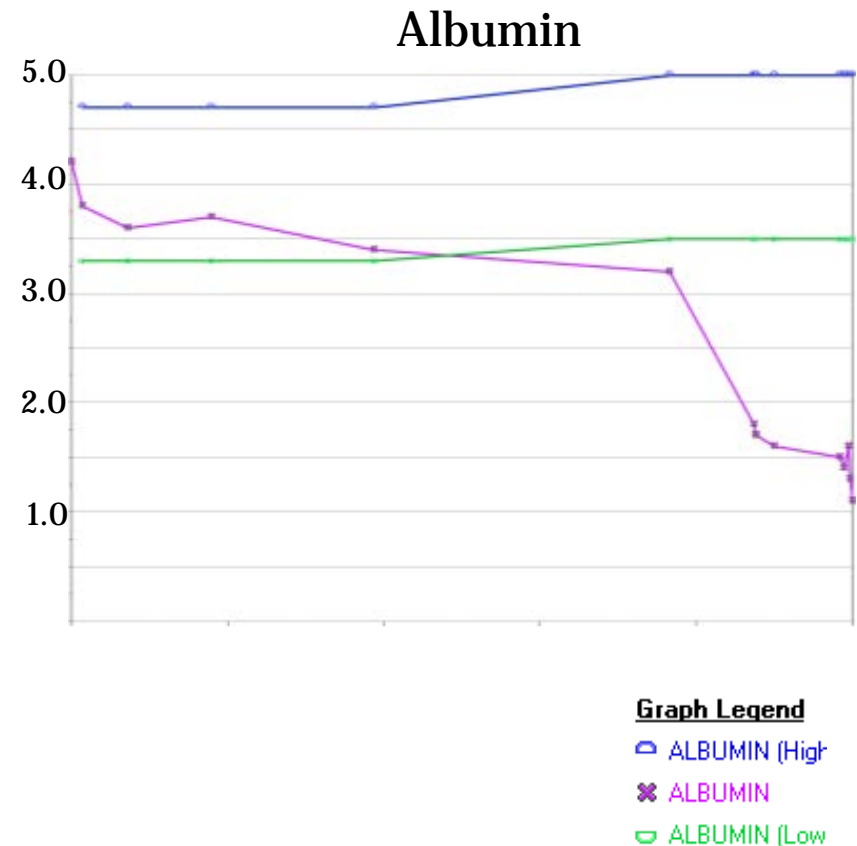


Tree-in-bud opacities



3.75 years

- Blood draining from wound site
- Albumin dropping (1.5 g/dL)
- White blood cell count rising (14 K/uL)
- Bronchopulmonary fistula identified
- Undergoes second surgery for debridement, flap repair and endobronchial stent placement





One month later (~4 years)

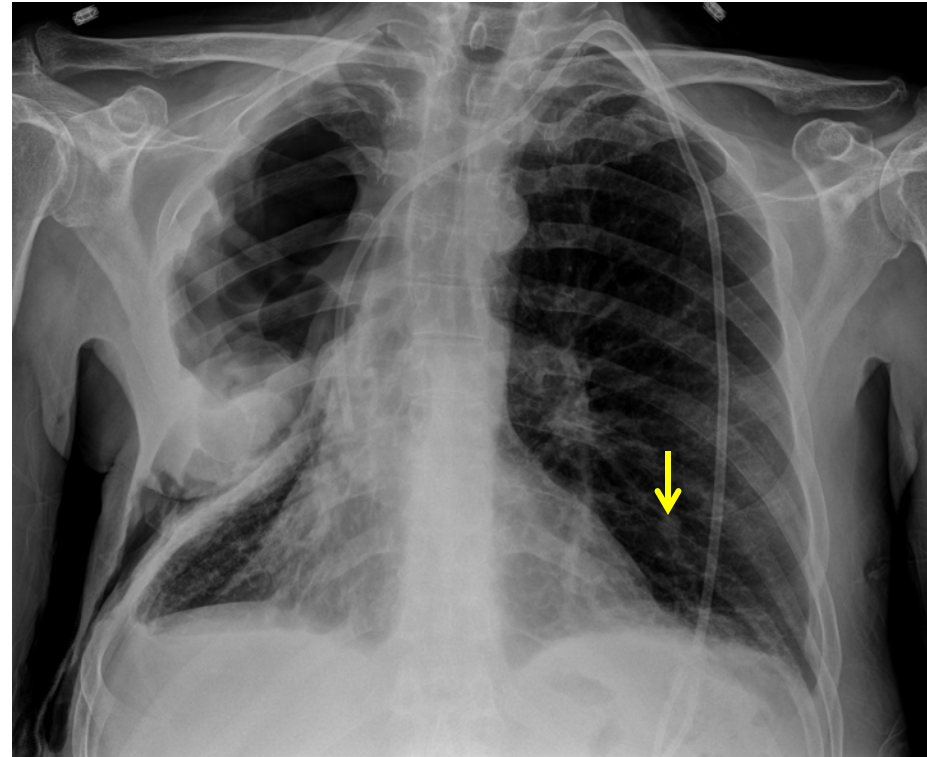
- Wound continues to drain pus and bleed.
- Heavy lifting at home resulted in sudden large amount of bleeding.
- Albumin at 1.1 g/dL in clinic
- Patient initially refuses to be admitted despite warnings he may have a heart attack
- Wife convinces him to get a transfusion
- Regular sputum cultures identify new organism

M. peregrinum

- Nonpigmented Rapid grower
- Very rare cause of pulmonary infections
- *M. fortuitum* complex
 - *Fortuitum, peregrinum, senegalense, setense, septicum, porcinum, houstonense, boenickei, brisbanense, neworleansense*
- Case reports of disease in previously healthy people (Nihon Kokyuki Gakkai Zasshi. 2010)

Two months later (4 years)

- Salvage therapy recommended by national Jewish
 - amikacin, cefoxitin, tigecycline, and clofazimine
- Improves initially then represents with air and pus leaking from chest wound.
- Undergoes another surgery to debride and close multiple fistulas.
- New sputum culture results. . .



M. fortuitum



- Rapid grower
- Non-pigmented
- Common mycobacterial pathogen
- Usually in skin and soft tissue infections
- Often nosocomial
- Macrolide and cephalosporin resistance is common
- 4-6 months of therapy recommended

Summary

<i>M. szulgai</i>	<i>M. abscesses</i>	<i>M. peregrinum</i>	<i>M. fortuitum</i>
Slow grower	Rapid grower	Rapid grower	Rapid grower
Rare	Common	Uncommon	Common
Fairly susceptible (except isoniazid)	Fairly resistant	Fairly susceptible	Fairly susceptible
Pigment in light only when grown at 25			No growth at 45C

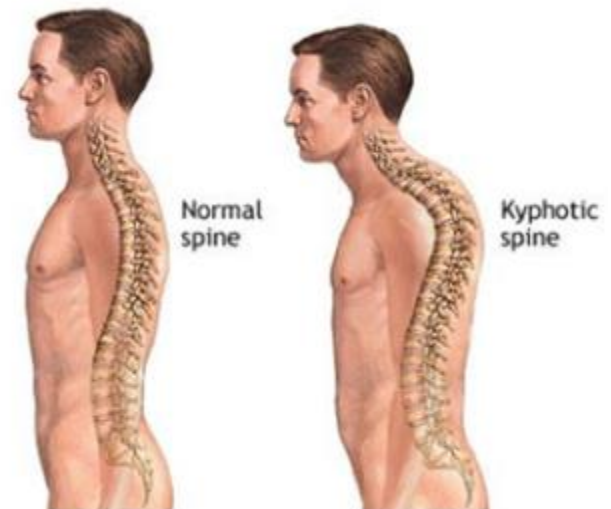
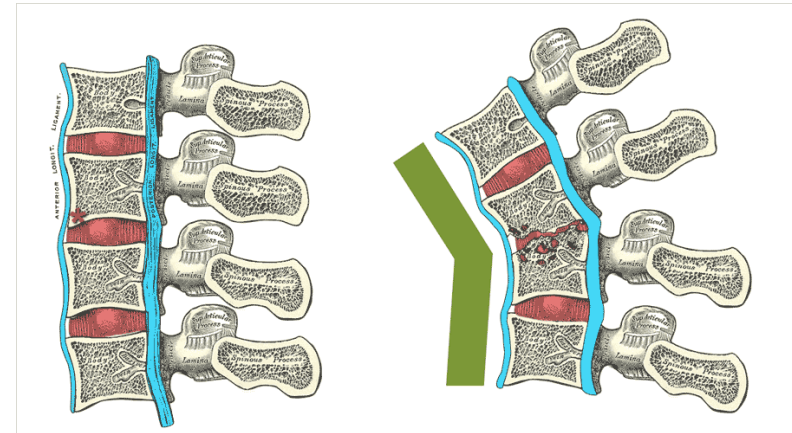


Case 2

Non- tuberculous spondylitis

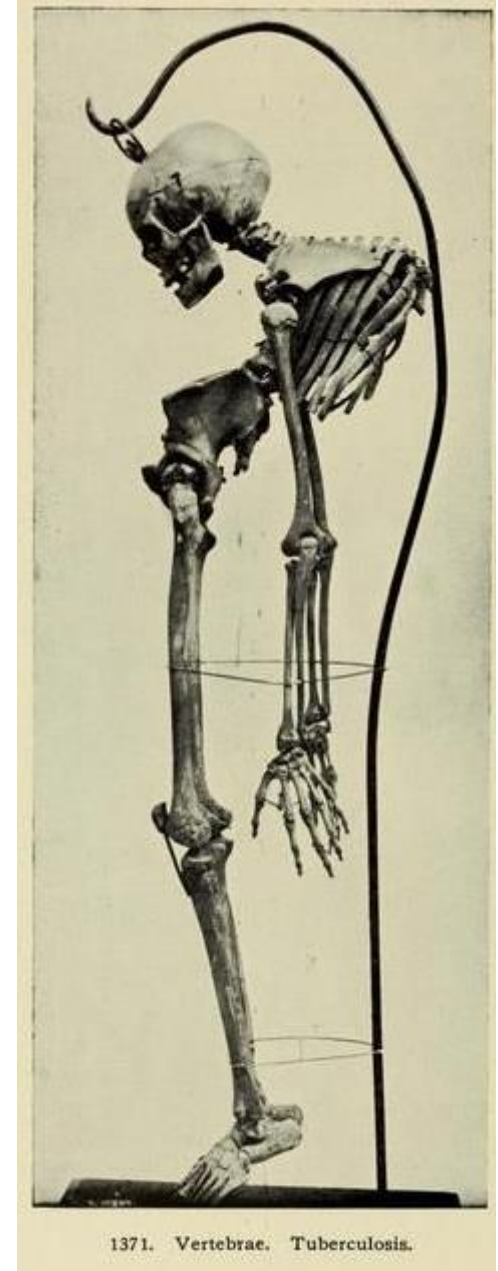
Pott's Disease

- Infection of the spine with *Mycobacterium*
- First described in 1779 by an English surgeon named Percivall Pott
- Causes destruction of the disc space and vertebral bodies, results in “wedging”
- Result in progressive kyphosis
- Can lead to neurologic deficits and severe deformity



Pott's Disease

- Most common site of mycobacterial osteomyelitis
- Most common in children and young adults
- Before anti-tuberculosis medications mortality was 20%
- Likely disseminates from a pulmonary source
 - Yet, most patients have no evidence of extra spinal disease
- Prognosis is best when treated early



Mycobacterium xenopi

- First isolated in 1959 from skin lesions on an adult female *Xenopus laevis* (African clawed frog)
- Recognized as a pathogen in 1965
- Slow growing
- Scotochromogen
- Optimal growth at 45 C
- Nest like colonies
- Treatment often requires 2+ years of ethambutol, rifampin and macrolide therapy

