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Editorial

Contents

Here's another issue of JHS loaded with lot of valuable information, kindly flip a few pages to believe us……

Mini review section - Acute respiratory tract infection (ARI) is a leading cause of morbidity and mortality worldwide. ARIs were responsible for about 20% of total deaths in children. ARIs affect children regardless of their economic status, with similar incidence rates in both developed and developing countries, but with a higher mortality rate in developing countries. Human metapneumovirus (hMPV) was first discovered in 2001 in the Netherlands, when the virus was isolated from a paediatric patient who had symptoms like those of hRSV infection. hMPV causes disease primarily in children but can infect adults and immunocompromised individuals as well. The clinical features of the illness caused by hMPV infection range from a mild upper respiratory tract infection to life-threatening severe bronchiolitis and pneumonia.

Current Trends section - A review of conventional and emerging technologies for hydrogels sterilization.

In Profile Scientist - Marie Curie, *née* Maria Sklodowska, was born in Warsaw on November 7, 1867, the daughter of a secondary-school teacher. She received a general education in local schools and some scientific training from her father. She became involved in a students' revolutionary organization and found it prudent to leave Warsaw, then in the part of Poland dominated by Russia, for Cracow, which at that time was under Austrian rule. In 1891, she went to Paris to continue her studies at the Sorbonne where she obtained Licenciateships in Physics and the Mathematical Sciences.

Bug of the month - 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.

Did You Know? - Using AI, scientists have designed proteins that say not so fast to toxins wielded by cobras and other venomous snakes. It's a proof-of-concept approach that could one day offer a new treatment for snakebites. In lab experiments, the custom proteins saved the lives of mice given an otherwise lethal dose of toxins, researchers report January 15 in *Nature*.

Best Practices - The impacts of climate change include warming temperatures, changes in precipitation, increases in the frequency or intensity of some extreme weather events, and rising sea levels. These impacts threaten our health by affecting the food we eat, the water we drink, the air we breathe, and the weather we experience.

Tickle yourself enjoying the jokes in our **Relaxed Mood** section.

Our JHS team is thankful to all our readers for their ever-increasing appreciation that has served as a reward & motivation for us. Looking forward for your continuous support.

Human metapneumovirus: review of an important respiratory Pathogen

Acute respiratory tract infection (ARI) is a leading cause of morbidity and mortality worldwide. ARIs were responsible for about 20% of total deaths in children. ARIs affect children regardless of their economic status, with similar incidence rates in both developed and developing countries, but with a higher mortality rate in developing countries. Human metapneumovirus (hMPV) was first discovered in 2001 in the Netherlands, when the virus was isolated from a paediatric patient who had symptoms like those of hRSV infection. hMPV causes disease primarily in children but can infect adults and immunocompromised individuals as well. The clinical features of the illness caused by hMPV infection range from a mild upper respiratory tract infection to life-threatening severe bronchiolitis and pneumonia.

Epidemiology

hMPV has been isolated on all continents and has a seasonal distribution. Outbreaks occur mainly in the spring and winter months – January to March in the northern hemisphere and June to July in the southern hemisphere. Being a respiratory infection, hMPV is transmitted by infectious airborne droplets. The incubation period varies from individual to individual but is commonly between 3 and 5 days.

hMPV is commonly found in the paediatric population, with high susceptibility rates in children less than 2 years old. hMPV infection in adults normally shows only mild flu-like symptoms. However, in some adult cases (especially elderly adults), severe complications such as chronic obstructive pulmonary disease (COPD) can occur. Dyspnoea is more likely in adults as compared to children. hMPV infection has also been reported in several immunocompromised patients, such as lung transplant recipients, patients with haematological malignancies, and hematopoietic stem cell transplant recipients.

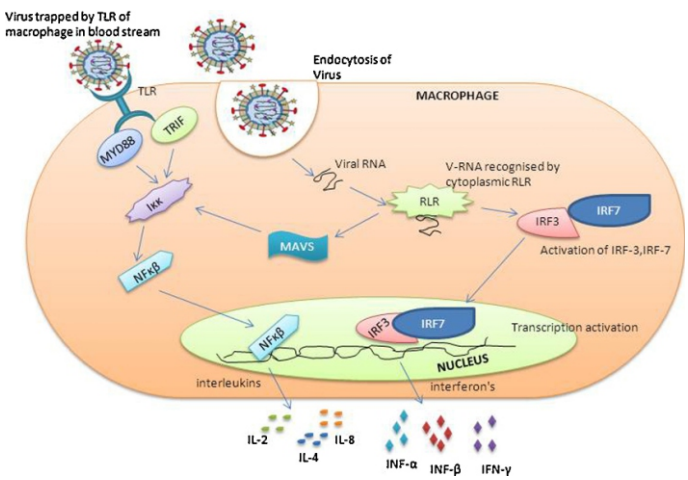
Risk factors associated with severe hMPV infection include premature birth, young age, pre-existing nosocomial infection, and underlying chronic pulmonary, heart, or neural disorders. About 40% of children hospitalized with hMPV infection were found to have underlying high-risk conditions, like asthma and chronic lung disease.

Clinical features

hMPV patients are generally diagnosed with bronchiolitis, bronchitis, and pneumonia. They show common symptoms like fever, cough, hypoxia, upper respiratory tract infection, lower respiratory tract infection, and wheezing. However, the most common causes of hospitalization are bronchiolitis and pneumonia. The average duration of fever in hMPV-positive cases is about 10 days, with a peak during the illness. Young adults with hMPV re-infection show mild cold and flu-like symptoms, with fever in a small proportion of infected cases.

However, in the case of elderly patients, re-infection can lead to severe symptoms (such as pneumonitis) and even to death. Wheezing is a common clinical symptom observed in multiple studies of children with hMPV associated lower respiratory tract infections. hMPV infections can lead to asthma exacerbations in small children and adults. hMPV acts as an enhancer of COPD and patients with COPD are more prone to hMPV infection.

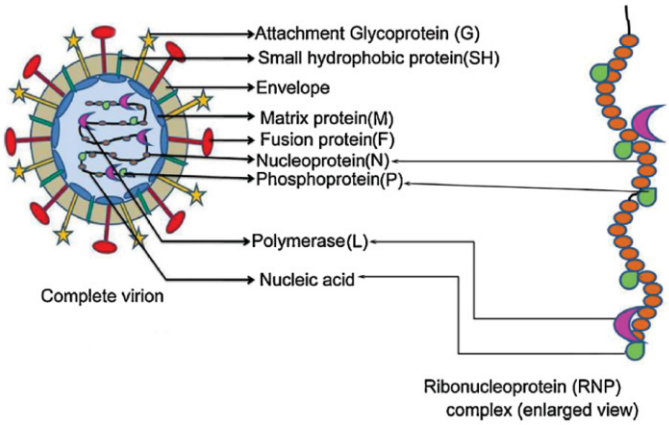
Pathogenecity



Molecular events in the pathogenesis of hMPV infection. Virus attachment to toll-like receptors (TLR) of macrophage and/or dendritic cells activates several adapter molecules of the immune system (TRIF and MYD88), which in turn activates nuclear factor kappa beta (NFkb). RNA of internalized virus is detected by cytoplasmic RIG1-like receptor (RLR), which in turn activates NFkb by activation of mitochondrial antiviral signalling protein (MAVS) and transcription activators interferon regulatory factors 3 and 7 (IRF-3 and IRF-7). Finally, NFkb and IRFs induce the production of several interferons and interleukins.

Diagnosis

Various cell lines, such as Vero cells,75 HEp-2 cells, Hep G2 cells,76 293 cells,29 and LLC-MK2 cells5 have been used for the growth and isolation of hMPV. Currently, the use of cell culture for the diagnosis of hMPV infection is uncommon and molecular methods like RT-PCR and/or real-time RT-PCR are more widely used. Many clinical laboratories do not at present have the capability to perform routine diagnostic RT-PCR for hMPV detection. For rapid and accurate diagnosis of hMPV infections, a combination of immunofluorescence assays and direct fluorescent antibody methods is used as the first line of diagnosis, followed by RT-PCR on the negative samples.



Treatment and Control Strategies

Using ribavirin, immunoglobulin, fusion inhibitors, and small interfering ribonucleic acids for the treatment and control of hMPV infection. The different strategies used to treat hMPV infection are reviewed in Table 1 below.

Human metapneumovirus (hMPV) appears to be as dangerous pathogen as hRSV in terms of morbidity and mortality. As an important respiratory pathogen, understanding hMPV pathogenesis and molecular constraints for severe disease is essential for the treatment of infection and for the development of an effective vaccine against hMPV.

Table

Different treatment strategies under development for the prevention of human metapneumovirus (hMPV) infection

Control strategy	Product	Human/animal model used	Results
Antivirals	Ribavirin	Tissue culture assay	Ribavirin along with intravenous immunoglobulin was found to have antiviral activity against hMPV in vitro
		Human	Oral ribavirin combined with intravenous immunoglobulin led to rapid and complete recovery in an immunocompromised child who was undergoing chemotherapy for Burkitt's lymphoma
Antibodies	Monoclonal antibody	Mice	On immunization in BALB/c mice, showed significantly reduced lung viral titres, decreased histopathological changes, and decreased airway obstruction post challenge with hMPV
		Hamster	Monoclonal antibodies against hMPV F protein showed protection against heterologous hMPV challenge in hamsters
		Mice	Human monoclonal antibody was able to cross-neutralize hMPV and hRSV and may be used as prophylaxis and therapy for severe hRSV and hMPV
Fusion inhibitors	Inhibitory peptides	Mice	Fusion peptides against heptad repeat A and B domains of F protein gave protection against lethal hMPV intranasal challenge in BALB/c mice. Post-challenge there was a significant decrease in lung viral load, pulmonary inflammation, levels of proinflammatory cytokines, and airway obstruction
RNA interference	SiRNA	LLC-MK2 cells	SiRNA targeting P and N genes of hMPV was able to inhibit replication of all subgroups of HMPV in vitro
		Mice	Dicer substrate SiRNA reduced lung viral titre post-challenge in mice
Inactivated vaccine	Heat inactivated vaccine	Mice	Immunization gave protective immunity against a homologous strain of hMPV followed by intranasal challenge in BALB/c mice
Epitope vaccine	T lymphocyte epitope vaccine	Mice	Immunization reduced viral load, lung pathology, and expression of Th2-type cytokines (IL-10, IL-4) after hMPV challenge
Chimeric vaccine	hMPV antigen on parainfluenza vaccine	African green monkeys, rhesus monkey	Intranasal immunization of African green monkeys induced hMPV-specific humoral and cell-mediated immune response and complete protection from wild-type hMPV challenge. In the rhesus monkey, this vaccine was found to be sufficiently attenuated
Subunit vaccine	hMPV F subunit vaccine	Hamster	Intranasal immunization with recombinant human PIV-1 expressing hMPV F protein vaccine showed high immunogenicity and protection in comparison to the ones expressing G and SH proteins
		Cotton rats	Immunization showed reduced nasal viral shedding in cotton rats after hMPV challenge, while the lung pathology was comparable to that of control mice
		Syrian golden hamsters	Immunization induced high virus neutralization titres against homologous virus. It also showed significantly reduced viral titres in nasal turbinates
		Cynomolgus macaques	Immunization induced hMPV F specific antibody response, neutralizing antibody, and a robust cellular immune response. However, the induced humoral response waned rapidly over time
VLP	Virus-like particles (VLPs)	Mice	Immunization induced cross-protective immunity in mice against both homologous and heterologous strains, along with reduced viral titres in the lungs of immunized animals
Live attenuated vaccine	ΔM2-2	Hamster	Attenuated and protective in hamsters against Wild type hMPV challenge
	ΔG, ΔSH, ΔM2-2	African green monkeys	ΔG and ΔM2-2 were sufficiently attenuated. After challenge with wild-type hMPV, virus shedding in the lower respiratory tract was undetectable
	ΔM2-2	Mice	Immunization induced complete protection against challenge with a homologous strain and cross-protective immunity against a heterologous strain

hRSV, human respiratory syncytial virus; SiRNA, small interfering RNA; IL, interleukin.

A review of conventional and emerging technologies for hydrogels sterilization

Hydrogels are three-dimensional polymeric networks with the ability to absorb large amounts of water and other biological fluids without dissolving. Their high-water content, flexibility, and softness make them structurally like living tissue.

This resemblance, together with general good biocompatibility, makes hydrogels ideal materials for several biomedical and health-related applications such as tissue regeneration, drug delivery, wound dressings, and contact lenses.

Sterility is an essential requisite for any biomaterial intended to be implanted or to be in close contact with living tissues (e.g. organs, or to replace part of it such as in bone defects and wounds).

Two main approaches can be followed to obtain a sterile product: **aseptic processing** or **terminal sterilization**.

Aseptic processing requires the sterilization of all raw materials and equipment involved in the production, as well as the assurance of operational conditions capable to maintain sterility. This is a costly procedure that requires the maintenance of an extremely controlled production environment and that does not offer the level of security of terminal methods. Thus, aseptic processing is only adopted when the terminal sterilization of the final product is not possible.

In **terminal sterilization**, the finished product is sterilized in its final package.
Common (final) sterilization methods include steam and dry heat, ionizing radiation, gas sterilization and sterilizing filtration. The adoption of this approach reduces the costs of production and enables the achievement of a higher sterility assurance level (SAL), a probabilistic parameter used to assess the effectiveness of a sterilization process.

A value of SAL $\leq 10^{-6}$, i.e. the probability of having not more than one viable microorganism in 10^{6} sterilized units of the final product, is usually a critical requirement for health care products and medicines.

However, exposition to the harsh physical or chemical conditions of the sterilization process can change the chemical, physical, and mechanical properties of the biomaterials or even lead to the formation of toxic residues.

Hydrogel classifications according to some of their features and final/functional properties

Feature: **Source**
Benefit: Natural origin comprises biomacromolecules, i.e., macromolecules formed by living organisms (e.g., proteins, nucleic acids, and polysaccharides).
Man-made: comprises macromolecules that are manmade.
Man-modified: comprises chemically modified biomacromolecules.

Feature: **Charge**
Benefit: Non-charged: comprised macromolecules having no anionic/cationic charges, or of the zwitterionic type (net charge is zero).
Charged: comprises macromolecules having anionic or cationic charges (net charge is not zero).
Zwitterionic: contains both anionic and cationic groups.

Feature: **Intramolecular structure**
Benefit: Homopolymers: derived from one species of monomer.
Copolymers: derived from more than one species of monomer.
Interpenetrating networks comprises two or more networks that are, at least, partially interlaced on a molecular scale but not covalently bonded to each other. These networks cannot be separated unless chemical bonds are broken.
Semi-interpenetrating networks comprises one (or more) networks and one (or more) linear or branched polymer(s), and where the latter can penetrate on a molecular scale of, at least, one of the former networks.

Feature: **Structure**
Benefit: Amorphous: comprises polymers that are in the amorphous state, i.e., in a state of matter that is characterized by the absence of long-range molecular order.
Crystalline/semicrystalline: comprises polymers having a significant fraction of material in the crystalline state, i.e., a state of matter that is ideally characterized by a three dimensional, long-range order on an atomic scale. It should be noted that polymers rarely crystallize completely and, therefore, there is always some amorphous material coexisting with the crystalline phases (thus presenting a specific degree of crystallinity).

Feature: **Degradability**
Benefit: Biodegradable: comprises polymers susceptible to degradation by biological activity (in specific biological environments) by lowering the molar masses of macromolecules that form the substances.
Non-biodegradable: comprises polymers not susceptible to degradation by biological activity (in specific biological environments) by lowering the molar masses of macromolecules that form the substances.

Feature: **Crosslinking**
Benefit: Physically crosslinked: comprises macromolecules having regions from which, at least, four chains emanate, and which are formed by the intermolecular or intramolecular interactions between existing macromolecules and other molecules that are present (e.g., ionic and electrostatic interactions).
Chemically crosslinked: comprises macromolecules having regions from which at least four chains emanate, and which are formed by reactions involving sites or groups on existing macromolecules, and other molecules that are present (e.g., covalent bonds).
Permanently crosslinked: crosslinked polymers (formed by covalent bonds, intermolecular or intramolecular interactions)

that are stable under the conditions of use of the material formed.
Transiently crosslinked: crosslinked polymers (formed by covalent bonds, intermolecular or intramolecular interactions) that are unstable under the conditions of use of the material formed.

Feature: **Response**
Benefit: Responsive: comprised by macromolecules that respond to external electrical, mechanical, thermal, light-induced or chemical stimulation (e.g., pH, ionic strength, electromagnetic field, electrical current, light/radiation, temperature, pressure, stress/shear, enzymes, oxidants/ reducers, etc.).
Non-Responsive: comprised by macromolecules that do not respond to external electrical, mechanical, thermal, light-induced or chemical stimulation (e.g., pH, ionic strength, electromagnetic field, electrical current, light/ radiation, temperature, pressure, stress/shear, enzymes, oxidants/ reducers, etc.).

Biomedical applications
Hydrogels have been extensively used in several fields. Several hydrogels have been proposed as drug delivery systems. Injectable hydrogels have attracted more attention in recent years. Others allow the controlled release of anticancer drugs. Some examples include doxazocin loaded in chitosan-PVA crosslinked hydrogels and 5-fluorouracil impregnated in chitosan *in situ* gelling hydrogel for injection.

Other innovative systems for drug delivery include 3D printing of hydrogels, and hydrogel-based microneedles.

Another application of hydrogels is their use as contact lenses. Hydrogel contact lenses have a wide range of characteristics, and silicone hydrogel lenses (containing siloxy groups) have a dominant position in the market due to their higher oxygen permeability and comfortable fit.

One of the advantages of hydrogel-based wound dressings are that it can decrease pain due to a cooling effect and low adherence to the tissue/wound. Hydrogel-based dressings are, in fact, promising systems since they can keep the wound moist and absorb the exudate: avoid adhesion to sensitive underlying tissue and reduce pain. hydrogel dressings may be impregnated with antimicrobial agents and may be used as drug-controlled release systems.

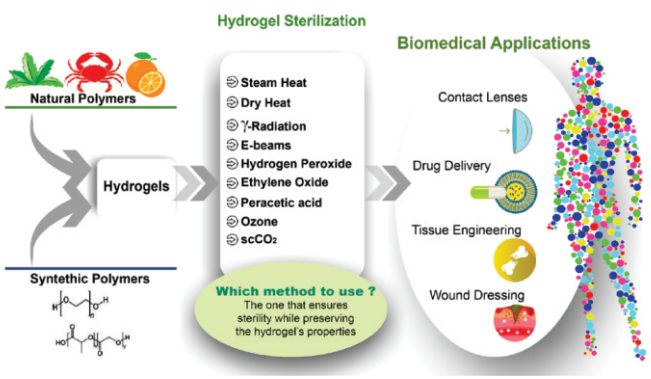
Due to its biocompatibility, low toxicity, and antimicrobial and haemostatic activity, among many others, chitosan has been a material of choice for the development of hydrogels for wound dressing. Alginate is also one of the most frequently used polymers. Being hydrophilic, it can easily absorb high volumes of wound exudate, as intended. Moreover, it has a haemostatic effect and increases cell migration.

Hydrogels present ideal characteristics for tissue engineering/ regenerative medicine, such as biocompatibility, biodegradability, highly porous structure, high water content, controllable physical properties and flexibility in fabrication. In addition, hydrogels present structures like the extracellular matrix of many tissues and can be delivered in a minimum invasive manner.

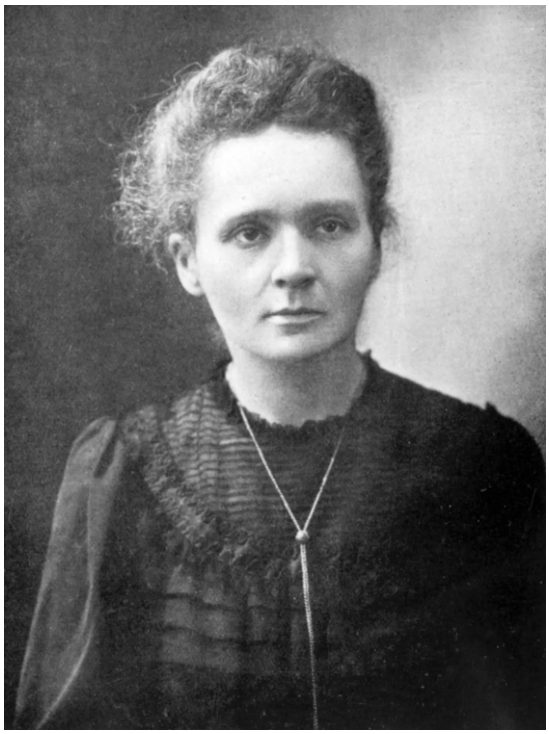
In tissue engineering, hydrogels can be applied as space-filling agents, delivery vehicles for bioactive substances able to influence cellular behaviour or three-dimensional structures that allow cell organization and present stimuli for tissue development.

Hydrogels can also be used to deliver bioactive substances to a target tissue, to promote angiogenesis and encapsulation of secretory cells. A scaffold used as a delivery vehicle allows local and specific delivery to the desired tissue, avoiding the drug degradation or its uptake by other tissues, to which it may be toxic.

In addition, hydrogel scaffolds can be applied for cell transplant and to engineer many tissues, such as cartilage, bone, muscle, fat, liver and neurons. Their highly hydrated three-dimensional network provides an ideal chemical and mechanical environment for cell adhesion, proliferation and differentiation, making them suitable for tissue development the mechanisms of degradation during the processing.



Marie Curie



Marie Curie, *née* Maria Sklodowska, was born in Warsaw on November 7, 1867, the daughter of a secondary-school teacher. She received a general education in local schools and some scientific training from her father. She became involved in a students' revolutionary organization and found it prudent to leave Warsaw, then in the part of Poland dominated by Russia, for Cracow, which at that time was under Austrian rule. In 1891, she went to Paris to continue her studies at the Sorbonne where she obtained Licenciateships in Physics and the Mathematical Sciences. She met Pierre Curie, Professor in the School of Physics in 1894 and in the following year they were married. She succeeded her husband as Head of the Physics Laboratory at the Sorbonne, gained her Doctor of Science degree in 1903, and following the tragic death of Pierre Curie in 1906, she took his place as Professor of General Physics in the Faculty of Sciences, the first time a woman had held this position. She was also appointed Director of the Curie Laboratory in the Radium Institute of the University of Paris, founded in 1914.

Her early researches, together with her husband, were often performed under difficult conditions, laboratory arrangements were poor and both had to undertake much teaching to earn a livelihood. The discovery of radioactivity by Henri Becquerel in 1896 inspired the Curies in their brilliant researches and analyses which led to the isolation of polonium, named after the country of Marie's birth, and radium. Mme. Curie developed methods for the separation of radium from radioactive residues in sufficient quantities to allow for its characterization and the careful study of its properties, therapeutic properties in particular.

Mme. Curie throughout her life actively promoted the use of radium to alleviate suffering and during World War I, assisted by her daughter, Irene, she personally devoted herself to this remedial work. She retained her enthusiasm for science throughout her life and did much to establish a radioactivity laboratory in her native city – in 1929 President Hoover of the United States presented her with a gift of $ 50,000, donated by American friends of science, to purchase radium for use in the laboratory in Warsaw.

Mme. Curie, quiet, dignified and unassuming, was held in high esteem and admiration by scientists throughout the world. She was a member of the Conseil du Physique Solvay from 1911 until her death and since 1922 she had been a member of the Committee of Intellectual Co-operation of the League of Nations. Her work is recorded in numerous papers in scientific journals and she is the author of *Recherches sur les Substances Radioactives* (1904), *L'Isotopie et les Éléments Isotopes* and the classic *Traité' de Radioactivité* (1910).

The importance of Mme. Curie's work is reflected in the numerous awards bestowed on her. She received many honorary science, medicine and law degrees and honorary memberships of learned societies throughout the world. Together with her husband, she was awarded half of the Nobel Prize for Physics in 1903, for their study into the spontaneous radiation discovered by Becquerel, who was awarded the other half of the Prize. In 1911 she received a second Nobel Prize, this time in Chemistry, in recognition of her work in radioactivity. She also received, jointly with her husband, the Davy Medal of the Royal Society in 1903 and, in 1921, President Harding of the United States, on behalf of the women of America, presented her with one gram of radium in recognition of her service to science.

For further details, cf. Biography of Pierre Curie. Mme. Curie died in Savoy, France, after a short illness, on July 4, 1934.

From *Nobel Lectures, Physics 1901-1921*, Elsevier Publishing Company, Amsterdam, 1967

This autobiography/biography was written at the time of the award and first published in the book series *Les Prix Nobel*. It was later edited and republished in *Nobel Lectures*. To cite this document, always state the source as shown above.

Jokes

Wife: If you keep losing your hair at this speed, I shall divorce you.

Husband: Oh my God! And I was stupid enough trying to save them!

Wife: What are ten years with me?

Husband: A second.

Wife: What is $1,000 for me?

Husband: A coin.

Wife: Ok, give me a coin.

Husband: Wait a second.

Husband: "Do you like beaches, sweetheart?"

Wife: "Yes, darling. The scenic views at the beach make me quite speechless!"

Husband: "Excellent, we're staying three weeks there."

Wife: "Darling, you never listen to me."

Husband: "Excuse me, what did you just say?"

Wife: "Why are you watching cooking shows if you can't cook?"

Husband: "Well, you watch romantic movies, don't you?"

Wife: "I love you."

Husband: "Is that you are talking or the wine?"

Wife: "It's me talking to the wine."

Human metapneumovirus (HMPV)

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.

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.

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.

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.

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.

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.

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.

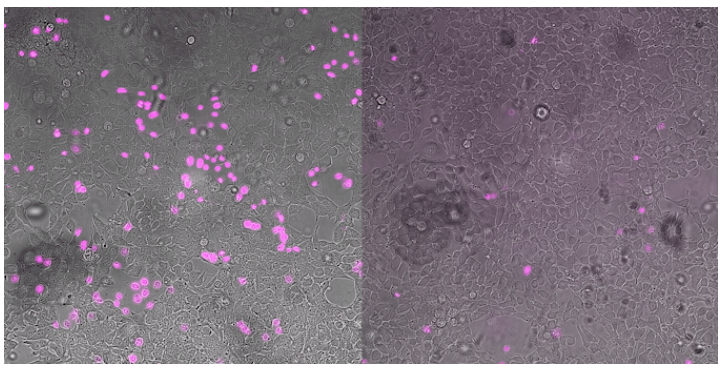
Treatment / Management

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.

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.

Artificial intelligence could take the bite out of snake venom.



Using AI, scientists have designed proteins that say not so fassst to toxins wielded by cobras and other venomous snakes. It's a proof-of-concept approach that could one day offer a new treatment for snakebites. In lab experiments, the custom proteins saved the lives of mice given an otherwise lethal dose of toxins, researchers report January 15 in *Nature*.

These proteins "are really doing their job," says Michael Hust, an antibody researcher at the Technical University of Braunschweig in Germany who was not involved with the new research. "The mice are surviving. This is what we all want."

The work represents the latest real-life application of work that earned three scientists the 2024 Nobel Prize in chemistry. In 2022, medical biotechnologist Timothy Jenkins spotted a preprint from the lab of David Baker, a biochemist at the University of Washington School of Medicine in Seattle and one of the Nobel awardees. The preprint described AI-designed proteins that stick like superglue to specific molecules.

That sparked an idea. Could the AI think up a design that clamps onto — and neutralizes — snake venom toxins?

Jenkins, of the Technical University of Denmark in Lyngby, had spent years trying to develop new therapies for snakebites. Worldwide, snakebites kill some 100,000 people each year. Venomous snakes can deliver a blizzard of toxins via their bite. Some of the most dangerous include molecules called three-finger toxins, which can paralyze muscles, stilling people's hearts and their ability to breath. Antivenoms exist, but the technology is outdated, Jenkins says. "There's not a lot of money in it, so not a lot of innovation has been attracted."

Current antivenom producers milk snakes to extract their venom, which is "like handling a live hand grenade," he says. A small dose of that venom gets injected into a horse or other large animal, from which producers later harvest antibodies.

When given to a snakebite victim, those antibodies bind to venom toxins and shut them down. But manufacturing antivenom is costly and time-consuming, so scientists have been searching for other methods. One option that's seen recent success is scanning a vast collection of lab-made antibodies to identify those that target particular toxins.

With AI, scientists can quickly and cost-effectively build toxin-targeting proteins from scratch. Jenkins and Baker paired up to create custom proteins using a generative AI model called RF diffusion. It's a free protein-design tool that shares some similarity with the AIs that generate images. Instead of conjuring up a picture of the pope in a puffer jacket, RF diffusion can concoct protein designs that match a molecule scientists want to target.

In the lab, human cells exposed to toxins from black-necked spitting cobra venom typically die off within about an hour and a half (left panel). Dying cells appear to light up like a pink Christmas tree. But treating the cells with designer proteins five minutes after toxin exposure fended off the lethal effects (right panel.) University of Washington Institute for Protein Design

Baker's team had previously trained the model on all known protein structures and their amino acid sequences, the string of molecular building blocks that fold up into a protein's 3-D shape. Then, the researchers computationally disassembled those shapes. That taught the model how to put together a complete protein from its components, like learning how to build a car engine by taking it apart.

Baker and Jenkins asked the AI to design proteins that would glom on to venom toxins. Then they manufactured the proteins in the lab. Like a magnetic cap covering the tip of a key so it no longer fits in a lock, the synthesized proteins prevented the toxin from docking onto cells.

The team injected 20 mice with the custom proteins 15 minutes after a lethal dose of cobra toxins or concurrently with the toxins. Every mouse survived. "We were very, very excited about this," Jenkins says. It was a stark demonstration of the proteins' powers. Next, the team wants to develop its proteins into an actual product it could test in people. Scientists will need to ensure the custom proteins are safe, and not binding unexpectedly in human tissues, Hust says.

Jenkins agrees. The new study is just a first step to defanging venoms' harms. "It was very much just proving that this extremely new technology works," he says.

Climate Impacts on Human Health

The impacts of climate change include warming temperatures, changes in precipitation, increases in the frequency or intensity of some extreme weather events, and rising sea levels. These impacts threaten our health by affecting the food we eat, the water we drink, the air we breathe, and the weather we experience.

Temperature-Related Impacts

Warmer average temperatures will lead to hotter days and more frequent and longer heat waves. These changes will lead to an increase in heat-related deaths. Adaptive responses, such as wider use of air conditioning, are expected to reduce the projected increases in death from extreme heat. Exposure to extreme heat can lead to heat stroke and dehydration, as well as cardiovascular, respiratory, and cerebrovascular disease. Certain types of populations are more vulnerable than others: for example, outdoor workers, student athletes, and homeless people tend to be more exposed to extreme heat because they spend more time outdoors. Additionally, young children, pregnant women, older adults, and people with certain medical conditions are less able to regulate their body temperature and can therefore be more vulnerable to extreme heat.

Air Quality Impacts

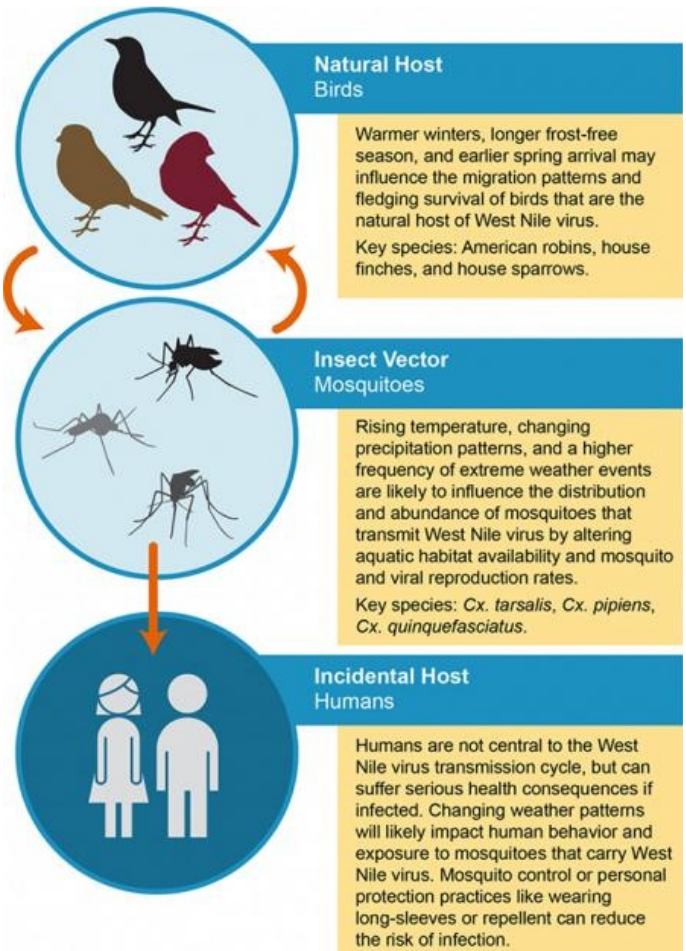
Changes in the climate affect the air we breathe both indoors and outdoors. Warmer temperatures and shifting weather patterns can worsen air quality, which can lead to asthma attacks and other respiratory and cardiovascular health effects. Wildfires, which are expected to continue to increase in number and severity as the climate changes, create smoke and other unhealthy air pollutants. Rising carbon dioxide levels and warmer temperatures also affect airborne allergens. Some particulate matter such as dust, wildfire smoke, and sea spray occur naturally, while some is created by human activities such as the burning of fossil fuels to produce energy. These particles may be emitted directly or may be formed in the atmosphere from chemical reactions of gases such as sulphur dioxide, nitrogen dioxide, and volatile organic compounds. Inhaling fine particles can lead to a broad range of adverse health effects, including lung cancer, chronic obstructive pulmonary disease (COPD), and cardiovascular disease.

Vector borne Diseases

Vector borne diseases are illnesses that are transmitted by disease *vectors*, which include mosquitoes, ticks, and fleas. These vectors can carry infectious pathogens, such as viruses, bacteria, and protozoa, from animals to humans. Changes in temperature, precipitation, and extreme events increases the geographic range of diseases spread by vectors and can lead to illnesses occurring earlier in the year. The geographic range of ticks that carry Lyme disease is limited by temperature. As air temperatures rise, ticks are likely to become active earlier in the season, and their range is likely to continue to expand northward. Typical symptoms of Lyme disease include fever, headache, fatigue, and a characteristic skin rash.

Water-Related Illnesses

People can become ill if exposed to contaminated drinking or recreational water. Climate change increases the risk of illness through increasing temperature, more frequent heavy rains and runoff, and the effects of storms. Health impacts may include gastrointestinal illness like diarrhoea, effects on the body's nervous and respiratory systems, or liver and kidney damage.



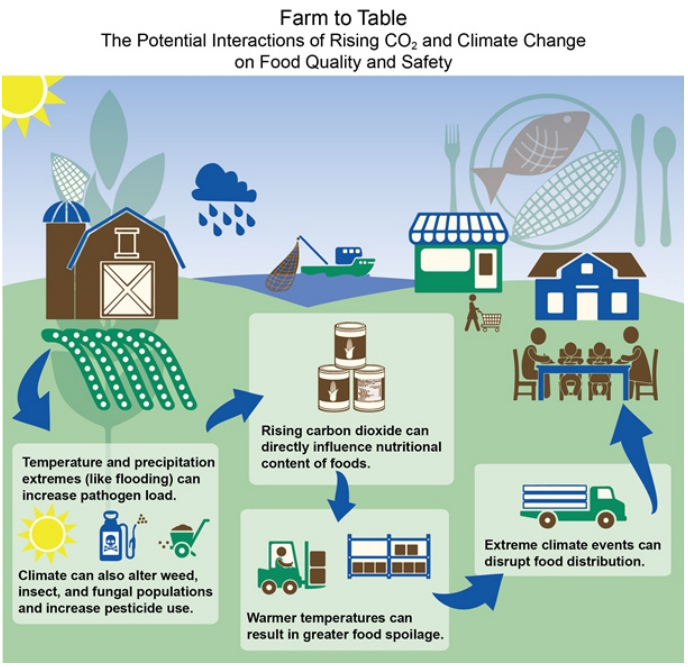
- Climate impacts can affect exposure to waterborne pathogens (bacteria, viruses, and parasites such as *Cryptosporidium* and *Giardia*); toxins produced by harmful algal and cyanobacterial blooms in the water; and chemicals that end up in water from human activities.
- Changing water temperatures mean that waterborne *Vibrio* bacteria and harmful algal toxins will be present in the water or in seafood at different times of the year, or in places where they were not previously threats.
- Runoff and flooding resulting from increases in extreme precipitation, hurricane rainfall, and storm surge will increasingly contaminate water bodies used for recreation (such as lakes and beaches), shellfish harvesting waters, and sources of drinking water.
- Extreme weather events and storm surges can damage or exceed the capacity of water infrastructure (such as drinking water or wastewater treatment plants), increasing the risk that people will be exposed to contaminants.

Food Safety and Nutrition

Climate change and the direct impacts of higher concentrations of carbon dioxide in the atmosphere are expected to affect food safety and nutrition. Extreme weather events can also disrupt or

slow the distribution of food.

- Higher air temperatures can increase cases of *Salmonella* and other bacteria-related food poisoning because bacteria grow more rapidly in warm environments. These diseases can cause gastrointestinal distress and, in severe cases, death.
- Climate change will have a variety of impacts that may increase the risk of exposure to chemical contaminants in food. For example, higher sea surface temperatures will lead to higher mercury concentrations in seafood and increases in extreme weather events will introduce contaminants into the food chain through stormwater runoff.
- Higher concentrations of carbon dioxide in the air can act as a "fertilizer" for some plants but lowers the levels of protein and essential minerals in crops such as wheat, rice, and potatoes, making these foods less nutritious.
- Extreme events, such as flooding and drought, create challenges for food distribution if roads and waterways are damaged or made inaccessible.



Mental Health

Any changes in a person's physical health or surrounding environment can also have serious impacts on their mental health. Experiencing an extreme weather event can cause stress and other mental health consequences, particularly when a person loses loved ones or their home. Individuals with mental illness are especially vulnerable to extreme heat. People taking medication for mental illness that makes it difficult to regulate their body temperature are particularly at higher risk of death during heat waves.

Highlights of the coming issue

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