[Template:Redirect4](/wiki/Template:Redirect4" \o "Template:Redirect4) [Template:Distinguish](/wiki/Template:Distinguish) [Template:Pp-semi](/wiki/Template:Pp-semi) [Template:Pp-move-indef](/wiki/Template:Pp-move-indef) [Template:Use dmy dates](/wiki/Template:Use_dmy_dates) [Template:Infobox medical condition](/wiki/Template:Infobox_medical_condition) **Influenza**, commonly known as "the **flu**", is an [infectious disease](/wiki/Infectious_disease) caused by an [influenza virus](/wiki/Influenza_virus).<ref name=WHO2014/> Symptoms can be mild to severe.<ref name=CDC2014Key>[Template:Cite web](/wiki/Template:Cite_web)</ref> The most common [symptoms](/wiki/Symptom) include: a high [fever](/wiki/Fever), [runny nose](/wiki/Rhinorrhea), [sore throat](/wiki/Sore_throat), [muscle pains](/wiki/Myalgia), [headache](/wiki/Headache), [coughing](/wiki/Cough), and [feeling tired](/wiki/Fatigue_(medical)). These symptoms typically begin two days after exposure to the virus and most last less than a week. The cough, however, may last for more than two weeks.<ref name=WHO2014/> In children, there may be [nausea](/wiki/Nausea) and [vomiting](/wiki/Vomiting), but these are not common in adults. Nausea and vomiting occur more commonly in the unrelated infection [gastroenteritis](/wiki/Gastroenteritis), which is sometimes inaccurately referred to as "stomach flu" or "24-hour flu".<ref name=Dub2011>[Template:Cite book](/wiki/Template:Cite_book)</ref> Complications of influenza may include [viral pneumonia](/wiki/Viral_pneumonia), secondary [bacterial pneumonia](/wiki/Bacterial_pneumonia), [sinus infections](/wiki/Sinus_infection), and worsening of previous health problems such as [asthma](/wiki/Asthma) or [heart failure](/wiki/Heart_failure).<ref name=CDC2014Key/><ref name=Harr2012/>

Three types of influenza viruses affect people, called Type A, Type B, and Type C.<ref name=Harr2012>[Template:Cite book](/wiki/Template:Cite_book)</ref> Usually, the virus is [spread through the air](/wiki/Airborne_disease) from coughs or sneezes.<ref name=WHO2014/> This is believed to occur mostly over relatively short distances.<ref name=Brankston2007>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> It can also be spread by touching surfaces contaminated by the virus and then touching the mouth or eyes.<ref name=CDC2014Key/><ref name=Brankston2007/> A person may be infectious to others both before and during the time they are showing symptoms.<ref name=CDC2014Key/> The infection may be confirmed by testing the throat, [sputum](/wiki/Sputum), or nose for the virus. A number of [rapid tests](/wiki/Rapid_influenza_diagnostic_test) are available; however, people may still have the infection if the results are negative. A type of [polymerase chain reaction](/wiki/Polymerase_chain_reaction) that detects the virus's [RNA](/wiki/RNA) is more accurate.<ref name=Harr2012/>

Frequent hand washing reduces the risk of infection because the virus is inactivated by soap.<ref name=Jeff2011>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Wearing a [surgical mask](/wiki/Surgical_mask) is also useful.<ref name=Jeff2011/> Yearly [vaccinations against influenza](/wiki/Influenza_vaccine) are recommended by the [World Health Organization](/wiki/World_Health_Organization) for those at high risk. The vaccine is usually effective against three or four types of influenza.<ref name=WHO2014/> It is usually well tolerated. A vaccine made for one year may not be useful in the following year, since the virus evolves rapidly. [Antiviral drugs](/wiki/Antiviral_drug) such as the [neuraminidase inhibitor](/wiki/Neuraminidase_inhibitor) [oseltamivir](/wiki/Oseltamivir), among others, have been used to treat influenza.<ref name=WHO2014/> Their benefits in those who are otherwise healthy do not appear to be greater than their risks.<ref name=Mich2013>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> No benefit has been found in those with other health problems.<ref name=Mich2013/><ref name=Ebe2013>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Influenza spreads around the world in a [yearly outbreak](/wiki/Flu_season), resulting in about three to five million cases of severe illness and about 250,000 to 500,000 deaths.<ref name=WHO2014>[Template:Cite web](/wiki/Template:Cite_web)</ref> In the Northern and Southern parts of the world outbreaks occur mainly in winter while in areas around the equator outbreaks may occur at any time of the year.<ref name=WHO2014/> Death occurs mostly in the young, the old and those with other health problems.<ref name=WHO2014/> Larger outbreaks known as [pandemics](/wiki/Pandemic) are less frequent.<ref name=Harr2012/> In the 20th century three [influenza pandemics](/wiki/Influenza_pandemic) occurred: [Spanish influenza](/wiki/Spanish_influenza) in 1918, [Asian influenza](/wiki/Asian_influenza) in 1958, and [Hong Kong influenza](/wiki/Hong_Kong_influenza) in 1968, each resulting in more than a million deaths.[[1]](#cite_note-1) The [World Health Organization](/wiki/World_Health_Organization) declared an outbreak of a new type of [influenza A/H1N1](/wiki/Influenza_A_virus_subtype_H1N1) to be a [pandemic in June 2009](/wiki/2009_flu_pandemic).[[2]](#cite_note-2) Symptoms of influenza can start quite suddenly one to two days after infection. Usually the first symptoms are chills or a chilly sensation, but fever is also common early in the infection, with body temperatures ranging from 38 to 39 °C (approximately 100 to 103 °F).[[6]](#cite_note-6) Many people are so ill that they are confined to bed for several days, with aches and pains throughout their bodies, which are worse in their backs and legs.<ref name=Merck>[Template:Cite web](/wiki/Template:Cite_web)</ref> Symptoms of influenza may include:

* [Fever](/wiki/Fever) and extreme coldness (chills [shivering](/wiki/Shivering), shaking ([rigor](/wiki/Rigor_(medicine))))
* [Cough](/wiki/Cough)
* [Nasal congestion](/wiki/Nasal_congestion)
* [Runny nose](/wiki/Rhinorrhea)
* [Sneezing](/wiki/Sneezing)
* [Body aches](/wiki/Myalgia), especially joints and throat
* [Fatigue](/wiki/Fatigue_(medical))
* [Headache](/wiki/Headache)
* Irritated, [watering eyes](/wiki/Tears)
* Reddened eyes, [skin (especially face)](/wiki/Flushing_(physiology)), mouth, throat and nose
* [Petechial rash](/wiki/Petechia)[[7]](#cite_note-7)\* In children, gastrointestinal symptoms such as [diarrhea](/wiki/Diarrhea) and [abdominal pain](/wiki/Abdominal_pain),<ref name=Richards/>[[8]](#cite_note-8) (may be severe in children with influenza B)[[9]](#cite_note-9)

It can be difficult to distinguish between the [common cold](/wiki/Common_cold) and influenza in the early stages of these infections,<ref name=Eccles>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> but a flu can be identified by a high fever with a sudden onset and extreme fatigue. Influenza is a mixture of symptoms of common cold and [pneumonia](/wiki/Pneumonia), body ache, headache, and fatigue. Diarrhea is not normally a symptom of influenza in adults,[[4]](#cite_note-4) although it has been seen in some human cases of the [H5N1](/wiki/H5N1) "bird flu"[[10]](#cite_note-10) and can be a symptom in children.<ref name=Richards>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The symptoms most reliably seen in influenza are shown in the table to the right.[[4]](#cite_note-4) Since [antiviral drugs](/wiki/Antiviral_drug) are effective in treating influenza if given early ([see treatment section](/wiki/#Treatment), below), it can be important to identify cases early. Of the symptoms listed above, the combinations of fever with cough, sore throat and/or nasal congestion can improve diagnostic accuracy.[[11]](#cite_note-11) Two [decision analysis](/wiki/Decision_analysis) studies[[12]](#cite_note-12)[[13]](#cite_note-13) suggest that *during local outbreaks* of influenza, the [prevalence](/wiki/Prevalence) will be over 70%,[[13]](#cite_note-13) and thus patients with any of these combinations of symptoms may be treated with [neuraminidase inhibitors](/wiki/Neuraminidase_inhibitors) without testing. Even in the absence of a local outbreak, treatment may be justified in the elderly during the [influenza season](/wiki/Flu_season) as long as the prevalence is over 15%.[[13]](#cite_note-13) The available laboratory tests for influenza continue to improve. The United States [Centers for Disease Control and Prevention](/wiki/Centers_for_Disease_Control_and_Prevention) (CDC) maintains an up-to-date summary of available laboratory tests.[[14]](#cite_note-14) According to the CDC, rapid diagnostic tests have a sensitivity of 50–75% and specificity of 90–95% when compared with [viral culture](/wiki/Viral_culture).[[15]](#cite_note-15) These tests may be especially useful during the influenza season (prevalence=25%) but in the absence of a local outbreak, or peri-influenza season (prevalence=10%[[13]](#cite_note-13)).

Occasionally, influenza can cause severe illness including primary viral pneumonia or secondary bacterial pneumonia.<ref name=New-England-Journal-Medicine-Hospitalized-H1N1-Patients-2009>[Hospitalized Patients with 2009 H1N1 Influenza in the United States, April–June 2009](http://www.nejm.org/doi/full/10.1056/NEJMoa0906695#t=abstract), New England Journal of Medicine, Jain, Kamimoto, et al., 12 November 2009.</ref><ref name=WHO-press-conference-Dr-Nikki-Shindo-12-Nov-2009>[Transcript of virtual press conference with Gregory Hartl, Spokesperson for H1N1, and Dr Nikki Shindo, Medical Officer, Global Influenza Programme, World Health Organization](http://www.who.int/mediacentre/vpc_transcript_12_november_09_nikki_shindo.pdf), 12 November 2009.</ref> The obvious symptom is trouble breathing. In addition, if a child (or presumably an adult) seems to be getting better and then relapses with a high fever, that is a danger sign since this relapse can be bacterial pneumonia.<ref name=NYTimesDeniseGradySept2009>[Report Finds Swine Flu Has Killed 36 Children](http://www.nytimes.com/2009/09/04/health/research/04flu-001.html?_r=1), New York Times, DENISE GRADY, 3 September 2009.</ref>

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## Virology[[edit](/index.php?title=(none)&action=edit&section=2)]

### Types of virus[[edit](/index.php?title=(none)&action=edit&section=3)]

[thumb|Structure of the influenza](/wiki/File:3D_Influenza_virus.png) [virion](/wiki/Wikt:virion). The [hemagglutinin](/wiki/Hemagglutinin) (HA) and [neuraminidase](/wiki/Neuraminidase)(NA) proteins are shown on the surface of the particle. The viral RNAs that make up the [genome](/wiki/Genome) are shown as red coils inside the particle and bound to [Ribonuclear Proteins](/wiki/Influenza_virus_nucleoprotein) (RNPs).

In [virus classification](/wiki/Virus_classification) influenza viruses are [RNA viruses](/wiki/RNA_viruses) that make up three of the five [genera](/wiki/Genera) of the family [Orthomyxoviridae](/wiki/Orthomyxoviridae):<ref name=Kawaoka>[Template:Cite book](/wiki/Template:Cite_book)</ref>

* [Influenzavirus A](/wiki/Influenzavirus_A)
* [Influenzavirus B](/wiki/Influenzavirus_B)
* [Influenzavirus C](/wiki/Influenzavirus_C)

These viruses are only distantly related to the [human parainfluenza viruses](/wiki/Human_parainfluenza_viruses), which are RNA viruses belonging to the [paramyxovirus](/wiki/Paramyxovirus) family that are a common cause of respiratory infections in children such as [croup](/wiki/Croup),[[16]](#cite_note-16) but can also cause a disease similar to influenza in adults.[[17]](#cite_note-17) A fourth family of influenza viruses has been proposed - influenza D.<ref name=Hause2014>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Collin2015>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Ducatez2015>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Song2016>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Sheng2014>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Quast2015>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Smith2016>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The type species for this family is Bovine Influenza D virus which was first isolated in 2012.

#### Influenzavirus A[[edit](/index.php?title=(none)&action=edit&section=4)]

This genus has one species, influenza A virus. Wild aquatic birds are the natural hosts for a large variety of influenza A. Occasionally, viruses are transmitted to other species and may then cause devastating outbreaks in domestic poultry or give rise to human influenza [pandemics](/wiki/Pandemic).<ref name=sobrino6>[Template:Cite book](/wiki/Template:Cite_book)</ref> The type A viruses are the most virulent human pathogens among the three influenza types and cause the severest disease. The influenza A virus can be subdivided into different [serotypes](/wiki/Serovar) based on the [antibody](/wiki/Antibody) response to these viruses.<ref name=hay/> The serotypes that have been confirmed in humans, ordered by the number of known human pandemic deaths, are:

* [H1N1](/wiki/H1N1), which caused [Spanish Flu](/wiki/Spanish_Flu) in 1918, and [Swine Flu](/wiki/2009_flu_pandemic) in 2009
* [H2N2](/wiki/H2N2), which caused [Asian Flu](/wiki/Asian_Flu) in 1957
* [H3N2](/wiki/H3N2), which caused [Hong Kong Flu](/wiki/Hong_Kong_Flu) in 1968
* [H5N1](/wiki/H5N1), which caused [Bird Flu](/wiki/Avian_influenza) in 2004
* [H7N7](/wiki/H7N7), which has unusual [zoonotic](/wiki/Zoonotic) potential[[18]](#cite_note-18)\* [H1N2](/wiki/H1N2), endemic in humans, pigs and birds
* [H9N2](/wiki/H9N2)
* [H7N2](/wiki/H7N2)
* [H7N3](/wiki/H7N3)
* [H10N7](/wiki/H10N7)
* [H7N9](/wiki/H7N9)

#### Influenzavirus B[[edit](/index.php?title=(none)&action=edit&section=5)]

[thumb|Influenza virus](/wiki/File:Influenza_nomenclature.svg) [nomenclature](/wiki/International_Committee_on_Taxonomy_of_Viruses) (for a [Fujian flu](/wiki/Fujian_flu) virus)

This genus has one species, influenza B virus. Influenza B almost exclusively infects humans<ref name=hay>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> and is less common than influenza A. The only other animals known to be susceptible to influenza B infection are the [seal](/wiki/Pinniped)[[19]](#cite_note-19) and the [ferret](/wiki/Ferret).[[20]](#cite_note-20) This type of influenza mutates at a rate 2–3 times slower than type A[[21]](#cite_note-21) and consequently is less genetically diverse, with only one influenza B serotype.<ref name=hay/> As a result of this lack of [antigenic](/wiki/Antigen) diversity, a degree of [immunity](/wiki/Immunity_(medical)) to influenza B is usually acquired at an early age. However, influenza B mutates enough that lasting immunity is not possible.<ref name=webster>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> This reduced rate of antigenic change, combined with its limited host range (inhibiting cross species [antigenic shift](/wiki/Antigenic_shift)), ensures that pandemics of influenza B do not occur.<ref name=Zambon>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

#### Influenzavirus C[[edit](/index.php?title=(none)&action=edit&section=6)]

This genus has one species, influenza C virus, which infects humans, dogs and pigs, sometimes causing both severe illness and local epidemics.[[22]](#cite_note-22)<ref name=Taubenberger2008/> However, influenza C is less common than the other types and usually only causes mild disease in children.[[23]](#cite_note-23)[[24]](#cite_note-24)

### Structure, properties, and subtype nomenclature[[edit](/index.php?title=(none)&action=edit&section=7)]

Influenzaviruses A, B and C are very similar in overall structure.[[25]](#cite_note-25) The virus particle is 80–120 [nanometers](/wiki/Nanometre) in diameter and usually roughly spherical, although filamentous forms can occur.[[26]](#cite_note-26)<ref name=Lamb>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> These filamentous forms are more common in influenza C, which can form cordlike structures up to 500 [micrometers](/wiki/Micrometre) long on the surfaces of infected cells.<ref name=Bouvier/> However, despite these varied shapes, the viral particles of all influenza viruses are similar in composition.<ref name=Bouvier/> These are made of a [viral envelope](/wiki/Viral_envelope) containing two main types of [glycoproteins](/wiki/Glycoprotein), wrapped around a central core. The central core contains the viral [RNA](/wiki/RNA) [genome](/wiki/Genome) and other viral proteins that package and protect this RNA. RNA tends to be single stranded but in special cases it is double.<ref name=Lamb/> Unusually for a virus, its genome is not a single piece of [nucleic acid](/wiki/Nucleic_acid); instead, it contains seven or eight pieces of segmented [negative-sense](/wiki/Negative-sense) RNA, each piece of RNA containing either one or two [genes](/wiki/Gene), which code for a gene product (protein).<ref name=Bouvier/> For example, the influenza A genome contains 11 genes on eight pieces of RNA, encoding for 11 [proteins](/wiki/Protein): [hemagglutinin](/wiki/Hemagglutinin_(influenza)) (HA), [neuraminidase](/wiki/Viral_neuraminidase) (NA), [nucleoprotein](/wiki/Influenza_virus_nucleoprotein) (NP), [M1](/wiki/M1_protein), [M2](/wiki/M2_protein), [NS1](/wiki/NS1_Influenza_Protein), NS2 (NEP: nuclear export protein), PA, PB1 (polymerase basic 1), PB1-F2 and PB2.<ref name=Ghedin>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Hemagglutinin (HA) and neuraminidase (NA) are the two large glycoproteins on the outside of the viral particles. HA is a [lectin](/wiki/Lectin) that mediates binding of the virus to target cells and entry of the viral genome into the target cell, while NA is involved in the release of progeny virus from infected cells, by cleaving sugars that bind the mature viral particles.[[27]](#cite_note-27) Thus, these proteins are targets for [antiviral drugs](/wiki/Antiviral_drugs).[[28]](#cite_note-28) Furthermore, they are [antigens](/wiki/Antigen) to which [antibodies](/wiki/Antibodies) can be raised. Influenza A viruses are classified into subtypes based on antibody responses to HA and NA. These different types of HA and NA form the basis of the *H* and *N* distinctions in, for example, *H5N1*.<ref name=Hilleman/> There are 16 H and 9 N subtypes known, but only H 1, 2 and 3, and N 1 and 2 are commonly found in humans.<ref name=Lynch>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

### Replication[[edit](/index.php?title=(none)&action=edit&section=8)]

[thumb|Host cell invasion and replication by the influenza virus. The steps in this process are discussed in the text.](/wiki/File:Virus_Replication_large.svg)

Viruses can replicate only in living cells.[[29]](#cite_note-29) Influenza infection and replication is a multi-step process: First, the virus has to bind to and enter the cell, then deliver its genome to a site where it can produce new copies of viral proteins and RNA, assemble these components into new viral particles, and, last, exit the host cell.<ref name=Bouvier>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Influenza viruses bind through [hemagglutinin](/wiki/Hemagglutinin) onto [sialic acid](/wiki/Sialic_acid) sugars on the surfaces of [epithelial cells](/wiki/Epithelium), typically in the nose, throat, and [lungs](/wiki/Lung) of mammals, and [intestines](/wiki/Intestine) of birds (Stage 1 in infection figure).<ref name=Wagner>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> After the hemagglutinin is [cleaved](/wiki/Proteolysis) by a [protease](/wiki/Protease), the cell imports the virus by [endocytosis](/wiki/Endocytosis).<ref name=Steinhauer>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

The intracellular details are still being elucidated. It is known that virions converge to the [microtubule](/wiki/Microtubule) organizing center, interact with acidic endosomes and finally enter the target endosomes for genome release.<ref name=Liu2011>Liu SL, Zhang ZL, Tian ZQ, Zhao HS, Liu H, Sun EZ, Xiao GF, Zhang W, Wang HZ, Pang DW (2011) Effectively and efficiently dissecting the infection of influenza virus by quantum dot-based single-particle tracking. ACS Nano</ref>

Once inside the cell, the acidic conditions in the [endosome](/wiki/Endosome) cause two events to happen: First, part of the hemagglutinin protein fuses the [viral envelope](/wiki/Viral_envelope) with the vacuole's membrane, then the M2 [ion channel](/wiki/Ion_channel) allows [protons](/wiki/Proton) to move through the viral envelope and acidify the core of the virus, which causes the core to disassemble and release the viral RNA and core proteins.<ref name=Bouvier/> The viral RNA (vRNA) molecules, accessory proteins and [RNA-dependent RNA polymerase](/wiki/RNA-dependent_RNA_polymerase) are then released into the [cytoplasm](/wiki/Cytoplasm) (Stage 2).[[30]](#cite_note-30) The M2 ion channel is blocked by [amantadine](/wiki/Amantadine) drugs, preventing infection.<ref name=Pinto>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

These core proteins and vRNA form a complex that is transported into the [cell nucleus](/wiki/Cell_nucleus), where the RNA-dependent RNA polymerase begins transcribing complementary positive-sense vRNA (Steps 3a and b).[[31]](#cite_note-31) The vRNA either is exported into the cytoplasm and translated (step 4) or remains in the nucleus. Newly synthesized viral proteins are either secreted through the [Golgi apparatus](/wiki/Golgi_apparatus) onto the cell surface (in the case of neuraminidase and hemagglutinin, step 5b) or transported back into the nucleus to bind vRNA and form new viral genome particles (step 5a). Other viral proteins have multiple actions in the host cell, including degrading cellular [mRNA](/wiki/MRNA) and using the released [nucleotides](/wiki/Nucleotide) for vRNA synthesis and also inhibiting [translation](/wiki/Translation_(biology)) of host-cell mRNAs.[[32]](#cite_note-32) Negative-sense vRNAs that form the [genomes](/wiki/Genome) of future viruses, RNA-dependent RNA polymerase, and other viral proteins are assembled into a virion. Hemagglutinin and neuraminidase molecules cluster into a bulge in the cell membrane. The vRNA and [viral core](/wiki/Capsid) proteins leave the nucleus and enter this membrane protrusion (step 6). The mature virus buds off from the cell in a sphere of host [phospholipid membrane](/wiki/Lipid_bilayer), acquiring hemagglutinin and neuraminidase with this membrane coat (step 7).[[33]](#cite_note-33) As before, the viruses adhere to the cell through hemagglutinin; the mature viruses detach once their [neuraminidase](/wiki/Neuraminidase) has cleaved sialic acid residues from the host cell.<ref name=Wagner/> After the release of new influenza viruses, the host cell dies.

Because of the absence of RNA [proofreading](/wiki/Proofreading_(biology)) enzymes, the RNA-dependent RNA polymerase that copies the viral genome makes an error roughly every 10 thousand nucleotides, which is the approximate length of the influenza vRNA. Hence, the majority of newly manufactured influenza viruses are mutants; this causes [antigenic drift](/wiki/Antigenic_drift), which is a slow change in the antigens on the viral surface over time.[[34]](#cite_note-34) The separation of the genome into eight separate segments of vRNA allows mixing or [reassortment](/wiki/Reassortment) of vRNAs if more than one type of influenza virus infects a single cell. The resulting rapid change in viral genetics produces [antigenic shifts](/wiki/Antigenic_shift), which are sudden changes from one antigen to another. These sudden large changes allow the virus to infect new host species and quickly overcome protective immunity.<ref name=Hilleman/> This is important in the emergence of pandemics, as discussed below in the section on [Epidemiology](/wiki/#Epidemiology).

## Mechanism[[edit](/index.php?title=(none)&action=edit&section=9)]

### Transmission[[edit](/index.php?title=(none)&action=edit&section=10)]

When an infected person sneezes or coughs more than half a million virus particles can be spread to those close by.[[35]](#cite_note-35) In otherwise healthy adults, influenza virus shedding (the time during which a person might be infectious to another person) increases sharply one-half to one day after infection, peaks on day 2 and persists for an average total duration of 5 days—but can persist as long as 9 days.<ref name=Carrat>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> In those who develop symptoms from experimental infection (only 67% of healthy experimentally infected individuals), symptoms and viral shedding show a similar pattern, but with viral shedding preceding illness by one day.[[36]](#cite_note-36) Children are much more infectious than adults and shed virus from just before they develop symptoms until two weeks after infection.[[37]](#cite_note-37) In immunocompromised people, viral shedding can continue for longer than two weeks.[[38]](#cite_note-38) Influenza can be spread in three main ways:<ref name=Weber>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>[[39]](#cite_note-39) by direct transmission (when an infected person sneezes mucus directly into the eyes, nose or mouth of another person); the airborne route (when someone inhales the [aerosols](/wiki/Particulate) produced by an infected person coughing, sneezing or spitting) and through hand-to-eye, hand-to-nose, or hand-to-mouth transmission, either from contaminated surfaces or from direct personal contact such as a hand-shake. The relative importance of these three modes of transmission is unclear, and they may all contribute to the spread of the virus.<ref name=Brankston2007/> In the airborne route, the droplets that are small enough for people to inhale are 0.5 to 5 [µm](/wiki/Μm) in diameter and inhaling just one droplet might be enough to cause an infection.<ref name=Weber/> Although a single sneeze releases up to 40,000 droplets,<ref name=Cole\_1998>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> most of these droplets are quite large and will quickly settle out of the air.<ref name=Weber/> How long influenza survives in airborne droplets seems to be influenced by the levels of [humidity](/wiki/Humidity) and [UV radiation](/wiki/UV_radiation), with low humidity and a lack of sunlight in winter aiding its survival.<ref name=Weber/>

As the influenza virus can persist outside of the body, it can also be transmitted by contaminated surfaces such as banknotes,<ref name=Thomas>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> doorknobs, light switches and other household items.<ref name=Merck/> The length of time the virus will persist on a surface varies, with the virus surviving for one to two days on hard, non-porous surfaces such as plastic or metal, for about fifteen minutes from dry paper tissues, and only five minutes on skin.<ref name=Moore>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> However, if the virus is present in mucus, this can protect it for longer periods (up to 17 days on banknotes).<ref name=Weber/><ref name=Thomas/> Avian influenza viruses can survive indefinitely when frozen.<ref name=cfsph>[Template:Cite web](/wiki/Template:Cite_web) p. 7</ref> They are inactivated by heating to 56 °C (133 °F) for a minimum of 60 minutes, as well as by acids (at pH <2).<ref name=cfsph/>

### Pathophysiology[[edit](/index.php?title=(none)&action=edit&section=11)]

[thumb|280px|The different sites of infection (shown in red) of](/wiki/Image:H1N1_versus_H5N1_pathology.png) [seasonal H1N1](/wiki/Influenza_A_virus_subtype_H1N1) versus [avian H5N1](/wiki/Influenza_A_virus_subtype_H5N1). This influences their lethality and ability to spread.

The mechanisms by which influenza infection causes symptoms in humans have been studied intensively. One of the mechanisms is believed to be the inhibition of [adrenocorticotropic hormone](/wiki/Adrenocorticotropic_hormone) (ACTH) resulting in lowered [cortisol](/wiki/Cortisol) levels.<ref name=jefferies1998>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Knowing which genes are carried by a particular strain can help predict how well it will infect humans and how severe this infection will be (that is, predict the strain's [pathophysiology](/wiki/Pathophysiology)).<ref name=Taubenberger2008>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Korteweg>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

For instance, part of the process that allows influenza viruses to invade cells is the [cleavage](/wiki/Proteolysis) of the viral [hemagglutinin](/wiki/Hemagglutinin) protein by any one of several human [proteases](/wiki/Protease).<ref name=Steinhauer/> In mild and avirulent viruses, the structure of the hemagglutinin means that it can only be cleaved by proteases found in the throat and lungs, so these viruses cannot infect other tissues. However, in highly virulent strains, such as H5N1, the hemagglutinin can be cleaved by a wide variety of proteases, allowing the virus to spread throughout the body.<ref name=Korteweg/>

The viral hemagglutinin protein is responsible for determining both which species a strain can infect and where in the human [respiratory tract](/wiki/Respiratory_tract) a strain of influenza will bind.[[40]](#cite_note-40) Strains that are easily transmitted between people have hemagglutinin proteins that bind to receptors in the upper part of the respiratory tract, such as in the nose, throat and mouth. In contrast, the highly lethal H5N1 strain binds to receptors that are mostly found deep in the lungs.[[41]](#cite_note-41) This difference in the site of infection may be part of the reason why the H5N1 strain causes severe viral pneumonia in the lungs, but is not easily transmitted by people coughing and sneezing.[[42]](#cite_note-42)[[43]](#cite_note-43) Common symptoms of the flu such as fever, headaches, and fatigue are the result of the huge amounts of proinflammatory [cytokines](/wiki/Cytokine) and [chemokines](/wiki/Chemokine) (such as [interferon](/wiki/Interferon) or [tumor necrosis factor](/wiki/Tumor_necrosis_factor-alpha)) produced from influenza-infected cells.<ref name=Eccles/>[[44]](#cite_note-44) In contrast to the [rhinovirus](/wiki/Rhinovirus) that causes the [common cold](/wiki/Common_cold), influenza does cause tissue damage, so symptoms are not entirely due to the [inflammatory response](/wiki/Inflammation).[[45]](#cite_note-45) This massive immune response might produce a life-threatening [cytokine storm](/wiki/Cytokine_storm). This effect has been proposed to be the cause of the unusual lethality of both the H5N1 avian influenza,[[46]](#cite_note-46) and the 1918 pandemic strain.[[47]](#cite_note-47)[[48]](#cite_note-48) However, another possibility is that these large amounts of cytokines are just a result of the massive levels of viral replication produced by these strains, and the immune response does not itself contribute to the disease.<ref name=Beigel>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

## Prevention[[edit](/index.php?title=(none)&action=edit&section=12)]

### Vaccination[[edit](/index.php?title=(none)&action=edit&section=13)]

[Template:Main](/wiki/Template:Main) [thumb|Giving an influenza vaccination](/wiki/File:Vaccination_US_Navy.jpg) The [influenza vaccine](/wiki/Influenza_vaccine) is recommended by the [World Health Organization](/wiki/World_Health_Organization) and United States [Centers for Disease Control and Prevention](/wiki/Centers_for_Disease_Control_and_Prevention) for high-risk groups, such as children, the elderly, health care workers, and people who have chronic illnesses such as [asthma](/wiki/Asthma), [diabetes](/wiki/Diabetes), [heart disease](/wiki/Heart_disease), or are immuno-compromised among others.[[49]](#cite_note-49)<ref name=cdcreport>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> In healthy adults it is modestly effective in decreasing the amount of influenza-like symptoms in a population.[[50]](#cite_note-50) Evidence is supportive of a decreased rate of influenza in children over the age of two.[[51]](#cite_note-51) In those with [chronic obstructive pulmonary disease](/wiki/Chronic_obstructive_pulmonary_disease) vaccination reduces exacerbations,[[52]](#cite_note-52) it is not clear if it reduces asthma exacerbations.[[53]](#cite_note-53) Evidence supports a lower rate of influenza-like illness in many groups who are immunocompromised such as those with: [HIV/AIDS](/wiki/HIV/AIDS), [cancer](/wiki/Cancer), and post organ transplant.[[54]](#cite_note-54) In those at high risk immunization may reduce the risk of [heart disease](/wiki/Heart_disease).<ref name=Udell-2013>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Whether immunizing health care workers affects patient outcomes is controversial with some reviews finding insufficient evidence[[55]](#cite_note-55)[[56]](#cite_note-56) and others finding tentative evidence.[[57]](#cite_note-57)[[58]](#cite_note-58) Due to the high [mutation rate](/wiki/Mutation_rate) of the virus, a particular influenza vaccine usually confers protection for no more than a few years. Every year, the World Health Organization predicts which strains of the virus are most likely to be circulating in the next year (see [Historical annual reformulations of the influenza vaccine](/wiki/Historical_annual_reformulations_of_the_influenza_vaccine)), allowing [pharmaceutical companies](/wiki/Pharmaceutical_company) to develop vaccines that will provide the best immunity against these strains.<ref name=WHOrecommendation/> The vaccine is reformulated each season for a few specific flu strains but does not include all the strains active in the world during that season. It takes about six months for the manufacturers to formulate and produce the millions of doses required to deal with the seasonal epidemics; occasionally, a new or overlooked strain becomes prominent during that time.[[59]](#cite_note-59) It is also possible to get infected just before vaccination and get sick with the strain that the vaccine is supposed to prevent, as the vaccine takes about two weeks to become effective.<ref name=CDCkeyfacts/>

Vaccines can cause the [immune system](/wiki/Immune_system) to react as if the body were actually being infected, and general infection symptoms (many cold and flu symptoms are just general infection symptoms) can appear, though these symptoms are usually not as severe or long-lasting as influenza. The most dangerous [adverse effect](/wiki/Adverse_effect) is a severe [allergic reaction](/wiki/Allergy) to either the virus material itself or residues from the hen eggs used to grow the influenza; however, these reactions are extremely rare.[[60]](#cite_note-60) The cost-effectiveness of seasonal influenza vaccination has been widely evaluated for different groups and in different settings.[[61]](#cite_note-61) It has generally been found to be a cost-effective intervention, especially in children[[62]](#cite_note-62) and the elderly,[[63]](#cite_note-63) however the results of economic evaluations of influenza vaccination have often been found to be dependent on key assumptions.[[64]](#cite_note-64)[[65]](#cite_note-65)

### Infection control[[edit](/index.php?title=(none)&action=edit&section=14)]

[Template:Further](/wiki/Template:Further) Reasonably effective ways to reduce the transmission of influenza include good personal health and hygiene habits such as: not touching your eyes, nose or mouth;[[66]](#cite_note-66) frequent [hand washing](/wiki/Hand_washing) (with soap and water, or with alcohol-based hand rubs);[[67]](#cite_note-67) covering coughs and sneezes; avoiding close contact with sick people; and staying home yourself if you are sick. Avoiding spitting is also recommended.<ref name=Aledort>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Although [face masks](/wiki/Surgical_mask) might help prevent transmission when caring for the sick,[[68]](#cite_note-68)[[69]](#cite_note-69) there is mixed evidence on beneficial effects in the community.<ref name=Aledort/>[[70]](#cite_note-70) Smoking raises the risk of contracting influenza, as well as producing more severe disease symptoms.[[71]](#cite_note-71)[[72]](#cite_note-72) Since influenza spreads through both [aerosols](/wiki/Particulate) and contact with contaminated surfaces, surface sanitizing may help prevent some infections.[[73]](#cite_note-73) [Alcohol](/wiki/Alcohol) is an effective sanitizer against influenza viruses, while [quaternary ammonium compounds](/wiki/Quaternary_ammonium_cation) can be used with alcohol so that the sanitizing effect lasts for longer.<ref name=McDonnell>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> In hospitals, quaternary ammonium compounds and [bleach](/wiki/Bleach) are used to sanitize rooms or equipment that have been occupied by patients with influenza symptoms.<ref name=McDonnell/> At home, this can be done effectively with a diluted chlorine bleach.[[74]](#cite_note-74) During past pandemics, closing schools, churches and theaters slowed the spread of the virus but did not have a large effect on the overall death rate.[[75]](#cite_note-75)[[76]](#cite_note-76) It is uncertain if reducing public gatherings, by for example closing schools and workplaces, will reduce transmission since people with influenza may just be moved from one area to another; such measures would also be difficult to enforce and might be unpopular.<ref name=Aledort/> When small numbers of people are infected, isolating the sick might reduce the risk of transmission.<ref name=Aledort/>

## Treatment[[edit](/index.php?title=(none)&action=edit&section=15)]

[Template:Main](/wiki/Template:Main)

People with the flu are advised to get plenty of rest, drink plenty of liquids, avoid using [alcohol](/wiki/Alcoholic_beverage) and [tobacco](/wiki/Tobacco_smoking) and, if necessary, take medications such as acetaminophen ([paracetamol](/wiki/Paracetamol)) to relieve the fever and muscle aches associated with the flu.[[77]](#cite_note-77) Children and teenagers with flu symptoms (particularly fever) should avoid taking [aspirin](/wiki/Aspirin) during an influenza infection (especially [influenza type B](/wiki/Influenzavirus_B)), because doing so can lead to [Reye's syndrome](/wiki/Reye's_syndrome), a rare but potentially fatal disease of the [liver](/wiki/Liver).[[78]](#cite_note-78) Since influenza is caused by a virus, [antibiotics](/wiki/Antibiotic) have no effect on the infection; unless prescribed for [secondary infections](/wiki/Secondary_infection) such as [bacterial pneumonia](/wiki/Bacterial_pneumonia). Antiviral medication may be effective, if given early, but some strains of influenza can show resistance to the standard antiviral drugs and there is concern about the quality of the research.[[79]](#cite_note-79)

### Antivirals[[edit](/index.php?title=(none)&action=edit&section=16)]

The two classes of antiviral drugs used against influenza are [neuraminidase inhibitors](/wiki/Neuraminidase_inhibitor) ([oseltamivir](/wiki/Oseltamivir) and [zanamivir](/wiki/Zanamivir)) and [M2 protein](/wiki/M2_protein) inhibitors ([adamantane](/wiki/Adamantane) derivatives).

#### Neuraminidase inhibitors[[edit](/index.php?title=(none)&action=edit&section=17)]

Overall the benefits of neuraminidase inhibitors in those who are otherwise healthy do not appear to be greater than the risks.<ref name=Mich2013/> There does not appear to be any benefit in those with other health problems.<ref name=Mich2013/> In those believed to have the flu, they decreased the length of time symptoms were present by slightly less than a day but did not appear to affect the risk of complications such as needing hospitalization or [pneumonia](/wiki/Pneumonia).<ref name=Ebe2013/> Previous to 2013 the benefits were unclear as the manufacturer ([Roche](/wiki/Hoffmann-La_Roche)) refused to release trial data for independent analysis.<ref name=CD008965>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Increasingly prevalent resistance to neuraminidase inhibitors has led to researchers to seek alternative antiviral drugs with different mechanisms of action.[[80]](#cite_note-80)

#### M2 inhibitors[[edit](/index.php?title=(none)&action=edit&section=18)]

The [antiviral drugs](/wiki/Antiviral_drug) [amantadine](/wiki/Amantadine) and [rimantadine](/wiki/Rimantadine) inhibit a viral [ion channel](/wiki/Ion_channel) ([M2 protein](/wiki/M2_protein)), thus inhibiting replication of the influenza A virus.<ref name=Pinto/> These drugs are sometimes effective against influenza A if given early in the infection but are ineffective against influenza B viruses, which lack the M2 drug target.[[81]](#cite_note-81) Measured resistance to amantadine and rimantadine in American isolates of [H3N2](/wiki/H3N2) has increased to 91% in 2005.[[82]](#cite_note-82) This high level of resistance may be due to the easy availability of amantadines as part of over-the-counter cold remedies in countries such as China and Russia,[[83]](#cite_note-83) and their use to prevent outbreaks of influenza in farmed poultry.[[84]](#cite_note-84)[[85]](#cite_note-85) The CDC recommended against using M2 inhibitors during the 2005–06 influenza season due to high levels of [drug resistance](/wiki/Drug_resistance).[[86]](#cite_note-86)

## Prognosis[[edit](/index.php?title=(none)&action=edit&section=19)]

Influenza's effects are much more severe and last longer than those of the [common cold](/wiki/Common_cold). Most people will recover completely in about one to two weeks, but others will develop life-threatening complications (such as [pneumonia](/wiki/Pneumonia)). Thus, influenza can be deadly, especially for the weak, young and old, or chronically ill.<ref name=Hilleman/> People with a [weak immune system](/wiki/Immunosuppression), such as people with advanced [HIV](/wiki/HIV) infection or transplant patients (whose immune systems are medically suppressed to prevent transplant organ rejection), suffer from particularly severe disease.[[87]](#cite_note-87) Pregnant women and young children are also at a high risk for complications.[[88]](#cite_note-88) The flu can worsen chronic health problems. People with emphysema, chronic bronchitis or asthma may experience [shortness of breath](/wiki/Dyspnea) while they have the flu, and influenza may cause worsening of [coronary heart disease](/wiki/Coronary_heart_disease) or [congestive heart failure](/wiki/Congestive_heart_failure).[[89]](#cite_note-89) [Smoking](/wiki/Tobacco_smoking) is another [risk factor](/wiki/Risk_factor) associated with more serious disease and increased mortality from influenza.[[90]](#cite_note-90) According to the World Health Organization: "Every winter, tens of millions of people get the flu. Most are only ill and out of work for a week, yet the elderly are at a higher risk of death from the illness. We know the worldwide death toll exceeds a few hundred thousand people a year, but even in developed countries the numbers are uncertain, because medical authorities don't usually verify who actually died of influenza and who died of a flu-like illness."[[91]](#cite_note-91) Even healthy people can be affected, and serious problems from influenza can happen at any age. People over 50 years old, very young children and people of any age with chronic [medical conditions](/wiki/Medical_conditions) are more likely to get complications from influenza, such as pneumonia, [bronchitis](/wiki/Bronchitis), [sinus](/wiki/Paranasal_sinus), and [ear infections](/wiki/Ear_infection).<ref name=CDCkeyfacts>[Key Facts about Influenza (Flu) Vaccine](http://www.cdc.gov/flu/protect/keyfacts.htm) CDC publication. Published 17 October 2006. Retrieved 18 October 2006.</ref>

In some cases, an [autoimmune](/wiki/Autoimmune) response to an influenza infection may contribute to the development of [Guillain-Barré syndrome](/wiki/Guillain-Barré_syndrome).<ref name=Sivadon-Tardy>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> However, as many other infections can increase the risk of this disease, influenza may only be an important cause during epidemics.<ref name=Sivadon-Tardy/>[[92]](#cite_note-92) This syndrome has been believed to also be a rare side effect of influenza vaccines. One review gives an incidence of about one case per million vaccinations.[[93]](#cite_note-93) Getting infected by influenza itself increases both the risk of death (up to 1 in 10,000) and increases the risk of developing GBS to a much higher level than the highest level of suspected vaccine involvement (approx. 10 times higher by recent estimates).[[94]](#cite_note-94)[[95]](#cite_note-95)

## Epidemiology[[edit](/index.php?title=(none)&action=edit&section=20)]

### Seasonal variations[[edit](/index.php?title=(none)&action=edit&section=21)]

[Template:Further2](/wiki/Template:Further2) [thumb|300px|Seasonal risk areas for influenza: November–April (blue), April–November (red), and year-round (yellow).](/wiki/Image:Influenza_Seasonal_Risk_Areas.svg) Influenza reaches peak prevalence in winter, and because the [Northern](/wiki/Northern_Hemisphere) and [Southern Hemispheres](/wiki/Southern_Hemisphere) have winter at different times of the year, there are actually two different flu seasons each year. This is why the World Health Organization (assisted by the [National Influenza Centers](/wiki/National_Influenza_Centers)) makes recommendations for two different vaccine formulations every year; one for the Northern, and one for the Southern Hemisphere.<ref name=WHOrecommendation>[Recommended composition of influenza virus vaccines for use in the 2006–2007 influenza season](http://www.who.int/csr/disease/influenza/2007northreport.pdf) WHO report 14 February 2006. Retrieved 19 October 2006.</ref>

A long-standing puzzle has been why outbreaks of the flu occur seasonally rather than uniformly throughout the year. One possible explanation is that, because people are indoors more often during the winter, they are in close contact more often, and this promotes transmission from person to person. Increased travel due to the Northern Hemisphere winter holiday season may also play a role.[[96]](#cite_note-96) Another factor is that cold temperatures lead to drier air, which may dehydrate mucus, preventing the body from effectively expelling virus particles. The virus also survives longer on surfaces at colder temperatures and aerosol transmission of the virus is highest in cold environments (less than 5 °C) with low relative humidity.[[97]](#cite_note-97) The lower air humidity in winter seems to be the main cause of seasonal influenza transmission in temperate regions.[[98]](#cite_note-98)[[99]](#cite_note-99) However, seasonal changes in infection rates also occur in tropical regions, and in some countries these peaks of infection are seen mainly during the rainy season.[[100]](#cite_note-100) Seasonal changes in contact rates from school terms, which are a major factor in other [childhood diseases](/wiki/List_of_childhood_diseases) such as [measles](/wiki/Measles) and [pertussis](/wiki/Pertussis), may also play a role in the flu. A combination of these small seasonal effects may be amplified by dynamical resonance with the endogenous disease cycles.[[101]](#cite_note-101) [H5N1](/wiki/H5N1) exhibits seasonality in both humans and birds.<ref name=WHOH5N1data>[WHO Confirmed Human Cases of H5N1](http://www.who.int/csr/disease/avian_influenza/country/en/) Data published by WHO Epidemic and Pandemic Alert and Response (EPR). Retrieved 24 October 2006</ref>

An alternative hypothesis to explain seasonality in influenza infections is an effect of [vitamin D](/wiki/Vitamin_D_and_influenza) levels on immunity to the virus.[[102]](#cite_note-102) This idea was first proposed by [Robert Edgar Hope-Simpson](/wiki/Robert_Edgar_Hope-Simpson) in 1965.[[103]](#cite_note-103) He proposed that the cause of influenza epidemics during winter may be connected to seasonal fluctuations of vitamin D, which is produced in the skin under the influence of solar (or artificial) [UV radiation](/wiki/Ultraviolet). This could explain why influenza occurs mostly in winter and during the tropical rainy season, when people stay indoors, away from the sun, and their vitamin D levels fall.

### Epidemic and pandemic spread[[edit](/index.php?title=(none)&action=edit&section=22)]

[Template:Further2](/wiki/Template:Further2)

[thumb|right|](/wiki/File:Antigenic_drift_vs_shift.png)[Antigenic drift](/wiki/Antigenic_drift) creates influenza viruses with slightly modified antigens, while [antigenic shift](/wiki/Antigenic_shift) generates viruses with entirely novel antigens.

As influenza is caused by a variety of species and strains of [viruses](/wiki/Virus), in any given year some strains can die out while others create [epidemics](/wiki/Epidemic), while yet another strain can cause a [pandemic](/wiki/Pandemic). Typically, in a year's normal two [flu seasons](/wiki/Flu_season) (one per hemisphere), there are between three and five million cases of severe illness and around 500,000 deaths worldwide,<ref name=Loz2012>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> which by some definitions is a yearly influenza epidemic.[[104]](#cite_note-104) Although the incidence of influenza can vary widely between years, approximately 36,000 deaths and more than 200,000 hospitalizations are directly associated with influenza every year in the United States.[[105]](#cite_note-105)[[106]](#cite_note-106) One method of calculating influenza mortality produced an estimate of 41,400 average deaths per year in the United States between 1979 and 2001.[[107]](#cite_note-107) Different methods in 2010 by the [Centers for Disease Control and Prevention](/wiki/Centers_for_Disease_Control_and_Prevention) (CDC) reported a range from a low of about 3,300 deaths to a high of 49,000 per year.[[108]](#cite_note-108) Roughly three times per century, a pandemic occurs, which infects a large proportion of the world's population and can kill tens of millions of people (see [pandemics section](/wiki/Influenza#Pandemics)). One study estimated that if a strain with similar [virulence](/wiki/Virulence) to the [1918 influenza](/wiki/1918_flu_pandemic) emerged today, it could kill between 50 and 80 million people.[[109]](#cite_note-109) [thumb|left|Antigenic shift, or reassortment, can result in novel and highly pathogenic strains of human influenza](/wiki/File:Influenza_geneticshift.svg) New influenza viruses are constantly [evolving](/wiki/Evolution) by [mutation](/wiki/Mutation) or by [reassortment](/wiki/Reassortment).<ref name=hay/> Mutations can cause small changes in the [hemagglutinin](/wiki/Hemagglutinin) and [neuraminidase](/wiki/Neuraminidase) [antigens](/wiki/Antigen) on the surface of the virus. This is called [antigenic drift](/wiki/Antigenic_drift), which slowly creates an increasing variety of strains until one evolves that can infect people who are immune to the pre-existing strains. This new variant then replaces the older strains as it rapidly sweeps through the human population, often causing an epidemic.[[110]](#cite_note-110) However, since the strains produced by drift will still be reasonably similar to the older strains, some people will still be immune to them. In contrast, when influenza viruses reassort, they acquire completely new antigens—for example by reassortment between avian strains and human strains; this is called [antigenic shift](/wiki/Antigenic_shift). If a human influenza virus is produced that has entirely new antigens, everybody will be susceptible, and the novel influenza will spread uncontrollably, causing a pandemic.[[111]](#cite_note-111) In contrast to this model of pandemics based on antigenic drift and shift, an alternative approach has been proposed where the periodic pandemics are produced by interactions of a fixed set of viral strains with a human population with a constantly changing set of immunities to different viral strains.[[112]](#cite_note-112) [thumb|The generation time for influenza (the time from one infection to the next) is very short (only 2 days). This explains why influenza epidemics start and finish in a short time scale of only a few months.](/wiki/File:Ferguson_influenza_generation_time_distribution.png)[[113]](#cite_note-113) From a public health point of view, flu epidemics spread rapidly and are very difficult to control. Most influenza virus strains are not very infectious and each infected individual will only go on to infect one or two other individuals (the basic reproduction number for influenza is generally around 1.4). However, the generation time for influenza is extremely short: the time from a person becoming infected to when he infects the next person is only two days. The short generation time means that influenza epidemics generally peak at around 2 months and burn out after 3 months: the decision to intervene in an influenza epidemic therefore has to be taken early, and the decision is therefore often made on the back of incomplete data. Another problem is that individuals become infectious before they become symptomatic, which means that putting people in quarantine after they become ill is not an effective public health intervention.[[113]](#cite_note-113) For the average person, viral shedding tends to peak on day two whereas symptoms peak on day three.<ref name=AmericanJournalEpidemiology2008/>

## History[[edit](/index.php?title=(none)&action=edit&section=23)]

[Template:See also](/wiki/Template:See_also)

### Etymology[[edit](/index.php?title=(none)&action=edit&section=24)]

The word *Influenza* comes from the [Italian language](/wiki/Italian_language) meaning "influence" and refers to the cause of the disease; initially, this ascribed illness to unfavorable [astrological](/wiki/Astrology) influences.[[114]](#cite_note-114) Changes in medical thought led to its modification to *influenza del freddo*, meaning "influence of the cold". The word *influenza* was first used in English to refer to the disease we know today in 1703 by J. Hugger of the University of Edinburgh in his thesis *De Catarrho epidemio, vel Influenza, prout in India occidentali sese ostendit*.[[115]](#cite_note-115)Archaic terms for influenza include *epidemic catarrh*, *grippe* (from the French, first used by Molyneaux in 1694 [[116]](#cite_note-116)), *sweating sickness*, and *Spanish fever* (particularly for the [1918 flu pandemic](/wiki/1918_flu_pandemic) strain).[[117]](#cite_note-117)

### Pandemics[[edit](/index.php?title=(none)&action=edit&section=25)]

[Template:Further2](/wiki/Template:Further2)

[thumb|The difference between the influenza mortality age distributions of the 1918 epidemic and normal epidemics. Deaths per 100,000 persons in each age group, United States, for the interpandemic years 1911–1917 (dashed line) and the pandemic year 1918 (solid line).](/wiki/File:W_curve.png)[[118]](#cite_note-118) [thumb|Thermal imaging camera and screen, photographed in an airport terminal in](/wiki/Image:Airport_Thermographic_Camera.jpg) [Greece](/wiki/Greece) during the 2009 flu pandemic. Thermal imaging can detect elevated body temperature, one of the signs of swine flu.

The symptoms of human influenza were clearly described by [Hippocrates](/wiki/Hippocrates) roughly 2,400 years ago.[[119]](#cite_note-119)[[120]](#cite_note-120) Although the virus seems to have caused epidemics throughout human history, historical data on influenza are difficult to interpret, because the symptoms can be similar to those of other respiratory diseases.[[121]](#cite_note-121)<ref name=Potter/> The disease may have spread from Europe to the Americas as early as the [European colonization of the Americas](/wiki/European_colonization_of_the_Americas); since almost the entire indigenous population of the Antilles was killed by an epidemic resembling influenza that broke out in 1493, after the arrival of [Christopher Columbus](/wiki/Christopher_Columbus).[[122]](#cite_note-122)[[123]](#cite_note-123) The first convincing record of an influenza pandemic was of an outbreak in 1580, which began in Russia and spread to Europe via Africa. In [Rome](/wiki/History_of_Rome#Renaissance_Rome), over 8,000 people were killed, and several Spanish cities were almost wiped out. Pandemics continued sporadically throughout the 17th and 18th centuries, with the pandemic of 1830–1833 being particularly widespread; it infected approximately a quarter of the people exposed.<ref name=Potter>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

The most famous and lethal outbreak was the [1918 flu pandemic](/wiki/1918_flu_pandemic) (Spanish flu pandemic) ([type A influenza](/wiki/Influenzavirus_A), [H1N1](/wiki/H1N1) subtype), which lasted from 1918 to 1919. It is not known exactly how many it killed, but estimates range from 50 to 100 million people.[[118]](#cite_note-118)<ref name=Knobler>[Template:Cite book](/wiki/Template:Cite_book)</ref><ref name=Patterson1>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> This pandemic has been described as "the greatest medical holocaust in history" and may have killed as many people as the [Black Death](/wiki/Black_Death).<ref name=Potter/> This huge death toll was caused by an extremely high infection rate of up to 50% and the extreme severity of the symptoms, suspected to be caused by [cytokine storms](/wiki/Cytokine_storm).<ref name=Patterson1/> Symptoms in 1918 were so unusual that initially influenza was misdiagnosed as dengue, [cholera](/wiki/Cholera), or typhoid. One observer wrote, "One of the most striking of the complications was hemorrhage from [mucous membranes](/wiki/Mucous_membrane), especially from the nose, stomach, and intestine. Bleeding from the ears and [petechial hemorrhages](/wiki/Petechia) in the skin also occurred."<ref name=Knobler/> The majority of deaths were from [bacterial pneumonia](/wiki/Bacterial_pneumonia), a [secondary infection](/wiki/Secondary_infection) caused by influenza, but the virus also killed people directly, causing massive [hemorrhages](/wiki/Bleeding) and [edema](/wiki/Edema) in the lung.<ref name=autogenerated1>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

The 1918 flu pandemic (Spanish flu pandemic) was truly global, spreading even to the [Arctic](/wiki/Arctic) and remote [Pacific islands](/wiki/Pacific_Islands). The unusually severe disease killed between 2 and 20% of those infected, as opposed to the more usual flu epidemic [mortality rate](/wiki/Mortality_rate) of 0.1%.<ref name=Taubenberger/><ref name=Knobler/> Another unusual feature of this pandemic was that it mostly killed young adults, with 99% of pandemic influenza deaths occurring in people under 65, and more than half in young adults 20 to 40 years old.[[124]](#cite_note-124) This is unusual since influenza is normally most deadly to the very young (under age 2) and the very old (over age 70). The total mortality of the 1918–1919 pandemic is not known, but it is estimated that 2.5% to 5% of the world's population was killed. As many as 25 million may have been killed in the first 25 weeks; in contrast, [HIV/AIDS](/wiki/AIDS) has killed 25 million in its first 25 years.<ref name=Knobler/>

Later flu pandemics were not so devastating. They included the 1957 [Asian Flu](/wiki/Asian_Flu) (type A, [H2N2](/wiki/H2N2) strain) and the 1968 [Hong Kong Flu](/wiki/Hong_Kong_Flu) (type A, [H3N2](/wiki/H3N2) strain), but even these smaller outbreaks killed millions of people. In later pandemics [antibiotics](/wiki/Antibiotic) were available to control secondary infections and this may have helped reduce mortality compared to the Spanish Flu of 1918.<ref name=Taubenberger/>

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Known [flu pandemics](/wiki/Flu_pandemic)[[1]](#cite_note-1)<ref name=Hilleman>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Potter/> | | | | | |
| **Name of pandemic** | **Date** | **Deaths** | [**Case fatality rate**](/wiki/Case_fatality_rate) | **Subtype involved** | [**Pandemic Severity Index**](/wiki/Pandemic_Severity_Index) |
| [**1889–1890 flu pandemic**](/wiki/1889–1890_flu_pandemic) **(Asiatic or Russian Flu)**[**[125]**](#cite_note-125)**|1889–1890** | **|0.15%** | **possibly** [**H3N8**](/wiki/H3N8) **or** [**H2N2**](/wiki/H2N2) | **N/A** |  |  |
| [**1918 flu pandemic**](/wiki/1918_flu_pandemic) **(Spanish flu)**[**[126]**](#cite_note-126)**|1918–1920** | **|2%** |  | 5 |  |  |
| [**Asian Flu**](/wiki/H2N2#Asian_flu) | 1957–1958 | 1 to 1.5 million | 0.13% | [H2N2](/wiki/H2N2) | 2 |
| [**Hong Kong Flu**](/wiki/H3N2#Hong_Kong_Flu) | 1968–1969 | 0.75 to 1 million | <0.1% | [H3N2](/wiki/H3N2) | 2 |
| [**Russian flu**](/wiki/Influenza_A_virus_subtype_H1N1#Russian_flu) | 1977–1978 | no accurate count | N/A | [H1N1](/wiki/H1N1) | N/A |
| [**2009 flu pandemic**](/wiki/2009_flu_pandemic)[**[127]**](#cite_note-127)**|2009–2010** | **105,700-395,600**[**[128]**](#cite_note-128) | **0.03%** |  | N/A |  |

The first influenza virus to be isolated was from poultry, when in 1901 the agent causing a disease called "fowl plague" was passed through [Chamberland filters](/wiki/Chamberland_filter), which have pores that are too small for [bacteria](/wiki/Bacteria) to pass through.[[129]](#cite_note-129) The [etiological](/wiki/Etiology) cause of influenza, the Orthomyxoviridae family of viruses, was first discovered in [pigs](/wiki/Pig) by [Richard Shope](/wiki/Richard_Shope) in 1931.[[130]](#cite_note-130) This discovery was shortly followed by the isolation of the virus from humans by a group headed by [Patrick Laidlaw](/wiki/Patrick_Laidlaw) at the [Medical Research Council](/wiki/Medical_Research_Council_(UK)) of [the United Kingdom](/wiki/United_Kingdom) in 1933.[[131]](#cite_note-131) However, it was not until [Wendell Stanley](/wiki/Wendell_Stanley) first crystallized [tobacco mosaic virus](/wiki/Tobacco_mosaic_virus) in 1935 that the [non-cellular](/wiki/Cell_(biology)) nature of viruses was appreciated.

[thumb|350px|The main types of influenza viruses in humans. Solid squares show the appearance of a new strain, causing recurring influenza pandemics. Broken lines indicate uncertain strain identifications.<ref name=Palese>](/wiki/Image:Influenza_subtypes.svg)[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

The first significant step towards preventing influenza was the development in 1944 of a killed-virus vaccine for influenza by [Thomas Francis, Jr.](/wiki/Thomas_Francis,_Jr.). This built on work by Australian [Frank Macfarlane Burnet](/wiki/Frank_Macfarlane_Burnet), who showed that the virus lost virulence when it was cultured in fertilized hen's eggs.[[132]](#cite_note-132) Application of this observation by Francis allowed his group of researchers at the [University of Michigan](/wiki/University_of_Michigan) to develop the first influenza vaccine, with support from the [U.S. Army](/wiki/United_States_Army).[[133]](#cite_note-133) The Army was deeply involved in this research due to its experience of influenza in [World War I](/wiki/World_War_I), when thousands of troops were killed by the virus in a matter of months.<ref name=Knobler/> In comparison to vaccines, the development of anti-influenza drugs has been slower, with [amantadine](/wiki/Amantadine) being licensed in 1966 and, almost thirty years later, the next class of drugs (the [neuraminidase inhibitors](/wiki/Neuraminidase_inhibitor)) being developed.<ref name=Lynch/>

## Society and culture[[edit](/index.php?title=(none)&action=edit&section=26)]

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Influenza produces [direct costs](/wiki/Variable_cost) due to lost [productivity](/wiki/Productivity) and associated medical treatment, as well as [indirect costs](/wiki/Indirect_costs) of preventative measures. In the United States, influenza is responsible for a total cost of over $10 billion per year, while it has been estimated that a future pandemic could cause hundreds of billions of dollars in direct and indirect costs.[[134]](#cite_note-134) However, the economic impacts of past pandemics have not been intensively studied, and some authors have suggested that the [Spanish influenza](/wiki/Spanish_flu) actually had a positive long-term effect on per-capita income growth, despite a large reduction in the working population and severe short-term [depressive](/wiki/Recession) effects.[[135]](#cite_note-135) Other studies have attempted to predict the costs of a pandemic as serious as the 1918 Spanish flu on the [U.S. economy](/wiki/Economy_of_the_United_States), where 30% of all workers became ill, and 2.5% were killed. A 30% sickness rate and a three-week length of illness would decrease the [gross domestic product](/wiki/Gross_domestic_product) by 5%. Additional costs would come from medical treatment of 18 million to 45 million people, and total economic costs would be approximately $700 billion.[[136]](#cite_note-136) Preventative costs are also high. Governments worldwide have spent billions of [U.S. dollars](/wiki/United_States_dollar) preparing and planning for a potential H5N1 avian influenza pandemic, with costs associated with purchasing drugs and vaccines as well as developing [disaster drills](/wiki/Emergency_management) and strategies for improved [border controls](/wiki/Border_control).<ref name=Rosenthal/> On 1 November 2005, [United States President](/wiki/President_of_the_United_States) [George W. Bush](/wiki/George_W._Bush) unveiled the National Strategy to Safeguard Against the Danger of Pandemic Influenza[[137]](#cite_note-137) backed by a request to [Congress](/wiki/United_States_Congress) for $7.1 billion to begin implementing the plan.[[138]](#cite_note-138) Internationally, on 18 January 2006, donor nations pledged US$2 billion to combat bird flu at the two-day International Pledging Conference on Avian and Human Influenza held in China.[[139]](#cite_note-139) In an assessment of the 2009 H1N1 pandemic on selected countries in the Southern Hemisphere, data suggest that all countries experienced some time-limited and/or geographically isolated socio/economic effects and a temporary decrease in tourism most likely due to fear of 2009 H1N1 disease. It is still too early to determine whether the H1N1 pandemic has caused any long-term economic impacts.[[140]](#cite_note-140) [thumb|upright|Chinese inspectors on an airplane, checking passengers for fevers, a common symptom of swine flu](/wiki/File:ChineseFluInspectors.JPG)

In March 2013, the Chinese government reported three cases of H7N9 influenza infections in humans. Two of whom had died and the third was critically ill. Although the strain of the virus is not thought to spread efficiently between humans,[[162]](#cite_note-162)[[163]](#cite_note-163) by mid-April, at least 82 persons had become ill from H7N9, of which 17 had died. These cases include three small family clusters in Shanghai and one cluster between a neighboring girl and boy in Beijing, raising at least the possibility of human-to-human transmission. WHO points out that one cluster did not have two of the cases lab confirmed and further points out, as a matter of baseline information, that some viruses are able to cause limited human-to-human transmission under conditions of close contact but are not transmissible enough to cause large community outbreaks.[[164]](#cite_note-164)[[165]](#cite_note-165)

### Swine flu[[edit](/index.php?title=(none)&action=edit&section=30)]

In pigs [swine influenza](/wiki/Swine_influenza) produces fever, lethargy, sneezing, coughing, difficulty breathing and decreased appetite.<ref name=Kothalawala>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> In some cases the infection can cause abortion. Although mortality is usually low, the virus can produce weight loss and poor growth, causing economic loss to farmers.<ref name=Kothalawala/> Infected pigs can lose up to 12 pounds of body weight over a 3- to 4-week period.<ref name=Kothalawala/> Direct transmission of an influenza virus from pigs to humans is occasionally possible (this is called [zoonotic](/wiki/Zoonosis) swine flu). In all, 50 human cases are known to have occurred since the virus was identified in the mid-20th century, which have resulted in six deaths.<ref name=Myers>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

In 2009, a swine-origin [H1N1](/wiki/H1N1) virus strain commonly referred to as "swine flu" caused the [2009 flu pandemic](/wiki/2009_flu_pandemic), but there is no evidence that it is endemic to pigs (i.e. actually a swine flu) or of transmission from pigs to people, instead the virus is spreading from person to person.[[166]](#cite_note-166)[[167]](#cite_note-167) This strain is a reassortment of several strains of H1N1 that are usually found separately, in [humans](/wiki/Human_influenza), [birds](/wiki/Avian_influenza), and pigs.[[168]](#cite_note-168)

## References[[edit](/index.php?title=(none)&action=edit&section=31)]

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* [Template:Cite journal](/wiki/Template:Cite_journal)
* Bernd Sebastian Kamps, Christian Hoffmann and Wolfgang Preiser (Eds.) [Influenza Report](http://www.InfluenzaReport.com/), 225 pp, PDF, free download. Flying Publisher 2006
* [Template:Cite book](/wiki/Template:Cite_book)
* [Template:Cite book](/wiki/Template:Cite_book)
* [Template:Cite journal](/wiki/Template:Cite_journal)
* ISBN 978-3-211-80892-4 The Influenza Viruses Hoyle L 1968 Springer Verlag

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* [Template:Cite journal](/wiki/Template:Cite_journal)
* [Epidemiology of WHO-confirmed human cases of avian influenza A(H5N1) infection](http://www.who.int/wer/wer8126.pdf)

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* [Template:Cite journal](/wiki/Template:Cite_journal)
* [WHO (PDF) contains latest Evolutionary "Tree of Life" for H5N1](http://www.who.int/csr/disease/avian_influenza/guidelines/recommendationvaccine.pdf) article *Antigenic and genetic characteristics of H5N1 viruses and candidate H5N1 vaccine viruses developed for potential use as pre-pandemic vaccines* published 18 August 2006
* [WHO's assessment of Flu Research](http://www.who.int/csr/resources/publications/influenza/WHO_CDS_EPR_GIP_2006_3C.pdf) as of November 2006.

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## External links[[edit](/index.php?title=(none)&action=edit&section=33)]

[Template:Sisterlinks](/wiki/Template:Sisterlinks)

* [ERS Online Course on Influenza](http://www.ers-education.org/pages/default.aspx?id=331)
* [Info on influenza](http://www.cdc.gov/flu/) at [CDC](/wiki/Centers_for_Disease_Control_and_Prevention)
* [Fact Sheet](http://www.who.int/mediacentre/factsheets/fs211/en/index.html) Overview of influenza at World Health Organization
* [The Multinational Influenza Seasonal Mortality Study (MISMS)](http://origem.info/misms/index.php) [Fogarty International Center](/wiki/Fogarty_International_Center)
* [Influenza Virus Resource](http://www.ncbi.nlm.nih.gov/genomes/FLU/flubiology.html) from the [NCBI](/wiki/National_Center_for_Biotechnology_Information)
* [European Influenza Surveillance Scheme](http://www.eiss.org/)
* [Online video discussing influenza outbreaks and spread of other infectious diseases](http://www.vega.org.uk/video/programme/6) (Vega Science Trust)
* [PATH Vaccine Resource Library influenza resources](http://www.path.org/vaccineresources/influenza.php)
* [Influenza Research Database](http://www.fludb.org/) – Database of influenza genomic sequences, serotypes, polymorphisms, structures, epitopes, drugs and related tools
* [? Recombinomics – What's New](http://www.recombinomics.com/whats_new.html): Up to date details of circulating strains.

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