Brigham and Women's Hospital
Founding Member, Mass General Brigham

Challenging Infectious Disease Cases

Cameron Nutt, MD
Associate Physician
BWH Division of Infectious Diseases
Instructor of Medicine
Harvard Medical School

Faculty: Cameron Nutt, MD

- Medical school: Harvard Medical School
- Residency: Brigham and Women's Hospital
- Fellowship: Mass General Brigham
- Instructor of Medicine at Harvard Medical School
- Clinical focus: long-acting injectable antiretroviral therapy, point-of-care ultrasound

Disclosures

- I have no disclosures to report.

Case 1:
Lung and Brain Masses

51F with remote 10-pack-year smoking history and no other PMH presenting to primary care clinic with suspected CAP

Initial primary care clinic evaluation:

- 2 weeks of non-productive cough and chills in early spring
- No sick contacts or environmental exposures beyond driving a convertible
- SARS-CoV-2, influenza A/B, RSV NP swab RT-PCRs negative
- Exam unremarkable beyond decreased air movement at R apex
- BMP, CBC with diff unremarkable
- CXR with RUL lobar consolidation; diagnosed with CAP
- Treated with:
  - Cefpodoxime 200mg PO Q12H x7d
  - Doxycycline 100mg PO Q12H x7d

51F with remote 10-pack-year smoking history and no other PMH treated for CAP with persistent RUL consolidation 1 month later

One month after initial symptoms:

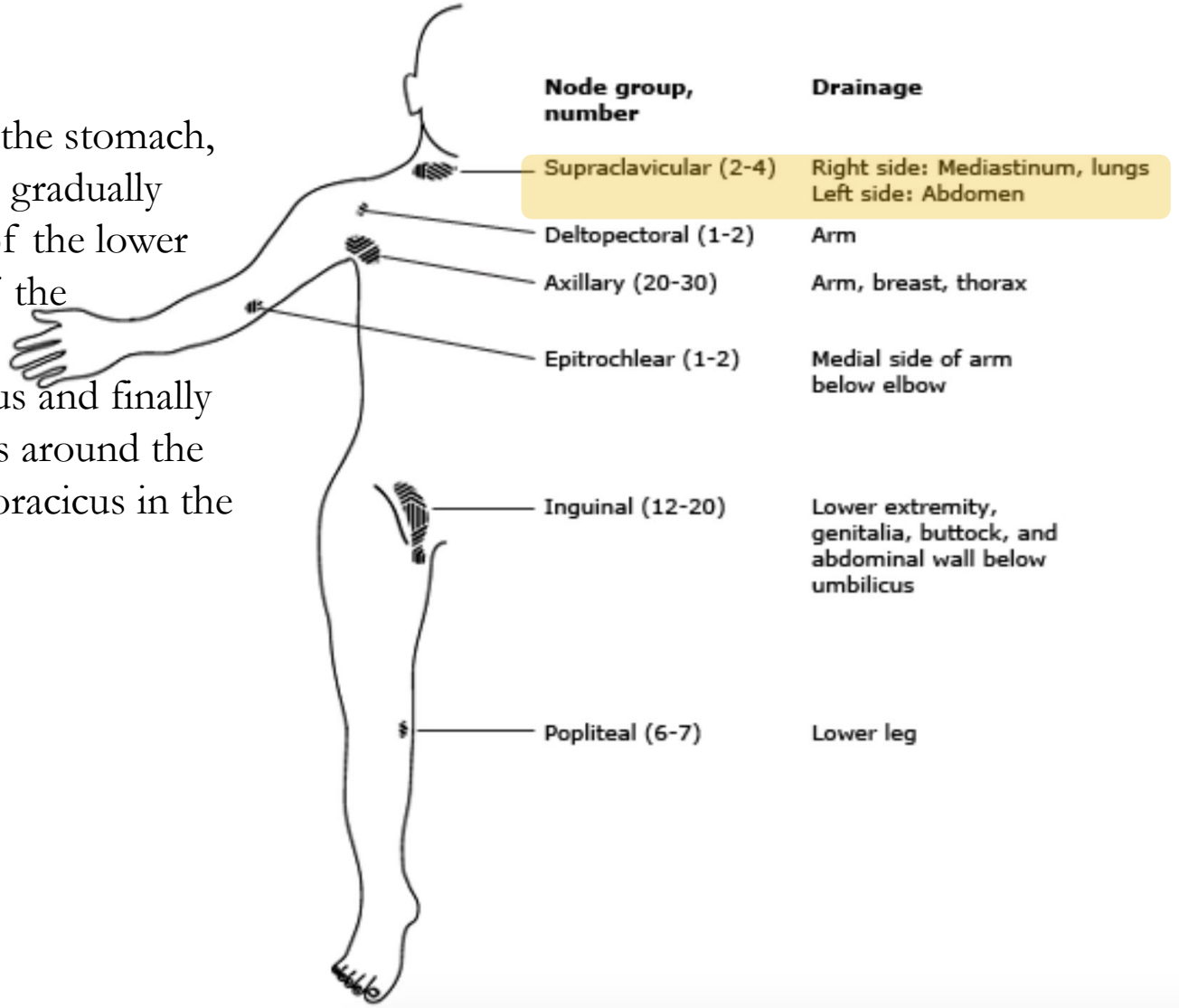
- Clinical improvement ("completely better")
- Interval CXR unchanged, with persistent RUL opacity
- CT chest (not available for review) with:
  - "RUL consolidation and small area of surrounding ill-defined groundglass."
  - "R perihilar (1cm) and R supraclavicular (6mm) lymph nodes also noted."
- Referred to thoracic surgery

Thoracic surgery evaluation:

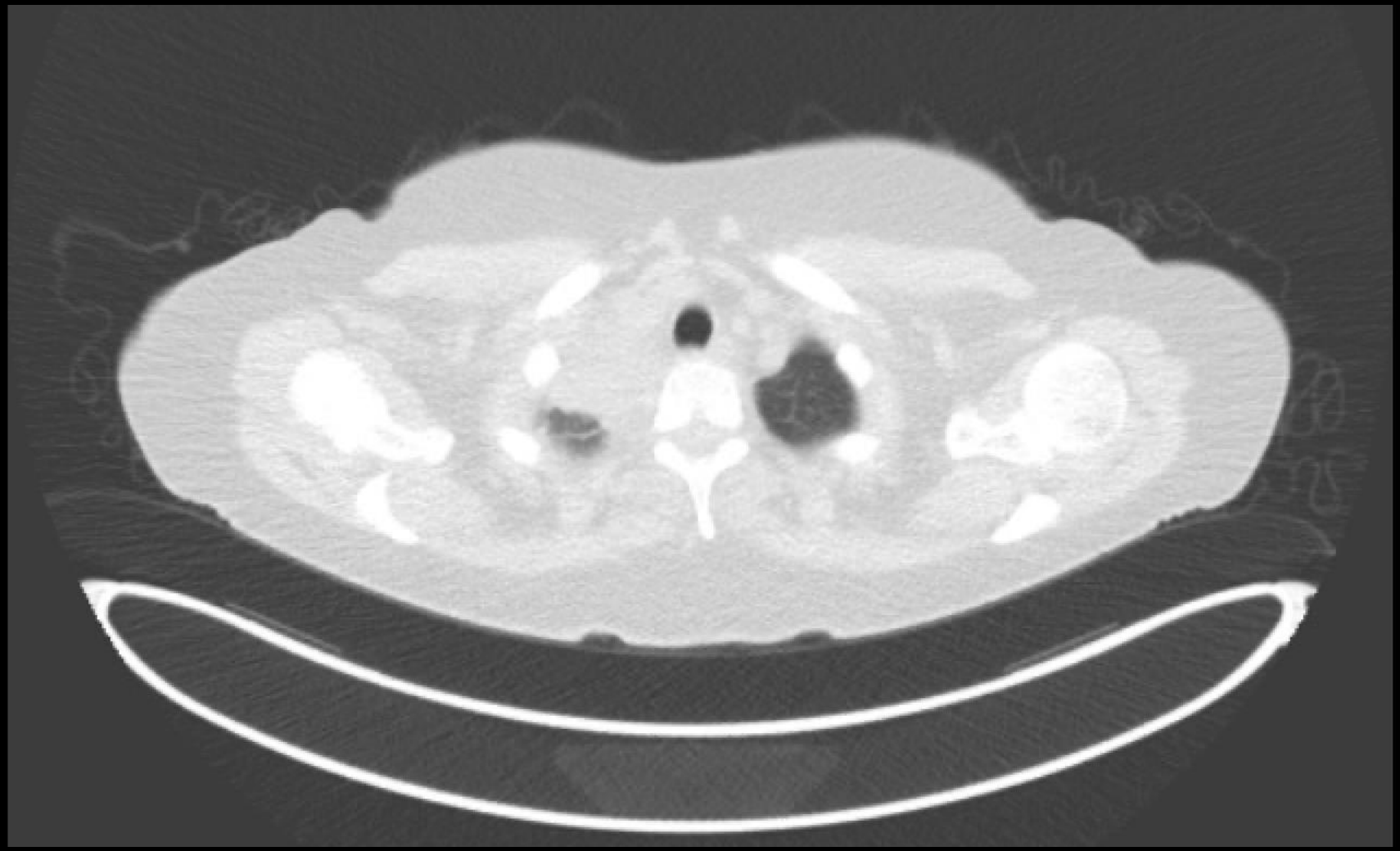
- "Suspect residual changes from pneumonia, as lung is often slow to heal radiographically compared to symptoms. Repeat CT in 8 weeks."
- Ordered repeat CT chest that was obtained 12 weeks later.

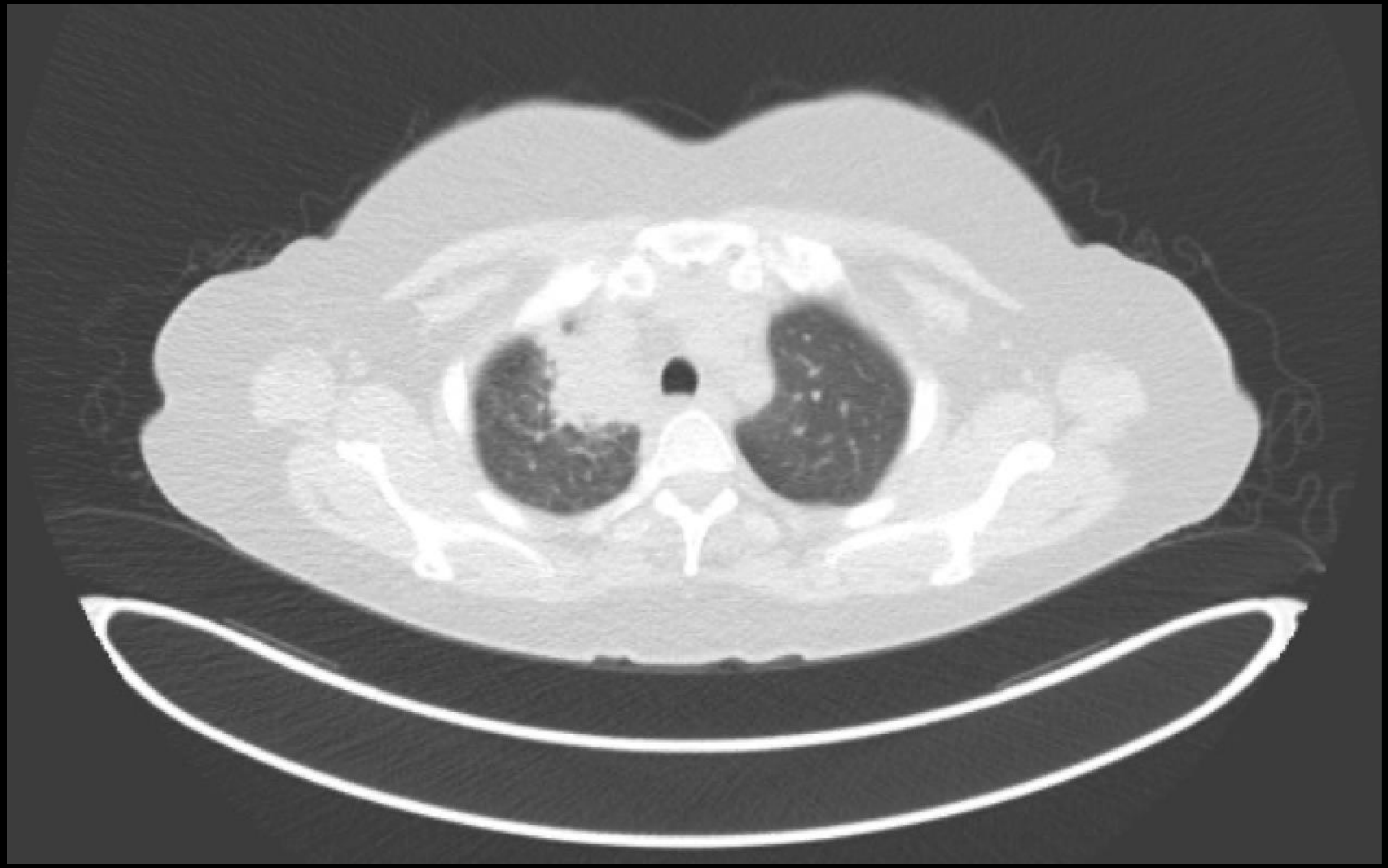
Supraclavicular Lymphadenopathy

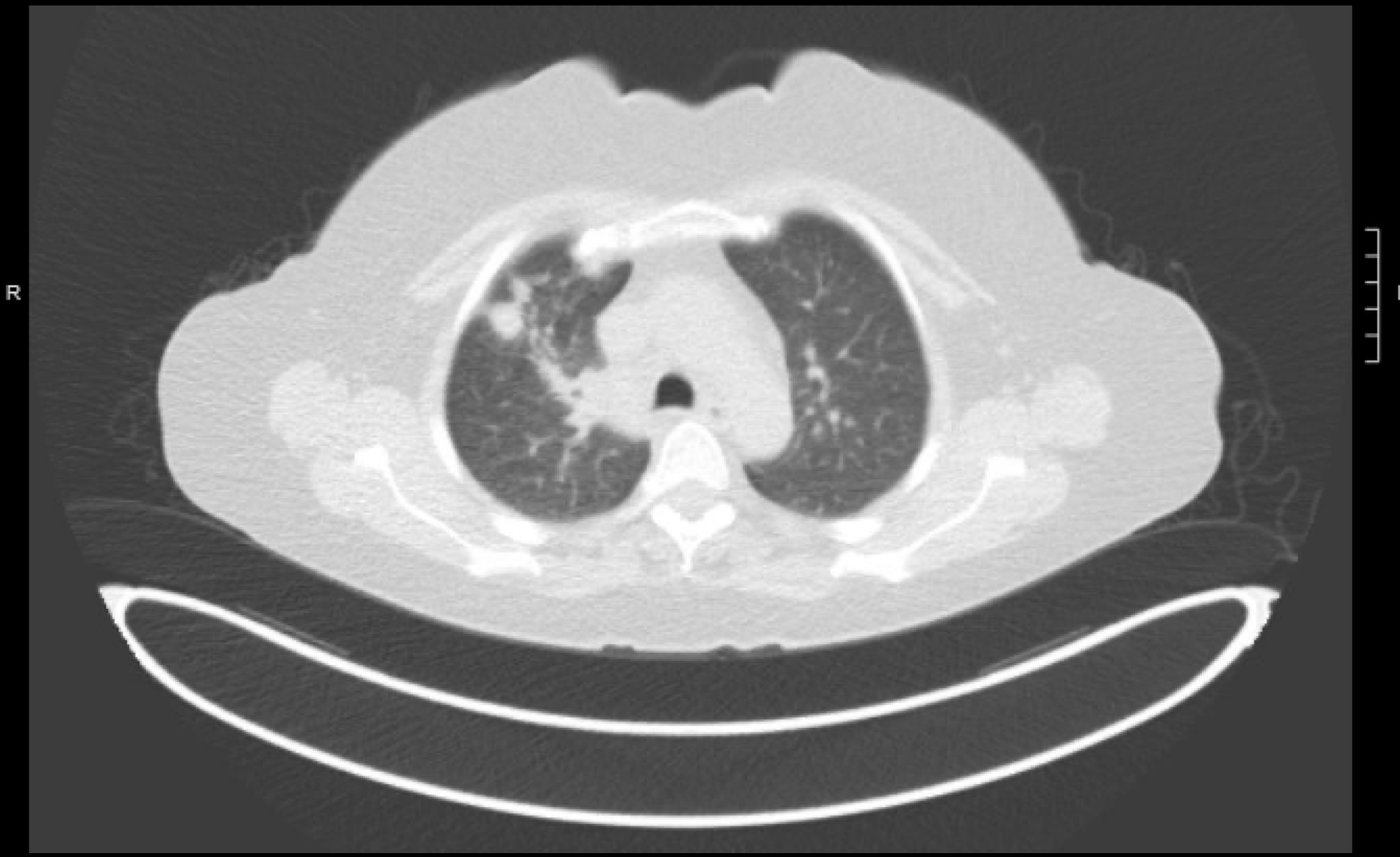
Virchow's Node:
"Particularly in cancer of the stomach, pancreas, etc., the process gradually spreads from the glands of the lower abdomen to the glands of the posterior mediastinum along the ductus thoracicus and finally involves the jugular glands around the junction of the ductus thoracicus in the left supraclavicular fossa"
—Rudolf Virchow, 1848

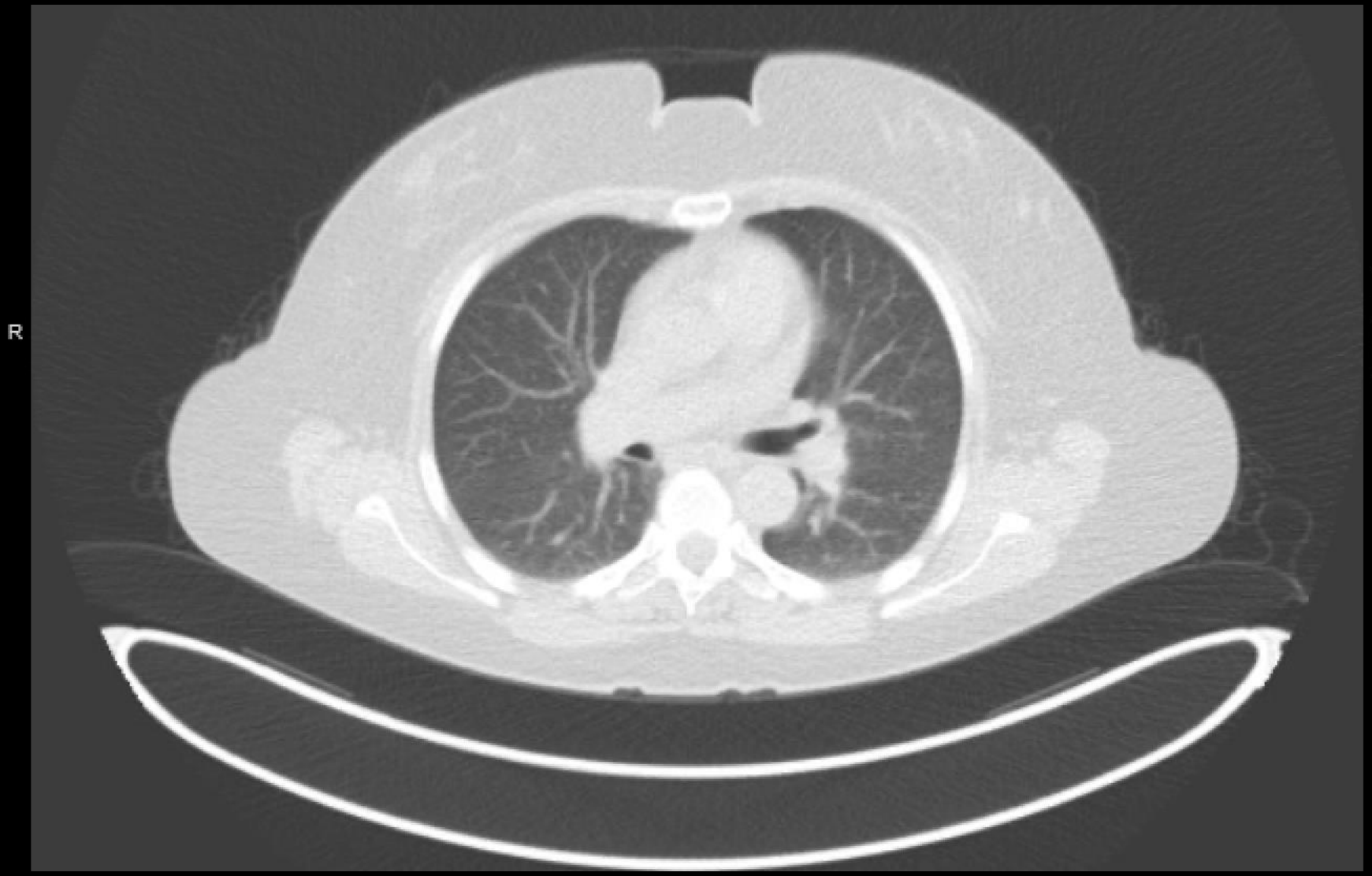


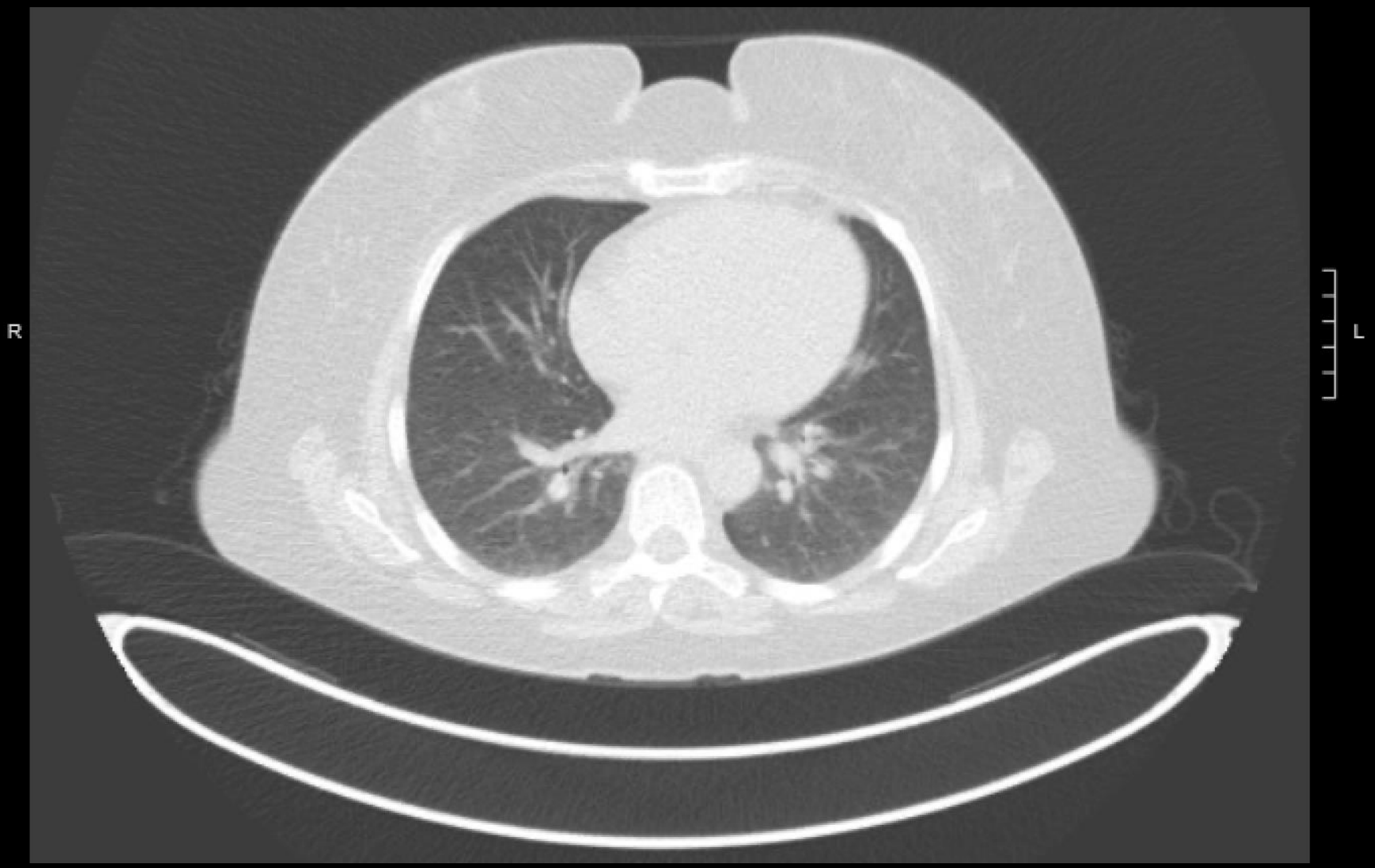
Virchow RLK. Zur Diagnose Der Krebse Im Unterleibe. *Med Ref* 1848; 45: 248.

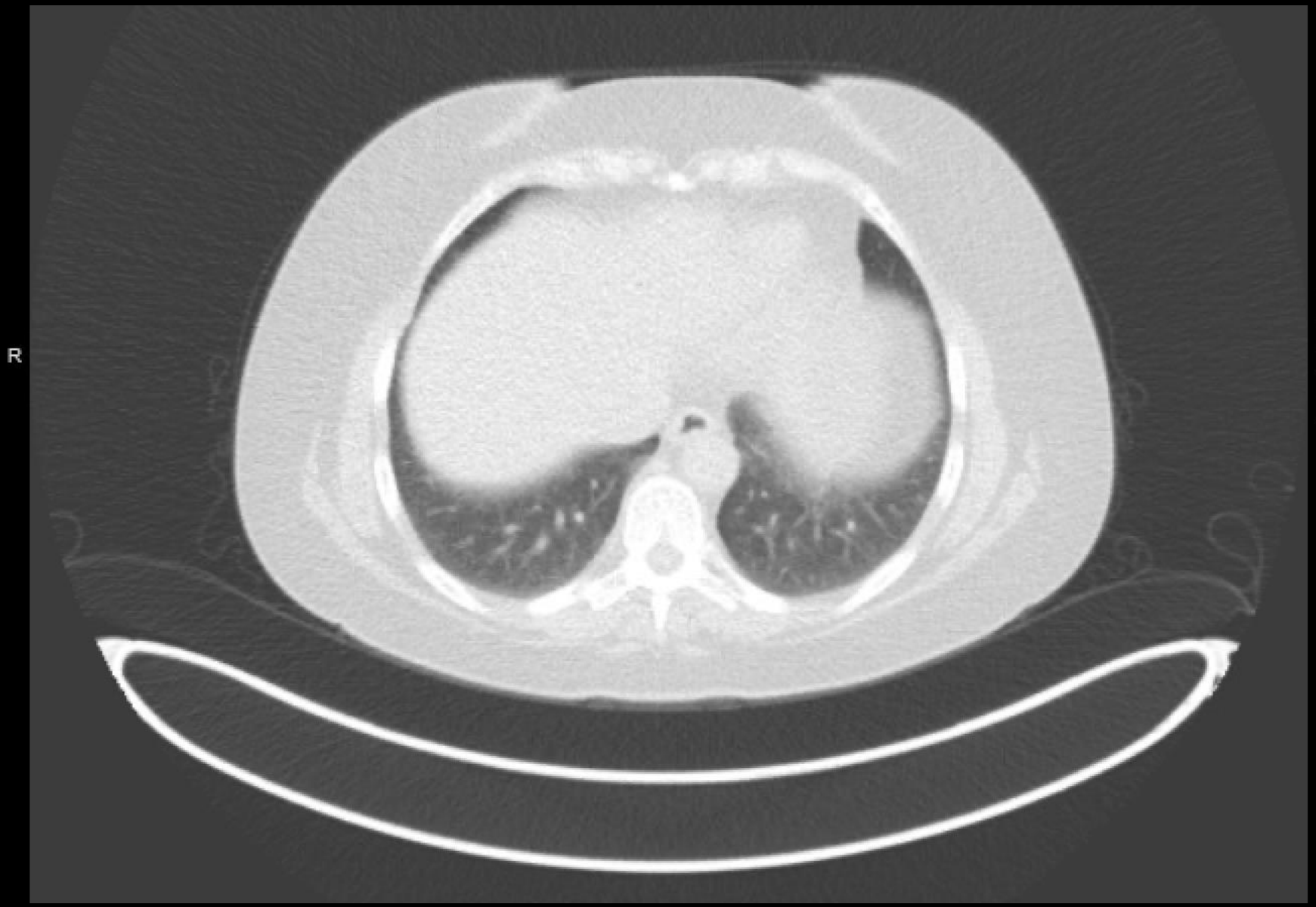

R
L


R
L


R
L


R
L


R
L


R
L

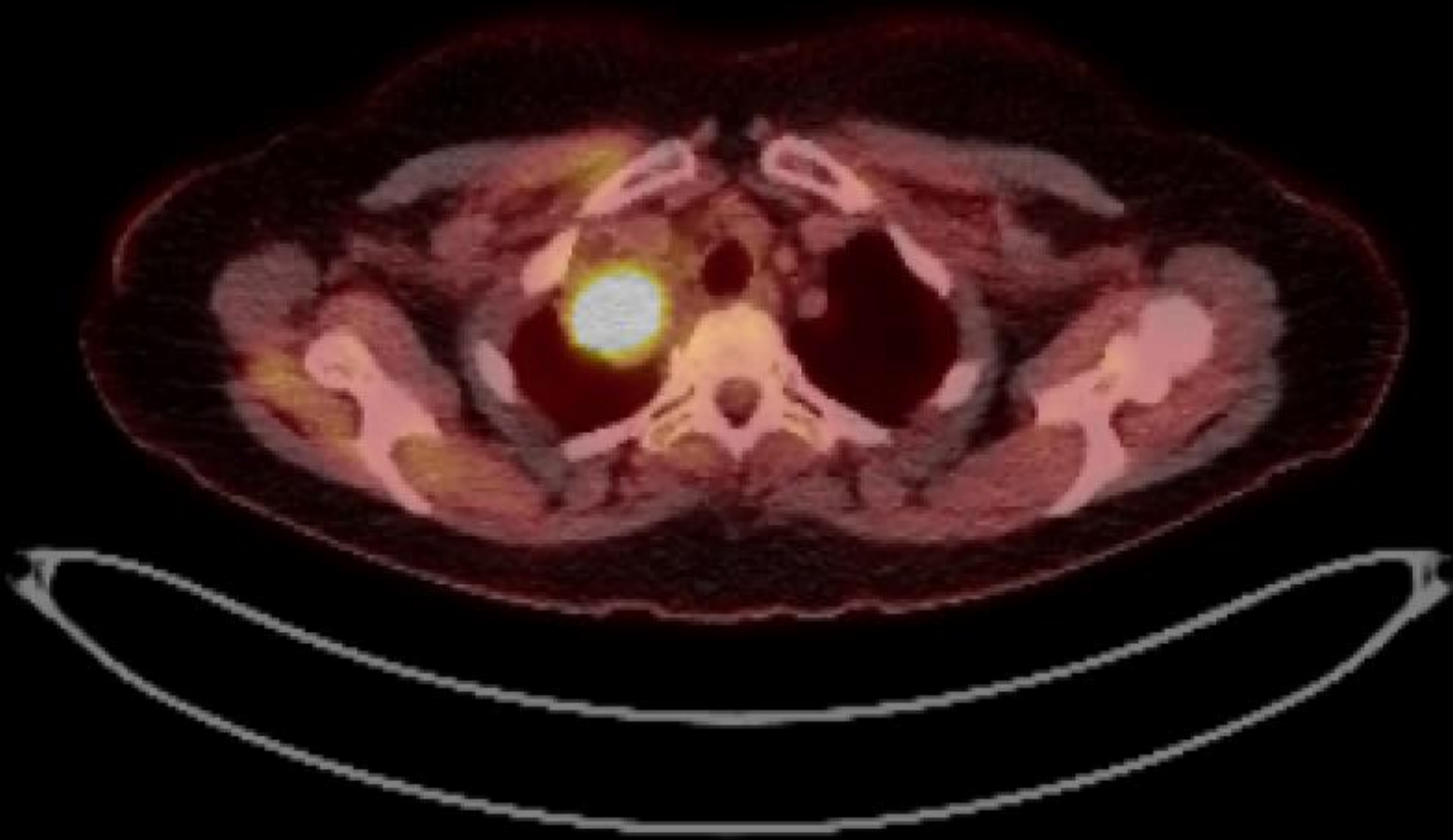
51F with remote ~10-pack-year smoking history and recent CAP with enlarging RUL consolidation 4 months later

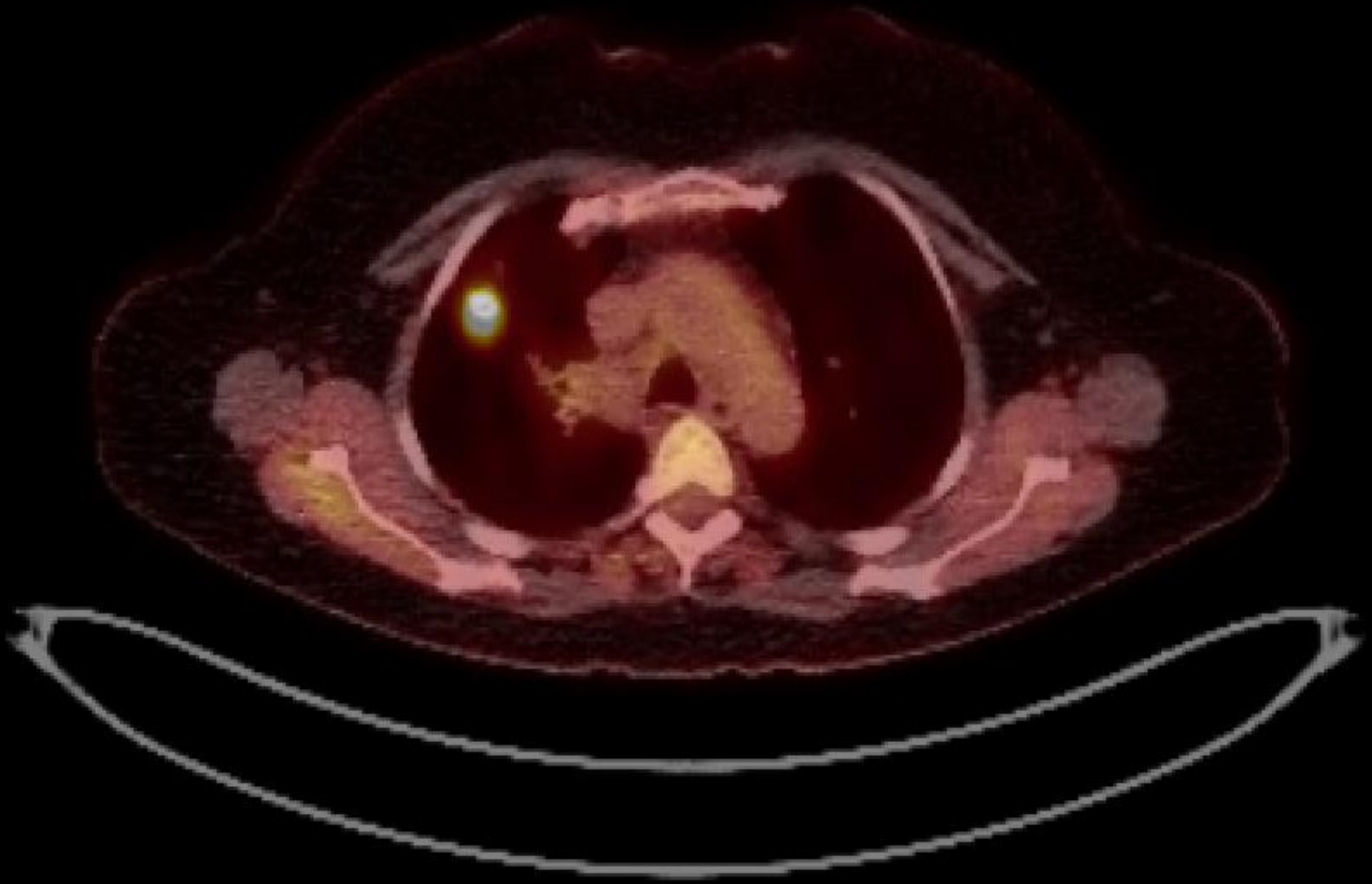
Four months after initial symptoms:

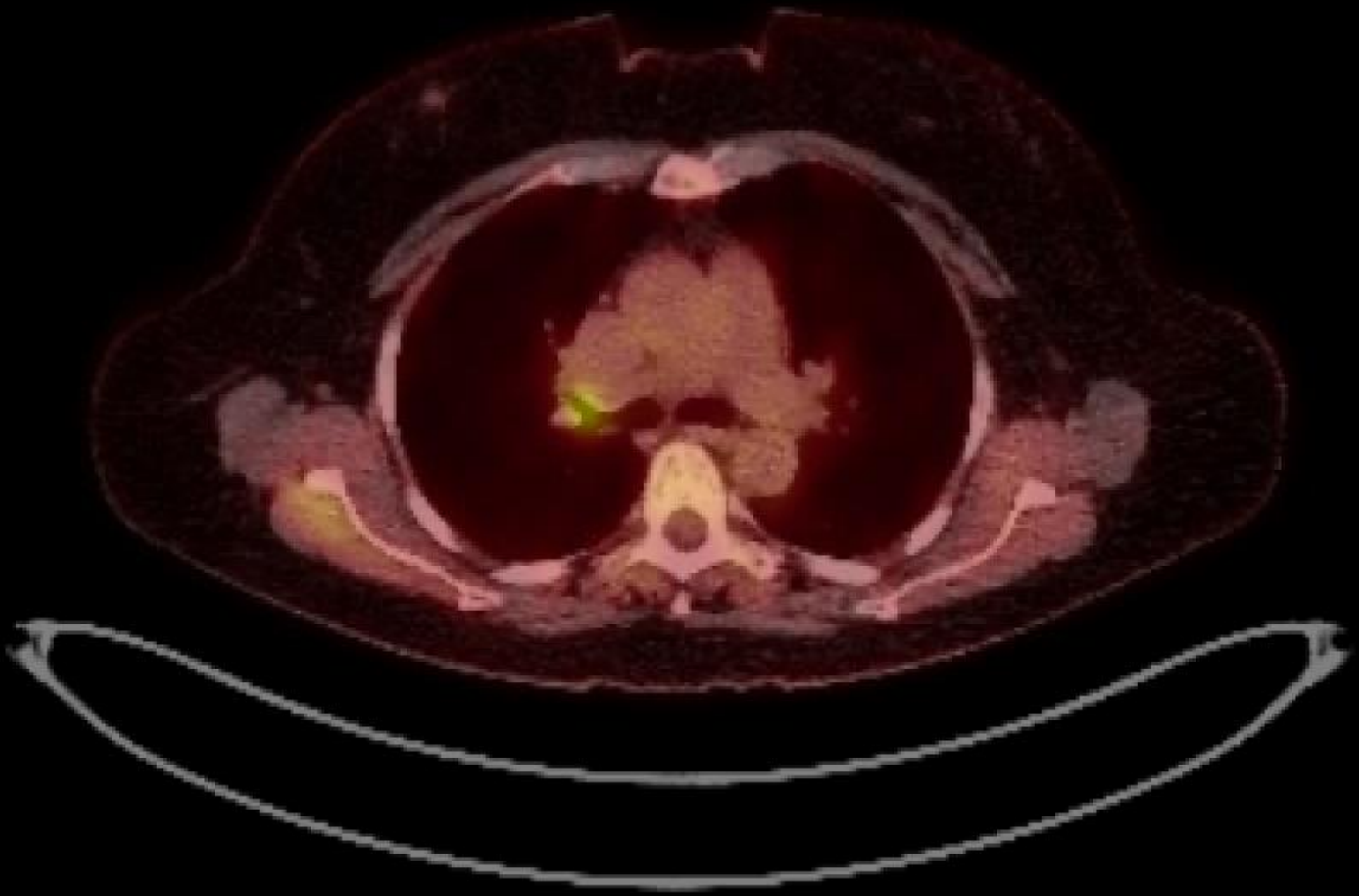
- "Interval enlargement of masslike consolidation at R lung apex concerning for enlarging malignancy such as worsening primary lung cancer. Adjacent satellite nodules with possible lymphangitic spread of tumor."
- "An infectious/inflammatory process such as a partially treated pneumonia is felt to be much less likely. R hilar node now 12mm."
- HIV AgAb negative
- BMP, LFTs, CBC with diff again unremarkable (no other labs collected)

Five months after initial symptoms:

- PET-CT performed





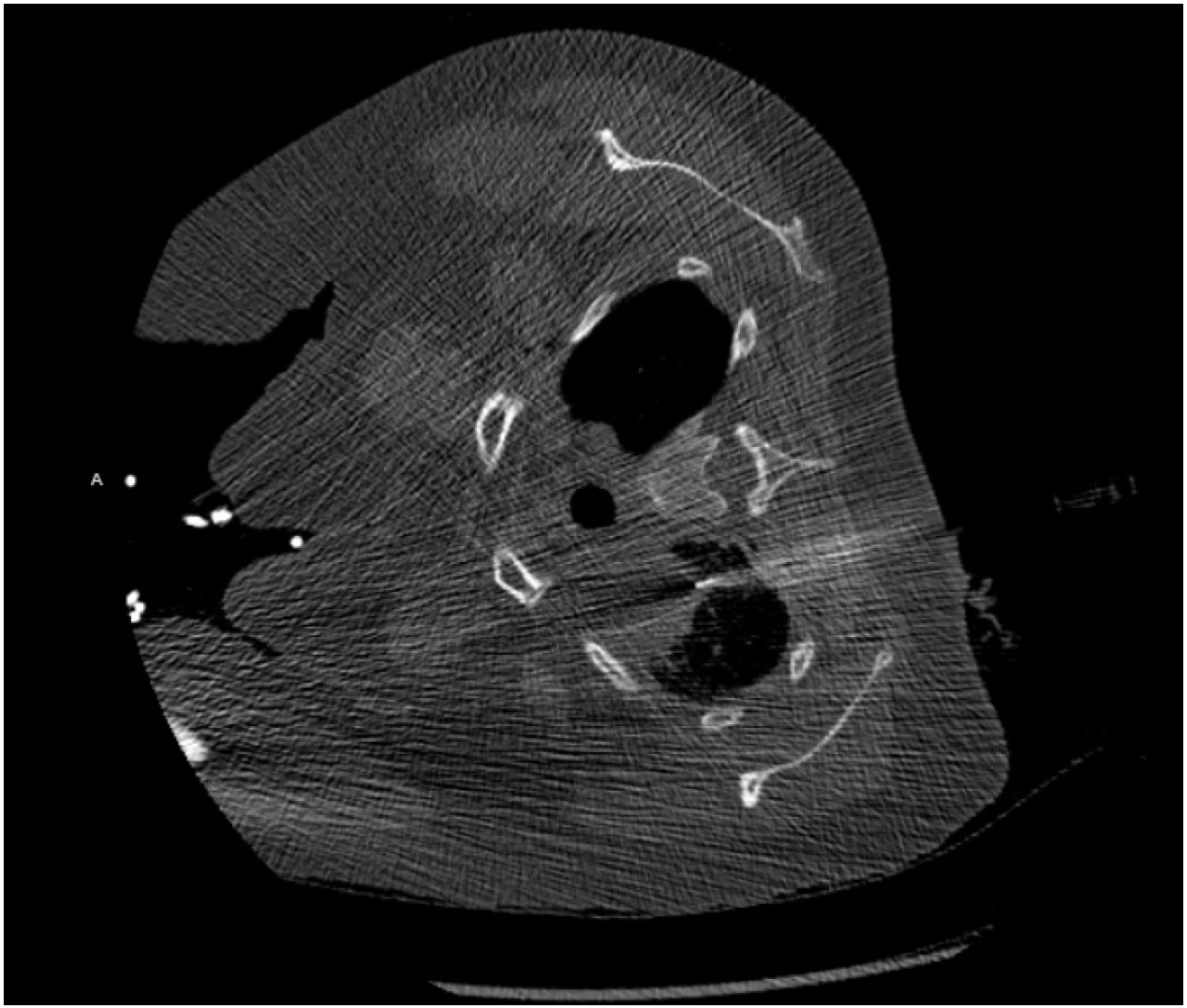


When Tumor Is The Rumor…

PET-CT Radiology Read:

- "Interval progression of R apical primary bronchogenic carcinoma/Pancoast tumor and R hilar nodal metastasis."
- "Mild FDG uptake of R supraclavicular and mediastinal nodes, nonspecific but suspicious for early nodal metastases. No abdominopelvic metastases."

Tissue Is The Issue…



While Cancer May Be The Answer…

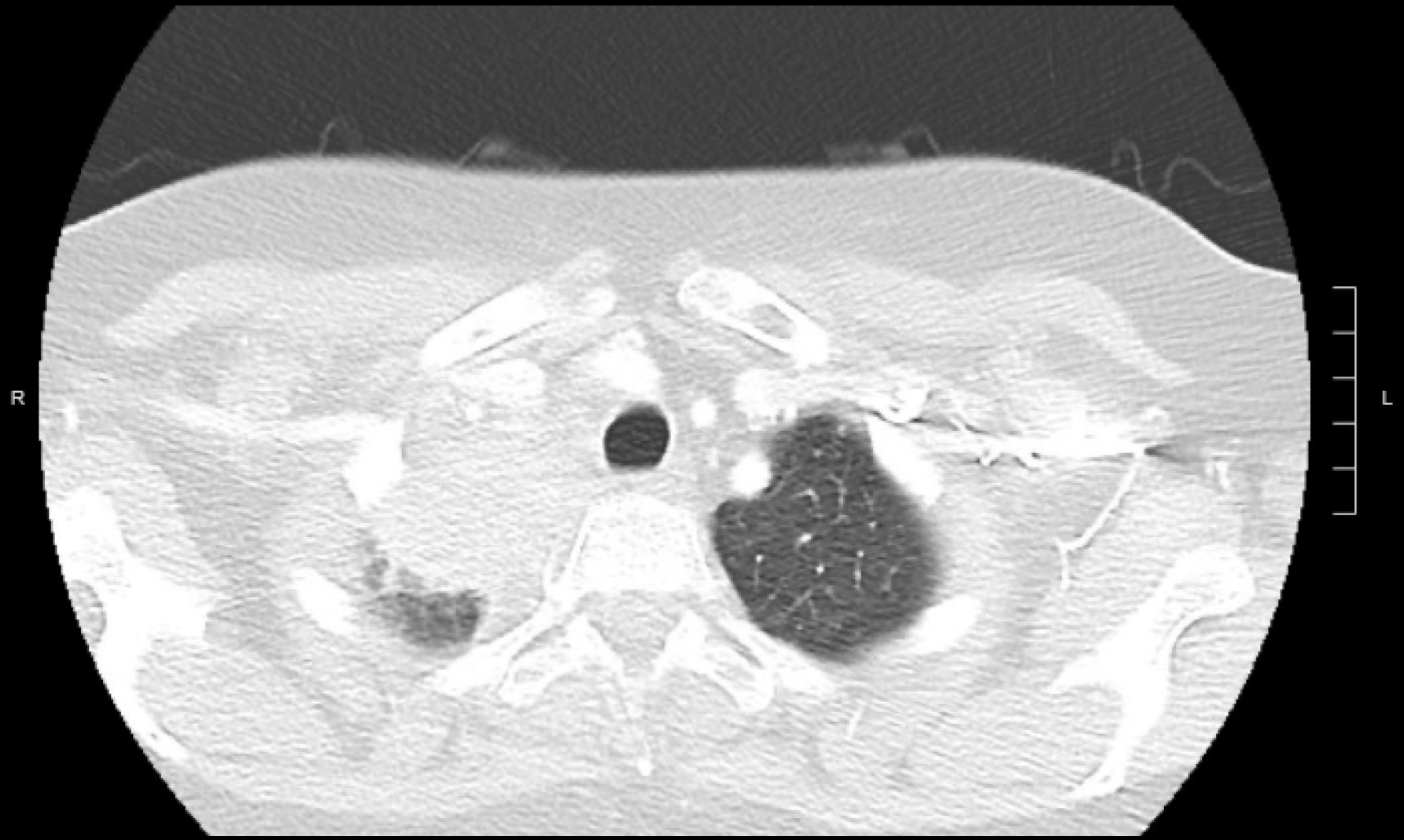
FINAL PATHOLOGIC DIAGNOSIS:
A. RIGHT LUNG, UPPER LOBE, NEEDLE CORE BIOPSY:
Benign lung parenchyma with chronic inflammation, extensive stromal fibrosis and reactive changes (see comment).

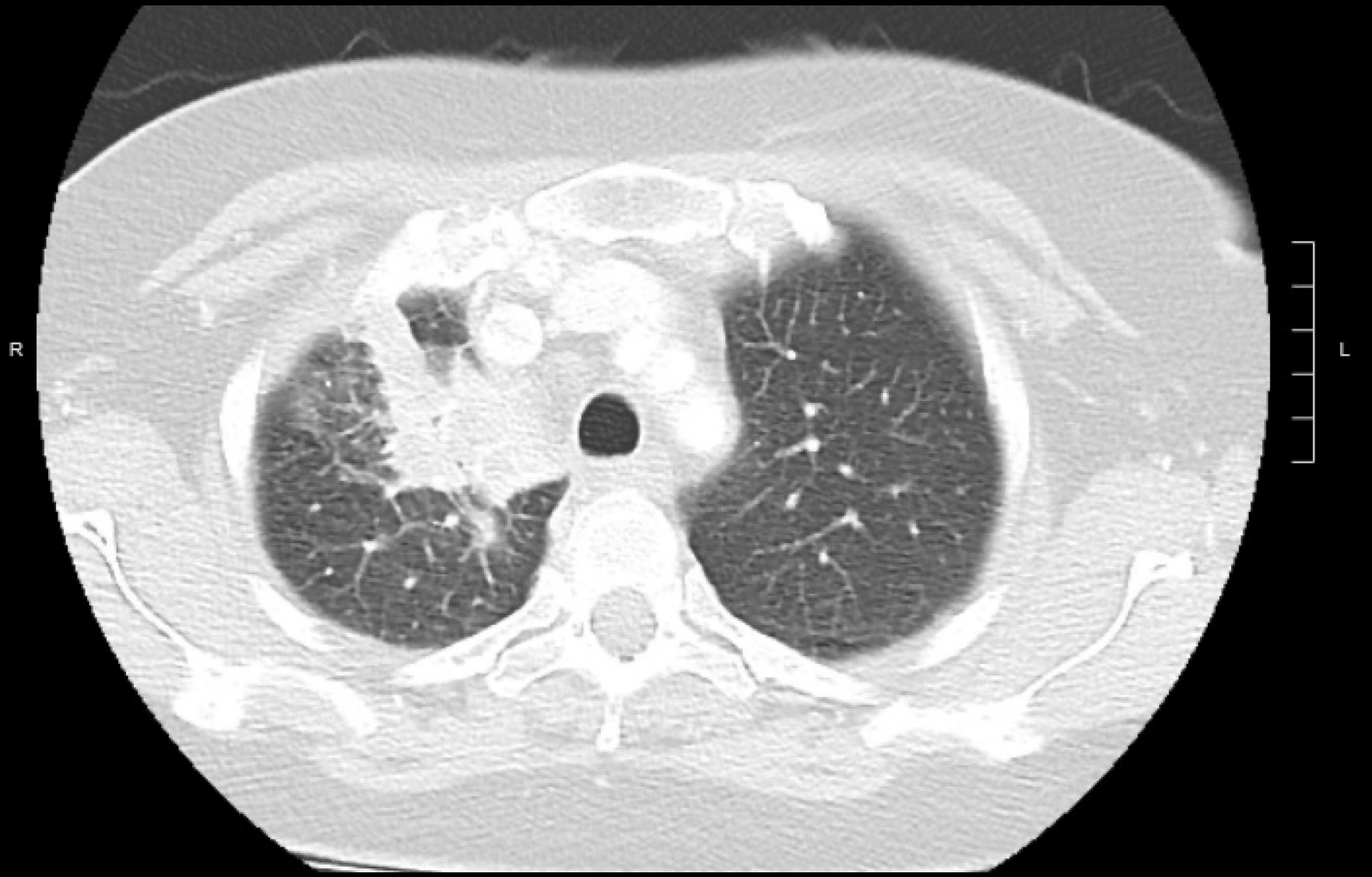
"TB, Or Not TB" Remains The Question

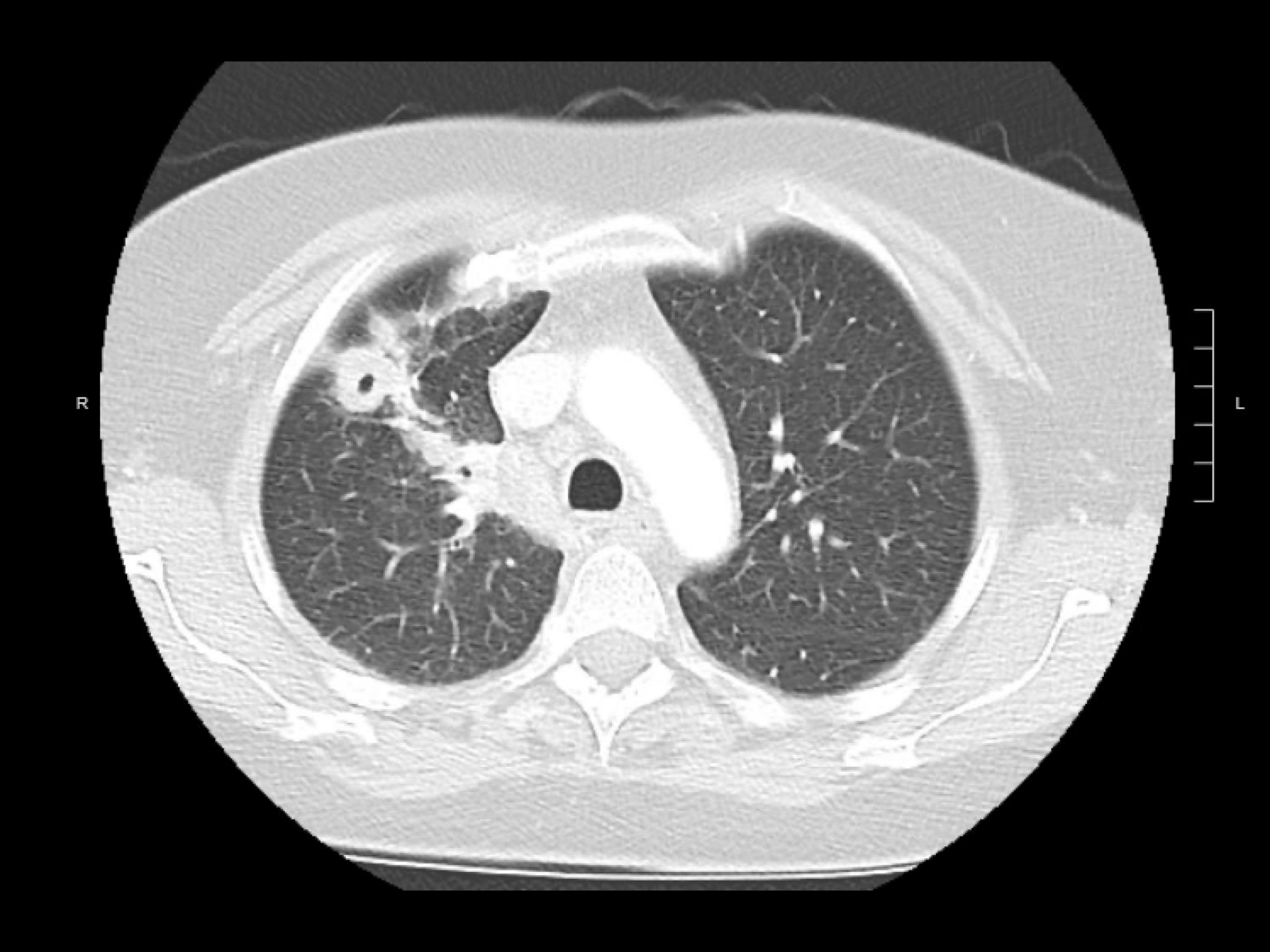
RUL mass biopsy, five months after initial symptoms:

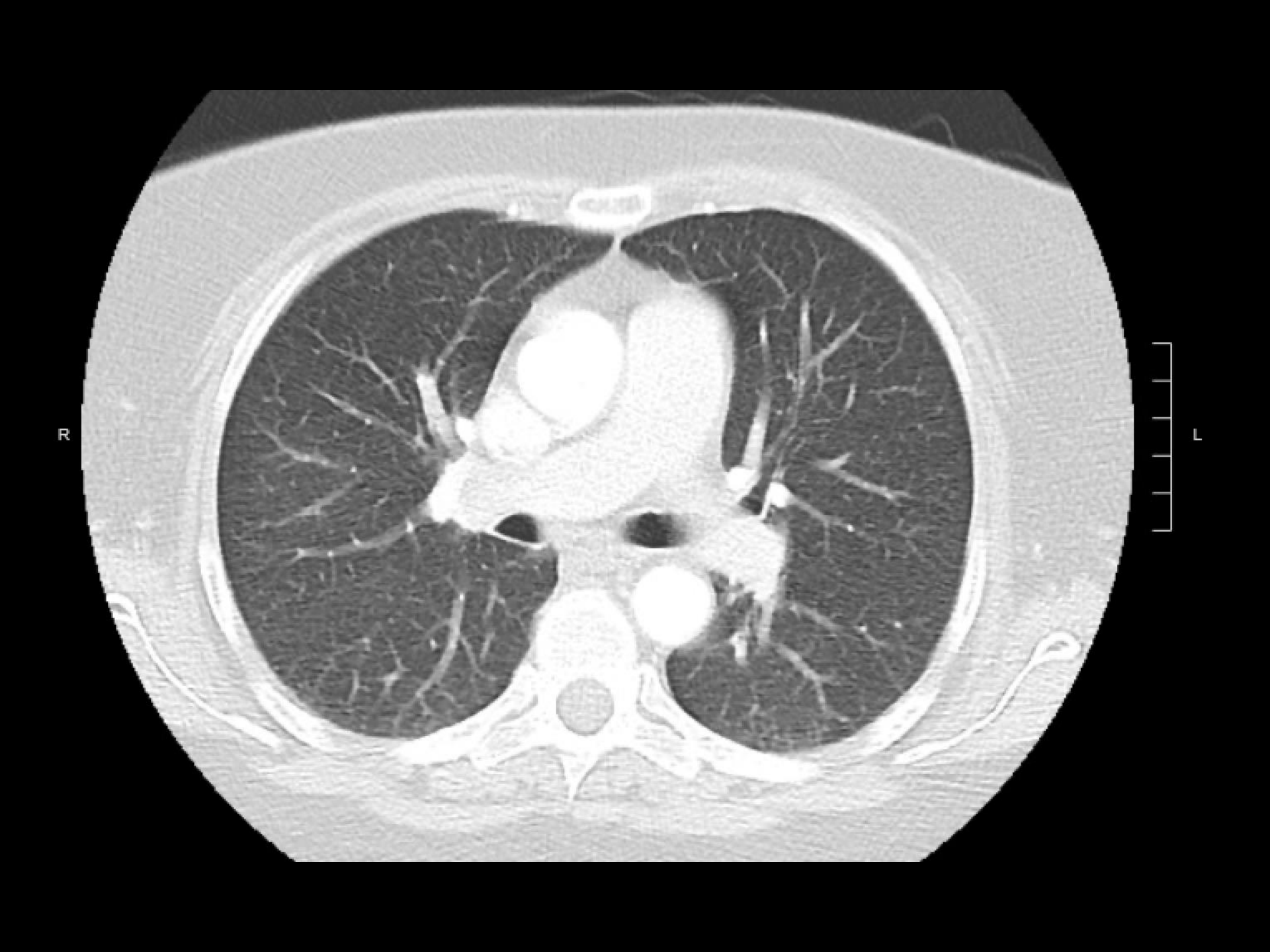
- **Gram stain**: no organisms seen
- **AFB stain**: no acid-fast bacilli observed
- **Aerobic culture**: no organisms isolated after 5 days
- **Anaerobic culture**: no organisms isolated after 14 days
- **Fungal culture**: no fungus isolated after 28 days
- **Mycobacterial culture**: no mycobacteria isolated after 56 days

After cultures finalized, yet another CT chest is obtained…


R
L


R
L

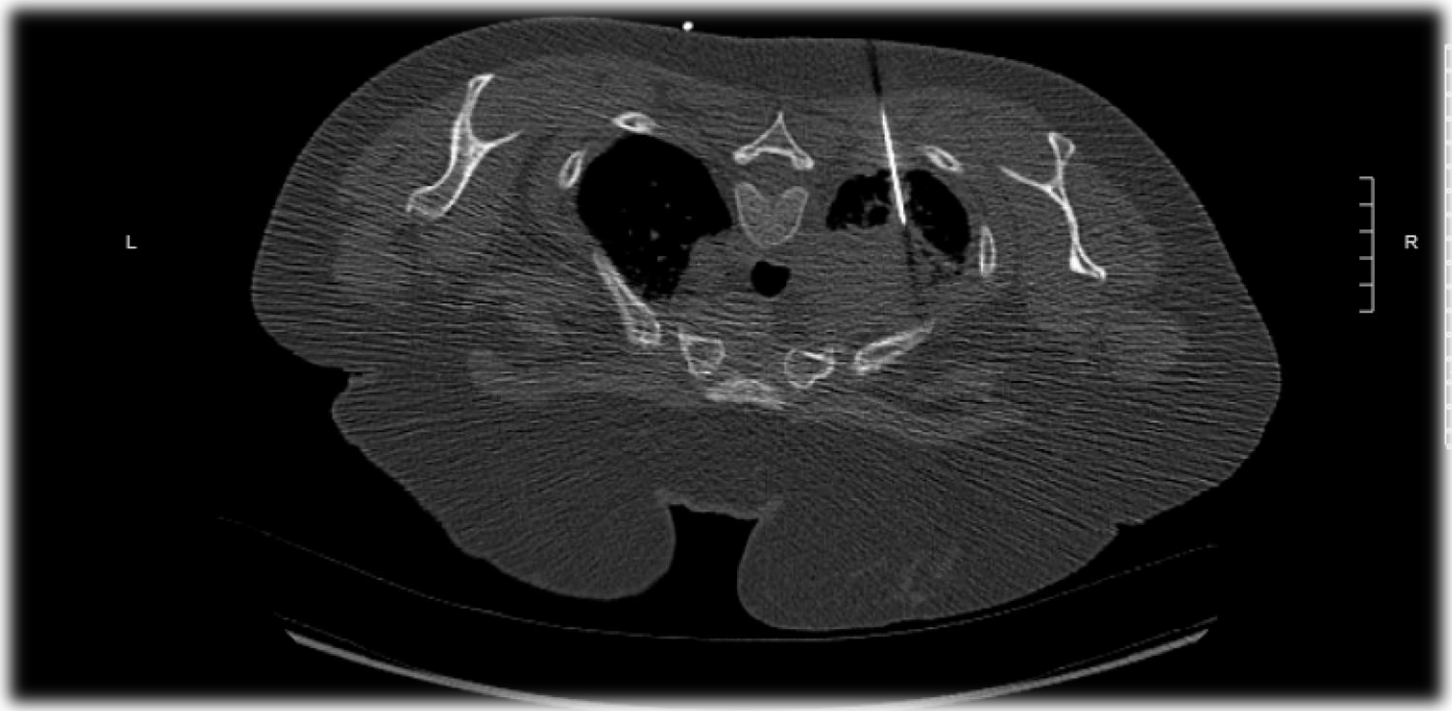

R
L


R
L

51F with remote smoking history and presumed CAP with enlarging RUL consolidation now with cavitary satellite lesion 7 months later

Radiology read, seven months after initial symptoms:

- "Interval growth of R apical mass and adjacent now cavitary nodule, highly suspicious for local malignancy progression. Enlarged lymph nodes unchanged. Worsening infection is a diagnosis of exclusion."
- Repeat CT-guided biopsy



Second CT-Guided Lung Biopsy

FINAL PATHOLOGIC DIAGNOSIS:
A. RIGHT UPPER LOBE LUNG MASS, NEEDLE CORE BIOPSY:
Fragments of benign alveolar lung tissue with fibrosis, patchy chronic inflammation, and reactive changes; see note.

Note: There is no evidence of malignancy in this biopsy specimen; multiple levels are examined. There is no evidence of storiform fibrosis. An immunohistochemical stain for CD138 (A1, A2) highlights few scattered plasma cells, which do not appear increased; CD138 stains predominantly alveolar epithelial cells. Overall, the findings are nonspecific. Correlation with clinicoradiologic findings is recommended to ensure adequate sampling of targeted lesion. Please see also the concurrent cytology specimen (XN21-3876).

RUL mass biopsy, eight months after initial symptoms:

- **Gram stain**: no organisms seen
- **AFB stain**: no acid-fast bacilli observed
- **Aerobic culture**: no organisms isolated after 5 days
- **Anaerobic culture**: no organisms isolated after 14 days
- **Fungal culture**: no fungus isolated after 28 days
- **Mycobacterial culture**: no mycobacteria isolated after 56 days

51F with remote smoking history and enlarging RUL consolidation with cavitary satellite lesion 8 months later, now with acute diplopia

Eight months after initial symptoms:

- 1d acute L retroorbital headache + vertical diplopia, worse when looking to L
- Exam with **direction-changing nystagmus + L vertical skew**
- Decreased RUL air movement; remainder of exam unremarkable

<u>HINTS</u> Exam:

51F with remote smoking history and enlarging RUL consolidation with cavitary satellite lesion 8 months later, now with acute diplopia

Eight months after initial symptoms:

- 1d acute L retroorbital headache + vertical diplopia, worse when looking to L
- Exam with **direction-changing nystagmus + L vertical skew**
- Decreased RUL air movement; remainder of exam unremarkable

HINTS Exam:

- **H**ead **I**mpulse
  - *Patient looks at your nose while you passively rotate their head*
  - **No saccade = ambiguous**
  - Catchup saccade = peripheral

51F with remote smoking history and enlarging RUL consolidation with cavitary satellite lesion 8 months later, now with acute diplopia

Eight months after initial symptoms:

- 1d acute L retroorbital headache + vertical diplopia, worse when looking to L
- Exam with **direction-changing nystagmus + L vertical skew**
- Decreased RUL air movement; remainder of exam unremarkable

HINTS Exam:

- **H**ead **I**mpulse
  - *Patient looks at your nose while you passively rotate their head*
  - **No saccade = ambiguous**
  - Catchup saccade = peripheral
- **N**ystagmus
  - Unidirectional (ie always L-beating) = peripheral
  - **Direction-changing = central**
  - Any vertical component = central

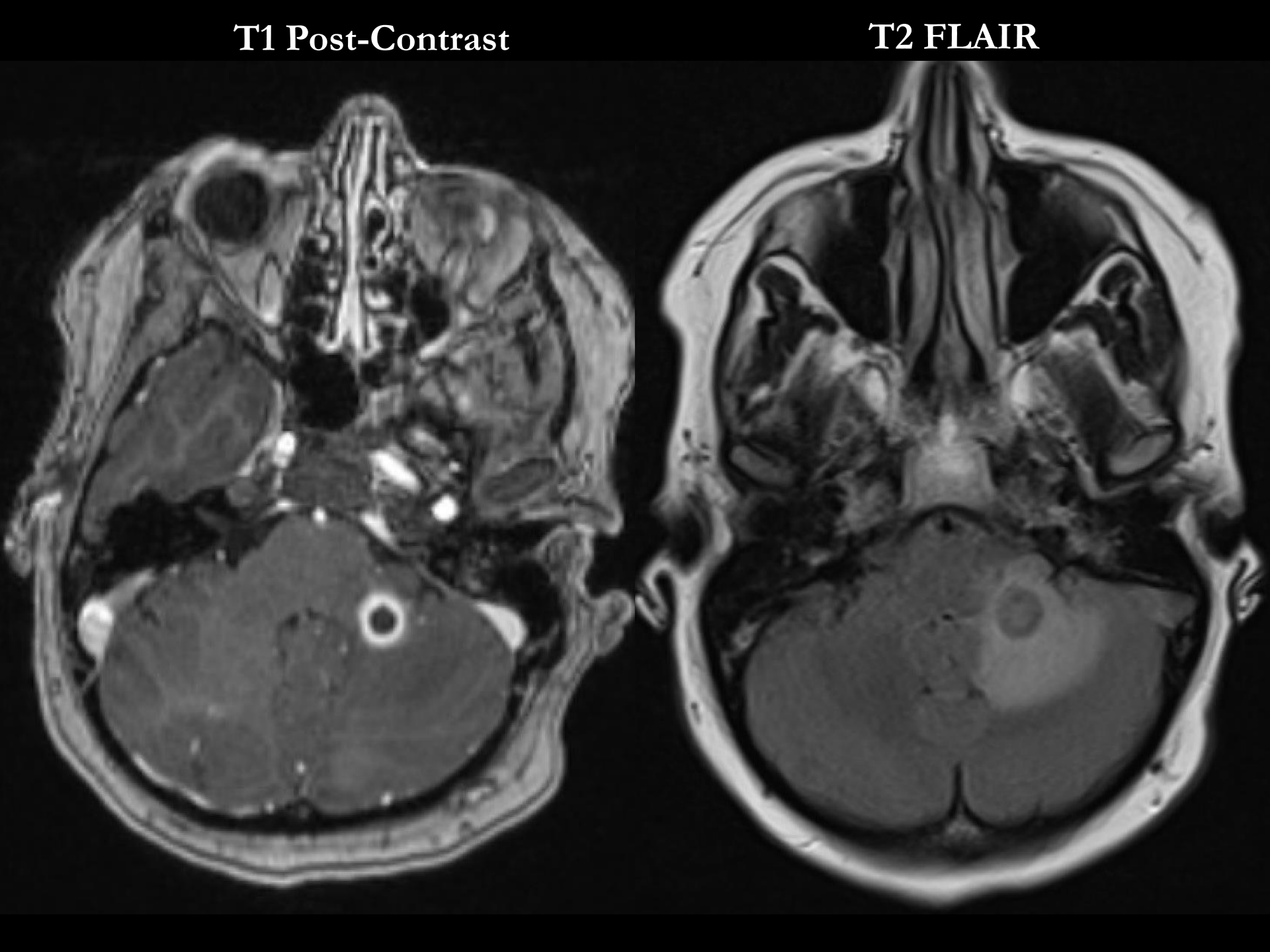
51F with remote smoking history and enlarging RUL consolidation with cavitary satellite lesion 8 months later, now with acute diplopia

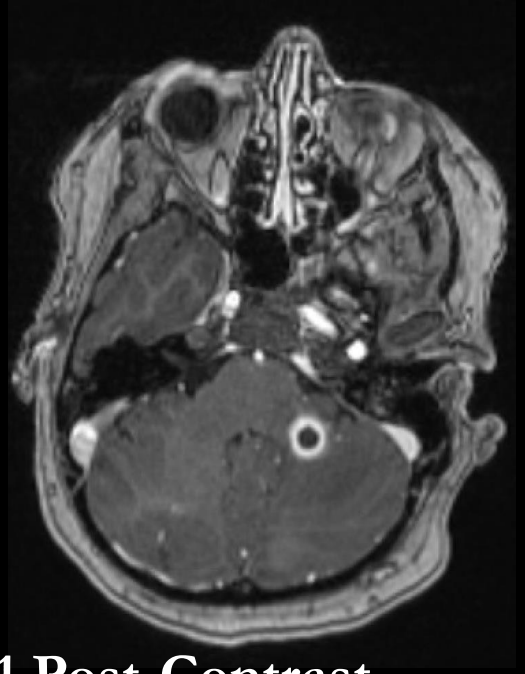
Eight months after initial symptoms:

- 1d acute L retroorbital headache + vertical diplopia, worse when looking to L
- Exam with **direction-changing nystagmus + L vertical skew**
- Decreased RUL air movement; remainder of exam unremarkable

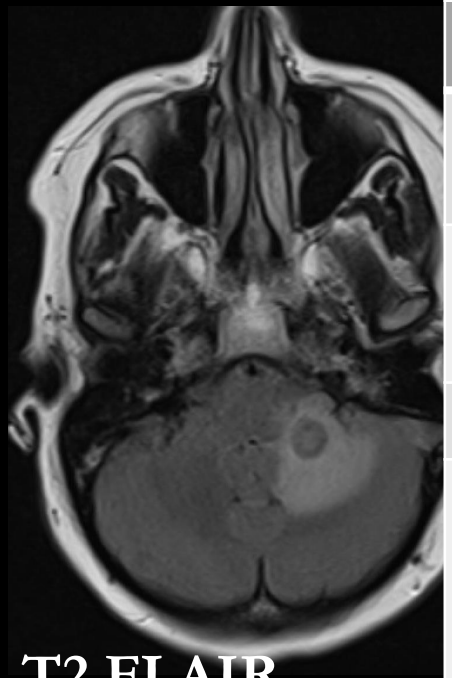
HINTS Exam:

- **H**ead **I**mpulse
  - *Patient looks at your nose while you passively rotate their head*
  - **No saccade = ambiguous**
  - Catchup saccade = peripheral
- **N**ystagmus
  - Unidirectional (ie always L-beating) = peripheral
  - **Direction-changing = central**
  - Any vertical component = central
- **T**est of **S**kew
  - *Cover patient's L eye, then R while observing their eyes*
  - **Any vertical skew or correction = central**


T1 Post-Contrast
T2 FLAIR

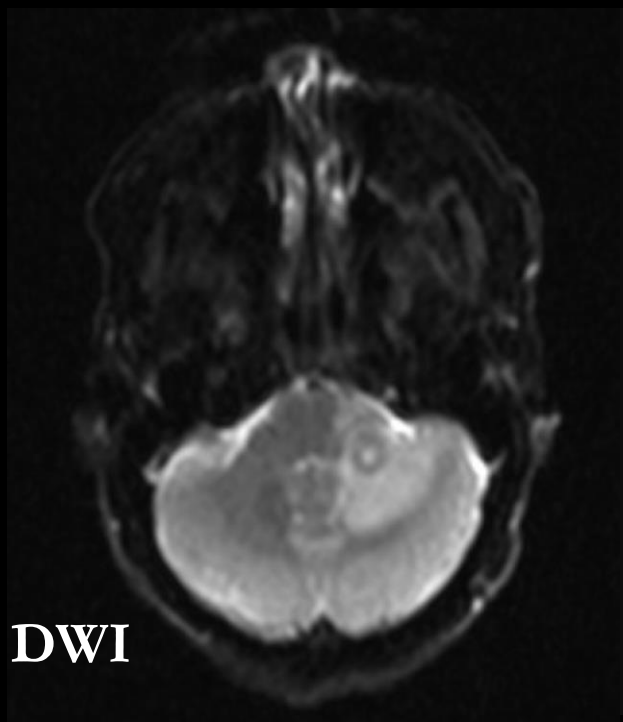


T1 Post-Contrast

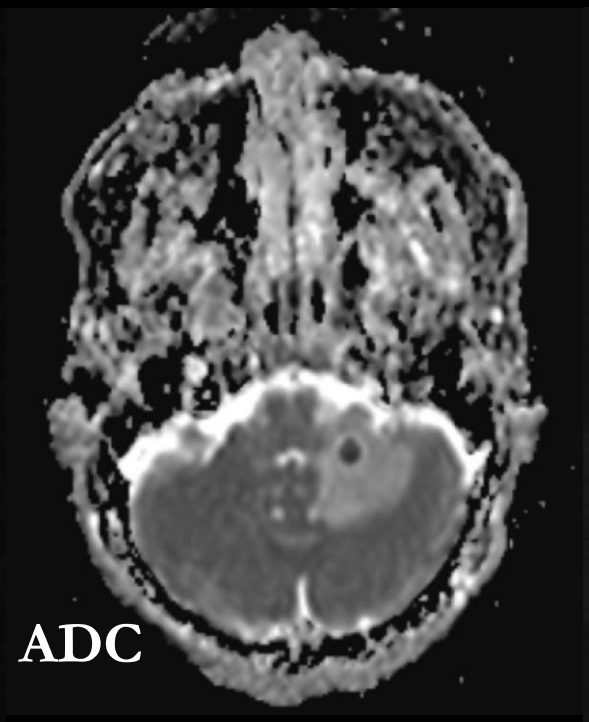


T2 FLAIR

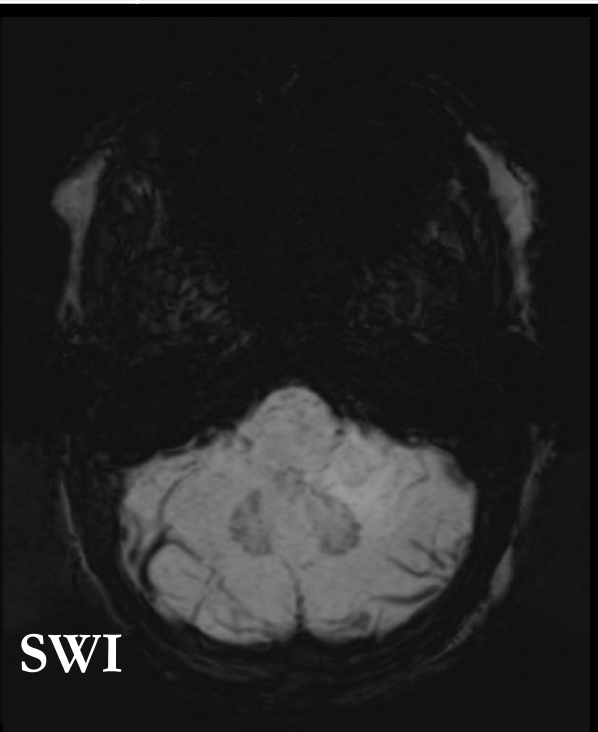
Sequence	Basic Use
T1 post-contrast	
T2 FLAIR	
SWI	
DWI/ADC	



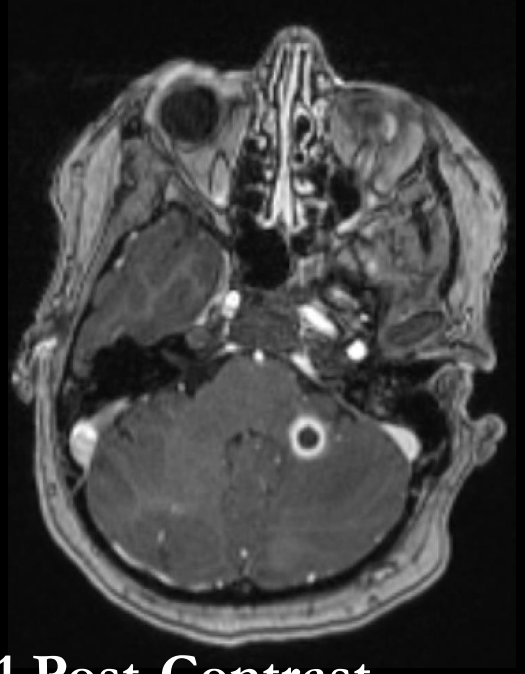
DWI



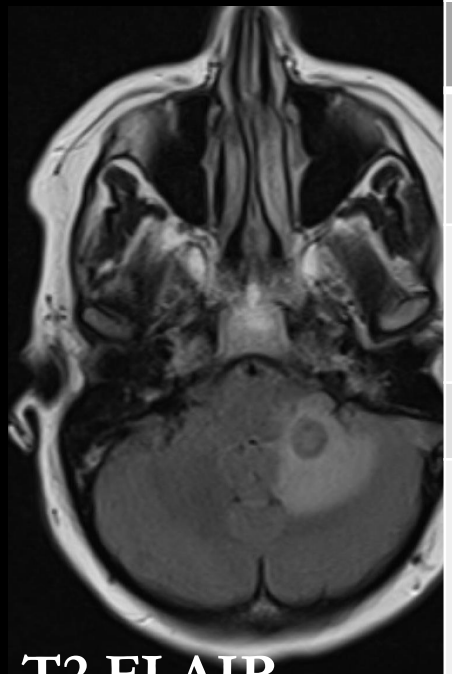
ADC



SWI

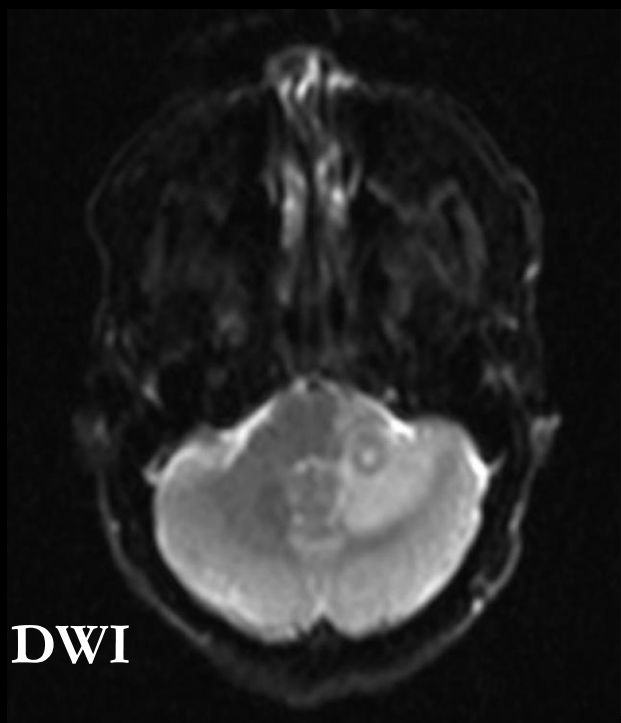


T1 Post-Contrast

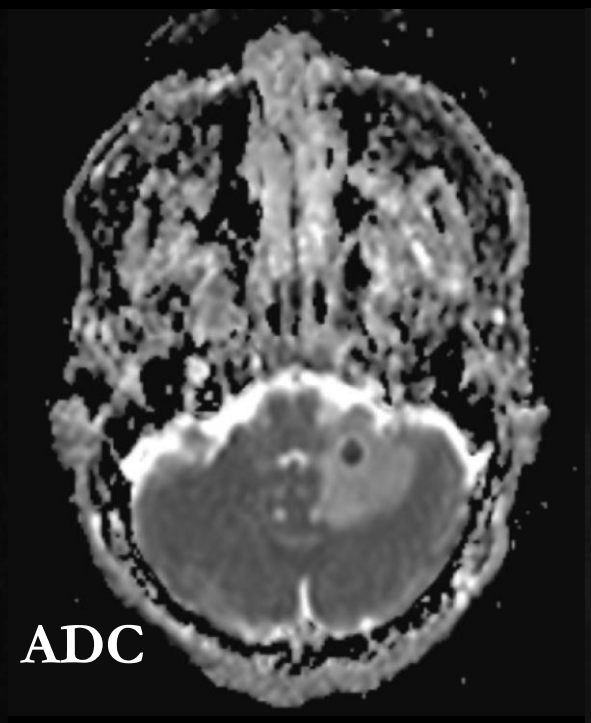


T2 FLAIR

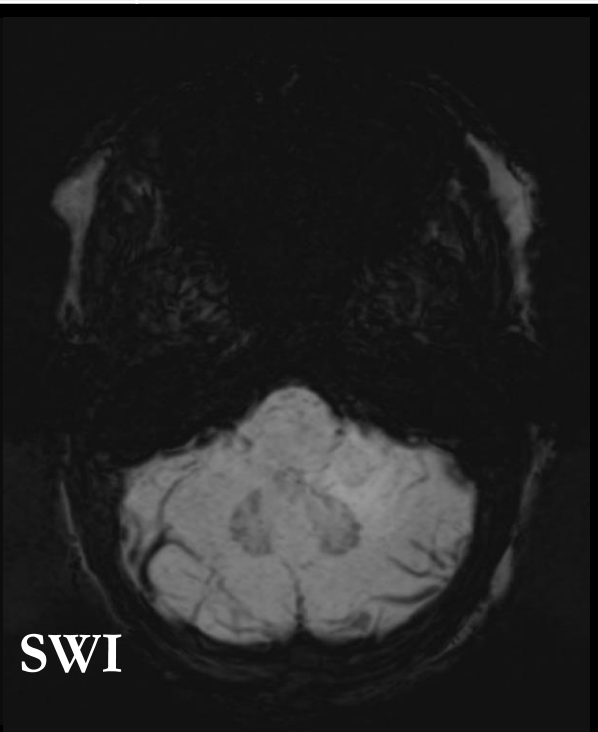
Sequence	Basic Use
T1 post-contrast	BBB interrupted?
T2 FLAIR	Edema? Structural abnormalities?
SWI	Blood = black
DWI/ADC	Diffusion restriction =DWI light/ADC dark (ischemia, inflammation / pus, demyelination)?



DWI



ADC



SWI

51F with remote smoking history with progressive multifocal RUL cavitary lesion now found to have L pontine ring-enhancing lesion

Eight months after initial symptoms:

- 1d acute L retroorbital headache and vertical diplopia
  - Diplopia worse when looking to L
- Exam with direction-changing nystagmus and L vertical skew; admitted
- MRI/MRA brain with:
  - "1.1cm enhancing focus in L brachium pontis with surrounding edema and central necrosis, concerning for a metastatic lesion."
  - "A focus of restricted diffusion centrally within this lesion may reflect necrosis or a developing abscess. Of note, lung and breast metastases may show restricted diffusion. The appearance is overall atypical for an acute infarct."
- Repeat CT chest with:
  - "Mildly increased size of R apical mass and adjacent cavitary nodule. Stable LAD."

Ddx for Concurrent Lung and Brain Masses

Non-Infectious

- Metastatic cancer
  - Lung
  - Breast
  - Melanoma
  - Colon
  - Renal
- Lymphoma
- Sarcoidosis
- Tuberous sclerosis
- Two separate processes

Infectious

- Endocarditis
- *Streptococcus pneumoniae*
- *Mycobacterium tuberculosis*
- *Nocardia* spp (100+)
- *Histoplasma capsulatum*
- *Blastomyces hominis*
- *Rhodococcus equi*
- *Toxoplasma gondii*
- *Cryptococcus neoformans*
- Mold (*Mucorales*, *Aspergillus* spp)

Lumbar Puncture

CSF Studies:

- Opening pressure: 15cm H2O [<20]
- Tube 4: 8 nucleated cells (89% lymphs, 11% monos), 4 RBCs
- Glucose 62 [40-70]
- Protein: 46.5 [10-44]
- Gram stain (CSF): negative
- Aerobic/anaerobic culture (CSF): no growth
- Cryptococcal antigen (CSF): negative
- Toxoplasma PCR (CSF): negative
- Nocardia PCR (CSF): negative
- Cytology (CSF): negative

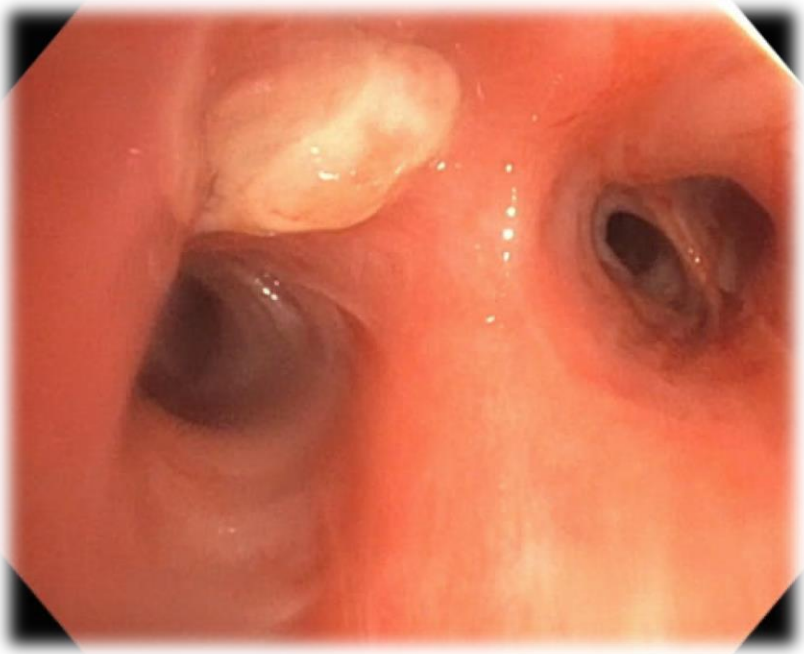
Tumor Is The Rumor, And TB Or Not TB Is The Question… Tissue Is Still The Issue!

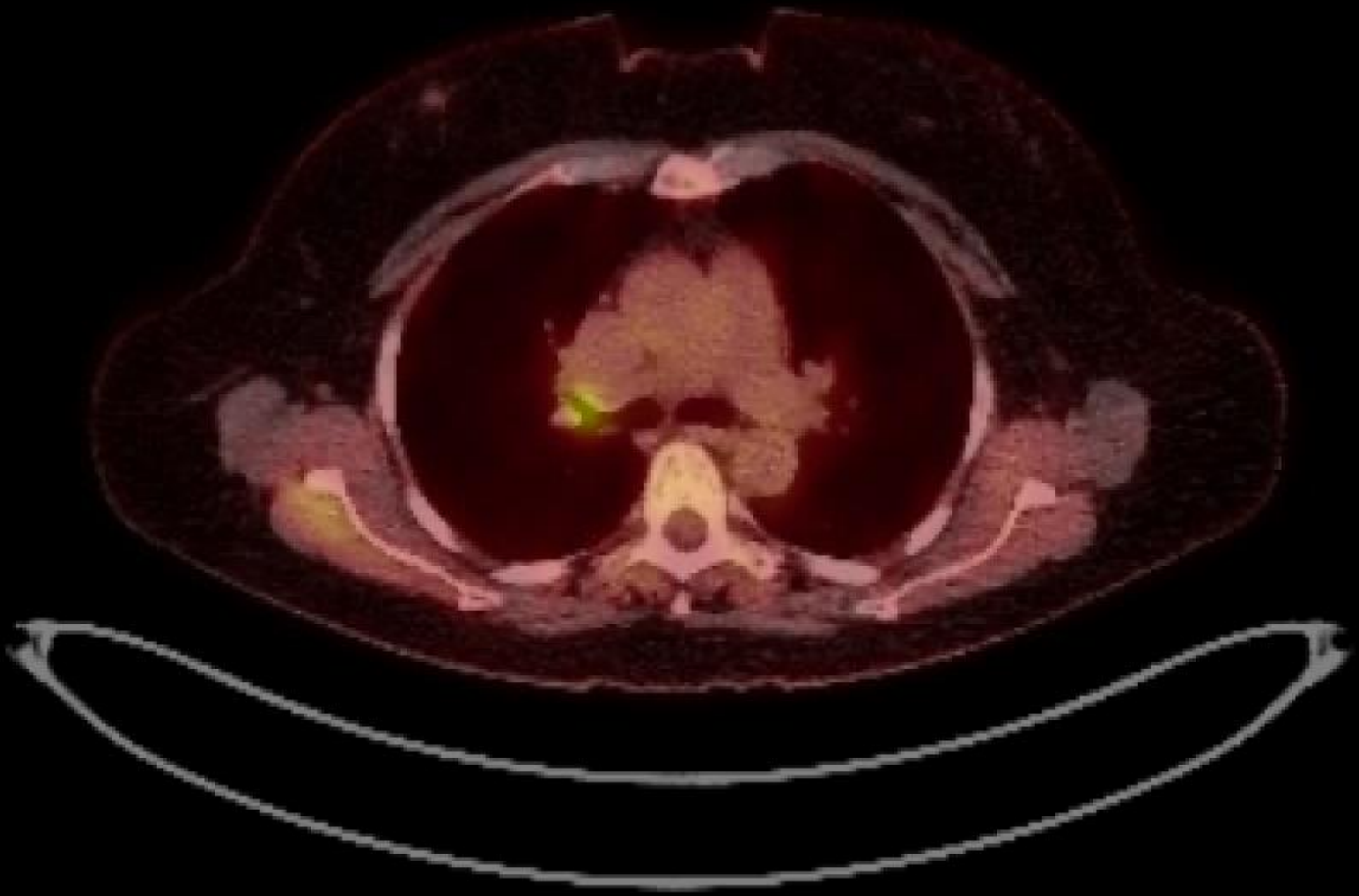
Labs:

- BMP, LFTs, CBC with diff unremarkable (again)
- ESR 44, CRP 18.7
- Blood cultures x2: no growth x3d
- T-spot: negative *(note: never rules out active TB!)*
- 1-3-Beta-D glucan: <31
- Galactomannan: 0.03
- Urine histoplasma Ag: negative
- Urine blastomyces Ag: negative
- HIV AgAb –ve (again)

Bronchoscopy with EBUS/RUL mass biopsy and RUL BAL

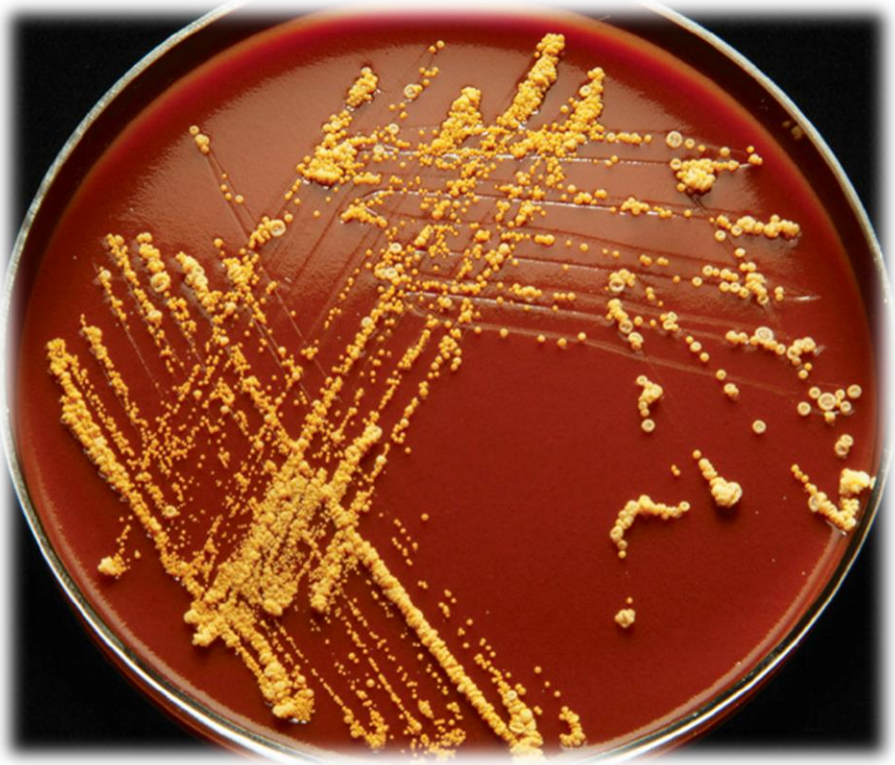
- **Biopsy**: frozen sections with no malignancy; full review pending
- **Gram stain**: few PMNs, no organisms seen
- **AFB stain**: no acid-fast bacilli observed
- **Aerobic culture**: no growth x1d
- **Anaerobic culture**: no growth x1d
- **Fungal culture**: pending
- **Mycobacterial culture**: pending

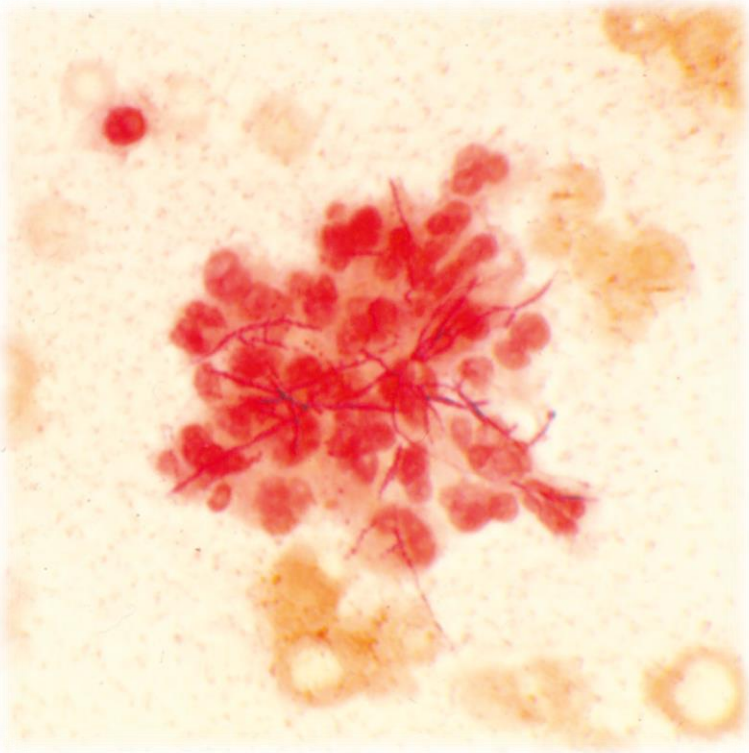




A Diagnostic Test Was Added On

11/08/2021 1325	11/23/2021 0651	Nocardia culture [917549468] (Abnormal) Bronchial alveolar lavage RIGHT UPPER LOBE	Final result	Component Special Requests Nocardia Culture	Value None NOCARDIA SPECIES ! Sent to University of Texas (Health Science Center)





Mandell, Douglas, and Bennett (Eds). *Principles and Practice of Infectious Diseases, 9th Edition*. Elsevier, 2019: Philadelphia, PA.

Case Resolution

- Started on TMP-SMX IV and imipenem IV while inpatient
- Discharged on high-dose TMP-SMX PO
- Full resolution of cough and diplopia 1 month later
- Full resolution of lung and brain lesions 2 months later

Key Learning Points

- Nocardia species are ubiquitous, gram-positive, partially Acid-fast filamentous branching rods acquired by environmental inhalation from soil/dust worldwide, and can cause pulmonary, CNS, cutaneous, and disseminated (2+ sites) disease.
- Nearly HALF of patients with pulmonary nocardiosis develop CNS involvement. While most patients who develop nocardiosis are immunocompromised, up to a third are not.
- Concomitant lung and brain masses can be caused by many cancers and infections (most notably tuberculosis and nocardiosis). Nocardia can be slowly progressive at first but is underdiagnosed and deadly in immunocompromised patients—please don't forget it!
- Partial treatment of mycobacteria or nocardia can cloud diagnostic pictures (transient improvement on treatment, then worsening) and decrease yield of respiratory cultures (classic = TB and levofloxacin for CAP).

Case 2:
Complete Heart Block

Mid-Summer Overnight Admission on the Cardiology Service

Patient**: 25-year-old male**
Length of stay**: 7 minutes**
Triage note:

ED Triage Notes Date of Service: 8/2/2019 4:30 PM
Registered Nurse
Emergency Medicine
Signed
Signed

3 days of feeling dizzy with stomach discomfort and today LOC then unwitnessed fall forward on his face.: contusions on his face. No lac, no bleeding more like a road rash. No H/A. Denies any drugs / alcohol. No CP, no SOB.

Mid-Summer Overnight Admission on the Cardiology Service

- No records available for review
- Initial vitals from triage:
  - T: 98.1F | P 49 | BP 128/58 | RR 16 | SaO2 99% on room air

Mid-Summer Overnight Admission on the Cardiology Service

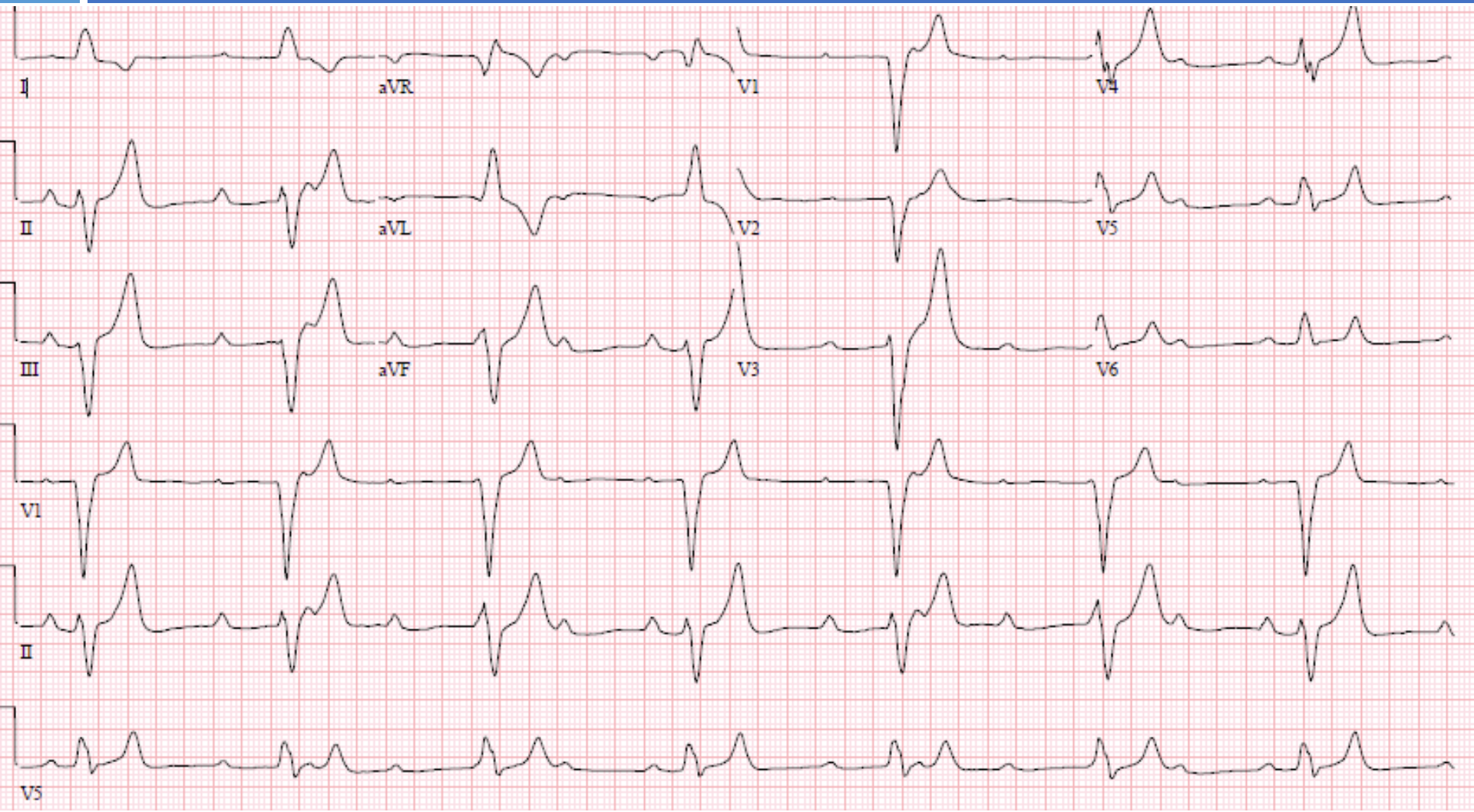
- No records available for review
- Initial vitals from triage:
  - T: 98.1F | P 49 | BP 128/58 | RR 16 | SaO2 99% on room air
- Brief history:
  - 25M with no documented past medical history
  - 2 days of progressive fatigue, occasional chills without taking temperature, and three episodes of transient dizziness ("I worried I was going to faint and had to sit down")
  - 1 episode of unwitnessed syncope with head strike and loss of consciousness of uncertain duration; colleague found him and called EMS
  - No chest pain, dyspnea, or involuntary movements he was aware of

Physical Exam

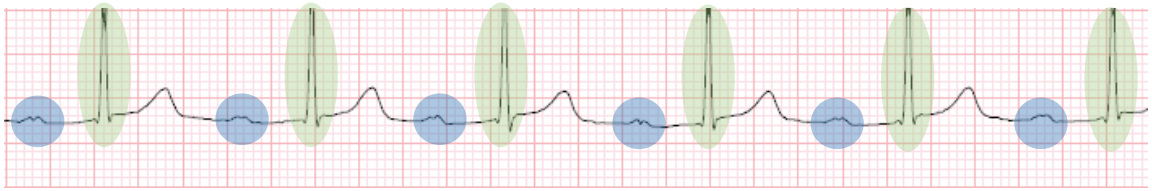
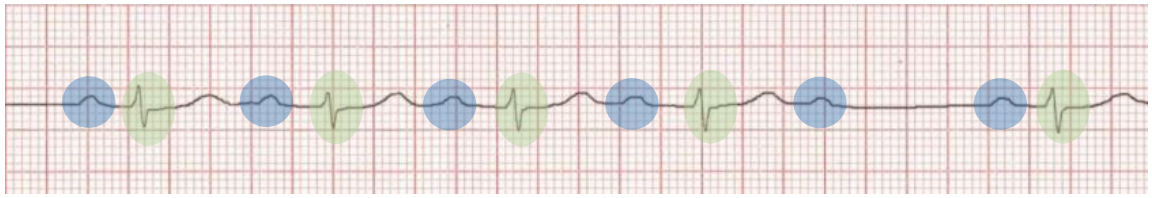
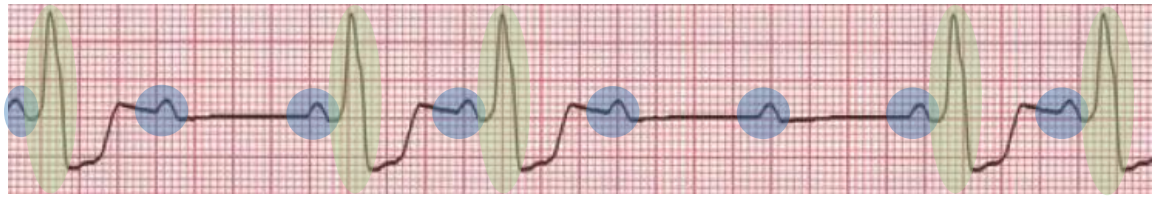
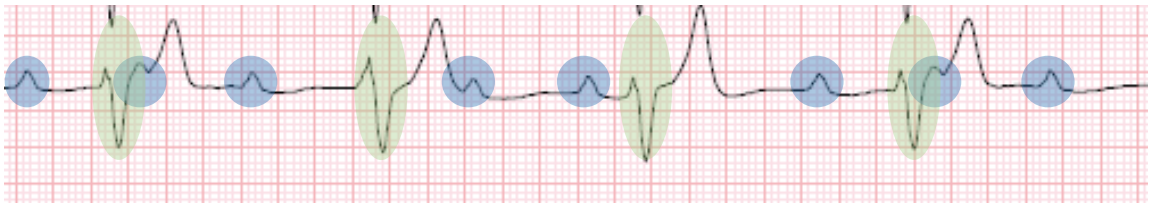
T: 98.1F | P 49 | BP 128/58 | RR 16 | SaO2 99% on room air

GEN: sitting upright on stretcher, no acute distress
HEENT: small lacerations over nose and forehead, no conjunctival injection/icterus, oropharynx clear, MMM
NECK: supple, no cervical or supraclavicular LAD
CV: very prominent JVP to 4cm above clavicle at 45 degrees, bradycardic with regular rhythm, no M/R/G, nl S1/S2
PULM: CTAB
ABD: soft, ND/NT, +BS
EXT: WWP, no edema
SKIN: no rashes noted over exposed skin

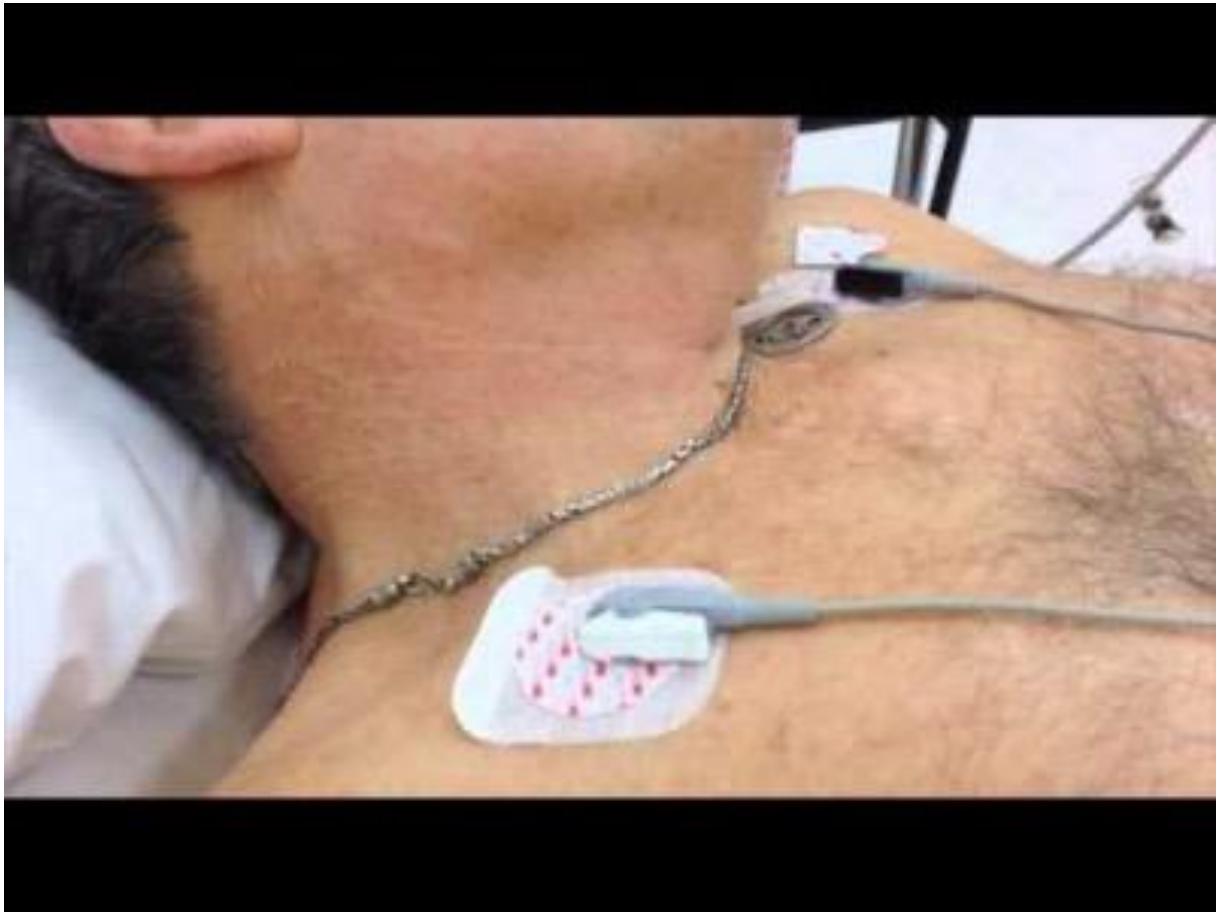
Initial ECG



Degrees of Heart Block on ECG

First degree		PR≥200ms
Second degree *Mobitz I* *(Wenckebach)*		Progressive PR interval prolongation before dropped QRS
Second degree *Mobitz II* *(Hay)*		Constant PR interval, then dropped QRS
Complete heart block		P and QRS unfollowed each other

A Key Exam Finding in Complete Heart Block



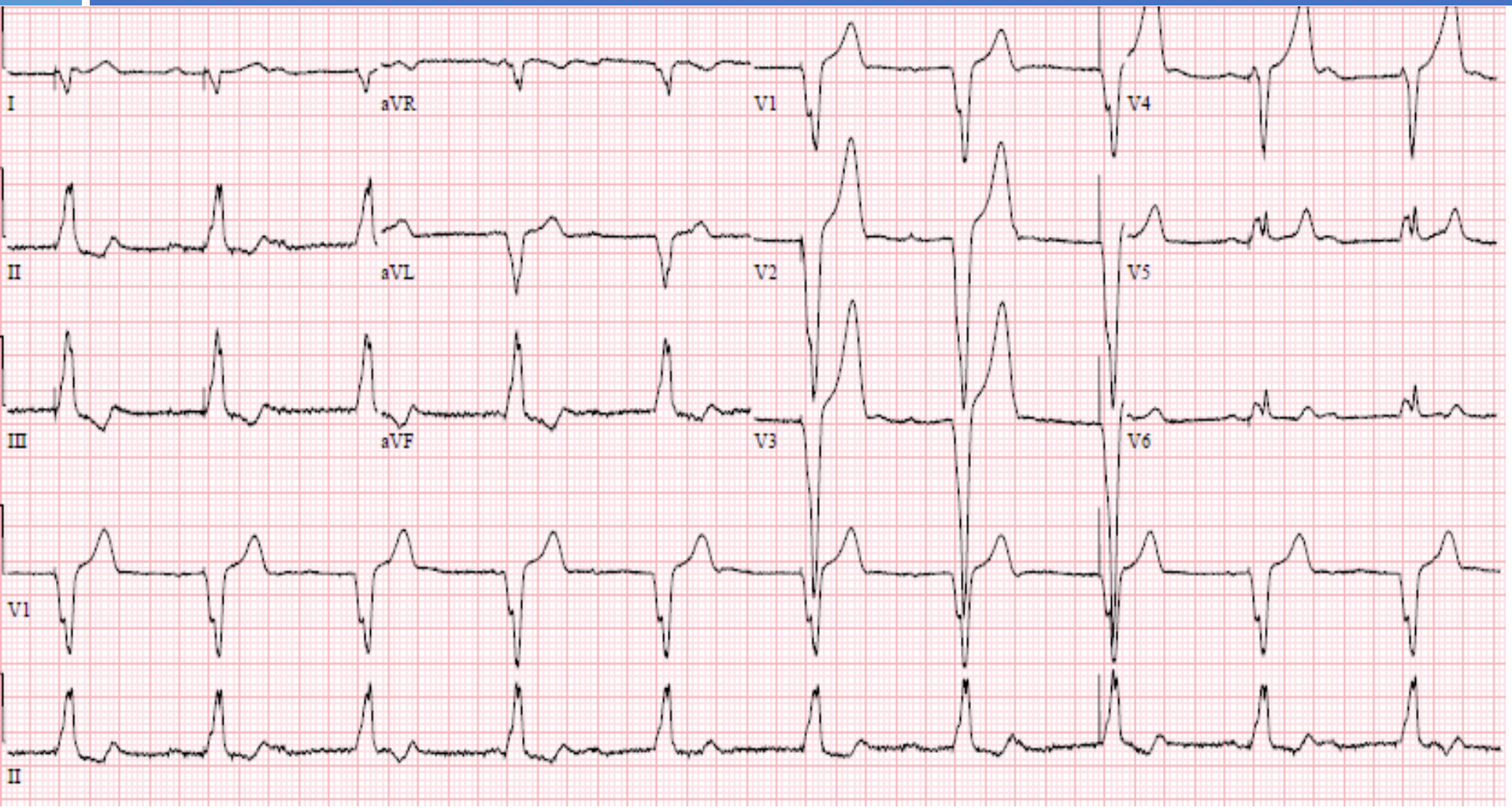
Cannon A Waves:

RA contracting against closed TV

- Complete heart block
- VT
- AVNRT

Tung MKY, Healy S. "Cannon A Waves." *NEJM* 2016; 374: e4.

S/p temp wire for CHB with wide-complex LBBB escape rhythm



Phew! Now Where Were We…?

History of the Present Illness
-25M with no known PMH
-Two days progressive fatigue and occasional chills w/o measured fevers
-Three episodes transient dizziness causing him to sit down
-One unwitnessed syncopal episode +HS + LOC (uncertain duration); colleague found him and called EMS
-No chest pain, dyspnea, or involuntary movements he was aware of
-ECG with complete heart block and LBBB junctional escape rhythm
-Now s/p temporary transvenous pacemaker

Social History:
-Immigrated to Boston from Dominican Republic five years prior to presentation
-Has not yet seen a doctor in the US
-No recent travel outside of Boston metro area
-Works downtown as a custodian
-Recalls no arthropod bites or recent rashes
-Recalls no recent sick contacts
-Never smoked
-No recreational drug use
-Rare social alcohol use

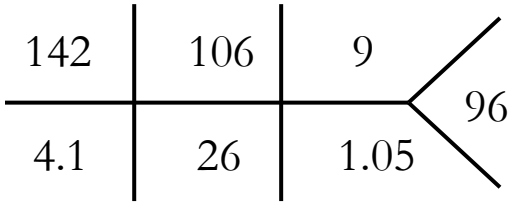
Past Medical/Surgical History:
-None

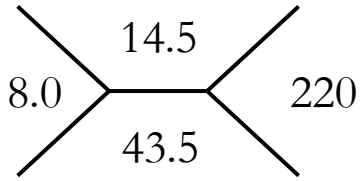
Family History:
-No known history of sudden death, cardiac disease, autoimmune disease, or CVA

Medications:
-None

Allergies:
-None known

Initial ED Labs





-Mg 2.2
-Ca 8.8
-ALT 37
-AST 31
-AP 159
-TB 0.6
-Alb 3.7
-T protein 6.7
-PT-INR 1.4

-Troponins 11, 11
-NT-proBNP 750
-TSH 1.0
-Hgb A1c 5.4%
-LDL 33
-HDL 28
-Total chol 76
-TGs 73

-Diff: 78% PMNs, 12.8% lymphs, 8.3% monos, 0.2% eos, 0.4% basos, 0.5% bands
-Ferritin 225
-Iron 93
-TIBC 249
-ESR 5
-CRP 32.6
-Blood cultures x2 pending

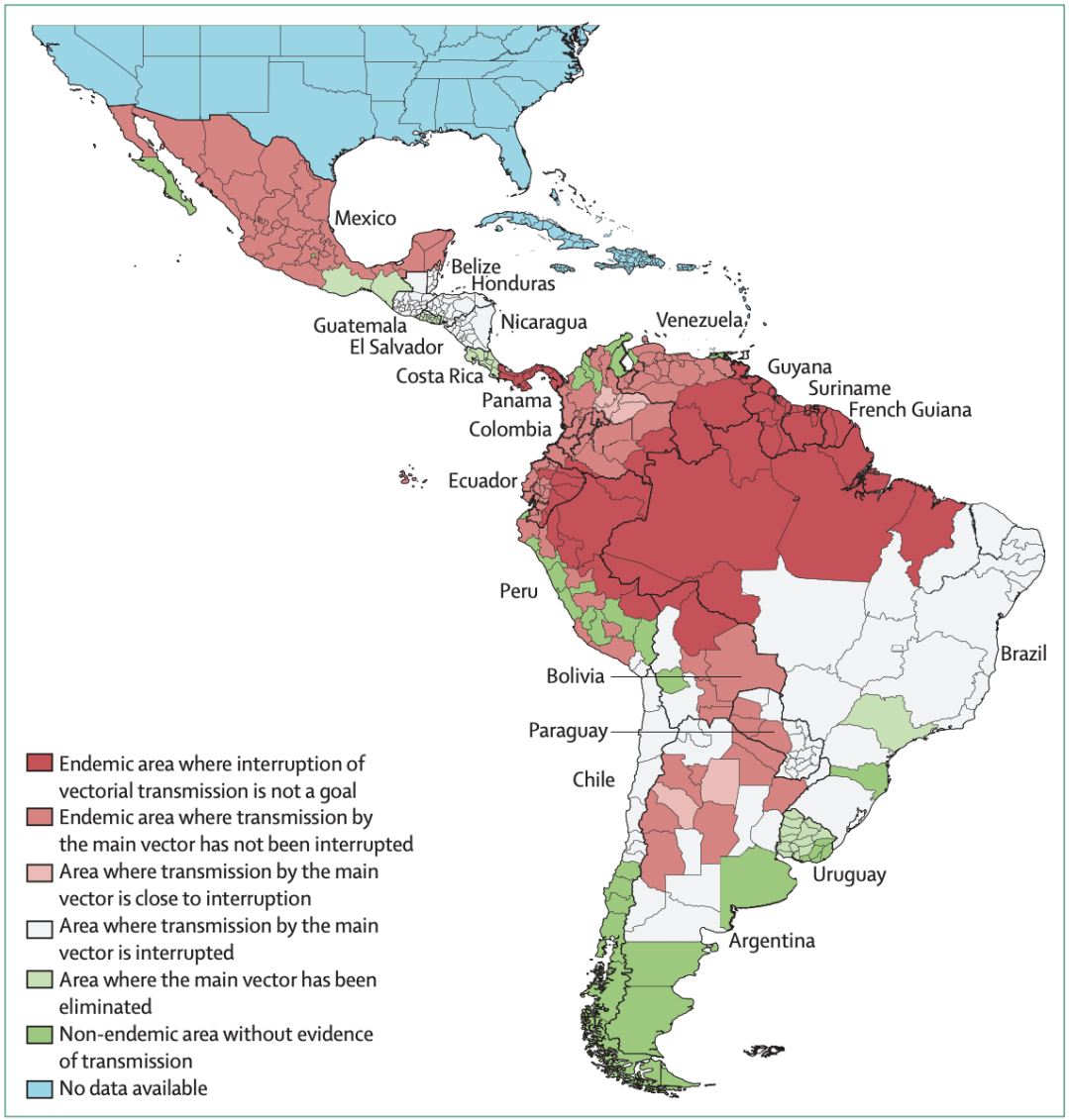
Differential Diagnosis for CHB (Not in Order)

- Conduction system fibrosis
  - Age-related
  - Chronic Chagas disease
- Structural congenital heart disease
- Infiltrative cardiomyopathy
  - Sarcoid
  - Amyloid
  - Hemochromatosis
- Acute/subacute infections
  - Viral myocarditis
  - Lyme carditis
  - Endocarditis with abscess
- Other inflammatory myocarditis
  - Giant cell
  - Eosinophilic
  - SLE
- Ischemia
- Severe hyperkalemia
- Severe hypo- or hyperthyroidism
- AV nodal blocking medications
- S/p cath or CT surgery

Differential Diagnosis for CHB (Not in Order)

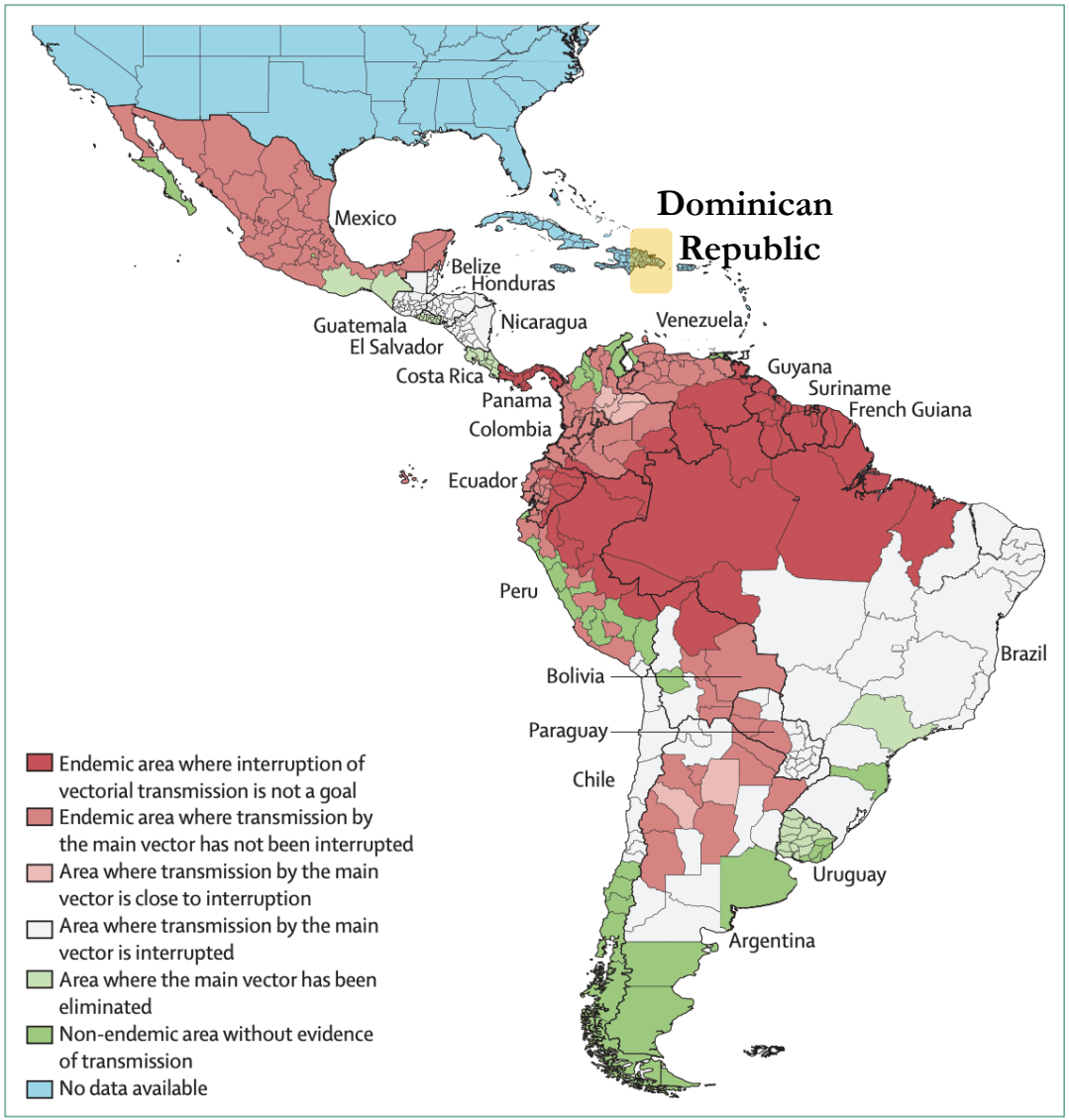
- Conduction system fibrosis
  - ~~Age-related~~
  - Chronic Chagas disease
- Structural congenital heart disease
- Infiltrative cardiomyopathy
  - Sarcoid
  - Amyloid
  - ~~Hemochromatosis~~
- Acute/subacute infections
  - Viral myocarditis
  - Lyme carditis
  - Endocarditis with abscess
- Other inflammatory myocarditis
  - Giant cell
  - Eosinophilic
  - SLE
- ~~Ischemia~~
- ~~Severe hyperkalemia~~
- ~~Severe hypo- or hyperthyroidism~~
- ~~AV nodal blocking medications~~
- ~~S/p cath or CT surgery~~

Trypanosoma cruzi (Chagas disease) epidemiology



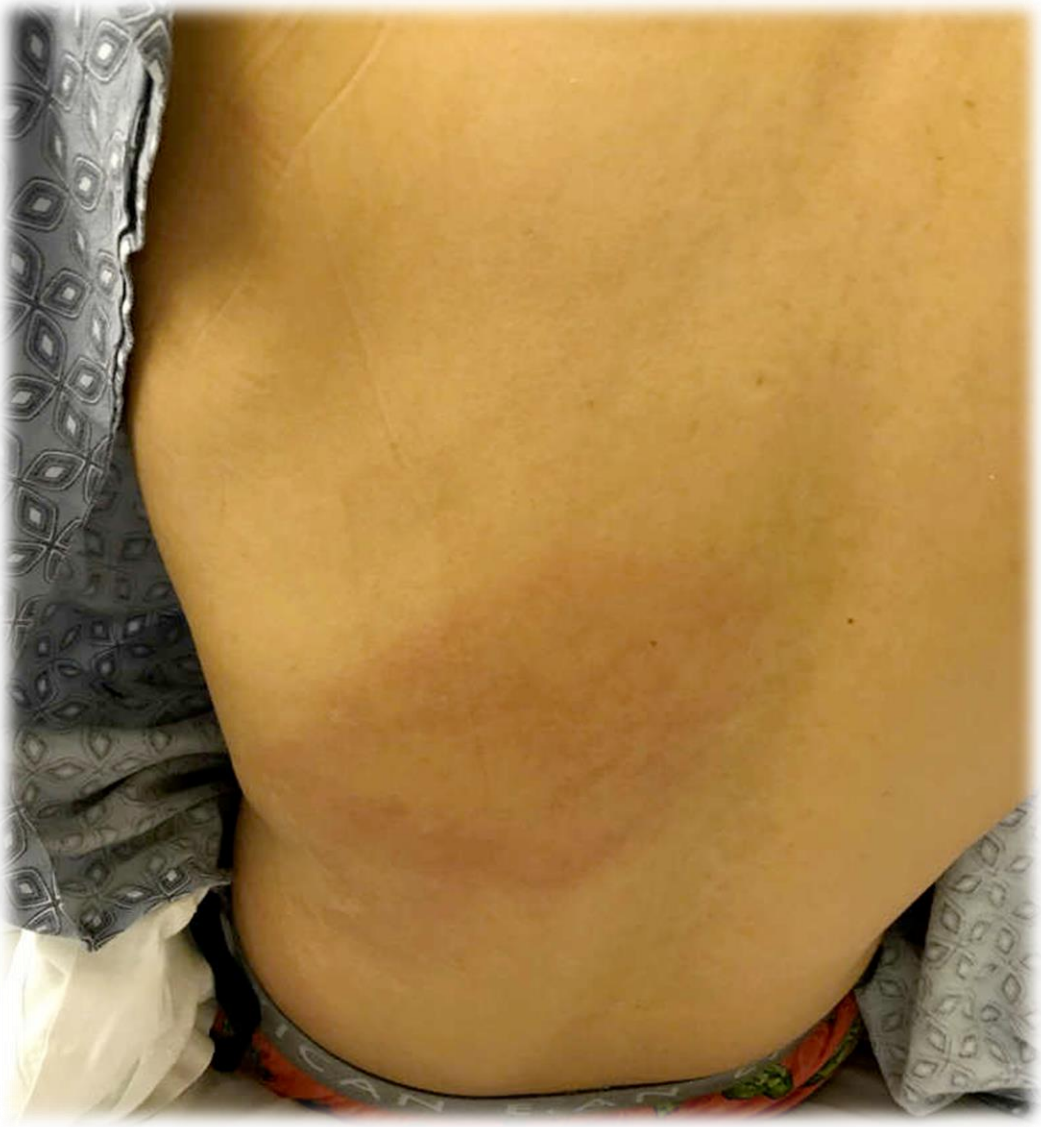
Pérez-Molina JA, Molina I. "Chagas Disease: Seminar." *Lancet* 2018; 391: 82-94.

Turnaround time for *T cruzi* serology: >2 weeks



Pérez-Molina JA, Molina I. "Chagas Disease: Seminar." *Lancet* 2018; 391: 82-94.

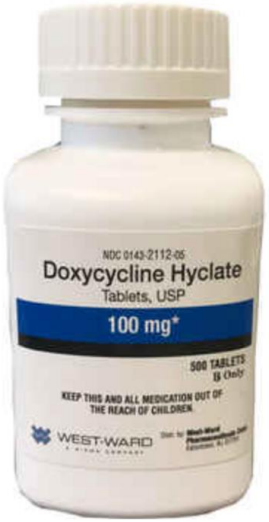
Or We Could Do a Full Physical Exam…



What Next?

Ceftriaxone 2g IV QD until PR interval ≤300ms

Note that 1st– and 2nd –generation cephalosporins have **NO effect in Lyme carditis*



Followed by **doxycycline 100mg PO BID** for 21-28 days total

Second Round of Labs

-ANA: +ve (1:160, nucleolar)
-ds-DNA Ab: negative
-Anti-Smith Ab: negative
-Anti-La Ab: negative
-Anti-Ro Ab: negative
-Anti-RNP Ab: negative
-ACE: negative

-HIV AgAb: negative
-Trypanosoma cruzi IgG: negative
-Lyme screen EIA: **positive** (resulted day 4)
-Lyme Western blot: **positive (IgM, IgG)** (day 10)
-Babesia parasite smear: negative
-Ehrlichiosis/anaplasmosis PCR: negative
-Treponema pallidum IgG: negative

Test Method:	Antibody Capture Enzyme Immunoassay (Borrelia burgdorferi 49736 strain)

Antibody Capture Enzyme Immunoassay

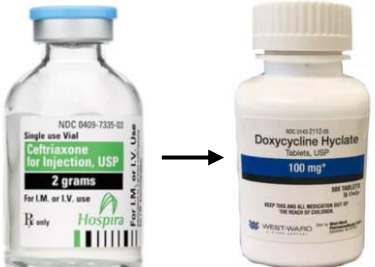
Test Date:	8/9/2019
IGM:	>23.2
IGG:	2.1
IGA:	>7.9

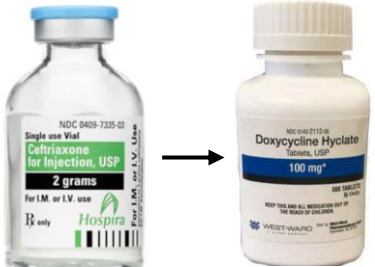
Values reflect the amount of B. burgdorferi-specific antibody corrected for background. Normal Range: No antibody detected at <0.8 for IgM and <1 for IgG and IgA.

Comment: IgM is Positive, IgG is Positive and IgA is Positive.

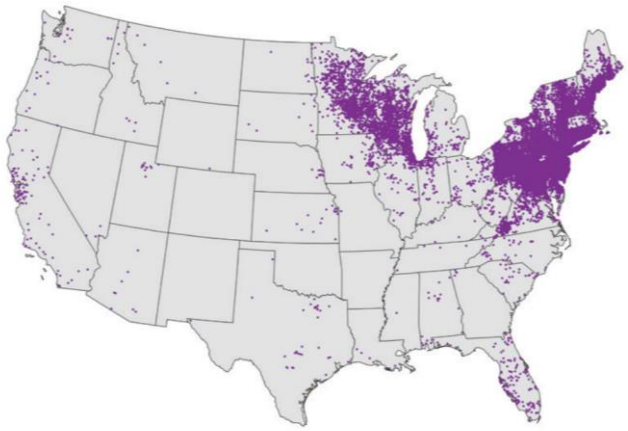
The Spectrum of Lyme Disease

Early Localized *1-2 weeks*	Early Disseminated *2 weeks to months*	Late Disseminated *Months to years*	Post-Treatment Syndrome *Months to years after effective tx*
Erythema migrans (EM) • Only in 75% of pts w/ confirmed Lyme • **NOT** a prerequisite for disseminated dz	Neurologic: • Bell's palsy • Radiculopathy • Lymphocytic meningitis	Arthritis with effusion • Monoarthritis • Oligoarthritis	Fatigue, myalgias, arthralgias, subjective cognitive changes
Fatigue, HA, myalgias, fever/chills, and/or arthralgias +/- EM	Carditis • Only **44%** of pts with complete heart block had preceding EM lesion	Neurologic: • Encephalomyelitis • Mononeuritis multiplex • Peripheral neuropathy	• Onset within 6 mos confirmed/treated dz • No alternative dx
	Multiple EM		
	Ocular disease (rare)		





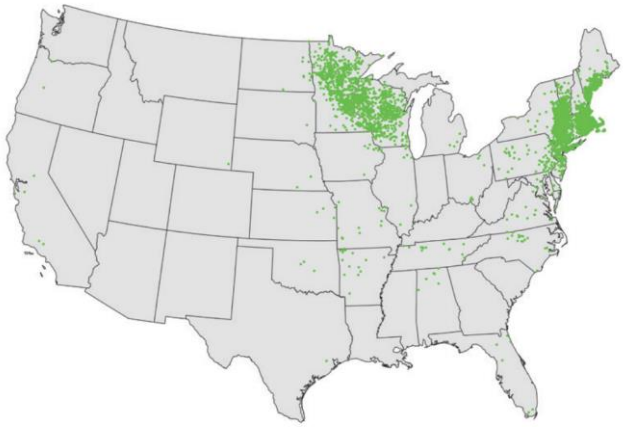
Just Because It's Lyme Doesn't Mean It's Not ALSO…



LYME DISEASE

EHRLICHIOSIS

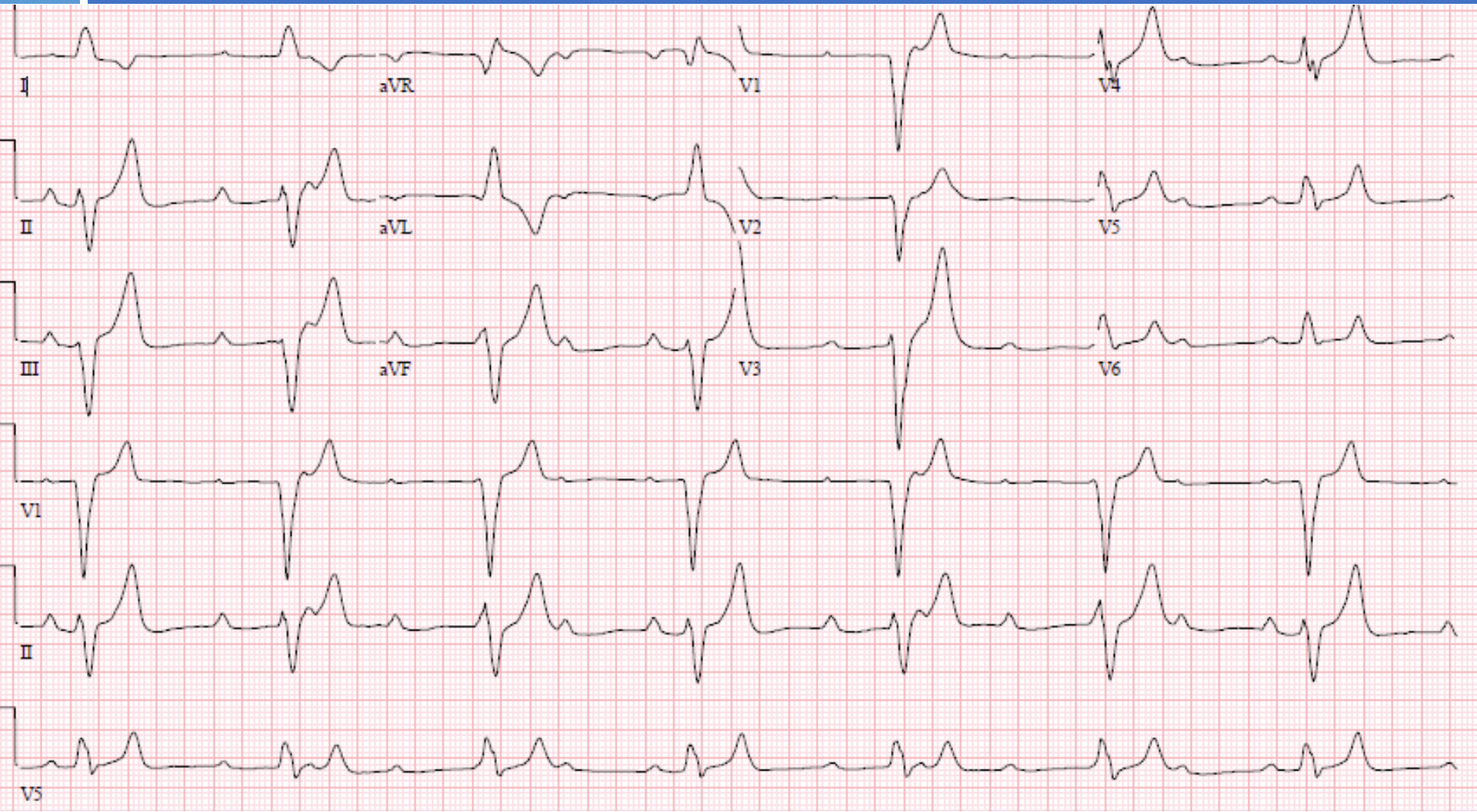
BABESIOSIS



ANAPLASMOSIS

CDC. "*Tickborne Diseases of the United States: A Reference Manual for Healthcare Providers*." CDC; Atlanta, GA: 2018.

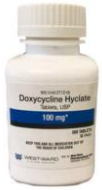
ECG on Presentation



ECG on Day 3 of  (Temp Wire Turned Off)

ECG on Day 4 of  (Temp Wire Turned Off)

ECG on Day 5 of  (Temp Wire Removed)

ECG on Day 6 of Abx, Day 1 of  (Pre-Discharge)

Key Learning Points

- Patients' epidemiologic risk factors warrant consideration, but we shouldn't anchor on them
- High-grade AV block can be the presenting symptom of Lyme disease, and Lyme carditis should be high on the differential diagnosis for young adults with complete heart block (CHB) during summer months in endemic regions.
- Up to half of patients with CHB due to Lyme carditis have no associated erythema migrans lesion, and many patients who do have a suspicious rash are not aware because these lesions are neither painful nor pruritic, demonstrating the importance of a full-body skin examination for patients with CHB.
- Recommended treatment for Lyme carditis resulting in symptomatic high-grade AV block includes daily IV ceftriaxone until the PR interval is less than 300ms (noting that 1st- and 2nd-generation cephalosporins have no effects), followed by twice-daily oral doxycycline for a total course of 21 to 28 days.
- Temporary pacing may be required for severe cases, but permanent pacemakers can almost always be avoided, as Lyme carditis has an excellent prognosis with prompt antibiotic treatment (which often must be initiated empirically, prior to return of serology and Western blot results).

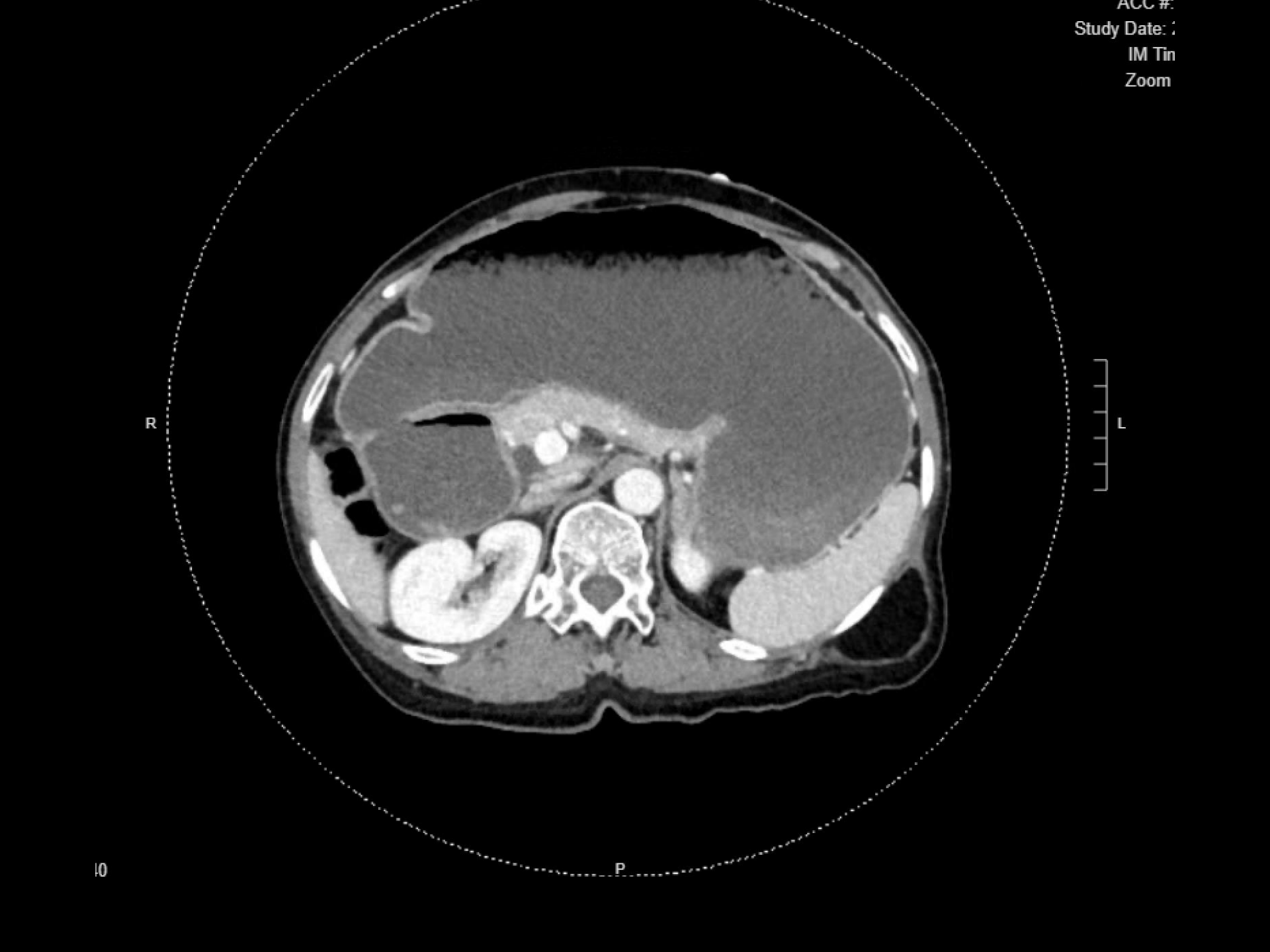
Case 3:
Small Bowel Obstruction

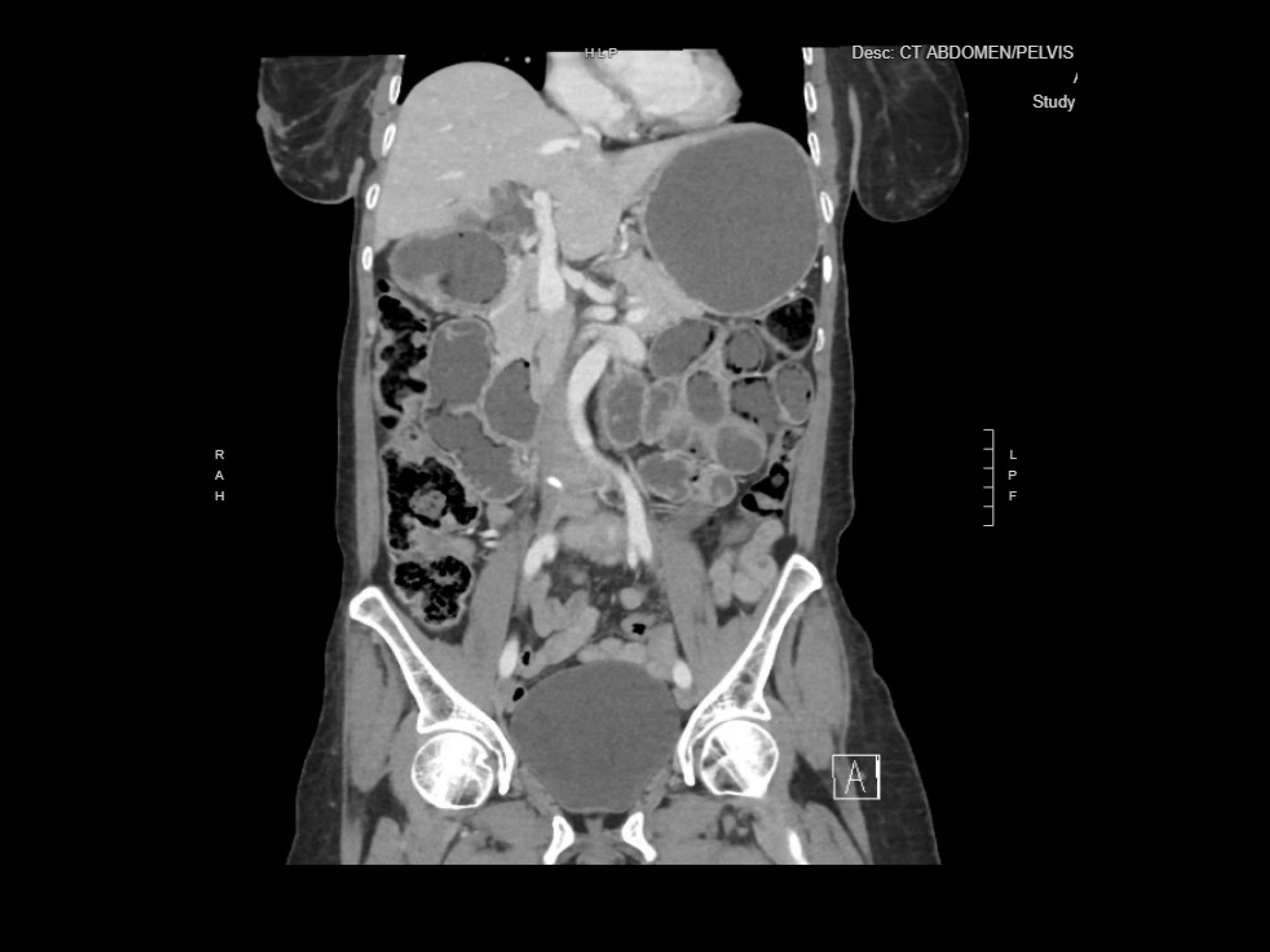
66F with previously treated pulmonary TB admitted with chronic post-prandial epigastric pain and 40 lbs weight loss

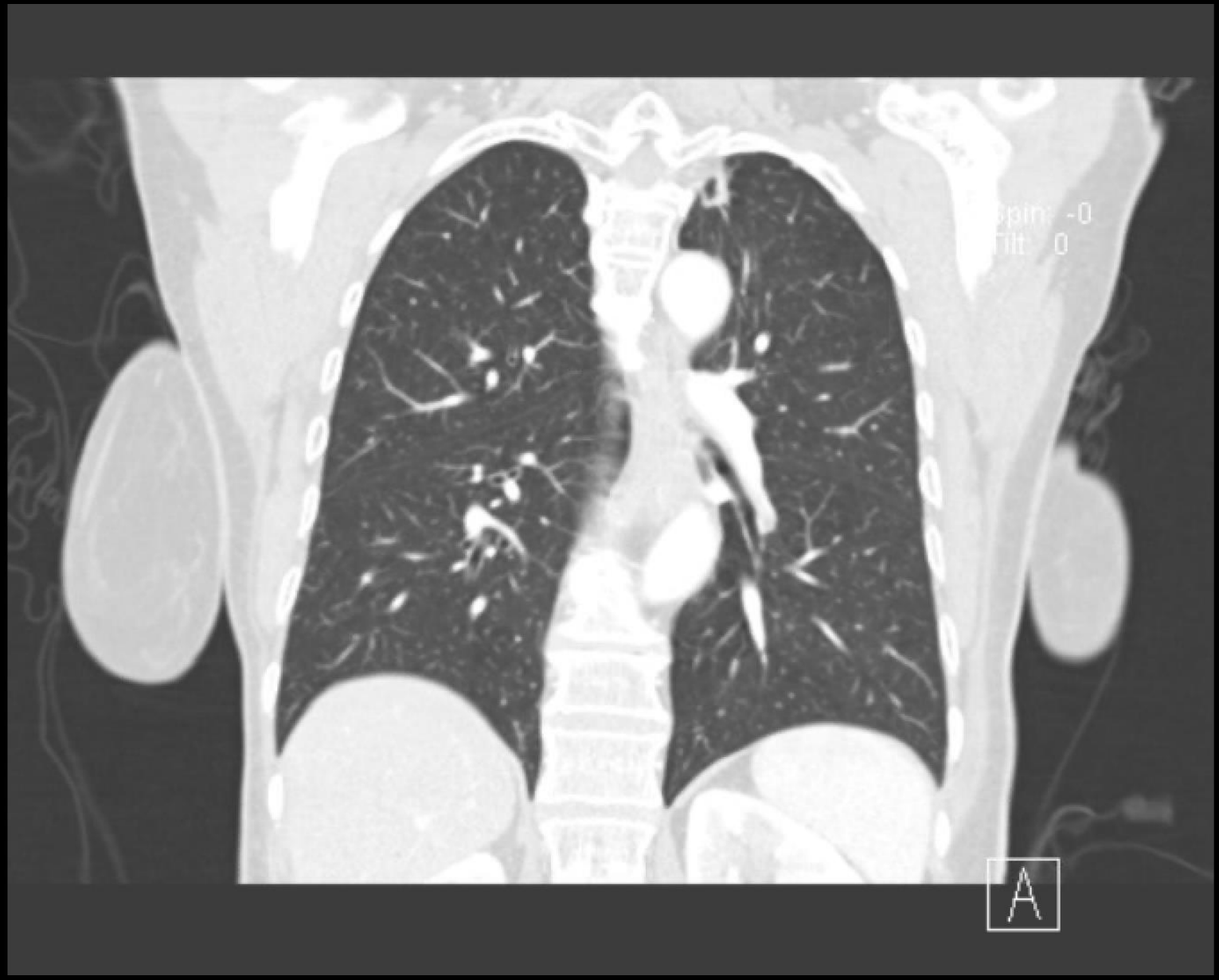
History of the Present Illness:
-Onset of slowly progressive postprandial substernal/epigastric pain 12 months ago
-Often accompanied by GERD, nausea, early satiety, constipation, intermittent subjective fevers, and non-productive chronic cough; all symptoms wax and wane in cycles
-No associated night sweats, diarrhea, hemoptysis, hematemesis, or hematochezia
-Pain steadily worsened over past 3 months, leading to avoidance of solids and loss of 40 lbs
-No current rashes, but had hyperpigmented streaky pruritic rash over her R thigh last month

Past Medical History:
-Remote pulmonary TB (>10 years ago, completed 6 months of RIPE per her report)
-Uterine fibroids s/p remote myomectomy via laparotomy (before 1990)
-HTN, prediabetes, MDD

Relevant Social History:
-Immigrated from Haiti in 2018
-Currently homeless, staying with friends and intermittently in shelters, and has had no access to medical care since prior to the COVID-19 pandemic


ACC #:
Study Date:
IM Tin
Zoom
R
L
P


H L P
Desc: CT ABDOMEN/PELVIS
Study
R
A
H
L
P
F
A

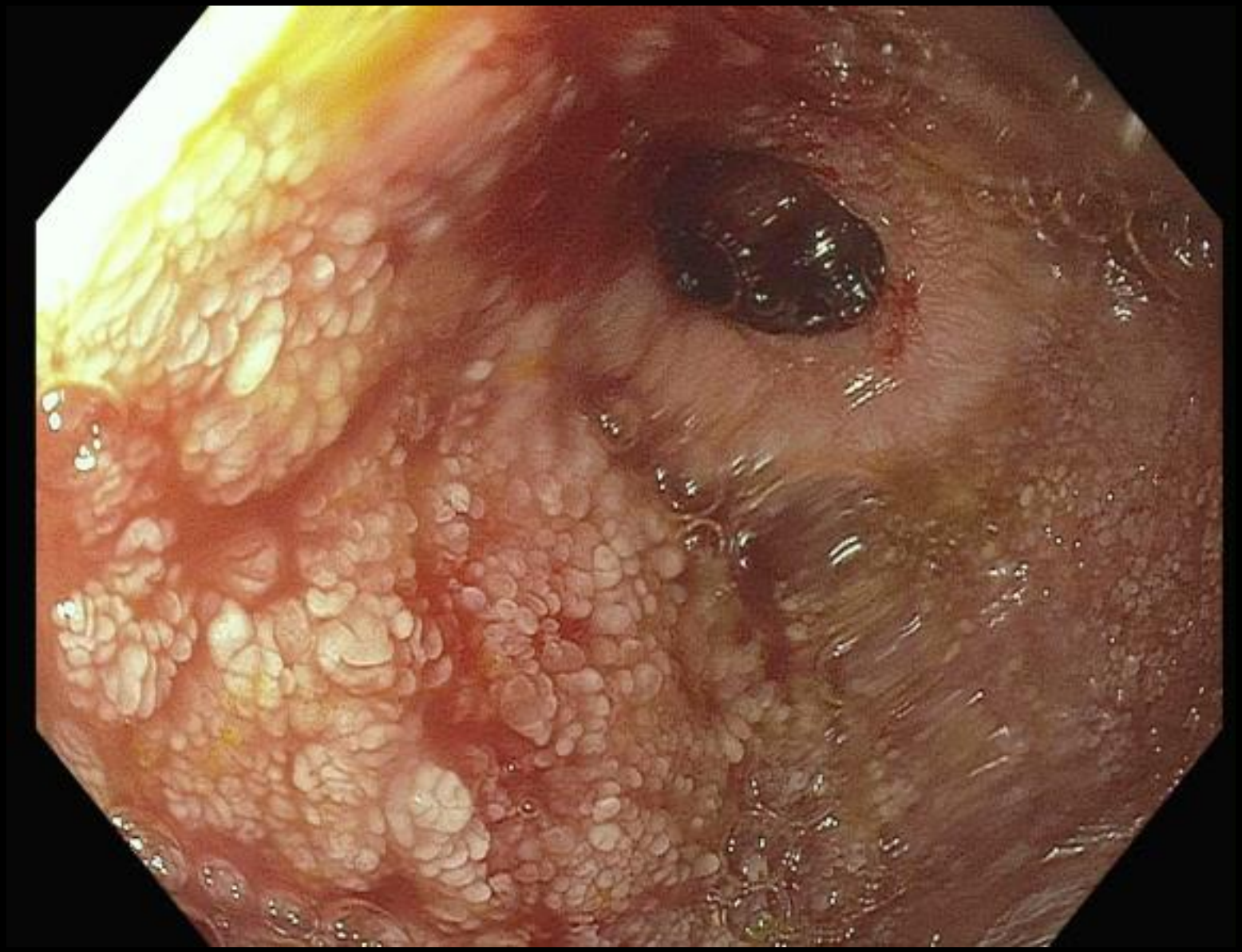

R
L
A

66F immigrant from Haiti with remote pulmonary TB admitted with chronic post-prandial epigastric pain, 40 lbs weight loss, and peripheral eosinophilia

Relevant Labs:
-WBC 12.6 (45.1% lymphs, 12.6% eos)
-Absolute eosinophil count 1590
-AST 26, ALT 19, AP 140, TB 0.3
-CRP 34.2, ESR 29
-CA 19-9 16, CEA 1.2, CA-125 7 (all normal)

Relevant Microbiology:
-HIV AbAg negative
-T Spot indeterminate
-Stool O&P not collected (constipation)
-Stool H pylori Ag not collected (constipation)

Hospital Course:
-Initial imaging concerning for SBO attributed to malignancy vs. adhesions (prior ex-lap)
-NGT placed with massive bilious output
-Gastroenterology service consulted and EGD performed on hospital day 2…

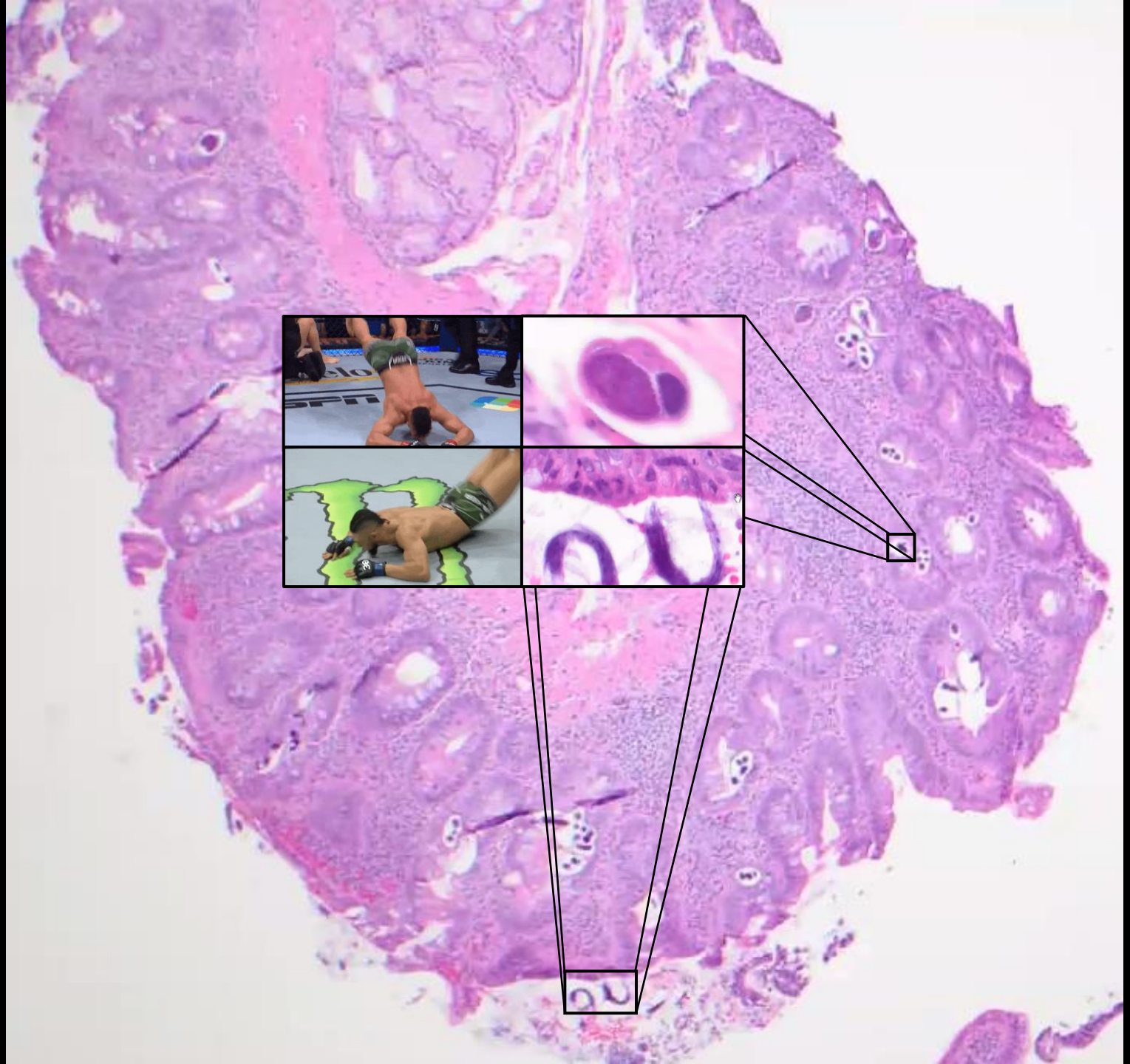


66F immigrant from Haiti with remote pulmonary TB admitted with intrinsic duodenal stenosis (causing 40 lb weight loss) and peripheral eosinophilia

Relevant Labs:
-WBC 12.6 (45.1% lymphs, 12.6% eos)
-Absolute eosinophil count 1590
-AST 26, ALT 19, AP 140, TB 0.3
-CRP 34.2, ESR 29
-CA 19-9 16, CEA 1.2, CA-125 7 (all normal)

Relevant Microbiology:
-HIV AbAg negative
-T Spot indeterminate
-Stool O&P not collected (constipation)
-Stool H pylori Ag not collected (constipation)

Hospital Course:
-Initial imaging concerning for SBO attributed to malignancy vs. adhesions (prior ex-lap)
-NGT placed with massive bilious output
-Gastroenterology service consulted and EGD performed on hospital day 2…
-Minimal improvement by hospital day 5, when preliminary pathology slides are reviewed...



Helminths That Can Penetrate Duodenum and Cause Peripheral Eosinophilia

Species	Route of transmission	Duodenal findings	Stool findings	Treatment
Toxocara spp.	Ingestion of eggs	Transient larvae in wall	None	Albendazole
Trichinella spp.	Ingestion of undercooked pork/game	Adults in wall	None	Albendazole
Ascaris lumbricoides	Ingestion of eggs	Adults in lumen	Eggs and adults	Albendazole
Tapeworms (*Taenia* spp, *Diphylobothrium* spp, *Hymenolepis nana*)	Ingestion of undercooked meat/fish/veggies	Adults in lumen	Eggs and proglottids	Praziquantel (if no neurocysticercosis)
Hookworms (*Necator americanus, Ancylostoma duodenale*)	Larvae penetrate skin (esp. feet)	Adults in lumen	Eggs	Albendazole
Strongyloides stercoralis	Larvae penetrate skin (esp. feet); prolonged autoinfection	Adults and eggs in wall; larvae in lumen	Larvae +/- eggs	Ivermectin

66F immigrant from Haiti with remote pulmonary TB admitted with intrinsic duodenal stenosis and peripheral eosinophilia

Historical labs from 2 outpatient encounters at another hospital 32 months prior:

66F immigrant from Haiti with remote pulmonary TB admitted with intrinsic duodenal stenosis and chronic eosinophilia

Historical labs from 2 outpatient encounters at another hospital 32 months prior:

-WBC 8.9 with 15.0% eosinophils (absolute 1300)

-Flow cytometry: "An aberrant non-clonal T cell population with irregular nuclear contours is observed comprising approximately 30% of the lymphoid gate which are CD4 positive, CD3 dim, CD7 negative and bright CD25 positive with normal expression of CD2 and CD5. CD8 positive cells are phenotypically normal and B cells are polytypic."

66F immigrant from Haiti with remote pulmonary TB admitted with intrinsic duodenal stenosis and chronic eosinophilia

Historical labs from 2 outpatient encounters at another hospital 32 months prior:

-WBC 8.9 with 15.0% eosinophils (absolute 1300)

-Flow cytometry: "An aberrant non-clonal T cell population with irregular nuclear contours is observed comprising approximately 30% of the lymphoid gate which are CD4 positive, CD3 dim, CD7 negative and bright CD25 positive with normal expression of CD2 and CD5. CD8 positive cells are phenotypically normal and B cells are polytypic."

66F immigrant from Haiti with remote pulmonary TB admitted with chronic eosinophilia and ivermectin-responsive intrinsic duodenal stenosis

Hospital Course:

-Started on ivermectin 200ug/kg PO Q24H

-Marked improvement by the next day, with resolution of obstructive symptoms and removal of NGT

-"Tylenol absorption test" confirms ability to absorb oral medications

-Previous planned endoscopic duodenal dilatation canceled

66F immigrant from Haiti with remote pulmonary TB admitted with chronic eosinophilia and ivermectin-responsive intrinsic duodenal stenosis

Hospital Course:

-Started on ivermectin 200ug/kg PO Q24H

-Marked improvement by the next day, with resolution of obstructive symptoms and removal of NGT

-"Tylenol absorption test" confirms ability to absorb oral medications

-Previous planned endoscopic duodenal dilatation canceled

Subsequent microbiology:

-*Strongyloides stercoralis* serology: negative

-Stool O&P x3 negative (not collected until day 6 of ivermectin after constipation resolved)

-Induced sputum x3 negative for helminth larvae

-Induced sputum AFB smear x3 negative, along with MTB/RIF PCR negative x1

66F with intrinsic duodenal stenosis due to severe gastrointestinal *Strongyloides stercoralis* infection, now rapidly improving on ivermectin

Hospital Course:

-Started on ivermectin 200ug/kg PO Q24H

-Marked improvement by the next day, with resolution of obstructive symptoms and removal of NGT

-"Tylenol absorption test" confirms ability to absorb oral medications

-Previous planned endoscopic duodenal dilatation canceled

Subsequent microbiology:

-*Strongyloides stercoralis* serology: negative

-Stool O&P x3 negative (not collected until day 6 of ivermectin after constipation resolved)

-Induced sputum x3 negative for helminth larvae

-Induced sputum AFB smear x3 negative, along with MTB/RIF PCR negative x1

Final pathology report:

Active gastritis and duodenitis with abundant larval and egg forms, morphologically consistent with Strongyloides infection.

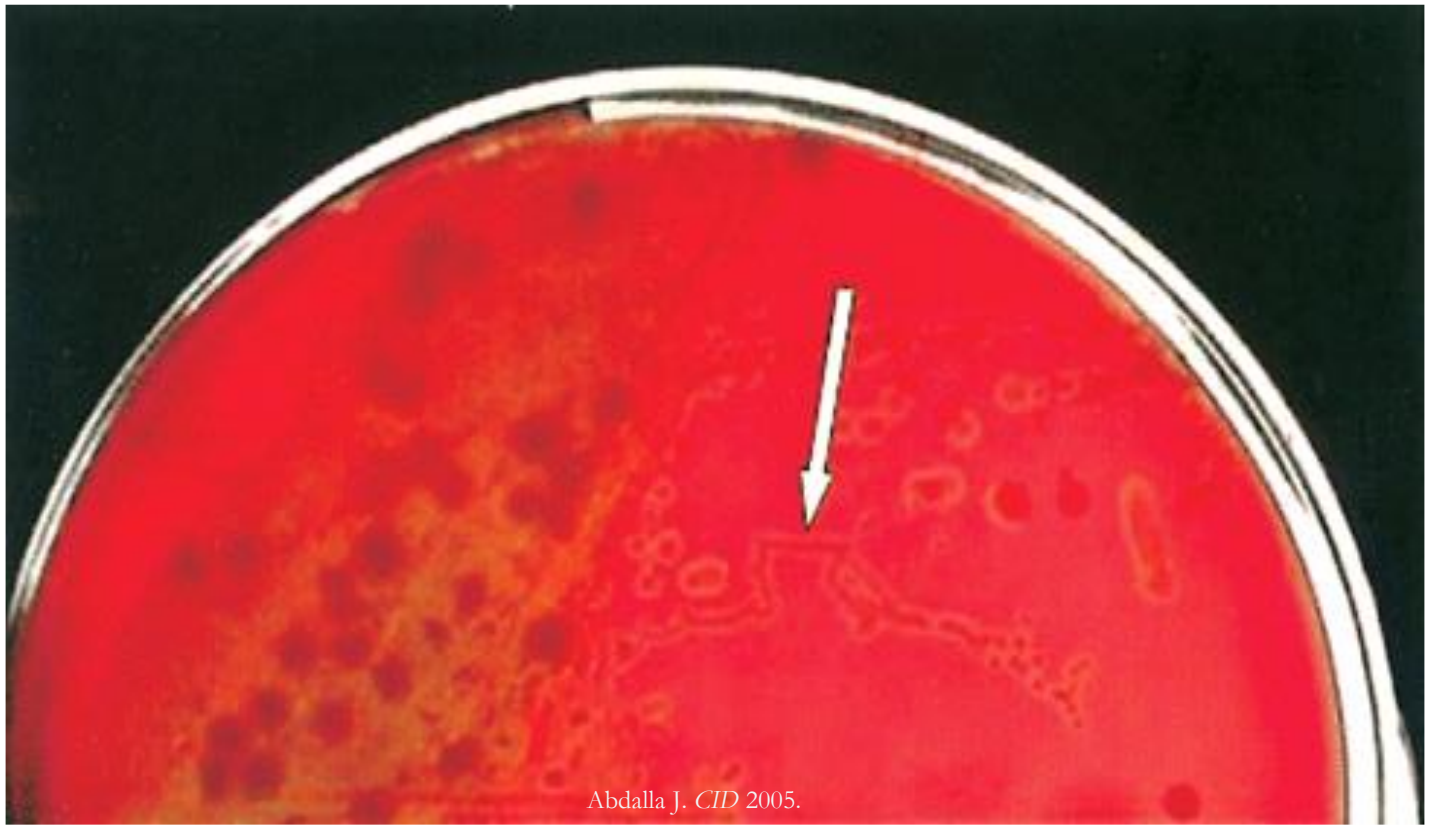
66F with intrinsic duodenal stenosis due to severe gastrointestinal *Strongyloides stercoralis* infection, now rapidly improving on ivermectin

...But why would a supposedly immunocompetent patient have such a heavy burden of infection?

...And why was her *Strongyloides* serology negative?

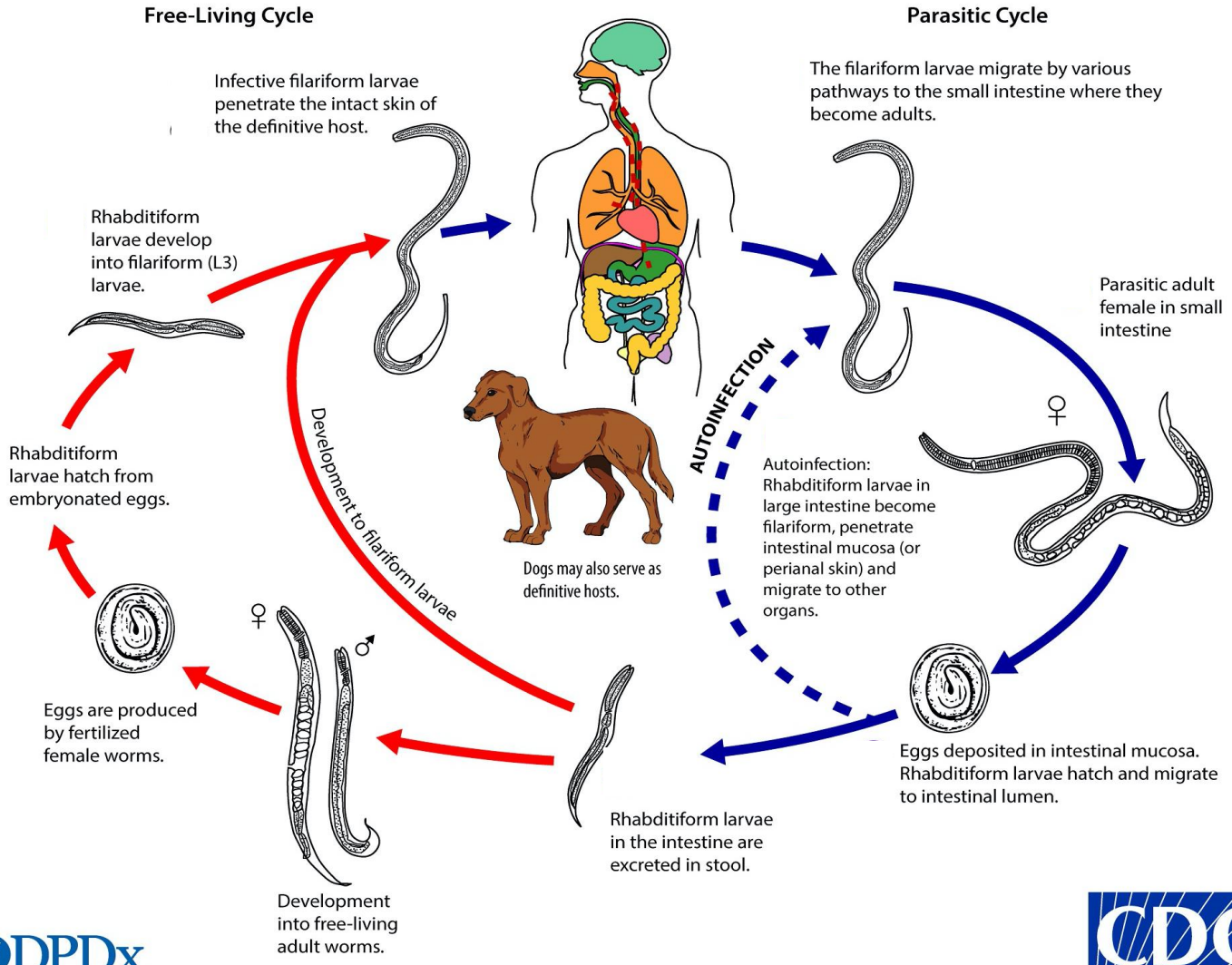
Strongyloides stercoralis: A Brief Primer

-Soil-transmitted nematode; prevalence not well understood
-Most estimates based on 1980s/1990s surveys suggesting burden of 30-100 million
-Recent spatiotemporal modeling estimates of prevalence range between 300-614 million
-Diagnosed by stool O&P (rhabditiform larvae), culture, serology (to soluble larva extract)
-Treated with ivermectin (binds helminth glutamate-gated Cl^- channels → hyperpolarization)



Abdalla J. *CID* 2005.

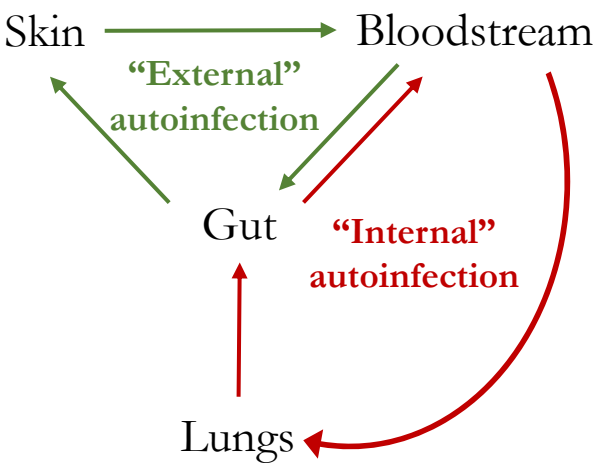
The *Strongyloides stercoralis* life cycle

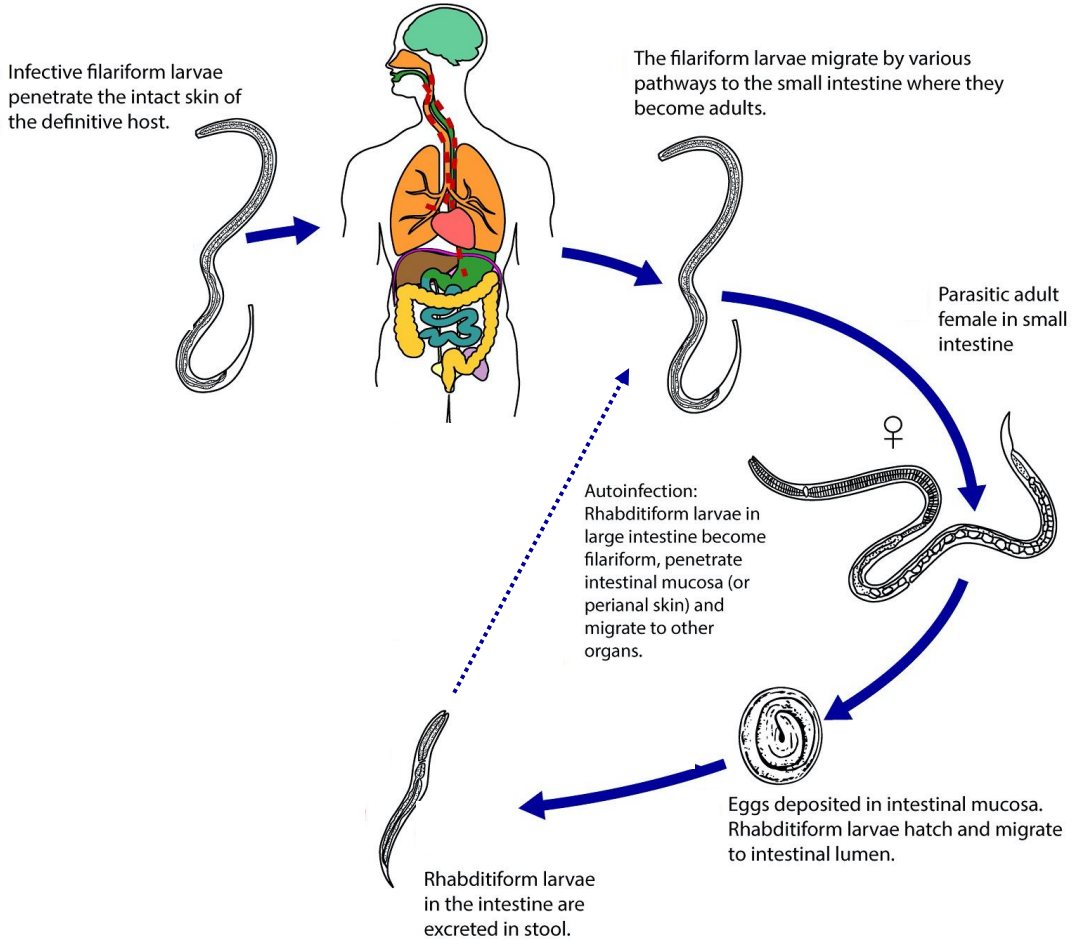


DPDx

CDC

The "Autoinfection Cycle"





The "Autoinfection Cycle"

Emerg Infect Dis. 2011 May; 17(5): 931–932.
doi: 10.3201/eid1705.100490

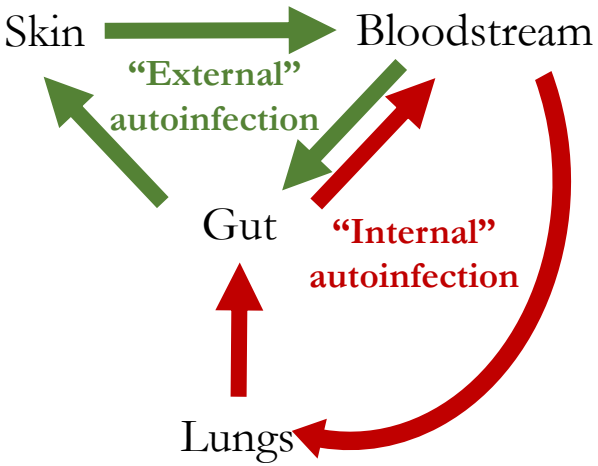
PMCID: PMC3321755
PMID: 21529417

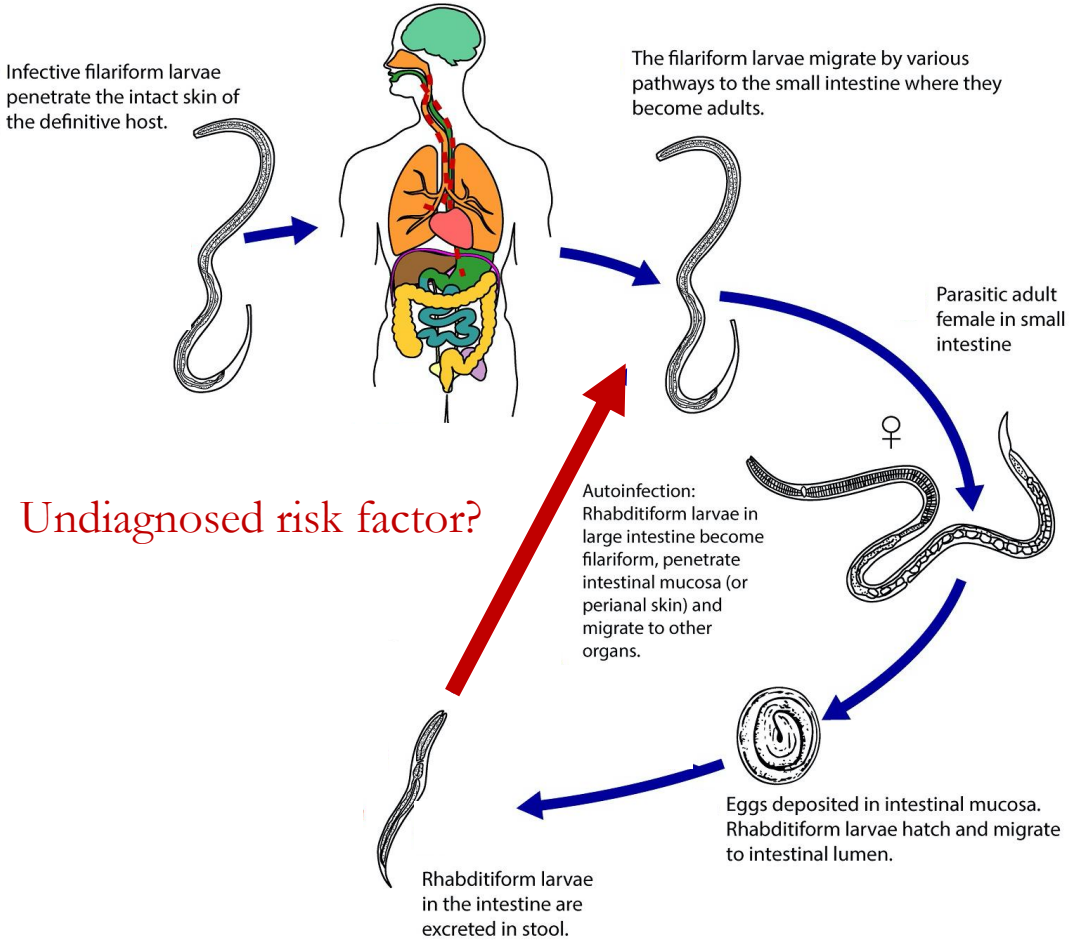
Strongyloidiasis in Man 75 Years after Initial Exposure

Virginie Prendki,[✉] Pierre Fenaux, Rémy Durand, Marc Thellier, and Olivier Bouchaud

"Endogenous autoinfection enables this nematode to develop into its host, which leads to the persistence of chronic infection several decades after a person has left a disease-endemic area. We encountered a case of prolonged strongyloidiasis with an infection going back >75 years."

Strongyloides Hyperinfection Syndrome





Strongyloides Hyperinfection Syndrome due to HTLV-1 Coinfection

-Serum HTLV-I PCR: **positive**

-Flow cytometry: An aberrant CD4+ CD3-dim T-cell population is identified. Review of the peripheral smear reveals that a subset of the lymphocytes has indented to convoluted or lobulated nuclei, condensed chromatin, and scant, pale cytoplasm.

Human T-Lymphotropic Virus Type 1: A Brief Primer

-First human retrovirus to be discovered (1980); paved the way for early "HTLV-III" research
-Prevalence poorly understood; outdated estimates suggest global burden of 10-20 million
-Highly concentrated among poor women in low-income countries
-Phylogenetic analyses suggest global dissemination in 17th century was linked to slave trade
-3 routes of transmission: vertical (breastfeeding) > sexual > parenteral (including IVDU)
-Selectively infects CD4+ T cells; clonal expansion > infection of new cells (unlike HIV)
-Highly oncogenic: adult T cell leukemia-lymphoma (2-4% lifetime risk) > cutaneous TCL
-Tropical spastic paraparesis / HTLV-1-associated myelopathy
-Co-infection with HIV-1 likely accelerates progression to AIDS
-Diagnosed by serology or serum PCR
-No effective vaccine or treatment, though 3TC and/or AZT often used in ATLL treatment

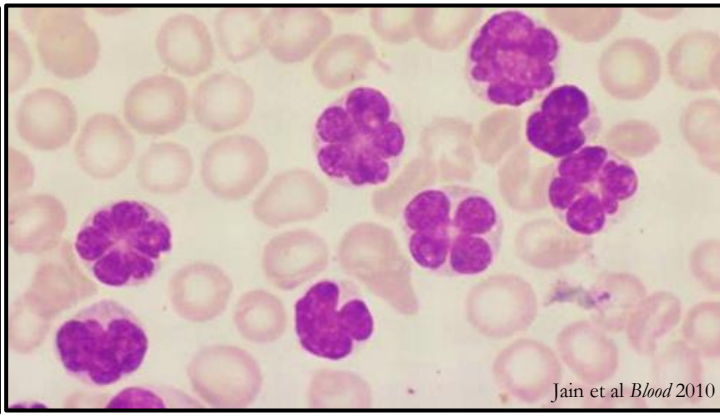
Proc. Natl. Acad. Sci. USA
Vol. 77, No. 12 pp. 7415–7419, December 1980
Medical Sciences

Detection and isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma

(mycosis fungoides/T-cell growth factor/RNA tumor virus/reverse transcriptase)

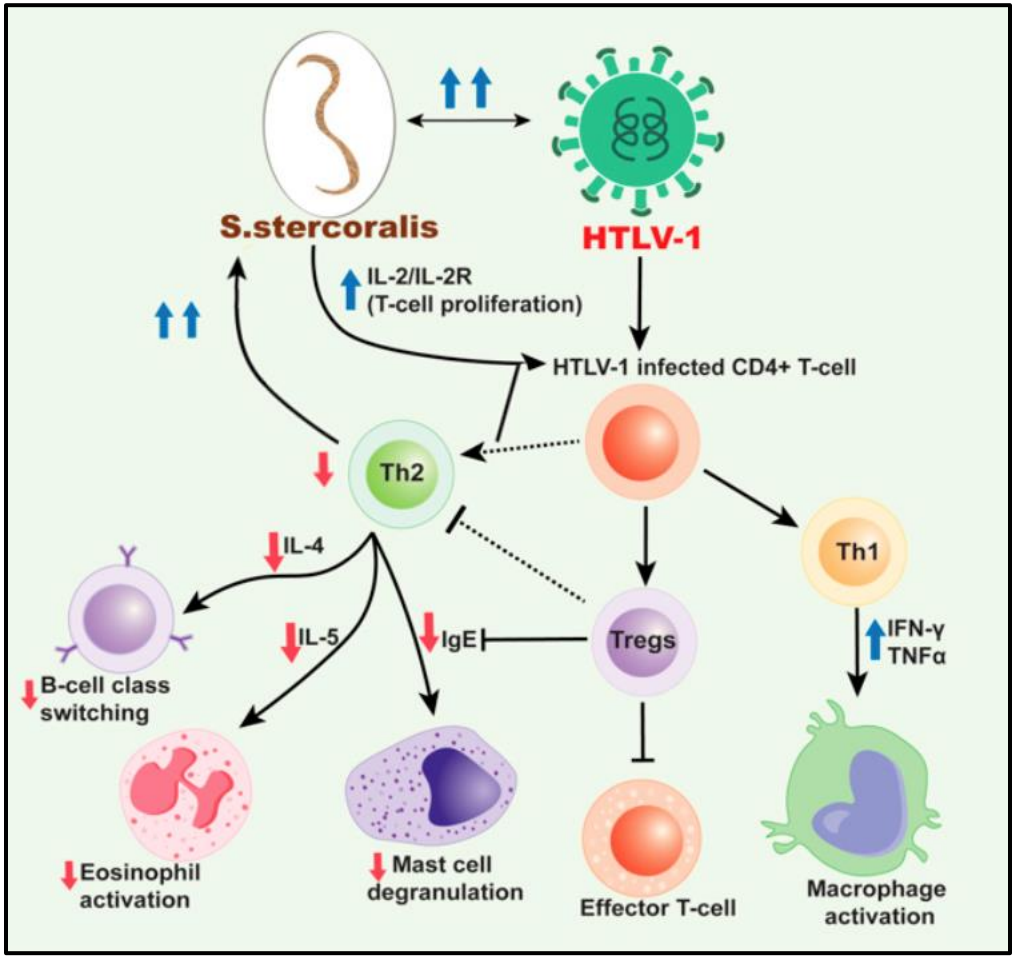
BERNARD J. POIESZ*, FRANCIS W. RUSCETTI*, ADI F. GAZDAR†, PAUL A. BUNN†, JOHN D. MINNA†, AND ROBERT C. GALLO*‡

*Laboratory of Tumor Cell Biology, Building 37, National Cancer Institute and †National Cancer Institute–Veterans Administration Oncology Branch, National Institutes of Health, Bethesda, Maryland 20205



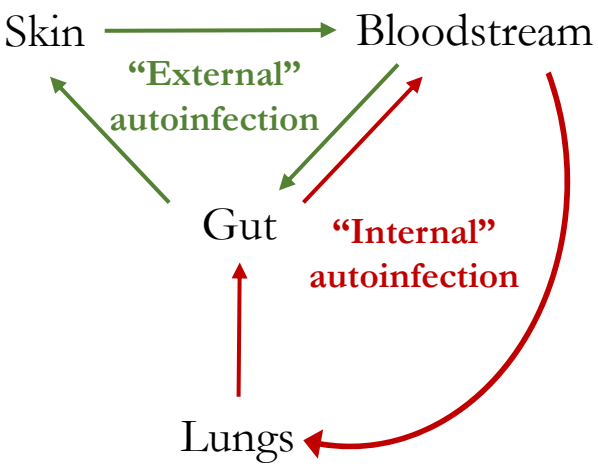
Jain et al *Blood* 2010

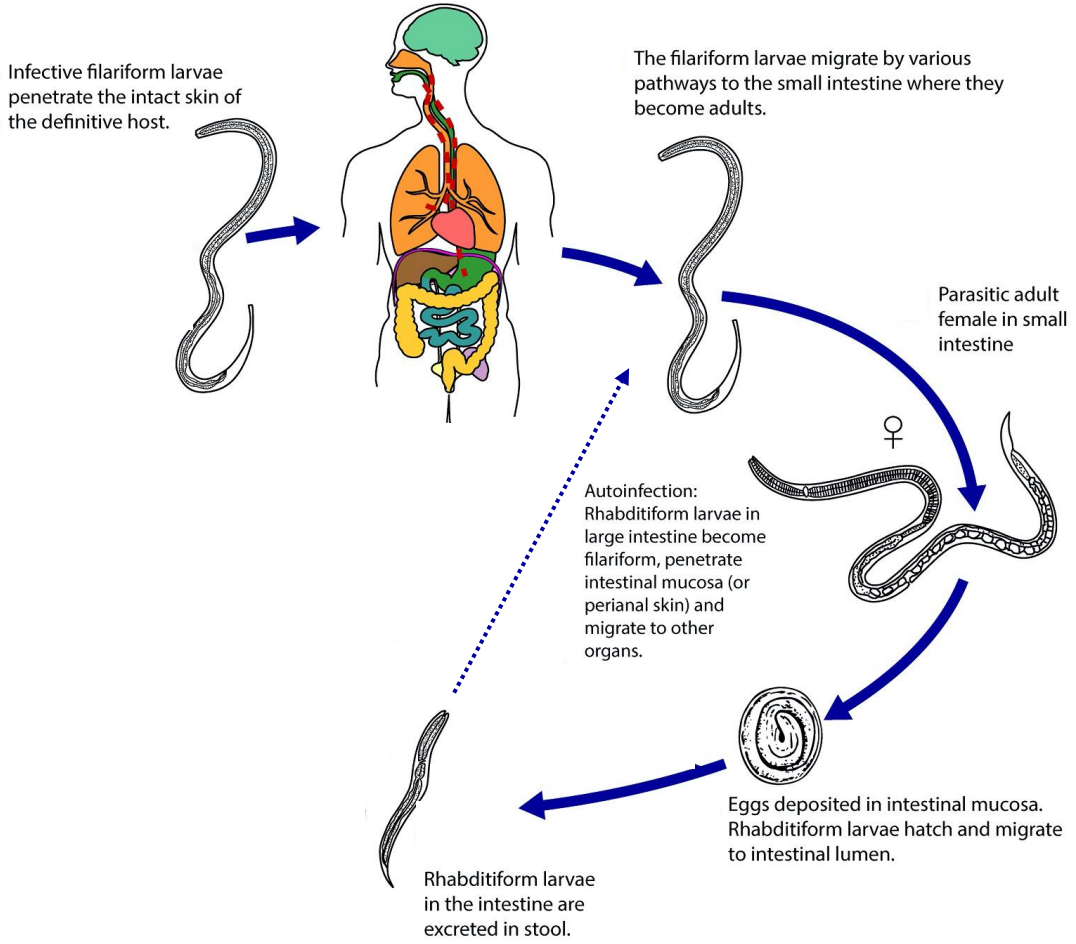
Mechanisms of HTLV-1 and Strongyloides Coinfection



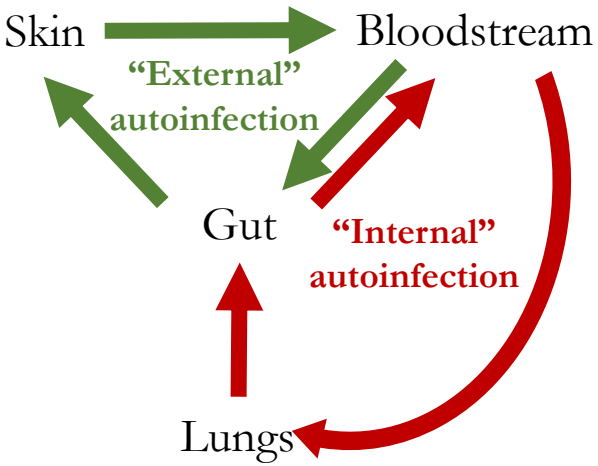
Dykie A, et al. Human T-Cell Leukemia Virus Type 1 and Strongyloides stercoralis: Partners in Pathogenesis. *Pathogens* 2020; 9: 904.

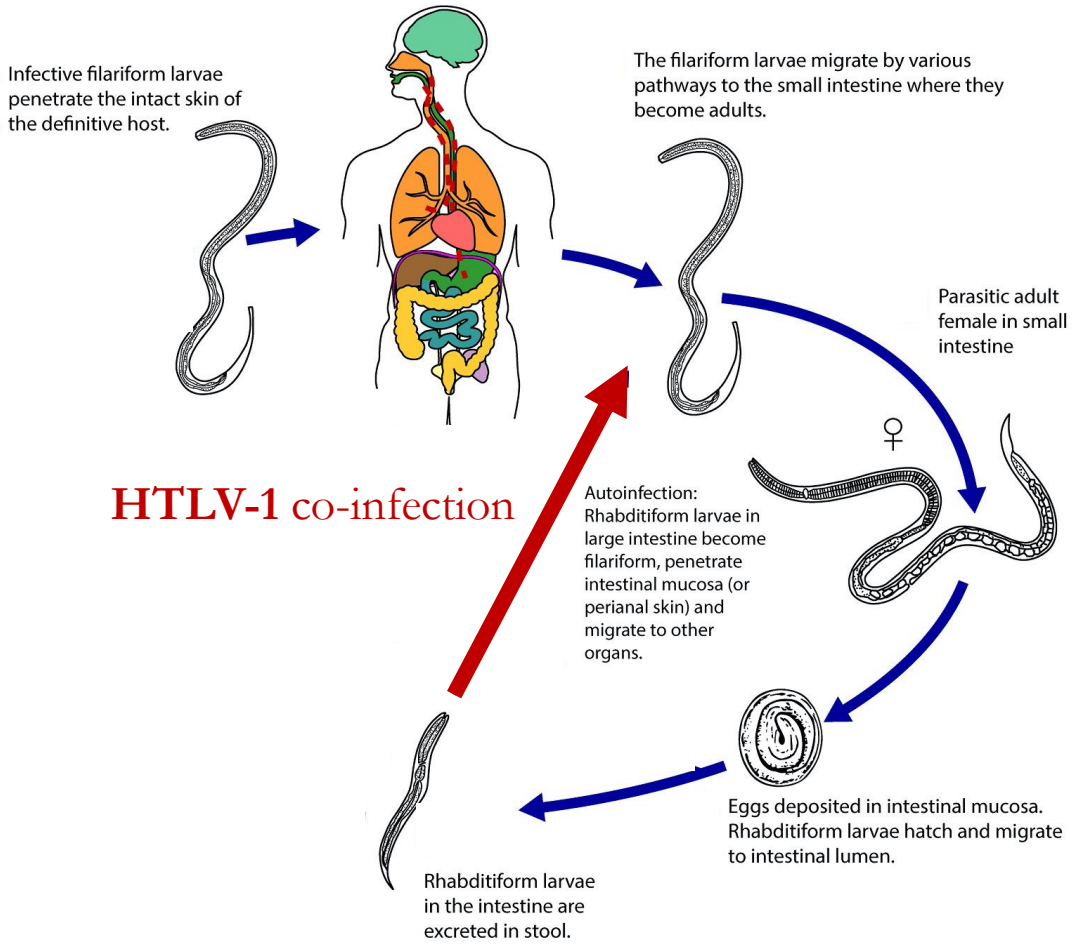
The "Autoinfection Cycle"



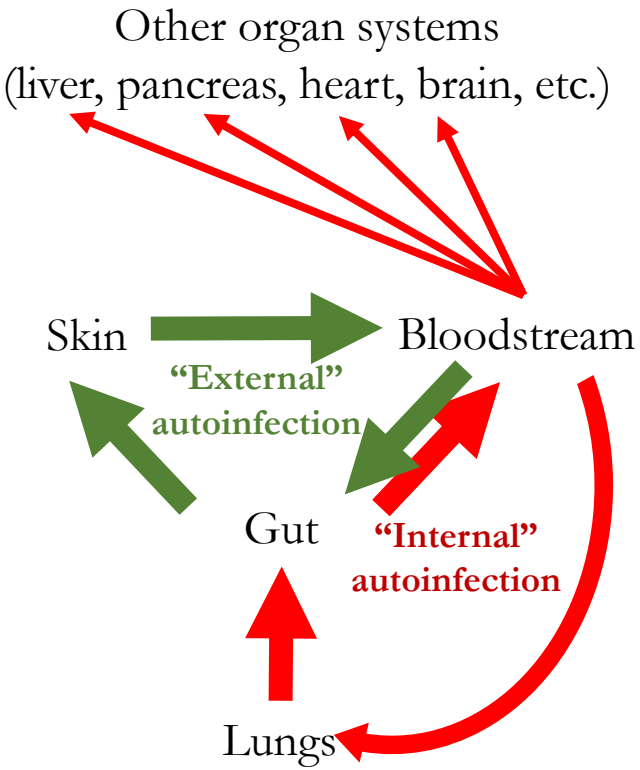


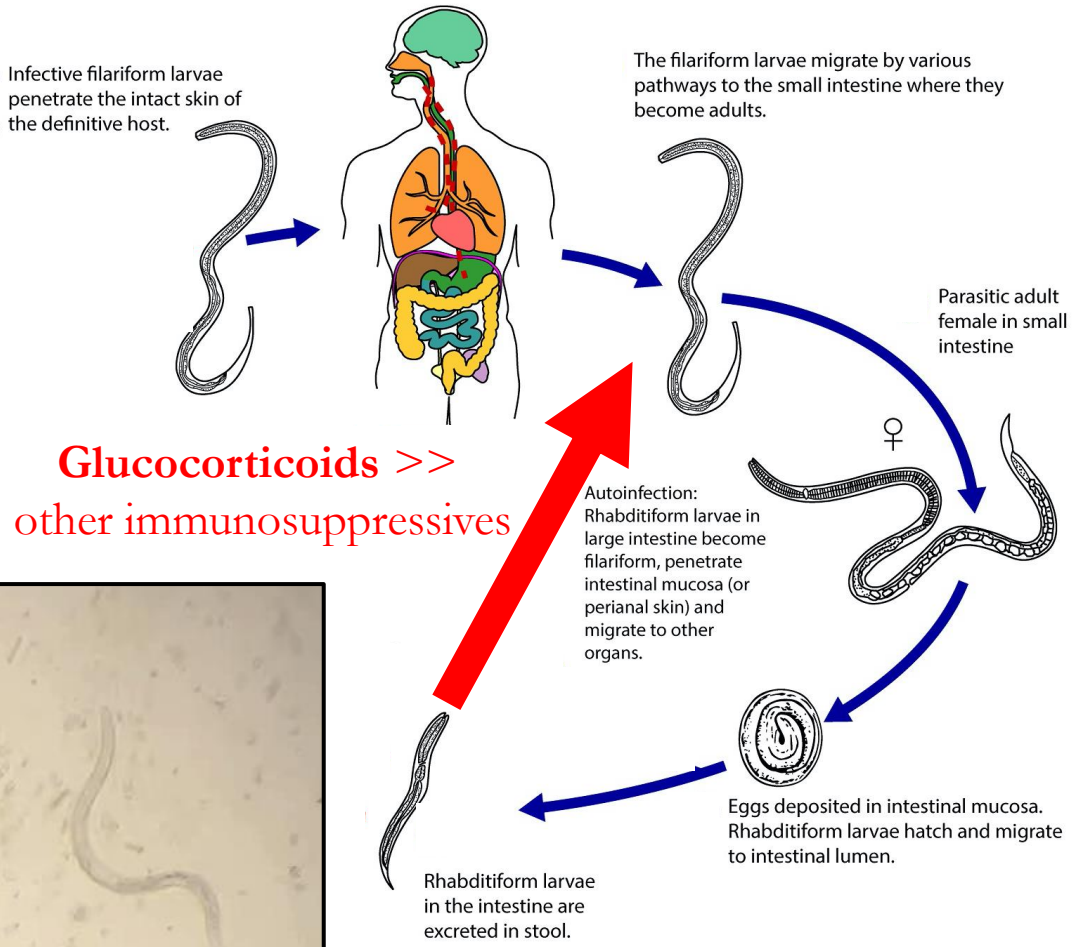
Strongyloides Hyperinfection Syndrome





Disseminated Strongyloides Infection





BAL wet mount from a different patient with a donor-derived infection after renal transplant

66F with intrinsic duodenal stenosis due to *Strongyloides stercoralis* hyperinfection syndrome due to chronic HTLV-1 infection

Clinical Course:

-Completed ivermectin 200ug/kg PO Q24H x14d

-Discharged free from all symptoms, with health insurance and a PCP

-Normal CT abdomen/pelvis 6 weeks later

-Outpatient evaluation by hematology/oncology led to determination that she did not currently have any evidence of smoldering ATLL; planned for close monitoring

-Followed closely by ID on monthly secondary prophylaxis with 1-day courses of ivermectin

Key Learning Points

- ***ALWAYS*** send *Strongyloides stercoralis* serology before immunosuppression in patients who have spent any significant amount of time in endemic settings (including the US Southeast), or just empirically treat with ivermectin if immunosuppression urgent
- A negative *S. stercoralis* serologic result is also essential to document prior to organ donation (regardless of whether the donor is living or deceased)
- Assess for HTLV-1 co-infection by serology or serum PCR in patients with symptomatic strongyloidiasis (especially if *S. stercoralis* serology is negative)
- Patients with HTLV-1 infection require long-term monitoring by oncology for ATLL

Case 4:
Fevers and Hypoxemia in a B-Cell-Depleted Host

Excerpts from your August 2021 twilight shift H&P

History of the Present Illness:
-1 week intermittent fevers to 102F at home
-Presented to local urgent care; dx with CAP
-Rx amoxicillin/azithromycin x1wk; no improvement
-Non-productive cough, dyspnea on exertion, and diffuse pleuritic chest discomfort evolved over week 2
-Re-presented to local community hospital with hypoxemia to mid-80s
-CT chest led to immediate bronchoscopy then transfer to BWH/DFCI

Social History:
-Lives with his wife and young daughter on apple orchard in rural central Maine
-Traveled to England years ago; otherwise has rarely left Maine
-No sick contacts; never known anyone with TB
-Never smoked, drinks a few ciders weekly, no recreational drug use

Past Medical/Surgical History:
-Chronic lymphocytic leukemia (dx 2016, Rai stage I, del11q, mutated IGHV)
-Multiple sclerosis (dx 2007)
-R hip fracture, s/p ORIF (2009)

Family History:
-Aunt with localized breast cancer (60s)
-Uncle with multiple myeloma (60s)
-Grandfather with prostate cancer (70s)
-No family history of leukemia or MS

Medications:
-Obinutuzumab (anti-CD20 mAb; last received 1d prior to first fever)
-Venetoclax (small molecule BCL-2 inhibitor)
-Allopurinol
-Baclofen PRN

Allergies:
-None known

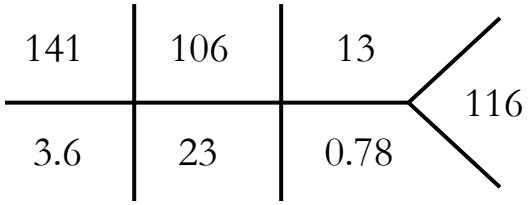
Relevant vaccines:
-SARS-CoV-2 mRNA vaccine x2 (4/2021, 5/2021)
-Tdap (7/2021)

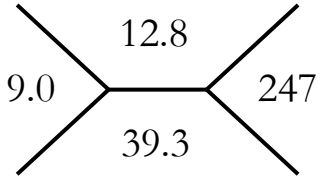
37M with CLL (on BCL-2i and anti-CD20 mAb) transferred from Maine with 2 weeks fevers, 1 week progressive DOE and cough, and new hypoxemia

T: 100.2F | P 84 | BP 121/70 | RR 22 | SaO2 94% on 2L NC

GEN: sitting upright in bed, no acute distress
HEENT: no conjunctival injection/icterus, oropharynx clear, MMM
NECK: shotty bilateral anterior and posterior cervical LAD
CV: RRR, no M/R/G, nl S1/S2
PULM: CTAB, no accessory respiratory muscle use
ABD: soft, ND/NT, +BS
EXT: WWP, no edema
SKIN: no rashes appreciated

37M with CLL (on BCL-2i and anti-CD20 mAb) transferred from Maine with 2 weeks fevers, 1 week progressive DOE and cough, and new hypoxemia





-Mg 2.2
-Ca 8.9
-ALT 50
-AST 41
-AP 73
-TB 0.3
-Alb 3.4
-T protein 5.6
-PT-INR 1.0

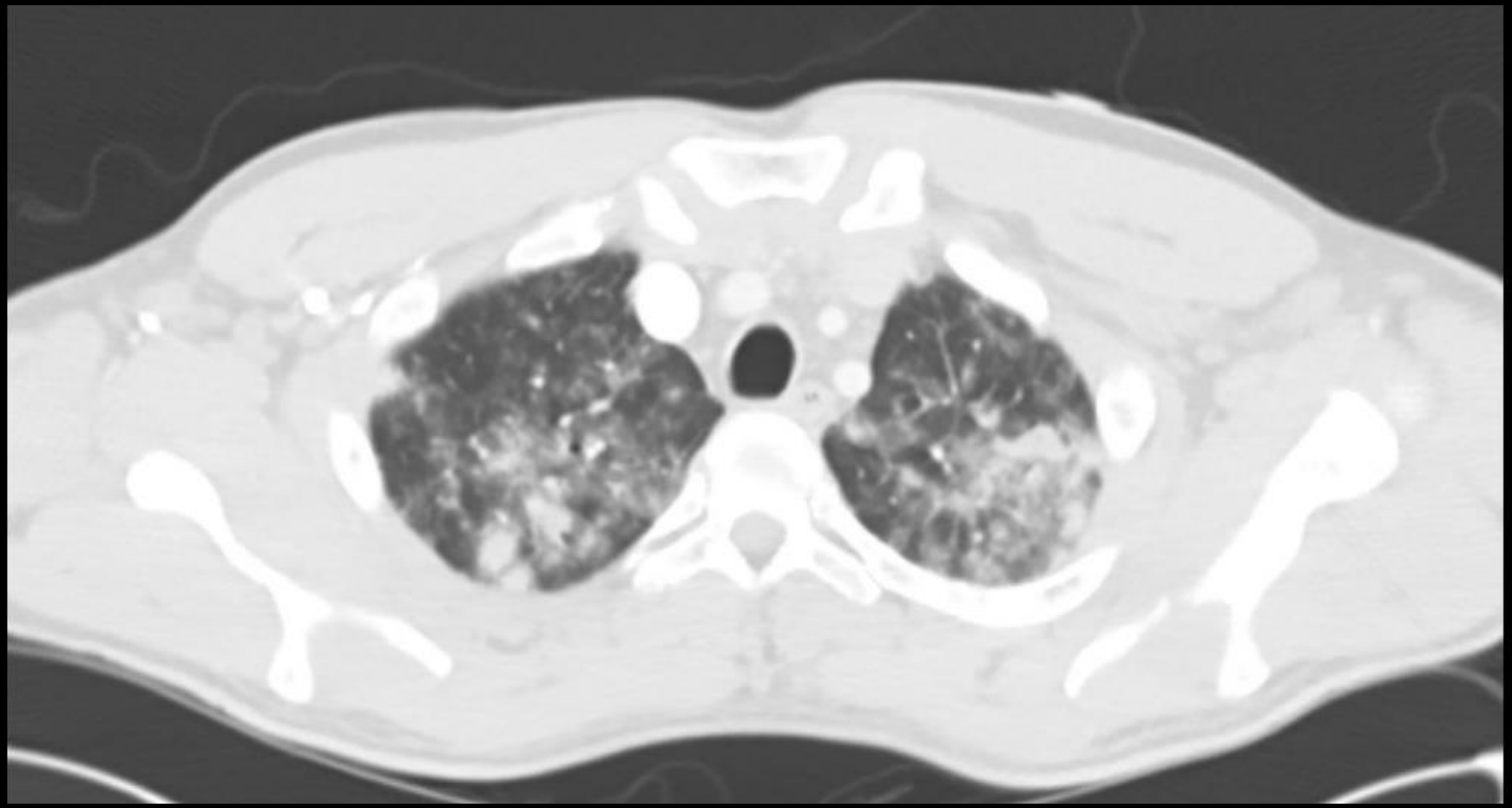
-Diff: 76% PMNs, 11.1% lymphs, 10.8% monos, 0% eos, 0.4% basos, 1.7% bands
-ANC 6840
-ALC 999

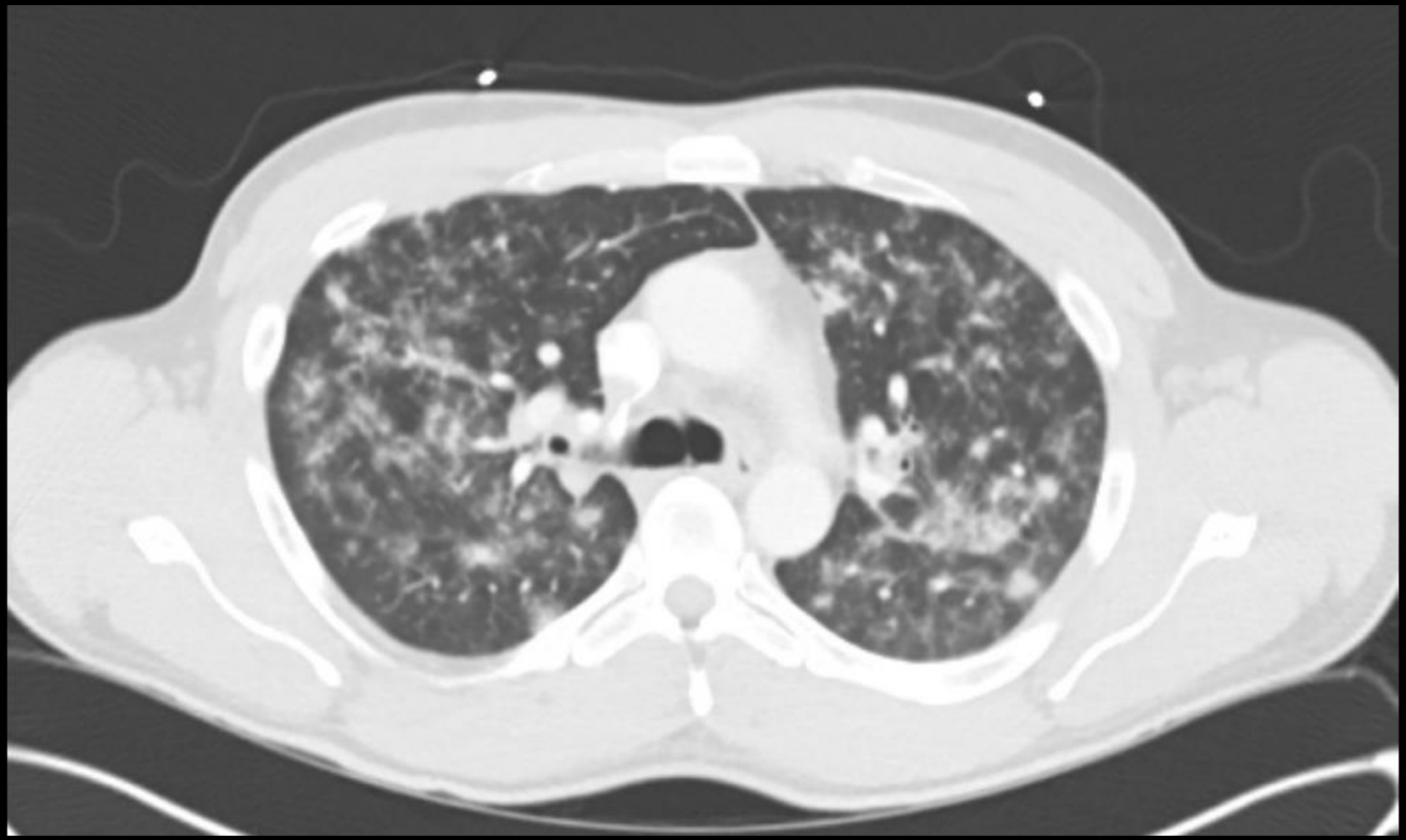
<u>Maine OSH bronchoscopy and other micro studies:</u>

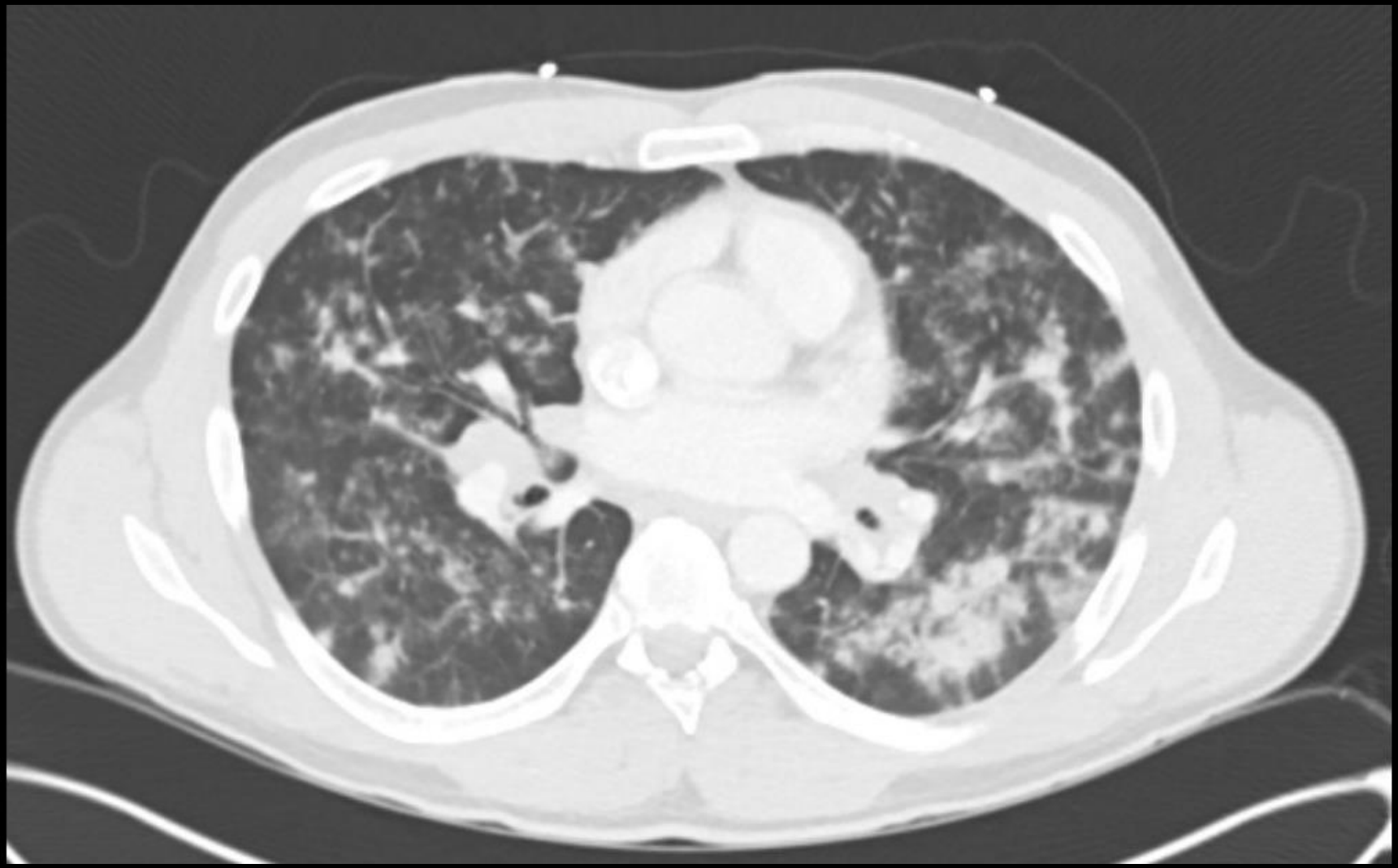
-Gram stain: few PMNs
-Wet prep: not performed
-Silver stain: negative
-AFB stain: negative

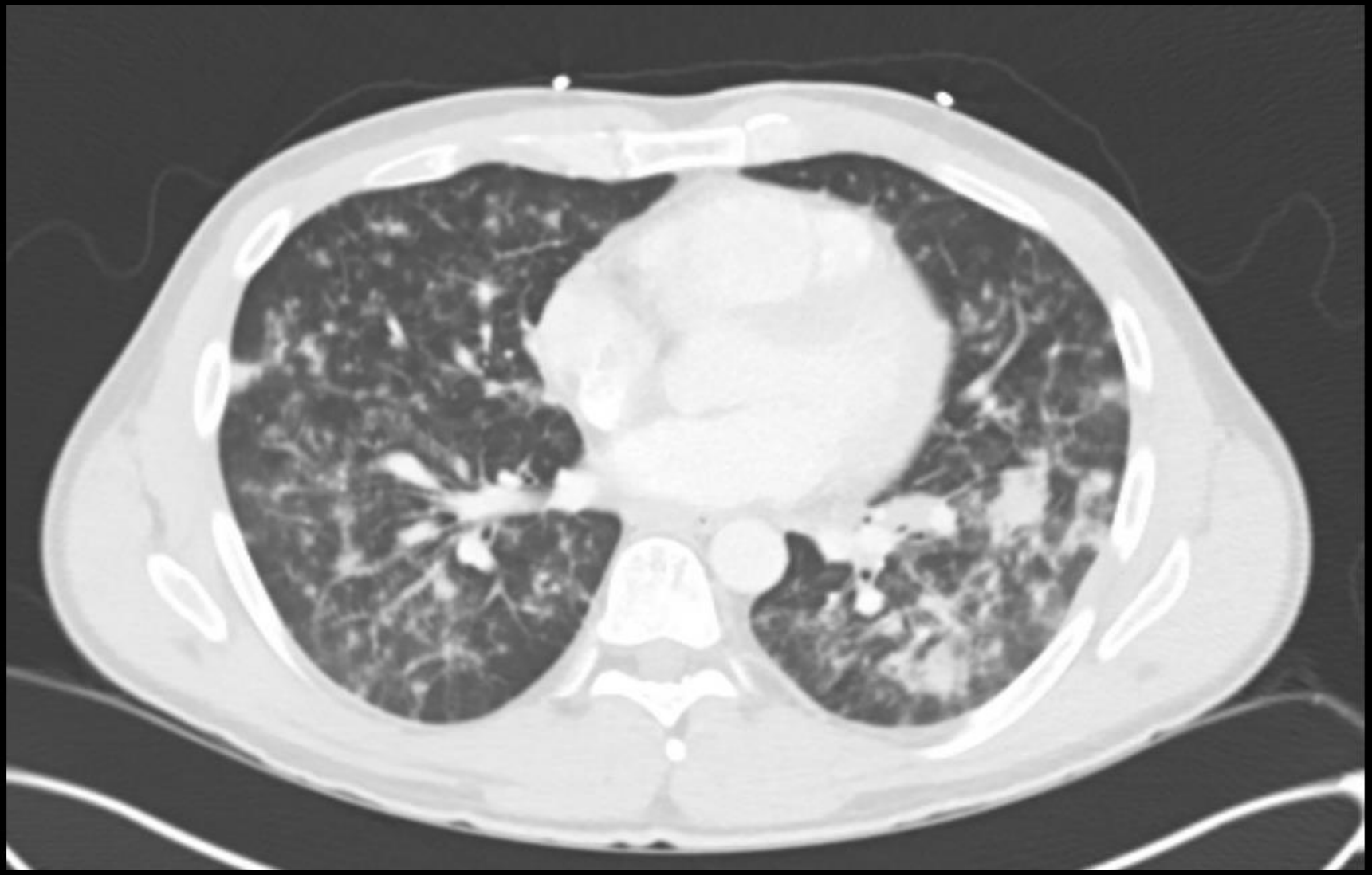
-Aerobic culture: pending
-Anaerobic culture: pending
-Fungal culture: pending
-Mycobacterial culture: pending

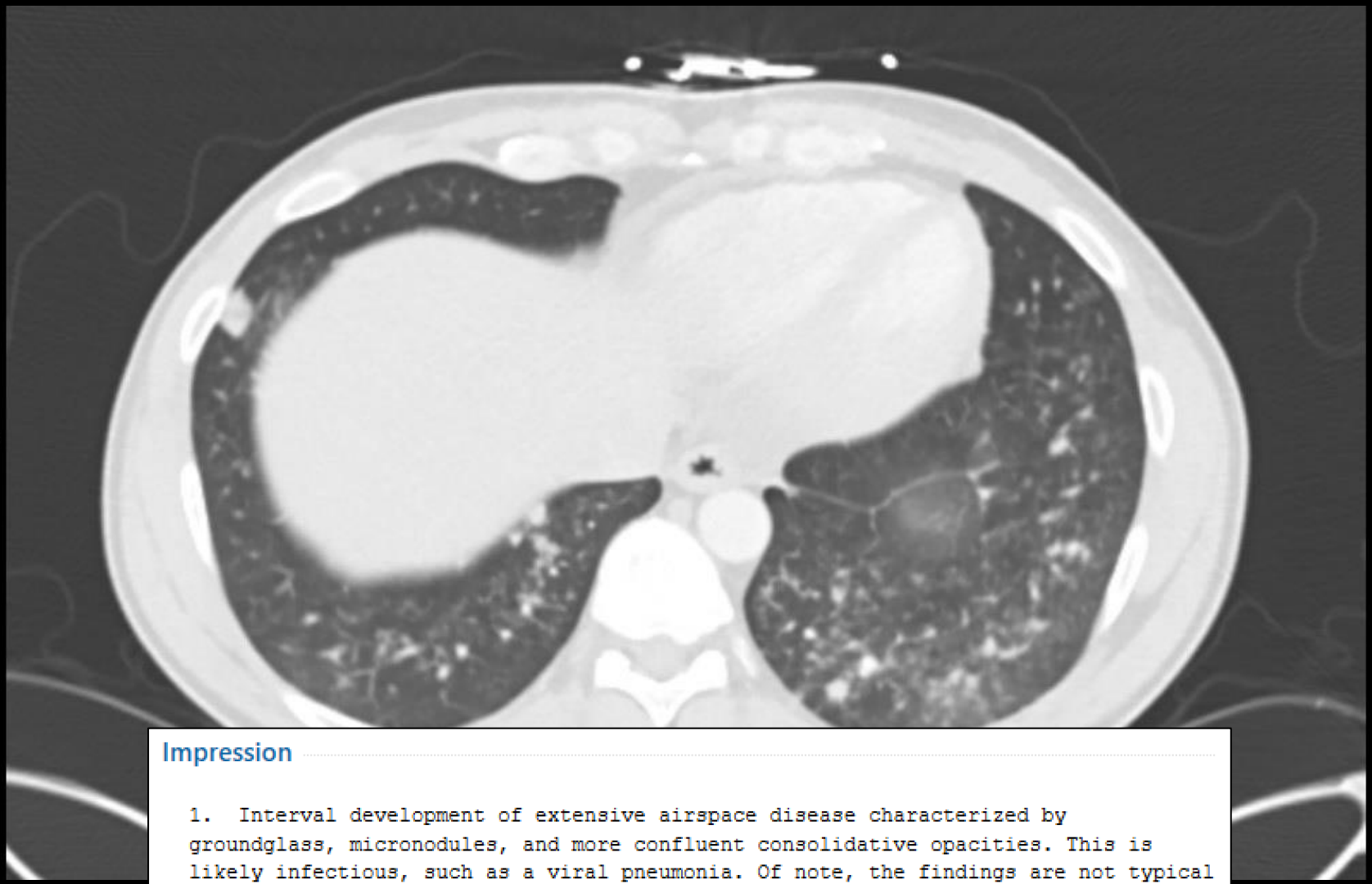
-Galactomannan: pending
-1-3-Beta-D glucan: pending
-Urine strep Ag: pending
-Urine legionella Ag: pending


R
L


R
L


R
L

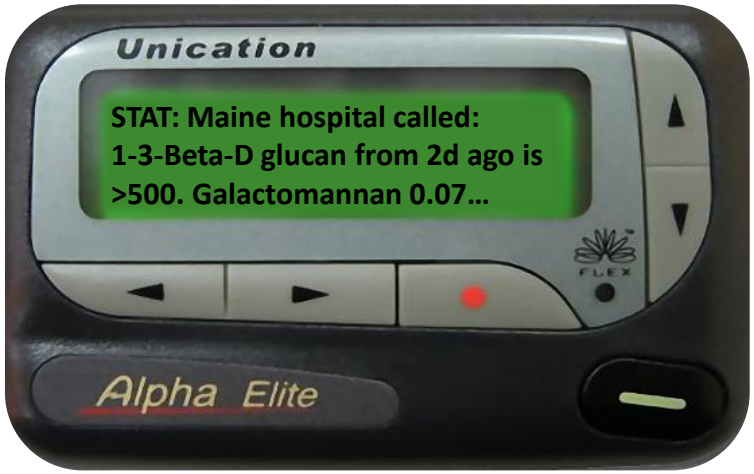

R
L



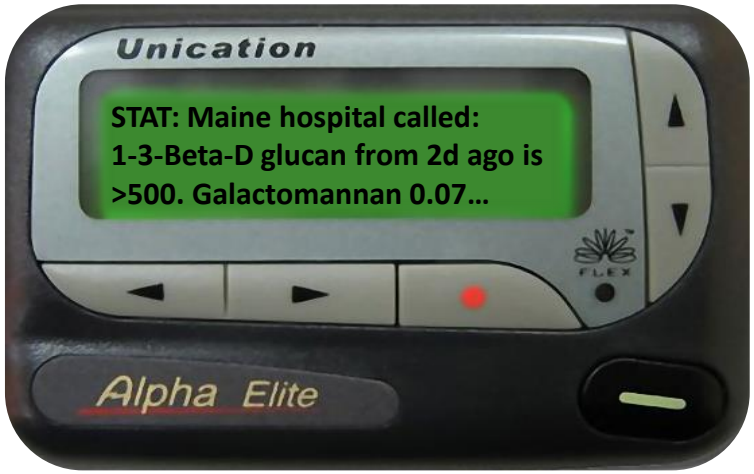
Impression

1. Interval development of extensive airspace disease characterized by groundglass, micronodules, and more confluent consolidative opacities. This is likely infectious, such as a viral pneumonia. Of note, the findings are not typical for pneumocystis pneumonia.
2. Decreasing multistation lymphadenopathy, consistent with chronic lymphocytic leukemia.

Sounds Like Our Patient Is A Very Fun Guy

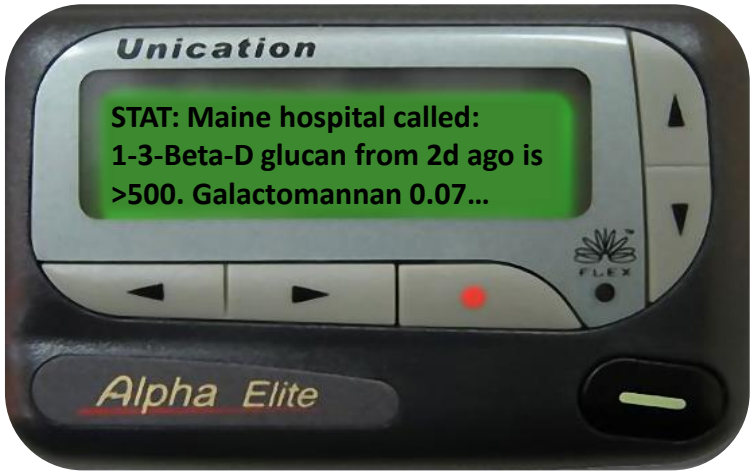


Sounds Like Our Patient Is A Very Fun Guy



1-3-BDG Elevated	1-3-BDG *NOT* elevated
Candidiasis	
Aspergillosis	
Pneumocystosis	
	Possible Causes of False+ 1-3-BDG

Sounds Like Our Patient Is A Very Fun Guy



1-3-BDG Elevated	1-3-BDG *NOT* elevated
Candidiasis	Mucormycosis
Aspergillosis	Blastomycosis
Pneumocystosis	Cryptococcosis
Histoplasmosis	**Possible Causes of False+ 1-3-BDG**
Coccidiomycosis	IVIG, IV albumin, defibrotide (common)
Paracoccidiomycosis	Retained gauze (cellulose)
Fusariosis	Cellulose HD membranes (not BWH's)
Trichosporonosis	Pseudomonas infection (rare)
Scedosporiosis	*NOT cefepime!*

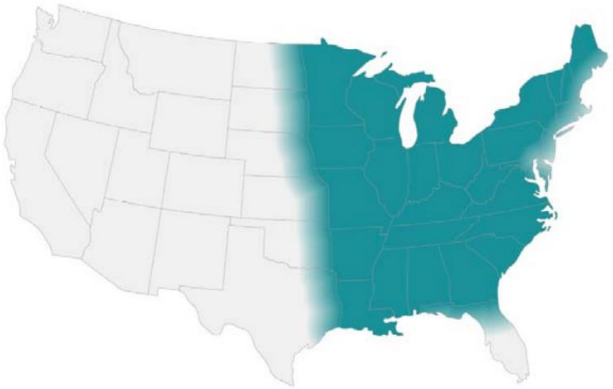
Initial "TB Rule-Out" for Inpatients

If active tuberculosis (pulmonary or extrapulmonary) is suspected...

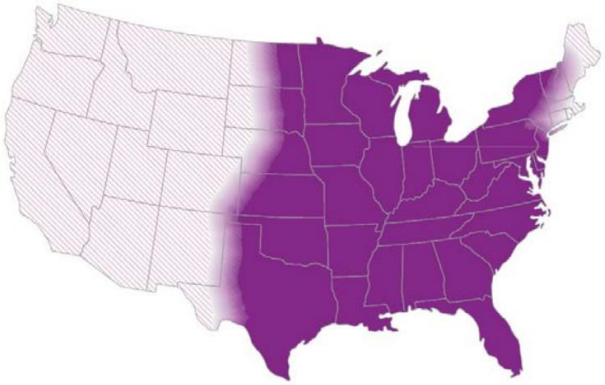
- Negative-pressure isolation room
- Airborne isolation (N95 mask required)
- Laboratory evaluation:
  - 3 sputum (vs induced sputum) samples for AFB smear and mycobacterial culture, approximately 8 hours apart
  - First sample should also be sent for GeneXpert MTB PCR
  - Current or past negative T-Spot (or Quantiferon Gold or PPD) does **NOT** rule out active tuberculosis

"Endemic Mycoses": Endemic *Where?*

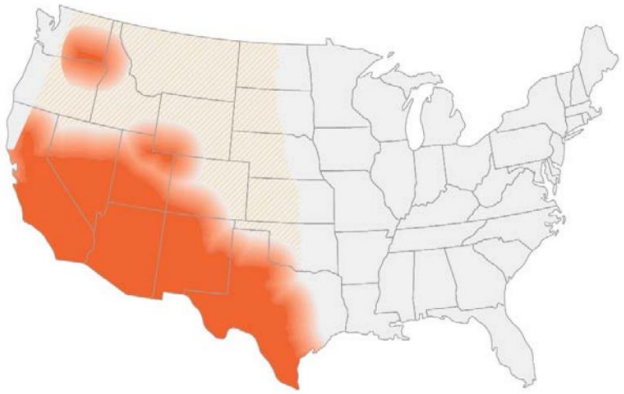
Blastomycosis



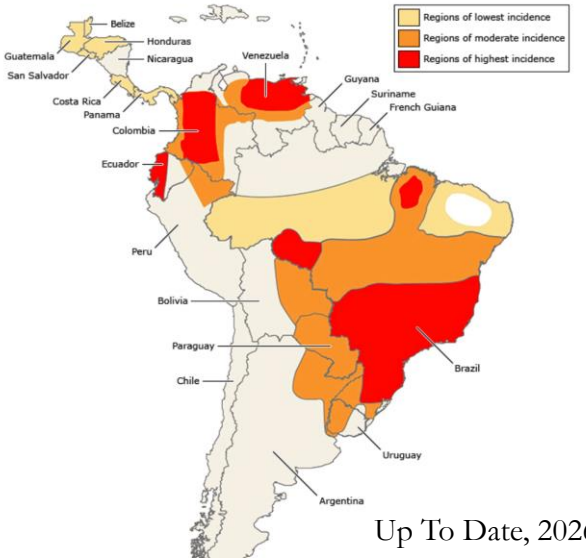
Histoplasmosis



Coccidioidomycosis (Valley fever)



Paracoccidiomycosis



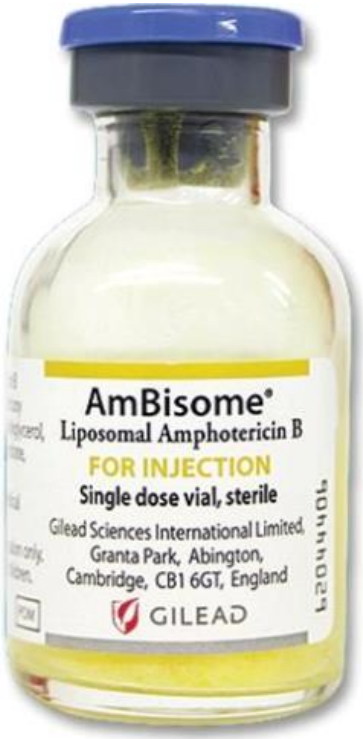
CDC, 2026

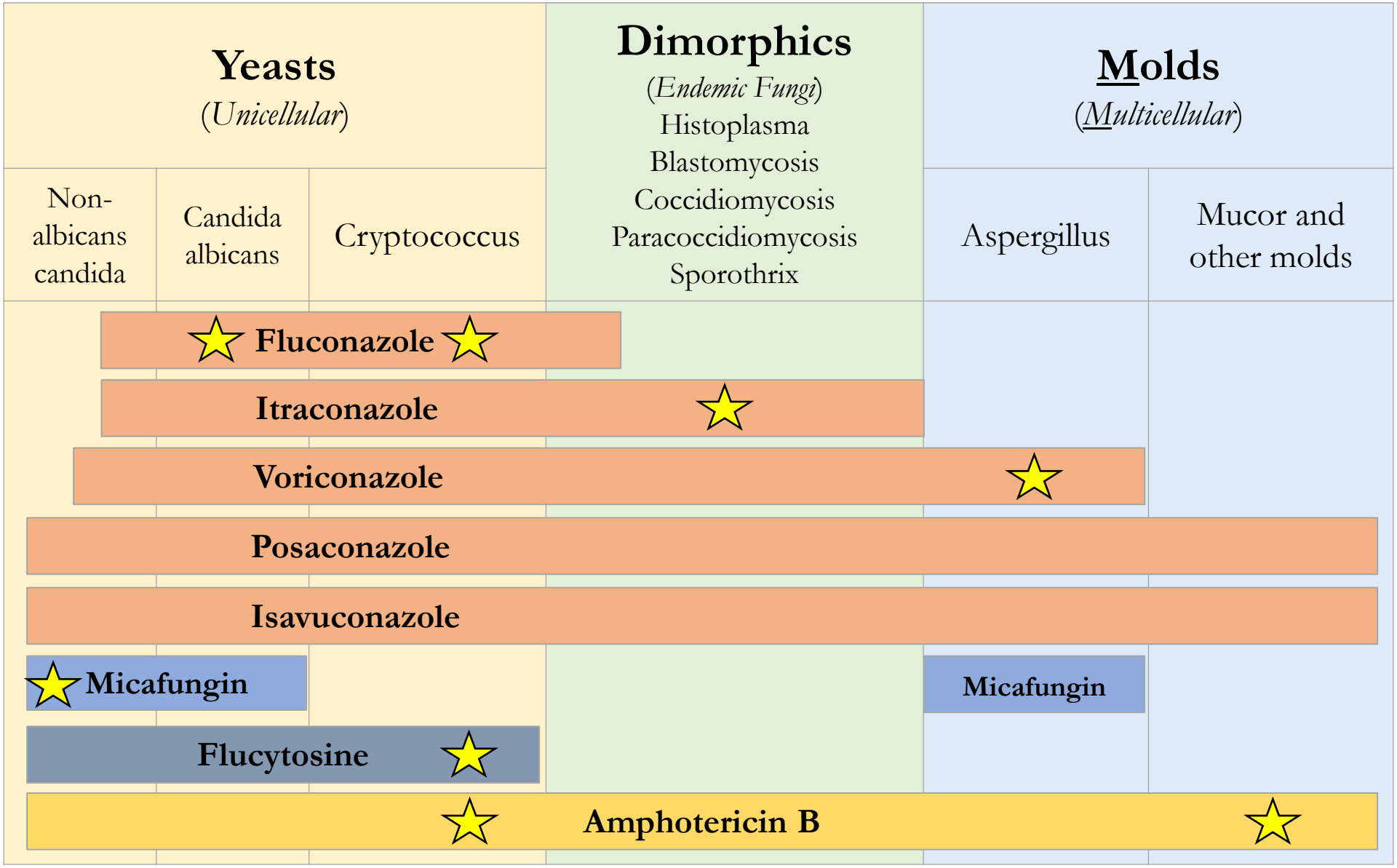
Up To Date, 2026


PSG410
Sunleaves
PERUVIAN
SEABIRD
GUANO
High Nitrogen
All Natural
Organic Fertilizer
12-11-2

Expanding the Differential

1. Histoplasmosis
2. Pneumocystis
3. Environmental mold (mucor > aspergillosis)
4. Blastomycosis / paracoccidiomycosis
5. Nocardiosis
6. Cryptococcosis
7. Non-TB mycobacterial infection





Adapted from: JA Freed and AJ Hale (www.idmodules.com).

★ = **first-line definitive therapy**

BAL and EBUS-guided biopsy planned... But this came back first!

KARIUS TEST REPORT
Karius ID: KA-135122

KARIUS clarity at speed™ | TEST

SPECIMEN TYPE: PLASMA

TEST RESULTS

MICROORGANISM DETECTED	DNA MOLECULES PER MICROLITER (MPM)*	REFERENCE INTERVAL (MPM)**

Microbial Cell-Free DNA: The ID "Cheat Code?"

KARIUS TEST REPORT
Karius ID: KA-135122

KARIUS clarity at speed™ | TEST

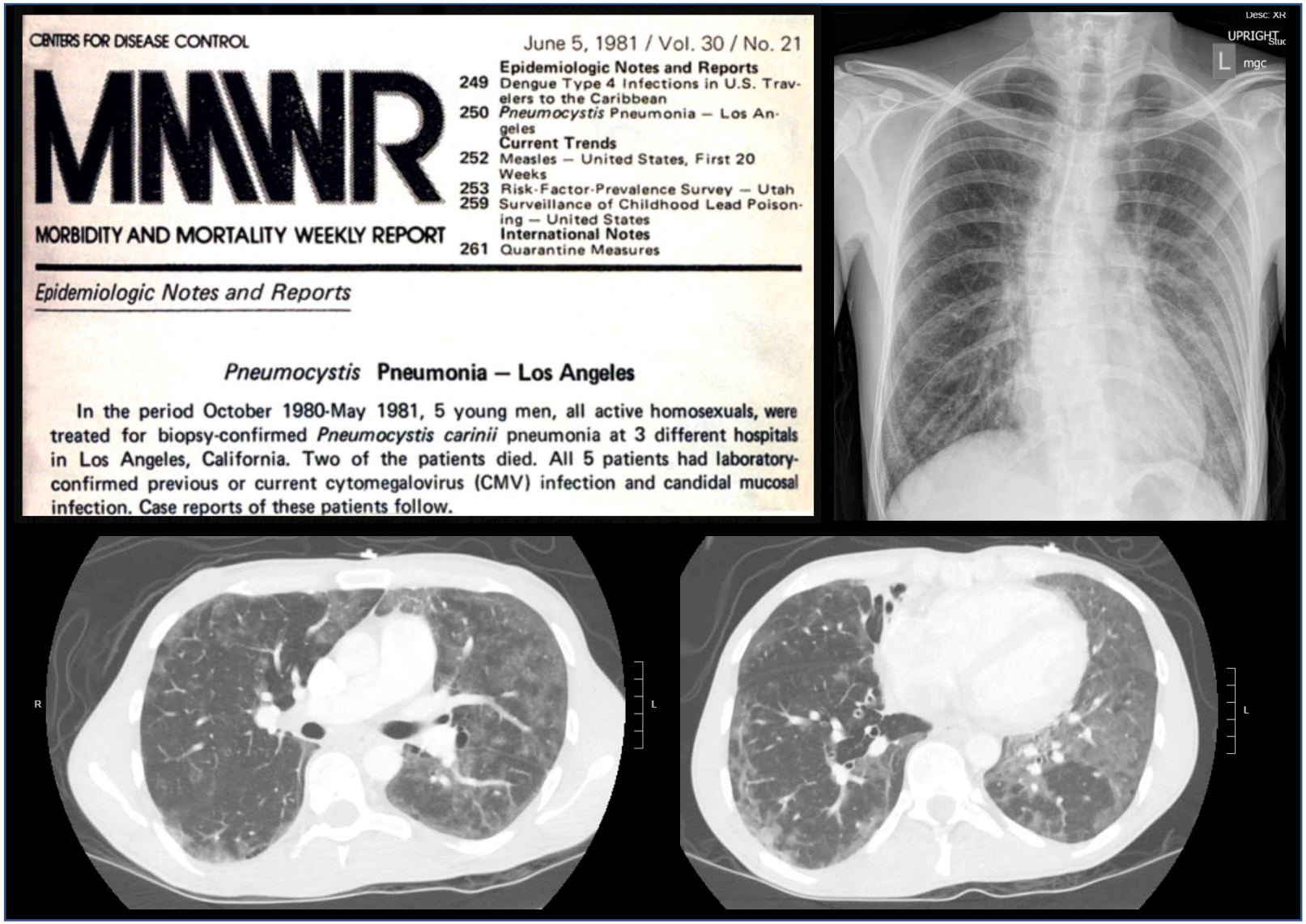
SPECIMEN TYPE: PLASMA

TEST RESULTS

MICROORGANISM DETECTED	DNA MOLECULES PER MICROLITER (MPM)*	REFERENCE INTERVAL (MPM)**
Pneumocystis jirovecii	6,493	< 10

Component	Value
CRYPTOCOCCAL AG	Negative
Component	Value
Histoplasma Ag, urine	Negative
Component	Value
UR BLASTOMYCES AG	Not Detected

The Most Famous Case Series in Medical History?



CENTERS FOR DISEASE CONTROL

June 5, 1981 / Vol. 30 / No. 21

MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

Epidemiologic Notes and Reports

Pneumocystis Pneumonia — Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

"Atypical" or Under-Recognized?

Vol. 291 No. 16 MEDICAL INTELLIGENCE — CROSS AND STEIGBIGEL 831

PNEUMOCYSTIS CARINII PNEUMONIA PRESENTING AS LOCALIZED NODULAR DENSITIES

ALAN S. CROSS, M.D., AND
ROY T. STEIGBIGEL, M.D.

SINCE roentgenographic examination of the chest is an initial form of evaluation of the dyspneic patient, an appreciation of the spectrum of roentgenographic findings that suggest the diagnosis of *Pneumocystis carinii* pneumonia will facilitate the diagnostic process. The chest roentgenogram findings beyond the "characteristic" picture, which is so often stressed, have been reviewed.[1] The patient described below initially had two discrete nodules that proved to be localized accumulations of pneumocystis organisms.

CASE REPORT

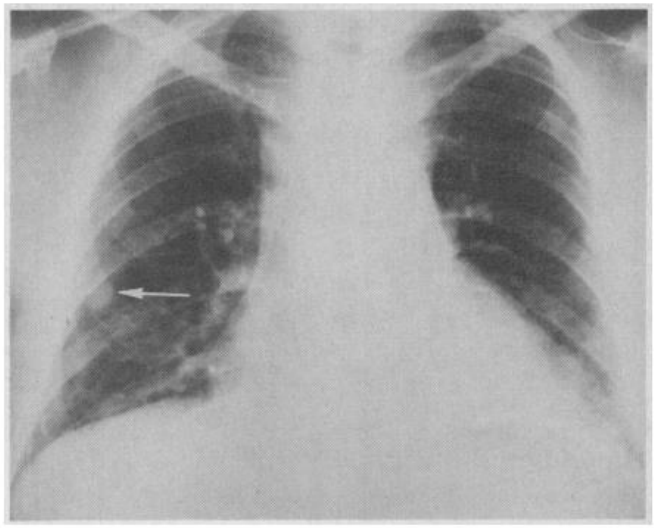


Figure 1. Film of the Chest Taken on the Ninth Hospital Day, Showing Nodules in the Superior Segment of the Right Lower Lobe (Arrow); a Bilateral Basilar Infiltrate Is Apparent.

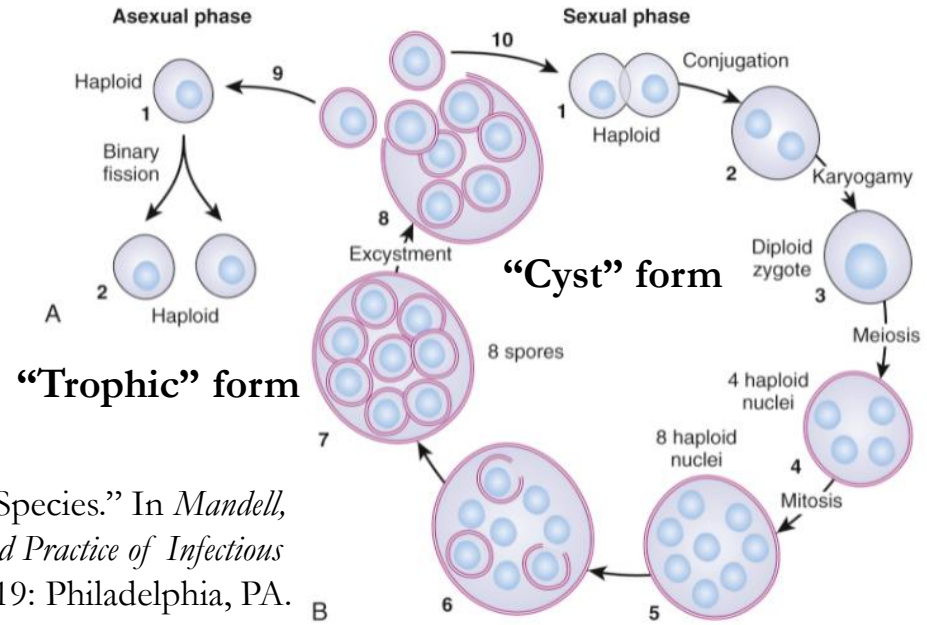
THE NEW ENGLAND JOURNAL OF MEDICINE Oct. 17, 1974

"In a small percentage of patients, cysts are in a necrotic area surrounded by palisades of epithelioid cells and a few giant cells, **very much resembling histoplasmosis**. CT is atypical for PJP, showing a reticulonodular pattern or rounded dense masses. **These patients often require biopsy for diagnosis because BAL for PCP is negative**."

Miller RF et al. "Pneumocystis Species." In *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 9th Edition.* Elsevier, 2019: Philadelphia, PA.

Pneumocystis jirovecii: What Is It?

- First described in 1906; initially thought by Chagas to be caused by a trypanosome
  - Not accurately noted to be a fungus until 1988
  - *P. carinii* = species infecting rats; *P. jirovecii* = species infecting humans
- Widely reported among malnourished orphans in Eastern Europe after WWII
  - Otherwise rare in literature prior to advent of transplantation and HIV pandemic
- 1980s-1990s: without ART, 80-90% of HIV patients eventually develop PJP at least once
- Remains leading cause of death among people living with HIV in US
- **Invariably fatal** if left untreated; response to treatment takes 4-8 days



Miller RF et al. "Pneumocystis Species." In *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 9th Edition.* Elsevier, 2019: Philadelphia, PA.

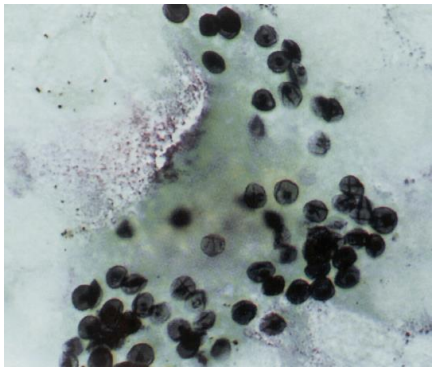
PJP: Who Gets Sick?

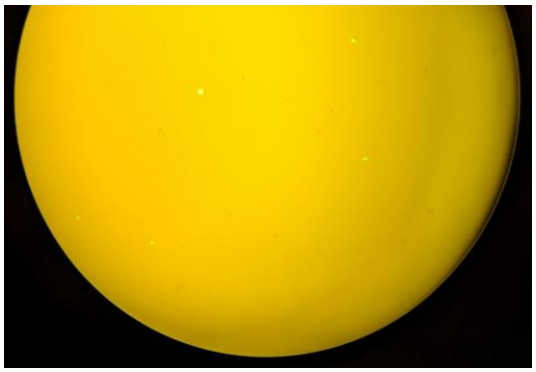
- Patients with HIV and other "acquired immunodeficiency syndromes"
- More fulminant and deadly presentation among patients with iatrogenic immunocompromised state
- Prednisone (or equivalent dose of another corticosteroid):
  - **20mg PO QD >4wks**
- Prednisone of ***any*** dose **>4wks PLUS:**
  - TNF blockade*
  - Anti-CD20 mAb*
  - Cyclosporine
  - Tacrolimus
  - MMF
  - Azathioprine
  - Cyclophosphamide

*** PJP cases documented without any additional agents, though this is not reflected in guidelines**

PJP: A Range of Clinical Presentations

HIV-positive PJP	HIV-negative PJP
Subacute fevers, non-prod. cough, DOE	Often fulminant respiratory failure
SaO2 often plummets with ambulation	SaO2 often plummets with ambulation
<10% in-hospital mortality	**30-60%** in-hospital mortality
High organism burden; more likely BAL+ve	Lower organism burden; often BAL—ve
"Classic" presentation predominates	Granulomatous PJP increasingly seen
May initially worsen with tx	4-8 days to signs of improvement on tx
High likelihood of IRIS once ART started	Higher risk of progression to ARDS
Severe disease highly steroid responsive	Weaker evidence for steroids, but may help



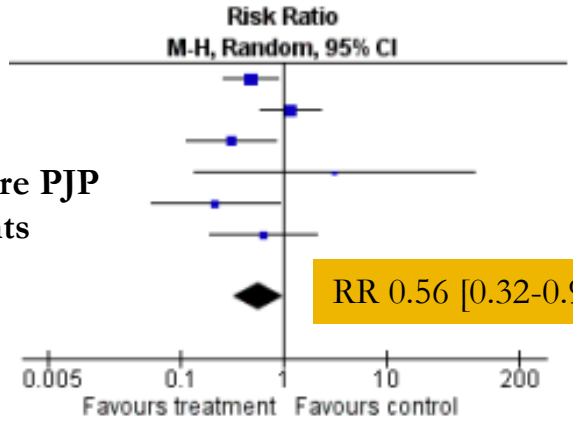


Miller RF et al. "Pneumocystis Species." In *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 9th Edition.* Elsevier, 2019: Philadelphia, PA.

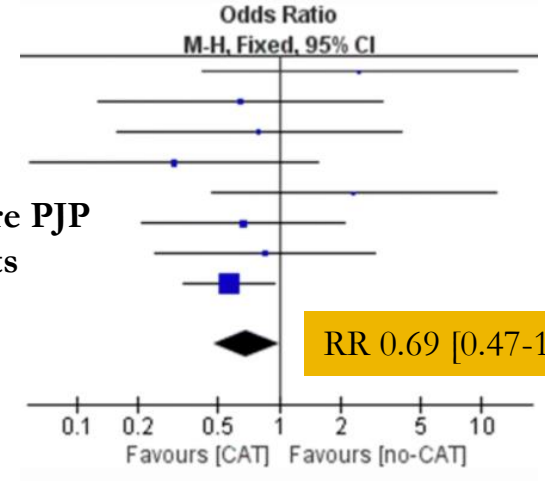
Brief Overview of Inpatient PJP Treatment

1. **TMP-SMX** (IV vs PO)
2. "Adjunctive" prednisone if progressive hypoxemia
3. If unable to take TMP-SMX and severely ill: clindamycin + primaquine
   (not in addition to TMP-SMX)

Prednisone for Severe PJP in HIV+ Patients



Prednisone for Severe PJP in HIV– Patients



Ewald et al. "Adjunctive Corticosteroids for PJP in Patients with HIV Infection." *Cochrane Database of Systematic Reviews* 2015; 4: CD006150.
Ding et al. "Adjunctive Corticosteroids May Be Associated with Better Outcome for Non-HIV PJP with Respiratory Failure: A Systematic Review and Meta-Analysis." *Annals of Intensive Care* 2020; 10: 34.

Any **Case of PJP in 2024 Is A Systems Failure**

- Effectiveness of PJP ppx: **85% reduction** in risk of infection
- NNT in population with clear indication: **19** to prevent 1 confirmed case

Current Options for PJP Prophylaxis

Agent	Effectiveness	Adverse effects
TMP-SMX (1st-line)	Best	Hypersensitivity, leukopenia, hyperK, pseudo-AKI, transaminase elevations, pruritus, nausea
Atovaquone (2nd-line)	High	Nausea/vomiting/diarrhea, pruritus, HA
Dapsone (3rd-line)	High	Agranulocytosis, hemolytic anemia (if G6PD-deficient)
Inhaled pentamidine	Poor	Seldom used due to limited efficacy in trials

Stern et al. "Prophylaxis for Pneumocystis Pneumonia in Non-HIV Immunocompromised Patients." *Cochrane Database of Systematic Reviews* 2014; 10: CD005590.

Key Learning Points

- Review the differential diagnosis for hypoxemic immunocompromised patients with diffuse bilateral GGOs +/- micronodules on chest CT
- Review the different presentations of PJP in HIV+ and HIV– patients
- Guidelines have not kept pace with explosion in immunosuppressive regimens; think mechanistically and don't forget about PJP ppx when starting/refilling/escalating immunosuppressive treatments
- Bactrim is best! Change your oncology patients back to TMP-SMX from atovaquone for PJP ppx when able
- Next-generation sequencing assays for microbial cell-free DNA in the peripheral blood may accelerate diagnosis in immunocompromised patients (but we shouldn't forget the basics)

Case 5:
Not Your Typical Raccoon Bite...

ID Curbside: “Can we give rabies vaccine?”

Initial ED presentation: 63yo homeless man with AUD who walked to the ED a from shelter for evaluation of recurrent falls and was found to have hyponatremia.

Curbside page: 63yo homeless man with AUD admitted from shelter with recurrent falls and found to have hyponatremia, now reporting a raccoon bite 3 weeks ago. Rabies ppx?

Chart review: 63yo homeless man with AUD, >40 pack-year smoking history, and chronic inactive HBV infection with seroconversion admitted from shelter with recurrent falls and found to have hyponatremia with CXR demonstrating “faint RUL airspace opacities that could reflect aspiration", now reporting a raccoon bite 3 weeks ago. T-Spot negative.

History from patient on formal evaluation: 63yo Cambodian refugee with prior shrapnel injuries from landmine injury during Cambodian genocide, untreated PTSD, long-standing heavy EtOH and nicotine use, prior outdoor residence in Arizona, and intermittent homelessness who has been living in a cave in a nearby park for the past 3 months, where he was bitten by a raccoon on the lower lip 3 week ago. He has also had progressive weight loss and a non-productive cough for >3 months, though presented for evaluation of recurrent falls.

T-Spot.TB	Negative

A negative test result does not exclude the possibility of exposure to or infection with Mycobacterium tuberculosis (M. tuberculosis). Patients with recent exposure to TB infected individuals exhibiting a negative T-SPOT.TB result should be considered for retesting within 6 weeks or if other relevant clinical symptoms indicate. Results from T-SPOT.TB testing must be used in conjunction with each individual's epidemiological history, current medical status, and results of other diagnostic evaluations.

Panel A Spot Count Corrected For Neg Control	0
Panel B Spot Count Corrected For Neg Control	0
Negative Control	Passed
Positive Control	Passed

Collected	Updated	Procedure	Result Status	Component	Value
06/16/2026 1651	06/28/2026 1442	Mycobacterial Culture/Smear [1804977603] (Abnormal) Sputum from Respiratory Tract	Preliminary result	Isolate Smear:	Results Updated P Acid Fast Bacilli ! P Identification to follow. Acid-fast bacilli present in liquid culture media. Few (2+) Acid-fast bacilli seen ! P Few (2+) Acid-fast bacilli seen ! P Few (2+) Acid-fast bacilli seen ! P
06/17/2026 0923	06/28/2026 1341	Mycobacterial Culture/Smear [1804682965] (Abnormal) Sputum from Respiratory Tract	Preliminary result	Component Isolate Smear:	Value Results Updated P Acid Fast Bacilli ! P Identification to follow. Acid-fast bacilli present in liquid culture media. Few (2+) Acid-fast bacilli seen ! P Few (2+) Acid-fast bacilli seen ! P
06/17/2026 0044	06/28/2026 1341	Mycobacterial Culture/Smear [1804570713] (Abnormal) Sputum from Respiratory Tract	Preliminary result	Component Isolate Smear:	Value Results Updated P Acid Fast Bacilli ! P Identification to follow. Acid-fast bacilli present in liquid culture media. — ! P Rare (1 +) acid-fast bacilli seen using the fluorochrome method. — ! P Rare (1 +) acid-fast bacilli seen using the fluorochrome method.

Mtb Complex PCR	Detected !
RIF Resistance	Not Detected

KatG(S315T) mutation not detected but all loci that may confer INH resistance are not tested with this assay.

Key Learning Points

- There is no formal "statute of limitations" on rabies post-exposure prophylaxis (sooner is better, but the incubation period is often >6 weeks)
- A negative interferon gamma release assay never rules out active tuberculosis
- Evaluation for active tuberculosis requires three sputum samples >8 hours apart sent for AFB smear and mycobacterial culture, with at least one sent for PCR testing
- Point-of-care molecular diagnostics can provide a rapid post-test probability of multidrug-resistant tuberculosis and guide empiric treatment

Thank You!

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Email: **ctnutt@bwh.harvard.edu**