

48 – Pneumonia: Some Cases that Could be on the Exam

Speaker: Paul Auwaerter, MD

IDBR
INFECTIOUS DISEASE BOARD REVIEW
AUGUST 20-24
2022

Pneumonia: Some Cases that Could be on the Exam

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Disclosures of Financial Relationships with Relevant Commercial Interests

- **Consultant:** EMD Serono, Humanigen
- **Ownership Interest:** Johnson & Johnson, Wellstat

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

Pathogen	Total (%)*
None	4380 (61.3)
Etiology	3279 (48.7)
• <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 (%)*
None	4380 (61.3)
Etiology	3279 (48.7)
• <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%

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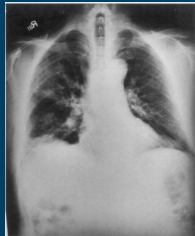
Case 1

- 55 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

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Chlamydia psittaci

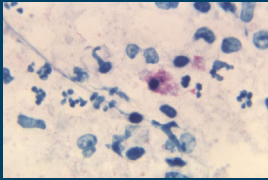
- AKA parrot fever, psittacosis, ornithosis
- Underdiagnosed
 - 1.03 % in studies of CAP
 - < 50 cases/yr in US
 - Most "atypical pneumonia"
- Risks: exposure to birds
 - May be healthy or ill
 - Pets, poultry, pigeons
 - Native birds
 - Lawn mowing



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

Microbiology

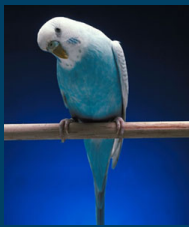
- Two states:
 - Extracellular: infectious, elementary body
 - Bird feces or respiratory secretions → aerosol → human
 - Direct contact
 - Intracellular: replicative



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 2016;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	More than sx	Multifocal
Low Na ⁺	-	-	-	++
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)

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

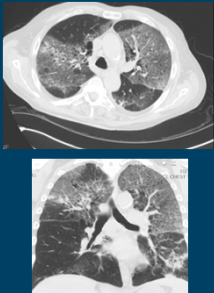
PMH: Diabetes, HTN, COPD, R BKA, bedbound
SH: 40 PPD smoker, now vaping, Baltimore MD resident, hx substance use
Meds: methadone, insulin, nifedipine, Lisinopril/HCT, inhalers

6.0 / 9.5 / 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
- Ceftaroline
- Daptomycin
- Strongyloides



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

48 – Pneumonia: Some Cases that Could be on the Exam

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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 (SpO₂) <90% on RA or PaO₂ <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%^B, 60%^P
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 acute/convalescent serology



Pre-intubation CXR

Legionella pneumonia

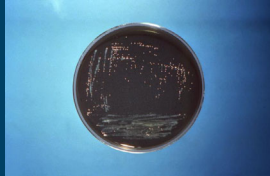
- Risks factors (and who to test)
 - Travel beyond home (e.g., hotel, hospital) last two weeks
 - May cause HAP
 - Severe pneumonia/ICU
 - Proximity to known outbreaks
 - Age > 50 yrs
 - Smoking
 - Comorbidities: diabetes, liver/renal dz, COPD, immunosuppressed
- Acquisition:
 - Aerosolization
 - Drinking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

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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

Legionnaires' disease is on the rise

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

Outbreaks: Known and **Unknown** Sources

MacIntyre CR, et al Emerg Microbes Infect 2016;7:36

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	Not FDA approved, home-brew tests, some are 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. <https://www.cdc.gov/legionella/clinicians/diagnostic-testing.html> (accessed 6/23/21)
Arai. J Clin Micro. 2016;54(2):401-11; Mulyerians, Eur J Clin Microbiol Infect Dis 2019

	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

23M cough, malaise, dyspnea, fever x 1 wk, just returning from overseas

PE: Appears ill, BP 98/70, P 100, T 38.5°C
No lymphadenopathy
Bronchial breath sounds lower fields, occasional wheezing
No murmur
No hepatosplenomegaly, abdominal tenderness
No rash

PMH: negative, no asthma

Meds: atovaquone/proguanil

ROS: no diarrhea, had rash on feet/legs post marathon now resolved

SH: Laguna Phuket (Thailand) triathlon 3 wks earlier

Non-smoker

Studies

WBC 18,000
63N, 13L, 24E

CXR: mild bilateral patchy infiltrates


Blood smear: no parasites

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Which of the following is the most likely explanation?

- A. Allergic bronchopulmonary aspergillosis
- B. Hookworm infection
- C. Malaria
- D. Tropical pulmonary eosinophilia
- E. Drug reaction



Löffler's syndrome

- Fever, malaise
- Respiratory symptoms: none—mild—moderate
- Migratory pulmonary infiltrates
- Peripheral eosinophilia
- Migration of parasites
- Dx:
 - Larvae in respiratory specimen
 - Stool O & P
- Treatment
 - Anti-helminthics
 - Corticosteroids
 - May spontaneously resolve

Acute eosinophilic pneumonia

- Features
 - Fever, cough
 - Hypoxemia
 - Diffuse, bilateral infiltrates
 - Eosinophils
 - Peripheral BAL (> 10%)
 - Lung biopsy
- Drug causes:
 - Antibiotics:
 - Daptomycin
 - 38 reported cases (2018)
 - Wate, elderly
 - Renal failure
 - Black box warning
 - Nitrofurantoin
 - Minocycline
 - Ampicillin
 - Sulfonamides
 - Others:
 - NSAIDs
 - Phenytoin
 - L-tryptophan


Uppal, Antimicrob Resist Infect Control 2016;5:55; Higashi, Intern Med 2018;57(2):253-258

Acute or chronic eosinophilic pneumonia

- Helminthic
 - Migration (Löffler's)
 - Ascaris
 - Hookworms
 - Strongyloides
 - Lung invasion
 - Paragonimiasis
- Tropical Pulmonary Eosinophilia
 - Wuchereria bancrofti
 - Brugia malayi
- Idiopathic hypereosinophilia
- Acute eosinophilic pneumonia
- Chronic eosinophilic pneumonia
- Allergic bronchopulmonary aspergillosis (ABPA)

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




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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

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	Limited FDA approvals, Expensive platforms needed	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

Viral Targets		
Adenovirus	Coxsackievirus HC41	Coxsackievirus B2/3
Cytomegalovirus CMV	Cytomegalovirus CC43	Human Herpesvirus 6
Human Rhinovirus/Enterovirus	Influenza A	Influenza A/H1N1
Influenza A/H3	Influenza A/H1-2009	Influenza B
Parainfluenza Virus 1	Parainfluenza Virus 2	Parainfluenza Virus 3
Parainfluenza Virus 4	Respiratory Syncytial Virus	
Bacterial Targets		
Streptococcus pneumoniae		
Chlamydia pneumoniae		
Mycoplasma pneumoniae		

Film Array
Multiplex, 20 pathogens
Results in 1 hr

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

Leons. *Front Microbiol*. 2016; 7: 448

Case 6

31F fever, cough, myalgia, headache, dyspnea over 1 week ago
• 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 (+)

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Case 6

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

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

Era of molecular diagnostics

- Increasing recognition of co-pathogens
 - Multiple viruses
 - Virus + bacteria
- Mixed infections:
 - Johansson CID 2010; 50:202
 - Pathogens detected: 67%
 - Mixed: 12%
 - Jain NEJM 2015;373:415
 - Pathogens detected: 38%
 - Mixed: 3%
- Still need to consider pathogens not in multiplex panels
- Positive values from asymptomatic controls
 - Especially viral
 - Prolonged shedding (especially immunocompromised)

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](#)