Pneumonia Potpourri

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

8/5/2025

1

Disclosures of Financial Relationships with Relevant Commercial Interests

- **Research:** Pfizer (investigational vaccine)
- **Consulting:** Medical-legal

2

Community-acquired Pneumonia: Meta-analysis Traditional Culture + PCR for "Atypicals" + Viruses

Pathogen	Total (%)*
None	4380 (61.3)
Pathogen detected	3279 (48.7)
Etiology Bacterial	
• *S. pneumoniae*	33%
• *H. influenzae*	8.6%
• *S. aureus*	4.9%
• *M. catarrhalis*	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

3

Community-acquired Pneumonia: Meta-analysis Traditional Culture + PCR for "Atypicals" + Viruses

Pathogen	Total (%)*
Etiology Viral & "Atypicals" And co-infections	
• *Mycoplasma pneumoniae*	8.9%
• *Legionella pneumoniae*	6.2%
• *C. pneumoniae*	2.9%
• *Pneumocystis*	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

4

Pneumonia Diagnostics

One commercially available PCR panel
- *Acinetobacter calcoaceticus-baumannii* complex
- *Enterobacter cloacae* complex
- *Escherichia coli*
- *Haemophilus influenzae*
- *Klebsiella aerogenes*
- *Klebsiella oxytoca*
- *Klebsiella pneumoniae* group
- *Moraxella catarrhalis*
- *Proteus* spp.
- *Pseudomonas aeruginosa*
- *Serratia marcescens*
- *Staphylococcus aureus*
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

Atypical Bacteria (Qualitative)
- *Chlamydia pneumoniae*
- *Legionella pneumophila*
- *Mycoplasma pneumoniae*

Viruses
- Adenovirus
- Coronavirus
- Human metapneumovirus
- Human rhinovirus/enterovirus
- Influenza A virus
- Influenza B virus
- Parainfluenza virus
- Respiratory syncytial virus

- Diagnostics for severe CAP and HAP/VAP
- What can be missed?
  - Molecular panels (examples)
    - Gram negatives
      - Stenotrophomonas
      - Citrobacter spp.
      - Other rare or nonspeciated Gram-negatives
    - Neisseria meningitidis
    - Atypical pathogens
      - Less sensitive
    - Tick-borne diseases and other less common causes
    - May miss polymicrobial cases
    - Fungal causes
      - Endemic fungi
      - Pneumocystis jiroveci
- Need clinical judgement to interpret both sputum culture and/or molecular tests (due to high sensitivity)

5

Question #1

PREVIEW QUESTION

IDBR INFECTIOUS DISEASE BOARD REVIEW 2025

- 35-year-old 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, 40ºC 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

6

Question #1

PREVIEW QUESTION

IDBR INFECTIOUS DISEASE BOARD REVIEW 2025

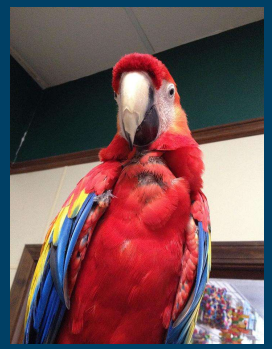
Which antibiotic will lead to the most rapid improvement?

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

7

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

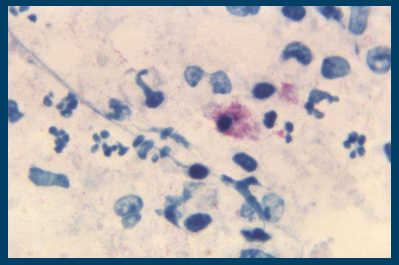


Hogerwerf L et al, Epidemiol Infect. 2017;145(15):3096

8

Microbiology

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



May appears as intracellular Gram negatives

9

Chlamydia psittaci

- Range of illness:
  - Mild, bronchitic to severe/ARDS
  - Clue: temperature/pulse dissociation
  - Also seen with Salmonella typhi, C burnetti, 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 Micrbiol Infect Dis 2018;90(3):167-170
Hogerwerf L et al, Epidemiol Infect 2017;145(15):3096-3105

10

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^+	-	-	-	++
Doxycycline response	Rapid, < 48h	Prompt	Prompt	Slower

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

11

Question #2

69-year-old M 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)

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, 02 sat 90% on 6L O_2
No lymphadenopathy, no JVD
Lungs: poor air movement, basilar crackles bilaterally
Cor: no murmur
Ext: no edema Skin: no rash

6.0 / 9.5 \ 300K 54%^{N}, 12%^{L}, 24%^{E}

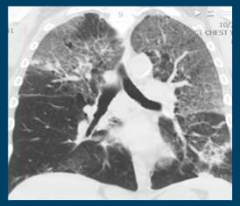
ESR 150 mm/hr NI LFTs
CRP 15 mg/dL (0.0-0.5)

12

Question #2

Which of the following is the most likely cause for the pneumonia?

A. Vaping-associated pulmonary injury (VAPI)
B. Allergic bronchopulmonary aspergillosis
C. Ceftaroline
D. Daptomycin
E. Strongyloides



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

13

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_2] <90% on RA or PaO_2 <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

14

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

15

Question #3

67-year-old M 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

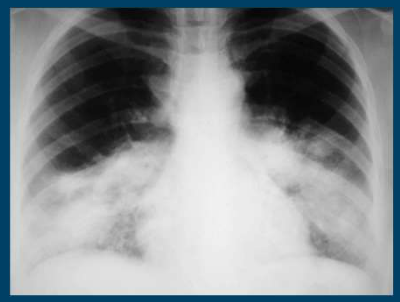
16

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?

A. Legionella urinary antigen
B. Legionella culture of respiratory secretions
C. Legionella Pneumonia Plus Film Array Panel (FDA-approved)
D. Legionella direct fluorescent antigen (DFA) stain of respiratory sample
E. Paired *Legionella pneumophila* acute/convalescent serology



Pre-intubation CXR

17

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

18

Legionella

- Environmental/water pathogen
  - Ponds, lakes
  - Water systems (hot > cold), chillers, misters, A/C
  - May be a 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)

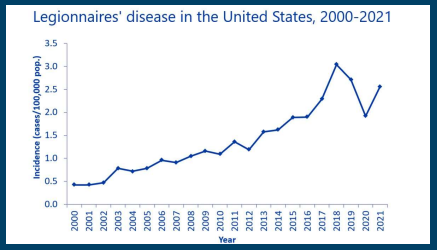
Legionella culture

Culture media: BCYE agar
Small, pearly white colonies

19

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



https://www.cdc.gov/legionella/php/surveillance/index.html (accessed 5/18/25)

20

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 *L. pneumophila* serogroup 1, rapid, may cross-react occasionally w/ other serogroups
PCR	95-99	99	FDA approved (2022) in some LRTI multiplex arrays, specific for *L. pneumophila.* Home brew/LDTs may offer broader *Legionella* spp. coverage
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; Muldyermans, Eur J Clin Microbiol Infect Dis 2019 *CDC preferred tests, obtain both in suspected patients

21

	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 %

22

Question #4

22-year-old M 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.

(+) fatigue, myalgia

PMH: negative

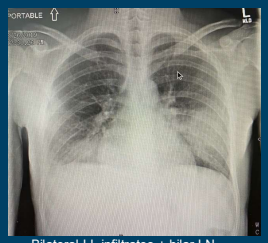
SH: Occasional MJ

PE: Appears ill, BP 98/70, P 110
T 39.5ºC, PaO_2 = 94%
No lymphadenopathy
Bronchial breath sounds lower fields with crackles bilaterally
No murmur
No hepatosplenomegaly, abdominal tenderness
No rash

23

Question #4

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



Bilateral LL infiltrates + hilar LN

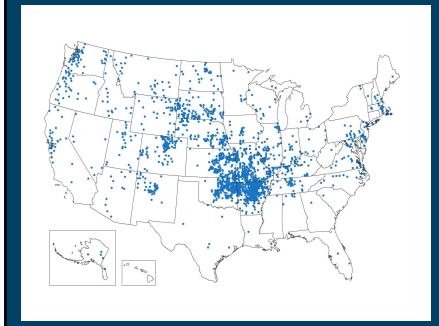
Consultant. 2020;60(11):27-29.

Which testing approach is most likely to confirm a diagnosis?

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

24

Francisella tularensis

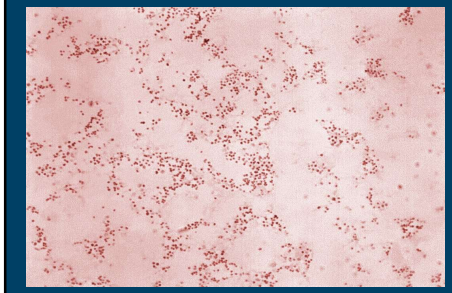


CDC Tularemia reported cases 2011-2020

- 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

25

Francisella tularensis



Gram stain photomicrograph, CDC

- 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

26

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

27

Question #5

- 18-year-old F c/o fever, dry hacking cough, malaise x 3d
- Allergy: erythromycin (N/V)
- Appears well, T38ºC, RR 16, P 80, BP 110/70
  - Oropharynx: normal
  - TMs: normal
  - Chest: some crackles left lower lobe

28

Question #5

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

29

Question #5

What is the most likely etiology?

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

30

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

31

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

32

Question #6

31-year-old F 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

33

Question #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 (+)

34

Question #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

35

Question #7

45-year-old M shepherd presents with 5d of dry cough, HA, fever and malaise in March

PMH: none

SH: Colorado, non-smoker. Helped with lambing in the past two weeks.

PE: RR 18 T101°F P90 BP 110/70

Non-toxic appearing

Chest: bibasilar rales

Labs: AST 58 ALT 89

CXR: bilateral patchy infiltrates

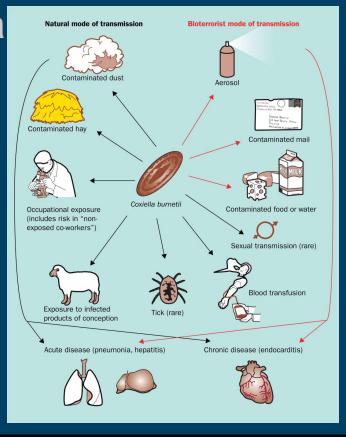
What antimicrobial would be the most appropriate?

A. Amoxicillin/clavulanate
B. Fluconazole
C. Gentamicin
D. Doxycycline
E. Ceftriaxone

36

Acute Q Fever Pneumonia

- *Coxiella burnetii* ~175 cases in US, 80% acute
  - Intracellular pathogen
  - Primary reservoirs: cattle, sheep, goats
  - Acquire by inhaling contaminated dust from feces, urine, birth material
  - Risk factors: male, living in or near an active ranch, drinking raw milk



Madariaga MG Lancet ID 2003;3(11):709

37

Q fever pneumonia

Diagnosis

- Two antigenic phases produce different antibodies
  - Phase I: antibodies associated with chronic infection.
  - Phase II: antibody responses are seen in acute infection.
- Acute disease (e.g., pneumonia): seroconversion or anti-Phase II Ab > Phase I.
  - Definitive: serology + whole blood PCR.

Treatment

- First-line treatment
  - Doxycycline (IV or PO)
- Alt: macrolides + rifampin, fluoroquinolones
- Note: post-infectious fatigue >6 months in 10%

MMWR 2013;62:1-30

38

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

39