## Influenza and other emerging respiratory viruses

Maria Zambon

#### Abstract

Acute lower respiratory tract infections (LRTIs) are a major worldwide health problem, particularly in childhood. About 30–50% of acute LRTIs are viral in origin with influenza A infection a key cause of explosive community outbreaks. Many different influenza A viruses occur naturally in animal reservoirs and present a constant threat of zoonotic infections and global pandemics. Since 2009, when pandemic (H1N1) influenza A emerged from a swine origin, there have been a number of different zoonotic influenza A transmissions into the human population, including H1N1 and H3N2 variant viruses in North America and H7N9 viruses in China. The segmented nature of the influenza A virus genome and the circulation of these viruses in wild bird, domestic poultry and mammalian reservoirs presents a continuous opportunity for reassortment of viral genes and the emergence of a novel pandemic virus. Constant vigilance is required.

The emergence of severe acute respiratory syndrome in 2003 and Middle East respiratory syndrome coronavirus in 2012, highlights the fact that other serious respiratory viral infections in humans may originate in animals. Enhanced awareness of the potential for serious human respiratory disease in association with travel, or animal exposure, should form part of clinical assessment. Rapid developments in genomic technology improve the ability to diagnose previously undetected pathogens.

Preventative measures for influenza include annual vaccination and treatment with antiviral drugs such as neuraminidase inhibitors, oseltamivir and zanamivir. Subtype-dependent resistance to antivirals can develop and should be closely monitored.

**Keywords** coronavirus; emerging; influenza; pandemic; respiratory; severe; virus; zoonosis

#### **Respiratory viruses**

Transmission of infections between humans through a respiratory route is well established and dependent on pathogens being carried in secretions that are transmitted between individuals as aerosols, droplets, secretions or via direct mucosal contact. Viruses have adapted to the human population over many millennia,<sup>1</sup> and many have now evolved to exclusive transmission in humans through the respiratory route, yet the disease

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### What's new?

- Emergence of Middle East respiratory syndrome coronavirus as a cause of sporadic, severe acute respiratory illness with a high fatality rate linked to unknown animal exposure in the Arabian peninsula
- Emergence of H7N9 influenza virus in humans exposed to poultry in China
- Recombination of avian, pig and human influenza viruses giving rise to new variants of H3N2 and H1N1 in swine in North America
- Introduction of live attenuated influenza vaccines in childhood in the UK

they cause is not restricted to the respiratory system. Examples of viruses causing systemic disease transmitted through the respiratory route include measles and erythrovirus B19. Other human viral infections cause respiratory system disease and transmit through respiratory secretions; for example, respiratory syncytial virus (RSV), rhinoviruses and human adapted strains of influenza A, which cause seasonal epidemics, and influenza B and C, which are human pathogens. The outcome of infection and clinical disease presentation is partly dependent on virus factors, which restrict viral replication to certain cell types (tissue tropism).

#### Viruses emerging into humans from animal hosts

Sporadic transmission of viruses from their natural animal host to humans can cause zoonotic infections with disease of varying severity and epidemic scale, depending on the virus. For many of these infections, humans are dead-end hosts. Such infections are usually well recognized, with effective control measures to limit human disease; examples include rabies. However, new infectious agents of man are described at regular intervals. For the last decade at least one significant new human pathogen has been identified almost every year, involving a diversity of organisms. The rate of identification of new viruses has increased in recent years with the application of genomics, which has facilitated the detection of organisms that could not previously be cultivated (Table 1).<sup>2</sup>

#### Characteristics of emerging virus infections

Approximately 75% of all newly described human pathogens (emerging diseases) are RNA viruses, many of which are transmitted through a mucosal or respiratory route. Not all of these cause serious human infections. Some may be viruses that have been in the human population for decades or even centuries without an animal reservoir, but through the application of improved diagnostic techniques are now recognized, such as human metapneumovirus (hMPV) (Table 2). Other newly described infections may have emerged very recently into the human population as a result of a species jump, such as human immunodeficiency virus (HIV), pandemic influenza, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome coronavirus (MERS-CoV). Such infections may first come to attention as a result of a severe undiagnosed respiratory

Co-evolution of viruses with humans	Acquisition from animals, now permanently established	Temporary residents, occasional zoonotic transmission
α β γ herpesviruses	Measles	Rabies
Papilloma + polyoma	HIV	Ebola
Hepatitis B	Smallpox	Lassa
	Human Influenza A H3N2	Hanta
	Influenza B	Nipah
	RSV	SARS
		H5N1
RSV, respiratory syncytial virus; SARS, severe a	acute respiratory syndrome.	

#### Table 1

Viruses in humans

illness, or an unusual severe illness requiring critical care, without obvious animal exposures, and may be detected as a result of an astute clinician requesting detailed diagnostic testing to rule out known infections. Evaluating the importance of a newly emerging virus is dependent on understanding the host range, disease and pathogenesis in man, transmissibility and likelihood of sustained transmission in human population.

#### Viruses with pandemic potential

The term pandemic is usually taken to indicate a very widespread epidemic with an infection that has the capacity to cause disease on a global scale. A new influenza A virus in the human population, known as pandemic influenza, has the greatest impact on human populations as a result of morbidity and mortality in all age groups,<sup>2</sup> but several other viruses, such as SARS coronavirus are also capable of causing significant clinical, economic and financial impact on a global level (Figures 1 and 2). In 2013, there is an unprecedented pandemic threat involving severe virus infections new to human populations. Two different viruses, influenza A H7N9<sup>3</sup> and MERS-CoV,<sup>4</sup> circulating in different animal reservoirs in China and the Arabian peninsula respectively, have caused fatalities in humans and demonstrated limited human-to-human transmission

#### Zoonotic origin of emerging viral pathogens in human disease

Virus (genus or type species)	Human disease	Animal source	Probability L = Likely P = Possible C = Confirmed
Calicivirus	Diarrhoea	Swine, cattle	L
Rotavirus	Diarrhoea	Swine, cattle	L
Ebola virus	Haemorrhagic fever	Monkeys	Р
Sin nombre virus	HFRS, HPS	Rodents	С
HIV	AIDS	Monkeys	L/C
HEV	Hepatitis	Swine	Р
Influenza virus	Influenza	Pigs	Reassortants L
		Horses	Reassortants L
		Birds	С
Hendravirus	Meningo-encephalitis	Fruit bat	L
		Tree shrew	L
Nipahvirus	Encephalitis	Pigs	L
		Dogs	Р
Metapneumovirus	Respiratory tract infection	Birds	Р
West Nile virus	Encephalitis	Birds	С
Cantalagovirus	Vesicular rash	Cattle	С
Borna disease virus	Encephalomyelitis	Horses	Р
BSE agent	nvCJD	Cattle	Р

BSE, bovine spongiform encephalopathy; HEV, hepatitis E virus; HFRS, haemorrhagic fever with renal syndrome; HPS, hantavirus pulmonary syndrome; nvCJD, new variant Creutzfeldt-Jacob disease.

#### Table 2

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