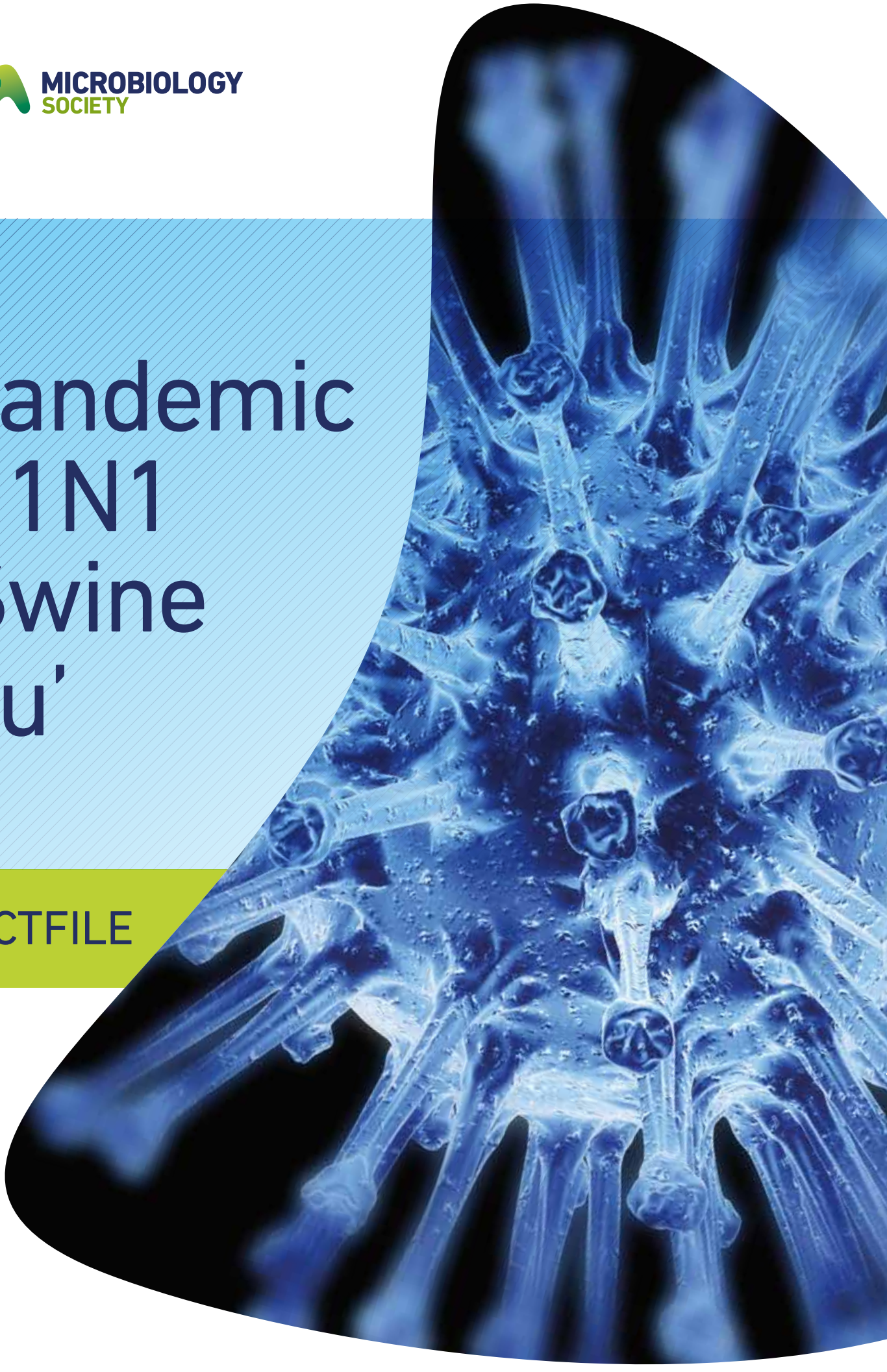
MICROBIOLOGY SOCIETY

Pandemic H1N1 'Swine flu'

FACTFILE



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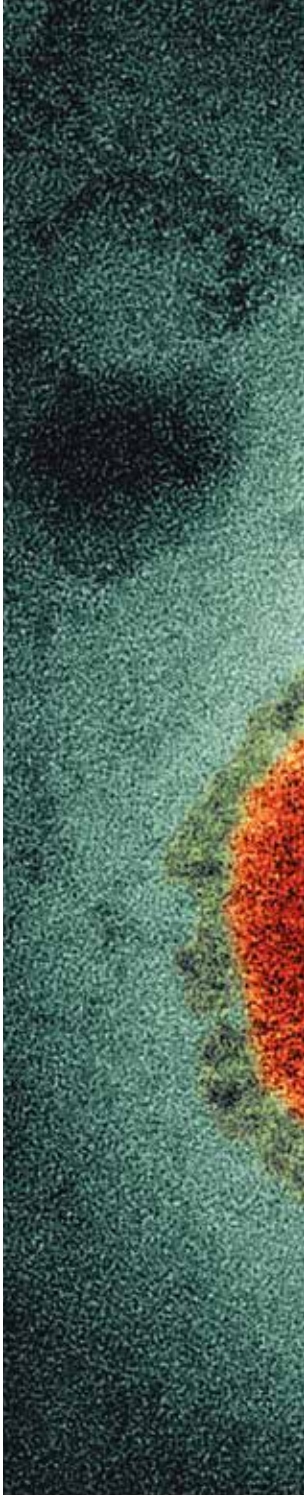
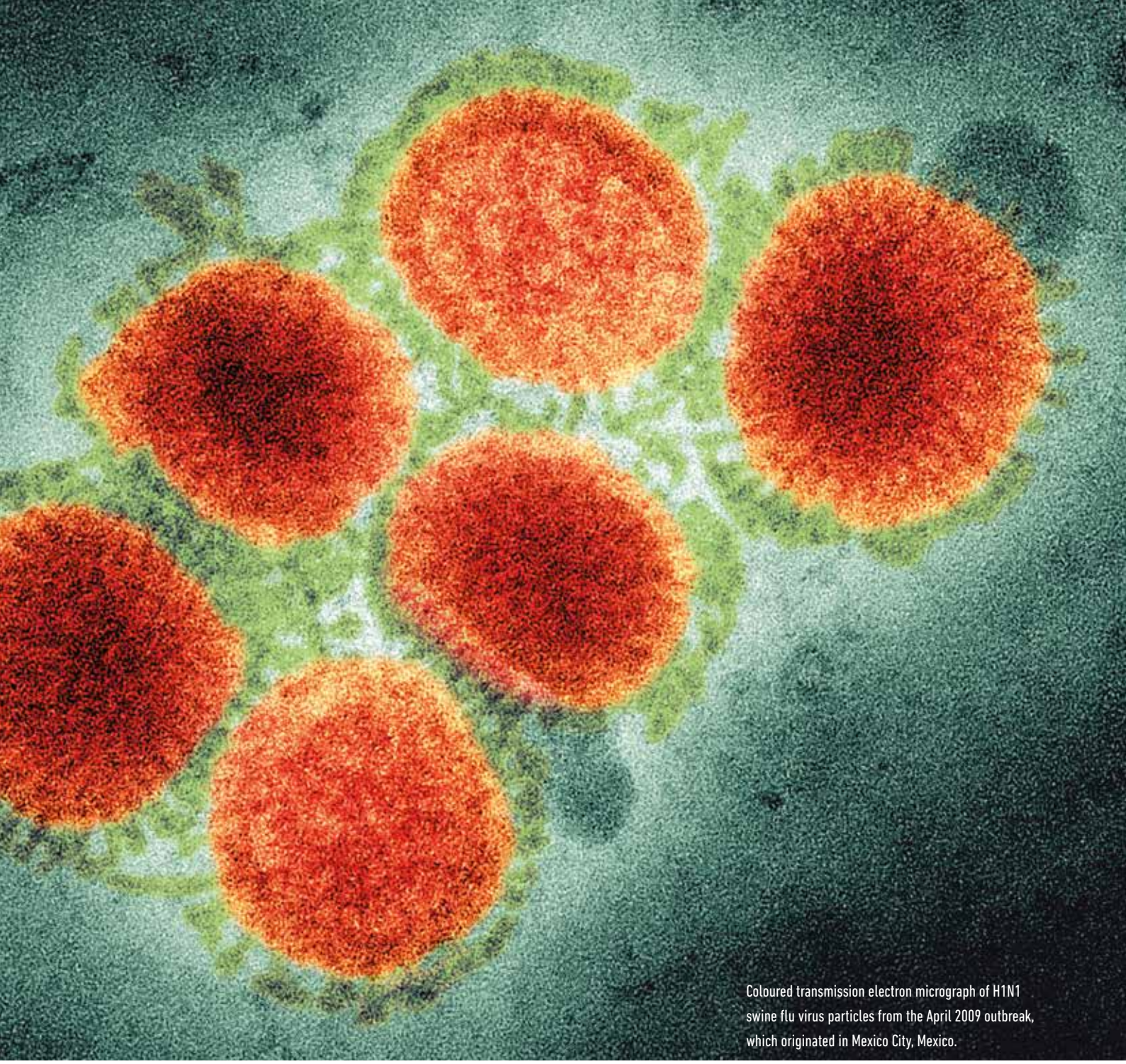


- **A novel influenza A H1N1 virus emerged from Mexico in April 2009 and spread so rapidly that the World Health Organization declared a global flu pandemic on 11 June.**
- **Symptoms can include fever, fatigue, lack of appetite, coughing and sore throat and, in about one quarter of cases, vomiting and diarrhoea.**
- **There were two peaks of infection in the UK, the first during the summer months and the second smaller peak over the traditional winter influenza season. In the post-pandemic period the virus reappeared, behaving as a seasonal strain.**

Influenza overview

Influenza viruses in human populations are usually classified as seasonal or pandemic. Seasonal influenza usually causes yearly epidemics in the old, the very young and those with underlying medical conditions, and is often associated with cold periods in temperate regions. An influenza virus becomes classified as pandemic when a novel strain emerges from an animal reservoir and is not only able to infect humans but also spreads quickly through the population across the globe irrespective of the season.

Typically, influenza viruses predominately circulate in birds; rarely they can infect and genetically adapt to replicate well in other animal hosts. Additionally, different viral strains can infect a single host and exchange that adapted genetic material, a process made easier as the genome is separated into eight segments, allowing mixing (reassortment) to occur and lead to development of a novel adapted strain. As the human population may not have encountered the virus before, it has little or no immunity (antibodies) to the novel strain. Such processes probably allowed the pandemics in 1918, 1957 and 1968 to occur. Each pandemic was caused by a different subtype of influenza, named for the outer spike proteins of the virus (H1N1, H2N2 and H3N2, respectively), which are the sections of the virus most recognised by the host antibodies.



Coloured transmission electron micrograph of H1N1 swine flu virus particles from the April 2009 outbreak, which originated in Mexico City, Mexico.

The 2009 H1N1 strain

The WHO named the new 2009 virus influenza A(H1N1)pdm09, but it was termed 'swine flu' in the media as the virus displayed genetic similarities with existing pig viruses. This influenza virus was the result of the reassortment of four different bird (avian) viruses that had adapted to use pigs (and a human intermediary) as hosts and mixing pots for several years, hence the name 'swine flu'. The new A(H1N1)pdm09 virus was able to transmit to humans and spread rapidly between them, and thus cause the 2009 pandemic. Since 2009, this virus has repeatedly transmitted back into pigs from humans. Other reassorted viruses have transmitted from pigs to humans, but they have not been able to transmit between humans as well as the A(H1N1)pdm09 virus.

Who is affected?

When the virus was originally detected, the news from Mexico was alarming – many of the cases resulted in critical illness and/or death; however, as the virus spread the number of severe cases in the infected population decreased. Unlike H5N1 ('bird flu' in the media) and other highly pathogenic influenza viruses, the pandemic H1N1 strain does not normally spread outside the respiratory tract; this is usually a trait associated with a milder seasonal disease. While there were severe and fatal cases requiring hospitalisation, most cases of A(H1N1)pdm09 flu in the UK were mild.

Treating illness

Pharmacist holding packets of Tamiflu™ (oseltamivir) capsules.

The normal recommended treatment for flu for healthy individuals is bed rest and a high fluid intake. Remedies containing paracetamol or ibuprofen will help ease symptoms such as a high temperature and muscle pain. Asprin is not recommended for children. Antibiotics are NOT effective against viruses such as influenza and should only be prescribed to treat confirmed secondary bacterial infections, which can lead to bacterial pneumonia.

Patients who are deemed to be at high risk (e.g. pregnant women, those with pre-existing medical conditions and young children) from pandemic or seasonal flu strains are prescribed antiviral medication. This must be taken quickly to be effective, ideally within 12–48 hours of onset of symptoms. Antiviral medications do not cure illness but they can reduce the length of symptoms by about a day and usually lessen their severity. Antivirals work by blocking the virus from replicating inside human cells or blocking the spread of virus from one infected cell to the next.

In certain situations (as happened early in the pandemic), antivirals can be given to prevent flu in healthy people who are exposed to the virus (prophylactic treatment). The A(H1N1)pdm09 strain has shown to be sensitive to antiviral medications oseltamivir (Tamiflu™), zanamivir (Relenza™) and peramivir. These antivirals work by blocking the release of the virus from infected cells by inhibiting a viral enzyme.

Influenza strains that were resistant to oseltamivir were first identified several years ago.

Oseltamivir-resistant A(H1N1)pdm09 influenza had been reported in <1% of cases in the last 6 years, according to Public Health England. Oseltamivir resistance most often occurs in patients who are immunosuppressed, who tend to clear the virus more slowly from the body.

Other drugs are being developed; some such as favipiravir target the viral replication machinery whereas others specifically seek to inhibit the virus by temporarily blocking specific host proteins that the virus needs to replicate or by manipulating specific aspects of the host's immune system. Neither favipiravir nor peramivir are, as yet, licensed for influenza treatment in the UK.

	Oseltamivir (Tamiflu)	**Zanamivir (Relenza)**
Safe for use in:	Adults, pregnant women, children and babies	Adults, pregnant women and children over 5
Method of administration:	Oral	Inhaled
Formulation:	Capsule or liquid	Dry powder
Adult dosage:	One 75 mg capsule per day for five days	Two 5 mg doses of powder per day for five days
Child dosage:	Weight-related	Same as adult dosage
Common side effects:	Nausea and vomiting	None

As observed in previous pandemics, the majority of the cases were in young people under 25, although a reasonable proportion of middle-aged people were also affected; this is in contrast to seasonal flu that predominantly affects the elderly, who have a less robust immune system. However, when they are infected, some groups have an increased risk of suffering from complications from an A(H1N1)pdm09 infection. These include the elderly, people with long-term health conditions including asthma, diabetes and obesity, women in the later stages of pregnancy and those with weakened immune systems.

The spread of disease

H1N1 infection spread rapidly in June and July 2009 as the majority of people were naïve to the virus and therefore had no antibodies to it. The number of new cases each week started to double and peaked at 100,000 per week in England. In October, the number of new cases per week started to increase again and a second, smaller peak of infection occurred. It was predicted that the second wave would coincide with peak seasonal flu season at the end of December/beginning of January; however, the number of new H1N1 cases did not reach the figures that were expected. The following influenza season, 2010–2011, saw a sustained number of A(H1N1)pdm09 infections in the young and middle-aged, and a higher-than-expected level of hospitalisation and critical care patients. The seasonal H1N1 and H3N2 viruses were supplanted by the newly emerged virus. However, since 2010–2011, both A(H1N1)pdm09 and A/H3N2 have circulated as the seasonal strains, with A(H1N1)pdm09 dominating the first season, then H3N2 the following two winters; currently each virus predominates on alternate flu seasons. Influenza B viruses have co-circulated throughout.

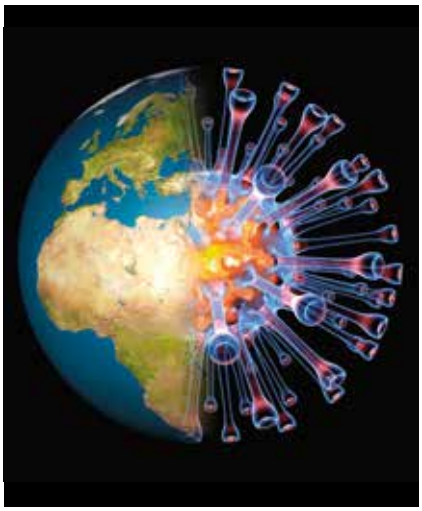


Illustration of a global influenza pandemic.

Phase	Containment phase	Treatment phase
Aim	Limit spread of infection	Minimise impact of pandemic
Action taken	Suspected cases tested to confirm H1N1 infection	Suspected cases no longer tested to confirm H1N1 infection
	Antiviral medication given to confirmed cases	Fast access to antivirals through National Pandemic Flu Service
	Schools closed (where medical advice deemed it appropriate)	H1N1 vaccine production fast-tracked
	Prophylactic treatment of close contacts of infected people with antiviral medication	Licensed H1N1 vaccine offered to vulnerable groups in order of priority

Dealing with the pandemic

Most countries, including the UK, had flu preparedness plans in place. In Britain, before a pandemic alert was issued by the WHO, preparations were already underway. Enough antiviral medication was stockpiled to treat half the population, and advance agreements with vaccine manufacturers were in place to quickly develop a vaccine against a new strain of flu. Vaccines, even when fast-tracked, take time to make. The first vaccine doses in the UK were not ready until 21 October 2009; so, when the A(H1N1)pdm09 strain first emerged, public health authorities focused their efforts on containing the spread of infection. As more and more people became infected, effort was centred upon treating the disease to minimise the impact of the pandemic. The UK officially moved from a containment phase to a treatment phase on 2 July 2009.

To ease the mounting pressure on GPs, the National Pandemic Flu Service was launched in the UK at the end of July. This service provided an online or telephone diagnosis of a patient's symptoms and gave them quick access to antiviral medication if necessary. Patients were advised to nominate a 'flu friend' to collect the medication for them to further limit the spread of infection.

Much was learnt from the 2009 pandemic; the preparedness plans have been modified for each stage of the next pandemic, as have the roles of the

UK government and health authorities outlined for the various phases of Detection, Assessment, Treatment, Escalation and Recovery (DATER). Surveillance programmes such as the First Few Hundred cases (FF100) will be used to ensure the response is proportionate to the risk posed by different viral strains. If the people contracting the disease suffer a mild illness such as in 2009, fewer resources will be assigned than if the pandemic is similar to that in 1918, where the death rates were very high. These plans are freely available on the UK Government Department of Health website.

National immunisation programme

Two vaccines were licensed for A(H1N1)pdm09 in the UK, Celvapan™ and Pandemrix™, and they were used as part of the national immunisation programme.

The groups of people who are most at risk from developing serious illness from A(H1N1)pdm09 were offered the vaccine first. These groups are:

- People aged between six months and 65 years with chronic health conditions
- All pregnant women
- People in close contact with those with compromised immune systems (e.g. AIDS sufferers)
- People aged 65 and over who normally receive the seasonal flu vaccine
- Children aged between six months and five years

In addition to these clinically at-risk groups, front-line health workers were

Patient receiving the H1N1 vaccine.

Vaccines

There are two main types of influenza vaccine, and both are made from a virus with the internal proteins of a safe vaccine strain and the outer spike proteins (HA and NA) of the virus strain recommended by the WHO that the population needs protecting against.

For the type used for the pandemic and seasonal adult vaccinations, the virus is inactivated, purified and then injected. The body's immune system sees the viral proteins as foreign and generates antibodies to the specific spike proteins. Although some people experience a few aches or a mild temperature after vaccination, these symptoms pass very quickly, as there is no virus to prolong the illness, and are an indication that their immune system is responding to the vaccine.

The second type of vaccine offered seasonally to children also contains the spike proteins of the recommended strains, but the internal body of the virus is crippled and unable to replicate well in the body; it is known as a Live Attenuated Influenza Vaccine. It generates a better immune response in children. In the UK, it is known as Fluenz™ and protects against two strains of influenza A and one or two strains of influenza B.

Some vaccines are produced in eggs, which act as ideal incubation chambers; others are grown in cell cultures. The main differences between pandemic and seasonal vaccines are time and number of strains. Planning for seasonal vaccination occurs 18 months before first delivery whereas the pandemic vaccines can be ready within five to six months. Seasonal vaccines provide protection from three to four strains of virus, whereas the pandemic vaccine protects against only one strain.

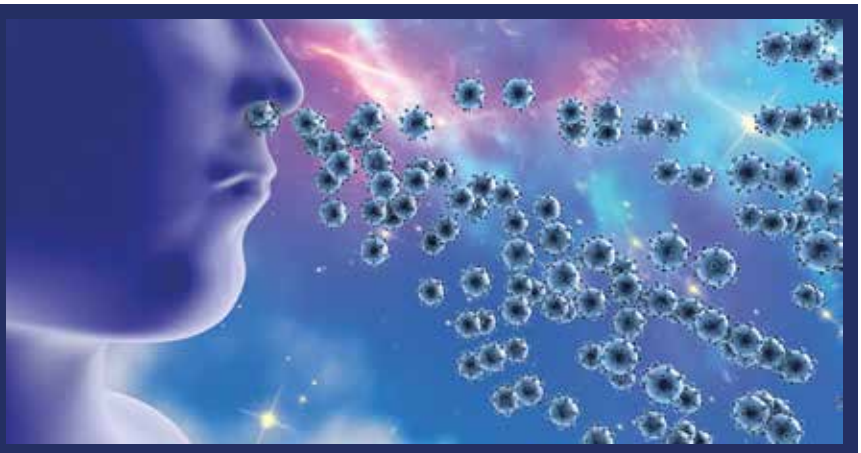
Doses of the 2015/2016 seasonal flu vaccine.

Vials of H1N1 vaccine.

Advice to the public

During the winter months and during a pandemic, spread of the virus can be reduced by a few simple methods summarised in the '**Catch it. Bin in. Kill it.**' campaign:

- sneezing into a tissue
- putting dirty tissues in the bin quickly
- washing hands frequently
- frequent cleaning of hard surfaces



Infection by respiratory viruses.

A scientist injects a solution of avian influenza viruses into a chicken egg.

also offered the vaccine to reduce the risk of them infecting more vulnerable patients. Researchers are attempting to make a universal influenza vaccine that will protect against all influenza A viruses by using a piece of viral spike protein found in all the viruses.

Where is the pandemic going?

There is constant surveillance across the globe investigating any new outbreaks of influenza, especially in regions where there is a high incidence of avian influenza such as H5N1 and H7N9. Both of these avian influenza viruses have displayed the capacity to jump from birds into humans and cause serious disease, but as yet there has been no sustained transmission between humans, which is required for a pandemic to occur. Because of the 'swine flu' pandemic in 2009, there has also been an increase in monitoring of influenza in pigs.

Sources of further information

Health Protection Agency **http://www.nhs.uk/conditions/pandemic-flu/Pages/Introduction.aspx**

World Health Organization **http://www.who.int/csr/disease/swineflu/en**

Centers for Disease Control and Prevention **http://www.cdc.gov/h1n1flu**

National Pandemic Flu Service **https://www.pandemicflu.direct.gov.uk**

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Picture credits

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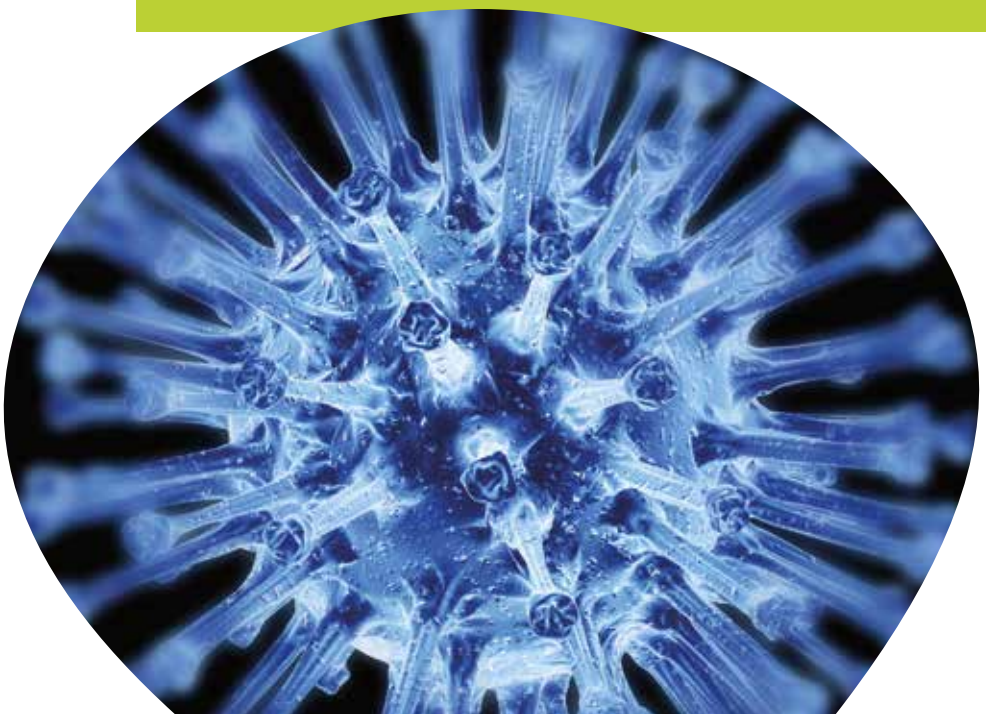
The Society produces and distributes a wide range of resources including videos to support microbiology teaching in schools and colleges.

For more information, see **www.microbiologyonline.org.uk** or contact the **Education Department, Microbiology Society, Charles Darwin House, 12 Roger Street, London WC1N 2JU, UK** (**education@microbiologysociety.org.uk**).



Front cover and right Computer artwork of an H1N1 influenza A virus particle (virion).