Influenza and other emerging respiratory viruses

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Abstract

Acute respiratory infections are one of the top five causes of mortality worldwide and contribute to >4 million deaths per year. Consequently, emerging respiratory viruses are a continuing threat to global health security and have the potential to affect our economies. Since the millennium, there have been around a dozen different outbreaks, several capturing international interest. The outbreak of severe acute respiratory syndrome coronavirus saw the beginning of an extensive global collaboration and has influenced many outbreak preparedness protocols now in place. Avian influenza is a particular threat, with cases of A(H5N1) and A(H7N9) reported most recently. Middle East respiratory syndrome coronavirus is causing continuing concerns with outbreaks in the Arabian Peninsula. Healthcare facilities worldwide play a crucial role in identifying threats and must be vigilant. Particularly important is identifying and managing emerging respiratory viruses when they are infrequently encountered. Surveillance, continuing research, vaccine and treatment developments are key to guiding the efforts and actions of healthcare workers, international health organizations, governments and other stakeholders. Each individual has a part to play in protecting our global health.

Keywords A(H1N1)pdm09; A(H5N1); A(H7N9); emerging; influenza; MERS-CoV; MRCP; outbreak; respiratory; SARS-CoV; virus

Key points

- Understand risk assessment. Know the key symptoms and signs for the emerging respiratory viruses and their specific management. Uphold basic hygiene principles and use of personal protective equipment
- Know how to contact public health professionals out of hours and inform them of notifiable diseases. Discuss with your local laboratory when an emerging respiratory virus is suspected
- Keep up to date with the latest emerging diseases. The following information sources can help: World Health Organization Disease Outbreak News online, Public Health England website announcement page and ProMED-mail website.

Introduction

A discussion of emerging respiratory viruses would not be complete without reference to the work of the World Health Organization (WHO). This organization closely monitors emerging respiratory viruses and assists countries with preparedness, prevention, response and recovery from these diseases, as well as aiming to reduce the threat to global health security (www.who.int).

A comprehensive list of emerging respiratory viruses is shown in Table 1. Here, we will focus on six key respiratory viruses: influenza viruses A(H5N1), A(H7N9), A(H1N1)pdm09 and seasonal influenza, and severe acute respiratory syndrome and Middle East respiratory syndrome coronaviruses (SARS-CoV, MERS-CoV). These have been selected because of their global impact, with high morbidity and mortality rates, and their importance in understanding emerging respiratory viruses.

In the clinical setting, it is important to be able to recognize symptoms and signs of these diseases, investigate and manage patients appropriately, and have an awareness of the public health impact and continuing research. With increasing globalization, particularly with travel and trade, a small epidemic can quickly develop into a pandemic, with little time to prepare a public health response. Clinicians are at the front line, and rapid recognition is critical in responding to these public health emergencies.

At the time of writing, the respiratory viruses considered as particular public health threats were A(H7N9) and MERS-CoV.[1] Even though it circulates widely, seasonal influenza, including H1N1, is less concerning because of immunity in the population, helped by vaccination; this therefore results in a more benign infection in many individuals.

The influenza viruses, four of which are discussed here – A(H5N1), A(H7N9), A(H1N1)pdm09, seasonal influenza – are grouped into three main types, A, B and C, all associated with human disease. Type A contains two subgroupings depending on the type of surface protein carried by the virus –haemagglutinin (H protein) or neuraminidase (N protein). Type A can infect many different animals as well as humans; its natural reservoir is aquatic birds. Type B circulates only in humans, and type C can infect humans and pigs, although infections are mild.

Influenza is notorious for its ability to change and present itself to the immune system as a newly encountered pathogen against which the body has no immunity. In *antigenic drift*, small genetic changes occur over time as the virus replicates. The changes are usually so small that the virus' antigenic properties remain the same and the immune system is able to recognize the

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Emerging respiratory viruses in chronological order over the past 20 years

Virus	Year	Region
Influenza A(H5N1)	1997	Hong Kong
Influenza A(H9N2)	1999	Hong Kong
Human metapneumovirus	2001	Netherlands
SARS coronavirus	2003	Hong Kong
Human coronavirus NL63	2004	Netherlands
Influenza A(H7N7)	2004	Netherlands
Human coronavirus HKU1	2005	China
Influenza A H1 triple reassortment	2005	USA
Triple reassortment H3N2 influenza A	2005	Canada
Bocavirus	2005	Sweden
Influenza A (H1N1)pdm09	2009	Mexico
Adenovirus 14	2010	USA
MERS coronavirus	2012	Saudi Arabia
Influenza A(H7N9)	2013	China

Source: Adapted from Al-Tawfiq JA et al. (see Further reading).

Table 1

pathogen (known as cross-protection). If these small changes accumulate, an antigenically different virus is produced to which the host has no immunity. The population is therefore able to catch flu more than once, and a new flu vaccine is produced each year according to the evolving viruses.

In *antigenic shift*, a major genetic change occurs resulting in new H or N proteins. Pandemics are often caused by recombinant viruses that derive some of their genetic material from an avian and some from a human influenza virus (known as reassortment). This mixing can occur when a host such as a pig is infected by the two viruses. The H and/or N proteins are derived from the avian virus and are antigenically different from those against which the population has immunity. A pandemic can then occur. Type A viruses undergo both antigenic drift and antigenic shift, whereas type B viruses change by antigenic drift.

Emerging respiratory viruses

Seasonal influenza

Seasonal influenza is a common cause of respiratory infection in humans during the winter months in both the northern and southern hemispheres. However, in tropical and subtropical areas, it can occur all year round. Because these viruses are continually evolving and new ones appearing, the population can become infected multiple times during their lifetime.

The disease is often mild but can sometimes be severe and is a cause of mortality in vulnerable individuals, particularly very young children, pregnant women and those who are elderly or immunocompromised. Worldwide, these annual epidemics result in around 250,000–500,000 deaths.[1] They also have a substantial economic impact through reduced workforce productivity and pressurizing health services. These viruses are transmitted from person to person by respiratory droplets (coughing, sneezing) or by touching infected surfaces.

Generally, two vaccines are developed each year to cover the current most prominent circulating strains for the northern and southern hemispheres. The WHO's Global Influenza Surveillance and Response System (GISRS) meets twice a year to update the vaccine. The 2017–2018 northern hemisphere vaccine currently contains three strains including H1N1, which caused the 2009 'swine flu' pandemic. Influenza types A and B are generally used in the vaccine. Type C strains cause such mild illnesses that they are not included.

The vaccine is available to everyone in the UK and is free for children aged 6 months to 2 years who are at risk of flu, pregnant women, adults at risk of flu, including healthcare workers, and all those aged 65 years and over.[2] The WHO recommends annual vaccination for all high-risk groups, and prioritization of pregnant women.

A(H1N1)pdm09 – swine flu

First identified in Mexico in April 2009, this was called swine flu because its genetic make-up was derived from a quadruple reassortment involving genes from pigs, birds and humans.[1] The virus established human-to-human transmission and spread rapidly through respiratory droplets and touching infected surfaces. However, it mostly caused mild infection because of a level of immunity in the older population. Some severe cases and deaths occurred, particularly in younger persons, including those in good health.

The pandemic was declared over in August 2010.[1] The WHO reported that >214 countries were affected, with >18,449 laboratory-confirmed deaths by the end of the pandemic.[1] The US Centers for Disease Control and Prevention (CDC) later estimated the total number of deaths (not all laboratory confirmed) as 284,000.[3] At the time, the pandemic was a major health concern because of its rapid spread and the lack of vaccine at the outset. H1N1 is now circulating as one of the seasonal flu viruses. With the increasing immunity in the population, it is now considered less of a global health threat.

A(H5N1) – avian flu

An outbreak of A(H5N1) occurred in Hong Kong in 1997. This was the first documented transmission of an avian influenza virus into the human population leading to disease. No cases were confirmed again until 2003, when a handful of cases were identified with a travel history to Fujian Province, China. The virus then spread through poultry in Asia and Europe, and cases have been detected in animals since then. Human cases have also occurred globally since 2003, affecting 16 countries, with Indonesia, Egypt and Viet Nam experiencing most cases and fatalities.[1]

To date, there have been 859 cases, 453 resulting in death.[1] In 2017, up until end July, there were three cases and one death, which were all in Egypt.[1] In the UK, no human cases had occurred and the virus had not been detected in animals since 2008.[1]

Most cases of A(H5N1) have been related to close contact with infected birds or environments. The virus does not transmit well from person to person, but this has occurred from close contact with family members. It is an important threat because of its high mortality rate, 60% in infected individuals, and continued sporadic presence.[1] If the virus mutates to become easily transmissible from person to person, the consequences could be substantial.

A(H7N9) – avian flu

In 2013, human infections with A(H7N9) were reported in southeastern China. As of 7 August 2017, a total of 1582 cases had been

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