



# Cross Canada Rounds – Short Cases

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- No disclosures

- Consent obtained for presentation of both cases



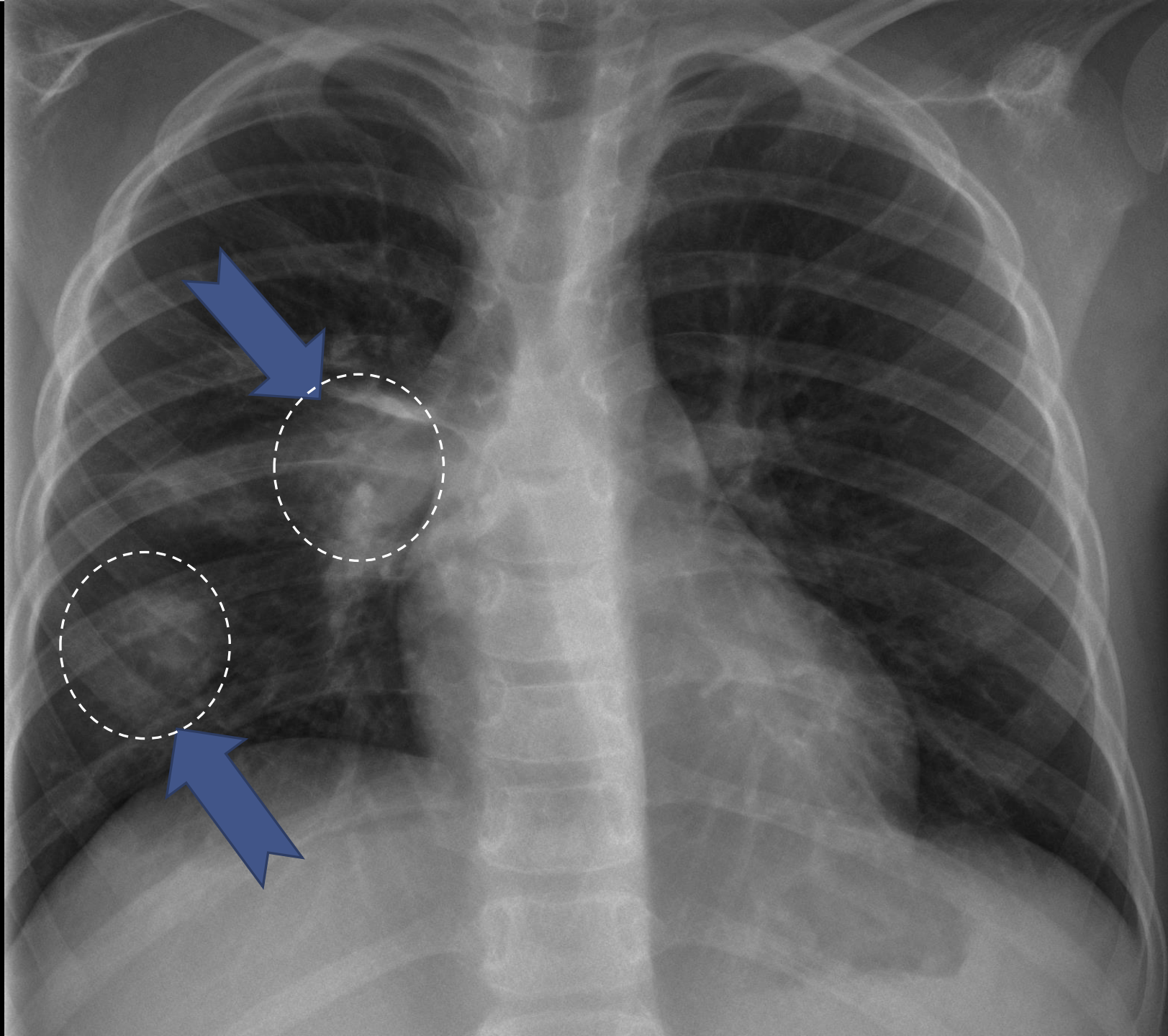
# Case 1

# Case Presentation



- 9 year old female
  - Refugee from Syria, living in Turkey prior to arrival
- Upon arrival in Canada, she was asymptomatic
  - History of small volume hemoptysis 1 month prior to arrival





# DDx of Cystic Chest Lesion?





# DDx of Cystic Chest Lesion -- BROAD

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- Infectious
  - Pneumonia
  - Abscess
  - Tuberculosis
  - Aspergillus
  - Hydatid Cysts
- Vascular lesion
  - Pulmonary Embolus
  - AVM
- Malignancy
  - Pleuropulmonary Blastoma
  - Carcinoma
  - Leiomyosarcoma
  - Neuroblastoma
- Congenital
  - CPAM
  - Bronchogenic Cyst



# Past Medical History

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- Small volume hemoptysis
  - Initially 3 years ago → “conservative management”
  - Re-occurred 1 month prior to admission
    - Intermittent, sputum streaked with blood
    - Occasional cough, clear sputum with “membrane” within
- Previous liver surgery
  - Resection of 2 “cysts” followed by “6 months of medication”
  - Complete resolution noted on imaging

# Physical Examination

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- Afebrile, RR: 18, O<sub>2</sub> Sats: 99% on RA
- HR: 90's, BP 90's/60's
- CVS:
  - Normal S<sub>1</sub>/S<sub>2</sub>, no murmurs. Well perfused.
- Resp:
  - Equal breath sounds bilaterally. No crackles or wheeze. No clubbing. No increased WOB.
- Abdo:
  - Soft, non tender, no HSM. Scar noted over RUQ.

# Work Up - Bloodwork

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- Hgb: 115
- WBC: 8.8
  - Eo: 0.2
  - Neut: 4.9
  - Lymph: 3.1
- CRP: 5.4
- **ESR: 33** (0-10)
- Lytes: normal
- BUN/Cr: normal
- LDH: 224
- Liver Enzymes: Normal
- Liver Function: Normal

# Initial Work Up: Infectious

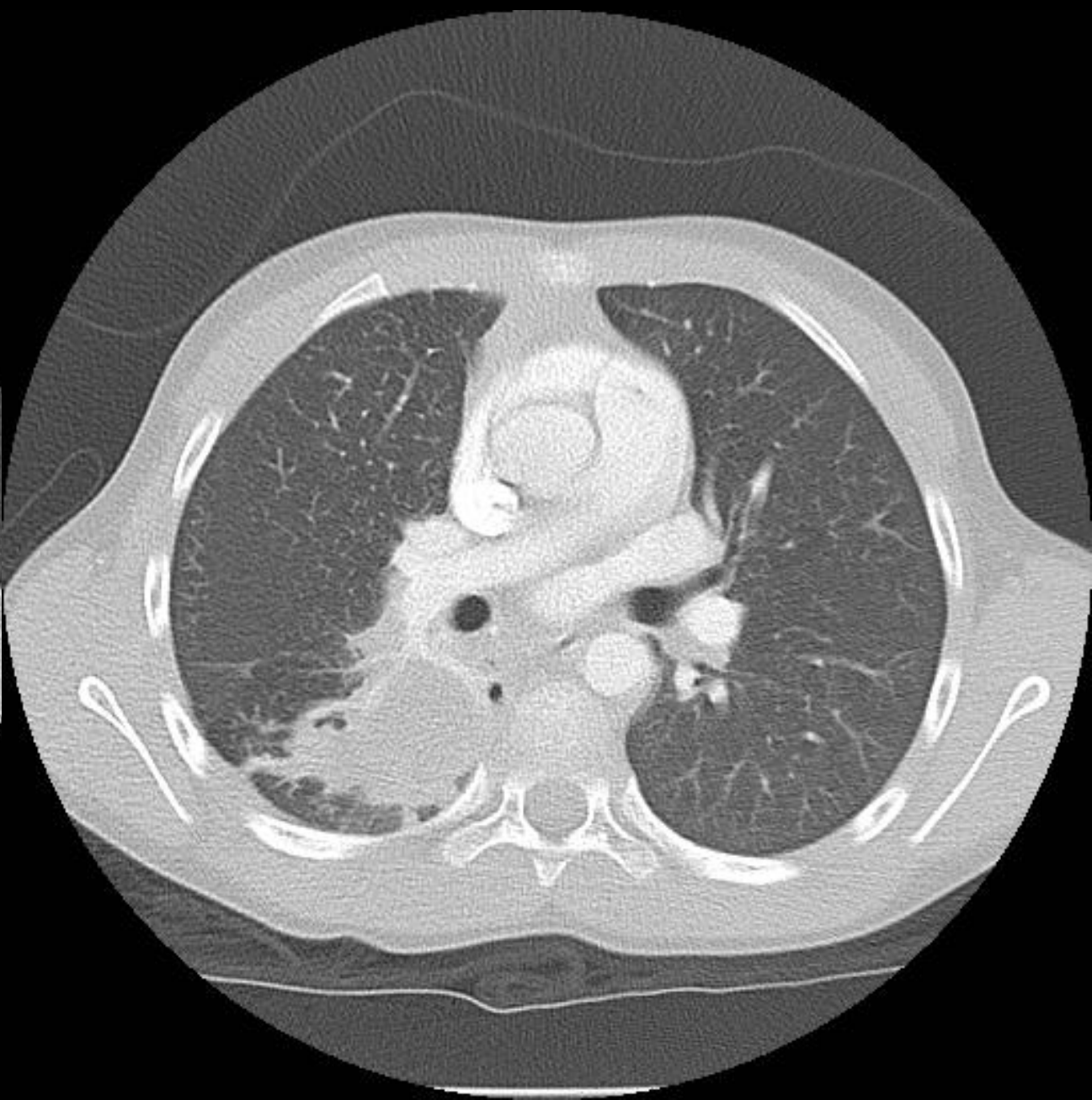
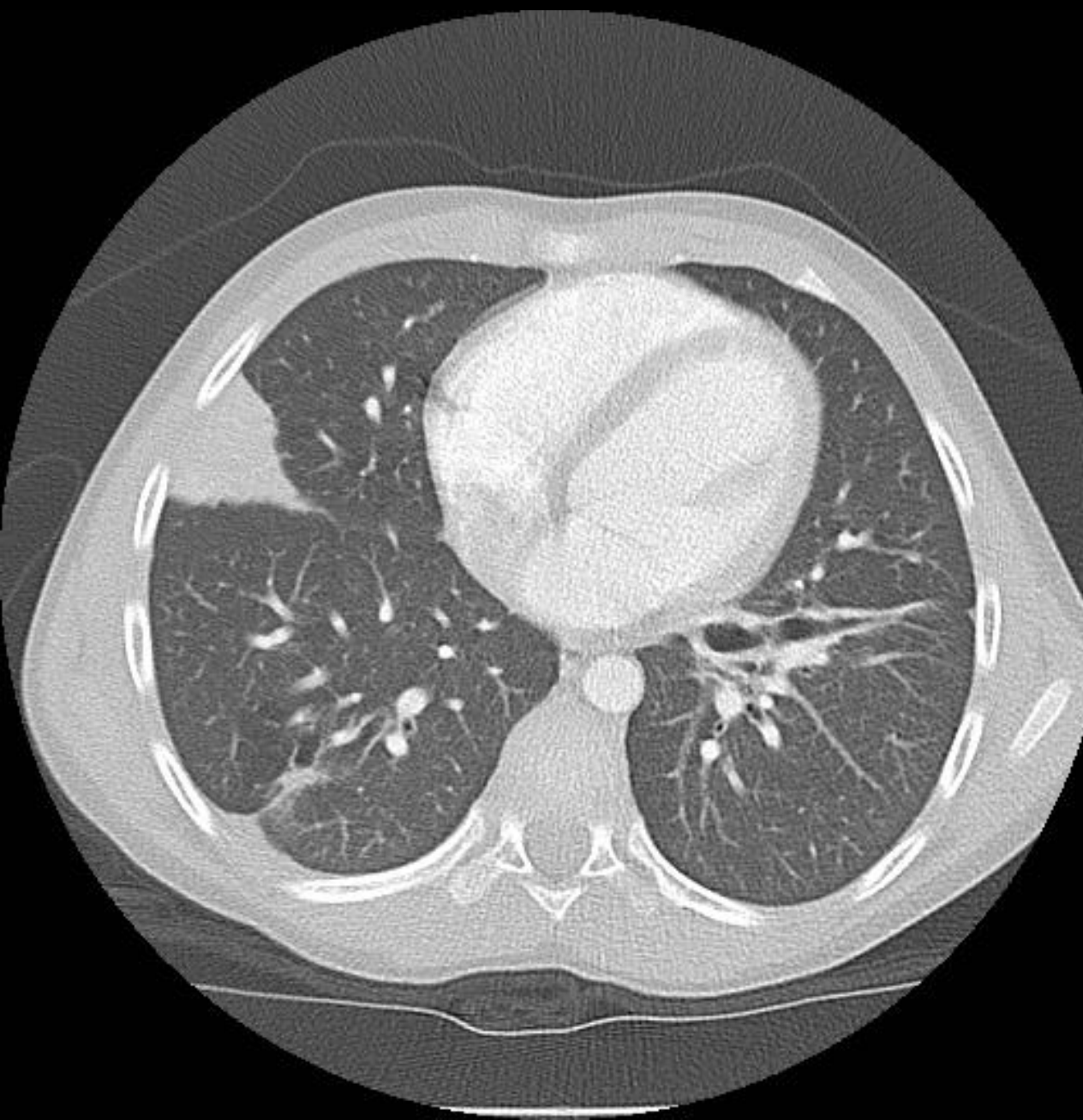
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- Sputum Culture for Mycobacterium:
  - No AFB seen
- Mantoux
  - Negative

# Work Up: Abdominal Imaging

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- U/S & CT:
  - 2 complex cystic lesions
    - Bi-lobed appearance
  - No rim enhancement
  - No blood flow noted within lesions
  - Cyst density consistent with fluid



# Updated DDx?





# Disease Confirmation



- *Echinococcus* Serology:
  - **Highly Positive**



# Echinococcosis

# Echinococcosis Etiology

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- Caused by 4 species of the *Echinococcus* family
  - ***E. granulosus***
    - **Cystic echinococcosis**
    - **Worldwide distribution**
  - *E. multilocularis*
    - Alveolar echinococcosis
    - Colder climates

# Echinococcus Life Cycle

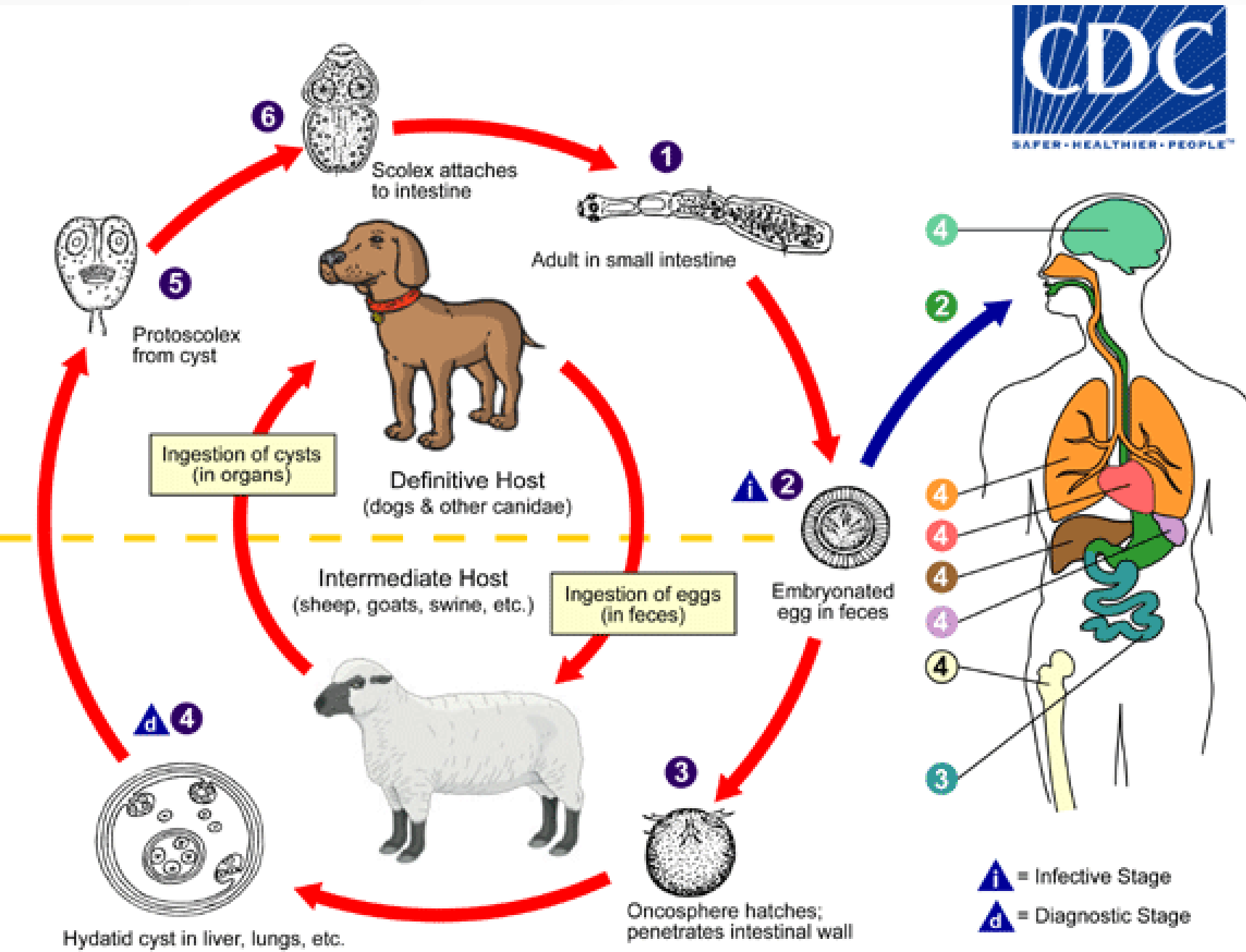
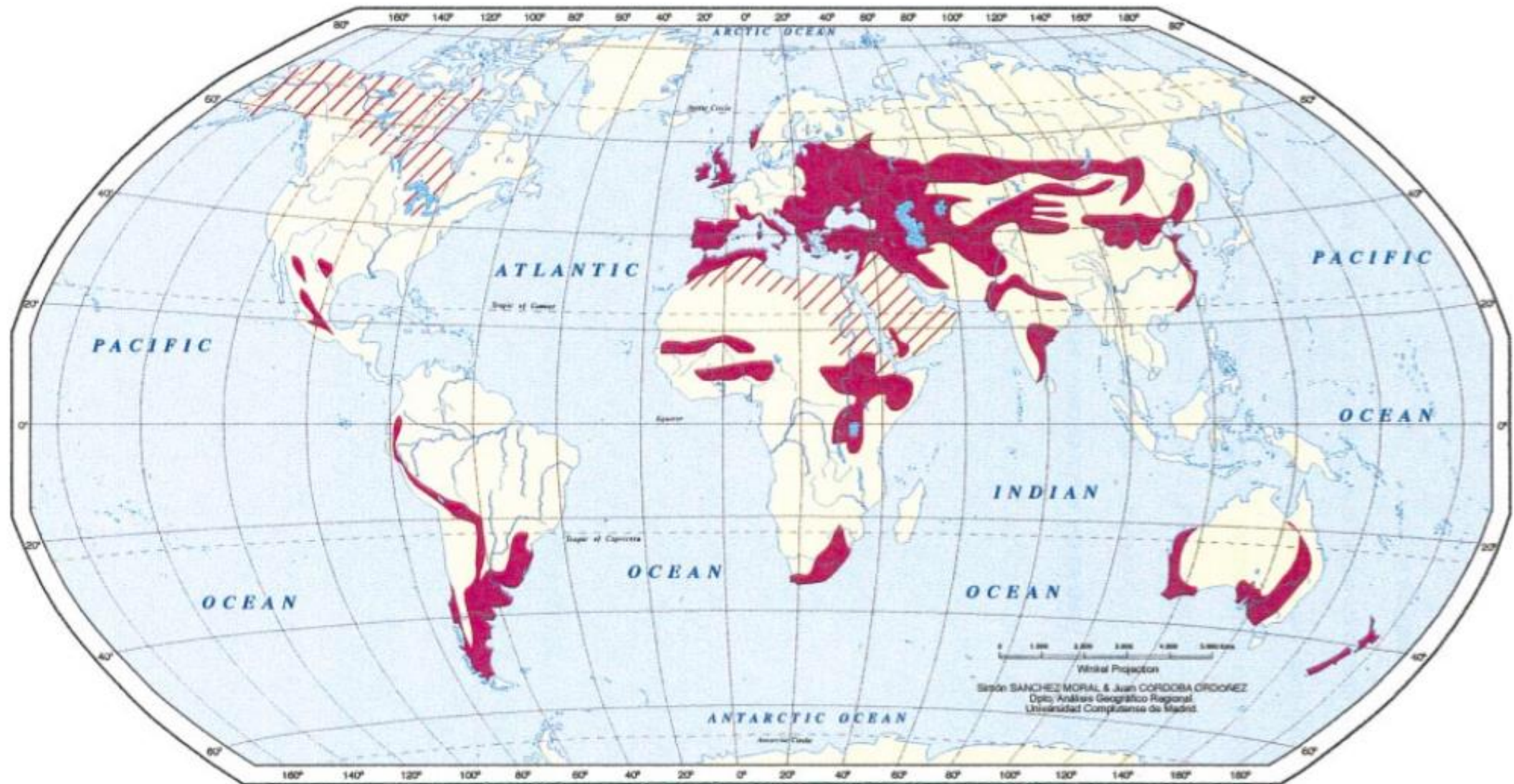


Image from CDC:  
<https://www.cdc.gov/parasites/echinococcosis/biology.html>

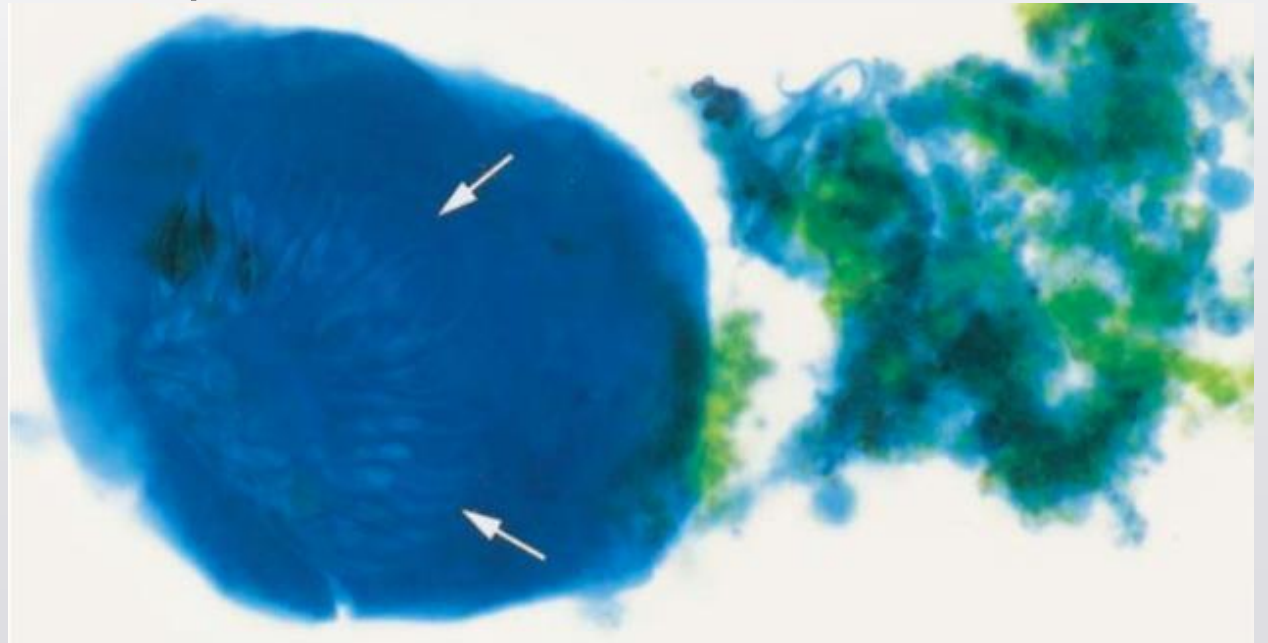
# E. granulos: Worldwide Distribution





# Cyst Growth

- Hydatid cyst slowly grows over time
  - Common in liver and lung
  - Rate of growth is dependent on surrounding tissue distensibility
    - Typically quoted rate of 1-5cm/yr
- Cysts layers
  - Endocyst
  - Ectocyst
  - Adventitia/Pericyst



# Symptoms



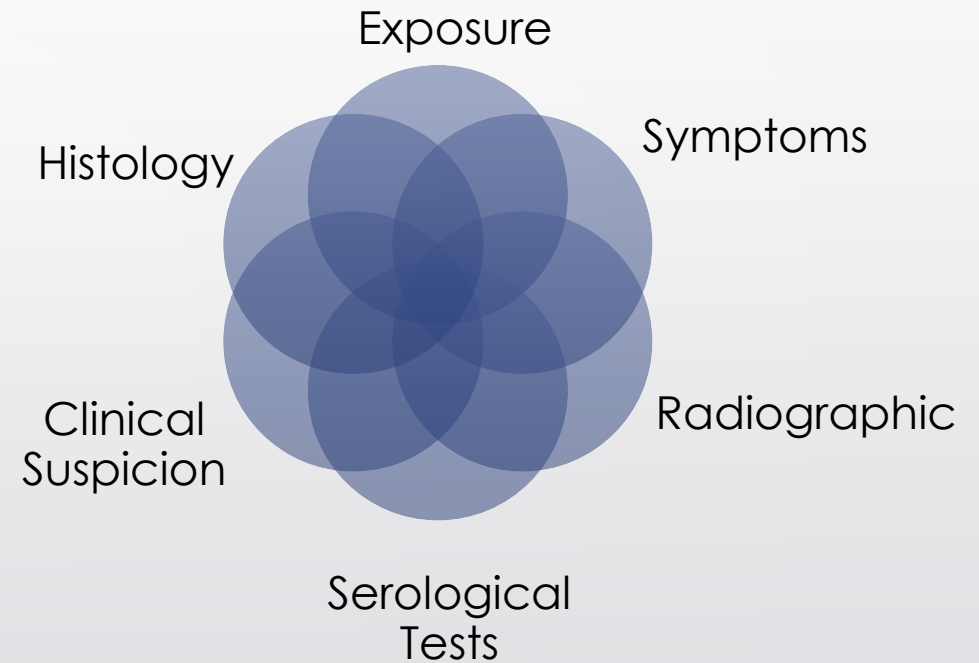
- Younger children are more commonly affected
  - Most are asymptomatic
- Tend to occur following cyst rupture
  - Contained
  - Communicating
- Leak of cystic fluid may cause anaphylaxis
- Symptoms:
  - Chest pressure/pain
  - Cough
    - May expectorate cystic elements
      - “Grape skins”
  - Wheeze
  - Hemoptysis
  - Fever
  - Malaise



# Diagnosis

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- Diagnosis depends on:
  - High clinical suspicion
  - History of travel to endemic area
  - Radiographic evidence
  - +/- Presence of cysts elsewhere
  - +/- Special tests
  - +/- Pathology



# Radiographic Findings

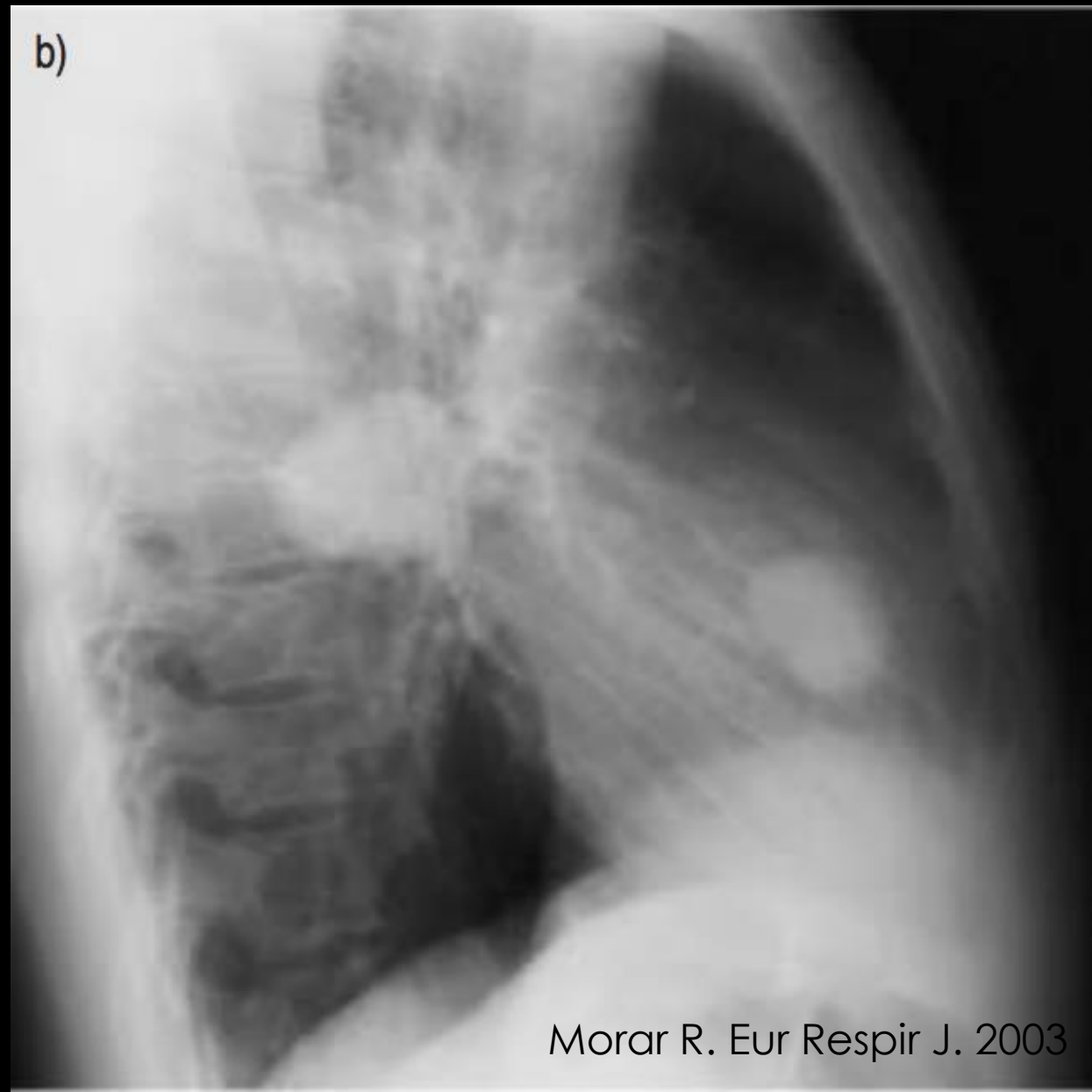


- Most common finding are cysts
  - Typically occur in lower lobes (60%)
  - Calcification is rare
- Over time:
  - Multiple cysts can form
  - Surrounding lung tissue affected
  - Erosion into surrounding airways
  - Variable degree of rupture/leakage

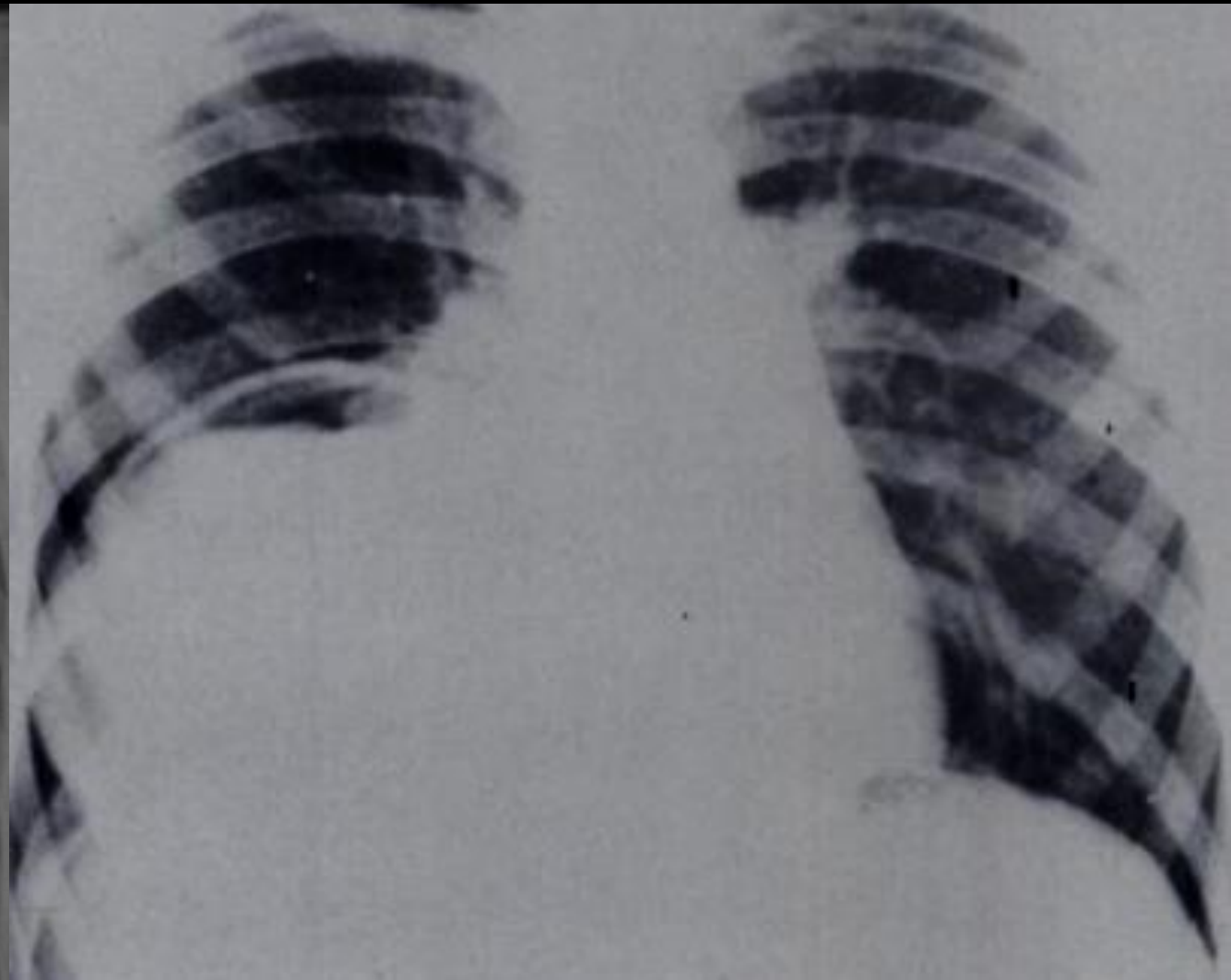
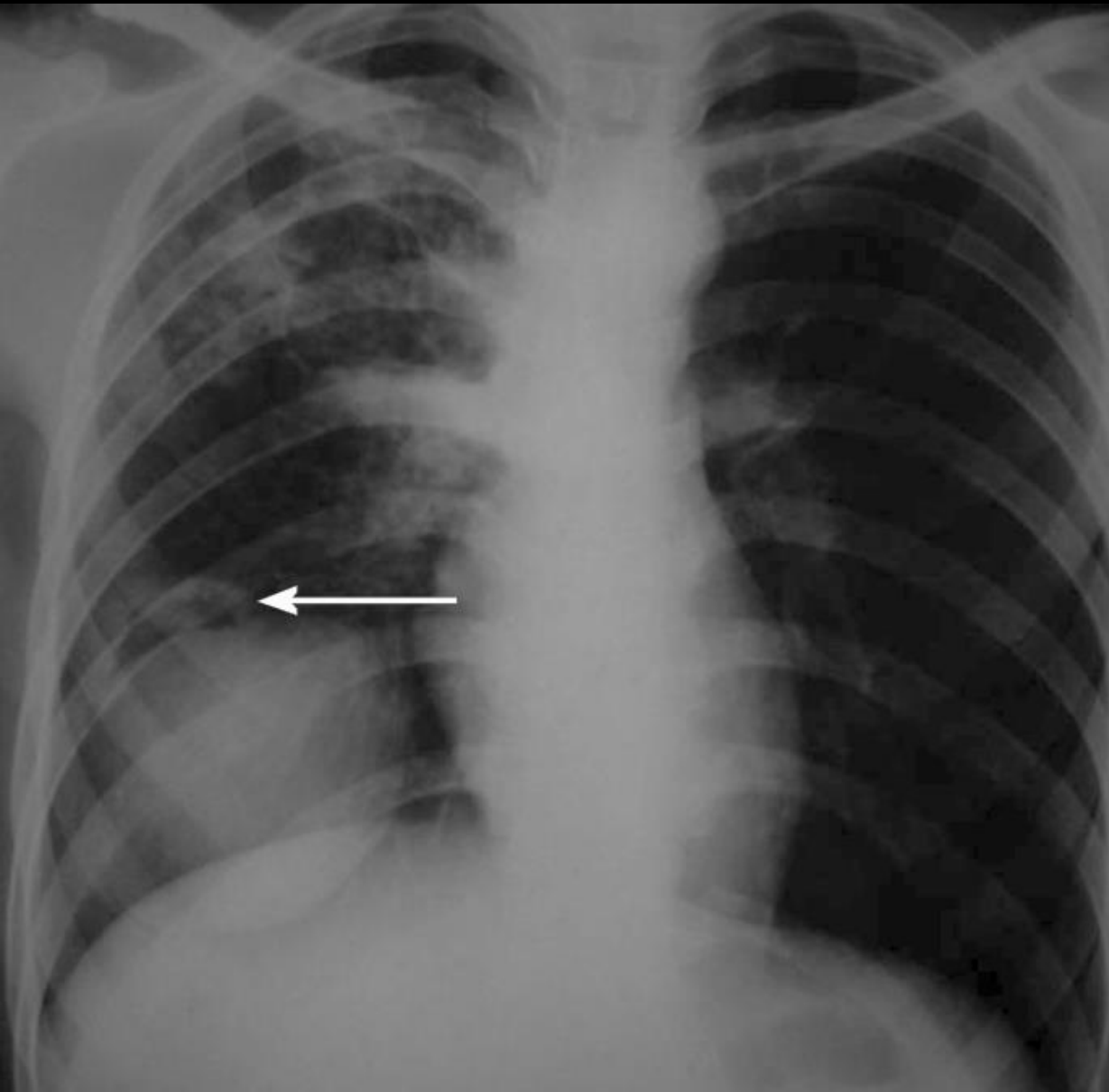


Influences  
radiographic  
findings

# Cysts



# Crescent Sign

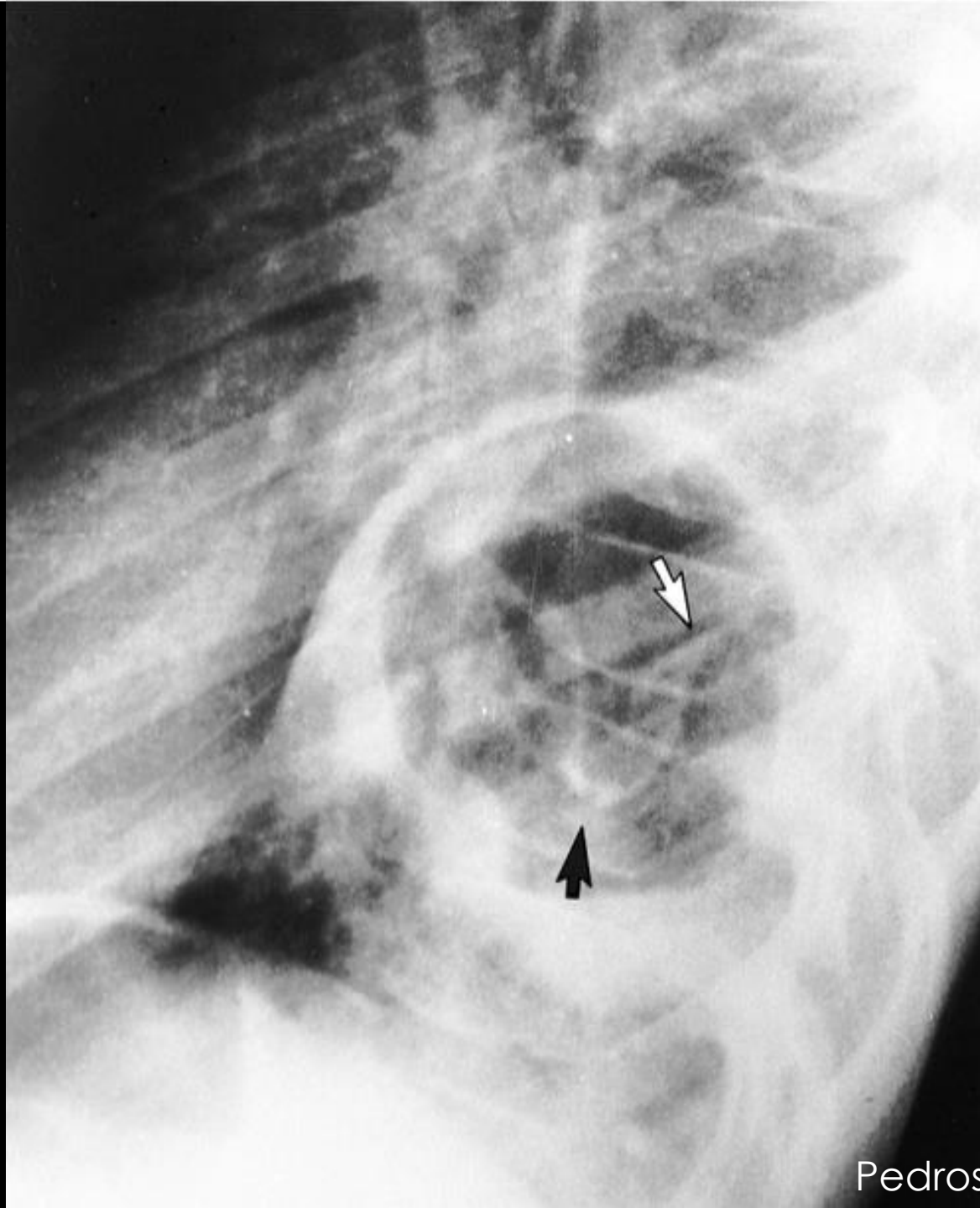


Garget et al, World J Radiol, 2016  
Balikian et al, Am J Roent Radium Ther Nucl Med, 1974

# Cumbo Sign

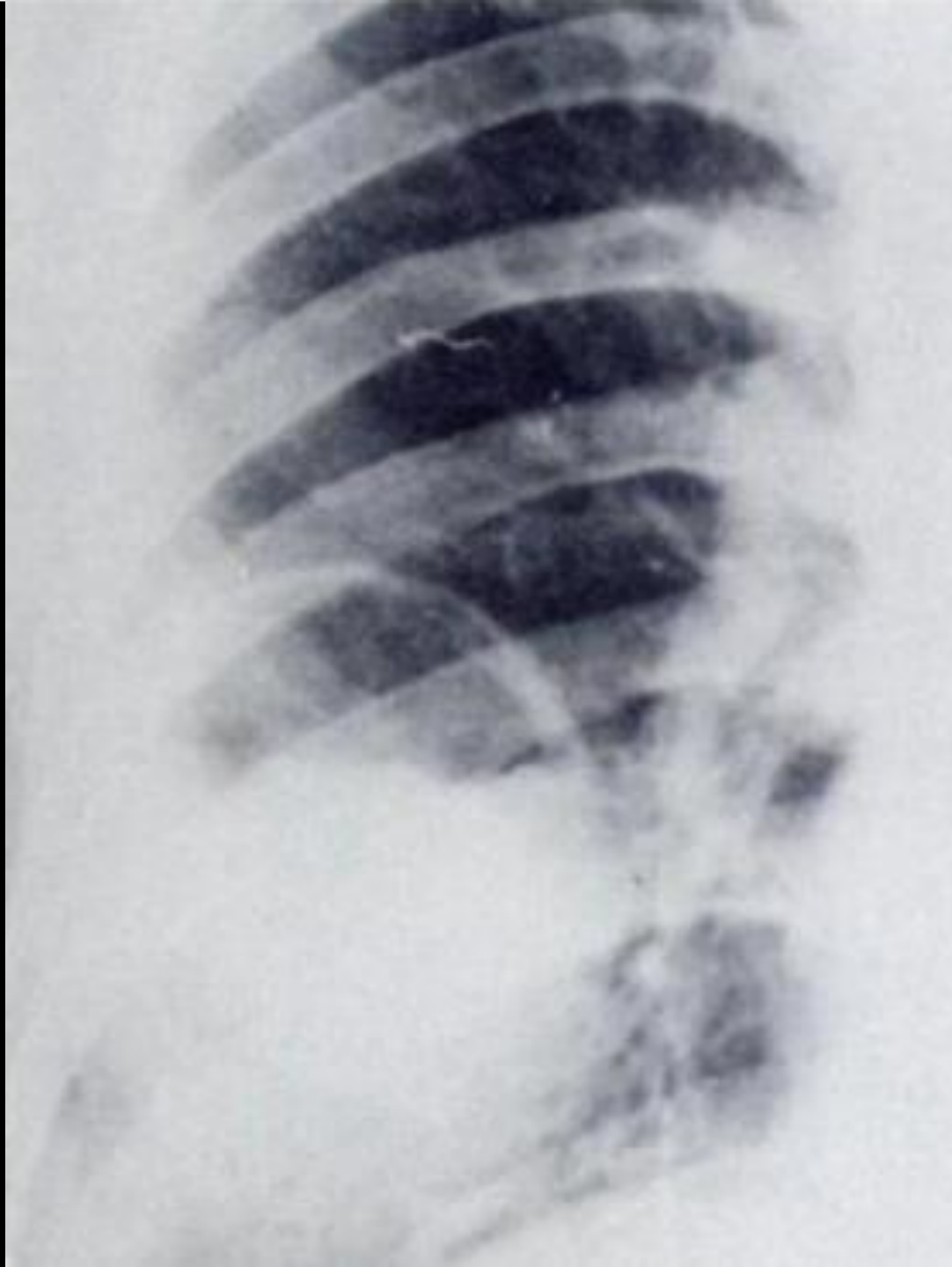


# Serpent Sign





# Water Lily Sign

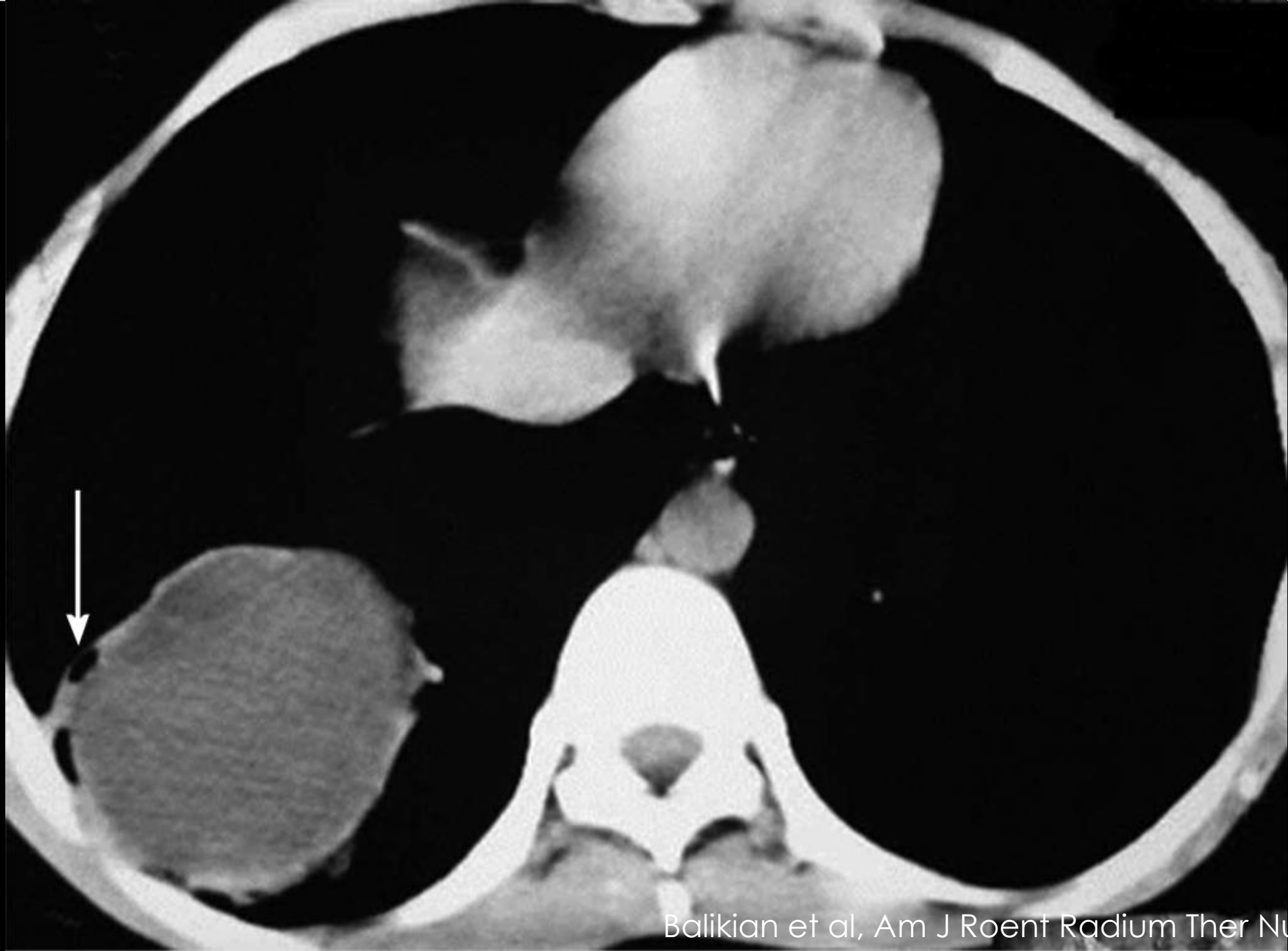


Balikian et al, Am J  
Roent Radium Ther Nucl  
Med, 1974



# Monod's Sign (Mass within a Cavity)





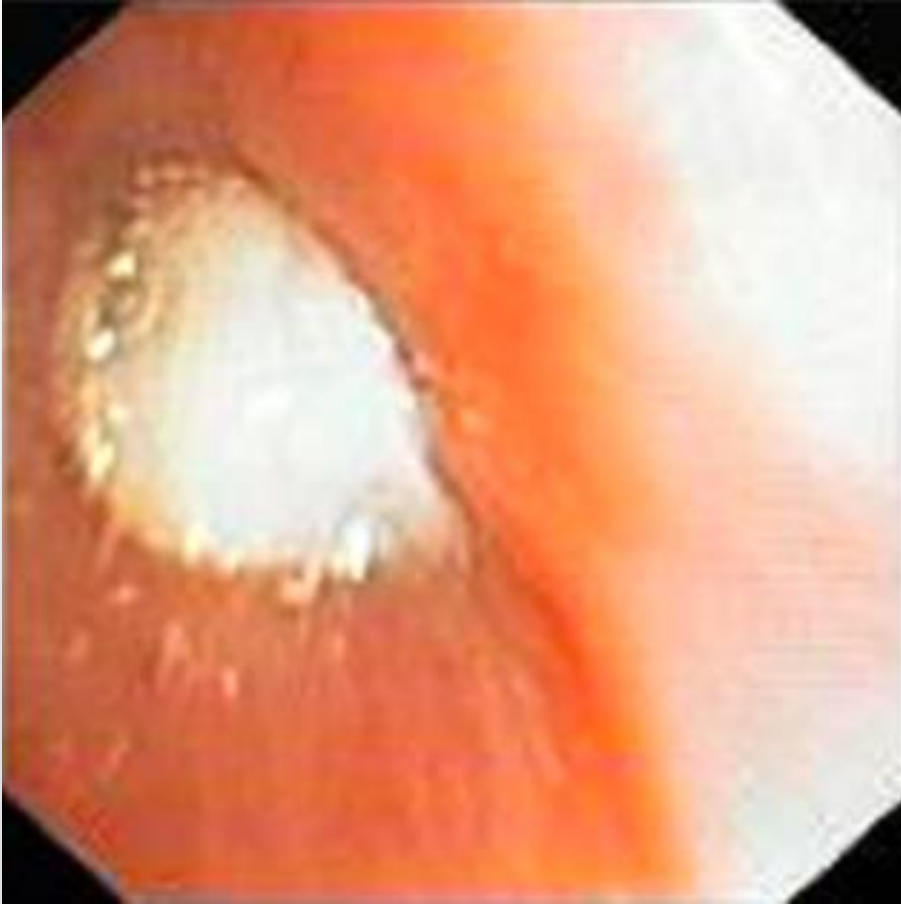
# Special tests

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- Serologic testing
  - Enzyme immunoassay
    - Specificity = 91.6%
    - Sensitivity = 97.8%
- Other tests
  - Latex agglutination
  - Indirect hemagglutination
  - Complement fixation
  - Casoni skin test
- Pathology
  - 3 layer cyst
  - Protoscolices

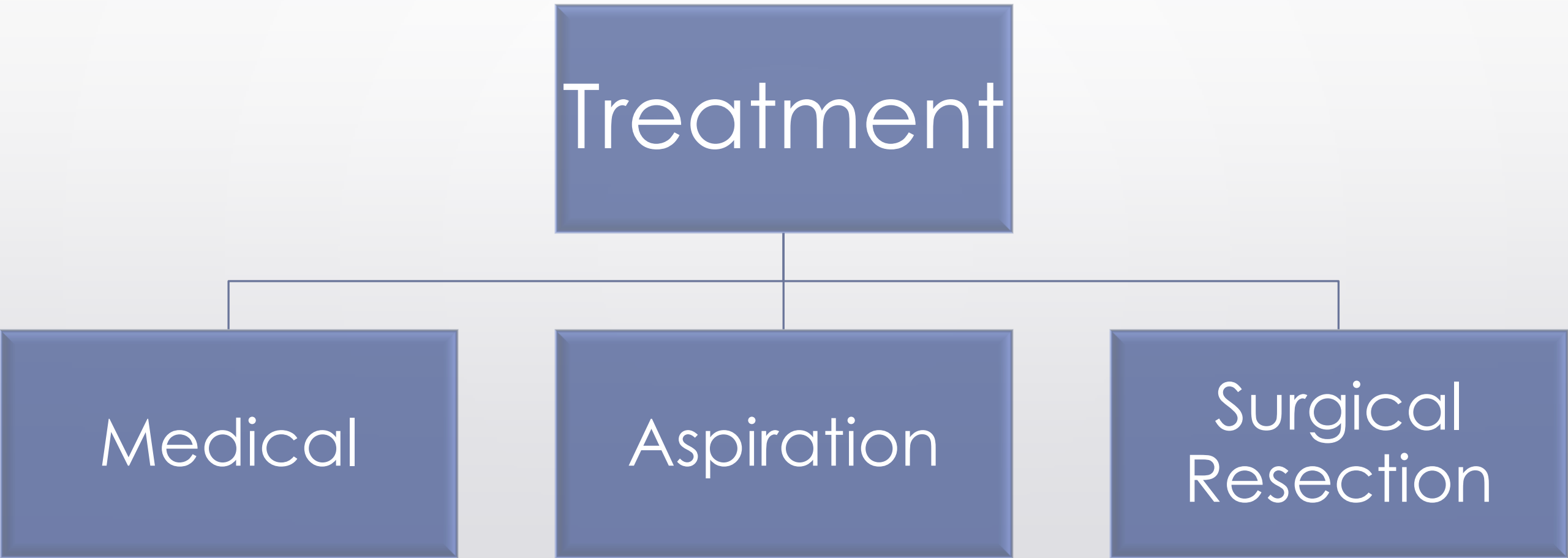
# Bronchoscopy

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# Treatment

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# Surgical Management



- Mainstay of treatment
- Eradication of parasite and cystic layers
  - Enucleation, wedge resection, lobectomy, pneumonectomy
- Risks/Complications:
  - Anaphylactic reactions
  - Infection: Cyst recurrence, abscess, empyema, sepsis
  - Leaks: Hydro/Pneumothorax

# Medical Management



- Indications:
  - Asymptomatic patient
  - Increased surgical morbidity/mortality risk
  - Multiple cysts
  - Disease recurrence not amenable to surgery
  - With intraoperative spillage from cyst
  - Pre-operatively to aid in removal



# Benzimidazoles



- Albendazole > Mebendazole
  - Albendazole: 10-15mg/kg/day
  - Mebendazole: 40-60mg/kg/day
- Treat for > 3-6 months
- +/- Addition of Praziquantel
- Contraindications
  - Pregnancy (first Trimester)
  - Large cysts at risk of rupture
  - Chronic liver disease or Bone Marrow suppression

# Percutaneous Aspiration



- Typically reserved for hepatic cysts
- Can confirm diagnosis
  - Evidence of protoscolices, hooklets and hydatid membranes
- Increases the risk of anaphylaxis, cysts fluid spillage
- Generally not considered first line for therapy


# *E. granulosus* var. *canadensis*

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- Similar life cycle
- More benign disease
  - Less frequently symptomatic
  - Smaller, delicate cysts
  - Potential for spontaneous cure
- Diagnostic approach similar to “typical” variant
- Treatment can consist of observation, medical therapy, or surgical management



Back to our case...

- 
- Initiated treatment with Albendazole and Praziquantel x 3 months
  - Chest and Abdominal imaging:
    - Improvement in cyst size
  - Given that lesions persist, continues on albendazole monotherapy
    - Plan to re-image in 3 months



Questions?



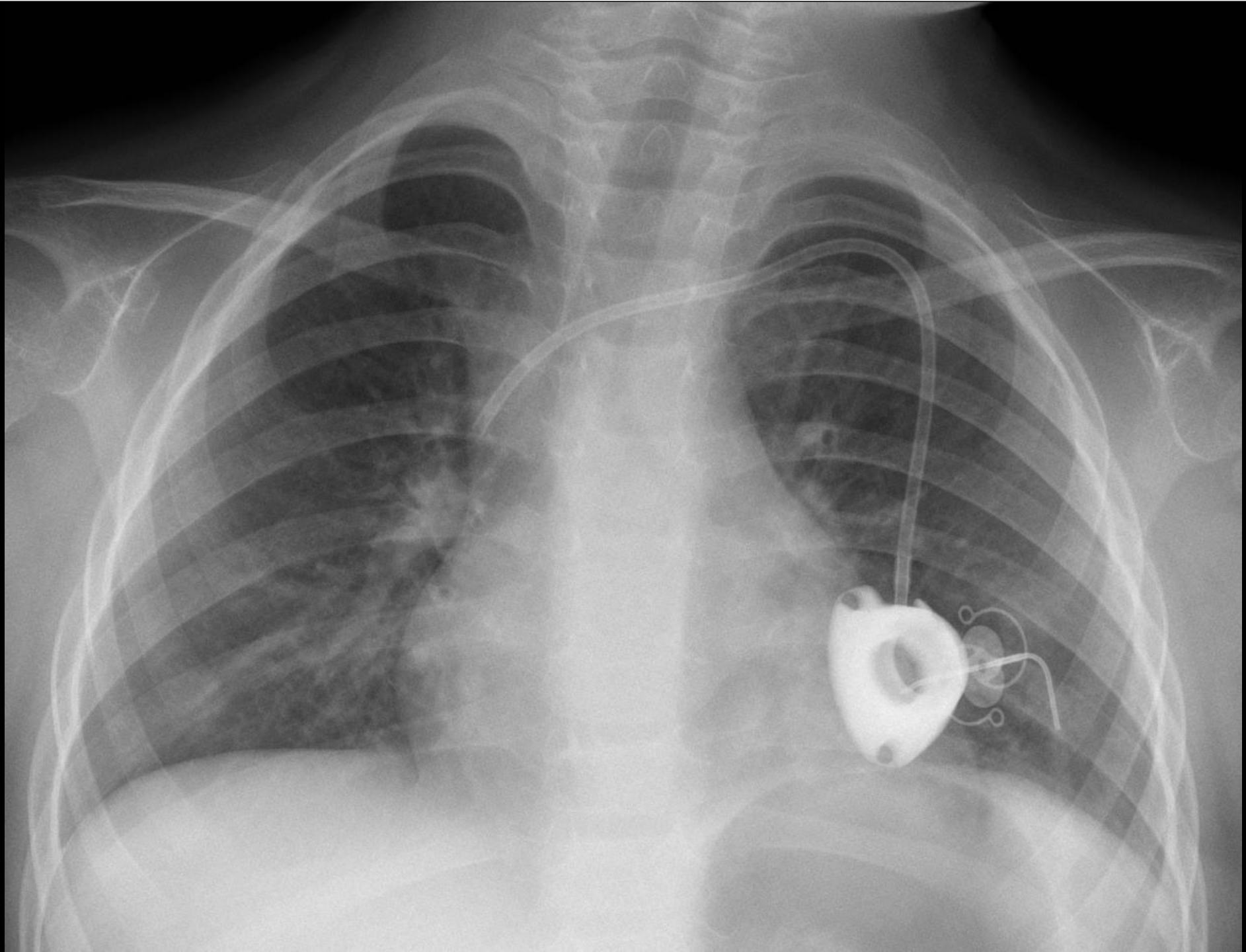


## Case 2

# Initial History



- 3 year, 8 month old female
  - Chromosomal deletion (9p23)
  - Global developmental delay
  - High Risk B Cell ALL
    - Maintenance phase chemotherapy
- History of febrile x 4 days, with cough and rhinorrhea
  - Not neutropenic



# Deterioration



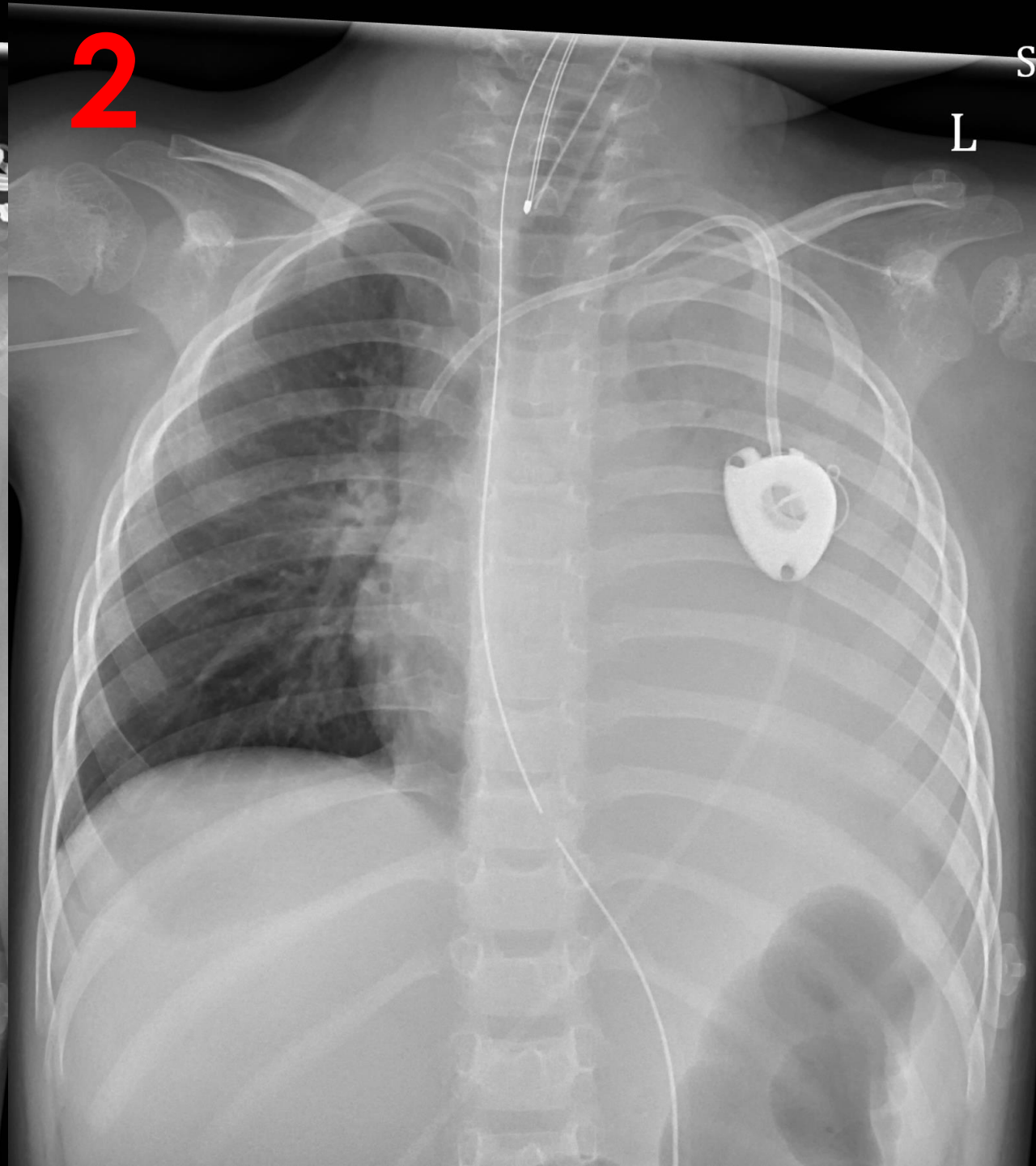
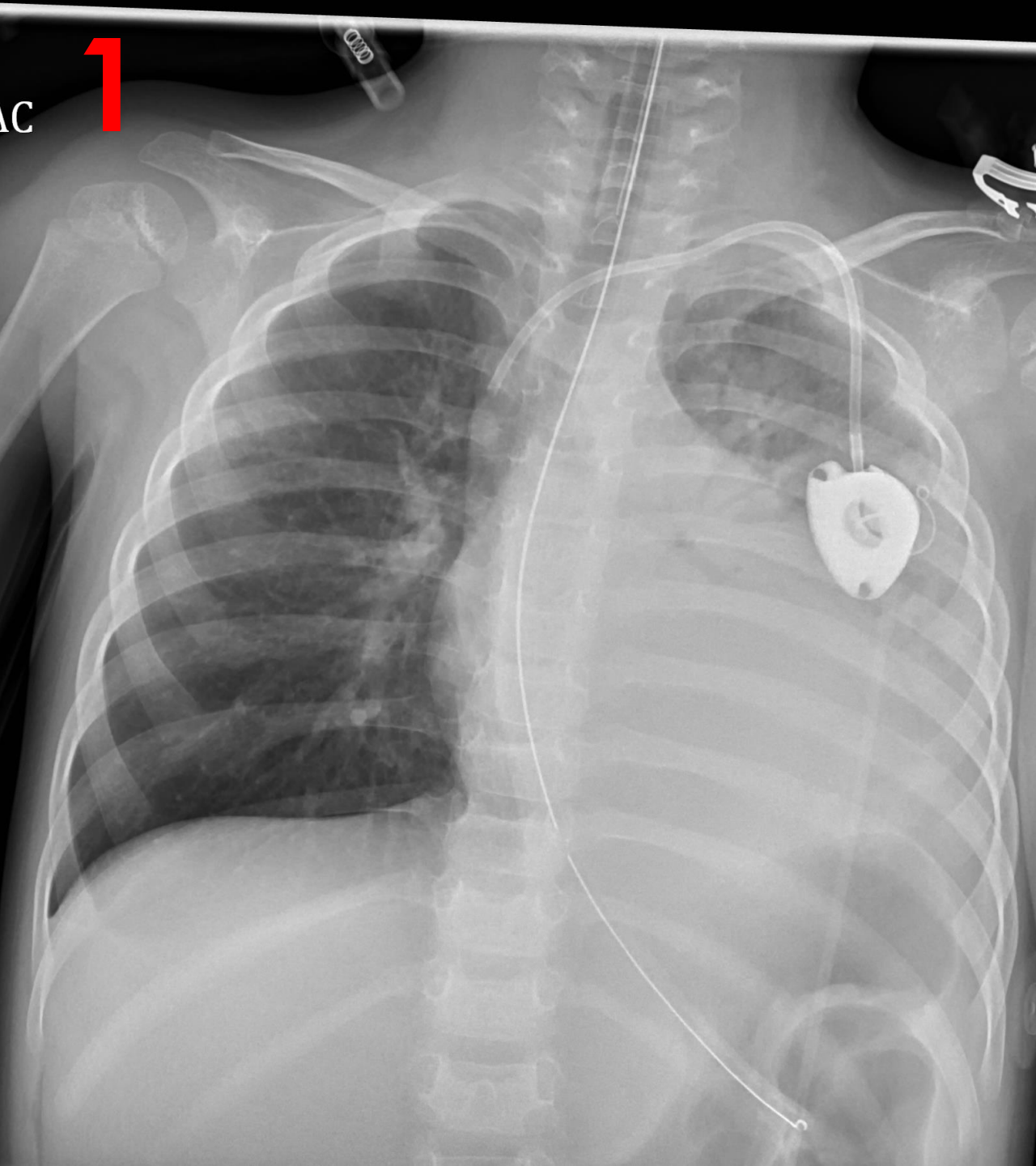
- Developed increased WOB
- Initial vitals:
  - Temp: 38°C HR: 167 BP: 95/52 RR: 60 O2 Sats: 80% on RA
- Exam:
  - Appeared unwell, dusky, tired
  - Increased WOB, grunting and suprasternal indrawing
  - Normal cardiac sounds, no murmur. Brisk capillary response
  - No organomegaly

# Work-up



- Hgb: **87** WBC: **0.8** PLT: 198
  - Neut: **0.5**, Lymph: 0, Mono: 0, Eo: 0
- CRP: **368**
- VBG: 7.42/36/23, Lactate: **1.8**
- Lytes: Na: **130**, K: 3.6
- Mild increase in Liver enzymes
- Normal Renal function







# Respiratory Intervention



- Oxygen applied, (3L) with initial improved saturation
  - WOB persisted despite BiPAP trial
- Ongoing tachypnea and WOB → intubated
  - $\text{FiO}_2 = 1.0$ , Pressure of 32/10 to maintain oxygen saturation
  - Transitioned to HFO
- Anti-infectives were broadened to Vancomycin, Meropenem, Azithromycin, TMP-SMX, and oseltamivir (Tamiflu)

# ECLS Activation



- Our patient continued to deteriorate
  - Escalating inotropic/chronotropic agents
  - Ongoing difficulty with oxygenation and ventilation
    - ABG: 6.83/139/23
- After discussion with family, cannulated for ECLS and transferred to regional ECLS center

# DDx of Rapidly Progressing Respiratory Failure?



# DDx of Rapidly Progressing Respiratory Failure?



- Given speed of deterioration:
  - Infectious etiology most likely
- Viral
  - Influenza
  - Enterovirus/Rhinovirus
  - RSV
  - CMV
  - ....
- Bacterial
  - S. pneumoniae, S. aureus, Haemophilus, Moraxella
  - Mycoplasma
  - PJP, Legionella
- Fungal *less likely* given rapid progression, but remains possible

# Infectious Workup



- Enterovirus/Rhinovirus positive
- ETT suction:
  - No organisms, no growth on culture
  - Pneumocystis not seen

# Bronchoscopy

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- Day # 4 of ECLS
  - Galactomannan negative
  - Pneumocystis negative
  - Bacterial and Fungal Culture negative
  - No AFB seen
  - Adenovirus NAT positive
- ***Legionella pneumophila*** (serogroup 6)

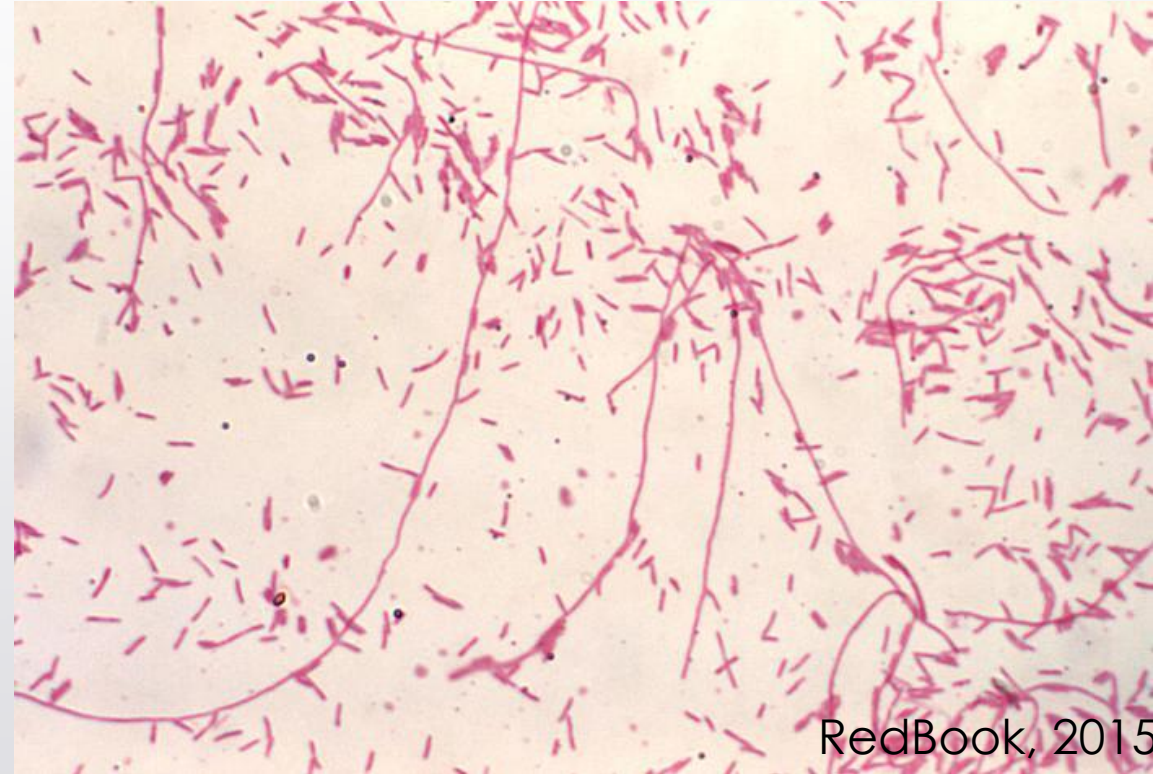




# Legionnaires Disease (Legionellosis)

# Microbiology & Environment

- *Legionella pneumophila* is a Gram-negative coccobacilli
  - 58 species
  - Multiple serogroups
    - Serogroup 1 (Lp1):
      - Most common subtype (~80%)
      - Most virulent subtype
- Ubiquitous in aqueous environments
- Survives as intracellular parasites in environment



RedBook, 2015

Cunha et al. Lancet, 2016  
Stout et al. NEJM, 1997

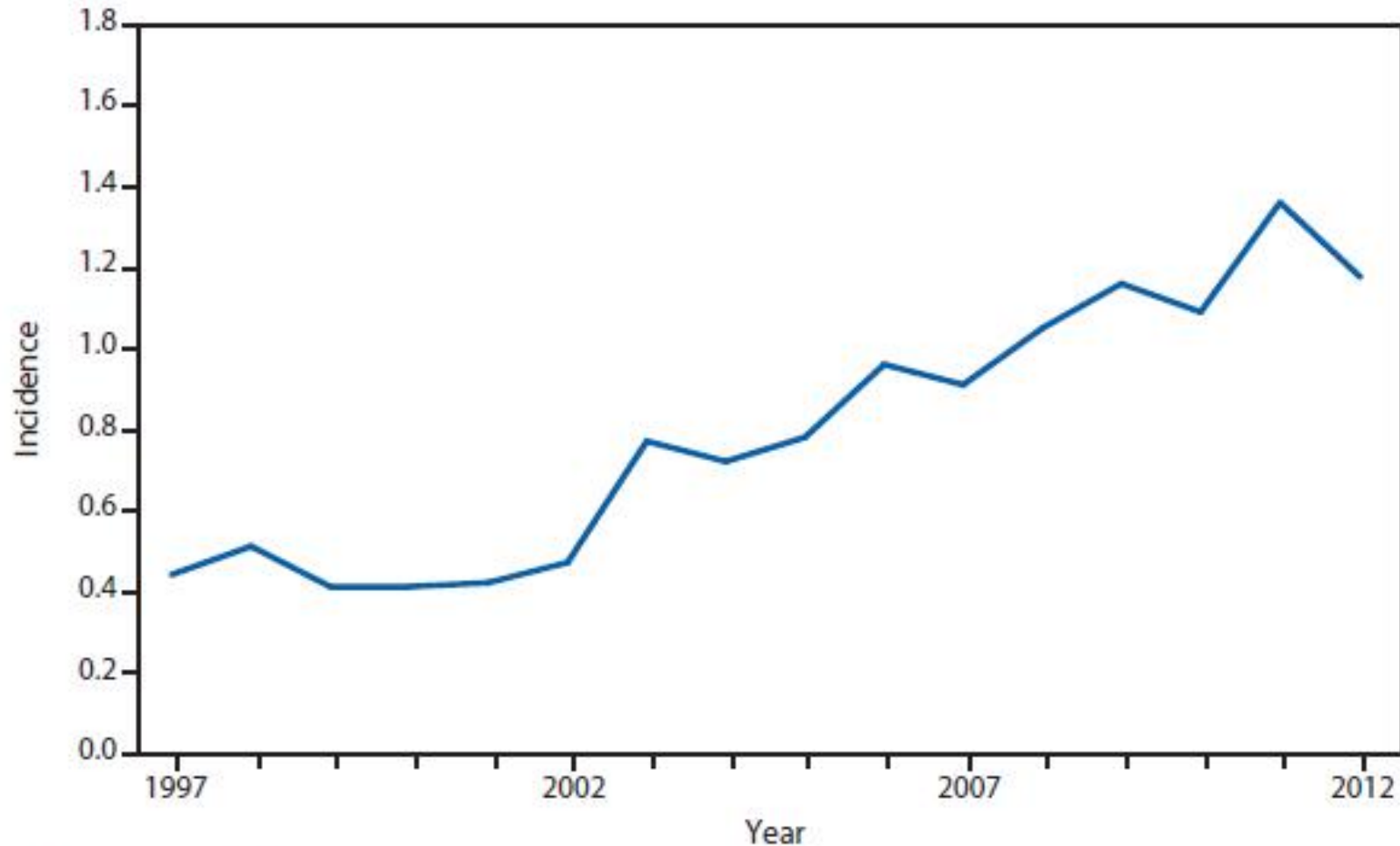
# Pathogenesis



- Transmission:
  - Inhalation, aspiration, or direct contact
  - Increased risk with cumulative exposure
- Infection of host cells
  - Flagellum, pili, and surface proteins to enter cells
  - Inhibition of phagocyte bactericidal function
    - Growth and replication occurs within host cells
  - Disruption of host cell membrane → *Legionella* expulsion

Mandell et al. Clin Infect Dis. 2016  
Cunha et al. Lancet, 2016  
Stout et al. NEJM, 1997

# Incidence



\* Per 100,000 population.

The incidence of legionellosis decreased slightly from 2011 to 2012, but a general increasing trend in disease began in 2003. Factors contributing to this increase include a true increase in disease transmission, greater use of diagnostic testing, and increased reporting.

Cunha et al. Lancet, 2016  
Redbook, 2015  
Stout et al. NEJM, 1997

# Risk Factors



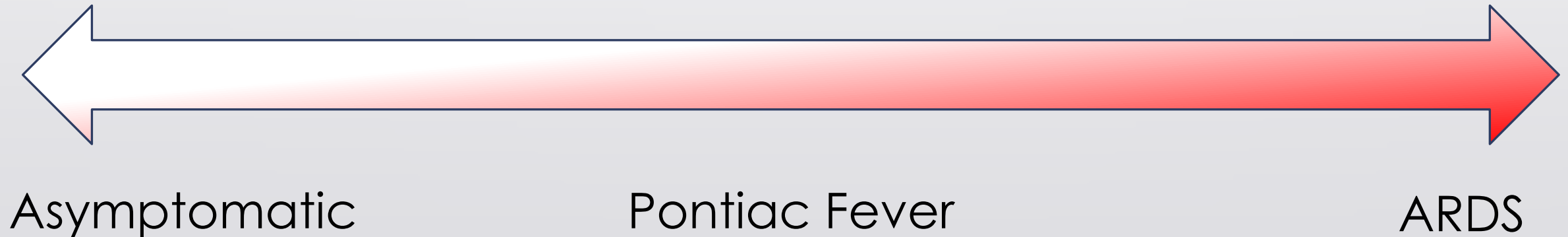
- Cigarette smoking
- Chronic Lung disease
- Malignancy/chemotherapy
- Surgery
- Neonates/premature infants
- Immunosuppression
  - Chronic steroid treatment
  - TNF- $\alpha$  treatment
  - Post transplant patients at high risk
- Neutropenia has NOT been identified as a risk factor

Greenberg et al. Lancet, 2006  
Cunha et al. Lancet, 2016  
Stout et al. NEJM, 1997



# Clinical Manifestations

- Often resembles pneumococcal pneumonia and Community Acquired Pneumonia (CAP)
  - Wide spectrum in disease from mild symptoms to severe pneumonia





# Symptoms



- Fever tends to occur in nearly all individuals (67-100%)
  - May not manifest with immunosuppression
- Symptoms
  - Cough (41-92%)
  - Chills (15-77%)
  - Dyspnea (36-56%)
  - Neurologic (38-53%)
  - Myalgia/arthralgia (20-43%)
  - Chest pain (14-50%)
  - Gastrointestinal (9-47%)

# Investigations

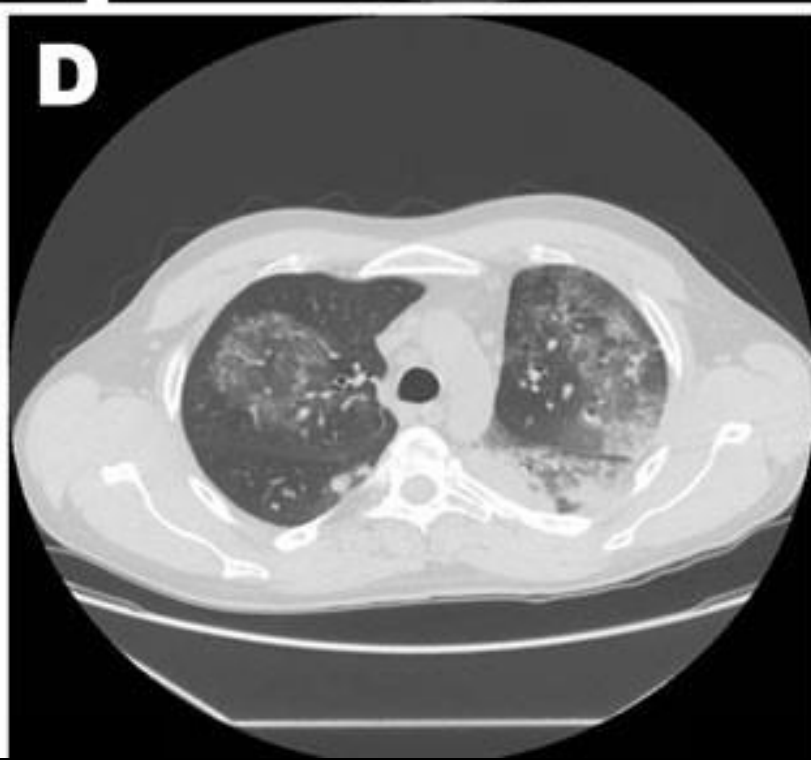
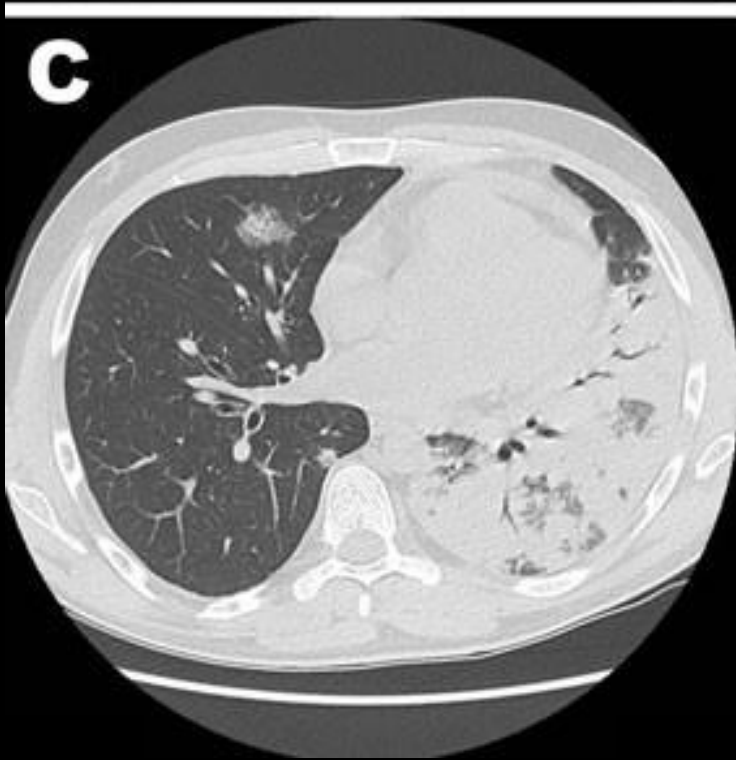
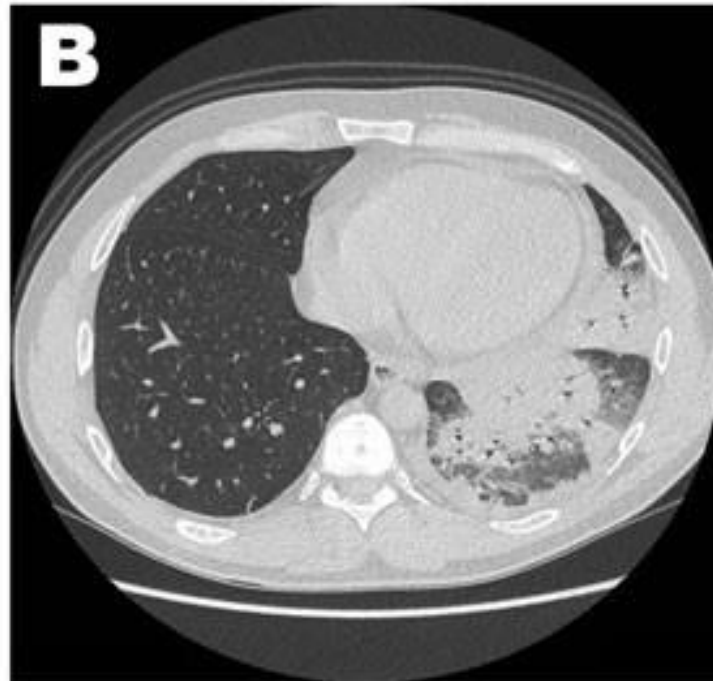


- **Radiographic:**

- No consistent/pathognomonic for *Legionella*
  - Patchy, unilobular infiltrate is most common
- Pleural effusion (15-50%)
- Cavitation can occur (18%)
- Nodular opacities (8%)

- **Laboratory**

- Hyponatremia
- Elevated inflammatory markers
- Leukocytosis/Leukopenia
- Elevated Creatine Kinase
- Myoglobinuria
- Watery sputum with few neutrophils



# Non-culture Diagnosis



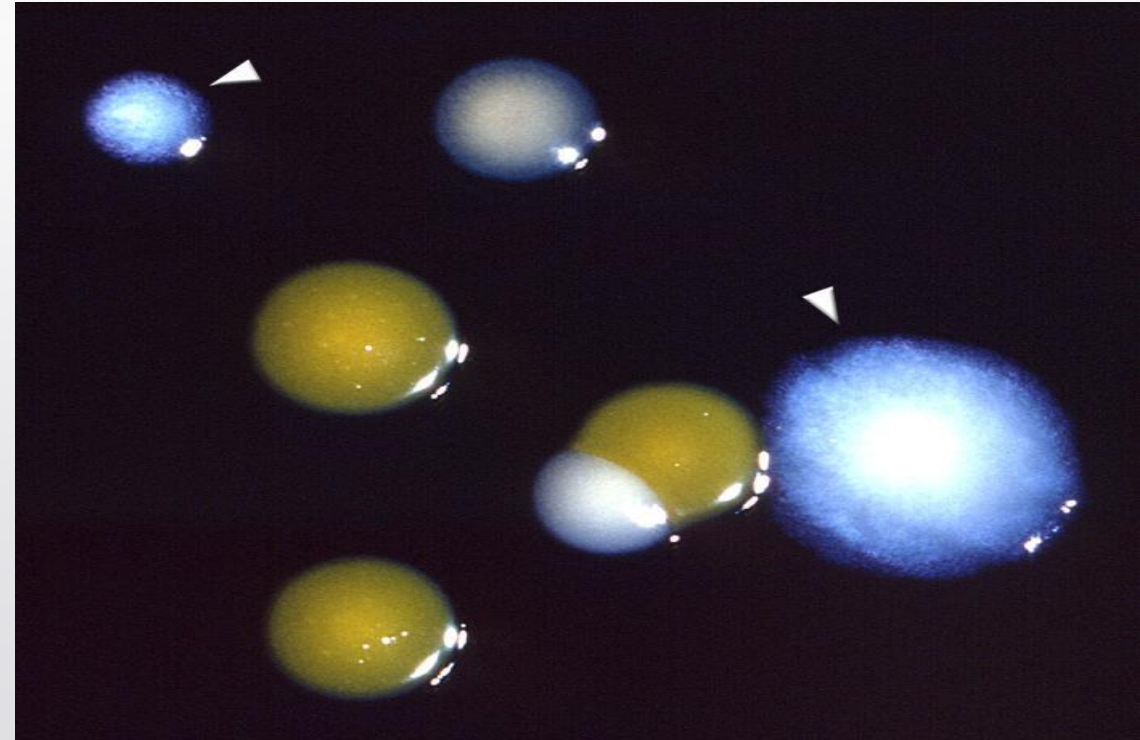
- Urinary Antigen
  - Fast
  - Specificity of 99%
  - Detects only Lp1 subgroup
  - Sensitivity 56-99%
    - Lower in immunocompromised patients
  - Ideal to combine with respiratory culture
- Immunofluorescence
  - Low sensitivity

Cunha et al. Lancet, 2016

Mandell et al. Clin Infect Dis. 2016

# Culture Diagnosis

- Gold standard
  - Detects all Legionella species and antibiotic susceptibilities
- Requires special culture media and environment for growth
  - Appropriate identification on requisition
- Samples should be obtained from suspected sites of infection



# Who to test?



- ATS and IDSA Adult Guidelines:
  - Severe Community Acquired Pneumonia (CAP)
  - Failure of outpatient therapy
  - Recent Travel
  - Pleural Effusion
  - Known *Legionella* outbreak



# Treatment



- B-lactams and aminoglycosides are ineffective
- First line:
  - Levofloxacin (Fluoroquinolone)
  - Azithromycin (Macrolide)
  - Doxycycline (Tetracycline)
- Extended course in high risk individuals
- Reporting to public health



# Mortality




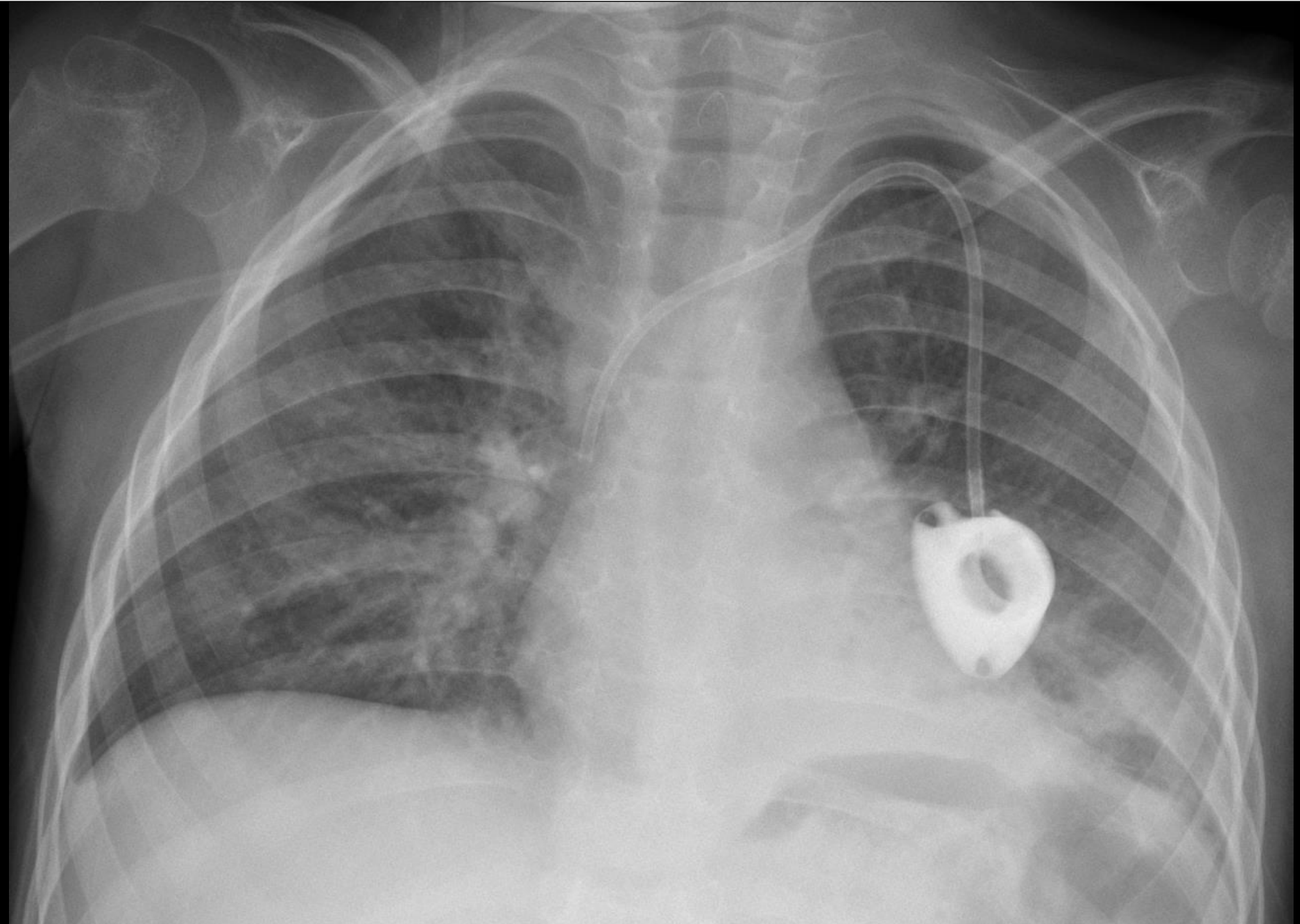
- Early identification and treatment initiation is key
- Overall pediatric mortality = 33%
- Increased mortality in:
  - < 1 year of age (50% vs 25%)
  - Immunosuppressed (42% vs 15%)
  - Inappropriate therapy (76% vs 24%)

Greenberg et al. Lancet, 2006  
Cunha et al. Lancet, 2016  
Stout et al. NEJM, 1997



Back to our Case...

- 
- Levofloxacin was added following identification of *Legionella*
  - Hemodynamics improved, decanulated from ECLS on day 10
  - Extubated to BiPAP on day 20
    - Quick transition to oxygen
    - On room air at time of discharge
  - Completed a 6 week course of Levofloxacin



# Source Identification?



- Public Health notified...
- Parents have a hot tub at home
  - Medical grade filters
- Legionella identified from hot tub water



Questions?

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