

New drug to boost defence against bird flu pandemic

Mark Henderson, Science Editor November 25, 2006

A new flu drug that can kill deadly strains of bird flu is promising to transform global preparations for an influenza pandemic.

Peramivir, an antiviral agent, could provide the world with a critical new line of defence against flu viruses with the potential to cause millions of deaths, such as the H5N1 avian strain, research has suggested.

Studies in the United States show that it should be more powerful and easier to give to seriously ill patients than either Tamiflu or Relenza, the two existing drugs for H5N1 flu.

Flu experts said that the advent of a third effective option could save hundreds of thousands of lives if H5N1 acquires the ability to pass easily from person to person the key trigger for a pandemic. H5N1 has already infected 258 people and killed 153, mainly in South-East Asia, and it has recently mutated in ways that make human infections more probable.

"We need as many good antiviral drugs for flu as we can develop," said Frederick Hayden, a World Health Organisation medical officer who has studied peramivir. "Having multiple options with different antiviral spectra is very desirable."

Peramivir has two important advantages over the other therapies. Tamiflu, which is taken orally, and Relenza, which is inhaled, are difficult to administer to unconscious patients. Peramivir does not have this problem because it is injected, and the first human studies have shown that it also reaches the bloodstream in higher concentrations and remains active for longer.

The new drug would also provide a valuable alternative if a pandemic strain were to evolve resistance to Tamiflu, the front-line treatment that has been stockpiled by many countries, including Britain. Some H5N1 viruses have already shown resistance to Tamiflu, and if such a strain became dominant the drug would become useless. This week, a report from the Royal Society urged the Government not to rely on it exclusively.

Laboratory tests show that peramivir is effective against every known variant of H5N1, and its greater potency means that the virus is less likely to acquire resistance.

It is also simple to manufacture from synthetic raw materials that are readily available in bulk. Tamiflu production has been delayed by a shortage of star anise, the plant from which the active ingredient comes.

Peramivir was developed by BioCryst Pharmaceuticals, based in Alabama. It said that facilities already exist that could make a billion doses a year; Roche can make only 400 million doses of Tamiflu a year. BioCryst recently completed successful safety trials on human volunteers, which also proved that both intramuscular (IM) and intravenous (IV) injections deliver high levels of the drug to the bloodstream.

Phase 2 trials of the IM formulation will start testing peramivir's effectiveness in more than 100 patients with seasonal flu from next week, and a similar study of the IV injection is due to begin in January. If these are successful, larger phase 3 trials would take place during next winter's flu season, and the drug could be marketed within two to three years.

If a flu pandemic were to start before then, peramivir could be made available as an emergency measure, as it already has a good safety record.

Protection for the masses

What is H5N1 flu? It is a strain of the influenza virus that has killed millions of birds, mainly in Asia and Africa. So far, 258 people have been infected and 153 have died, according to World Health Organisation figures

Why is it a concern? The virus has a mortality rate of 59 per cent. The "Spanish flu" of 1918-19 killed 20 million to 50 million people

How likely is a pandemic? We don't know. The chances of H5N1 passing from person to person are small, but the virus has acquired two mutations that allow it to infect people more easily. Even if it does not trigger a pandemic, another flu virus that does is likely to emerge some time soon. Pandemics tend to be cyclical, roughly every 40 years. The last one occurred in 1968.

What can be done about it? There are two main options: vaccines and antiviral drugs. Vaccines, which use a dead or weakened virus to stimulate immunity, can be designed only once the precise pandemic strain is known. A vaccine would take seven to nine months to develop

What are the drugs? Tamiflu, or oseltamivir, is the front-line treatment. It does not stop people becoming infected, but reduces symptoms and the probability of transmission. It is made by Roche. The other drug is Relenza, or zanamivir, made by GlaxoSmithKline. It is inhaled rather than taken orally. An injectable version is being developed

How do they work? Both drugs block a key protein called neuraminidase the "N" of H5N1 which allows the virus to replicate and spread. The class is known as the neuraminidase inhibitors.