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Human Metapneumovirus

Authors

Sanaa Uddin[1]; Meagan Thomas[2].

Affiliations

[1] Michigan State University College of Osteopathic Medicine
[2] Garden City Hospital, Michigan State University

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Continuing Education Activity

Human **metapneumovirus** is an important pathogen that causes upper and/or lower respiratory tract infections. It does require the clinician to be knowledgeable about a patient's underlying medical conditions and symptoms to determine the severity of the infection. This activity reviews the evaluation and treatment of human **metapneumovirus** and highlights the role of the interprofessional team in evaluating and treating patients with this condition.

Objectives:

- Identify the etiology of human **metapneumovirus** medical conditions and emergencies.
- Outline the evaluation of human **metapneumovirus**.
- Review the management options available for human **metapneumovirus**.

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Introduction

Human **metapneumovirus** (HMPV) is a common cause of respiratory tract infections in children, adults, elderly, and immunocompromised patients. In 2016, it was reclassified from the *Paramyxovirdae* family to the *Pneumoviridae* family. This virus is comprised of genetic groups A and B that are each divided into subclasses consisting of A1, A2, B1, B2 with year to year variability. HMPV was initially discovered in 2001 in the Netherlands but has been found across the globe. It is spread predominately by respiratory droplets from those who have been infected with the virus.

Infection with HMPV usually occurs by the age of 5 years with reinfection that can occur throughout life. The most predominant clinical scenario caused by HMPV infection is upper and/or lower respiratory tract infections, with lower respiratory tract infections being among the most common. Lower respiratory tract infections due to HMPV can lead to pneumonia, bronchiolitis, as well as acute asthma exacerbations. The mainstay of treatment is supportive care measures with supplemental oxygen, antipyretic agents, and hydration with intravenous fluids if needed.[1][2][3][4]

Etiology

Human **metapneumovirus** is a lipid-enveloped single-stranded, negative-sense non-segmented RNA virus that was reclassified in 2016 from the *Paramyxovirdae* family to the *Pneumoviridae* family and the ***Metapneumovirus*** genus. It is spread by infectious respiratory droplets. Severe infection with HMPV has been associated with premature birth, immunocompromised status, and underlying chronic pulmonary, neural, or heart disorders.[2][3][5]

Epidemiology

In 2001, human **metapneumovirus** was first identified in the Netherlands causing clinical symptoms in children, however serological studies demonstrated that this pathogen was already circulating in the Netherlands in 1958. Although infections with HMPV may be reported year-long, peak infection of HMPV in the northern

hemisphere occurs in late winter and early spring, but infection can be found globally across all continents. The four different subgroups A1, A2, B1, B2 have not been known to cause varying levels of severity of infection compared to one another. In addition, there is not a predominance of one strain versus the others.

HMPV is more commonly found in the pediatric population, predominately in children less than 2 years of age with an average age of 22 months. Approximately 90 to 100% of children are infected by HMPV by the age of 5 to 10 years old according to seroprevalence studies. About 5 to 10% of pediatric hospitalizations are a result of HMPV causing acute lower respiratory tract infections. On average, children who are less than 6 months of age with HMPV infection were three times as likely to be hospitalized compared to children between the ages of 6 months to 5 years. [6]

Re-infection may occur due to different viral genotypes or insufficient immunity acquired from the initial infection. Although adults typically only experience mild flu-like symptoms, complications can be seen in the elderly, immunocompromised, or those individuals with chronic lung diseases.[1][2][3][7][8]

Pathophysiology

Human **metapneumovirus** is spread from person to person via respiratory droplets. The incubation period of HMPV ranges between 3 to 5 days and varies between individuals. After inoculation within the nasopharyngeal mucosa, the virus can rapidly spread into the respiratory tract. HMPV contains approximately eight genes that code for nine different proteins responsible for infecting host cells. With the help of the attachment glycoprotein (G), the fusion glycoprotein (F) is responsible for transmembrane fusion by binding itself to integrins on host cell surfaces in order to facilitate entry into the host cell. Subsequently, the viral nucleocapsid enters the host cell's cytoplasm and undergoes replication. HMPV induces the response of various chemokines and cytokines such as IL-6, IFN-alpha, TNF-alpha, IL-2, and macrophage inflammatory proteins leading to peribronchiolar and perivascular infiltration and inflammation. The inflammatory process also results in monocyte and lymphocyte influx within the airway endothelium. These responses combined lead to pulmonary inflammation causing the respiratory manifestations of cough, mucous production, fever, dyspnea.[1][3][5]

History and Physical

Human **metapneumovirus** can present as either upper respiratory tract infection or lower respiratory tract infection.

- Common symptoms of **upper respiratory tract infection** include cough, rhinorrhea, congestion, and sore throat.
- **Lower respiratory tract infection** symptoms include wheezing, fever, cough, dyspnea, hypoxia. More often, lower respiratory tract infections in children cause bronchiolitis, acute asthma exacerbations, croup, and pneumonia. This may necessitate hospital admission, depending on the severity of symptoms.
- In adults, HMPV can cause pneumonia, acute asthma exacerbations, and acute exacerbations in chronic obstructive pulmonary disease.
- **Gastrointestinal symptoms** such as diarrhea, nausea, and vomiting have also been noted. Abnormal tympanic membrane suggestive of acute otitis media can also occur. These symptoms can be quite severe in adults with comorbidities, age greater than 65 years old, and immunocompromised patients, including those with HIV, cancer, immunomodulatory therapy, and transplant recipients.[1][3][5][7][8][9]

Evaluation

Identification of HMPV does not require confirmatory testing but is based on a clinical diagnosis majority of the time. However, there are laboratory tests that can be utilized,

Most commonly, confirmation of infection by HMPV is done by reverse transcriptase-polymerase chain reaction (RT-PCR) from nasopharyngeal swabs.

Radiographic findings on a chest X-ray are typically nonspecific unless HMPV leads to the development of bronchiolitis or pneumonia. Findings include lobar infiltrates, peribronchial cuffing, hypermutation, or diffuse

perihilar infiltrates. It is crucial to assess vital signs and to perform a thorough physical examination looking for signs of respiratory distress and hydration status in order to determine which supportive care measures are necessary.[1][7][9]

Treatment / Management

The primary mainstays of treatment are supportive measures. Anti-pyretic medications such as acetaminophen and ibuprofen are given for those patients with fever. If the patient appears dehydrated and cannot tolerate oral hydration, intravenous fluid hydration is indicated. Additionally, patients with HMPV may require supplemental oxygen support such as high flow nasal cannula or even mechanical ventilation in severe cases causing acute respiratory failure, especially in those patients who have pre-existing respiratory or cardiac illness as well as those who are immunocompromised. Most patients do undergo a full recovery. However, every patient with HMPV should be placed on droplet precautions to limit and prevent spread. There is no current vaccine available for HMPV. However, there have been various vaccines against different structures of HMPV that have been tested on non-human primates and rodents that appear promising, however, none have been tested on human volunteers.[1][3][8][10]

Differential Diagnosis

The differential diagnosis for symptoms resembling HMPV infection includes noninfectious causes such as acute asthma and acute, chronic obstructive pulmonary disease exacerbations. Bacterial infections causing pneumonia can demonstrate a similar clinical picture. Other viruses must also be considered, including coronaviruses, rhinovirus, adenovirus, parainfluenza virus, respiratory syncytial virus, and influenza A and B.[3][9]

Prognosis

Human **metapneumovirus** carries a good prognosis. It does require the clinician to be attuned to a patient's underlying medical conditions as well as signs to determine the severity of infection, including dyspnea, hypoxia, and the use of accessory muscles. Typically, supportive care measures are sufficient, and patients undergo a full recovery. Reinfection can occur, demonstrating short-lived and incomplete immunity to HMPV.[1][3][9]

Complications

Within certain patient populations, HMPV can cause severe illness requiring hospitalization. Among those are patients who are immunocompromised or have a pre-existing cardiac or respiratory condition. These patients are more susceptible to developing acute respiratory failure requiring high flow oxygen support, with some patients even deteriorating enough to require mechanical ventilation. In these cases, patients need to be admitted to the intensive care unit for close monitoring.[1][8]

Deterrence and Patient Education

Instructions for wiping down surfaces at home are essential to disclose to patients and patients' families. Appropriate hand washing is paramount, as well as droplet precautions.[1]

Pearls and Other Issues

Further treatment options are under research for HMPV. A nucleoside analog called ribavirin is an antiviral drug approved for the treatment of a closely related virus called RSV (respiratory syncytial virus), which causes similar symptoms as HMPV. In patients diagnosed with HMPV, ribavirin combined with intravenous immunoglobulin suggests a possible benefit for the treatment option in premature infants and immunocompromised patients. *In vitro* studies have demonstrated antiviral activity by decreasing HMPV replication and, thus, pulmonary inflammation.

One clinical study did use oral and aerosolized ribavirin along with intravenous immunoglobulin in 9 immunocompromised patients with two patients undergoing successful treatment. This does demonstrate a possible option for therapy, but further research must be undertaken. However, both ribavirin and intravenous immunoglobulin are expensive. Additionally, ribavirin has a teratogenic effect. Aerosolized ribavirin given by a small particle aerosol generator would need to be administered under extreme caution by a licensed respiratory therapist who is not pregnant nor has plans to become pregnant.[3][8][10][11]

Enhancing Healthcare Team Outcomes

HMPV infection can lead to visits to the Emergency Department or a primary care physician's office. An interprofessional team approach is an important component of disease prevention, recognition, and treatment. If the patient is stable for treatment as an outpatient, the doctor and nurse need to educate parents and patients on proper handwashing and the importance of wiping down surfaces with disinfectants at home. This is crucial when there are other members of the family at home, especially those who are susceptible to infections.

In the hospital setting, the nurse should ensure that the patient is under respiratory droplet precautions and placed in a separate part of the hospital, especially if being admitted in order to prevent transmission. The doctor, nurse, patient, the parents of the patient, or anyone involved in the direct care of the patient should wear a mask to cover their nose and mouth. They should also wash/sanitize their hands before entering and exiting the room. The doctor should also verify the patient's medical history in order to determine illness severity, progression, and those who are at high risk.

While the workup of the patient is in progress, the nurse should alert the doctor regarding changes in vital signs and respiratory status. This helps identify the need for acute management for the patient, such as supplemental oxygen or mechanical ventilation. If needed, the pharmacist can help educate patients and parents that treatment is mainly supportive, and there are no pharmacological treatments available for HMPV. These measures enhance patient-centered care to improve outcomes and provide safety for the patient with HMPV as well as others.[1][8][10] [Level 5]

Review Questions

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