

## ABOUT INFLUENZA

July 2009

Influenza, commonly called the flu, is a highly contagious infection of the respiratory tract that spreads from person-to-person through infectious respiratory secretion droplets caused by coughing or sneezing. Influenza outbreaks occur almost every year and their severity varies considerably. One unique aspect of influenza compared with other viruses, is its ability to continuously change over time, usually by mutation. This characteristic enables the virus to evade the immune system of its host, making people susceptible to the flu throughout their entire life. When infected with the virus, a person develops an antibody that works against that virus. Once the virus changes, however, the previous antibody is unable to recognize it, necessitating an entirely new antibody to fight off the virus. These modifications make it necessary for individuals to receive a different influenza vaccination each year, compared with one vaccination that would grant lifetime immunity.

### **Morbidity and Mortality**

Each year approximately 5-15% of the world's population contracts influenza and on average 3 to 5 million people suffer severe illness. An estimated 250,000 to 500,000 people die annually from influenza-related complications. Occasionally a major genetic shift in the influenza virus results in a deadly new virus strain to which the human population does not have immunity, and a global pandemic outbreak occurs. The Spanish influenza pandemic, the most severe outbreak of influenza to date, occurred from 1918 to 1920 and caused deaths worldwide ranging in estimation from 20 to 60 million. In 2004, a new highly pathogenic strain of avian influenza, H5N1, spread across Asia, infecting poultry and humans. Although the virus is incapable of sustained human-to-human transmission, the virus continues to mutate. According to the World Health Organization, as of March 5, 2008, 371 people had been infected with H5N1 virus across 14 countries, resulting in 235 deaths.

While the flu affects individuals of all ages, approximately 90% of flu-related deaths occur among individuals above the age of 65. People with chronic medical conditions and young children also have a higher risk of suffering influenza complications.

### **Geographical Distribution**

The influenza virus occurs worldwide. In temperate regions, influenza occurs during the winter months, affecting the northern hemisphere from November to March and the southern hemisphere from April to September. In tropical regions influenza may occur at any time of the year.

### **Transmission**

Influenza transmission occurs mostly by breathing in respiratory droplets that enter the air when an infected person coughs or sneezes. Transmission also occurs through direct contact with respiratory droplets or secretions, followed by touching the nose or mouth.

### **Symptoms**

Influenza leads to a variety of symptoms, ranging from mild to severe. Common symptoms include fever, headache, muscle ache, extreme fatigue, sore throat, cough and nasal congestion. While symptoms usually abate within one to two weeks, a common misconception about influenza is that the symptoms of stomach flu (vomiting, diarrhea, and nausea) are related to influenza. Stomach flu is commonly caused by bacteria or parasites and is rarely related to the influenza virus.

### Influenza antibodies H1N1 and H5N1

There is a growing fear within the medical community concerning the potential reoccurrence of a pandemic influenza outbreak, similar to the 1918 'Spanish flu' pandemic. A pandemic can start when a new influenza virus subtype emerges that meets three conditions: it infects humans causing serious illness; it spreads easily; and there is sustained human-to-human transmission of the virus.

Crucell has discovered the first human monoclonal antibodies for the prevention and treatment of the 'bird flu' strain H5N1, as well as H1N1, which is similar to the strain responsible for the devastating pandemic in 1918. The antibodies provide immediate protection and neutralize a broad range of H5N1 and H1N1 strains in pre-clinical models. In December 2008, Crucell presented data showing that the mAb CR6261 was 100% successful in preventing infection with H5N1. When given after H5N1 infection, Crucell's mAb demonstrated the ability to prevent death and cure disease in all cases. The mAb also performed significantly better than the anti-influenza drug oseltamivir for the prevention and treatment of H1N1 infection, illustrating the potential use for seasonal applications as well. This is especially important as the resistance of influenza strains for oseltamivir is rapidly increasing.

*Crucell's monoclonal antibodies against influenza strongly outperforms oseltamivir in preclinical tests.*

#### Resistance of influenza (H1N1) against oseltamivir is almost universal

- ① 98% United States
- ② 13-82% South America (6 countries)
- ③ 97% European Union
- ④ 45% Russian Federation
- ⑤ 93% Japan
- ⑥ 91% Philippines
- ⑦ 100% South Africa
- ⑧ 94% Australia
- ⑨ 31% Southern hemisphere (16 countries)



Source: WHO, January 2009.