


# 33 – Pneumonia

Speaker: Paul Auwaerter, MD



**Pneumonia**

Paul G. Auwaerter, MD  
Sherrilyn and Ken Fisher Professor of Medicine  
Clinical Director, Division of Infectious Diseases  
Johns Hopkins University School of Medicine

7/1/2024



**• Disclosures of Financial Relationships with Relevant Commercial Interests**

- Consultant: Gilead, Shionogi
- Research Grant: Pfizer
- Ownership Interest: Johnson & Johnson

**Community-acquired Pneumonia: Meta-analysis**  
Traditional culture + PCR for "atypicals" + viruses

Pathogen	Total (%)*
None	4380 (61.3)
Pathogen detected	3279 (48.7)
<b>Etiology Bacterial</b>	
• <i>S. pneumoniae</i>	33%
• <i>H. influenzae</i>	8.6%
• <i>S. aureus</i>	4.9%
• <i>M. catarrhalis</i>	2.4%
• Gram negatives	6.0%
• Mycobacteria	1.8%
• Other bacteria	1.94%

- 12 modern studies
  - 2005-2019
  - Inpatient n = 4399
  - In- & outpatient = 2752
  - Outpatient = 0
- Hospital mortality: 12-15%

Shoar and Musher, Pneumonia (2020) 12:11      \*Etiologic agents percentages

**Community-acquired Pneumonia: Meta-analysis**  
Traditional culture + PCR for "atypicals" + viruses

Pathogen	Total (%)*
<b>Etiology Viral &amp; "Atypicals" And co-infections</b>	
• <i>Mycoplasma pneumoniae</i>	8.9%
• <i>Legionella pneumoniae</i>	6.2%
• <i>C. pneumoniae</i>	2.9%
• <i>Pneumocystis</i>	0.2%
• Influenza	9.2%
• Rhinovirus	11.5%
• Parainfluenza or RSV	9.3%
• Bacterial + viral coinfection	5.9%

- 12 modern studies
  - 2005-2019
  - Inpatient n = 4399
  - In- & outpatient = 2752
  - Outpatient = 0

Shoar and Musher, Pneumonia (2020) 12:11      \*Etiologic agents percentages

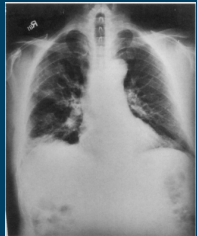
**Case 1**

- 35 M 6d fever, malaise, severe headache, dry cough, myalgia
- PMH: HTN
- Meds: Lisinopril/HCT
- SH: Married, suburban Maryland,
  - Works in long-term care facility
  - Visited pet shop 10d earlier  
Parakeets, cockatiels
  - Confided infidelity in last month

Exam: ill-toxic, 40°C P88  
BP100/70 RR18 O2 97% RA  
Lungs: clear  
Neck: supple  
Cor: no murmurs  
Skin: no rashes  
LP: pending  
Labs:  
WBC 5200, 26% B  
Sputum: 1+ PMNs, no organisms

**Question 1**

Which antibiotic will lead to the most rapid improvement?




- A. Ceftriaxone
- B. Gentamicin
- C. Doxycycline
- D. Trimethoprim/sulfamethoxazole

# 33 – Pneumonia

Speaker: Paul Auwaerter, MD

## Chlamydia psittaci

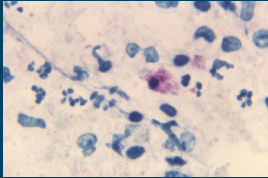
- AKA parrot fever, psittacosis, ornithosis
- Underdiagnosed
  - 1.03 % in studies of CAP
  - < 50 cases/yr in US
  - Most "atypical pneumonia"
- Risks: exposure to birds
  - May be healthy or ill
  - Pets, poultry, pigeons
  - Native birds
    - Lawn mowing



Hogerwerf L et al, Epidemiol Infect. 2017;145(15):3096

## Microbiology

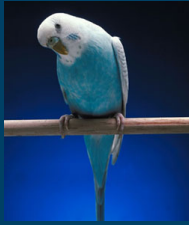
- Two states:
  - Extracellular: infectious, elementary body
    - Bird feces or respiratory secretions → aerosol → human
    - Direct contact
  - Intracellular: replicative



May appear as intracellular Gram negatives

## Chlamydia psittaci

- Range of illness:
  - Mild, bronchitic to severe/ARDS
  - **Clue:** temperature/pulse dissociation
  - Also seen with Salmonella typhi, C. burnetii, Chlamydia, Dengue
- Diagnosis:
  - Molecular/PCR, sputum (best)
  - Acute/convalescent serology (microimmunofluorescence, MIF)
  - Culture: tissue culture (difficult)
- Treatment:
  - Preferred: doxycycline
  - Alternatives:
    - Macrolides
    - Fluoroquinolones



Wolff BJ et al, Diagn Microbiol Infect Dis 2018;90(3):167-170  
Hogerwerf L et al, Epidemiol Infect 2017;145(15):3096-3105

## Helpful clues for "Atypical" CAP

Clinical feature	C. psittaci	C. pneumoniae	M. pneumoniae	L. pneumophila
Cough	++	+	++	+
Sputum	-	+	++	+++
Sore throat	-	++	-	-
Headache	+++	+	-	+
Confusion	+	-	-	++
CXR change	Minimal	Minimal	Worse than sx	Multifocal
Low Na <sup>+</sup>	-	-	-	++
Doxycycline response	Rapid, < 48h	Prompt	Prompt	Slower

Adapted from Stewardson, Grayson. Inf Dis Clin N Amer 2010; 24(1):7

## Case 2

69M c/o fever and dyspnea x 3 days  
-Dry cough, pleuritic chest pain  
-In nursing facility for L foot, C1-2, L4-5 osteomyelitis + MRSA bacteremia

Vancomycin (5d, rash) → Ceftriaxone (4d, hives) → Daptomycin (11d)

PMH: Diabetes, HTN, COPD, R BKA, bedbound

SH: 40 PPD smoker, now vaping, Baltimore MD resident, hx substance use

Meds: methadone, insulin, nifedipine, Lisinopril/HCT, inhalers

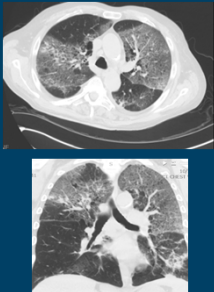
PE: T101.4°F, P 106, RR 24, O2 sat 90% on 6L O<sub>2</sub>  
No lymphadenopathy, no JVD  
Lungs: poor air movement, basilar crackles bilaterally  
Cor: no murmur  
Ext: no edema Skin: no rash

9.5  
6.0 ——— 300K 54%N, 12%L, 24%E  
ESR 150 mm/hr NI LFTs  
CRP 15 mg/dL (0.0-0.5)

## Question 2

The pneumonia is most caused by

- Vaping-associated pulmonary injury (VAPI)
- Allergic bronchopulmonary aspergillosis
- Ceftriaxone
- Daptomycin
- Strongyloides



Case courtesy of L. Leigh Smith, M.D.

# 33 – Pneumonia

Speaker: Paul Auwaerter, MD

### Acute eosinophilic PNA due to daptomycin [FDA black box warning]

- May present like atypical pneumonia or interstitial fibrosis
- Acute
  - Older men (40% > 60 yrs)
  - Daptomycin duration median 19d [2-54d]
  - Fever, dyspnea and cough
  - Hypoxemia
    - Pulse oxygen saturation (SpO<sub>2</sub>) <90% on RA or PaO<sub>2</sub> <60 mmHg
  - Diffuse pulmonary opacities
- Need to exclude alternative causes
  - e.g., fungal or parasitic PNA
  - Improvement with drug cessation
- Hypersensitivity reaction (early)
  - Acute & subacute
  - Ground glass findings +/- effusions
  - Eosinophilia (peripheral or BAL)
    - BAL cell count > 25% eosinophils
- Later presentations
  - Interstitial pneumonitis
  - Bronchiolitis obliterans
  - Mixed ground glass, fibrosis, consolidation

Hirai et al. J Infect Chemother 2017;23(4):245  
Lai et al. CID 2010;5(1):737

### Drug-induced pneumonitis/pneumonia

- Treatment:
  - Discontinue = resolution
  - Corticosteroids: no proven role, but often used
    - If significant hypoxemia: prednisone 40-60 mg PO daily with taper x 14d.
- Other drugs: incomplete list
  - Antibiotics:
    - INH
    - Daptomycin
    - Nitrofurantoin
    - Sulfonamide abx
    - Mirocycline
    - Ampicillin
  - CV:
    - Amiodarone
    - Flecainide
  - Chemotherapy:
    - Bleomycin
  - Others
    - NSAIDs
    - Phenytoin

### Case 3

67M COPD, alcoholic liver disease, diabetes, pancreatic CA

POD #5 s/p Whipple developed nausea, vomiting, fever, cough, confusion and hypoxemia → respiratory failure

Labs  
WBC 18,000 15%<sup>B</sup>, 60%<sup>P</sup>  
Glucose 310 Na 128 sCr 1.7  
AXR: no ileus

Intubation → ICU, respiratory sample:  
Heavy PMNs, no organisms on Gram stain


Therapy:  
Vancomycin and piperacillin/tazobactam x 3 d

No improvement, febrile, respiratory culture negative  
ID consultation called

### Question 3

You are aware of a recent *Legionella mcdadei* outbreak in the hospital. Which test below, would most help you securing a diagnosis of *L. mcdadei* pneumonia?


- Legionella urinary antigen
- Legionella culture of respiratory secretions
- Legionella PCR, respiratory
- Legionella direct fluorescent antigen (DFA) stain of respiratory sample
- Paired *Legionella pneumophila* acute/convalescent serology



Pre-intubation CXR

### Legionella pneumonia

- Risks factors (and who to test)
  - Travel beyond home (e.g., hotel, hospital) last two weeks
    - May cause HAP
  - Severe pneumonia/ICU
  - Proximity to known outbreaks
  - Age > 50 yrs
  - Smoking
  - Comorbidities: diabetes, liver/renal dz, COPD, immunosuppressed
- Acquisition:
  - Aerosolization
  - Drinking water (aspiration)

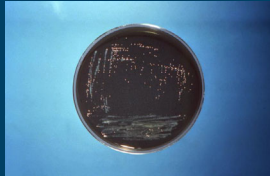


1976 Bellvue Stratford Hotel, Philadelphia

### Legionella

- Environmental/water pathogen
  - Ponds, lakes
  - Water systems (hot > cold), chillers, misters, A/C
  - May be nosocomial pathogen
- Legionellosis
  - Legionnaires' disease (99%)
    - Pneumonia
    - Most typical of the atypicals
  - Pontiac Fever (1%)
    - Febrile, flu-like illness
- Microbiology: 60 species
  - L. pneumophila* serotype 1 (most common)

Legionella culture



Culture media: BCYE agar  
Small, pearly white colonies

# 33 – Pneumonia

Speaker: Paul Auwaerter, MD

## Outbreaks: **Known** and Unknown Sources

- 5,000 cases/year U.S.
  - 20 Outbreaks
- 4X > cases since 2000
- 90% of CDC investigations caused by insufficient water system management
- WHERE?
  - Hotels
  - Long-term Care Facilities
  - Hospitals

SOURCE: National Notifiable Diseases Surveillance System, CDC, 2006-2014

## Legionella diagnostics

Test	Sensitivity (%)	Specificity (%)	Notes
Culture*	20-80	100	Slow, technically difficult, BCYE agar Detects all species
Urinary Ag*	70-100	95-100	Only <i>L. pneumophila</i> serogroup 1, rapid, may cross-react occasionally w/ other serogroups
PCR	95-99	99	FDA approved (2022) in some LRTI multiplex arrays, specific for <i>L. pneumophila</i> .
DFA	25-75	≥ 95	Technically demanding
Paired serology	80-90	> 99	Not helpful for acute care, 5-10% population with (+) titers

Source: CDC, Legionella Testing and Specimen Collection (accessed 7/10/24)  
Avni, J Clin Micro. 2016;54(2):401-11; Muldergans, Eur J Clin Microbiol Infect Dis 2019 \*CDC preferred tests, obtain both in suspected patients

	Legionnaires' disease	Pontiac fever
Clinical	Pneumonia	Flu-like symptoms
CXR	Consolidation, multifocal	No infiltrates
Epidemiology	Sporadic & epidemic	Epidemic
Onset after exposure	2-10 days	24-48 hrs
Attack rate	< 5%	> 90% (including healthy)
Diagnosis	Sputa: Culture Molecular tests DFA Urine antigen	No recovery of organism by culture Acute/convalescent serology Urine antigen, up to 50% in some reports
Mortality	10-30%	0 %

## Case 4

22M landscaper who mows lawns in Ozarks of Arkansas has 5 days of fever, chills and dry cough presenting in early July. He has run over several animal burrows with the mower.

PE: Appears ill, BP 98/70, P 110  
T 39.5°C, PaO<sub>2</sub> = 94%  
No lymphadenopathy  
Bronchial breath sounds lower fields with crackles bilaterally  
No murmur  
No hepatosplenomegaly, abdominal tenderness  
No rash

(+) fatigue, myalgia

PMH: negative

SH: Occasional MJ

## Case 4

WBC 18,500 88%N PLT 280K  
ALT 267 U/L  
CK 3280 U/L

Bilateral LL infiltrates + hilar LN  
Consultant. 2020;60(11):27-29.

Select the testing approach most likely to confirm a diagnosis:

- Respiratory viral panel (RSV, Influenza, SARS-CoV-2)
- Rickettsia rickettsii* acute and convalescent serology
- Whole blood Ehrlichia chaffeensis PCR
- Francisella tularensis* acute and convalescent serology
- Blood culture yielding *Yersinia pestis*

## Francisella tularensis

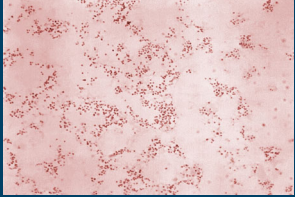
CDC Tularemia reported cases 2011-2020

- Small aerobic Gram negative pleomorphic coccobacillus
- Transmission:
  - US: biting flies (deer flies), ticks
  - Europe: mosquitoes
  - Also: aerosol, contaminated mud/water, infected carcasses, animal bites
- Risk groups:
  - Lab personnel, farmers, landscapers, vets, hunters/trappers, meat handlers
- Bioterrorism agent, Class A
- Inhaled infectious doses: ~10-50 organisms

# 33 – Pneumonia

Speaker: Paul Auwaerter, MD

### Francisella tularensis



- Small aerobic Gram negative pleomorphic coccobacillus
- Six illness patterns
  - Ulceroglandular (most common ~200 cases/yr)
  - Glandular
  - Oculoglandular
  - Pharyngeal
  - Typhoidal
  - Pneumonic
- Routine cultures often negative or offer incorrect identification
  - Notify lab if suspicious
- Acute/convalescent serology confirms most cases

Gram stain photomicrograph, CDC


### Francisella tularensis

- Differential diagnosis of pneumonic tularemia includes:
  - Plague (*Y. pestis*)
  - Anthrax (*B. anthracis*)
  - Consider bioterrorism
- Treatment
  - Fluoroquinolones
  - Aminoglycosides
    - Streptomycin
    - Gentamicin
  - Tetracyclines (mild-moderate cases)
- Limited data to suggest optimal choices

Nelson CA. CID 2024;78(S1):S15-28

### Case 5:

- 18F c/o fever, dry hacking cough, malaise x 3d
- Allergy: erythromycin (N/V)
- Appears well, T38°C, RR 16, P 80, BP 110/70
  - Oropharynx: normal
  - TMs: normal
  - Chest: some crackles left lower lobe



### Case 5

- Azithromycin prescribed
- Next day, full body rash and mucosal lesions develop



### Case 5

What is the most likely etiology?

- A. *Mycoplasma pneumoniae*
- B. Enterovirus D68
- C. Measles
- D. Lyme disease
- E. Drug reaction (azithromycin)

### *Mycoplasma pneumoniae*

- “Walking pneumonia”
  - CXR: appears worse than patient
- < 10% may have extra-pulmonary manifestations
  - Stevens-Johnson syndrome (SJS), E. multiforme
    - Most common infectious cause (children/adolescents)
    - Male > female
  - Hemolytic anemia
  - Hepatitis
  - CNS: encephalitis, meningitis

# 33 – Pneumonia

Speaker: Paul Auwaerter, MD

### Mycoplasma pneumoniae

Finding/method	Pro	Con	Notes
Bullous myringitis		Description w/ experimental infection	Urban legend that is wrong or if true, rare
Molecular	High sensitivity & specificity	FDA approved, Expensive platforms needed, multiplex	New gold standard In house assays not standardized
Serology	Available commercially	Non-specific Acute/convalescent	False +’s and –’s Not timely
Culture	100% specific Antibiotic susceptibilities	Poor sensitivity Time consuming	Only reference labs Special transport media Difficult to perform
Cold agglutinin titers	Occur in 50-70%	Non-specific	Association w/ hemolysis

### Respiratory Molecular Targets, a current FDA-approved example

- Viruses:
  - Adenovirus
  - Coronaviruses 229E, HKU1, NL63, OC43
  - SARS-CoV-2
  - Human metapneumovirus
  - Rhinovirus/enterovirus
  - Influenza A, A/H1, A/H3, A1-2009, B
  - Parainfluenza 1, 2, 3, 4
  - RSV
- Bacteria
  - *Bordetella parapertussis*
  - *Bordetella pertussis*
  - *Chlamydia pneumoniae*
  - *Mycoplasma pneumoniae*

Film Array, NP swab  
Multiplex, 22 pathogens  
Results in 1 hr

Viruses and some bacteria  
Sensitivity: 87, 98-100%  
Specificity: 89, 99-100%

Kilano, T. et al. (2020) J Infect Chemother. 26 (1):82-85

### Case 6

31F fever, cough, myalgia, headache, dyspnea over 1 week ago; February


- No help w/ azithromycin x 3d
- 18 mos daughter, recent bronchitis

PMH: not significant  
SH: ½ ppd smoker

PE: ill  
T38.3, RR 35, BP 125/70, P 128

Coarse breath sounds, rales bilateral and decreased L base

### Case 6



Data:  
WBC: 11, 300 38%P, 48%B

RA ABG: 7.37/35/58

Sputum Gram stain: > 25 WBC/hpf  
Some Gram (+) cocci  
Sputum Cx: pending

Respiratory Film Array:  
Influenza (+)  
RSV (+)

### Case 6

Pt placed on oseltamivir, ceftriaxone and azithromycin. Which of the below should be recommended by the ID consultant?

- Disregard RSV as likely false positive
- Institute ribavirin PO for RSV
- Continue ceftriaxone, but replace azithromycin with moxifloxacin
- Change from oseltamivir to peramivir injection
- Attempt aspiration of left pleural fluid, start linezolid

### Era of molecular diagnostics

- Increasing recognition of co-pathogens
  - Multiple viruses
  - Virus + bacteria
- Comprehensive multiplex Lower respiratory panels available, now including *Legionella pneumophila*
- Mixed infections:
  - Johansson CID 2010; 50:202
    - Pathogens detected: 67%
    - Mixed: 12%
  - Jain NEJM 2015;373:415
    - Pathogens detected: 38%
    - Mixed: 3%
- Beware: Positive values from asymptomatic controls
  - Especially viral
  - Prolonged shedding (especially immunocompromised)

## 33 – Pneumonia

Speaker: Paul Auwaerter, MD

### GOOD LUCK ON THE EXAM

"In the Mortality Bills, pneumonia is an easy second, to tuberculosis; indeed in many cities, the death rate is now higher, and it has become, to use the phrase of Bunyan 'the captain of the men of death.'"

— [William Osler](#)