1. **What is *Mycoplasma pneumoniae* (Mp)?**

*Mycoplasma pneumoniae* (Mp) is one of three species of mycoplasma that cause infection in humans. Mycoplasmas are ubiquitous organisms and the smallest bacteria that can survive alone in nature. Mycoplasmas are fastidious and differ from other bacteria in that they lack a rigid cell wall, making them difficult to grow in culture. As a result, they are rarely grown in clinical laboratories.

2. **What is the epidemiology of *Mp***?

Recent studies suggest that *Mp* infections are much more common than previously recognized. Infection occurs most frequently during the fall and winter but may develop year-round. Epidemics of *Mp* occur every 3-7 years and vary in geographic size. Traditionally, *Mp* was thought to be primarily a disease of adolescents and adults, with historical data suggesting that *Mp* was responsible for up to 50% of community acquired pneumonia (CAP) in college students and military recruits. The organism is now recognized as a common cause of upper and lower respiratory tract infections in children and is a leading cause of bacterial CAP in school-aged children and adolescents in the United States.

3. **What are the clinical manifestations of *Mp***?

The most commonly recognized manifestation of *Mp* infections is respiratory disease. The majority of younger children with *Mp* infections may be asymptomatic or experience only mild respiratory symptoms (fever, malaise, upper respiratory congestion, pharyngitis, otitis media, and/or tracheobronchitis causing cough). Symptoms in older children can be more severe and can progress to lower respiratory tract disease. While most children with *Mp* are managed as outpatients, infections culminating in CAP are typically associated with fever and may be severe enough to warrant hospitalization. In severe cases, *Mp* has been associated with necrotizing pneumonia and chronic lung disease. *Mp* is also a common trigger for asthma exacerbations, responsible for 20% of asthma hospitalizations in one pediatric study.

*Mp* is a known cause of encephalitis, thought to be responsible for up to 6% of cases. The most common presenting symptoms of *Mp* encephalitis include altered mental status (50%), seizures (40%), focal neurological symptoms (37%), and hallucinations (18%). It is estimated that approximately 1-7% of children hospitalized with *Mp* disease develop CNS symptoms. The majority of children with *Mp*-associated encephalitis have a history of preceding respiratory symptoms, typically 7-10 days prior to the onset of CNS symptoms.

*Mp* is an increasingly recognized cause of Stevens Johnson Syndrome (SJS). SJS is an immune-mediated disease characterized by a prodromal illness followed by severe mucocutaneous symptoms, typically involving blistering lesions of the skins and mucous membranes (oropharynx, conjunctivae, and/or genital). SJS can result in severe morbidity from scarring of mucosal surfaces, leading to blindness as well as urethral and esophageal strictures. In children, SJS is typically associated with medication use (most commonly anticonvulsants or antibiotics) or due to infections, such as *Mp*. Interestingly, SJS due to *Mp* is characterized by more severe mucous membrane involvement and may have little or no skin involvement in contrast to drug-associated SJS.

Outbreaks of SJS are exceedingly rare. However, in 2013 we experienced a small outbreak of 9 cases of *Mp*-associated SJS at CHCO. The spectrum of *Mp*-associated SJS disease at CHCO was consistent with previous reports, including severe mucositis and milder skin manifestations. Several children had significant morbidity during their hospitalizations. Our study of these patients suggests that clinicians should have a high suspicion for *Mp*-associated SJS when disease is characterized by radiographic pneumonia, preceding respiratory symptoms, fewer skin manifestations, and elevated erythrocyte sedimentation rate (ESR).

Skin involvement is common with *Mp* infections, with *Mp* pneumonia thought to be associated with rash in 3–33% of patients. *Mp* can be detected from blisters of patients with SJS. Other rare diseases associated with *Mp* infections include thrombotic thrombocytopenic purpura (TTP), autoimmune hemolytic anemia, carditis, arthritis, myoglobinuria, and pancreatitis.
4. How is Mp transmitted?

Mp is transmitted from person to person by infected respiratory droplets during close contact. The incubation period after exposure averages three weeks. Mp is highly contagious and has a documented household transmission rate of 40% and a transmission rate within nursing homes of 25%. Transmission is thought to occur in 2-week cycles. Children are thought to be the primary reservoir of human disease. Asymptomatic carriage after infection can persist for weeks to months.

5. How do you diagnose Mp?

Traditionally, Mp infections were diagnosed by serology. Assays that detect Mp-specific IgG and/or IgM are commercially-available, but interpretation of results is problematic. IgM may not appear until 7 days or longer after infection. IgM can persist for months so a single positive IgM result may not indicate current infection. In addition, IgM may not appear with recurrent infections. IgG titers typically peak at 3-4 weeks, with a fourfold or greater increase in titer in paired sera indicative of infection. Diagnosis can be delayed in an acutely ill patient by the need for a convalescent serum. Serologic tests also fail to distinguish Mp disease from asymptomatic carriage. Mp-specific IgM and IgG assays are no longer available at CHCO.

PCR-based assays have replaced serology for the diagnosis of most Mp infections. Single-plex Mp PCR tests are available at reference laboratories that can accommodate a wide range of specimen types. Currently, CHCO uses the FilmArray® (BioFire Diagnostics) Respiratory Pathogen Panel for rapid detection of Mp (and common respiratory viruses) in nasopharyngeal and lower respiratory tract specimens. Identification of Mp by PCR from a patient with compatible clinical manifestations suggests causation. Positive Mp PCR results however should be interpreted cautiously, particularly in non-classic presentations, as PCR can detect asymptomatic infection.

Non-specific indicators of Mp infection include appearance of cold-agglutinins and an elevated ESR. Cold agglutinins are antibodies that bind to red blood cells resulting in clot formation or clumping (agglutination) when exposed to colder temperatures outside of the body. Cold agglutination testing is no longer available at CHCO. The binding of cold agglutinins to erythrocytes can also results in an elevated ESR, which is commonly observed in patients with Mp disease.

6. How do you treat Mp disease?

Treatment for Mp disease remains controversial. This is due to some studies suggesting that the clinical manifestation of Mp disease may be due to the host’s inflammatory response to the Mp organisms rather than a direct result of Mp infection. However, current national guidelines recommend treatment for children with suspected Mp disease. First line therapy for the treatment of Mp associated CAP is macrolide antibiotics (typically azithromycin 10 mg/kg [max dose 500] on day 1, followed by 5 mg/kg [max dose 250 mg] on days 2-5, once a day). Local resistance rates to macrolides are approximately 5%. Worldwide, however, macrolide resistance is much higher, approaching 80-100% in some parts of Asia. Importantly, Mp organisms are resistant to cell wall active agents, including penicillins and cephalosporins. Other antimicrobials with activity against Mp include fluorquinolones and doxycycline though local resistance rates are unknown.

References:

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