

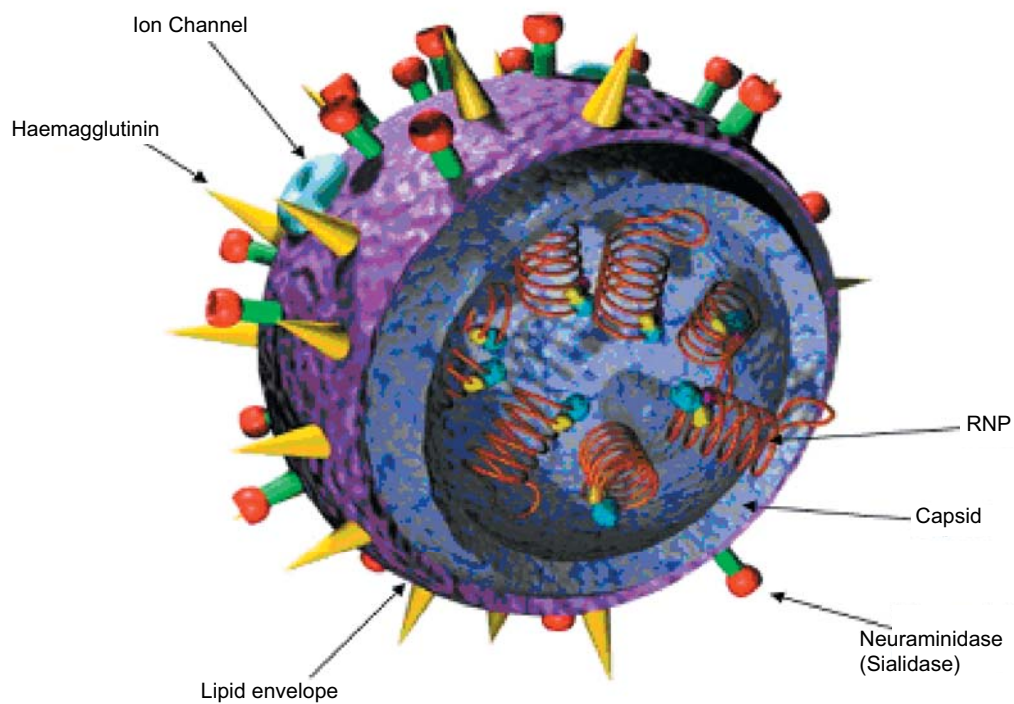
Spotlight on Influenza – Separating Fact from Fiction in the Fight against Influenza



PharmaVentures
Experts in deals and alliances

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THE INFLUENZA VIRUS

Introducing influenza

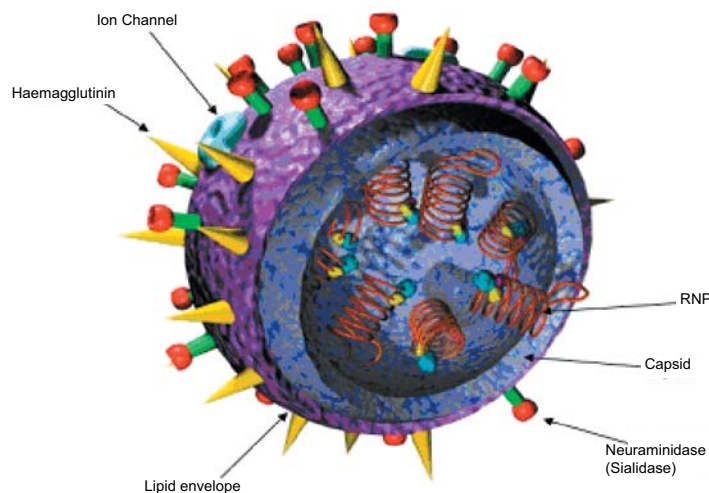
Despite being a mere tenth of a micrometer in size, the influenza virus is a pathogen with global prominence. Influenza sweeps rapidly around the world in seasonal epidemics affecting 5-15% of the population and causing up to half a million deaths each year.

Viral make-up

Although first isolated in the 1930s, the biological makeup of the influenza virus was not revealed until 1943 with the first glimpse of its structure in the electron microscope. Structurally speaking, an influenza virus particle consists of a core of single strands of RNA, containing all the necessary genes for the virus to survive and reproduce within host cells, wrapped in protein coats called nucleoproteins. This combination of vital genetic material and protein forms a helical structure known as the nucleocapsid.

Each strand of influenza virus RNA is covered with a protein coat called nucleoprotein. Coating the viral core is another layer of material called the matrix protein (M1) membrane and overlying this is a lipid envelope. The nucleocapsid and matrix proteins don these fatty coats when they become wrapped in cell membrane whilst budding from the infected cells (*Figure 1*).

Figure 1 - The influenza virus.



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From the surface of the influenza virus protrude two different types of glycoprotein molecules: haemagglutinin (H) and neuraminidase (N). The H and N proteins form the characteristic spikes of the influenza virus and aid in viral attachment and penetration, and release of progeny virus from infected cells, respectively. In an immune capacity, H and N proteins function as antigens and hence are fundamental to influenza vaccine development. Overall, the influenza virus genome is divided into eight segments which facilitates frequent, natural genetic reassortments and fuels the virus' high mutation rates, periodically resulting in new influenza strains that can result in influenza outbreaks.

triggering the latest slew of avian infections in Turkey. Experts have been tracking this strain since 1997 when it first revealed its ability to jump the species barrier and cause severe human disease with an outbreak of infected humans in Hong Kong. Despite the destruction of over 150 million birds, the H5N1 virus is now considered to be endemic in several regions of Southeast Asia. As of January 2006, there have been 148 confirmed human cases of H5N1 from the latest outbreak, and a total of 79 deaths (*Table 1*).

In the past, two other avian influenza strains have demonstrated the ability to infect humans, H9 and H7, but no previous outbreaks have been as severe as those caused by the H5N1 variant.

Viral targets for therapeutic intervention – Vaccination versus antivirals

There are two prongs to therapeutic targeting of the influenza virus – vaccination and antiviral therapy.

Overall, vaccines fall into one of three types:

- Whole virus vaccines – consisting of whole inactivated virus particles
- Split vaccines – comprising virus particles partially disrupted by detergent
- Subunit vaccines – containing purified envelope antigens, i.e. essentially consisting of haemagglutinin and neuraminidase from which other virus components have been removed

Vaccination

Vaccination is the cornerstone and primary means of influenza prevention, a stance supported by the World Health Organisation (WHO). Unlike antivirals, vaccines hold the ability to induce immunity, which is typically produced 2 to 3 weeks after a single vaccine dose. The primary principle underlying vaccination is the production of antibodies against haemagglutinin and neuraminidase proteins purposefully introduced into a healthy person by the vaccine vehicle. Among healthy adults, vaccination is very effective and reduces laboratory-confirmed illness in 70-90% of vaccinees. For the general elderly population, vaccination may reduce hospitalisations by 25-39% and overall mortality by 39-75%. The benefits conferred on nursing home residents by influenza vaccines are even greater, with a 50% reduction in the risk of hospitalisation, a 60% drop in pneumonia risk and a 68% fall in all-cause death. Advantages of vaccination also extend beyond the individual vaccine recipient. As an undertaking, vaccination not only decreases the risk of illness for the vaccinee but helps prevent the spread of the influenza virus and limits its role in the potential development of life-threatening complications.

AN EYE ON THE INFLUENZA MARKET: ANALYSING MARKET DIMENSIONS

Current market size

The influenza market is substantial in scope and size. In June 2005, GSK estimated that the influenza market could more than double from its then value of US\$1.3-1.6 B to a value of US\$2.9-3.7 B in 2010. Over the last couple of years, there has been a marked increase in interest in the antiviral field as a whole, concomitant with a surge in enthusiastic pharmaceutical endeavour targeted at highly prevalent diseases, such as influenza (Figure 5).

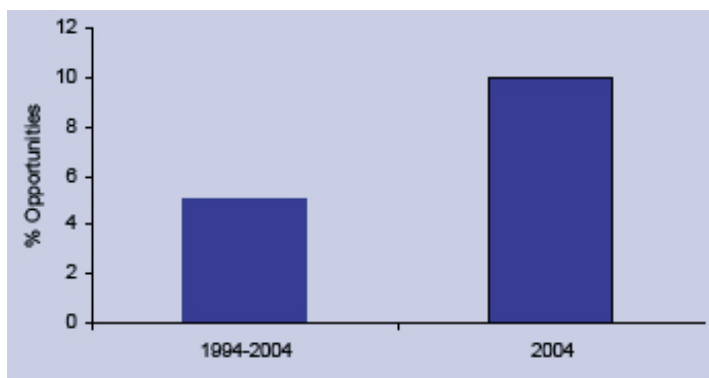


Figure 5 - Opportunities in anti-infective/antiviral fields.

Data adapted from Figure 8.3 in Facts and Trends in Deal Making - A Perspective on the Pharma and Biotech Industries, *PharmaVentures 2005*, 73.

Disease impact

Seasonal influenza epidemics affect between 5% and 15% of the population and are responsible for between 3 and 5 million cases of severe illness. In total, an estimated 250,000 to 500,000 deaths occur each year as a result of influenza infection. In an average year in the US, influenza causes more than 200,000 hospitalisations and is responsible for around 36,000 deaths, primarily in the over-65 population. Collectively, influenza and pneumonia are the 7th leading cause of death in the UK, killing more people than any other infectious disease.

Health care costs, lost days of work and education and general social disruption all contribute to the economic burden of influenza. The annual direct medical costs of influenza are estimated at US\$3 to US\$5 billion, with the figure rising to between US\$12 and US\$14 billion when indirect costs of a severe influenza epidemic, including lost work days, are also factored into the calculation.

Examining interventions

Over 50 countries have government-funded national influenza immunisation programs and vaccine is available commercially in many others. As a guide to the number of individual vaccinations carried out annually, in 2000 approximately 234 million of the world's 6 billion population received influenza vaccines.