A visit to the dentist

- Part 2 -

CLINID conference
Hunter Ratliff
05/15/2025

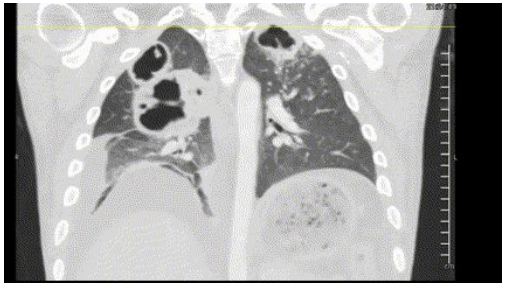
Ages, dates, and other identifying information may have been changed
I have no conflict of interest in relation to this presentation

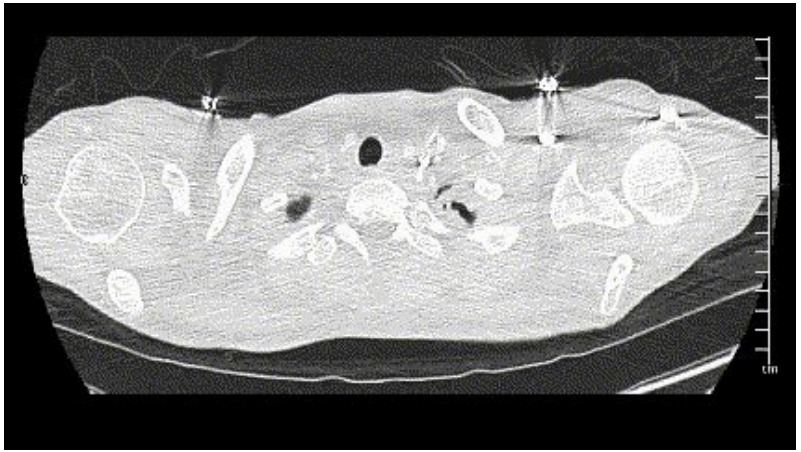
Updates on prior cases

Case #1

Case 1: Kleb/Crypto

A **27 y/o M** with PMH including **poorly controlled DM**, recent NSTI of groin p/w chronic groin **wound drainage** & productive cough and found to have **numerous cavitary lesions**





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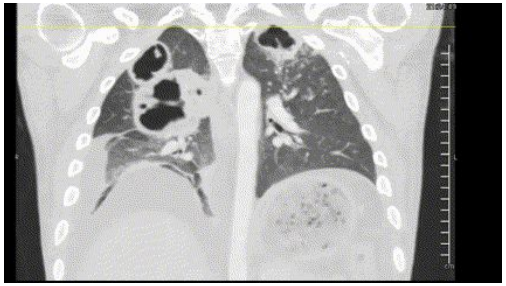
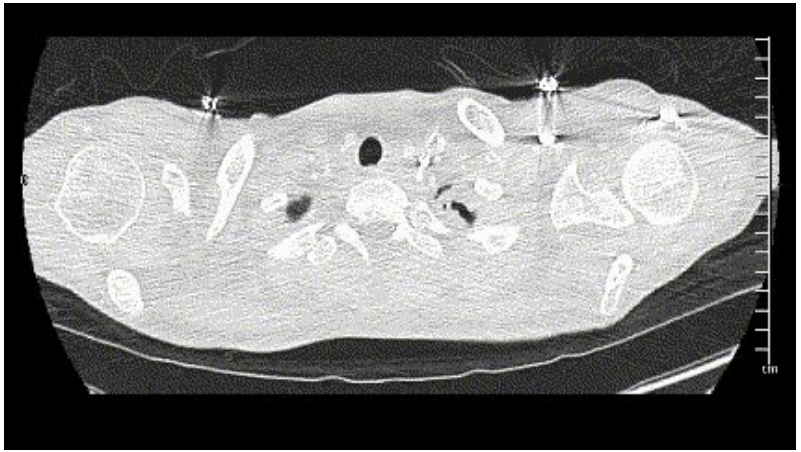
Micro	Result
BAL (routine)	>100k **mucoid kleb pneumo**

Date	CrAG
Day 2	**1 : 1280**
Day 3	**1 : 320**





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- **Augmentin** (6 weeks)
  - ➢ Repeat CT
- **Fluconazole** (6 months?)

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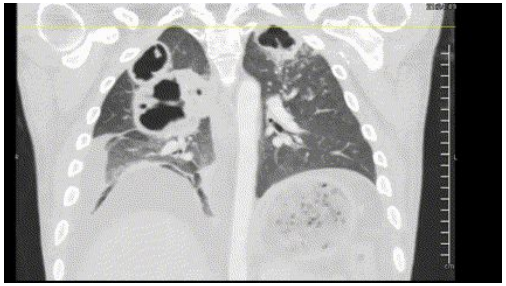

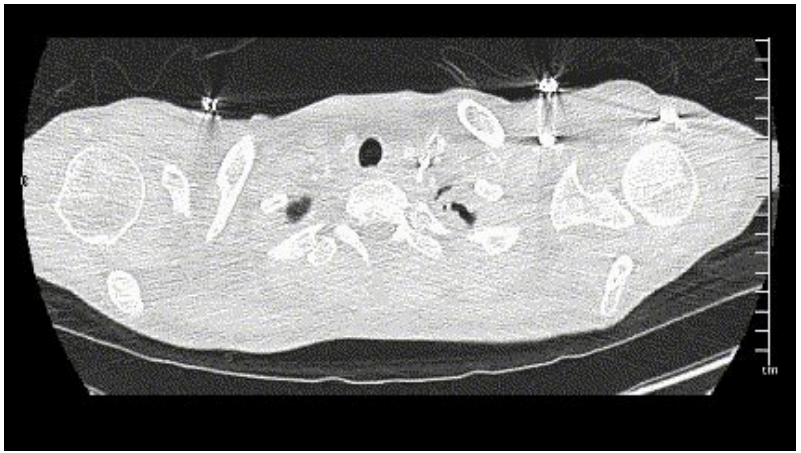

Case 1: Updates since conference

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Telephone		
Patient Message		
Appointment	WVU RUBY CT CAP..	
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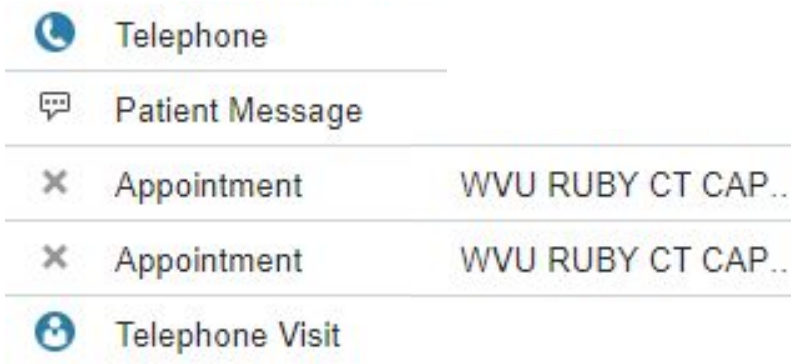
Telephone Visit		

Plan:
- Will obtain repeat CT chest to assess radiographic response to treatment
- Ordered repeat labs (CBC, CMP, CRP) as we don't have any labs since he left WVUH
- Appears he has been lost to pulm follow up, will refer to Wheeling pulm clinic
- Prefers to follow with ID closer to home, so will refer to Wheeling ID as well
- Refilled fluconazole, anticipate duration of 6-12 months
- Given clinical stability (admittedly, only able to base this off HPI) will hold off further antibacterials until CT chest is back

RTC: 1 mo (Prefers Wheeling)

Hunter Ratliff, MD

Case 1: Updates since conference



- Hopelessly lost to follow up
- No imaging
- Does refill his fluconazole

Case 1: Updates since conference

Admitted to Ruby

- Admitted with..?

Case 1: Updates since conference

Admission (Discharged)	Inpatient	Uncontrolled type 1 diabet...
Admission (Discharged)	Inpatient	Cavitary lung disease
ED to Hosp-Admission (Dis...	Inpatient	DKA (diabetic ketoacidosis)
ED to Hosp-Admission (Dis...	Inpatient	Hyperglycemia
ED to Hosp-Admission (Dis...	Observation	DKA (diabetic ketoacidosis)
Admission (Discharged)	Observation	DKA (diabetic ketoacidosis)
ED to Hosp-Admission (Dis...	Inpatient	Acute metabolic encephal...
ED to Hosp-Admission (Dis...	Inpatient	DKA (diabetic ketoacidosis)
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Admitted to Ruby (DKA)

- No real infectious concerns
- They get a CT chest (as one does for DKA)

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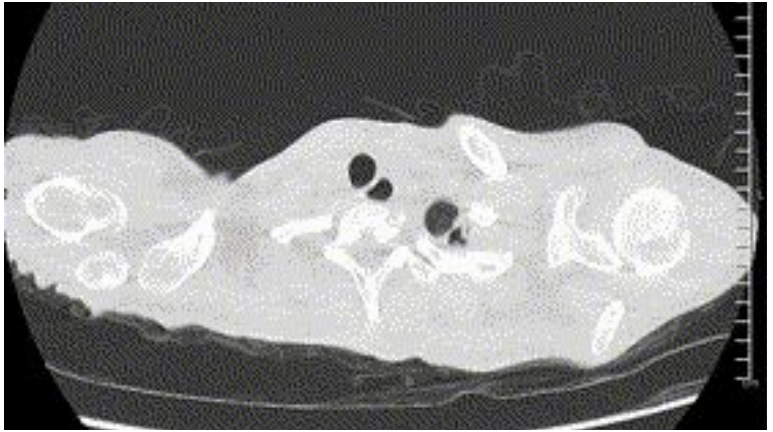
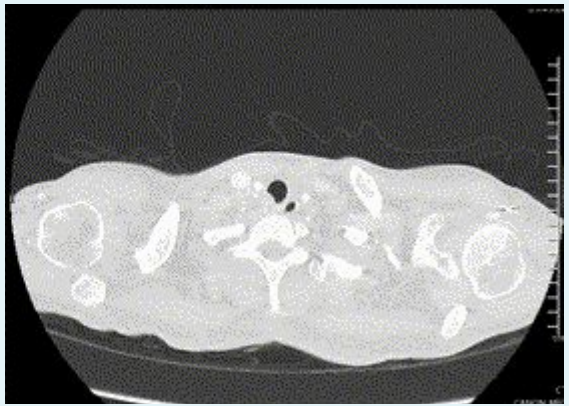


Case 1: Updates since conference

Last conference (2 months ago)



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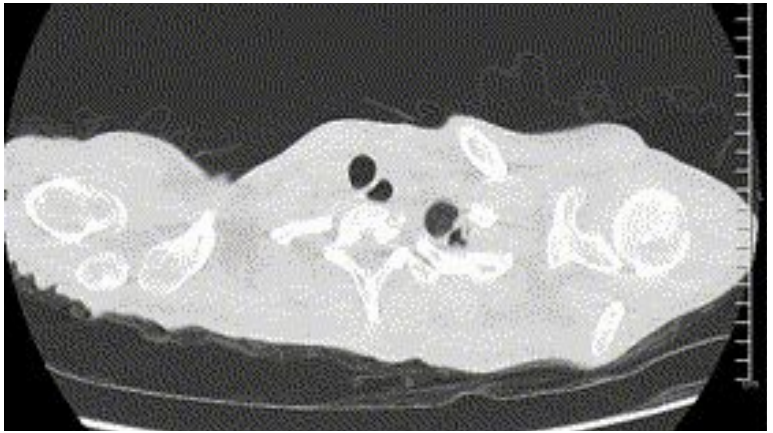
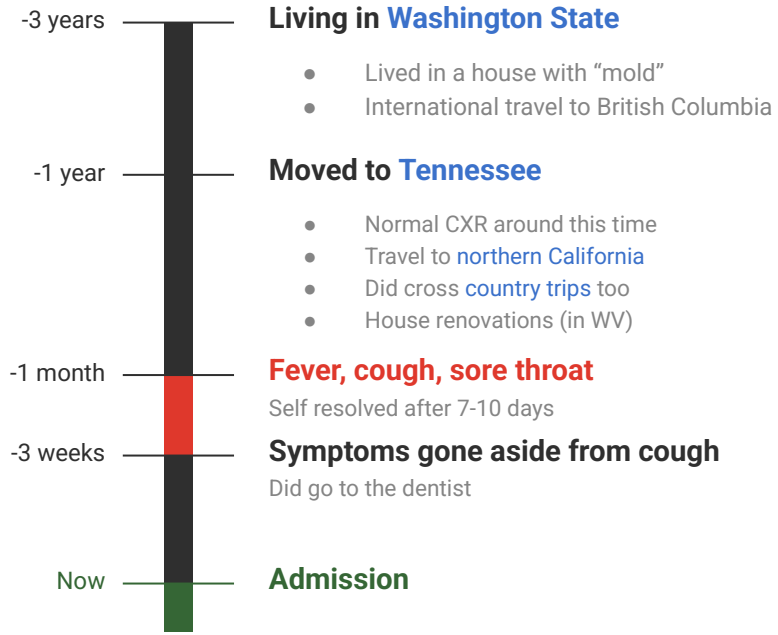


Case #2

Case 2: Coccidioides

A **22 y/o M** with no PMH who p/w **subacute cough** x 1 month. Found to have a new 4cm RUL cavity, 1cm LLL nodule (vs XR 14 mo ago)



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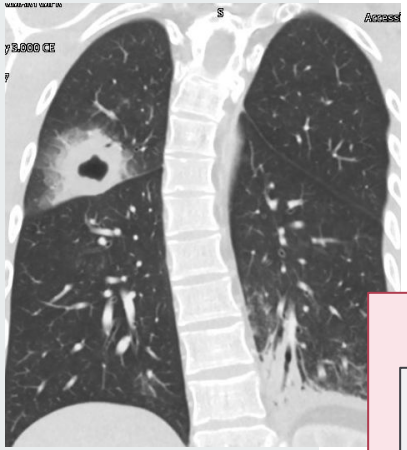

-3 years — **Living in Washington State**

- Lived in a house with "mold"
- International travel to British Columbia

-1 year — **Moved to Tennessee**

- Normal CXR around this time
- Travel to northern California
- Did cross country trips too
- House renovations (in WV)

-1 month — **Fever, cough, sore throat**

Self resolved after 7-10 days

-3 weeks — **Symptoms gone aside from cough**

Did go to the dentist

Now — **Admission**

Coccidioides antibody, serum

Complement fixation	**Immunodiffusion**
Antibody detected (**1:2**)	Antibody not detected

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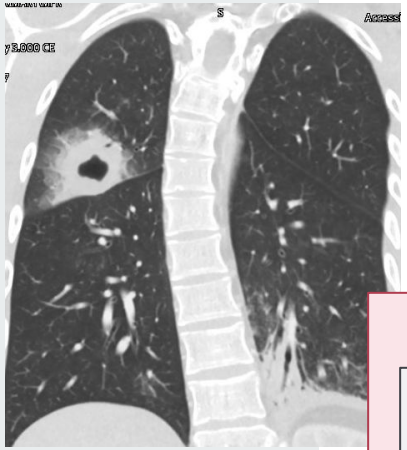

Augmentin (4 weeks)

-3 years — **Living in Washington State**

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Case 1: Updates since conference

Office Visit	O..	N..	PULMONARY-POC
CT Scan	H..	W..	CT RUBY
Nurse Triage			PULMONARY-POC
Documentation ...			INFECTIOUS DISEA
Documentation ...			INFECTIOUS DISEA
ED to Hosp-Ad...	I...		8ESD - Decicco, Dar

Spoke with patient on [redacted] Reviewed lab results with the patient. Patient denies antibiotic side effects. States he still has to clear his throat sometimes and has an occasional cough. Denies further symptoms. Overall feels improved since hospitalization. Patient inquired about stopping antibiotics at this time since he's completed almost 3 weeks of therapy. Explained discussion with Dr. Juskowich - okay to stop at this time per patient request. Encouraged patient to keep ID follow up appointment and reach out to the clinic if he develops any new symptoms or clinically worsens in any way. Patient displayed understanding. He denied any further questions.

Of note, patient stated he would need to reschedule ID follow up. Patient to request adjustment via MyChart.

Amy Spigelmyer, PharmD, BCIDP
Infectious Diseases Clinical Pharmacist

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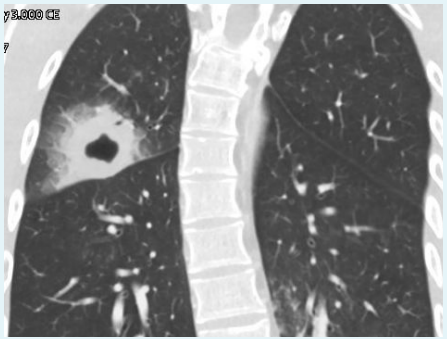
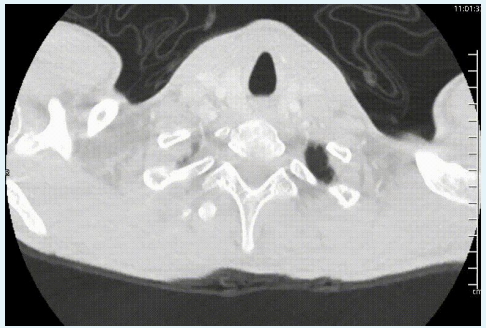
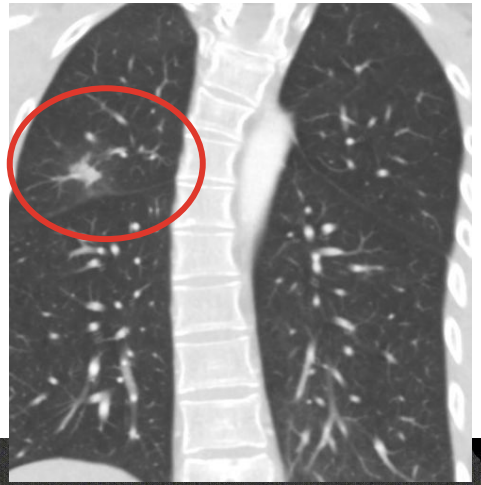
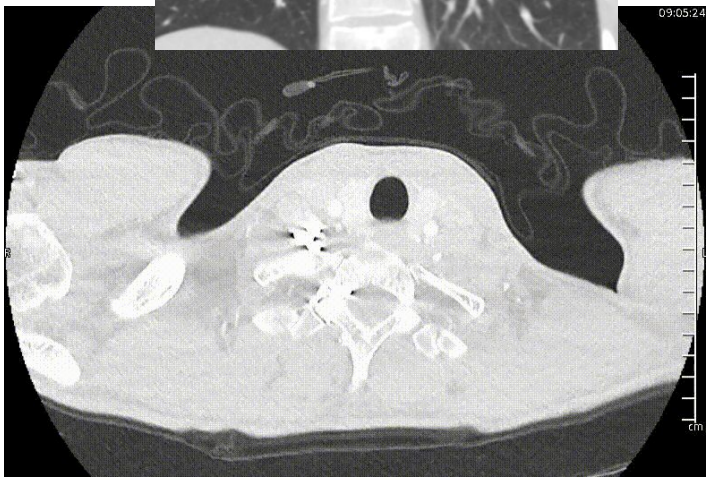
Office Visit	O..	N..	PULMONARY-POC
CT Scan	H..	W..	CT RUBY
Nurse Triage			PULMONARY-POC
Documentation ...			INFECTIOUS DISEA

Last conference (1.5 months ago)









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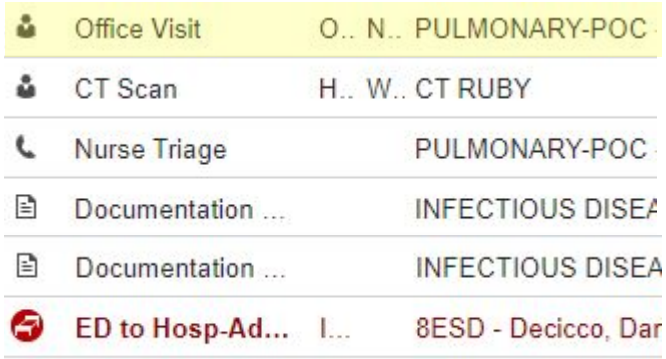

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ED to Hosp-Ad...	I...		8ESD - Decicco, Dar

Pulmonology clinic

- Doing great
- RTC: PRN

New cases!

Case #3

Case 3: HPI

A **60 y/o M** with PMH including untreated large granular lymphocytic leukemia, TTP (on pred 20) p/w

- **Hypoxia**
- **AMS**
- **Hyponatremia**

Case 3: HPI

A **60 y/o M** with PMH including untreated large granular lymphocytic leukemia, TTP (on pred 20) p/w **AMS, hyponatremia, & hypoxia**

- Generally feeling weak for **past week**
- **Productive** cough
- Unable to ascertain further symptoms

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Medical Hx / medications
Leukemia: Not on meds / chemo

Admission one ***month ago*** for non-ID reasons

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- Productive cough
- Unable to ascertain further symptoms

Medical Hx / medications

Leukemia: Not on meds / chemo

Admission one ***month ago*** for non-ID reasons

- Dx with **hyperviscosity syndrome**, perhaps MGUS?
- Also had w/up for *thrombocytopenia*, favored to be **TTP**
  - Start prednisone 20
  - No PJP ppx

Case 3: HPI

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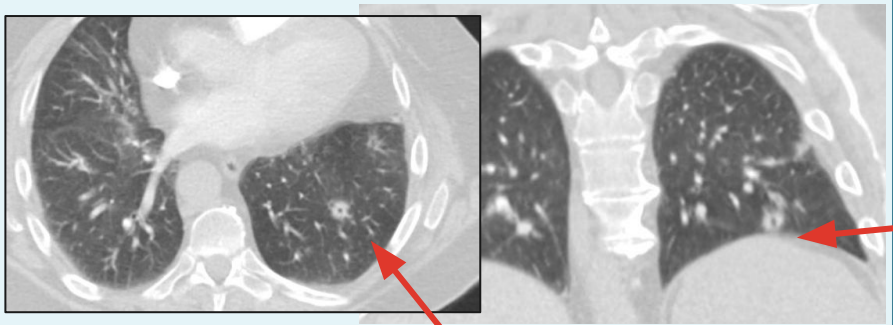
1.5 months ago



Medical Hx / medications

Leukemia: Not on meds / chemo

Admission one ***month ago*** for non-ID reasons

- Dx with **hyperviscosity syndrome**, perhaps MGUS?
- Also had w/up for *thrombocytopenia*, favored to be **TTP**
  - Start prednisone 20
  - No PJP ppx
- Incidental **left lower lobe** lung mass
  - 10 x 12 mm

Case 3: Exposure History

Geographic & Travel	• Lives in West Virginia • Never international travel
Occupational	• **Cattle farmer**
Substance & needles	• No EtOH, tobacco, drugs • No needle exposures
Animals	• Cattle
Exposures & hobbies	• Does work outdoors, namely with the cattle • No known TB risk factors

Case 3: Exam (per MICU note)

Vitals: 36.5 | 71 | **101/63** | 96%
General: appears chronically ill
Eyes: Conjunctiva clear, Pupils equal and round, Sclera non-icteric
HENT: Head atraumatic and normocephalic. **Vesicular/blisters under lower lip**. Two ulcers on lower lip that is blood filled but contained.
Neck: Trachea Midline
Lungs: Clear to auscultation bilaterally
Cardiovascular: Regular rate and rhythm, no murmur, click, rub or gallop
Abdomen: Soft, non-tender, Bowel sounds normal, non-distended
Extremities: No cyanosis or edema
Skin: Skin warm and dry
Neurologic: Alert and oriented x 3. **Answers questions but has confusion**.

Case 3: Labs

CBC	Result
WBC	**23.7**
Hgb	9.5
Platelets	**113**
Neut %	25%
Lymph %	**72%**
Eos %	0%

Chem7	Result
Na	**107**
K	2.9
Cl	**82**
HCO3	12
Cr	1.16

Misc	Result
sOsm	288
Lactate	**5.3**
LFTs	WNL

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CBC	Result
WBC	**23.7**
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Chem7	Initial
Na	**107**
K	2.9
Cl	**82**
HCO3	12
Cr	1.16

5 hour repeat

Chem7	Repeat	VBG
Na	**127**	131
K	3.4	3.8
Cl	102	99
HCO3	16	20
Cr	1.32	---

Misc	Initial	Repeat
sOsm	288	281
Lactate	**5.3**	2.6
LFTs	WNL	

[Q3.1] DDx

free response, vote

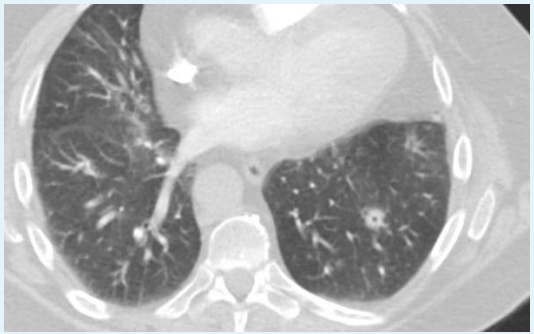
[Q3.2] Additional work up?

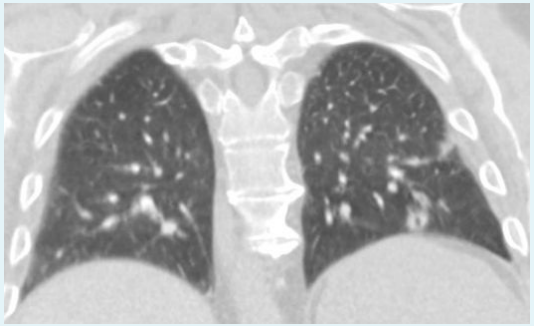
Word cloud

Case 3: Imaging

A **60 y/o M** with PMH including untreated large granular lymphocytic leukemia, TTP (on pred 20) p/w **AMS, hyponatremia, & hypoxia**

1.5 months ago

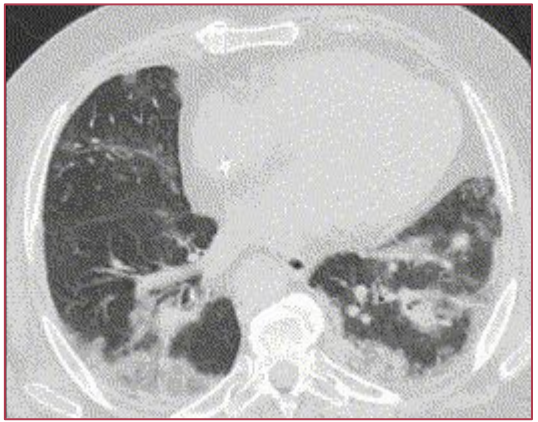


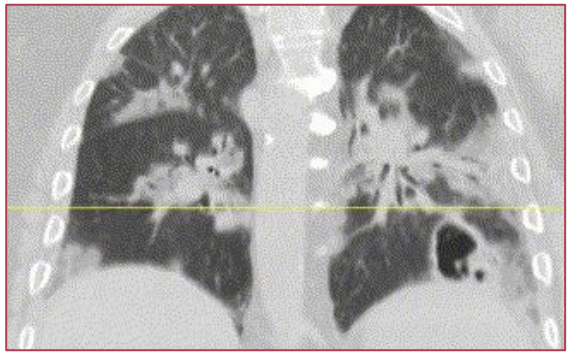


Case 3: Imaging

Interval increased size of a LLL lesion with cavitation (1.2 → 2.8 cm). A halo of groundglass opacity surrounds this consolidation

Impression: Constellation of findings are compatible with fungal infection in the lung, with concern for focal invasive aspergillosis





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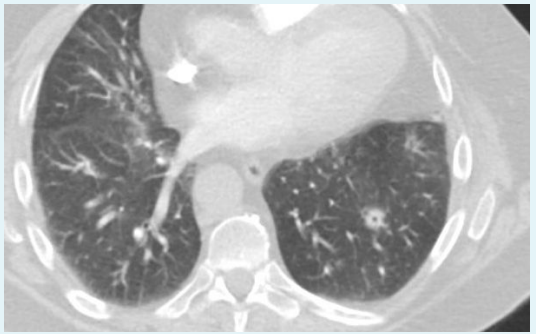
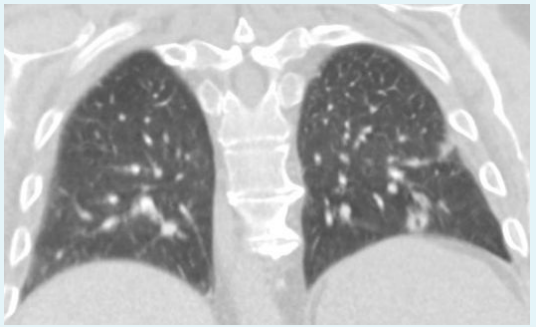
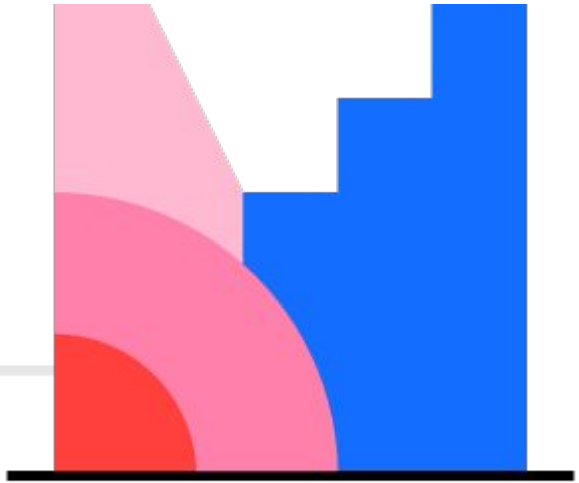




[Q3.3] invasive aspergillosis or something else?

Slider response (disagree vs agree)



This is invasive aspergillosis (specifically)

This is a fungal infection

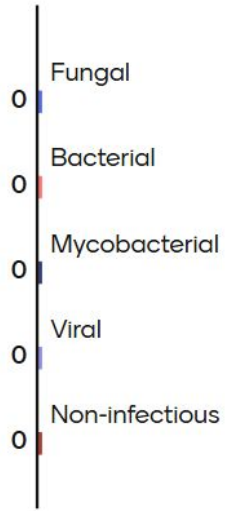
This is a cavitary pneumonia

Strongly disagree

Strongly agree

[Q3.4] What's going on?

Distribute responses (on 100pt scale)



Mentimeter

Case 3: Workup

Serum / Urine	Result
Histo Ag	
Blasto Ag	
Crypto Ag	
Fungitell	
Asp GM	
Legionella Ag	
QuantGOLD	

BAL	Result
Asp GM	
Asp PCR	
MTB PCR	
PJP PCR	
Legionella DNA	

Resp Biofire	Result
...	

Micro	Result
Blood	
Urine	
BAL (routine)	
BAL (AFB)	
BAL (fungal)	

Case 3: Workup

Serum / Urine	Result
Histo Ag	Neg
Blasto Ag	Neg
Crypto Ag	Neg
Fungitell	<31
Asp GM	Neg
Legionella Ag	**Pos**
QuantGOLD	Neg

BAL	Result
Asp GM	
Asp PCR	
MTB PCR	
PJP PCR	
Legionella DNA	

Resp Biofire	Result
…	

Micro	Result
Blood	
Urine	
BAL (routine)	
BAL (AFB)	
BAL (fungal)	

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Crypto Ag	Neg
Fungitell	<31
Asp GM	Neg
Legionella Ag	**Pos**
QuantGOLD	Neg

BAL	Result
Asp GM	Neg
Asp PCR	Neg
MTB PCR	Neg
PJP PCR	Neg
Legionella DNA	Neg

Resp Biofire	Result
...	

Micro	Result
Blood	
Urine	
BAL (routine)	
BAL (AFB)	
BAL (fungal)	

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Histo Ag	Neg
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Fungitell	<31
Asp GM	Neg
Legionella Ag	**Pos**
QuantGOLD	Neg

BAL	Result
Asp GM	Neg
Asp PCR	Neg
MTB PCR	Neg
PJP PCR	Neg
Legionella DNA	Neg

Micro	Result
Blood	
Urine	
BAL (routine)	
BAL (AFB)	
BAL (fungal)	

Resp Biofire	Result
Metapneumovirus	**Pos**
Parainfluenza 4	**Pos**

Case 3: Workup

Serum / Urine	Result
Histo Ag	Neg
Blasto Ag	Neg
Crypto Ag	Neg
Fungitell	<31
Asp GM	Neg
Legionella Ag	**Pos**
QuantGOLD	Neg

BAL	Result
Asp GM	Neg
Asp PCR	Neg
MTB PCR	Neg
PJP PCR	Neg
Legionella DNA	Neg

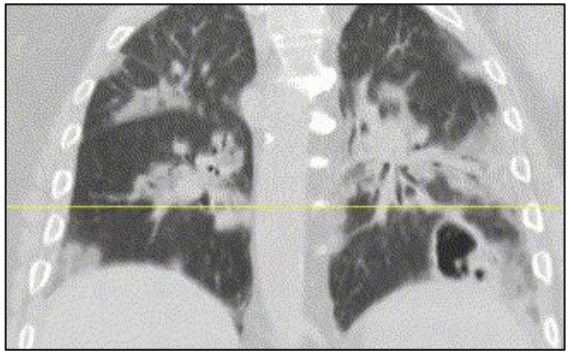
Micro	Result
Blood	Neg
Urine	Neg
BAL (routine)	NG
BAL (AFB)	NG
BAL (fungal)	**C. tropicalis**

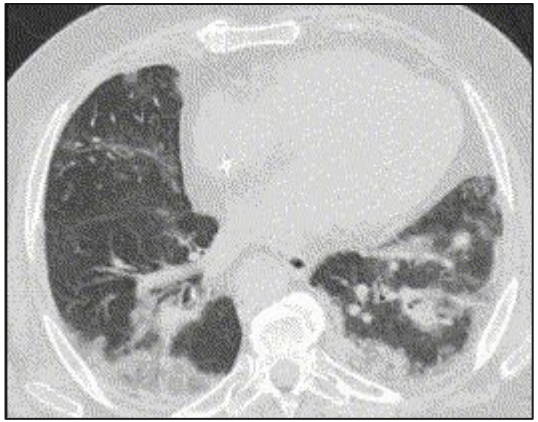
Resp Biofire	Result
Metapneumovirus	**Pos**
Parainfluenza 4	**Pos**

Case 3: Summary

A **60 y/o M** with PMH including untreated T-cell LGL, ITP/TTP (on pred 20) p/w AMS, ~~hyponatremia~~, & hypoxia found to have expanding LLL cavitary lesion w/ halo sign

- Biofire: **hMPV**, **paraflu**
- Urine **legionella**: positive
- BAL: normal





[Q3.5] DDx now?

What is driving his pulmonary process?

Distribute responses (on 100pt scale)

0	Good old HCAP
0	Invasive aspergillosis
0	PJP
0	Other fungal pneumonia
0	Legionella
0	Mycobacterial
0	hMPV &/or parainfulenza
0	Other viral pneumonia (e.g. CMV, HSV)
0	Q fever / coxi
0	Other infectious cause, not listed
0	Non-infectious

[Q3.6] How long to treat for legionella

Guess the number

Case 3: Hospital course

Legionella

- Improved with 2 weeks of **levofloxacin**

Fungal pneumonia?

- Initially on AmBisome
- Transitioned to **voriconazole** once all the studies came back normal
- Plan for **3+ month** course with reimaging

Case 3: Hospital course

Legionella

- Improved with 2 weeks of **levofloxacin**
- Quickly **worsened after stopping**
  - Improved with resuming
- Extended course to total of **4 weeks**

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CMV viremia (skipped over this)
Treated with **Valcyte** until virally suppressed
PCR: 15k → 544

Herpes labialis: Treated with Valcyte (due to above)

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Steroids/PJP
Remained on steroids so started **atovaquone** 1500 q24h

Case 3: Hospital course

Legionella

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- Extended course to total of **4 weeks**

Fungal pneumonia?

- Initially on AmBisome
- Transitioned to **voriconazole** once all the studies came back normal
- Plan for **3+ month** course with reimaging

Some concerns for drug interactions, so **switched vori to Cresemba**

CMV viremia (skipped over this)
Treated with **Valcyte** until virally suppressed
PCR: 15k → 544

Herpes labialis: Treated with Valcyte (due to above)

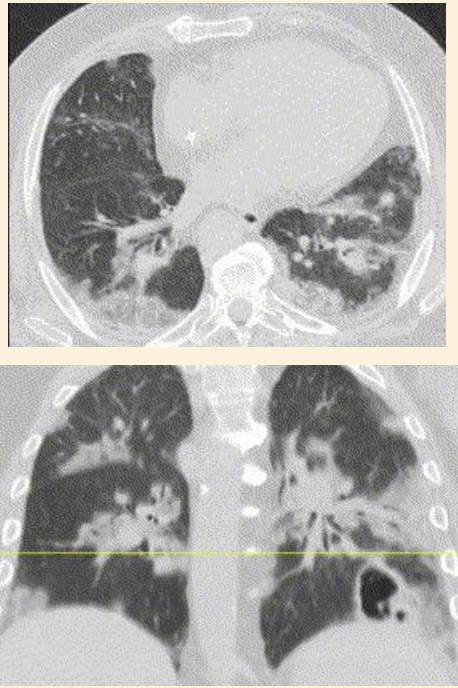
Steroids/PJP
Remained on steroids so started **atovaquone** 1500 q24h

Case #3.5
He’s back...

Case 4: HPI

A **60 y/o M** with PMH including untreated large granular lymphocytic leukemia, TTP (on **pred 20** for past two months), recent admission for legionella p/w **worsening respiratory status**

Recent admission

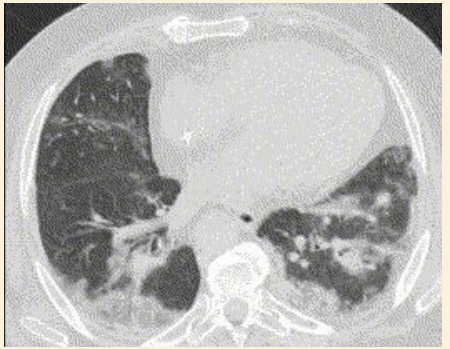


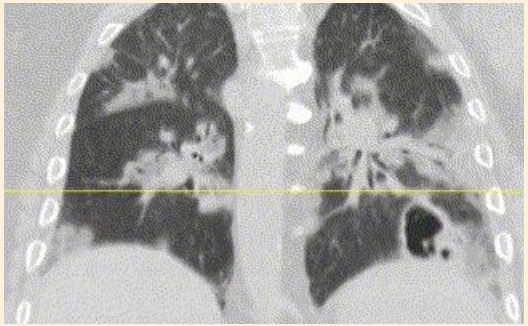
Case 4: HPI

A **60 y/o M** with PMH including untreated large granular lymphocytic leukemia, TTP (on **pred 20** for past two months), recent admission for legionella p/w **worsening respiratory status**

Only was out of the **hospital for 1-2 days**, now **intubated**

Recent admission





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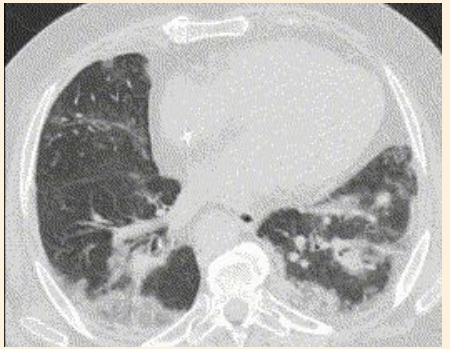
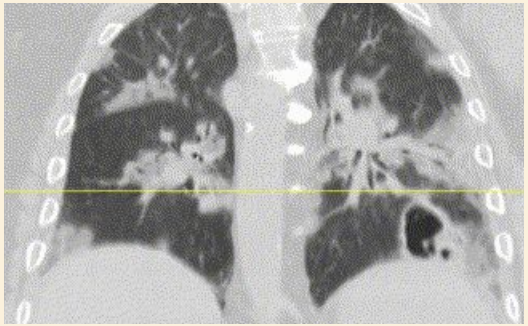
Only was out of the **hospital for 1-2 days**, now **intubated**

Respiratory status has declined **despite**:

- Negative workup (aside from legionella & viruses)
- Levofloxacin
- Cresemba
- Valcyte
- Atovaquone ppx

Recent admission





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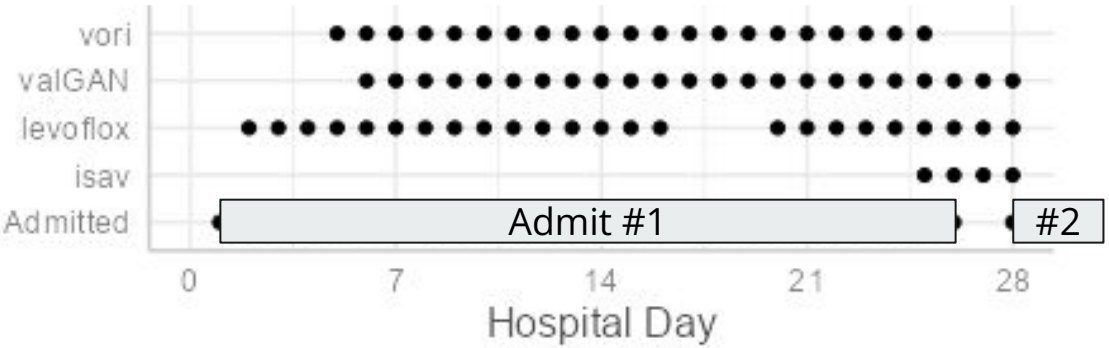

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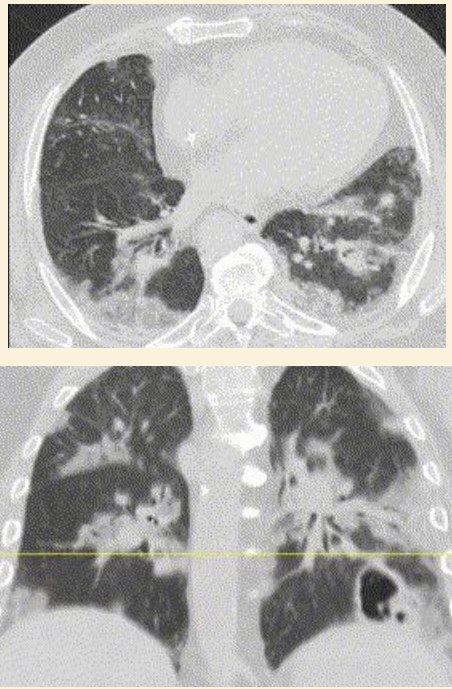

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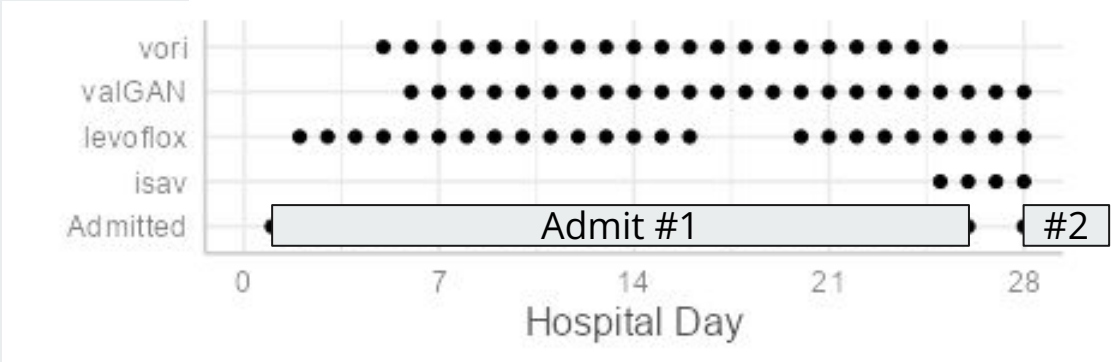
Only was out of the **hospital for 1-2 days**, now **intubated** despite levofloxacin, Cresemba, Valcyte, & atovaquone



[Q4.1] DDx now? Why is he getting worse?

Free response

Case 4: Prior workup (last admission)

Serum / Urine	Result
Histo Ag	Neg
Blasto Ag	Neg
Crypto Ag	Neg
Fungitell	<31
Asp GM	Neg
Legionella Ag	**Pos**
QuantGOLD	Neg

BAL	Result
Asp GM	Neg
Asp PCR	Neg
MTB PCR	Neg
PJP PCR	Neg
Legionella DNA	Neg

Micro	Result
Blood	Neg
Urine	Neg
BAL (routine)	NG
BAL (AFB)	NG
BAL (fungal)	**C. tropicalis**

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Serum / Urine	Result
Histo Ag	Neg
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Crypto Ag	Neg
Fungitell	<31
Asp GM	Neg
Legionella Ag	**Pos**
QuantGOLD	Neg

BAL	Result
Asp GM	Neg
Asp PCR	Neg
MTB PCR	Neg
PJP PCR	Neg
Legionella DNA	Neg

Micro	Result
Blood	Neg
Urine	Neg
BAL (routine)	NG
BAL (AFB)	NG
BAL (fungal)	**C. tropicalis** **Nocardia nova**

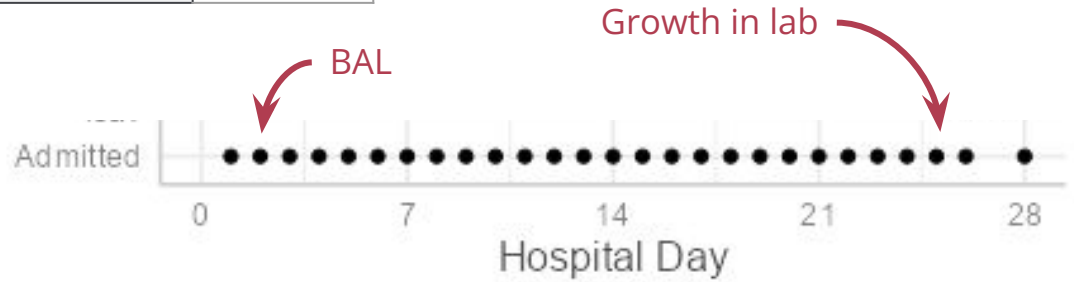
24 days after BAL

Case 4: Prior workup (last admission)

Serum / Urine	Result
Histo Ag	Neg
Blasto Ag	Neg
Crypto Ag	Neg
Fungitell	<31
Asp GM	Neg
Legionella Ag	**Pos**
QuantGOLD	Neg

BAL	Result
Asp GM	Neg
Asp PCR	Neg
MTB PCR	Neg
PJP PCR	Neg
Legionella DNA	Neg

Micro	Result
Blood	Neg
Urine	Neg
BAL (routine)	NG
BAL (AFB)	NG
BAL (fungal)	**C. tropicalis** **Nocardia nova**



Cases 3-4: Nocardia nova

- Very, **very late growth of Nocardia** (24 days after BAL)

Tobramycin	32 (R)
Linezolid	1 (S)
Bactrim	.25/4.8 (S)
Doxycycline	8 (R)
Ciprofloxacin	16 (R)
Augmentin	128 (R)
Moxifloxacin	4 (R)
Amikacin	<0.5 (S)
Imipenem	2 (S)
Ceftriaxone	32 (I)
Clarithromycin	<.03 (S)
Minocycline	4 (I)

Cases 3-4: Nocardia nova

- Very, **very late growth of Nocardia** (24 days after BAL)
- Missed during prior admission
  - To be fair, he was discharged the next day and readmitted 2 days later
  - So while Nocardia Tx wasn't started until 28 days after BAL, only went 4 days without treatment (from time of results)

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Cases 3-4: Nocardia nova

- Very, **very late growth of Nocardia** (24 days after BAL)
- Missed during prior admission
  - To be fair, he was discharged the next day and readmitted 2 days later
  - So while Nocardia Tx wasn't started until 28 days after BAL, only went 4 days without treatment (from time of results)
- Multiple other (non-infectious issues) developed while in MICU (stokes, CRRT, etc)
- Went CMO after palliative consult

Tobramycin	32 (R)
Linezolid	1 (S)
Bactrim	.25/4.8 (S)
Doxycycline	8 (R)
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Case #5

Case 5: HPI

A **37 y/o M** with PMH including poorly controlled DM (A1c **9.7**), TBI, sacral decubitus ulcer p/w **DKA & hypoxia**

Case 5: HPI

A **37 y/o M** with PMH including poorly controlled DM (A1c 9.7), TBI, sacral decubitus ulcer p/w **DKA & hypoxia**

- **Influenza A positive** on admission
- Respiratory status improved a little, but then worsened

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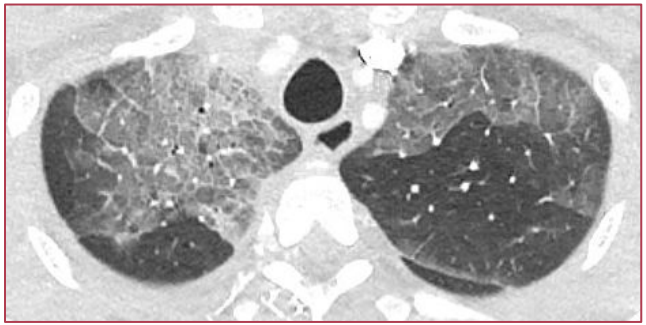
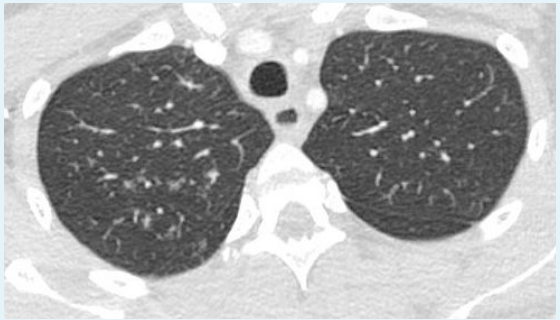


A week ago (admission)



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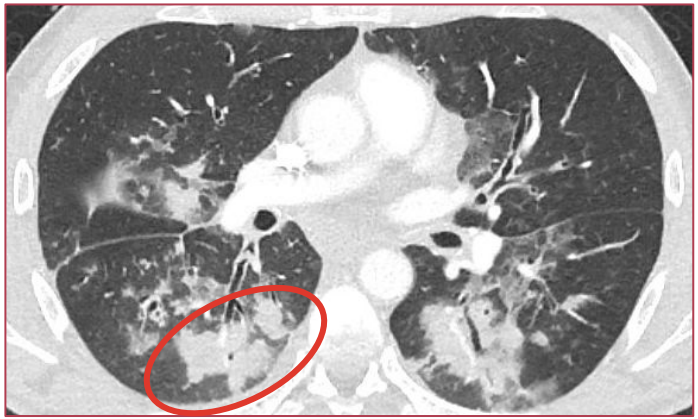

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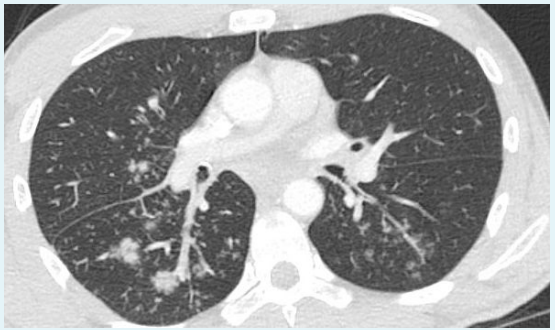

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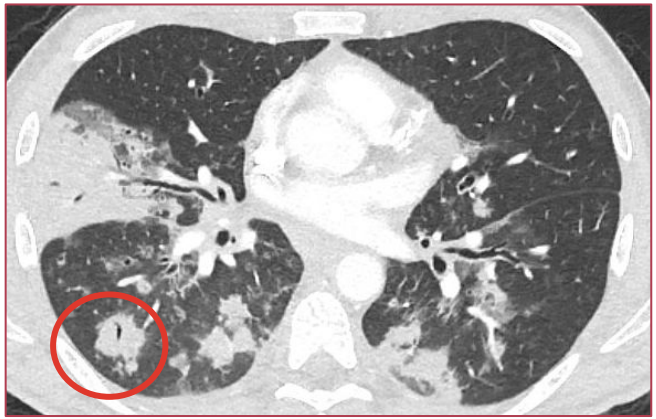

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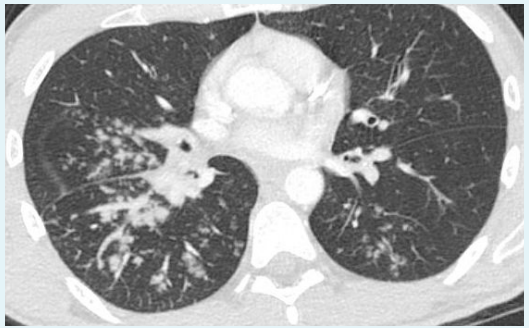

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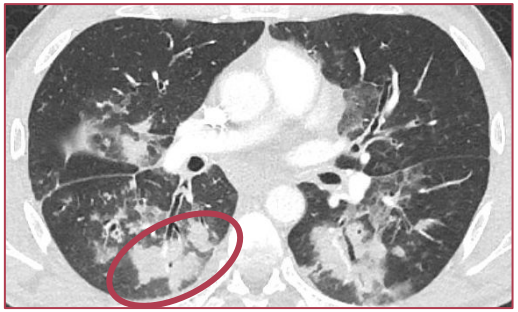

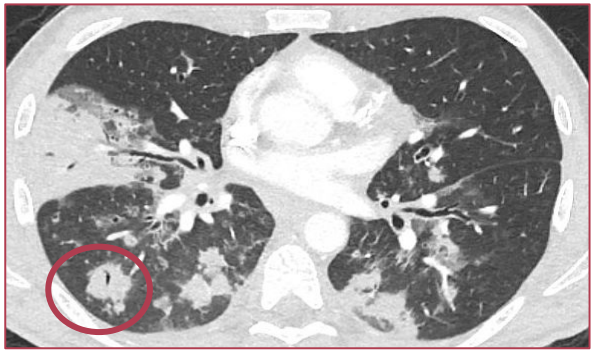

DDx?
(No MentiMeter for this one)

Case 5: HPI

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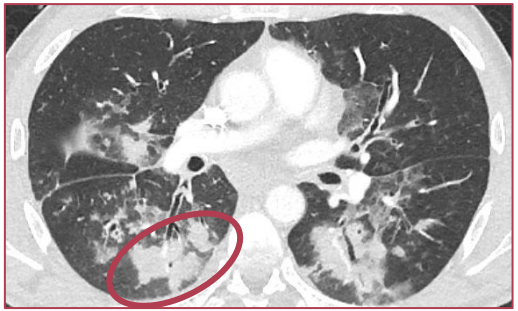

- **Influenza A positive** on admission
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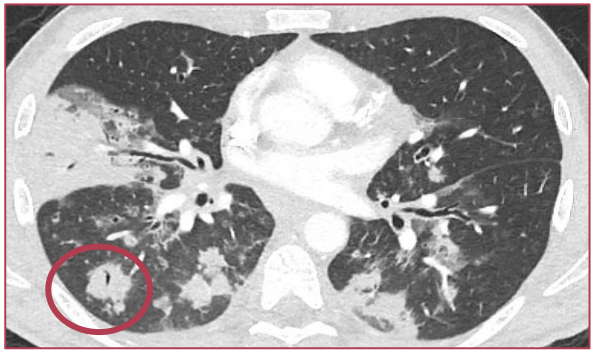
- Initial BCx: **MRSA** (1 of 2 sets)



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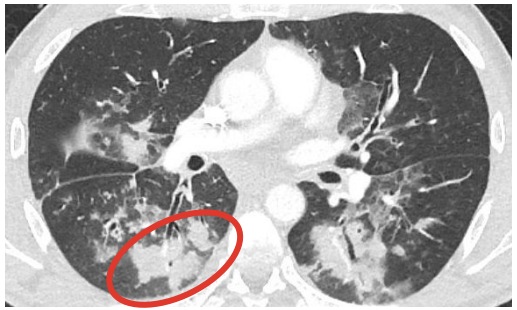

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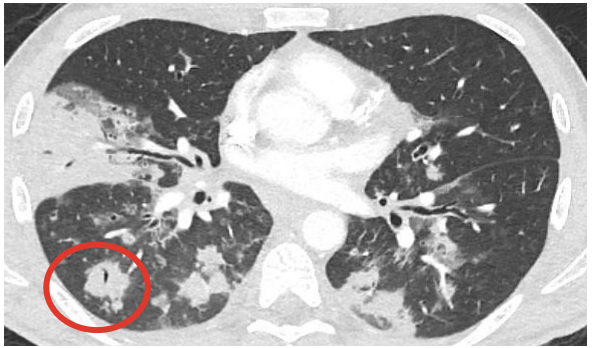


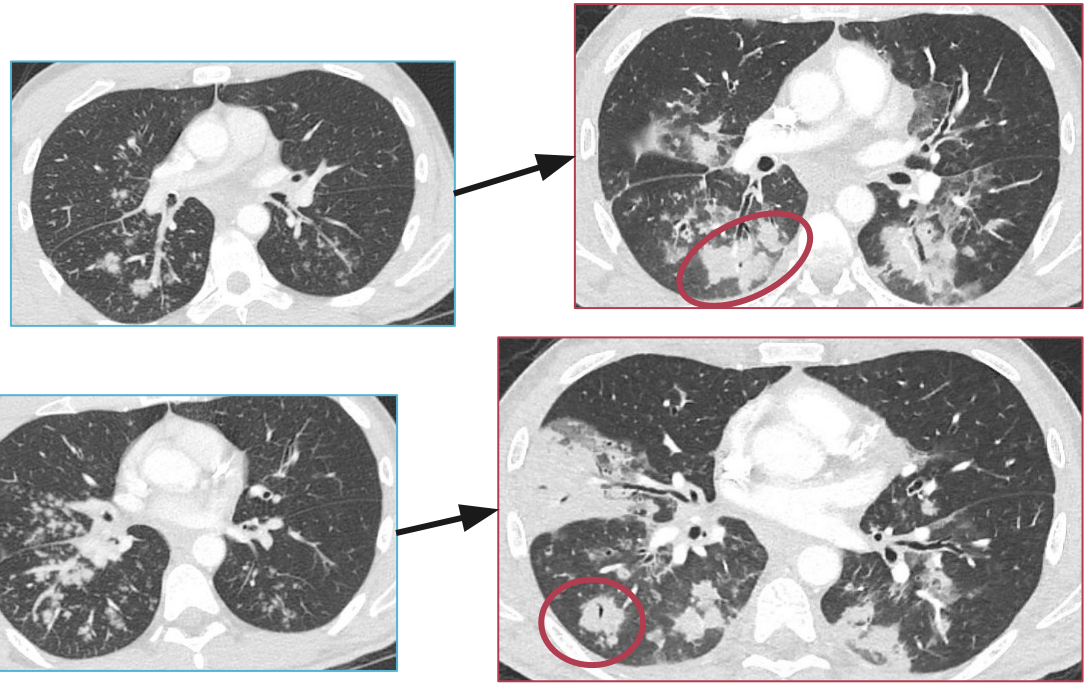
- Initial BCx: **MRSA** (1 of 2 sets)
- TTE: No valvular pathology
- Couldn't produce sputum

Case 5: Staph aureus *

Risk factors / clues

- Recent **influenza**
- Immunocompromise (DM)
- **Necrotizing pneumonia**

* Presumed to be from *Staph aureus*, since he improved on Zyvox (but took his time to get better)



Case #6

Case 6: HPI

A **30 y/o F** with PMH including tobacco use p/w **worsening cough**

Case 6: HPI

A **30 y/o F** with PMH including tobacco use p/w **worsening cough**

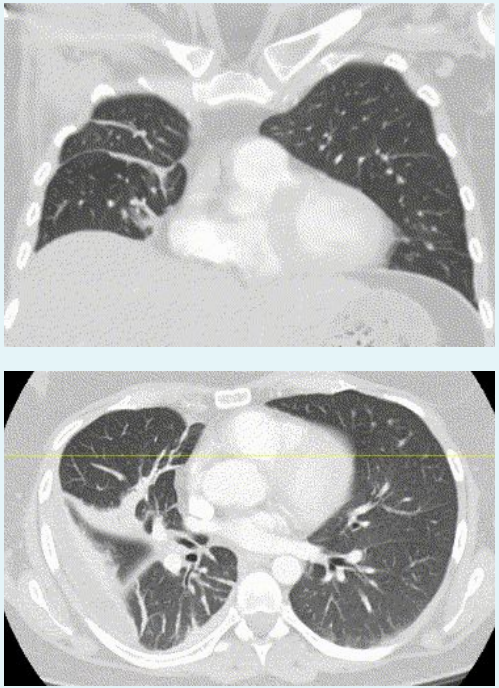
- Chronic, nonproductive cough for past year
  - Worsened in **past two months**
  - Now some **dyspnea**, **chronic leukocytosis**

Case 6: HPI

A **30 y/o F** with PMH including tobacco use p/w **worsening cough**

- Chronic, nonproductive cough for past year
  - Worsened in **past two months**
  - Now some dyspnea, chronic leukocytosis
- Two months ago, CT in ED showed **right pleural effusion**
  - Symptoms not improved with **doxycycline & cefpodoxime**

Two months ago

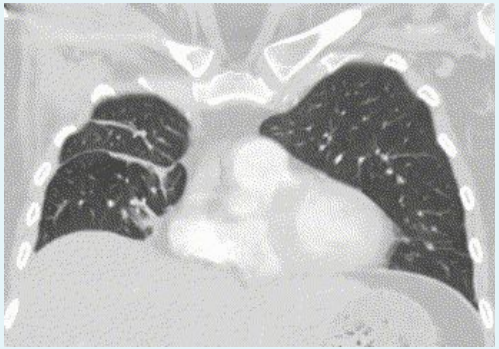


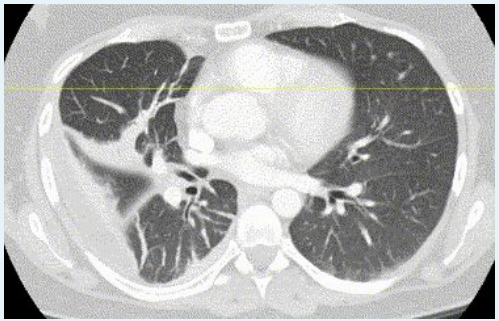
Case 6: HPI

A **30 y/o F** with PMH including tobacco use p/w **worsening cough**

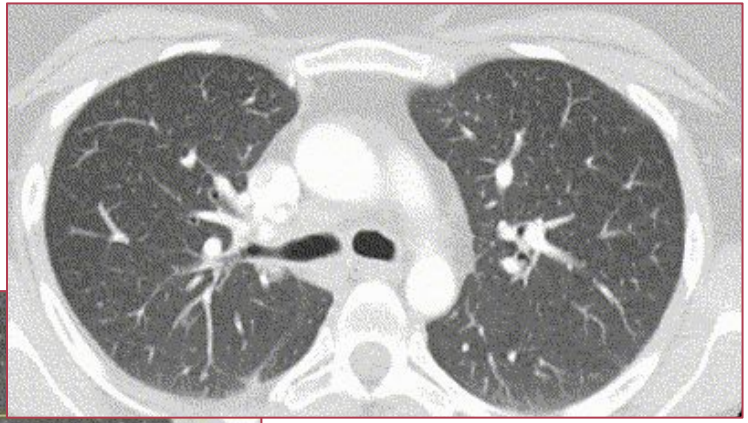
- Chronic, nonproductive cough for past year
  - Worsened in **past two months**
  - Now some dyspnea, chronic leukocytosis
- Two months ago, CT in ED showed **right pleural effusion**
  - Symptoms not improved with **doxycycline & cefpodoxime**
- No overt fevers, but **chills & anorexia** for **past month**
- Had seen CT surgery a month ago, who ordered repeat CT
  - Repeat CT prompted this admission

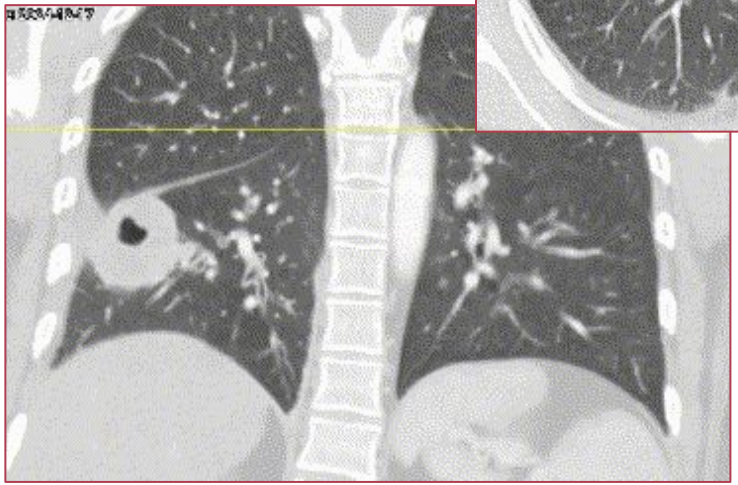
Two months ago



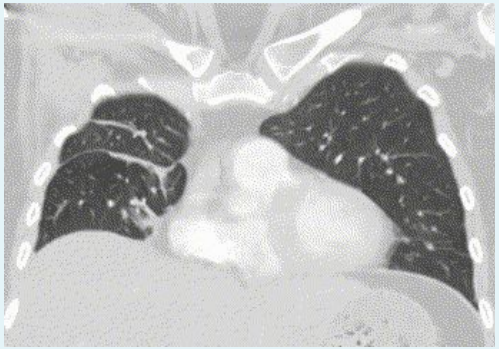


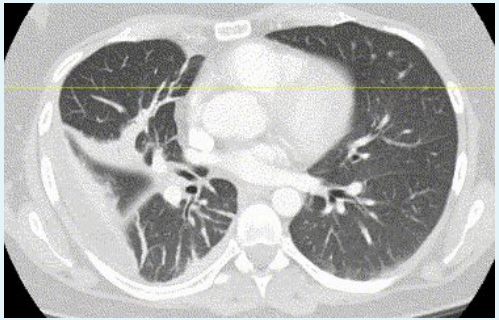
Case 6: Imaging





Two months ago





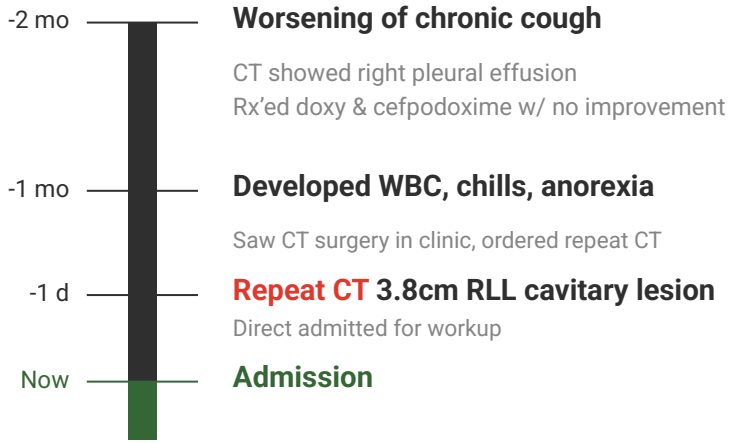
Case 6: Social & Exposure History

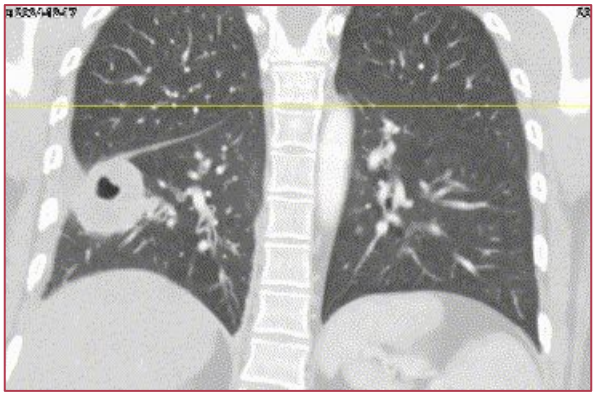
Geographic & Travel	• Resides in in house a mile out of town (in the woods) • Lives with boyfriend and two kids • No recent foreign or domestic travel. Never international travel
Occupational	• Not working, takes care of the kids (6 & 8 years old)
Substance & needles	• Social use of EtOH • **Smokes 1 ppd** • **Used to smoke weed** (many years ago); never IVDU • Remote hx of unprofessional tattoos
Animals	• Cats, dogs, snakes at home • No frequent bird exposures, but has **cared for her parents chickens** in the past
Exposures & hobbies	• No known TB risk factors, including incarceration, homelessness, healthcare exposures, known contacts with TB, international travel • In the past year, she has **gone in caves** (unclear if there were bats)

Case 6: Summary

A **30 y/o F** with PMH including tobacco use p/w **worsening cough** x2 months after **right pleural effusion** that was unimproved with doxy & cefpodoxime.

- **Systemic symptoms** x1 month
- CT chest now with 3.8cm RLL cavitary lesion
- Smoker, birds, caves





[Q6.1] DDx

free response, vote

[Q6.2] Additional work up?

Word cloud

Case 6: DDx?

Serum / Urine	Result
Histo Ag	
Blasto Ag	
Crypto Ag	
Fungitell	---
Asp GM	
Legionella Ag	---
Strep pneumo Ag	
QuantGOLD	---

BAL	Result
Asp GM	
Asp PCR	
MTB PCR	---
PJP PCR	
Legionella DNA	---

Micro	Result
Blood	
BAL (routine)	
BAL (AFB)	
BAL (fungal)	

Case 6: DDx?

Serum / Urine	Result
Histo Ag	Neg
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Micro	Result
Blood	
BAL (routine)	
BAL (AFB)	
BAL (fungal)	

Additional HPI
Extensive **dental work** six months ago

Case 6: DDx?

Serum / Urine	Result
Histo Ag	Neg
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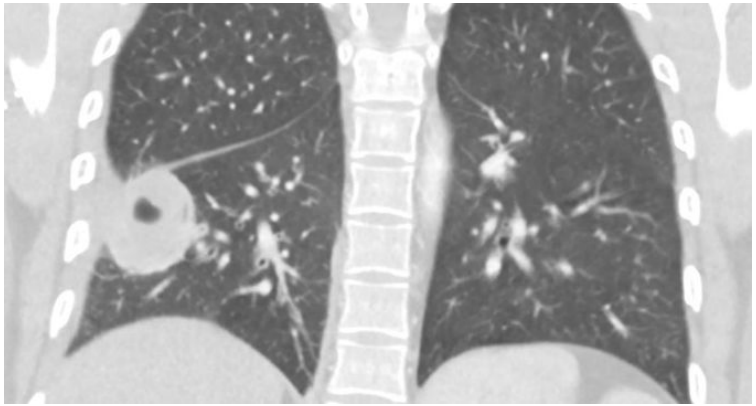
Legionella DNA	---

Micro	Result
Blood	NG
BAL (routine)	**4+ Strep anginosus**
BAL (AFB)	NG
BAL (fungal)	NG

Case 6: Strep anginosus

Hospital course

- TTE normal
- Rx: **ceftriaxone** & **flagyl** (**4 weeks**)
- Repeat CT outpatient



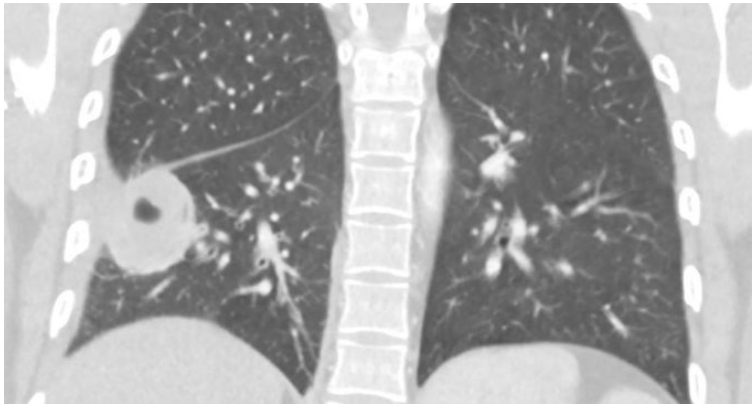
Case 6: Strep anginosus

Hospital course

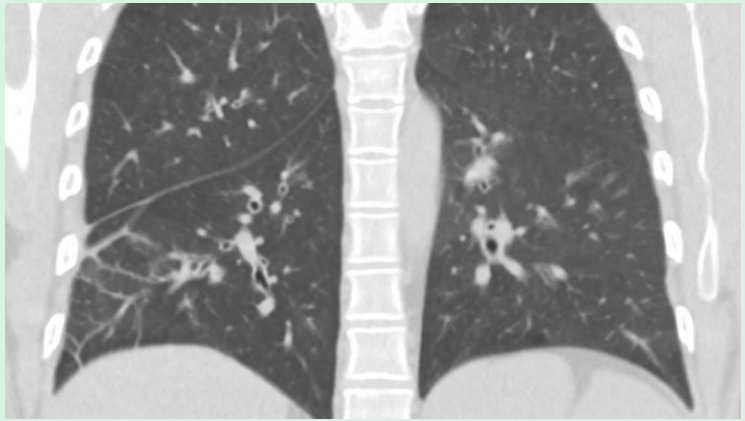
- TTE normal
- Rx: **ceftriaxone & flagyl** (**4 weeks**)
- Repeat CT outpatient

Clinic

- Doing well after 4 weeks of OPAT
- Hadn't gotten repeat CT, so extended duration by **2 weeks** with **cefpodoxime & flagyl**
- CT (at 7 weeks) **near complete resolution**



After treatment



Discussion

Links to articles discussed here

Legionella & Hyponatremia

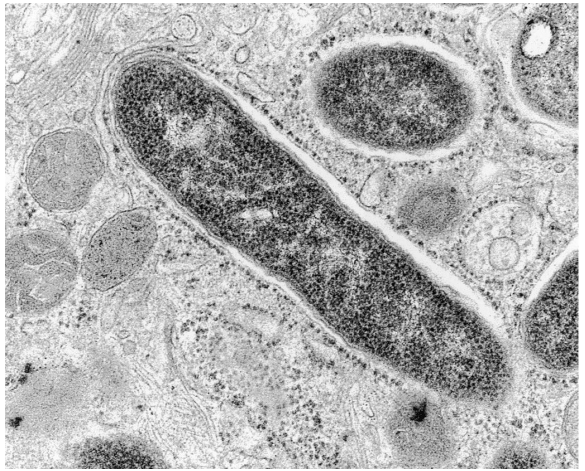
Learning objectives

- Recognize the spectrum of **clinical manifestations** seen in Legionella infections
- Discuss the various **testing modalities** used to diagnose Legionella
- Compare the **common treatments** used in Legionnaires' disease, including duration of treatment
- Appraise the literature regarding **hyponatremia in Legionella** (& critique what I learned in medical school)

Legionnaires' disease [1]

Bacterial pneumonia caused by Legionella

- Intracellular small gram-negative bacilli
  - Fun fact: Coxiella burnetii (Q fever) is closest living relative to Legionella
- Classically associated with pulse temperature dissociation, pulmonary symptoms, hyponatremia, elevated LFTs [5]
  - More on this later
- Often associated with altered mental status, with a normal neurologic exam



Legionella cavitation? [9]

Cavitary disease is quite **rare**, but has been described (2009 review of 79 cases) [9]

- 90% are **immunosuppressed** at baseline (35% SOT)
  - 70% were on **steroids** at time of diagnosis
- **One in four** died

	Solid organ transplantation	22	35.5%	
	Hematological malignancy	7	11.3%	*
	Collagen vascular diseases	6	9.7%	
	Neoplasms	6	9.7%	
	HIV infection	3	4.8%	*
	Alchoholism	1	1.6%	**
	COPD	3	4.8%	**
	Others	10	16.1%	
	No known underlying diseases	6	9.7%	
Outcome	survived	45	72.6%	
	dead	17	27.4%	

*: B lymphoma in HIV infection

**: co-morbidity of COPD and alchoholism

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Unclear if they looked at co-infections
(more on this later)

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Legionella: Testing

Urine antigen

- Urine antigen is ideal test (in terms of sensitivity & specificity)
  - Only for serogroup 1
- Antigenuria may persist for weeks, even after pneumonia has resolved

DFA

- Less sensitive, and prone to false positives if lab is inexperienced
- Can be done of fixed lung tissue

Test / Specimen	Sensitivity	Specificity
Culture	20 - 95%	100%
Urine antigen	60 - 95%	>99%
Immunofluorescence microscopy	20 - 50%	99%
PCR (sputum, urine)	70 - 95%	95 - 99%

Optimal approach
Some authors [1] suggest more than one test (e.g. urine antigen + PCR) to increase yield

Legionella: Treatment

- Generally, fluoroquinolones (FQ) are about as effective as macrolides
- Little head-to-head comparisons of FQ vs azithromycin
- Retrospective study of critically ill patients found reduced mortality for levoflox vs non-azithro macrolides [2]
- Propensity matched analyses showed similar outcomes between levofloxacin & azithro [3][4]

Legionella: Treatment [1]

- Duration is normally similar to that of other forms of CAP
  - Similar principles apply for lung abscesses (may need prolonged extension)
  - Relapse has been described in immunocompromise
- No benefit to combo therapy, even in severe disease / immunosuppression [2]

Legionella: Treatment [1]

- Up to **10%** of patients with Legionella may have **co-infections with other pathogens**
  - Includes typical respiratory bacteria (H flu, pneumococcus), staph aureus
  - Also PJP, **nocardia**, aspergillus, tuberculosis, cryptococcus
  - More common in immunosuppression & severe disease

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- Generally, patients respond well to therapy
  - Within **hours to days**
  - Radiographic findings may lag
- Failure to respond to therapy should prompt **search for alternative causes**

Legionella & hyponatremia

Classically, legionella is associated with hyponatremia…

- I thought it might be interesting to look up why
- Then I remembered why I don’t like sodium

Why the low sodium?

Multiple choice

Mentimeter

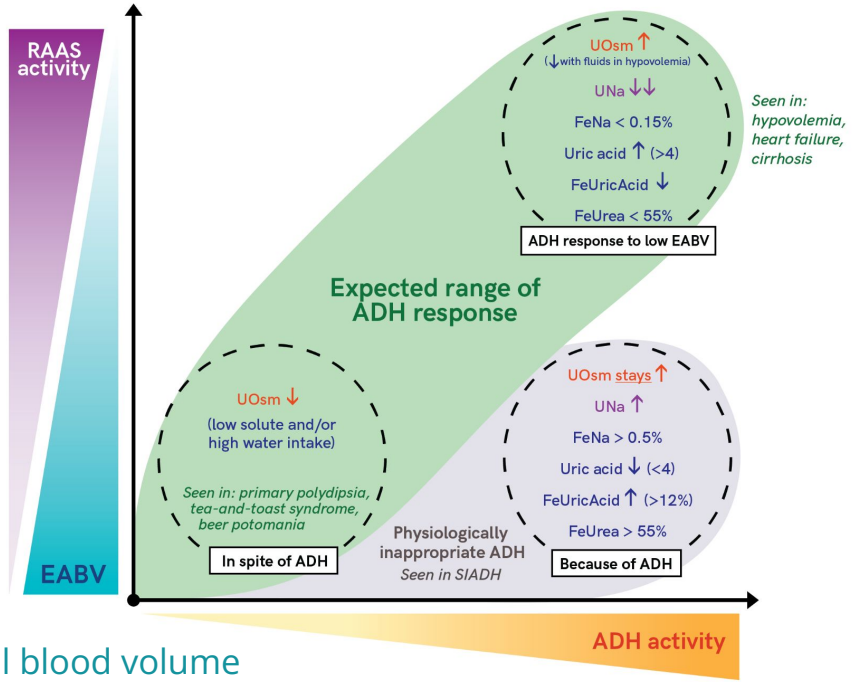
Quick refresher

- Hyponatremia is a problem with water retention, not salt *per se*
- ADH makes the kidneys hold on to water

CORE IM

VISUALIZING HYPOTONIC HYPONATREMIA

UNa reveals RAAS activity. UOsm reveals ADH activity.
ADH secretion is appropriate only when RAAS is active.



EABV = Effective arterial blood volume

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- ↑↑ ADH makes sense when kidneys think there is low blood volume (**EABV**)
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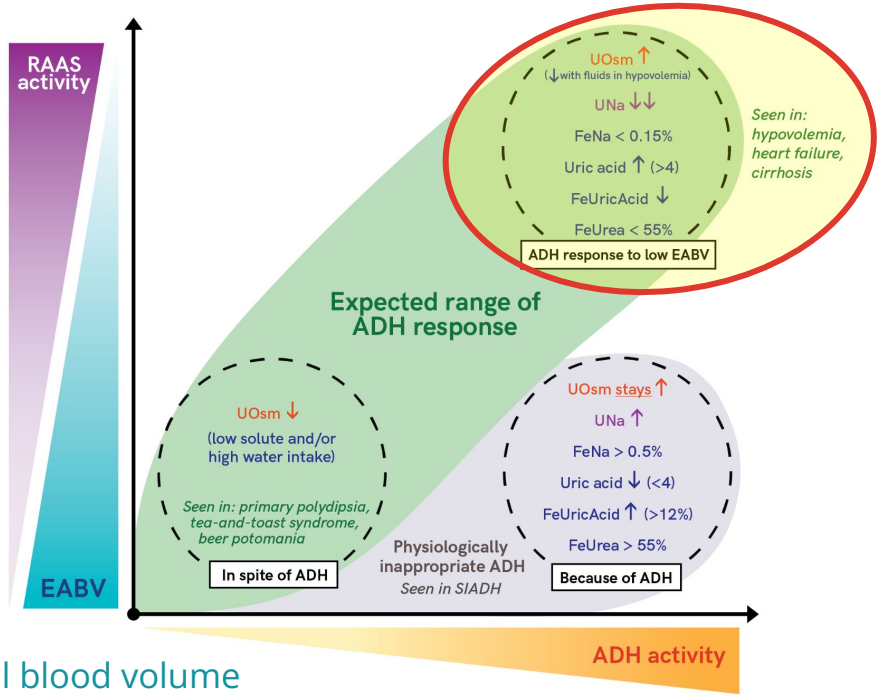

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- SIADH: ↑↑ ADH disproportionate to ↓**EABV**

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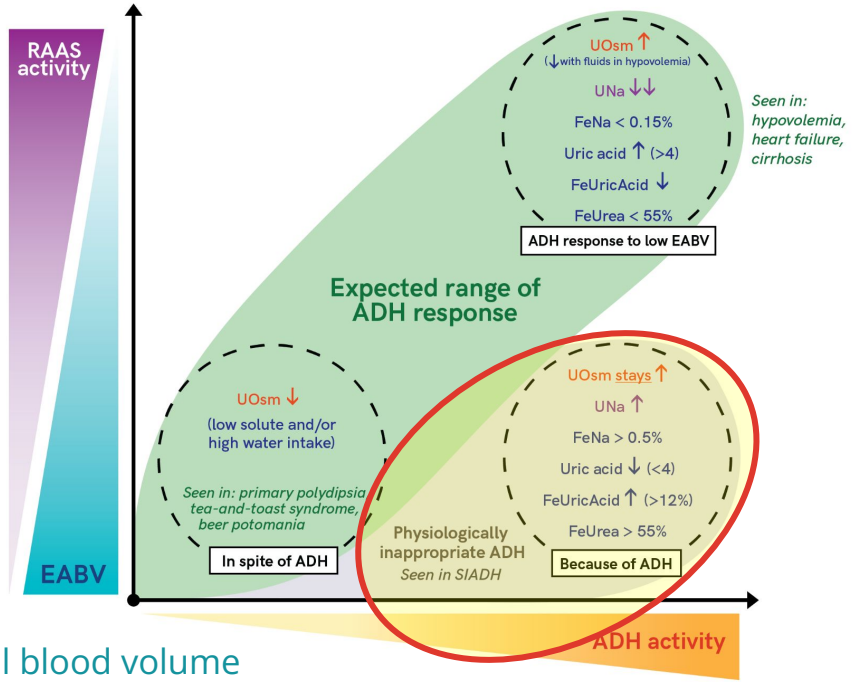

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- SIADH: ↑↑ ADH disproportionate to ↓**EABV**

There is also **renal salt wasting** (formerly cerebral salt wasting), *too complicated* to discuss here

- Appears similar to SIADH but *better* with normal saline (not water restriction)

CORE IM

VISUALIZING HYPOTONIC HYPONATREMIA

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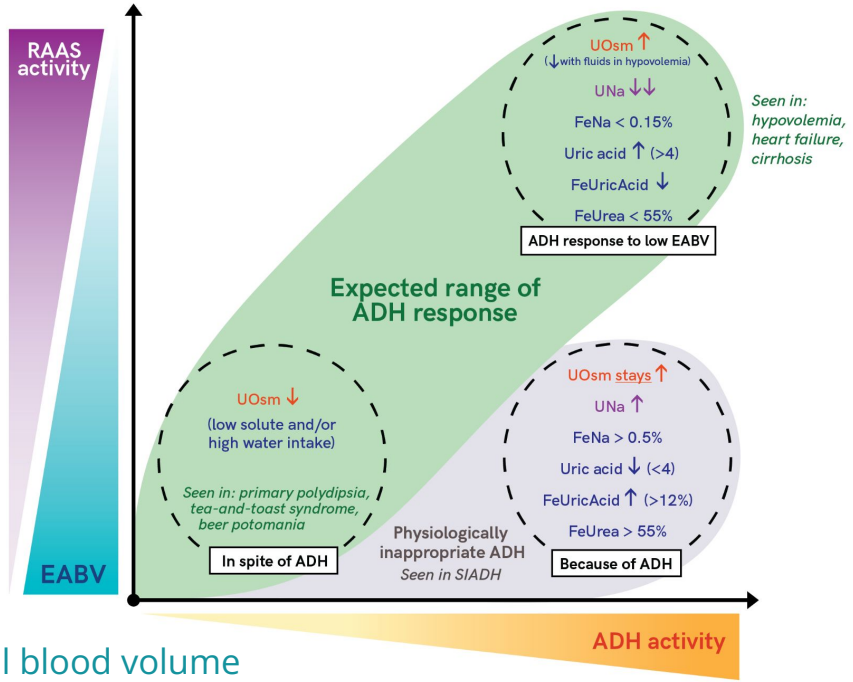

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Does Legionella cause hyponatremia?

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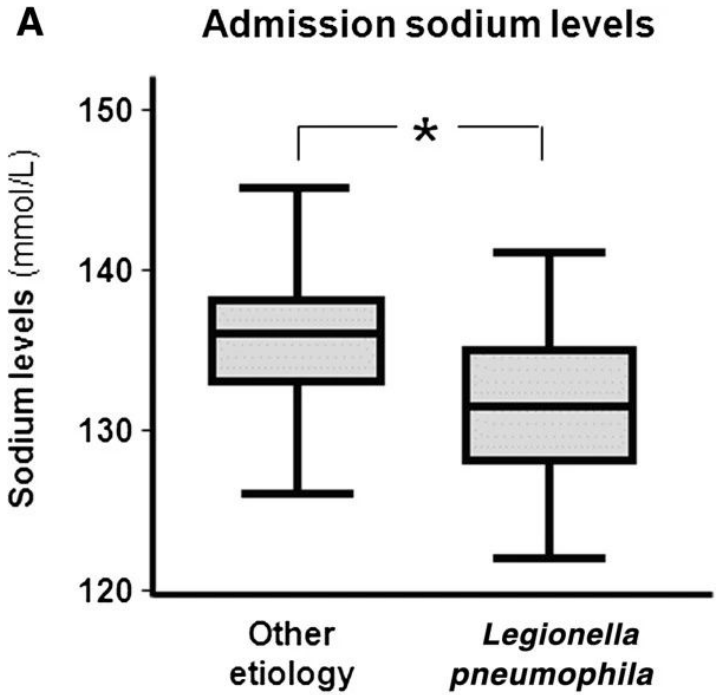
- Used left over blood to measure **copeptin**, in addition to serum sodium levels (on admission)

Copeptin / CT-ProVasopressin
C terminal provasopressin (referred to as **CT-ProVasopressin** in the article) is a stable laboratory surrogate of ADH levels

Schuetz et al (2013) [5]

Patients with **Legionnaires' disease**

- More frequently had **low sodium levels**
  - Defined as Na < 130 (mmol/L)
  - 44.4% vs 8.2% ($p < 0.01$)



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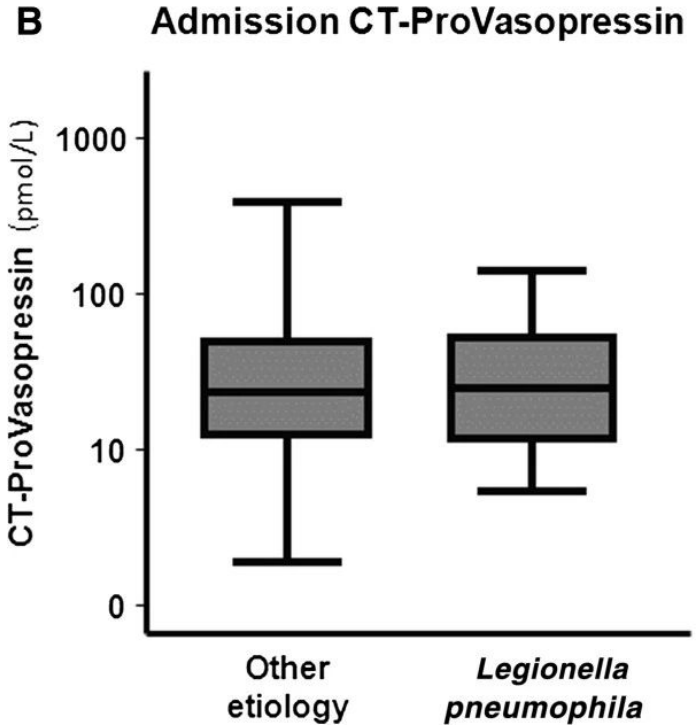
  - 39.4 ±7 vs 51.2 ±2.7 ($p = 0.43$)



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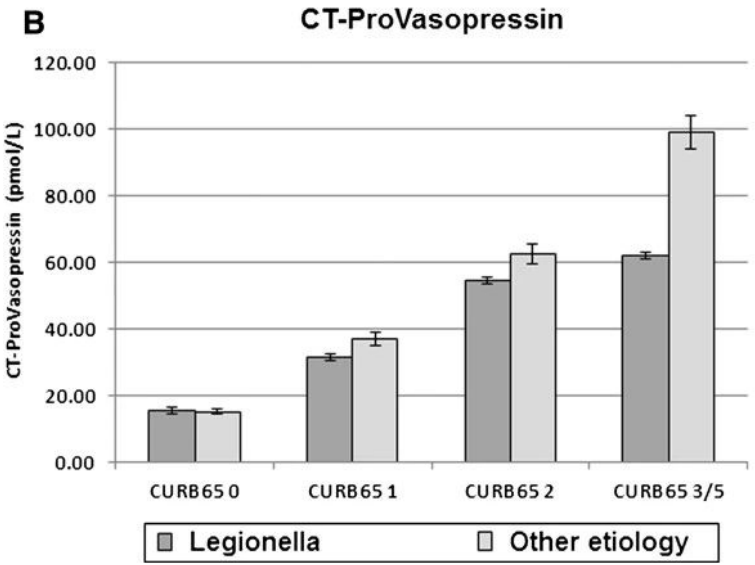

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Author's conclusions

Although legionella is associated with hyponatremia, there is **no evidence that ADH is driving this process**.

Rather, an **ADH-independent process** may be driving hyponatremia, such as **direct renal effects** of cytokines or toxins, as well as **natriuretic hormones**

Why it matters?

Volume management with sepsis & ARDS is challenging

- Fluid restricting when it's not ADH makes things worse

If not SIADH, then what *does* cause hyponatremia?

- Not a whole lot on the pathophysiology that I could find on PubMed
- A few interesting case reports on **acquired Fanconi syndrome** in Legionella

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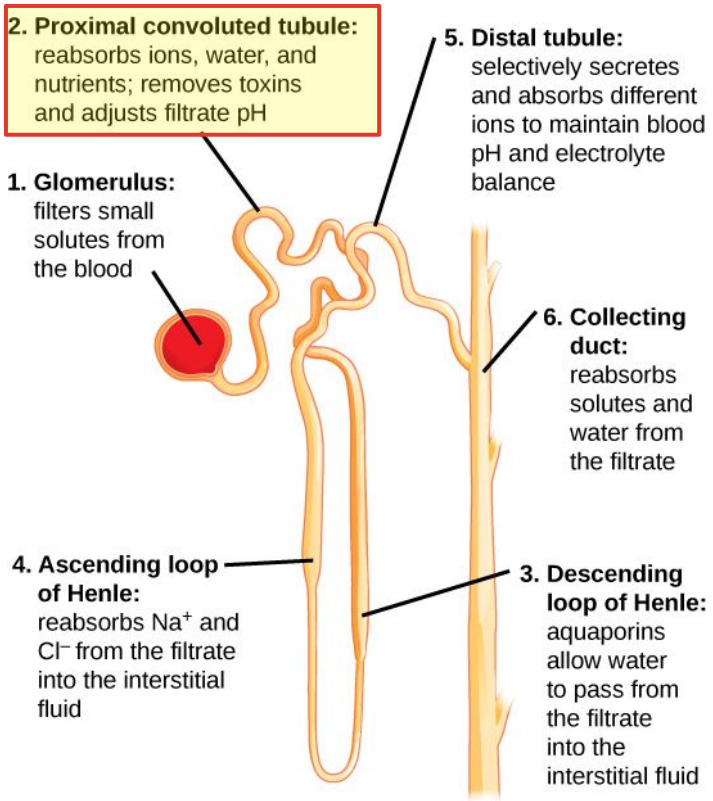
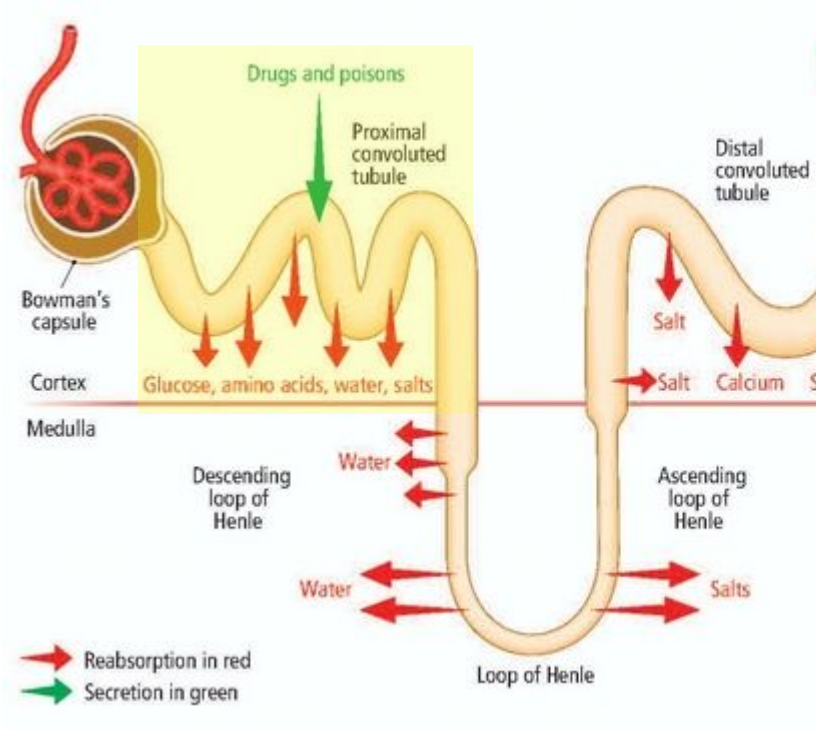
Fanconi syndrome (more nephrology)

- **Fanconi syndrome** is generalized dysfunction of the PCT
- Same syndrome that occurs with **aminoglycosides**, **tenofovir**, **tetracyclines**



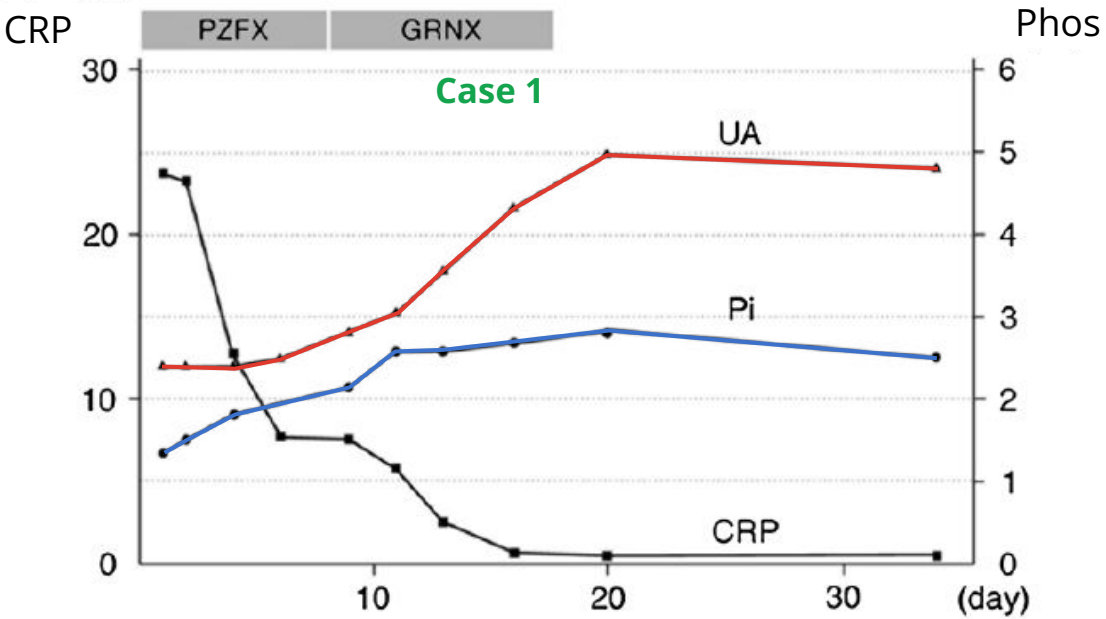
Fanconi syndrome (more nephrology)

- **Fanconi syndrome** is generalized dysfunction of the PCT
- PCT reabsorbs key nutrients, such as phosphate, glucose, and amino acids
- **Results in**:
  - Hypokalemia
  - **Hypophosphatemia**
  - **Hypouricemia**
  - Metabolic acidosis
- +/- hyponatremia (collecting duct can compensate, with use of ADH)



Kinoshita-Katahashi et al (2013) [6]

Case report of 2 cases of acquired Fanconi syndrome + Legionella out of Japan



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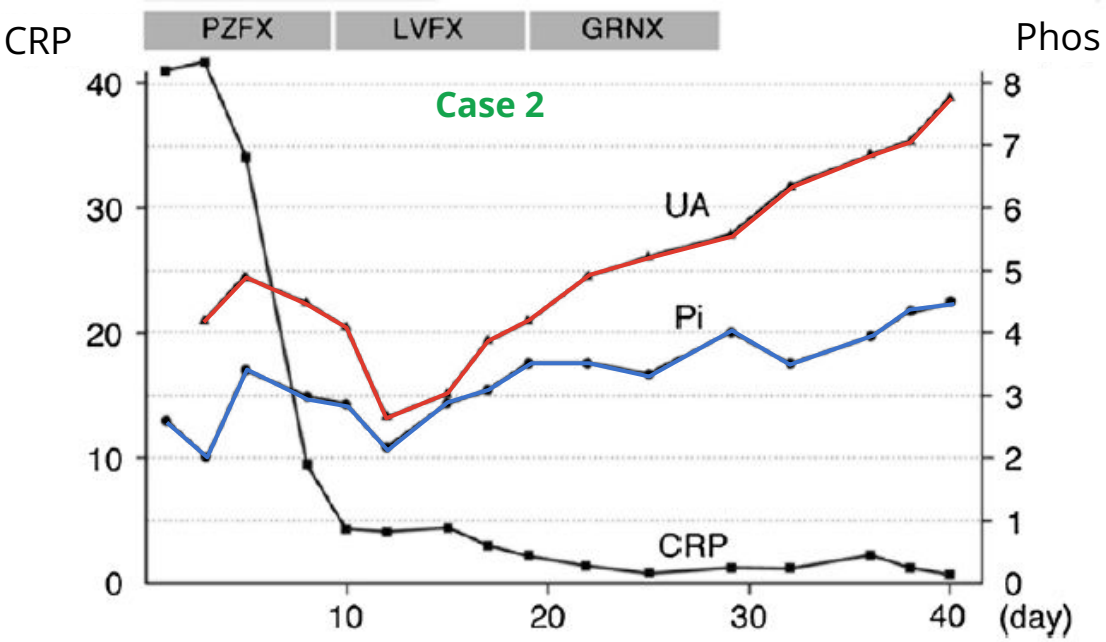

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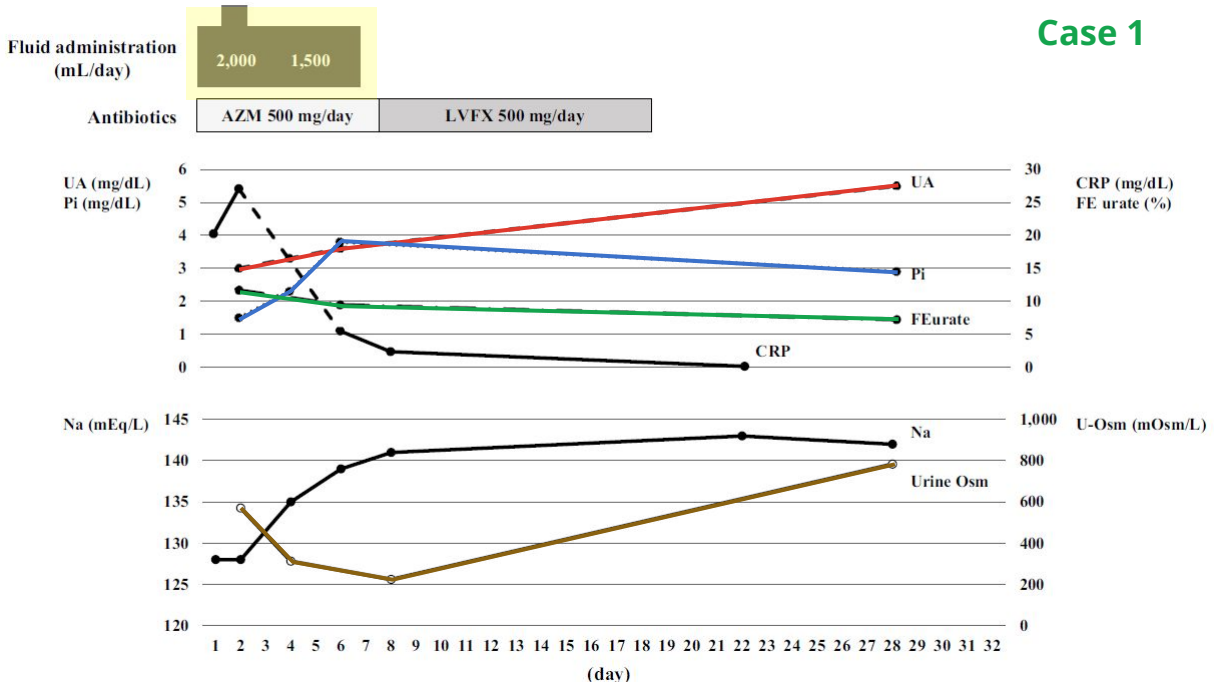

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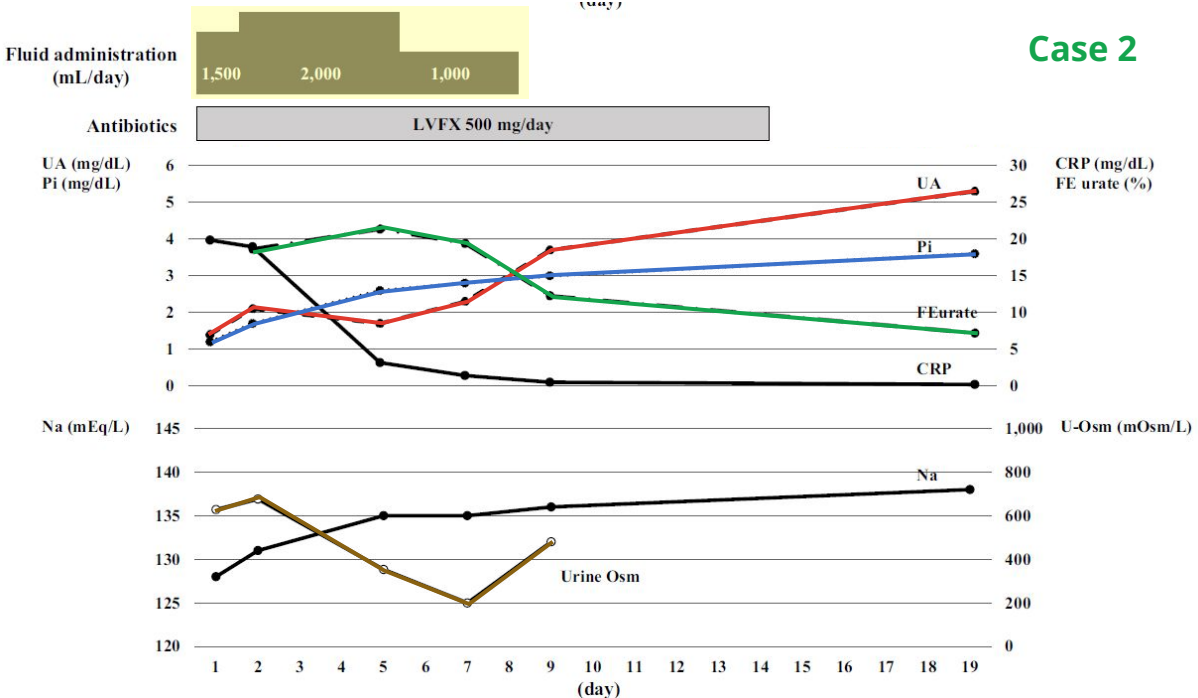

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Speculation

An additional case report [8] discusses evidence of **Legionella involvement in the kidneys** themselves

- Specifically, an autopsy case report showed **positive immunofluorescence** in the renal **proximal tubules**

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- This may imply that the kidneys (PCT specifically) are taking more of a hit than previously expected

Table Legionnaire's Disease: Six Clinical Predictors and Diagnostic Eliminators in Adults Admitted with Pneumonia*

Diagnostic Predictors	Diagnostic Eliminators
Clinical Predictors • Fever (>102°F)	Clinical Eliminators • Sore throat • Severe myalgias
Laboratory Predictors† • Highly elevated ESR (>90 mm/h) or CRP (>180 mg/L) • Highly elevated ferritin levels (>2 × normal) • Hypophosphatemia (on admission/early) • Highly elevated CPK (>2 × normal) • Microscopic hematuria (on admission)	Laboratory Eliminators • Leukopenia • Thrombocytopenia • Negative chest x-ray (no infiltrates)
Legionnaire's disease very likely if >3 predictors present	Legionnaire's disease very unlikely if <3 predictors or >3 diagnostic eliminators present

CPK = creatinine phosphokinase test; CRP = C-reactive protein; ESR = erythrosedimentation rate.

*Pulmonary symptoms: shortness of breath, cough, and so forth with fever and a new focal/segmental infiltrate on chest x-ray.

†Otherwise unexplained. If finding is due to an existing disorder, it should not be used as a clinical predictor.

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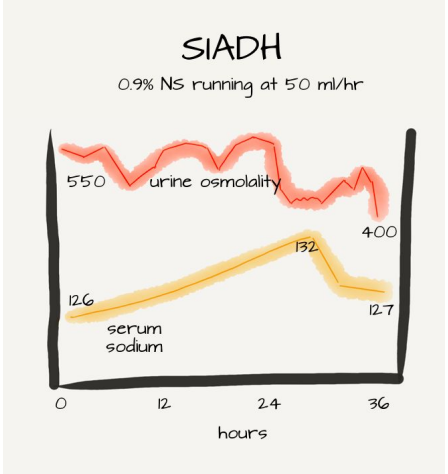
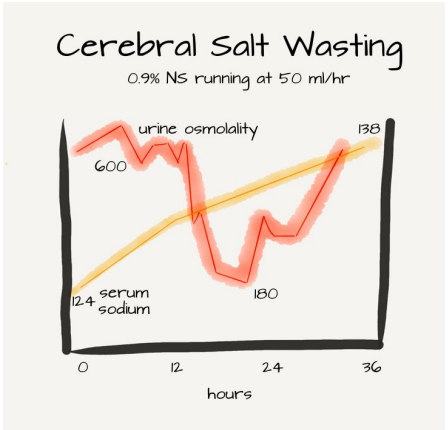
Renal salt wasting?



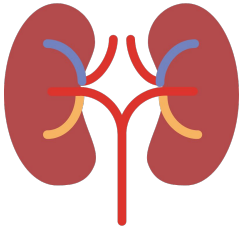


https://ajkdblog.org/2018/03/15/nephmadness-2018-hyponatremia-region/

Learning points & take aways

Learning points & take aways

- When testing for legionella, combination testing (e.g. uAg + PCR) is best
- Legionella rarely causes cavitary disease (though can happen in immunocompromise)
- Up to 10% of patients with Legionella will have co-infections with other pathogens
  - May be typical respiratory bacteria (H flu, pneumococcus), staph aureus
  - But don't forget about PJP, **nocardia**, aspergillus, tuberculosis, cryptococcus
- Legionella can cause hyponatremia
  - Traditionally thought to be from SIADH
  - An analysis of trial data (Schuetz et al [5]) suggests it is *not* from SIADH
  - Possibly mediated by direct injury to the kidney?
- Prior talks
  - Nocardia: www.hunterratliff1.com/talk/cid-2024-09/
  - Hyponatremia (for ABIM): www.hunterratliff1.com/talk/acp_prep/



Slides available on hunterratliff1.com/talk/; Citations available via QR code or via the "citations" button on the website