

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

Speaker: Paul Auwaerter, MD



Pneumonia: Some Cases that Could be on the Exam

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Disclosures of Financial Relationships with Relevant Commercial Interests

- Consultant: Pfizer, EMD Serono
- Ownership Interest: Johnson & Johnson

Community-acquired Pneumonia:

Pathogen ^{1a}	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% historically¹
 - Culture
 - Serology
 - Antigen detection
 - Molecular methods
- EPIC study (2015)²
 - Pathogen only detected in 38%
 - Viral 23% (rhinovirus 9%)
 - Bacterial 11%

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

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

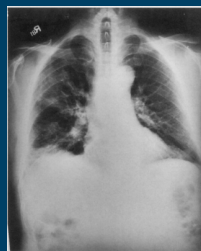
Exam: ill-toxic, 40°C P88
BP100/70 RR18 O2 97% RA
Lungs: clear
Neck: supple
Cor: no murmurs
Skin: no rashes
LP: pending
Labs:
WBC 5200, 26% B
Sputum: 1+ PMNs, no organisms

Question 1



Which antibiotic will lead to the most rapid improvement?

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



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



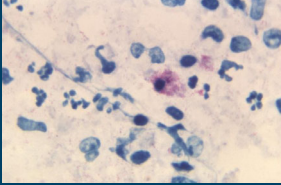
Hogerwerf L et al. Epidemiol Infect. 2017;145(15):3096

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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

Chlamydia psittaci

- Range of illness:
 - Mild, bronchitic to severe/ARDS
 - Clue:** temperature/pulse dissociation
 - Also seen with Salmonella typhi, 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
Hogenwerf 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) → Ceftaroline (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

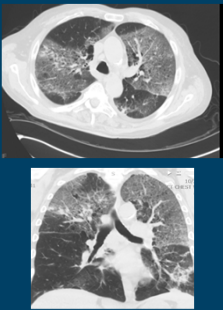
6.0 \times 9.5 \times 300K 54%^N, 12%^L, 24%^E

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.

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;51(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

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

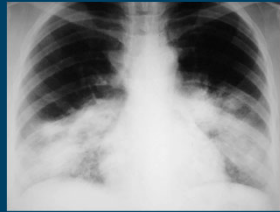
Therapy:
 Vancomycin and piperacillin/tazobactam x 3 d

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)

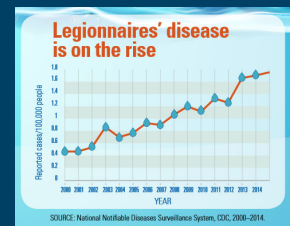
Legionella culture



Culture media: BCYE agar
 Small, pearly white colonies

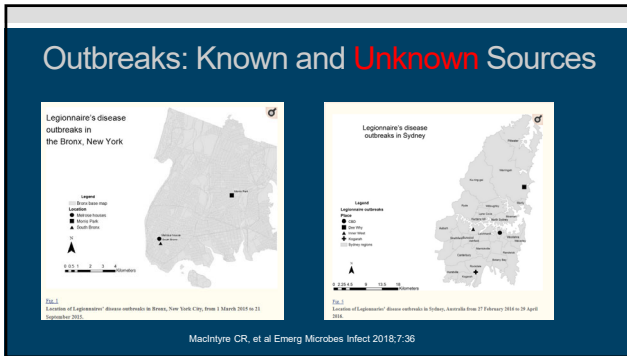
Outbreaks: Known and Unknown Sources

- 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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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)
Aron, J Clin Micro, 2016;54(2):401-11; Muddiyirama, 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: atovoquone/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

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

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

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

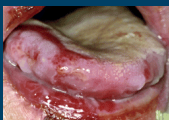


PREVIEW QUESTION



Case 5

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



PREVIEW QUESTION

Case 5

What is the most likely etiology?

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



PREVIEW QUESTION

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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

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	Coronavirus HCoV-229E	Coronavirus NL63
Coronavirus 229E	Coronavirus OC43	Human Metapneumovirus
Human Rhinovirus/Echovirus	Influenza A	Influenza AH1
Influenza AH3	Influenza AH1 2009	Influenza B
Parainfluenza Virus 1	Parainfluenza Virus 2	Parainfluenza Virus 3
Parainfluenza Virus 4	Respiratory Syncytial Virus	
Bacterial Targets		
Corynebacterium pertussis		
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

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

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

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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)