Infections Due to Mycoplasmas

Chapter 193 | Part 5 – Infectious Diseases: Bacterial

KEY CLINICAL POINTS

1. Mycoplasmas are the smallest organisms capable of independent replication (150–350 nm) and lack a cell wall.
2. Absence of a cell wall renders beta-lactam antibiotics (penicillins, cephalosporins) ineffective.
3. M. pneumoniae is the most frequently detected 'atypical' organism in community-acquired pneumonia in adults.
4. Macrolide resistance in M. pneumoniae is high in Asia (34–76%) and rising in the US (10.2% in 2018).
5. Treatment of acute M. pneumoniae pneumonia with macrolides significantly shortens duration of fever and cough.
6. Corticosteroids are not routinely recommended but may be considered for severe or macrolide-refractory cases.
7. Erythema multiforme major (Stevens-Johnson syndrome) is the most clinically significant skin eruption associated with M. pneumoniae.
8. M. pneumoniae pneumonia is often self-limited, but appropriate antimicrobial therapy significantly reduces morbidity.
9. Urogenital mycoplasmas are associated with genitourinary tract disorders and neonatal infections.
10. Diagnosis relies on PCR of respiratory secretions or serology (paired acute and convalescent samples).

1. DEFINITION & OVERVIEW

- **Classification:** Prokaryotes of the class Mollicutes
- **Size:** 150–350 nm (among the smallest prokaryotic genomes)
- **Cell Wall:** Absent; bound only by a cell membrane
- **Resistance:** Inactive to beta-lactams (penicillins, cephalosporins) due to lack of cell wall
- **Nutrient Requirement:** Host for exogenous nutrients (amino acids, fatty acids, cholesterol)
- **Culture Requirements:** Requires complex fastidious media
- **Pathogenic Species:**
  - M. pneumoniae (Respiratory tract)
  - M. hominis (Genitourinary tract, neonatal infections)
  - M. genitalium (Genitourinary tract, neonatal infections)
  - Ureaplasma urealyticum (Genitourinary tract, neonatal infections)
  - Ureaplasma parvum (Genitourinary tract, neonatal infections)

2. EPIDEMIOLOGY

- **Incidence:** Upper respiratory illness occurs up to 20× more frequently than pneumonia
- **Transmission:** Respiratory droplets
- **Clinical Presentation Rate:** 80% of exposed individuals develop clinical disease
- **Incubation Period:** 2–4 weeks
- **Outbreak Settings:** Common in institutional settings (military bases, schools, summer camps)
- **Epidemiological Pattern:** Endemic with sporadic epidemics every 4–7 years
- **Intrafamilial Attack Rates:**
  - Children: Up to 84%
  - Adults: 41%

2.1 Prevalence Statistics

- **2002–2015 Studies (Adults):**
  - M. pneumoniae: 7.2%
  - C. pneumoniae: 4.3%
  - Legionella species: 2.8%
- **1996–2001 Studies (6207 adults):**
  - M. pneumoniae: 22.7%
  - C. pneumoniae: 11.7%
  - Legionella species: 4.6%

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3. PATHOGENESIS

- **Extracellular Behavior:** Generally acts extracellularly but may replicate within human cells
- **Attachment Mechanism:** Mediated by terminal organelle with adhesins and accessory proteins
- **Tissue Injury Mechanisms:**
  - Hydrogen peroxide production
  - ADP-ribosylating/vacuolating cytotoxin (similar to pertussis toxin)
  - Lipoproteins activate Toll-like receptors (TLR2) on macrophages
- **Immune System Interaction:**
  - Innate Immunity: Primary defense in lungs
  - Cellular Immunity: May exacerbate lung disease
  - Humoral Immunity: Prevents dissemination; immunodeficiency increases risk of disseminated infection (arthritis, meningitis)
- **Host Response:**
  - Lack of cell wall components (lipopolysaccharide, peptidoglycan) reduces innate immune stimulation
  - Lipoproteins activate TLR2 pathways
  - Lung biopsies show monocytic infiltrates and polymorphonuclear exudates

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4. CLINICAL FEATURES

- **Respiratory Manifestations:**
  - Symptoms: Pharyngitis, tracheobronchitis, reactive airway disease/wheezing, cough (most common; nonproductive), headache, malaise, chills, fever

– Physical Exam: Wheezes/rales in ~80% of patients with pneumonia

– Radiographic Findings: Peribronchial pneumonia (most common), thickened bronchial markings, interstitial infiltrates, subsegmental atelectasis, segmental/lobar consolidation, pleural effusions (up to 20% on lateral decubitus)

– Clinical Course: Resolution in 2–3 weeks without treatment; treatment shortens duration of symptoms; potential for long-term recurrent wheezing

- **Extrapulmonary Manifestations:**

– Dermatologic: Erythematous (macular/maculopapular), vesicular, bullous, petechial, urticarial rashes; Exanthem in 17% of patients with pneumonia

– **Most Clinically Significant Skin Condition:** Erythema multiforme major (Stevens-Johnson syndrome)

– Neurologic: Meningoencephalitis/encephalitis (5–7%), Guillain-Barré syndrome, aseptic meningitis, cranial neuropathy, acute psychosis, cerebellar ataxia, demyelinating disease, thromboembolic events, transverse myelitis

– Hematologic: Hemolytic anemia (week 2–3), aplastic anemia, cold agglutinins, DIC, hypercoagulopathy

– Other: Hepatitis, glomerulonephritis, pancreatitis, myocarditis, pericarditis, rhabdomyolysis, arthritis (septic/reactive)

– Septic arthritis: Common in hypogammaglobulinemic patients

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5. DIFFERENTIAL DIAGNOSIS

- **Atypical Pneumonia:**

– M. pneumoniae is the most frequently detected 'atypical' organism in adults

– Comparison: C. pneumoniae (4.3% in 2002–2015) and Legionella species (2.8% in 2002–2015)

– Key Differentiator: Failure to respond to penicillin/cephalosporin (beta-lactam resistance)

- **Otitis Media:**

– Little evidence supports M. pneumoniae as a significant cause of otitis media ◦ Associated condition: Bullous myringitis

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6. INVESTIGATIONS & DIAGNOSIS

1. **Respiratory PCR:**

→ Recommended for routine use

→ Sensitivity: 65–90%

→ Specificity: 90–100%

2. **Serologic Studies (ELISA):**

→ Requires paired acute and convalescent serum samples

→ Timing: Antibodies may not develop until week 2; IgM can persist up to 1 year

→ Sensitivity: 55–100%

→ Specificity: 55–100%

3. **Respiratory Culture:**

→ Not routinely used due to slow growth (weeks) and low yield

→ Sensitivity: ≤60%

→ Specificity: 100%

→ Use if resistance is suspected; available via culture/PCR

Table 193-1 Reference:

- Respiratory culture: Sensitivity ≤60%, Specificity 100%
- Respiratory PCR: Sensitivity 65–90%, Specificity 90–100%
- Serologic studies: Sensitivity 55–100%, Specificity 55–100%

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7. MANAGEMENT & TREATMENT

1. **Macrolides (First-line):**

→ Azithromycin: 500 mg day 1, then 250 mg/d days 2–5

→ Clarithromycin/erythromycin: 500 mg twice daily for 7–14 days

→ Note: High resistance in Asia (34–76%); rising in US (10.2% in 2018)

2. **Tetracyclines:**

→ Doxycycline: 100 mg twice daily for 7–14 days

3. **Fluoroquinolones:**

→ Levofloxacin/moxifloxacin: 500 mg once daily for 7–14 days

→ Gemifloxacin: 320 mg once daily for 7–14 days

→ Note: Ciprofloxacin and ofloxacin are not recommended (high MICs, poor efficacy)

4. **Corticosteroids:**

→ Not routinely recommended for community-acquired pneumonia

→ May be considered for severe or macrolide-refractory cases

5. **Urogenital Mycoplasmas:**

→ Azithromycin, clarithromycin, erythromycin, doxycycline

Table 193-2 Reference (Antimicrobial Agents of Choice):

- M. pneumoniae: Azithromycin, clarithromycin, erythromycin, doxycycline, levofloxacin, moxifloxacin, gemifloxacin (not ciprofloxacin or ofloxacin)
- Ureaplasma urealyticum/parvum: Azithromycin, clarithromycin, erythromycin, doxycycline
- Mycoplasma hominis: Doxycycline, clindamycin
- Mycoplasma genitalium: Azithromycin, moxifloxacin, doxycycline

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8. PROGNOSIS & COMPLICATIONS

1. **Resolution & Recovery:**

  – Symptoms typically resolve in 2–3 weeks without treatment
  – Appropriate therapy significantly reduces morbidity and shortens duration of fever/cough
  – Critical illness: Uncommon
  – Death: Rare

– Long-term: Recurrent wheezing may follow resolution

2. **Resistance Impact:**
   – Macrolide-resistant infections lead to longer symptom duration and reduced treatment efficacy
   – Resistance rates:
   – Asia: 34–76%
   – US (2018): 10.2%
   – Eastern US (2015–2018): 15.2–21.7%
   – Western US (2015–2018): 1.9–2.8%
3. **Extrapulmonary Complications:**
   – Erythema multiforme major, neurologic syndromes, and disseminated infection in immunocompromised patients

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9. SPECIAL CONSIDERATIONS

- **Immunocompromised Hosts:**
  – Higher risk for disseminated infection (arthritis, meningitis, osteomyelitis)
- **Urogenital Transmission:**
  – Associated with genitourinary disorders and neonatal infections

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10. KEY PEARLS & CLINICAL TRAPS

- **Structural Defect:** Lack of cell wall → inherent resistance to beta-lactams
- **Clinical Trap:** Non-specific symptoms (pharyngitis, cough) can lead to delayed diagnosis; do not underestimate potential for severe extrapulmonary manifestations like Erythema multiforme major.
- **Resistance Awareness:** Macrolide resistance is a significant factor in treatment planning, especially in Asia and the Eastern US.

REFERENCE TABLES

TABLE 193-1

Diagnostic Tests for Respiratory Mycoplasma pneumoniae Infection a TEST Respiratory culture Respiratory PCR Serologic...

TEST	SENSITIVITY, %	SPECIFICITY, %
Respiratory culture	≤60	100
	65–90	
Serologic studiesb	55–100	55–100

TABLE 193-2

Antimicrobial Agents of Choice for Mycoplasma Infectionsa

ORGANISM(S)	DRUGS
Mycoplasma pneumoniae	Azithromycin, clarithromycin, erythromycin, doxycycline, levofloxacin, moxifloxacin, gemifloxacin (not ciprofloxacin or ofloxacin)

ORGANISM(S)	DRUGS
Mycoplasma hominis	Doxycycline, clindamycin