Atypical Pneumonia

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📌 Pneumonia

🔘 Definition

- Pneumonia = Inflammation of alveoli and interstitium of lungs due to infective origin → consolidation occurs.

- Alveoli become filled with:

  - Inflammatory exudates
  - Bacteria
  - WBCs

    → Appears as opaque shadows on chest X-ray.

🔷 Classification of Pneumonia

1. Community-acquired pneumonia (CAP)

2. Hospital-acquired pneumonia (HAP) / Healthcare-associated pneumonia (HCAP)

3. Ventilator-associated pneumonia (VAP)

4. Opportunistic pneumonia

Etiology

1 Community-Acquired Pneumonia (CAP)

Bacteria:

- *Streptococcus pneumoniae* (most common)
- *Haemophilus influenzae*
- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Coxiella burnetii* (Q fever)
- *Haemophilus parainfluenzae*
- *Moraxella catarrhalis*
- *Staphylococcus aureus* (esp. post-viral)
- *Legionella pneumophila*

Viruses:

- Respiratory syncytial virus (RSV)
- Influenza, Parainfluenza
- Adenovirus
- Coronavirus (incl. COVID-19)

2 Hospital-Acquired Pneumonia (HAP / HCAP)

- *Enterobacteriaceae* (E. coli, Klebsiella)
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus* (including MRSA)
- *Acinetobacter baumannii*

3 Ventilator-Associated Pneumonia (VAP)

- *Acinetobacter sp.*
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus* & MRSA
- *Enterobacteriaceae*
- *Candida sp.*
- *Aspergillus sp.*
- *Haemophilus sp.*

📊 Typical vs. Atypical Pneumonia (Comparison Table)

Feature	Atypical Pneumonia ◌	Typical Pneumonia ◍
Etiology	*Mycoplasma pneumoniae, Legionella pneumophila, Chlamydia pneumoniae,* viruses, fungi, protozoa	*Streptococcus pneumoniae, H. influenzae, Klebsiella pneumoniae,* mixed oral flora
Onset	Gradual	Abrupt
Cough	Dry	Productive
Sputum	Scanty, mucoid	Purulent

Extrapulmonary symptoms	Prominent (myalgia, fatigue, nausea, vomiting, diarrhea)	Usually absent

✵ Atypical Pneumonia

◈ What is it?

- Infection of pulmonary parenchyma by atypical pathogens.
- "Does not resemble pneumococcal pneumonia."
- Usually community-acquired.
- Does not respond to usual antibiotics.
- Causes a milder form of pneumonia → "Walking Pneumonia."
- Gram stain: usually negative (exception: *Legionella*).
- Conventional cultures: negative.

◈ Clinical Features

- Gradual onset

- Dry / nonproductive cough (sometimes with scanty, whitish, non-bloody sputum)
- Sore throat, ear pain possible
- Constitutional symptoms: fever, headache, malaise, myalgia
- Chest X-ray: Interstitial infiltrates (diffuse, patchy)
- Recovery: spontaneous in 10–14 days

◈ Chest Examination

- Findings do not correlate with X-ray (disproportionately mild on auscultation compared to radiology).
- Edema + exudation → alveolo-capillary block → respiratory distress.

Etiological Agents of Atypical Pneumonia

Classical Causes:

1. *Mycoplasma pneumoniae*

2. *Chlamydia pneumoniae*

3. *Legionella pneumophila*

Other Causes:

4. *Chlamydia psittaci* (bird exposure)

5. *Coxiella burnetii* → Q fever

6. Viruses:

   - Influenza virus
   - RSV
   - SARS-CoV, MERS-CoV, COVID-19 coronavirus
   - Adenoviridae
   - Varicella (chickenpox pneumonia)

⚠ Risk Factors for Atypical Pneumonia

- Person-to-person spread (esp. *Mycoplasma, Chlamydia*)

- Closed populations: schools, offices, military barracks 🏫
- *Legionella*: fresh water & man-made water systems (air conditioning, whirlpools, respiratory equipment, cooling towers)
- Young, otherwise healthy individuals 🧒🎓
- Cigarette smoking 🚬
- Pre-existing lung disease (e.g., COPD)
- Weakened immunity (e.g., steroids, HIV)

📌 Flowchart: Types of Pneumonia by Source

Infective Agent

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Community-Acquired Pneumonia (CAP)

→ Bacteria (*S. pneumoniae, H. influenzae, Mycoplasma,*

Chlamydia, Legionella)

→ Viruses (RSV, Influenza, Coronavirus, Adenovirus)

Hospital-Acquired Pneumonia (HAP/HCAP)

→ *Enterobacteriaceae, Pseudomonas, MRSA, Acinetobacter*

Ventilator-Associated Pneumonia (VAP)

→ *Acinetobacter, Pseudomonas, MRSA, Candida, Aspergillus, Enterobacteriaceae*

📌 Mycoplasma pneumoniae

◈ General Characteristics

- Smallest free-living organism (0.3 μm).
- No cell wall → resistant to β-lactam antibiotics (penicillins, cephalosporins).
- Poorly Gram-stainable.

- Cell membrane contains cholesterol (unusual for bacteria, resembles eukaryotic membranes).
- Requires lipids for growth on artificial media.
- Slow grower: visible colonies in ~1 week.
- Colonies show "fried-egg" appearance (raised center, thinner periphery).

◈ Pathogenesis & Mechanism of Inflammation

- Rod-shaped, tapered tip with specific adhesion proteins → attaches firmly to respiratory epithelium.
- No invasion, but:
    - Inhibits ciliary motion → epithelial necrosis.
    - Produces H_2O_2 → tissue injury.
- Only 1 serotype, but reinfection possible.
- Triggers autoantibody formation:

- Cold agglutinins (IgM against RBC I antigen) → hemolytic anemia.
- Autoantibodies against brain, lung, liver tissue.

◈ Laboratory Diagnosis

- Cold agglutinin test: IgM titer ≥ 1:128 → recent infection.
- Complement fixation test → confirmation.
- PCR & ELISA → specific & sensitive.

◈ Clinical Features

- Common cause of CAP in children & adults, especially in winter ❁.
- Accounts for 2–30% of adult pneumonia cases.
- Gradual onset: flu-like prodrome → headache, malaise, fever, sore throat.
- Dry, nonproductive cough.

- Physical signs are minimal compared to severity of symptoms.

- May involve multiple systems (extrapulmonary manifestations).

◈ Complications

- Neurological: aseptic meningitis, cerebellar ataxia, transverse myelitis, peripheral neuropathy.

- Hematological: hemolytic anemia due to cold agglutinins.

- Dermatological: erythema multiforme, erythema nodosum, urticaria.

- Cardiac: pericarditis, myocarditis.

- Joints: arthritis, arthralgia.

- GIT: nausea, vomiting, diarrhea, rarely pancreatitis.

📌 Flowchart: Mycoplasma pneumoniae Infection

Attachment to Respiratory Epithelium

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Inhibition of Ciliary Action + H_2O_2 release

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Epithelial Necrosis

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Inflammatory Response

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Autoantibodies (Cold Agglutinins, Organ-specific)

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Clinical Features → Respiratory symptoms + Extrapulmonary complications

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📌 Chlamydia Species

◈ General Characteristics

- Obligate intracellular bacteria (cannot synthesize ATP).

- Three important species infect humans:

  1. C. trachomatis
  2. C. pneumoniae
  3. C. psittaci

1 Chlamydia trachomatis

- Eye: conjunctivitis, trachoma (leading cause of preventable blindness worldwide).

- Respiratory: pneumonia in newborns (during delivery) & adults.

- Genital tract: urethritis, lymphogranuloma venereum.

- Most common bacterial cause of STD.

- Associated with Reiter's syndrome (autoimmune: arthritis, urethritis, conjunctivitis).

2 Chlamydia pneumoniae

- Infects humans only.
- Transmission: aerosol, person-to-person.
- Responsible for 5-15% of CAP.
- Reinfection common.
- Incubation: 3-4 weeks.

Clinical features:

- Gradual onset, may improve then worsen again.
- Initial URTI symptoms → bronchitis/pneumonia.
- Most cases mild or asymptomatic.
- Prolonged bronchitis with productive cough.
- Hoarseness + headache common.
- Fever uncommon.
- Symptoms may persist for weeks-months despite

therapy.

- Severity usually due to secondary infection or co-existing illness (e.g., diabetes).

Complications:

1. Sinusitis, otitis media
2. New-onset asthma after infection
3. Endocarditis, myocarditis

3 Chlamydia psittaci

- Causes Psittacosis (Ornithosis) = systemic infection often with pneumonia.
- Reservoir: birds (parrots, pigeons, poultry) & some mammals.
- Risk groups: pet shop workers, poultry workers.
- Respiratory features: fever, cough, dyspnea, myalgia, headache.

- Systemic involvement:
    - CNS: hearing loss, transverse myelitis, meningoencephalitis.
    - CVS: culture-negative endocarditis, myocarditis, pericarditis.
    - Liver: hepatomegaly, jaundice.

📊 Quick Comparison Table: Chlamydia Species

Species	Diseases	Natural Hosts	Mode of Transmission to Humans	Immuno logic Types	Diagnosis	Treatment
C. tracho matis	Urethritis Pneumonia Conjunctivitis Lympho – granuloma venereum Trachoma	Humans	Sexual contact Perinatal transmission	>15 types	Inclusions in epithelial cells (Giemsa stain) Immunofluore scence Cell culture	Doxycyclin e, Erythromy cin
C. pneu moniae	Atypical pneumonia	Humans	Respiratory droplets	1 type	Serologic test	Doxycyclin e
C. psittaci	Psittacosis (pneumonia)	Birds	Inhalation of dried bird feces	1 type	Serologic test (cell culture rarely done)	Doxycyclin e

📌 Legionella pneumophila

General Characteristics

- Discovered during 1976 Legionnaires' disease outbreak (American Legion convention).
- Aerobic, motile, non-encapsulated, faintly Gram-negative bacilli.
- Requires iron + cysteine for growth → explains initial culture failure.
- Incubation period: 2–10 days.
- Causes:
    - Legionnaires' disease → severe atypical pneumonia.
    - Pontiac fever → mild flu-like illness without pneumonia.

Epidemiology

- Associated with environmental water sources:
    - Air conditioners

    - Cooling towers
    - Hospital water taps, sinks, showers

- Replicates inside free-living amoebae → enhances survival.

- Amoebae can encyst → protect Legionella in harsh conditions.

- No person-to-person spread (important distinguishing feature).

🧬 Pathogenesis

- Portal of entry: Respiratory tract (inhalation of aerosols).

- In severe cases → bacteremia.

- Virulence factor: Lipopolysaccharide (endotoxin).

- Causes vascular endothelial damage (esp. in brain, kidneys).

- Host defense: Cell-mediated immunity crucial.

- Risk factors:
    - Older men, smokers 🚬, alcoholics 🍺
    - Immunocompromised (AIDS, cancer, transplant, corticosteroids).

🩺 Clinical Features

Spectrum:

- Mild form (Pontiac fever): flu-like, self-limited, no pneumonia.
- Severe form (Legionnaires' disease): atypical pneumonia.

Findings in severe disease:

- Mild influenza-like prodrome: headache, myalgia.
- Pneumonia with systemic features:
    - Mental confusion 😵
    - Non-bloody diarrhea 💩

    - Proteinuria + microscopic hematuria (renal involvement).
    - Hyponatremia ($Na^+ \leq 130$ mEq/L) → characteristic clue.

- Respiratory: minimally productive cough, dyspnea, pleuritic chest pain, hemoptysis.

- Symptoms resolve in 7–10 days (mild cases).

Extrapulmonary involvement:

- CVS: myocarditis, pericarditis, endocarditis ♡

- Renal: glomerulonephritis

- GIT: pancreatitis, peritonitis

- Neurological: focal deficits, encephalopathy

Diagnosis

- Chest X-ray: nonspecific, cannot reliably distinguish from other pneumonias.

- Physical chest signs minimal (disproportionately mild).
- Lab diagnosis:
  - PCR (most sensitive).
  - Serology/culture (need iron & cysteine, rarely available in routine labs).
- Diagnosis often clinical → treated empirically as atypical pneumonia.

💊 Treatment

- First-line: Macrolides (azithromycin, clarithromycin).
- Erythromycin: less tolerated, limited efficacy.
- Severe cases: Rifampicin + macrolide.
- Alternatives: Tetracyclines (doxycycline), fluoroquinolones.
- Duration: 2–3 weeks (longer than typical CAP due to intracellular persistence).

📊 Table: Legionella vs Other Atypical Pneumonias

Feature	Legionella pneumophila	Mycoplasma pneumoniae	Chlamydia pneumoniae
Reservoir	Water sources (AC, showers, cooling towers)	Human-to-human	Human-to-human
Transmission	Aerosol from environment	Droplet/contact	Droplet/contact
Onset	Moderate (2–10 days)	Gradual	Gradual
Special Clues	Hyponatremia, diarrhea, confusion	Cold agglutinins, rash, CNS	Hoarseness, prolonged bronchitis
Spread	No person-to-person	Yes	Yes
Therapy	Macrolides ± rifampicin, fluoroquinolones	Macrolides, tetracyclines	Macrolides, tetracyclines

📌 Flowchart: Clinical Spectrum of Legionella Infection

Exposure to Contaminated Water Source

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Inhalation of Aerosolized Bacteria

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Replication inside Macrophages + Amoebae

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Two Clinical Outcomes:

1. Pontiac Fever

→ Mild, flu-like illness
→ No pneumonia
→ Resolves spontaneously

2. Legionnaires' Disease

→ Severe atypical pneumonia
→ CNS, renal, GIT, CVS involvement
→ Hyponatremia, confusion, diarrhea
→ Requires antibiotic therapy