Novel and Re-Emerging Human Respiratory Viruses

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ABSTREACT

Respiratory infections are major causes of morbidity and mortality worldwide. Viruses are considered an important cause of respiratory disease in both the community and hospital settings and are associated with infection at all levels of the respiratory tract. Respiratory viruses have been grouped into six distinct families including the *Paramyxoviridae, Orthomyxoviridae,Picornaviridae, oronaviridae, Adenoviridae and Herpesviridae*. However, this list of pathogens was extended with the discovery of novel respiratory viruses. The recent advances in molecular technology have enabled the detection of several new viral agents in specimens collected from the human respiratory tract.

The hMPV was first described in 2001, and is considered a significant respiratory pathogen, particularly of children. The most closely related human virus is the hRSV, with similar epidemiological and clinical characteristics. However on the basis of morphological, biochemical and genetic analyses, hMPV seemed to be closely related to aMPV-C, thus it was classified in the same genus *Metapneumovirus*.

Key Word

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LIST OF COMMON ABBREVIATIONS*

aMPV	Avian metapneumovirus
aMPV-C	Avian metapneumovirus serotype C
ARTI	Acute respiratory tract infection
CoV(s)	Coronavirus(es)
E protein	Envelope protein
F protein	Fusion protein
G protein	Attachment glycoprotein
HA	Haemagglutinin
HBoV	Human bocavirus
hMPV	Human metapneumovirus
HPAI	Highly pathogenic avian influenza viruses
hRSV	Human respiratory syncytial virus
KIV	KI polyomavirus
L protein	Large polymerase protein
LRTI(s)	Lower respiratory tract infection(s)
M protein	Membrane protein or Matrix protein
MAbs	Monoclonal antibodies

** **Abbreviations that have been mentioned more than ten times.***

N protein	Nucleocapsid protein
NA	Neuraminidase
NS protein	Non-structural protein
OC	Organ culture
ORF(s)	Open reading frame(s)
P protein	Phosphoprotein
PCR	Polymerase chain reaction
PIV(s)	Parainfluenza virus(es)
PIV3	Parainfluenza virus type 3
RT-PCR	Reverse transcription -polymerase chain reaction
S protein	Spike glycoprotein
SARS	Severe acute respiratory syndrome
SH protein	Small hydrophobic protein
URTI	Upper respiratory tract infection
VP1 and VP2	Virus proteins 1, 2
WUV	WU polyomavirus

[*] ***Abbreviations that have been mentioned more than ten times.***

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GENERAL OVERVIEW

Respiratory infections are major causes of morbidity and mortality worldwide. In children younger than five years old, acute respiratory tract infection (ARTI) is the leading cause of death **(Bryce *et al.*, 2005)**. The burden of respiratory tract infections is not limited to the pediatric population. Pneumonia, influenza and influenza-like illnesses are the sixth leading cause of death for all age groups **(Barlett *et al.*, 2000)**.

Although the clinical features of respiratory tract infections are easily recognized, the etiology of a large proportion of disease remains undetermined. For community-acquired pneumonia, the infectious agent responsible for disease is identified in only 50% of cases, despite the sensitivity of diagnostic tests such as polymerase chain reaction (PCR) and serological methods **(Ruiz *et al.*, 1999; Zambon *et al.*, 2001)**.

Viruses are an important cause of respiratory diseases in both the community and hospital settings. They are associated with infections at all levels of the respiratory tract. Viruses are responsible for a significant number of cases with upper respiratory tract symptoms as well as laryngotracheobronchitis (croup), bronchiolitis and pneumonia. They are a well-recognized cause of severe and life-threatening infections in the immunocompromised, the elderly, neonates and individuals with compromised cardiac or pulmonary systems. Moreover, they are also responsible for more 'trivial' asymptomatic infections and mild symptomatology in a community setting. Seasonal outbreaks of respiratory virus infections account for a considerable proportion of medical consultations **(Hibbitts and Fox, 2002)**.

The importance of viral respiratory tract infections (VRTIs) is immense. There are considerable costs associated with VRTIs in terms of decreased productivity and time lost from work or school, visits to healthcare providers and amount of drugs prescribed. Another important factor contributing to the impact of VRTIs is the inappropriate use of antibiotics; this significantly adds to the cost of management and to the increasing prevalence of antibiotic resistant bacteria **(File, 2003a)**.

Viruses spread in respiratory droplets, aerosols and saliva by close contact and on hands. Similar respiratory symptoms can be caused by several different viruses, as seen in Table 1 **(Murray 2005a)**.

Table 1: Oral and respiratory diseases caused by viruses.

Disease	**Etiologic Agent**
Common cold (including pharyngitis)	Rhinovirus* Coronavirus* Influenza viruses Parainfluenza viruses Respiratory syncytial virus Metapneumovirus Adenovirus Enterovirus
Pharyngitis	Herpes simplex virus Ebstein-Barr virus Adenovirus* Coxsackie A virus* (herpangina, hand-foot-and-mouth disease) and other enteroviruses.
Croup, tonsillitis, laryngitis and bronchitis (children younger than two years)	Parainfluenza virus 1* Parainfluenza virus 2 Influenza virus Adenovirus Ebstein-Barr virus
Bronchiolitis	Respiratory syncytial virus* (infants) Metapneumovirus Parainfluenza virus 3* (infants and children) Parainfluenza viruses 1 and 2
Pneumonia	Respiratory syncytial virus* (infants) Metapneumovirus Parainfluenza virus* (infants) Influenza virus* Adenovirus Varicella-zoster virus (primary infection of adults or immunocompromised hosts) Cytomegalovirus (infection of immunocompromised hosts) Measles

*Most common causal agents.

(Murray, 2005a)

Although the etiology of the majority of lower respiratory tract infections (LRTIs) is thought to be viral, yet in only 40% of cases can a viral agent be identified, even with the use of genomic amplification methods **(File, 2003b; Louie *et al.*, 2005)**. In children, human respiratory syncytial virus (hRSV), parainfluenza viruses (PIVs) and influenza viruses are known as the major causes of bronchiolitis and pneumonia. However, in up to a third of these cases, an infectious agent cannot be identified, thus suggesting that previously unidentified viruses may be circulating **(Kahn, 2007)**.

Following the boom in respiratory virology in the 1960s, species of rhinoviruses, coronaviruses (CoVs), enteroviruses (EVs), adenoviruses, PIVs and hRSV were added to influenza and measles viruses as causes of respiratory tract infections. In restricted patient groups, such as the immunocompromised, members of the family of herpesviruses including herpes simplex (HSV), cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus (EBV) and human herpes virus 6 (HHV-6) have also been associated with respiratory disease. More than 200 antigenically distinct viruses have been documented as causes of sporadic or epidemic respiratory infections in infants, children and adults. However, this varied and diverse group can be divided among six distinct families: *Paramyxoviridae, Orthomyxoviridae, Picornaviridae, Coronaviridae, Adenoviridae and Herpesviridae* **(Mackie, 2003)**.

Recent advances in molecular technology have enabled the detection of several new viral agents in specimens collected from the human respiratory tract and thus this list of pathogens was extended with the discovery of novel viruses such as human metapneumovirus (hMPV), human bocavirus (HBoV), the NL63 and HKU1 CoVs, KI and WU polyomaviruses and the giant mimivirus **(Sloots *et al.*, 2008)**.