

# 44 – Pneumonia: Some Cases that could be on the Exam

Speaker: Paul Auwaerter, MD

**2020 INFECTIOUS DISEASE BOARD REVIEW**

**Pneumonia: Some Cases that Could be on the Exam**

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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

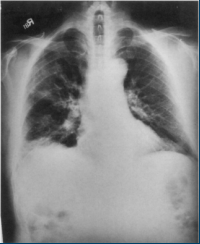
Exam: ill-toxic, 40°C P88  
BP100/70 RR18 O2 97% RA  
Lungs: clear  
Neck: supple  
Cor: no murmurs  
Skin: no rashes  
LP: pending  
Labs:  
WBC 5200, 26% B  
Sputum: 1+ PMNs, no organisms

### Disclosures of Financial Relationships with Relevant Commercial Interests

- Scientific Advisory Board – DiaSorin, Adaptive BioTherapeutics
- Grantee – MicroBplex, NIH/SBIR (Lyme disease diagnostics)
- Equity – JNJ

### Question 1

Which antibiotic will lead to the most rapid improvement?



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

### Community-acquired Pneumonia:

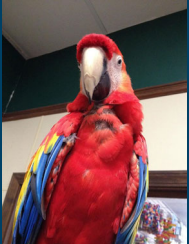
Pathogen <sup>1a</sup>	Cases (%)
<i>Streptococcus pneumoniae</i>	20-60
<i>Haemophilus influenzae</i>	3-10
<i>Staphylococcus aureus</i>	3-5
Gram-negative bacilli	3-10
<i>Legionella</i> species	2-8
<i>Mycoplasma pneumoniae</i>	1-6
<i>Chlamydia pneumoniae</i>	4-6
Viruses	2-15
Aspiration	6-10
Others	3-5

- Pathogen identification
  - 39-76% historically<sup>1</sup>
    - Culture
    - Serology
    - Antigen detection
    - Molecular methods
  - EPIC study (2015)<sup>2</sup>
    - Pathogen only detected in 38%
      - Viral 23% (rhinovirus 9%)
      - Bacterial 11%

<sup>1</sup>Mandell, et al. CID 2003;37(11):1405  
<sup>2</sup>Jain, et al. NEJM 2015;373:835

### *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



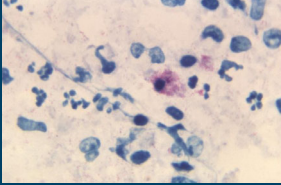
Hogenweir L et al. Epidemiol Infect. 2017;145(15):3096

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## Microbiology

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



May appear as intracellular Gram negatives

## 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 O<sub>2</sub>  
 No lymphadenopathy, no JVD  
 Lungs: poor air movement, basilar crackles bilaterally  
 Co: 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  
 CRP 15 mg/dL (0.0-0.5)      NI LFTs

## Chlamydia psittaci

- Range of illness:
  - Mild, bronchitic to severe/ARDS
  - Clue: temperature/pulse dissociation
- Diagnosis:
  - Molecular/PCR, sputum (best)
  - Acute/convalescent serology (microimmunofluorescence, MIF)
  - Culture: tissue culture (difficult)
- Treatment:
  - Preferred: doxycycline
  - Alternatives:
    - Macrolides
    - Fluoroquinolones

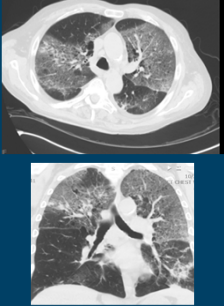


Woff BJ et al. Diagn Microbiol Infect Dis. 2018;9(3):167-170  
 Hogenwerf L et al. Epidemiol Infect 2017; 145(15):3098-3105

## 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.

## 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 <sup>+</sup>	-	-	-	++
Doxycycline response	Rapid, < 48h	Prompt	Prompt	Slower

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

## Acute eosinophilic PNA due to daptomycin

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

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## 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
    - Minocycline
    - Ampicillin
  - CV:
    - Amiodarone
    - Flecainide
  - Chemotherapy:
    - Bleomycin
  - Others
    - NSAIDs
    - Phenytoin

## 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

## 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

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

## 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

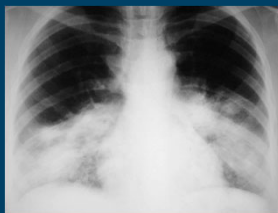


Culture media: BCYE agar  
Small, pearly white colonies

## 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?

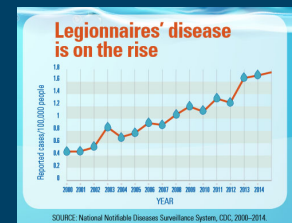
- Legionella urinary antigen
- Legionella culture of respiratory secretions
- Legionella PCR, respiratory
- Legionella direct fluorescent antigen (DFA) stain of respiratory sample
- Paired Legionella acute/convalescent serology



Pre-intubation CXR

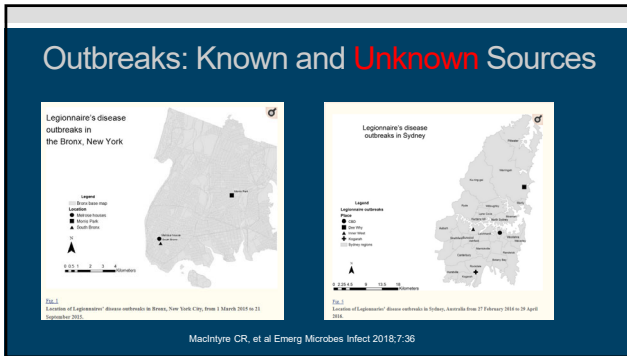
## Outbreaks: Known and Unknown Sources

- 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



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### 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: atovoquone/proguanil

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

SH: Laguna Phuket (Thailand) triathlon 3 wks earlier

Non-smoker

### 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	Unknown	Unknown	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, [cdc.gov/legionella/clinicians/diagnostic-testing](http://cdc.gov/legionella/clinicians/diagnostic-testing) (accessed 7/16/2019)

### Studies

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

CXR: mild bilateral patchy infiltrates

Blood smear: no parasites

	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%

Which of the following is the most likely explanation?

- Allergic bronchopulmonary aspergillosis
- Hookworm infection
- Malaria
- Tropical pulmonary eosinophilia
- Drug reaction

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## 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

## 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



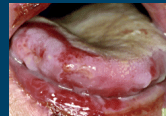
## Acute eosinophilic pneumonia

- Features
  - Fever, cough
  - Hypoxemia
  - Diffuse, bilateral infiltrates
  - Eosinophils
    - Peripheral
    - BAL (> 10%)
    - Lung biopsy
- Drug causes:
  - Antibiotics:
    - Daptomycin
      - 38 reported cases (2018)
      - Male, 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

## Case 5

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



## 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

What is the most likely etiology?

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

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## 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

## Case 6

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

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

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

Coarse breath sounds, rales bilateral and decreased L base

PMH: not significant  
SH: ½ ppd smoker

## 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

## 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 (+)

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

Viral Targets		
Adenovirus	Coronavirus NL63	Coronavirus NL63
Coronavirus 229E	Coronavirus OC43	Human Metapneumovirus
Human Rhinovirus/Enterovirus	Influenza A	Influenza A/H1
Influenza A/H3	Influenza A/H1N1 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%

## 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

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### Era of molecular diagnostics

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