Searchers map the global spread of drug-resistant influenza

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In the new movie "Contagion," fictional health experts scramble to get ahead of a flu-like pandemic as a drug-resistant virus quickly spreads, killing millions of people within days after they contract the illness.

Although the film isn't based entirely on reality, it's not exactly science fiction, either.

"Certain strains of influenza are becoming resistant to common treatments," said Ira M. Longini, a professor of biostatistics in the University of Florida College of Public Health and Health Professions, the UF College of Medicine, and the UF Emerging Pathogens Institute. "We've been able to map out globally how this phenomenon is happening."

Longini is among a team of researchers who have published this month in the Royal Society journal *Interface* and explain how seasonal H1N1 influenza became resistant to oseltamivir, otherwise known as Tamiflu, the most widely used antiviral agent for treating and preventing flu. The scientists say that a combination of genetic mutations and human migration through air travel can lead to the rapid global spread of drug-resistant strains.

"If you see resistant strains in parts of the world where no one is taking antiviral drugs, that's the smoking gun that the resistant strain must be transmitting," said Longini, who also worked on this research at the Fred Hutchinson Cancer Research Center in Seattle.

In some situations, drug-resistant bacteria and viruses can spread when drugs are overused. The scientists explored this theory using a mathematical model that simulates the spread of influenza across 321 cities connected by air travel. Using this model, they found that oseltamivir use had not been nearly widespread enough to promote the spread of antiviral resistance after it arose. However, the resistant strain probably originated in one person taking the drug.

"Oseltamivir is an important prophylactic, or preventative agent, against future flu viruses, including a potential H5N1, or 'bird flu,' pandemic," said Dennis Chao, the lead author of the paper and a staff scientist at the Center for Statistics and Quantitative Infectious Diseases at the Fred Hutchinson Cancer Research Center.

However, influenza can mutate, making the drug less effective. It had been believed that this mutation would not spread because it makes the flu less transmissible in people not taking the drug.

"The fact that it spread so quickly in seasonal H1N1 between 2006 and 2008 took everyone by surprise," Chao said.

The researchers say that the mutation may have "hitchhiked" on one or more other mutations that made the drug-resistant influenza strain more transmissible. They suggest that because strains of influenza turn over so rapidly, there are many opportunities for these types of mutations to arise in an otherwise highly transmissible strain and become widespread, and it can become the dominant strain within a couple of years, making the drug useless.

"For the next pandemic, we should have all the available drugs at our disposal as a first line of defense to both prevent infection and to treat the most vulnerable," Longini said. "Or else, the chance that the next pandemic influenza strain is resistant goes up. We know something like

'Contagion' could happen for influenza."

Provided by University of Florida

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