Mycoplasma pneumoniae

Diagnosis and treatment for paediatric care providers

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Mycoplasma pneumoniae

What health-care providers need to know

The purpose of this document is to provide an overview of *Mycoplasma pneumoniae* diagnosis and treatment, as is relevant to the paediatric care provider.

How common are Mycoplasma pneumoniae infections and when do they usually occur?

Typically, *M. pneumoniae* season is late summer to fall when it is estimated to account for approximately 4-8% of community acquired pneumonia.[1] Rates usually decline as winter approaches at the start of viral respiratory season. Outbreaks (epidemics) occur every 3 to 7 years, when *M. pneumoniae* can account for up to 20-40% of community acquired bacterial pneumonia cases.[1]

Since the summer of 2024, an increase in *M. pneumoniae* infections has been noted in several jurisdictions, with the highest increase noted in children.[2] Both the number of confirmed *M. pneumoniae* cases and percent positivity has increased compared to both 2023 and prior to the COVID-19 pandemic.

What clinical syndromes are caused by Mycoplasma pneumoniae?

M. pneumoniae infection has a range of clinical presentations including asymptomatic colonization, mild respiratory disease, pneumonia, and extrapulmonary manifestations. Colonization can persist for weeks to months following infection; colonization rates as high as 50% have been reported during outbreaks.[3]

Mycoplasma pneumoniae most commonly affects the respiratory system and is a cause of atypical pneumonia in children. There are no clinical, laboratory, or chest x-ray findings that can **reliably** distinguish between "typical pneumonia" (*Streptococcus pneumoniae*, Group A Streptococcus) and atypical pneumonia. Features that have classically been associated with atypical pneumonia include[4]:

- Older age, ≥ 5 years old
- Subacute onset with constitutional symptoms (e.g., malaise, myalgia, headache, rash)
- Prominent and gradually worsening cough
- Minimal leukocytosis
- Nonlobar infiltrate
- Extrapulmonary manifestations or complications (e.g., polymorphous mucocutaneous eruptions, hemolytic anemia, hepatitis, pancreatitis, myopericarditis, encephalitis or meningitis or other immune-mediated neurological syndromes)

How is Mycoplasma pneumoniae infection *diagnosed?*

Mycoplasma pneumoniae testing is available, but molecular (PCR) detection cannot differentiate between disease and colonization. Children with pneumonia caused by *M. pneumoniae* can test positive – but so can asymptomatic children, or children with pneumococcal or viral pneumonia and *M. pneumoniae* colonization or co-infection.

In general, testing is indicated only if it will alter management. In settings where the turnaround time for results is long (e.g., >5-7 days), or follow-up may not be feasible (e.g., emergency department with high volume), an empiric treatment approach may be preferred over testing. See indications for empiric treatment below.

If PCR testing is being performed for *M. pneum*oniae, a throat swab is preferred over a nasopharyngeal swab.[5,6]

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Indications for Testing:

- Patients with pneumonia being admitted to the ICU with severe or life-threatening illness*
- Patient with pneumonia at high risk for complications (and where confirmed diagnosis may impact the need for further work-up). For example, immunocompromised hosts, underlying pulmonary disease (cystic fibrosis, asthma), sickle cell disease
- Diagnostic work-up for extra-pulmonary disease – recent or current respiratory symptoms with hemolytic anemia, encephalitis, arthritis or mucocutaneous disease (Reactive mucocutaneous eruption – RIME)
- Patients with suspected bacterial pneumonia (lobar), with worsening symptoms or persistent fever after 72 hours of beta-lactam therapy (testing or can consider empiric *M. pneum*oniae treatment)
- Patients with suspected viral or atypical infection with worsening symptoms after 72 hours, persistent fever for >5-7 days or persistent symptoms (excluding isolated cough) for more than 2 weeks not on antibiotics.**

*Consideration can be given to testing all hospitalized patients with pneumonia
**Testing for pertussis should also be considered for cough lasting 2 or more weeks without an apparent cause

How should Mycoplasma pneumoniae infection be treated?

It is difficult to quantify the benefit of antimicrobial treatment for most *M. pneumoniae* infections. Most patients recover **without antibiotics.**

If treatment is indicated, macrolides are first line for treatment. *Mycoplasma pneu*moniae is naturally **resistant** to beta-lactams (such as amoxicillin) that are commonly used to treat community-acquired pneumonia (CAP).

Macrolide-resistant *M. pneumoniae* varies by region. Rates as high as 80-90% have been reported in China. Latest estimates of macrolide resistance in Ontario are around 16%.[7] But surveillance is limited as testing is often not completed. Treatment of macrolide-resistant disease with macrolides generally results in only 1-2 days more fever than treatment of macrolide-sensitive disease with macrolides.

Community-acquired Pneumonia Management (See outpatient algorithm below)

- Amoxicillin remains the first line treatment for “typical bacterial pneumonia” as it covers *Streptococcus pneumoniae* and Group A Streptococcus, which tend to be more severe.
- Macrolide monotherapy should not be used in this situation, given high macrolide resistance amongst *Streptococcus pneumoniae* and Group A Streptococcus isolates.

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Indications for *Mycoplasma pneumoniae* directed therapy:

Empiric treatment:

- Children with community acquired pneumonia and worsening symptoms (excluding isolated cough) after 72 hours of beta-lactam therapy (testing or empiric treatment)
- Severe or life-threatening illness (e.g., admission to the ICU with pulmonary or extrapulmonary manifestations)
- Patients with suspected atypical pneumonia with persistent symptoms (excluding isolated cough) for more than 1-2 weeks where a household member has *M. pneumoniae* pneumonia or other *M. pneumoniae* conditions such as RIME or encephalitis.
- When testing is not available, consideration can be given to empirically treating individuals with a high clinical suspicion for *M. pneumoniae* infection (age > 5 years, subacute onset, non-toxic, prominent cough, minimal leukocytosis, nonlobar infiltrate, extrapulmonary manifestations (headache, sore throat, conjunctivitis, rash)

Confirmed infection (PCR positive) treatment:

- Persistent or severe symptoms (inpatients and outpatients)
- Patients at high risk for complications (e.g immunocompromised, sickle cell disease, asthma)
- Extrapulmonary manifestations*

*The role of treatment of immune-mediated extrapulmonary manifestations is unclear, but should be considered especially if respiratory symptoms are also present.

Antimicrobial Choice:

- *Mycoplasma pneumoniae* is resistant to antibiotics that inhibit cell wall synthesis (beta-lactam antibiotics); in addition, susceptibility testing is not done on isolates from PCR samples.
- ***Macrolides*** are the treatment of choice for *Mycoplasma pneumoniae* infections
    - Azithromycin is reasonable for confirmed infections or outpatient empiric treatment courses (better tolerated and shorter course).
    - Clarithromycin is preferred over azithromycin for empiric treatment due to less impact on resistance development. It has a shorter half-life which is helpful, especially if treatment will be discontinued based on a negative test.
    - Macrolide resistance in *Streptococcus pneumoniae* is up to 50% depending on the region and therefore should be used cautiously as monotherapy for CAP.
- ***Tetracyclines (i.e. doxycycline)*** and ***fluoroquinolones (i.e. levofloxacin)*** are second line agents that can be used for patients with confirmed *M. pneumoniae* infection where macrolides are contraindicated or there are worsening symptoms after 48-72 hours or inadequate response after 5 days.
- ***Levofloxacin and doxycycline*** are considered second line agents for the following reasons:
    - Macrolide antibiotics have a lower risk of severe adverse effects than fluoroquinolones and tetracyclines.
    - Fluoroquinolone overuse can lead to Gram negative resistance in the community, reducing the efficacy for treatment of ESBL infections, e.g, UTI.
    - For patients with non-responding pneumonia, particularly with hilar adenopathy, pulmonary tuberculosis (TB) must be considered. Fluoroquinolone monotherapy can lead to resistant strains of TB.
    - Suspensions are not commercially available for levofloxacin or doxycycline

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Dosing guidelines for select antimicrobials when indicated for community-acquired pneumonia (CAP):

Antimicrobial	Dosing Guidance	Treatment Duration	Additional Comments
Amoxicillin	40-90mg/kg/day divided TID or 80-90mg/kg/day divided BID	5 days	First line therapy for CAP
Clarithromycin	7.5 mg/kg/dose PO q12h (Dose limit: 1g/day)	7 days	
Azithromycin	10 mg/kg/dose PO q24h on Day 1 (Dose limit: 500 mg/dose), THEN 5 mg/kg/dose q24h (Dose limit: 250 mg/dose) for 4 days	5 days	
Levofloxacin	≥6 months and <5 years – Levofloxacin 10 mg/kg/dose PO/IV q12h (Dose limit: 750 mg/dose) ≥5 years –Levofloxacin 10 mg/kg/dose q24h PO/IV (Dose limit: 750 mg/dose)	7 days	No commercially available suspension.
Doxycycline	2mg/kg/dose PO q12h (Dose limit: 100mg/dose)	7 days	Typically reserved for children 8 years and older. No commercially available suspension.

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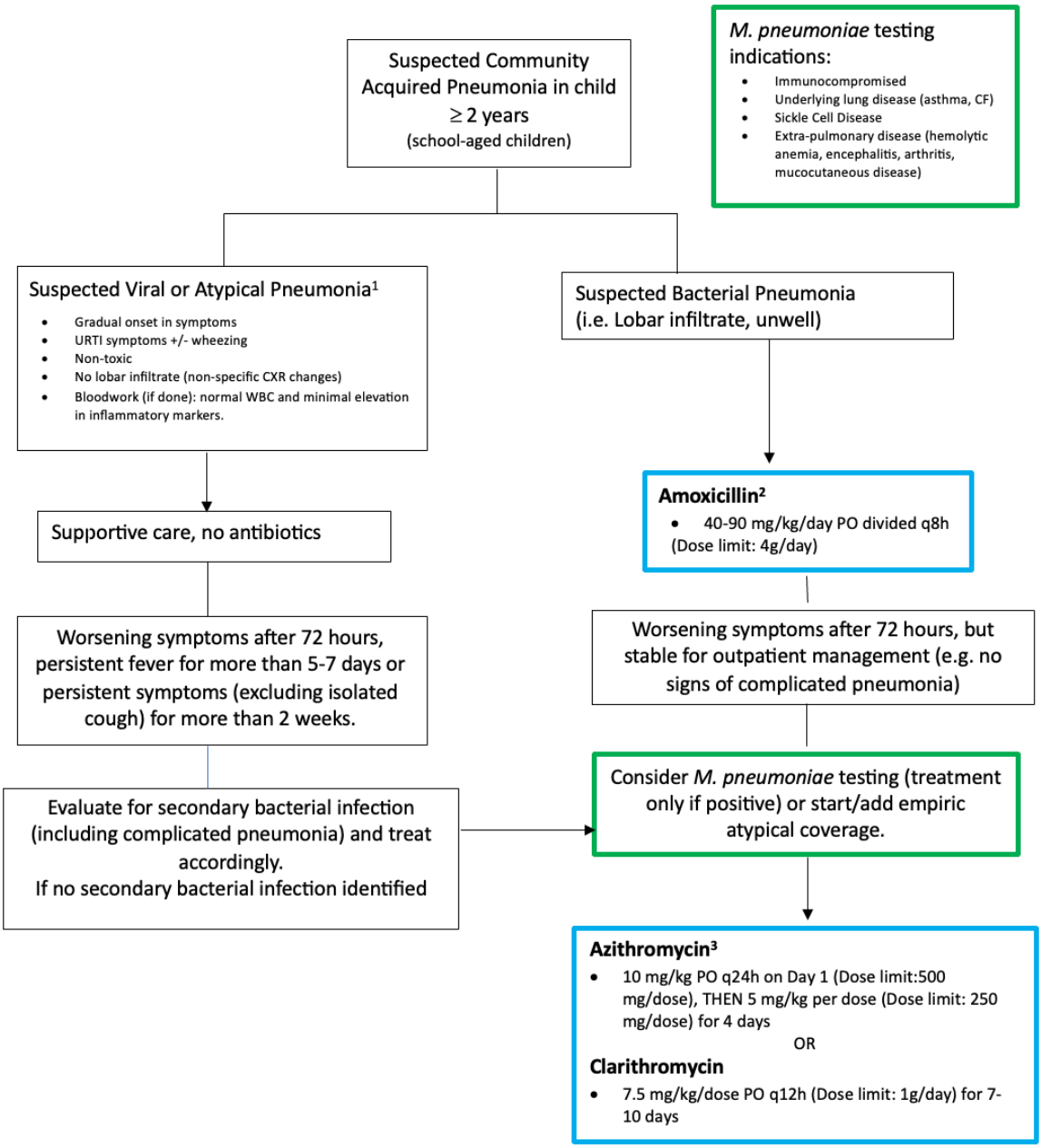
Community Acquired Pneumonia – Outpatient Management Algorithm



Key Points:

1. Most patients with a mild *M. pneumoniae* infection will recover **without antibiotics.**
2. Either **low dose amoxicillin** (40-50 mg/kg/day) or **high dose amoxicillin** (80-90 mg/kg/day) divided 3 times a day can be used in most jurisdictions as *Streptococcus pneumoniae* susceptibility to penicillin remains high. Alternatively, if twice a day dosing is prescribed, higher dose amoxicillin should be used (45 mg/kg/dose PO q 12 h, maximum 4 g/day)
3. **Macrolides** alone should not be used alone if *Streptococcus pneumoniae* is suspected due to high resistance rates (up to 50%)

Additional Treatment Considerations

Levofloxacin and **Doxycycline** should be reserved for patients with confirmed M. pneumoniae infections where IV therapy is needed (levofloxacin), there is severe disease, or lack of response after 48-72 hours of macrolide therapy (levofloxacin or doxycycline)
Amoxicillin/clavulanate would add coverage for infections with beta-lactamase producing organisms (e.g. Haemophilus influenzae, *Moraxella catarrhalis*) as well as methicillin susceptible *Staphylococcus aureus*, but these are less common causes of pneumonia in children.

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