About Flu A & B

What is Influenza?
Influenza virus infections rank as one of the most common infectious diseases in humankind. Approximately 21 million people died worldwide in the 1918-1919 influenza pandemic.

Influenza usually occurs in the autumn and winter months in the Northern (October to April) and Southern (April to September) hemispheres and is characterised by explosive outbreaks lasting for six to eight weeks.

Who is at risk?

Everyone is at risk of developing Influenza. Every year, 100 million people are affected in Europe, Japan and the USA alone. Up to one in ten adults and one in three children can be affected by influenza annually. Certain groups of patients are at particularly high risk of developing the virus and additional complications. These include:

- Elderly patients (over 65 years old)
- Individuals whose immune system is compromised e.g by HIV treatment or steroid use
- Young children
- Patients suffering from chronic illnesses e.g. chronic respiratory, cardiac or renal disease
- Diabetics

What are the symptoms of Influenza?

The most defining characteristic of influenza is that symptom onset is sudden. Symptoms associated with Influenza may include:

· Fever/chills
· Cough
· Headaches
· Fatigue/weakness
· Muscle aches and pains

These symptoms are a direct consequence of viral replication and are different to symptoms associated with the common cold. The symptoms associated with Influenza can last for five to seven days, whilst fatigue and weakness can persist for up to two to three weeks.

How does Influenza spread to others?

The virus usually enters the body through mucus membranes in the mouth, nose or eyes. When a person with the flu coughs or sneezes, the virus becomes airborne and can be inhaled by anyone nearby. The incubation period ranges from 18 to 72 hours during which time the infected person is already likely to spread the virus to other people.

How is Influenza diagnosed?

A number of traditional tests can be used in the diagnosis of influenza (see table below). Tests are most useful when they are likely to give a doctor results that will help with diagnosis and treatment decisions. During a respiratory illness outbreak, however, testing for influenza can be very helpful in determining if influenza is the cause of the outbreak.

Appropriate samples for influenza testing can include a nasopharyngeal or throat swab, nasal wash, or nasal aspirates, depending on which type of test is used. (See table) Samples should be collected within the first 4 days of illness.
During outbreaks of respiratory illness when influenza is suspected, some samples should be tested by both rapid tests and by viral culture. The collection of some samples for viral culture is essential for determining the influenza subtypes and strains causing illness, and for surveillance of new strains that may need to be included in the next year's influenza vaccine. During outbreaks of influenza-like illness, viral culture also can help identify other causes of illness when influenza is not the cause.

Procedure	Influenza Types Detected	Acceptable Specimens	Time for Results
Rapid test	A and B	NP swab, nasal wash, throat swab, nasal aspirate, sputum	<30 mins
Enzyme Immuno Assay (EIA)	A and B	NP swab, throat swab, nasal wash, bronchial wash	2 hours
Immunofluorescence DFA Antibody Staining	A and B	NP swab, nasal wash, bronchial wash, nasal aspirate, sputum	2-4 hours
RT-PCR [5]	A and B	NP swab, throat swab, nasal wash, bronchial wash, nasal aspirate, sputum	1-2 days
Viral culture	A and B	NP swab, throat swab, nasal wash, bronchial wash, nasal aspirate, sputum	5-10 days
Serology	A and B	paired acute and convalescent serum samples	>2 weeks

Epidemic and Pandemic

Influenza epidemics can occur virtually every year, the extent and severity of each one varies widely. Pandemics – a worldwide epidemic can occur every 10 to 40 years and can affect up to 50% of the population.

Pathophysiology
Influenza results from infection with 1 of 3 basic types of virus, A, B, or C, which are classified within the family *Orthomyxoviridae*.

Influenza A and B most commonly cause disease in humans. Influenza A is a zoonotic infection that also infects pigs, birds, horses, and seals. The 1918 pandemic that resulted in millions of human deaths worldwide is believed to have originated from pigs.

The RNA core consists of 8 gene segments surrounded by a coat of 10 (influenza A) or 11 (influenza B) proteins. From a clinical viewpoint, the most significant surface proteins are hemagglutinin and neuraminidase. The viruses are typed based on these proteins. For example, influenza A (H3N2) expresses hemagglutinin 3 and neuraminidase 2.

The most common prevailing human influenza A subtypes are H1N1 and H3N2. Each year, the distributed vaccine contains A strains from H1N1 and H3N2, along with an influenza B strain.

In 1997, an avian subtype, H5N1, was first described in Hong Kong. Infection was confirmed in only 18 individuals, but 6 died. In January 2004, an epidemic occurred in domesticated birds in Southeast Asia (primarily Vietnam). The H5N1 flu appears to be transmissable from birds to humans but not from human to human. As a result of the poultry outbreak, more than a dozen people died.

Experts are concerned that a slight mutation could convert H5N1 to a strain that would spread from human to human. Such a strain could spread rapidly and result in very high human mortality rates around the world.

In March 1999, another avian subtype, H9N2, was described in 2 young children. Despite concern, no further outbreak of H9N2 infection occurred. Similar to H5N1 flu, experts are also concerned that a virulent strain of H9N2 influenza may mutate to allow human-to-human infection and that such a strain may possess the triad of infectivity, lethality, and transmissibility.

Influenza virus infection occurs after transfer of respiratory secretions from an infected individual to a person who is immunologically susceptible. If not neutralised by secretory antibodies, the virus invades airway and respiratory tract cells. Once within host cells, cellular dysfunction and degeneration occur, along with viral replication and release of viral progeny. Systemic symptoms result from inflammatory mediators, similar to other viruses. The incubation period ranges from 18-72 hours.

Viral shedding

A virus remains in cells in the body after first infection in a dormant form. At some point this latency ends and the virus multiplies and becomes transmittable, excreting itself from the infected host cell. Viral shedding occurs at onset of symptoms or just before the onset of illness (0-24 hours). Shedding continues for 5-10 days. Young children may shed virus longer, placing others at risk for contacting the virus. Viral shedding gives clinicians the ability to detect the virus.

What is the burden of Influenza on the healthcare sector and industry?

Healthcare

- Each year, influenza causes a 30–50% increase in primary care consultations. Complications due to Influenza, such as sinusitis, bronchitis and pneumonia generate additional costs for the healthcare system.
- During epidemics, the rate of hospital admissions may increase by 2 or 3 fold.

Industry

- Influenza has been estimated to account for one tenth of all sickness absences from work.
- After return from work, 80% of adults find that their work performance is reduced.
- Lost productivity costs $12 billion each year in the US alone

Vaccination

The prevention strategies for influenza infection focus on vaccination of vulnerable groups and aim to try and prevent infection. In general, studies suggest that vaccines are between 70-90% effective, but can be less effective in some patient populations, e.g. in the elderly with an effectiveness of 30-40%. If an unpredicted new strain of virus appears after the vaccine has been manufactured and distributed to individuals who have received the vaccine will not be protected.

Surveillance ensures that influenza vaccine produced each year is effective against the appropriate strain and produced in good time. The World Health Organisation (WHO) co-ordinates information exchange in the global surveillance of influenza, and advices on the formulation of vaccines against the virus.

What treatment is available for influenza sufferers?

The vast majority of patients use over the counter medications, such as paracetamol, to reduce the symptoms of influenza, but these agents do not attack the influenza virus itself and therefore the illness continues, which increases the risk of secondary complications. Antibiotics, such as penicillin, which are designed to kill bacteria, cannot attack the virus. Therefore antibiotics have no role in treating influenza in otherwise healthy people although they are used to treat complications.

For several years, four antiviral drugs that act by preventing influenza virus replication have been available. They differ in terms of their pharmacokinetics, side effects, routes of administration, target age groups, dosages, and costs.

When taken before infection or during early stage of the disease (within two days of illness onset), antivirals may help prevent infection, and if infection has already taken hold, their early administration may reduce the duration of symptoms by one to two days.

For several years, amantadine and rimantadine were the only antiviral drugs. However, whilst relatively inexpensive, these drugs are effective only against type A influenza, and may be associated with severe adverse effects (including delirium and seizures that occur mostly in elderly persons on higher doses). When used for prophylaxis of pandemic influenza at lower doses, such adverse events are far less likely. In addition, the virus tends to develop resistance to these drugs.

A newer class of antivirals, the neuraminidase inhibitors has been developed, that attack the virus. NIAs target one of the two major surface structures of the influenza virus, the neuraminidase protein. The neuraminidase active site is virtually the same in all common strains of influenza. If neuraminidase is inhibited, the virus is not able to infect new cells. Neuraminidase inhibitors that have been developed include, zanamivir (Relenza) and oseltamivir (Tamiflu®), have fewer adverse side effects (although zanamivir may exacerbate asthma or other chronic lung diseases) and the virus less often develops resistance. However, these drugs are expensive and currently not available for use in many countries. In severe influenza, admission to hospital, intensive care, antibiotic therapy to prevent secondary infection and breathing support may be required.