



Pneumonia

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Disclosures of Financial Relationships with Relevant Commercial Interests

- Research: Pfizer (investigational Lyme disease vaccine)
- Consulting: medical-legal, Tonix Pharmaceuticals, Tarsus Pharmaceuticals

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%

Shoar and Musher, Pneumonia (2020) 12:11

- 12 Modern studies
 - 2005-2019
 - Inpatient n = 4399
 - In & outpatient = 2752
 - Outpatient = 04
- Hospital mortality: 12-15%

*Etiologic agents percentages

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%

Shoar and Musher, Pneumonia (2020) 12:11

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

*Etiologic agents percentages

Question #1

- 67M c/o fever, slightly productive cough and dyspnea x 10 days
 - Received rituximab 2 mos earlier for granulomatosis with polyangiitis
 - On prednisone 40 mg daily
- All: sulfa (rash), azithromycin (n/v)
- **PMH:** HTN, HLD
 - **SH:** Non-smoker, Baltimore resident, retired, no pets
 - **Meds:** lisinopril, atorvastatin, dapsons
- T101.4°F, P 106, RR 24, O2 sat 88% RA
 - No lymphadenopathy, no JVD
 - Lungs: basilar crackles bilaterally
 - Cor: no murmur
 - Ext: no edema
 - Skin: no rash
- WBC 7,800/μL 85%N 5%L 5%M 4%E 1%B
 - sCr 1.0 mg/dL
 - UA non-active sediment
 - Methemoglobin %: normal
 - Sputum: Light PMNs, no organisms
 - Sputum Film array: negative

Question #1

Which of the following is the appropriate next step?

- A. Begin meropenem plus doxycycline
- B. Repeat sputum expectoration for dedicated *P. jirovecii* PCR
- C. Obtain BAL including *P. jirovecii* PCR
- D. Obtain serum galactomannan and begin voriconazole
- E. Increase prednisone to 60 mg daily



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PJP in Patients without HIV

- Lower organism burden in non-HIV patients
 - Scant sputum; microscopy may miss
 - Commercial film arrays don't assess for PJP
 - BAL PJP PCR ± serum β-D-glucan w/ suspicion
- May present as "CAP"
 - Include CAP pathogens, OIs
- Prophylaxis doesn't exclude PJP

References: Sarasombath PT et al. Front Microbiol. 2021;12:729193. Ramirez JA et al. Chest. 2020;158:1896–1911. Shoham S, Prone MVD. Emerging Transplant Infections. Springer; 2021:1183–1208. BIOPIRE FILMARRAY Pneumonia Panel target menu, bioMérieux.

Pneumonia Diagnostics

One commercially available PCR panel

- *Acinetobacter calcoaceticus-baumannii* complex
- *Enterobacter cloacae* complex
- *Escherichia coli*
- *Hemophilus 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* (only this species)
- *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 on expectorated sputum?
 - Molecular panels (examples)
 - Gram negatives
 - *Stenotrophomonas*
 - *Citrobacter* spp.
 - Other rare or non-specified 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 jirovecii*
 - Need clinical judgment to interpret both sputum culture and/or molecular tests (due to high sensitivity)

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Question #2

- 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, 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 #2

Which antibiotic will lead to the most rapid improvement?

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



Question #2

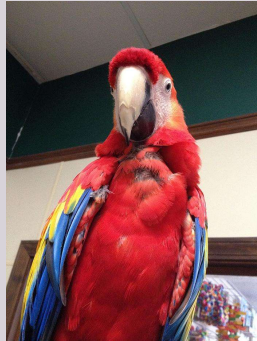
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Chlamydia psittaci

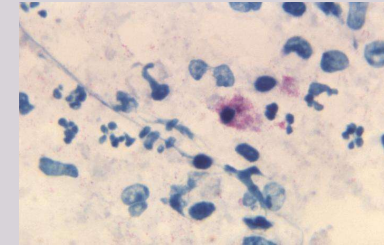
- AKA parrot fever, psittacosis, ornithosis
- Underdiagnosed
 - 1.03 % in studies of CAP
 - < 50 cases/yr in US
 - Most “atypical pneumonia”
- Risks: exposure to birds
 - May be healthy or ill
 - Pets, poultry, pigeons
 - Native birds
 - Lawn mowing



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

Microbiology

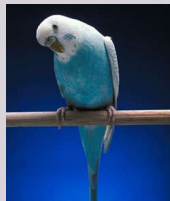
- Two states:
 - Extracellular: infectious, elementary body
 - Bird feces or respiratory secretions → aerosol → human
 - Direct contact
 - Intracellular: replicative



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

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

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
 - 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

Labs

- WBC 18,000 15%^B, 60%^P
- Glucose 310 Na 128 sCr 1.7
- AXR: no ileus

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

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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 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)

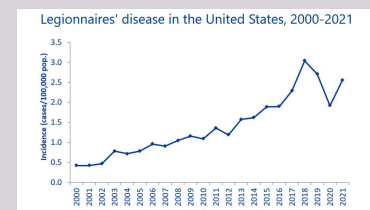
Legionella Culture



Culture media: BCYE agar
Small, pearly white colonies

Outbreaks: Known and Unknown Sources

- 8,442 cases in '21 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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<https://www.cdc.gov/legionella/php/surveillance/index.html> (accessed 7/18/26)

Legionella Diagnostics

Test	Sensitivity (%)	Specificity (%)	Notes
Culture*	20-80	100	Slow, technically difficult on BCYE agar Detects all species/serotypes
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> . Home brew/LDTs may offer broader <i>Legionella</i> 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 7/18/26)
Avni, J Clin Micro. 2016;54(2):401-11; Mulderymans, 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 the organism by culture Acute/convalescent serology Dx by epidemiology/serology
Mortality	10-30%	0 %

Question #4

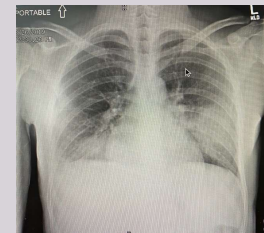
- 22-year-old M landscaper who mows lawns in Ozarks of Arkansas has 5 days of fever, chills and dry cough presenting in early July. He has run over several animal burrows with the mower.
- (+) fatigue, myalgia
- PMH: negative
- SH: Occasional MJ
- PE: Appears ill, BP 98/70, P 110
- T 39.5°C, PaO₂ = 94%
- No lymphadenopathy
- Bronchial breath sounds lower fields with crackles bilaterally
- No murmur
- No hepatosplenomegaly, abdominal tenderness
- No rash

Question #4

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*

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.

Question #4

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*

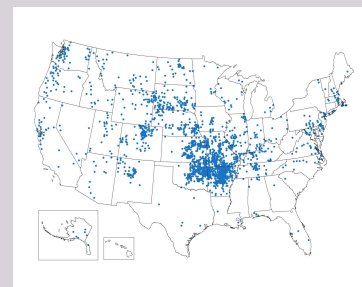
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CK 3280 U/L



Bilateral LL infiltrates + hilar LN

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

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

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

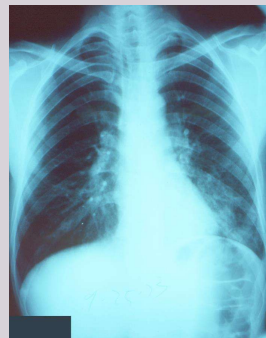
Francisella tularensis

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

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

Question #5

- 18-year-old F 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



Question #5

- Azithromycin prescribed
- Following day, develops severe painful oral erosions, hemorrhagic lip crusting, and bilateral conjunctivitis with targetoid vesicles on extremities



Question #5

What is the most likely etiology?

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

Question #5: More than “Walking Pneumonia”

What is the most likely etiology?

- A. *Mycoplasma pneumoniae**
- B. Enterovirus D68
- C. Measles
- D. Lyme disease
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Mycoplasma pneumoniae

- “Walking pneumonia”
 - CXR: appears worse than the patient
- ~25% may have extra-pulmonary manifestations
 - *M. pneumoniae*-induced rash and mucositis (MIRM)
 - MIRM/RIME (reactive infectious mucocutaneous eruptions):
 - Prominent oral, ocular, or genital mucositis with sparse vesiculobullous or targetoid skin lesions; may resemble SJS/TEN.
 - Most common infectious cause (children/adolescents)
 - Male > female
 - Often ≥ 2 involved mucosal sites
 - 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	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

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

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 (+)

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

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- E. **Attempt aspiration of left pleural fluid, start linezolid***



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

Question #7

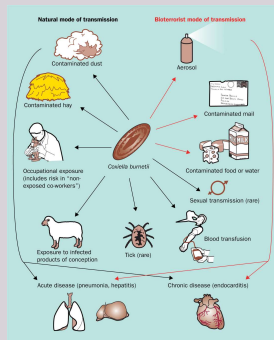
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- B. Fluconazole
- C. Gentamicin
- D. Doxycycline***
- E. Ceftriaxone

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



SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

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

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

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