Patient

View this article online at: patient.info/doctor/influenza

Influenza

Synonym: *flu* See also the article on Influenza Vaccination

What is influenza?[1]

Influenza, also known as flu, is an acute respiratory illness due to infection with RNA viruses of the family Orthomyxoviridae (influenza viruses).

It is highly infectious and transmission occurs via droplets, aerosols or direct contact with respiratory secretions from an infected person, and the usual incubation period is 1-3 days.

Uncomplicated influenza is an acute respiratory infection caused by influenza A or B viruses that is usually self-limiting in the general population.

Complicated influenza is more severe and is associated more often with influenza A infection rather than influenza B infection. It is defined by signs and symptoms that require hospital admission, involve the lower respiratory tract, central nervous system, or cause significant exacerbation of an underlying medical condition. Treatment may require more aggressive supportive care or hospitalisation, including treatment with antibiotics and/or antivirals.

Types of influenza virus (pathogenesis)

There are three serotypes - A, B and C.[2] Influenza A and B viruses cause most clinical disease:

- A is the more frequent and the cause of major influenza outbreaks.
- B tends to circulate with A in yearly outbreaks and causes less severe illness.
- C tends to cause a mild or asymptomatic illness akin to the common cold.

Influenza A serotypes are further categorised by their surface antigens:

- H: haemagglutinin - facilitates entry of the virus into the host respiratory cell.
- N: neuraminidase - facilitates release of virions from the infected host cells.

There are 15 H and 9 N subtypes of the A virus in aquatic birds, which together with pigs (often termed the 'mixing vessel' for scrambling human and avian virus genetic material) are the natural reservoir of the virus.

The influenza virus undergoes minor mutations to one or both of its surface antigens - **antigenic drift**. This causes seasonal epidemics where people have only partial immunity from previous infection.

In influenza A alone, major and sudden changes in the H and N antigens produce a new virus subtype - **antigenic shift**. There is little population immunity to the new form and a major epidemic may ensue.

Influenza-like illness presents with similar symptoms to influenza, but it is caused by a virus other than influenza A, B, or C - eg, respiratory syncytial virus.

How common is influenza? (Epidemiology) [1] [2]

Influenza usually occurs in the UK during the winter months, typically between December and March.

In 1997, the normal seasonal activity in England was defined as 30–200 consultations per week, with over 200 consultations per week indicating an epidemic.

In 2017/18:

- Moderate to high levels of influenza activity were observed in the UK with co-circulation of influenza B and influenza A(H3).
- In England, syndromic surveillance indicators peaked in week 2 of 2018 at 42.5 per 100,000 population.

- In England, weekly rates of GP consultations for influenza-like illness peaked in week 3 of 2018 at 54.1 per 100,000. Rates remained at or above the baseline threshold (13.1 per 100,000) for 14 weeks until week 12 of 2018.
- By age group, activity peaked at the highest levels in those aged 45-64 years and 65-74 years in week 2 (74.4 per 100,000, and 58.4 per 100,000 respectively).

When a disease outbreak leads to an unexpected increase in the number of disease cases in a specific geographical area, it is called an epidemic. A pandemic is when a disease spreads over several countries or continents, usually affecting a large number of people.[3]

There have been four pandemics in the last 100 years. The effects can be devastating; the 1918 outbreak killed around 21 million worldwide (that is 6 x more casualties than in the First World War):

- The most recent was swine influenza virus (H1N1v) in 2009. Swine influenza A virus was quite different to previous viruses. The human community initially had little immunity to it. The young were at most risk and those aged over 60 years at least risk.[4] Epidemics occurred worldwide in 209 countries, with considerable morbidity and an estimated 100,00–400,00 deaths worldwide.[5]

However, the severity of seasonal flu is easily underestimated. In the UK, seasonal flu claims an average of around 10,000 lives annually (ranging from less than 1,000 to more than 20,000). The annual flu vaccine is generally only 40-60% effective against the year's new strains and there remains debate about how effective existing antivirals for influenza are.[3]

At-risk groups[1] [2]

'At-risk group' includes people aged over 65 years, children aged under 6 months, pregnant women (at any stage of pregnancy, or women up to two weeks postpartum), and people with any of the following conditions:

- Asplenia or dysfunction of the spleen.

- Chronic respiratory disease, including:
    - Chronic obstructive pulmonary disease, chronic bronchitis and emphysema, bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis, and bronchopulmonary dysplasia.
    - Asthma that requires continuous or repeated use of inhaled or systemic corticosteroids or with previous exacerbations requiring hospital admission.
    - Children who have previously been admitted to hospital for lower respiratory tract disease.
- Chronic heart disease - including congenital heart disease, hypertension with cardiac complications, chronic heart failure, and individuals requiring regular medication or follow-up for coronary heart disease.
- Chronic kidney disease - including chronic kidney disease stage 3, 4 or 5, chronic kidney failure, nephrotic syndrome, and kidney transplantation.
- Chronic liver disease - including cirrhosis, biliary atresia, and chronic hepatitis:
    - Chronic neurological conditions, including stroke and transient ischaemic attack. Conditions in which respiratory function may be compromised (for example, polio syndrome).
    - Individual assessment should also be considered in clinically vulnerable individuals including those with cerebral palsy, learning disabilities, multiple sclerosis and related or similar conditions; or hereditary and degenerative disease of the nervous system or muscles; or severe neurological disability.
- Diabetes mellitus, including type 1 diabetes and type 2 diabetes.

- Immunosuppression due to disease or treatment, including:
    - People undergoing chemotherapy (or radiotherapy) leading to immunosuppression.
    - People undergoing bone marrow transplant.
    - HIV infection (all stages).
    - Individuals treated with, or likely to be treated with, systemic steroids for more than one month at dosages equivalent to prednisolone 20 mg or more daily (at any age) or, for children weighing less than 20 kg, a dose of 1 mg or more per kg body weight per day.
    - Multiple myeloma.
    - Genetic disorders affecting the immune system (for example, IRAK-4, NEMO, complement disorder).
- Morbid obesity (body mass index of 40 or more).

Residents of nursing homes are particularly at risk of serious complications because of their age, high rate of chronic disease and living in a closed community. In pregnant women there is a slight increase in perinatal mortality rate, as well as early and late fetal deaths.

Flu symptoms[1] [2]

Transmission is either by:

- Droplet due to coughing/sneezing.
- Direct nasal or eye contact with hands carrying the virus.

After an incubation period of one to three days the patient commonly presents with rapid onset of:

- Anorexia.
- Malaise.
- Headache (retro-orbital).
- Fever.

- Myalgia.
- Non-productive cough and sore throat.

Nasal discharge/obstruction and sneezing can occur but are not usually prominent features of the illness. Fever may not be seen in older patients. Gastrointestinal symptoms are not usual but may occur in a minority of patients.

Swine flu is similar to the usual human seasonal influenza infection, with most cases in adults and children being mild.

Clinicians are encouraged to diagnose swine flu based on symptoms if there is a pyrexia (≥38°C), fever or history of fever **and** flu-like illness (two or more of the following symptoms: cough, sore throat, rhinorrhoea, widespread muscle and joint aches, headache).

There may also be any of the following: fatigue, loss of appetite and sometimes diarrhoea, nausea, vomiting, otitis media and (rarely) cerebral irritability ± seizures.[4]

Most symptoms typically last for 3-5 days but cough, tiredness and malaise may last for 1-2 weeks. Infectivity continues for five days from onset, although children can remain infectious for two weeks, and the severely immunocompromised can shed virus for weeks.

Atypical symptoms of flu in children

In H1N1 influenza these include haematemesis, photophobia, chest pain, epistaxis, croup, apnoea and rigors.

Very young children and babies can present with apnoea, reduced tone and poor feeding (without classical influenza features) and may exhibit a sudden severe collapse (apparent life-threatening episode).[4]

With all influenzas, neonates and infants may present with drowsiness, lethargy, poor feeding, apnoea or fever, pneumonia or otitis media.

Differential diagnosis[1]

The most important are listed below:

- Common cold/upper respiratory tract infection.
- Pharyngitis - multiple aetiologies.
- Meningitis.
- Bacterial or viral lower respiratory tract infection, including pneumonia.
- Malaria or dengue in returning travellers.
- Infectious mononucleosis.
- Cytomegalovirus.
- Acute HIV seroconversion illness.

In pregnant women, always consider pulmonary embolus (chest pain, tachypnoea and tachycardia) and pre-eclampsia (epigastric pain, headaches and elevated blood pressure).

Investigations

The diagnosis is a clinical one so investigations are usually reserved for community surveillance purposes. Available tests include:

- Direct viral culture of nasopharyngeal swabs/aspirates.
- Immunofluorescence of nasopharyngeal swabs/aspirates.
- Acute and convalescent sera, 10-14 days apart.
- Polymerase chain reaction.
- Rapid bedside antigen tests. These currently have low positive predictive values.[6]

Flu treatment and management

General advice[1]

- Drink adequate fluids to avoid dehydration.
- Take paracetamol or ibuprofen for symptomatic relief.
- Rest in bed if feel fatigued.

- Stay off work or school if feel unable to attend (about 1 week is adequate for most people).
- Fever and associated systemic symptoms of uncomplicated influenza usually resolve after about 1 week, although some symptoms (such as cough and fatigue) may persist for up to 2 weeks after resolution of fever.
- Routine follow up is not necessary but seek medical advice should the condition deteriorate, particularly if shortness of breath or pleuritic chest pain, or haemoptysis (may indicate pneumonia secondary to bacterial superinfection).
- Follow-up appointment if no improvement after 1 week (still significantly ill) or if deteriorating.
- Lower threshold for seeking help if caring for a young child or baby with influenza.

NB: aspirin should be avoided in children aged under16 years, due to the danger of Reye's syndrome.

Pharmacological [7]

The antivirals oseltamivir and zanamivir are used for both treatment and post-exposure prophylaxis of influenza, although there is evidence that some strains of influenza are more likely to develop resistance to oseltamivir. Amantadine hydrochloride is not recommended for the treatment or post-exposure prophylaxis of influenza A. Specialist advice is available through local health protection teams and public health virologists.

Treatment of suspected or confirmed influenza

Where treatment with oseltamivir is indicated, it should be started as soon as possible, ideally within 48 hours of symptom onset. There is evidence to suggest that the risk of mortality may be reduced even if treatment is started up to 5 days after symptom onset. Treatment initiation beyond 48 hours of onset is unlicensed and clinical judgement should be used.

Where treatment with inhaled zanamivir is indicated, it should also be started as soon as possible, ideally within 48 hours (36 hours in children) of symptom onset. Treatment initiation beyond this time is unlicensed and clinical judgement should be used.

Where treatment with intravenous zanamivir is indicated, it should be commenced as soon as possible and within 6 days of symptom onset.

Uncomplicated influenza:

- For patients who are otherwise healthy (excluding pregnant females), no antiviral treatment is usually needed. For those considered to be at serious risk of developing complications, offer oseltamivir.
- For patients in an at-risk group (including pregnant females but excluding those who are severely immunosuppressed), offer oseltamivir. Do not wait for laboratory test results to treat. For pregnant females who meet additional criteria for requiring zanamivir first-line, treatment should be discussed with a local infection specialist.
- For severely immunosuppressed patients, consider the subtype of influenza causing the infection, or if not yet known, take into account the current dominant circulating strain. Offer oseltamivir first-line unless the strain has a higher risk for oseltamivir resistance, in which case inhaled zanamivir should be offered. For patients unable to use inhaled zanamivir due to underlying severe respiratory disease or inability to use the device (including children under 5 years), offer oseltamivir and assess response to therapy.
- For patients with suspected or confirmed oseltamivir resistant influenza, offer inhaled zanamivir. For patients unable to use inhaled zanamivir, consider intravenous zanamivir [unlicensed indication].

Complicated influenza

- All patients should be tested and treated, often in hospital. Do not wait for laboratory test results to treat. For patients who are not severely immunosuppressed, oseltamivir should be offered first-line. If there is a risk of reduced gastrointestinal absorption, or if initial oseltamivir treatment is unsuccessful, offer inhaled zanamivir. For pregnant females who meet additional criteria for requiring zanamivir first-line, treatment should be discussed with a local infection specialist.

- For severely immunosuppressed patients, consider the dominant circulating strain of influenza to guide treatment. Offer oseltamivir first-line unless the strain has a higher risk for developing oseltamivir resistance, in which case inhaled zanamivir should be offered.
- For patients with suspected or confirmed oseltamivir resistant influenza, offer inhaled zanamivir.
- For patients unable to use inhaled zanamivir, or for those with severe complicated illness such as multi-organ failure, consider intravenous zanamivir.

A Cochrane review found[8] :

- Oseltamivir and zanamivir have small, non-specific effects on reducing the time to alleviation of influenza symptoms in adults, but not in asthmatic children.
- Using either drug as prophylaxis reduces the risk of developing symptomatic influenza.
- Treatment trials with oseltamivir or zanamivir do not settle the question of whether the complications of influenza (such as pneumonia) are reduced.
- The use of oseltamivir increases the risk of adverse effects, such as nausea, vomiting, psychiatric effects and renal events in adults and vomiting in children.
- Lower bioavailability may explain the lower toxicity of zanamivir compared to oseltamivir.

Oseltamivir may be ineffective in neonates but can be used for treatment or post-exposure prophylaxis of influenza in children under 1 year of age.[7]

Safety data are limited but either oseltamivir or zanamivir can be used in women who are pregnant or breastfeeding when the potential benefit outweighs the risk such as during a pandemic. Oseltamivir is preferred for women who are breastfeeding.

- At-risk patients include those aged over 65 years or those who have one or more of the following conditions:

    - Chronic respiratory disease, including asthma and chronic obstructive pulmonary disease (COPD).
    - Chronic heart disease.
    - Chronic kidney disease.
    - Chronic liver disease.
    - Chronic neurological disease.
    - Immunosuppression.
    - Diabetes mellitus.
    - Pregnancy.

Follow-up

Consider follow-up (particularly in frail people) after about one week, to confirm symptoms are improving and to exclude the development of secondary complications.

Advise the person that they should seek urgent medical attention if they develop shortness of breath or pleuritic chest pain, or if they start to cough up blood.

Arrange a follow-up appointment if there is no improvement after one week (that is, they are still significantly ill) or if they are deteriorating.

Have a lower threshold for seeking help if they are caring for a young child or baby with influenza, as children cannot accurately communicate their symptoms.

Complications with flu[1]

- Respiratory:
  - Acute bronchitis.
  - Exacerbations of asthma and chronic obstructive pulmonary disease.
  - Otitis media.
  - Pneumonia (secondary bacterial infection, particularly *Staphylococcus aureus*, or primary viral infection.
  - Sinusitis.
- Non-respiratory:
  - Cardiac complications: myocarditis, pericarditis, exacerbation of underlying cardiac disease.
  - Febrile convulsions.
  - Myalgia, myositis and rhabdomyolysis.
  - Neurological: Reye's syndrome, encephalomyelitis, transverse myelitis, Guillain-Barré syndrome, aseptic meningitis, and encephalitis.
  - Toxic shock syndrome.
- Pregnancy:
  - Women and their unborn children are at high risk of morbidity and mortality.
  - It can cause preterm labour and low birth weight.
  - The highest risk of morbidity is in the third trimester.

Prognosis[2]

Estimates of excess winter deaths potentially attributable to influenza range from less than 1,000 (2005 to 2006, 2006 to 2007 and 2008 to 2009) to greater than 20,000 (2014 to 2015 and 2017 to 2018).

The risk of serious illness from influenza is higher amongst children under 6 months of age, older people and those with underlying health conditions (such as respiratory or cardiac disease, chronic neurological conditions or immunosuppression) and pregnant women.

Influenza during pregnancy may also be associated with perinatal mortality, prematurity, smaller neonatal size and lower birth weight.

Typically, seasonal influenza (H3N2) has a greater effect on mortality rates in the elderly but H1N1 tends to affect children and young adults.[9]

Influenza prevention

See also the separate Influenza Vaccination article.

Post-exposure prophylaxis[7]

Contacts in an at-risk group who are not adequately protected through vaccination (either due to infection by a different circulating strain or exposure within 14 days post-vaccination), should be offered prophylaxis following exposure to a person in the same household or residential setting with influenza-like illness (when influenza is circulating). Certain populations that are susceptible to localised outbreaks (such as those in care homes, prisons or detention centres), may be considered for antiviral prophylaxis regardless of vaccination status.

Prophylaxis should be started as soon as possible following exposure, ideally within 48 hours for oseltamivir and 36 hours for inhaled zanamivir. Initiation beyond these times is unlicensed and specialist advice should be sought.

For patients in an at-risk group (including pregnant females but excluding severely immunosuppressed patients and children aged under 5 years), offer oseltamivir first-line regardless of the risk for resistance of the circulating or index case strain. For pregnant females who meet additional criteria for requiring zanamivir first-line, treatment should be discussed with a local infection specialist. For patients exposed to a strain with suspected or confirmed oseltamivir resistance, offer inhaled zanamivir.

For severely immunosuppressed patients (excluding children aged under 5 years), offer oseltamivir if the risk for oseltamivir resistance is low. However, if the risk for oseltamivir resistance is high, suspected or confirmed, offer inhaled zanamivir. For patients at higher risk of oseltamivir resistance who are unable to use inhaled zanamivir (due to underlying severe respiratory disease or inability to use the device), offer oseltamivir and advise patients to seek immediate medical attention if symptoms develop subsequently. For patients exposed to suspected or confirmed oseltamivir resistant influenza who are unable to use inhaled zanamivir, specialist advice should be sought and patients monitored closely for influenza-like illness, with arrangements made for prompt treatment if symptoms develop.

For children aged under 5 years in an at-risk group (including severely immunosuppressed children), offer oseltamivir first-line regardless of the risk of resistance for the circulating or index case strain. However, if the child is exposed to suspected or confirmed oseltamivir resistant influenza, monitor closely for influenza-like illness and promptly commence treatment if symptoms develop. Seek specialist advise if the child is severely immunosuppressed.

Further reading

- Amantadine, oseltamivir and zanamivir for the treatment of influenza; NICE Technology appraisal guidance, February 2009
- Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza; NICE Technology Appraisal Guidance, September 2008
- Influenza treatment and prophylaxis using anti-viral agents; UK Health Security Agency. Published January 2014, last updated December 2021.

Authored by:	Peer Reviewed by: Dr Krishna Vakharia, MRCGP	
Originally Published: 20/11/2023	Next review date: 01/09/2023	Document ID: doc_2323

View this article online at: patient.info/doctor/influenza

Discuss Influenza and find more trusted resources at Patient.