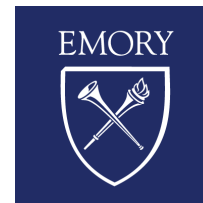



Mycoplasma: What, Where, When, & Why Now?

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Disclosures

- Received travel and lodging support to attend the International Scientific Association of Probiotics and Prebiotics international conference, Sitges, June 2022
 - Voting member of the FDA VRBAC
 - Receive a stipend for my role as Deputy Editor of *The Journal of the Pediatric Infectious Diseases Society (JPIDS)*
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Objective:

To describe the epidemiology, diagnostics, clinical manifestations, and management of *Mycoplasma pneumoniae* infections




History of *Mycoplasma*


- 1930s, noted people with respiratory symptoms that lasted for a longer duration, with less severity, and non-response to antibiotics
- 1944, scientists discovered an agent that causes “atypical” pneumonia and later named it *Mycoplasma pneumoniae*.
- “mycoplasma,” = Greek for “fungus-formed.”
- now known to be a bacterium that can survive and replicate external to cells, without a definite cell wall (implications for therapy)



***Mycoplasma pneumoniae* Epidemiology (1)**

- Infections occur sporadically, both endemic and epidemic, affecting all ages, with variable attack rates
 - Epidemics in late summer and fall; endemic - variation by year and geographical areas
 - *M. pneumoniae* associated with outbreaks in schools and congregate settings
 - Transmission occurs through inhalation of droplets or by direct contact; secondary cases among contacts being common
 - Incubation period 6 - 32 days and transmissibility can be extended up to 20 days; duration of immunity is unknown
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***Mycoplasma pneumoniae* Epidemiology (2)**

- **Cyclical increases in *M. pneumoniae* every 3 – 5 years due to changes in circulating strains**
 - **Mitigation measures of *COVID-19* pandemic = decline in *M. pneumoniae* detections**
 - **Autumn 2023, increase in *M. pneumoniae* infections in China and other countries**
 - **Data from CDC's National Syndromic Surveillance Program and the New Vaccine Surveillance Network showed an increase in *M. pneumoniae* in the United States beginning in fall 2023, though below pre-pandemic levels**
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***Mycoplasma pneumoniae* – Autumn 2023, Asia**

- **November 2023, China's respiratory disease surveillance system indicated an increase in outpatient consultations and pediatric hospital admissions for pneumonia due to *Mycoplasma pneumoniae* since May 2023 and for RSV, adenovirus, and influenza since October 2023**
- **Attributed increase to elimination of COVID-19 restrictions and the start of the winter season.**
- **Increase in respiratory disease activity occurred earlier than expected, no new or unusual pathogens**
- **The Korea Disease Control and Prevention Agency (KDCA) reported in November 2023 an increase in infections in children due to *M. pneumoniae***

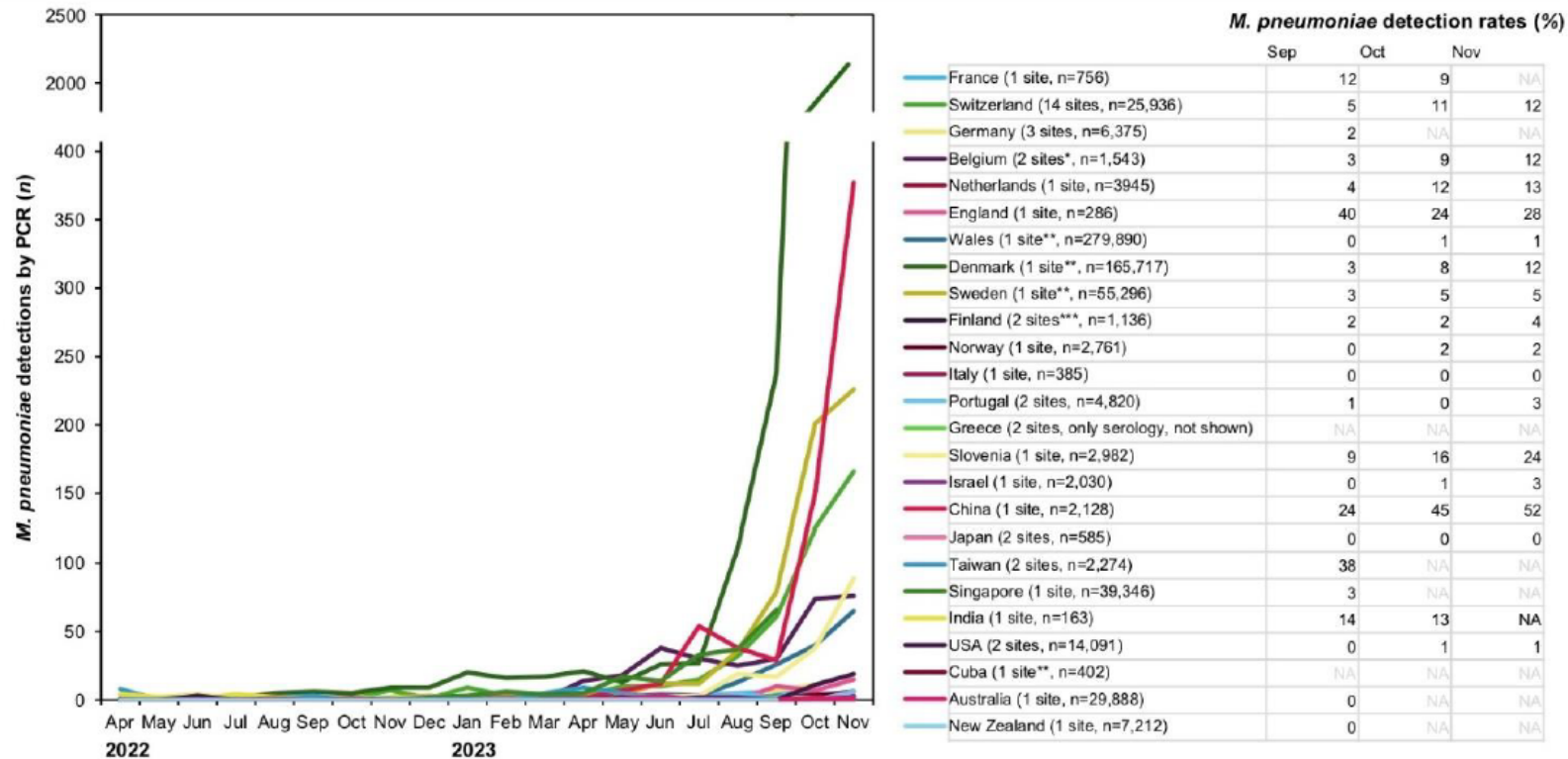


***Mycoplasma pneumoniae* – Autumn 2023, Europe**

- ECDC reported increases in *M. pneumoniae* detections in Denmark, France, Ireland, the Netherlands, Norway and Sweden in all age groups; predominantly among children and adolescents.
- French Public Health Agency reported unusual increases in respiratory infections from *M. pneumoniae* were detected in schools and intensive care units in several regions
- The Statens Serum Institut of Denmark reported an epidemic increase in respiratory infections attributed to *M. pneumoniae*, with 541 new cases in late November 2023; national epidemics occurring every four years, mainly affecting children aged 6 to 12 years in autumn and winter



Figure 1: Detection of *M. pneumoniae*, April 2022 to November 2023. Study Group for Mycoplasma and Chlamydia Infections – ESGMAC



Update: December 8, 2023. Please see previous publications for data after the implementation of non-pharmaceutical interventions against COVID-19 in March 2020, as well as detailed information on sites and reporting characteristics:

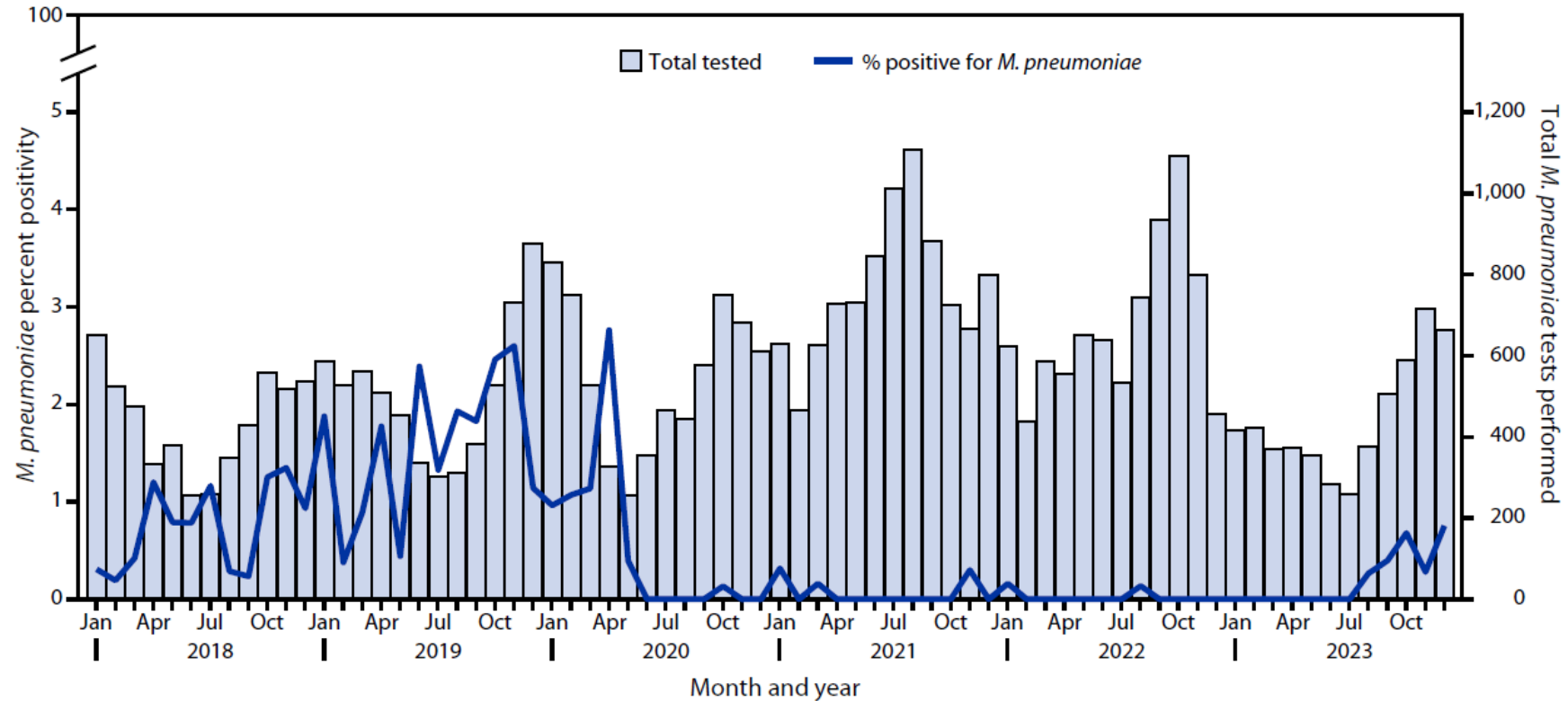
- **1st year** (Apr 1, 2020–Mar 31, 2021): [Euro Surveill. 2022 May;27\(19\):2100746](https://doi.org/10.1093/euro/27.19/2100746)
- **2nd year** (Apr 1, 2021–Mar 31, 2022): [Lancet Microbe. 2022 Dec;3\(12\):e897](https://doi.org/10.1016/j.lanmic.2022.12.012)
- **3rd year** (Apr 1, 2022–Mar 31, 2023): [Lancet Microbe. 2023 Oct;4\(10\):e763](https://doi.org/10.1016/j.lanmic.2023.04.010)
- **4th year** (Apr 1, 2023–Sep 30, 2023): [Lancet Microbe. 2023 Nov 23;S2666-5247\(23\)00344-0](https://doi.org/10.1016/j.lanmic.2023.11.003)

- * 1 site (national surveillance) with only positive test numbers (but not the total number of tests)
- ** National surveillance
- *** 1 site (national surveillance) with combined serology and PCR with no distinction possible between the detection methods (not shown)
- NA Data is coming soon


Source: European Society of Clinical Microbiology and Infections. Study of the international collaborative network established by the Study Group for Mycoplasma and Chlamydia Infections. Basel; ESCMID: ESGMAC MAPS; 2023. Disponible en: <https://www.escmid.org/research-projects/study-groups/study-groups-g-n/mycoplasma-and-chlamydia/esgmac-maps-study>

Mycoplasma pneumoniae Surveillance U.S.

FIGURE. Monthly number of *Mycoplasma pneumoniae* tests performed and percentage of positive test results among children and adolescents with acute respiratory illness — four sites, New Vaccine Surveillance Network, 2018–2023



***Mycoplasma pneumoniae* Pathophysiology**


- ***M. pneumoniae* prevents mucociliary clearance mechanisms from removal**
 - ***M. pneumoniae* damage the respiratory epithelial cells at the base of cilia → local cytotoxic effects**
 - ***M. pneumoniae* produce Community Acquired Respiratory Distress Syndrome (CARDS) toxin → colonization → inflammation and airway dysfunction**
 - **Residence on surface of the respiratory epithelial cells with ability to invade tissues and replicate intracellularly**
 - **Could lead to post-infectious or chronic complications**
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M. pneumoniae Diagnostics

- **Culture**: performed by reference laboratories; not valuable for clinical decision-making
- **Serological testing**: lacks specificity; acute and convalescent specimens
- **Molecular testing**: improved sensitivity and specificity over culture; results applicable in real time; most detect multiple respiratory organisms
- **Public health laboratories**: can type strains and perform antibiotic susceptibility.

***Mycoplasma pneumoniae* Clinical Presentations (1)**

- **Symptom onset often gradual progressing to more severe symptoms of fever and cough, dyspnea, dry cough → productive non-bloody sputum**
 - **Symptoms: headache, malaise, paroxysmal cough, sore throat**
 - **In addition, chest auscultation may show scattered or localized rhonchi and expiratory wheezes.**
 - **Duration of symptoms: days to months**
 - **Concurrent bacterial infection and rare post-infectious complications (CNS manifestations and Stevens Johnson syndrome); fatalities rare**
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***Mycoplasma pneumoniae* Clinical Presentations and Complications (2)**

- **Children < 5 years of age: subclinical symptoms**
 - **coryza, wheezing, without fever, diarrhea, and vomiting**
- **Exacerbation of asthma and severe pneumonia**
- **Non-pulmonary manifestations**
 - **Encephalitis**
 - **Hemolytic anemia**
 - **Renal dysfunction**
 - **Myalgias, arthralgias, or polyarthropathies**
 - **Septic arthritis**
 - **Skin disorders can include erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis**

Dermatologic Manifestations of *M. pneumoniae*




<https://dermnetnz.org/topics/mycoplasma-pneumoniae-infection>

***Mycoplasma*-Induced Rash with Mucositis (MIRM)**

- Mucosal eruption often with minimal skin changes, differs from Stevens-Johnson and erythema multiforme
- Average 12 years of age
- Oral, ocular, urogenital lesions
- Skin lesions vesiculobullous or target-like, and usually situated acraly, less frequent
- Classification of MIRM:
 1. Classic MIRM - atypical pneumonia with mucositis, plus a non-mucosal rash
 2. MIRM sine rash - atypical pneumonia with mucositis
 3. Severe MIRM - atypical pneumonia with mucositis (greater than 2 sites have been reported), - the cutaneous rash is extensive with widespread non-mucosal blisters or flat atypical target lesions.

***Mycoplasma pneumoniae* – Antimicrobials**

- Adequate antimicrobial treatment may decrease the duration of symptoms and may result in radiological and clinical improvement
 - Absence cell wall → resistance to beta lactam antimicrobials
 - Macrolides (azithromycin, clarithromycin) are recommended in children and adults
 - Alternatives include tetracyclines (doxycycline) for those over 8 years of age and quinolones (levofloxacin, moxifloxacin) in adults
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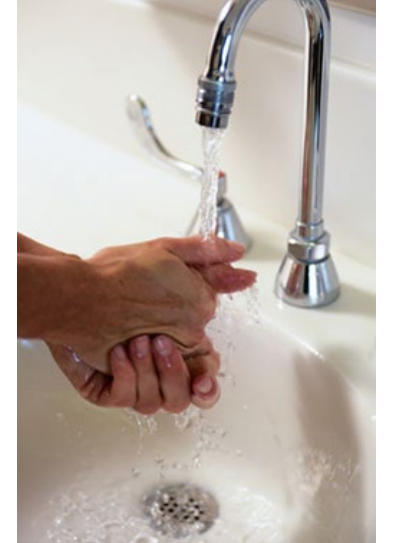
***M. pneumoniae* – Antimicrobial Resistance**

- **Resistance to macrolides has been emerging in *M. pneumoniae***
 - **Canada: About 12%**
 - **China: About 80%**
 - **Europe: 5- 20%**
 - **Japan: > 50%**
 - **United States: 10%**
- **Clinical correlations of longer duration of symptoms fever and cough with infections attributed to macrolide-resistant strains.**
- **Consider alternatives (e.g., doxycycline, levofloxacin, moxifloxacin) if concern for macrolide resistance**


<https://www.cdc.gov/pneumonia/atypical/mycoplasma/surv-reporting.html>

Infection Prevention

- 1. Spread through contact with droplets**
- 2. Hand hygiene**
- 3. Separation of symptomatic and asymptomatic**
- 4. Reduction in gathering, crowding**
- 5. Prophylaxis may be considered in group settings**



Take Aways

- 1. Consider *Mycoplasma pneumoniae* as an etiology of respiratory symptoms, especially during outbreaks**
 - 2. Consider extra-pulmonary post-infectious complications of *M. pneumoniae***
 - 3. Consider the addition of a macrolide for management and an alternative if non-response and/or concern for resistance**
 - 4. Hand hygiene is the mainstay of prevention along with separation of ill and well**
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