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Review Article

Human Metapneumovirus in Focus: Emerging Insights into a Silent Respiratory Threat

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ABSTRACT

Human Metapneumovirus (HMPV) is a significant etiological agent of acute respiratory tract infections, with its most pronounced impact observed in the pediatric population. It also poses a substantial threat to elderly individuals and immunocompromised adults, often leading to severe complications. Despite being formally identified in 2001, serological evidence indicates the virus has been circulating in humans since at least the late 1950s, with its delayed discovery largely due to its fastidious growth requirements in cell culture. Human Metapneumovirus shares considerable genetic homology with avian metapneumovirus, suggesting a potential zoonotic origin, and is classified within the Metapneumovirus genus alongside Respiratory Syncytial Virus (RSV). The clinical manifestations of Human Metapneumovirus infection, which include bronchiolitis and pneumonia, closely mirror those of RSV, complicating differential diagnosis based on symptomatology alone. Confirmatory diagnosis relies on molecular methods such as PCR. At present, no targeted antiviral therapy exists; clinical management is primarily supportive, encompassing oxygen supplementation and fluid maintenance. Prevention centers on stringent hygiene measures and, for select high-risk groups, immunoprophylaxis. A comprehensive understanding of HMPV's pathology, diagnostic approaches, and therapeutic limitations is vital for mitigating its public health burden, particularly among vulnerable groups.

Keywords: HMPV, Respiratory illness, Pneumovirus, Antibody.

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INTRODUCTION

Human Metapneumovirus (HMPV) is a prominent cause of acute respiratory disease worldwide, especially among infants and young children. Although it was first isolated and characterized in 2001, retrospective analyses of serum samples confirm its presence in human populations for several decades prior. The initial challenges in identifying the virus were related to its poor growth in conventional cell cultures, as it replicates slowly and requires specific additives like trypsin for propagation. These technical hurdles impeded research until modern virological methods, particularly molecular techniques, facilitated its detection and classification.

Phylogenetically, Human Metapneumovirus is closely aligned with avian metapneumovirus, a pathogen affecting poultry, hinting at a possible historical cross-species transmission event. In the Metapneumovirus genus, only Human Metapneumovirus and Respiratory Syncytial Virus (RSV) are established human pathogens, both inducing a similar spectrum of respiratory diseases. Human Metapneumovirus is a leading cause of bronchiolitis and pneumonia in children, and its clinical features are often nonspecific, overlapping significantly with RSV and other common respiratory viruses, making etiological distinction impossible without laboratory confirmation.

While pediatric infections are most frequent, Human Metapneumovirus can also lead to serious disease in adults, particularly the elderly and immunocompromised. Infections in these demographics are associated with higher rates of severe morbidity and hospitalization. Given its substantial impact on global health across all ages, Human Metapneumovirus continues to be a critical focus of infectious disease and virological research (Hoogen *et al*., 2001; Garcia-Moliner, 2013).

ETIOLOGY

Human Metapneumovirus (HMPV) is an enveloped, negative-sense, single-stranded RNA virus. It was originally classified within the Paramyxoviridae family but was subsequently reclassified into the Pneumoviridae family under the Metapneumovirus genus in 2016. The primary mode of human-to-human transmission is through inhalation of infectious respiratory droplets expelled by infected individuals; indirect transmission via fomites is also possible (Uche and Guerrero-Plata, 2018; Panda *et al*., 2014).

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Populations at elevated risk for severe Human Metapneumovirus disease include infants born prematurely, immunocompromised patients, and those with underlying chronic medical conditions such as respiratory diseases (e.g., COPD, asthma), cardiovascular disorders, or neurological impairments. These comorbidities can amplify the severity of the viral infection, potentially leading to serious complications that necessitate hospital admission and intensive supportive care. The significant disease burden imposed by Human Metapneumovirus underscores the necessity for ongoing research into effective preventive measures (Freymuth *et al.*, 2008; National Library of Medicine, 2025).

EPIDEMOLOGY

First identified in 2001 in nasopharyngeal samples from Dutch children with acute respiratory infections, Human Metapneumovirus (HMPV) has since been recognized as a globally significant pathogen. Serological evidence indicates the virus has been circulating in humans since at least the late 1950s, suggesting a long history of undetected infection prior to its discovery. The delay in identification was primarily due to the virus's poor growth in conventional cell cultures, which was overcome with the use of tertiary monkey kidney cells and trypsin-containing media (Van den Hoogen *et al.*, 2001).

Molecular Epidemiology and Genotypes

Human Metapneumovirus is an enveloped negative-sense single-stranded RNA virus belonging to the family Pneumoviridae, genus Metapneumovirus. Molecular analysis reveals two major genetic lineages, A and B, which are further subdivided into four subgroups: A1, A2, B1, and B2. These subgroups are defined by genetic variation, particularly in the surface glycoproteins (Fusion [F] and Attachment [G]), which are major targets for the host immune response. All four subgroups co-circulate globally with considerable genetic diversity, and multiple subgroups are often detected within a single season. There is no consistent evidence that any one subgroup is associated with more severe disease, though some studies suggest temporal and geographical variations in subgroup dominance may influence seasonal incidence and clinical presentation (Inagaki *et al.*, 2020).

Seasonal and Geographic Trends

Human Metapneumovirus demonstrates a distinct seasonal pattern in temperate climates, with annual epidemics typically occurring in the late winter and early spring, often following or overlapping with the Respiratory Syncytial Virus (RSV) and influenza season. This seasonality is less pronounced in tropical regions, where transmission can occur year-round with increased activity during the rainy season. The virus is endemic worldwide, with nearly all individuals seroconverting by the age of 5-10 years (Inagaki *et al.*, 2020; Vinci *et al.*, 2018).

Disease Burden

The pediatric population, especially young children, bears the highest disease burden. The peak incidence of severe infection occurs in children under two years of age, with the average age of first infection around 22 months. Human Metapneumovirus is a leading cause of Acute Lower Respiratory Tract Infections (ALRTI), accounting for 5-10% of pediatric hospitalizations for pneumonia and bronchiolitis. Infants under six months old are at the greatest risk, exhibiting hospitalization rates three times higher than those of children aged 6 months to 5 years (Inagaki *et al.*, 2020).

A key feature of Human Metapneumovirus epidemiology is its capacity for re-infection throughout life due to incomplete and transient immunity following natural infection. While re-infections in healthy adults are usually mild or asymptomatic, the virus remains a significant cause of morbidity and mortality in older adults (≥65 years), immunocompromised individuals, and those with underlying cardiopulmonary conditions. In these high-risk groups, Human Metapneumovirus infection can lead to severe complications, including exacerbations of Chronic Obstructive Pulmonary Disease (COPD), asthma, congestive heart failure, and pneumonia requiring hospitalization (Vinci *et al.*, 2018; Haas *et al.*, 2013).

PATHOPHYSIOLOGY

Human Metapneumovirus spreads primarily through respiratory droplets when infected individuals cough or sneeze. Following exposure, the virus typically incubates for 3-5 days before symptoms appear, though this period may vary. Infection begins when viral particles colonize the nasopharyngeal mucosa, subsequently migrating to the lower respiratory tract. The viral genome contains eight genes that generate nine proteins crucial for host cell invasion. Among these, two structural proteins - the attachment Glycoprotein (G) and Fusion glycoprotein (F) - are particularly important for pathogenesis. The F protein specifically interacts with host cell integrins, facilitating viral entry through membrane fusion. After penetration, the viral genetic material is released into the host cell cytoplasm, initiating replication.

The host immune system responds to Human Metapneumovirus infection by producing an array of inflammatory mediators, including IL-6, IFN-alpha, TNF-alpha, IL-2, and macrophage inflammatory proteins. These signaling molecules promote immune cell migration, resulting in characteristic peribronchiolar and perivascular infiltration. The inflammatory cascade involves monocyte and lymphocyte recruitment to airway tissues, creating localized inflammation. These pathological changes underlie the typical clinical presentation of HMPV infection, which includes respiratory manifestations such as productive cough, fever, mucus hypersecretion, and breathing difficulties (dyspnea). The severity of symptoms often correlates with the extent of pulmonary inflammation.

- Key features of HMPV pathogenesis.
- Respiratory droplet transmission with 3- 5-day incubation.
- Initial nasopharyngeal infection progressing to lower airways.
- Viral entry mediated by F glycoprotein-integrin interaction.
- Robust cytokine/chemokine response (IL-6, TNF-α, etc.).
- Inflammatory cell infiltration causing airway obstruction.
- Characteristic respiratory symptom constellation.

This complex interplay between viral replication and host immune response determines both disease presentation and clinical outcomes in infected individuals (Freymuth *et al.*, 2008b).

SIGNS AND SYMPTOMS

In young children, Human Metapneumovirus and Respiratory Syncytial Virus (RSV) infections produce nearly identical symptoms, often leading to diagnoses of pneumonia, bronchiolitis, or bronchitis. Common clinical features include fever, cough, wheezing, hypoxia, and concurrent upper and lower respiratory tract involvement (Panda *et al.*, 2014; Boivin *et al.*, 2003). While fever typically persists for about 10 days in hMPV-infected children, its intensity may fluctuate throughout the illness. Wheezing is particularly prominent in pediatric cases of Human Metapneumovirus-associated lower respiratory tract infections (Williams *et al.*, 2005).

Although fever is uncommon in Human Metapneumovirus-infected adults, reinfected individuals may exhibit mild cold- or flu-like symptoms. Most cases present as self-limiting upper respiratory infections (rhino-pharyngo-laryngitis), resolving within a week (Hamelin *et al.*, 2005). The most frequent symptoms include cough (90% of cases), rhinitis with nasal congestion and discharge (70%), and hoarseness (50-67%). Notably, while fever occurs in only 4% of adults, it affects 50-80% of pediatric cases (Falsey and Walsh, 2006).

Older adults with Human Metapneumovirus reinfections face an elevated risk of severe complications, including pneumonitis and fatal outcomes (Falsey *et al.*, 2003). Emerging research also suggests a potential link between pediatric HMPV infections and central nervous system disorders, such as encephalitis and febrile seizures (Arnold *et al.*, 2009).

Accurate diagnosis based solely on clinical presentation remains challenging, as Human Metapneumovirus symptoms overlap with those of other respiratory viruses. The pathogen can cause a wide range of infections, from upper respiratory conditions (rhinitis, pharyngitis, otitis media, conjunctivitis) to lower respiratory diseases (pneumonia, bronchiolitis) (Spaeder *et al.*, 2013). Additional high-risk groups include pregnant individuals, who may experience severe complications (Lenahan *et al.*, 2015), and lung transplant recipients, in whom HMPV infection can contribute to chronic allograft dysfunction (Zwart *et al.*, 2021).

DIAGNOSIS

The diagnostic landscape for Human Metapneumovirus is fraught with challenges that impede rapid and accurate identification.*In vitro* studies demonstrate that Human Metapneumovirus produces characteristic cytopathic effects in cell culture, though these develop slowly and may include syncytia formation, cell rounding, and detachment from the culture surface. The virus's sluggish replication kinetics necessitate combining traditional culture methods with ancillary techniques for optimal detection. Immunological methods such as direct fluorescent antibody testing and ELISA, which employ HMPV-specific antibodies to identify viral antigens, significantly improve diagnostic sensitivity compared to relying solely on cytopathic observation, yet their availability is often limited to specialized laboratories (Tollefson *et al.*, 2010).

A critical analytical challenge is the widespread implementation gap between advanced molecular techniques and routine clinical practice. While modern diagnostics have shifted from cell culture to molecular methods, with RT-PCR and real-time RT-PCR emerging as gold standards due to their superior sensitivity and specificity, many clinical laboratories still lack access to these technologies. Recent advances include the development of multiplex PCR assays capable of simultaneously detecting hMPV alongside other respiratory pathogens, offering more comprehensive diagnostic capabilities. However, the high cost and technical expertise required for these assays create significant barriers to adoption, particularly in resource-limited settings (Bellau-Pujol *et al.*, 2005; Litwin and Bosley, 2013).

Consequently, many facilities still rely on less sensitive first-line methods like direct fluorescent antibody testing and immunofluorescence, reserving RT-PCR only for confirmation of negative specimens. This diagnostic algorithm can lead to underreporting and misdiagnosis, as the clinical presentation of HMPV is nonspecific and mimics other respiratory viral infections. The absence of standardized, accessible, and cost-effective diagnostic tools remains a substantial obstacle to understanding the true burden of HMPV and implementing appropriate infection control measures (Jokela *et al.*, 2010; Ma *et al.*, 2010).

In cases where neurological involvement is suspected, brain MRI may reveal multiple cortical and subcortical lesions suggestive of HMPV-associated encephalitis. Cerebrospinal fluid analysis with PCR has successfully identified viral presence in some reported

cases, providing definitive diagnostic confirmation, though this is not part of routine practice (Schildgen *et al*., 2005).

MANAGEMENT

The management of HMPV presents substantial clinical challenges due to the absence of approved targeted antiviral therapies. Current practice emphasizes supportive care as the mainstay of treatment, which, while essential, highlights a significant therapeutic gap. Several investigational therapies show potential but face considerable hurdles (Wyde *et al*., 2003b; Kitanovski *et al*., 2013b; Ulbrandt *et al*., 2006b). Experimental approaches under investigation include ribavirin, intravenous immunoglobulins, fusion inhibitors, and RNA interference technologies (siRNAs) (Corti *et al*., 2013; Deffrasnes *et al*., 2007; Darniot *et al*., 2012). A critical analysis of ribavirin reveals a complex profile. While it demonstrates*in vitro* antiviral activity against HMPV through its guanosine analog structure that disrupts viral transcription, its clinical efficacy remains uncertain and poorly documented in controlled studies. The drug may also modulate host immune responses, further complicating its therapeutic profile. Additionally, ribavirin exhibits teratogenic properties requiring strict handling protocols, presents administration challenges as aerosolized delivery necessitates specialized equipment and trained respiratory therapists, and carries high treatment costs that create accessibility barriers (Park *et al*., 2012).

For severely immunocompromised patients (e.g., transplant recipients or oncology patients), combination therapy with ribavirin and immunoglobulins may be considered as a last resort, despite inconsistent evidence regarding outcomes. The lack of robust clinical trial data means such decisions must rely on anecdotal evidence and individual clinician experience, requiring careful risk-benefit analysis and shared decision-making between clinicians and patients (Raza *et al*., 2007; Hamelin *et al*., 2010). More promisingly, the engineered monoclonal antibody mAb 338, which targets the HMPV fusion protein, has shown effectiveness in animal studies, but human data are still lacking (Bergh *et al*., 2022).

The use of anti-inflammatory corticosteroids has been employed empirically in some cases, though robust clinical data supporting their efficacy are lacking, and their immunosuppressive effects might theoretically worsen viral replication in certain scenarios (González *et al*., 2018). This underscores the fundamental challenge in HMPV management: balancing inflammatory response control without compromising viral clearance.

Supportive measures remain fundamental, including antipyretics (acetaminophen/ibuprofen) for fever management and IV rehydration when oral intake is inadequate (Choi *et al*., 2019; Velayutham *et al*., 2022). Severe respiratory cases, particularly in high-risk patients, may require advanced oxygen support, including mechanical ventilation. Fortunately, most patients achieve full recovery with appropriate supportive care. Infection control measures should include droplet precautions, while vaccine development remains an urgent unmet need in the global effort to reduce HMPV morbidity and mortality (Siegel *et al*., 2007).

PREVENTION

Effective prevention of Human Metapneumovirus (HMPV) transmission currently relies on non-pharmaceutical interventions, which present implementation challenges in both community and healthcare settings. Rigorous hand hygiene, droplet precautions, and minimizing direct contact with infected individuals form the cornerstone of prevention strategies. However, the effectiveness of these measures is often limited by variable compliance and the fact that infected individuals may shed the virus for extended periods-ranging from days to weeks-during both active illness and early recovery, often before symptoms appear or after they resolve (Siegel *et al*., 2007).

A significant logistical challenge in healthcare settings involves cohorting patients to prevent nosocomial transmission. HMPV-positive patients should be isolated from those with Respiratory Syncytial Virus (RSV) to reduce the risk of severe co-infections. This requires rapid and accurate diagnostic capabilities that many facilities lack. Special care must be taken to limit exposure to immunocompromised individuals, who are most vulnerable to severe disease but are often concentrated in healthcare environments where exposure risk is highest.

Emerging evidence suggests that vaccination may play a future role in mitigating HMPV-related complications, but no licensed vaccine currently exists. Interestingly, the nine-valent Pneumococcal Conjugate Vacciogne (PCV9) has been associated with decreased hospitalization rates and reduced severity of HMPV illness, particularly in vulnerable pediatric populations such as children with HIV, possibly due to prevention of bacterial superinfection (Sepúlveda-Pachón *et al*., 2024). This indirect benefit highlights the complex interplay between viral and bacterial pathens but does not address the fundamental need for a specific HMPV vaccine, the development of which remains hampered by incomplete understanding of correlates of immune protection and the technical challenges of creating a vaccine that provides lasting immunity against multiple HMPV strains (Hermos *et al*., 2010).

DIFFERENTIAL DIAGNOSIS

The clinical presentation of Human Metapneumovirus (HMPV) infection often resembles various other respiratory conditions, necessitating comprehensive diagnostic evaluation. Non-infectious respiratory disorders, including acute asthma attacks and COPD exacerbations, can produce symptoms nearly identical to HMPV infection. The differential diagnosis should also include bacterial pneumonia, which shares many clinical features with severe HMPV cases.

Furthermore, HMPV infection must be distinguished from other viral respiratory pathogens, particularly:

- Coronaviruses (including seasonal varieties and SARS-CoV-2).
- Rhinovirus.
- Adenovirus.
- Parainfluenza viruses.
- Respiratory Syncytial Virus (RSV).
- Influenza viruses (types A and B).

Accurate diagnosis requires careful clinical assessment combined with appropriate laboratory testing to differentiate between these potentially overlapping conditions (Schildgen *et al.*, 2011).

PROGNOSIS

Most patients with Human Metapneumovirus (HMPV) infection experience complete recovery with supportive care, demonstrating an overall positive prognosis. However, healthcare providers should conduct thorough evaluations of comorbid conditions and vigilantly monitor for clinical indicators of severe disease progression, including:

- Respiratory distress (dyspnea).
- Oxygen desaturation (hypoxia).
- Increased work of breathing evidenced by accessory muscle use.

Notably, natural infection does not confer long-term immunity, leaving individuals susceptible to recurrent HMPV infections due to the transient and partial protective immune response generated following initial exposure (Schildgen *et al.*, 2011).

COMPLICATIONS

Human Metapneumovirus (HMPV) poses significant risks for immunocompromised individuals and those with pre-existing cardiopulmonary conditions, often resulting in serious complications requiring inpatient management. These high-risk patients frequently develop severe respiratory compromise that may progress to acute respiratory failure. Clinical management often involves escalating respiratory support, ranging from high-flow oxygen therapy to invasive mechanical ventilation in critical cases. Due to the potential for rapid clinical deterioration, such patients typically necessitate Intensive Care Unit (ICU) admission for continuous monitoring and specialized interventions (Vinci *et al.*, 2018; Haas *et al.*, 2013).

DETERRENCE AND PATIENT EDUCATION

Effective containment of Human Metapneumovirus (HMPV) requires comprehensive patient and family education regarding transmission prevention.

Key preventive measures include:

Environmental disinfection - Regular cleaning of high-touch surfaces with appropriate disinfectants.

Hand hygiene - Frequent handwashing with soap and water or alcohol-based sanitizers.

Respiratory etiquette - Implementation of droplet precautions, including proper mask usage and cough hygiene.

These evidence-based interventions can significantly reduce viral transmission in both household and community settings (Vinci *et al.*, 2018).

PEARLS AND OTHER ISSUES

Current research continues to evaluate novel treatment approaches for Human Metapneumovirus (HMPV). Among the most promising candidates is ribavirin, a nucleoside analog antiviral currently approved for Respiratory Syncytial Virus (RSV) management. Preliminary evidence indicates potential therapeutic benefits when combining ribavirin with Intravenous Immunoglobulin (IVIG), particularly for vulnerable populations including immunocompromised individuals and preterm neonates.

In vitro investigations demonstrate ribavirin's capacity to inhibit HMPV replication and attenuate associated pulmonary inflammation. Limited clinical data from a trial involving nine immunocompromised patients receiving combination therapy (oral/aerosolized ribavirin plus IVIG) showed partial efficacy, with two cases demonstrating positive outcomes. However, several limitations constrain widespread adoption:

Safety concerns: Ribavirin exhibits teratogenic properties requiring strict handling protocols.

Administration challenges: Aerosolized delivery necessitates specialized equipment and trained respiratory therapists (with pregnancy contraindications).

Economic factors: High treatment costs present accessibility barriers.

These findings underscore the need for larger, controlled studies to establish definitive efficacy and safety profiles before clinical implementation (Shahda *et al.*, 2010).

CONCLUSION

Human Metapneumovirus (HMPV) is a significant and pervasive respiratory pathogen with a substantial global health impact, particularly on young children, the elderly, and immunocompromised individuals. Despite its identification over two decades ago, clinical management remains reliant on supportive care, as no vaccines or specific antiviral therapies are approved for use. The challenges in culturing the virus and its clinical similarity to other respiratory infections, especially RSV, continue to complicate diagnosis and surveillance.

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ABBREVIATIONS

HMPV: Human Metapneumovirus; **COPD:** Chronic Obstructive Pulmonary Disease; **ELISA:** Enzyme-Linked Immunosorbent Assay; **F protein:** Fusion glycoprotein; **G protein:** Attachment glycoprotein; **ICU:** Intensive Care Unit; **IFN-α:** Interferon-alpha; **IL-2:** Interleukin-2; **IL-6:** Interleukin-6; **IV:** Intravenous; **IVIG:** Intravenous Immunoglobulin; **mAb:** Monoclonal Antibody; **MRI:** Magnetic Resonance Imaging; **PCV9:** Nine-valent Pneumococcal Conjugate Vaccine; **PCR:** Polymerase Chain Reaction; **RSV:** Respiratory Syncytial Virus; **RT-PCR:** Reverse Transcription Polymerase Chain Reaction; **siRNA:** Small Interfering RNA; **TNF-α:** Tumor Necrosis Factor-alpha.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

Significant knowledge gaps persist, underscoring urgent research priorities. First, the development of an effective vaccine is paramount. While some monoclonal antibodies show promise in preclinical studies, their translation to clinical practice requires accelerated investment and research to protect vulnerable populations. Second, there is a critical need for affordable, rapid, and accessible diagnostic tools. The current reliance on PCR-based methods limits timely diagnosis in resource-limited settings, hindering appropriate patient management and obscuring the true burden of disease. Finally, enhanced genomic surveillance, particularly in Low- and Middle-Income Countries (LMICs), is essential to understand the global circulation of HMPV genotypes, its seasonality, and its contribution to pediatric mortality in regions with high rates of respiratory illness.

Addressing these priorities-vaccine development, the creation of point-of-care diagnostics, and the establishment of robust surveillance systems-is crucial to mitigating the impact of this silent respiratory threat and reducing the global health burden of HMPV.

REFERENCES

Arnold, J. C., Singh, K. K., Milder, E., Spector, S. A., Sawyer, M. H., Gavali, S., and Glaser, C. (2009). Human metapneumovirus associated with central nervous system infection in children. The Pediatric Infectious Disease Journal, *28*(12), 1057-1060. https://doi.org/10.1097/INF.0b013e3181acd221

Bellau-Pujol, S., Vabret, A., Legrand, L., Dina, J., Gouarin, S., Petitjean-Lecherbonnier, J., Pozzetto, B., Ginevra, C., and Freymuth, F. (2005). Development of three multiplex RT-PCR assays for the detection of 12 respiratory RNA viruses. Journal of Virological Methods, *126*(1-2), 53-63. https://doi.org/10.1016/j.jviromet.2005.01.020

Boivin, G., De Serres, G., Côté, S., Gilca, R., Abed, Y., Rochette, L., Bergeron, M. G., and Déry, P. (2003). Human metapneumovirus infections in hospitalized children. Emerging Infectious Diseases, *9*(6), 634-640. https://doi.org/10.3201/eid0906.030017

Choi, S., Hong, S., Huh, J. W., Jung, J., Kim, M. J., Chong, Y. P., Kim, S., Sung, H., Koo, H. J., Do, K., Lee, S., Lim, C., Kim, Y. S., Woo, J. H., and Koh, Y. (2019). Outcomes of severe human metapneumovirus-associated community-acquired pneumonia in adults. Journal of Clinical Virology, *117*, 1-4. https://doi.org/10.1016/j.jcv.2019.05.007

Corti, D., Bianchi, S., Vanzetta, F., Minola, A., Perez, L., Agatic, G., Guarino, B., Silacci, C., Marcandalli, J., Marsland, B. J., Piralla, A., Percivalle, E., Sallusto, F., Baldanti, F., and Lanzavecchia, A. (2013). Cross-neutralization of four paramyxoviruses by a human monoclonal antibody. Nature, *501*(7467), 439-443. https://doi.org/10.1038/nature12442

Darniot, M., Schildgen, V., Schildgen, O., Sproat, B., Kleines, M., Ditt, V., Pitoiset, C., Pothier, P., and Manoha, C. (2012). RNA interference *in vitro* and *in vivo* using DsiRNA targeting the nucleocapsid N mRNA of human metapneumovirus. Antiviral Research, *93*(3), 364-373. https://doi.org/10.1016/j.antiviral.2012.01.004

Deffrasnes, C., Hamelin, M., Prince, G. A., and Boivin, G. (2007). Identification and evaluation of a highly effective fusion inhibitor for human metapneumovirus. Antimicrobial Agents and Chemotherapy, *52*(1), 279-287. https://doi.org/10.1128/AAC.00793-07

De Zwart, A., Riezebos-Brilman, A., Lunter, G., Vonk, J., Glanville, A. R., Gottlieb, J., Permpalung, N., Kerstjens, H., Alffenaar, J., and Verschuuren, E. (2021). Respiratory syncytial virus, human metapneumovirus, and parainfluenza virus infections in lung transplant recipients: A systematic review of outcomes and treatment strategies. Clinical Infectious Diseases, *74*(12), 2252-2260. https://doi.org/10.1093/cid/ciab969

Falsey, A. R., and Walsh, E. E. (2006). Viral pneumonia in older adults. Clinical Infectious Diseases, *42*(4), 518-524. https://doi.org/10.1086/499955

Falsey, A. R., Erdman, D., Anderson, L. J., and Walsh, E. E. (2003). Human metapneumovirus infections in young and elderly adults. The Journal of Infectious Diseases, *187*(5), 785-790. https://doi.org/10.1086/367901

Freymuth, F., Vabret, A., Legrand, L., Dina, J., Gouarin, S., Cuvillon-Nimal, D., and Brouard, J. (2008). Métapneumovirus humain. Pathologie Biologie, *57*(2), 133-141. https://doi.org/10.1016/j.patbio.2008.04.005

Freymuth, F., Vabret, A., Legrand, L., Dina, J., Gouarin, S., Cuvillon-Nimal, D., and Brouard, J. (2008b). Métapneumovirus humain. Pathologie Biologie, *57*(2), 133-141. https://doi.org/10.1016/j.patbio.2008.04.005

Garcia-Moliner, M. L. (2013). Human Metapneumovirus. In Viruses and the Lung (pp. 101-107). Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-642-40605-8_12

González, L. A., Vázquez, Y., Mora, J. E., Palavecino, C. E., Bertrand, P., Ferrés, M., Contreras, A. M., Beckhaus, A. A., Riedel, C. A., and Bueno, S. M. (2018). Evaluation of monoclonal antibodies that detect conserved proteins from respiratory syncytial virus, metapneumovirus and adenovirus in human samples. Journal of Virological Methods, *254*, 51-64. https://doi.org/10.1016/j.jviromet.2018.01.011

Haas, L., Thijsen, S., Van Elden, L., and Heemstra, K. (2013). Human metapneumovirus in adults. Viruses, *5*(1), 87-110. https://doi.org/10.3390/v5010087

Hamelin, M. E., Côté, S., Laforge, J., Lampron, N., Bourbeau, J., Weiss, K., Gilca, R., DeSerres, G., and Boivin, G. (2005). Human metapneumovirus infection in adults with community-acquired pneumonia and exacerbation of chronic obstructive pulmonary disease. Clinical Infectious Diseases, *41*(4), 498-502. https://doi.org/10.1086/431981

Hamelin, M., Gagnon, C., Prince, G. A., Kiener, P., Suzich, J., Ulbrandt, N., and Boivin, G. (2010). Prophylactic and therapeutic benefits of a monoclonal antibody against the

fusion protein of human metapneumovirus in a mouse model. Antiviral Research, *88*(1), 31-37. https://doi.org/10.1016/j.antiviral.2010.07.001

Hermos, C. R., Vargas, S. O., and McAdam, A. J. (2010). Human metapneumovirus. Clinics in Laboratory Medicine, *30*(1), 131-148. https://doi.org/10.1016/j.cll.2009.10.002

Inagaki, A., Kitano, T., Nishikawa, H., Suzuki, R., Onaka, M., Nishiyama, A., Kitagawa, D., Oka, M., Masuo, K., and Yoshida, S. (2020). The epidemiology of admission-requiring pediatric respiratory infections in a Japanese community hospital using multiplex PCR. Japanese Journal of Infectious Diseases, *74*(1), 23-28. https://doi.org/10.7883/yoken.JJID.2020.154

Jokela, P., Piiparinen, H., Luiro, K., and Lappalainen, M. (2010). Detection of human metapneumovirus and respiratory syncytial virus by duplex real-time RT-PCR assay in comparison with direct fluorescent assay. Clinical Microbiology and Infection, *16*(10), 1568-1573. https://doi.org/10.1111/j.1469-0691.2010.03191.x

Kitanovski, L., Kopriva, S., Pokorn, M., Dolničar, M. B., Rajić, V., Stefanović, M., and Jazbec, J. (2013b). Treatment of severe human metapneumovirus (HMPV) pneumonia in an immunocompromised child with oral ribavirin and IVIG. Journal of Pediatric Hematology/Oncology, *35*(7), e311-e313. https://doi.org/10.1097/MPH.0b013e3182915d2d

Lenahan, J. L., Englund, J., Tielsch, J., Katz, J., Khatry, S., Leclerq, S. C., Kuypers, J., Steinhoff, M. C., and Chu, H. Y. (2015). Human metapneumovirus infection in pregnant and postpartum women. Open Forum Infectious Diseases, *2*(suppl_1). https://doi.org/10.1093/ofid/ofv133.402

Litwin, C. M., and Bosley, J. G. (2013). Seasonality and prevalence of respiratory pathogens detected by multiplex PCR at a tertiary care medical center. Archives of Virology, *159*(1), 65-72. https://doi.org/10.1007/s00705-013-1794-4

Ma, Y., *et al.* (2010). Detection of human metapneumovirus in clinical specimens using PCR. Journal of Clinical Microbiology, *48*(9), 3324-3329.

National Library of Medicine. (2025, January 1). Human metapneumovirus. PubMed. https://pubmed.ncbi.nlm.nih.gov/32809745/

Panda, S., Mohakud, N. K., Pena, L., and Kumar, S. (2014). Human metapneumovirus: review of an important respiratory pathogen. International Journal of Infectious Diseases, *25*, 45-52. https://doi.org/10.1016/j.ijid.2014.03.1394

Park, S., Baek, S., Lee, S., Choi, S., Kim, Y. S., Woo, J. H., Sung, H., Kim, M., Kim, D., Lee, J., Lee, J., Lee, K., and Kim, S. (2012). Efficacy of oral ribavirin in hematologic disease patients with paramyxovirus infection: Analytic strategy using propensity scores. Antimicrobial Agents and Chemotherapy, *57*(2), 983-989. https://doi.org/10.1128/AAC.01961-12

Raza, K., Ismailjee, S. B., Crespo, M., Studer, S. M., Sanghavi, S., Paterson, D. L., Kwak, E. J., Rinaldo, C. R., Pilewski, J. M., McCurry, K. R., and Husain, S. (2007). Successful outcome of human metapneumovirus (HMPV) pneumonia in a lung transplant recipient treated with intravenous ribavirin. The Journal of Heart and Lung Transplantation, *26*(8), 862-864. https://doi.org/10.1016/j.healun.2007.05.020

Schildgen, O., Glatzel, T., Geikowski, T., Scheibner, B., Simon, A., Bindl, L., Born, M., Viazov, S., Wilkesmann, A., Knöpfle, G., Roggendorf, M., and Matz, B. (2005). Human metapneumovirus RNA in encephalitis patient. Emerging Infectious Diseases, *11*(3), 467-470. https://doi.org/10.3201/eid1103.040676

Schildgen, V., Van Den Hoogen, B., Fouchier, R., Tripp, R. A., Alvarez, R., Manoha, C., Williams, J., and Schildgen, O. (2011). Human metapneumovirus: Lessons learned over the first decade. Clinical Microbiology Reviews, *24*(4), 734-754. https://doi.org/10.1128/CMR.00015-11

Sepúlveda-Pachón, I. T., Dunne, E. M., Hanquet, G., Baay, M., Menon, S., Jodar, L., Gessner, B. D., and Theilacker, C. (2024). Effect of pneumococcal conjugate vaccines on viral respiratory infections: a systematic literature review. The Journal of Infectious Diseases, *230*(3), e657-e667. https://doi.org/10.1093/infdis/jiae125

Shahda, S., Carlos, W., Kiel, P., Khan, B., and Hage, C. (2010). The human metapneumovirus: a case series and review of the literature. Transplant Infectious Disease, *13*(3), 324-328. https://doi.org/10.1111/j.1399-3062.2010.00575.x

Siegel, J. D., Rhinehart, E., Jackson, M., Chiarello, L.; the Healthcare Infection Control Practices Advisory Committee. (2007). Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. CDC. https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html

Spaeder, M. C., Custer, J. W., Bembea, M. M., Aganga, D. O., Song, X., and Scafidi, S. (2013). A multicenter outcomes analysis of children with severe viral respiratory infection due to human metapneumovirus. Pediatric Critical Care Medicine, *14*(3), 268-272. https://doi.org/10.1097/PCC.0b013e3182720fc7

Tollefson, S. J., Cox, R. G., and Williams, J. V. (2010). Studies of culture conditions and environmental stability of human metapneumovirus. Virus Research, *151*(1), 54-59. https://doi.org/10.1016/j.virusres.2010.03.018

Uche, I. K., and Guerrero-Plata, A. (2018). Interferon-mediated response to human metapneumovirus infection. Viruses, *10*(9), 505. https://doi.org/10.3390/v10090505

Ulbrandt, N. D., Ji, H., Patel, N. K., Riggs, J. M., Brewah, Y. A., Ready, S., Donacki, N. E., Folliot, K., Barnes, A. S., Senthil, K., Wilson, S., Chen, M., Clarke, L., MacPhail, M., Li, J., Woods, R. M., Coelingh, K., Reed, J. L., McCarthy, M. P., . . . Suzich, J. A. (2006b). Isolation and characterization of monoclonal antibodies which neutralize human metapneumovirus *in vitro* and *in vivo*. Journal of Virology, *80*(16), 7799-7806. https://doi.org/10.1128/JVI.00318-06

Van Den Bergh, A., Bailly, B., Guillon, P., Von Itzstein, M., and Dirr, L. (2022). Antiviral strategies against human metapneumovirus: Targeting the fusion protein. Antiviral Research, *207*, 105405. https://doi.org/10.1016/j.antiviral.2022.105405

Van den Hoogen, B. G., de Jong, J. C., Groen, J., *et al.* (2001). A newly discovered human pneumovirus isolated from young children with respiratory tract disease. Nature Medicine, *7*, 719-724. https://doi.org/10.1038/89098

Velayutham, T. S., Ivanciuc, T., Garofalo, R. P., and Casola, A. (2022). Role of human metapneumovirus glycoprotein G in modulation of immune responses. Frontiers in Immunology, *13*. https://doi.org/10.3389/fimmu.2022.962925

Vinci, A., Lee, P. J., and Krilov, L. R. (2018). Human metapneumovirus infection. Pediatrics in Review, *39*(12), 623-624. https://doi.org/10.1542/pir.2017-0213

Williams, J. V., Crowe, J. E., Jr, Enriquez, R., Minton, P., Peebles, R. S., Jr, Hamilton, R. G., Higgins, S., Griffin, M., and Hartert, T. V. (2005). Human metapneumovirus infection plays an etiologic role in acute asthma exacerbations requiring hospitalization in adults. The Journal of Infectious Diseases, *192*(7), 1149-1153. https://doi.org/10.1086/444392

Wyde, P. R., Chetty, S. N., Jewell, A. M., Boivin, G., and Piedra, P. A. (2003b). Comparison of the inhibition of human metapneumovirus and respiratory syncytial virus by ribavirin and immune serum globulin *in vitro*. Antiviral Research, *60*(1), 51-59. https://doi.org/10.1016/S0166-3542(03)00153-0

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