Severe form of influenza can be treated more effectively

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With flu season now underway, a study by Ryerson researcher Catherine Beauchemin has found a more effective way to treat the most severe form of the virus.

Flu season is upon us and while getting the nasty bug is bad news, the good news is it's now possible to treat the severe form of the virus more effectively, according to a Ryerson University researcher. Though

Canada is not expecting a pandemic flu season this winter Health Canada reports that about 4,000 to 8,000 Canadians die each year from flu-related pneumonia.

Catherine Beauchemin is a professor in the Department of Physics and lead author of the study Neuraminidase inhibitors for treatment of human and avian strain influenza: A comparative modeling study. The study focuses on the treatment of severe influenza—not the kind that produces pesky symptoms such as cough, fever, chills, muscle ache and fatigue, but the kind that leads to acute respiratory illness and possible hospitalization and death.

Traditional flu treatment protocols recommend that neuraminidase inhibitors (NAIs) —drugs that prevent the virus from being released from the cell that produced it—be administered within two days of infection and continued for only five days. Beauchemin, however, found that for the severe form of the virus, treatment with Tamiflu (the most frequently prescribed NAI) can still be effective even when treatment is started as late as six to eight days after infection. The study also found that Tamiflu treatment should be continued beyond five days to prevent the infection from reactivating.

“For severe flu, such as bird flu, people keep getting worse after the two-day mark, and typically show up at the hospital six to eight days after they feel the first symptoms. If they are still very sick at that point this means the virus is still very much at work,” Beauchemin says. “We show that NAI treatment after the two-day mark in these cases is still a valid treatment option. That is, if you're still producing the flu virus, the treatment will still work.”

The study, which was co-authored by Ryerson postdoctoral fellow Hana Dobrovolny and others, is based on the results of a mathematical model the group created to simulate real flu infections in a patient. The model

was used to reproduce data from patients in Vietnam who became infected with bird flu. The model tracked how the flu interacted with two types of cells: those preferred by the virus and easy to infect, and those harder to infect. The latter included cells that are protected by the body's immune reaction to the virus as well as those cells located in the harder-to-reach lower respiratory tract. While these cells are more resistant to regular flu they can still get infected by more severe flu, such as bird flu. The study explored what happened to an infection when the researchers changed how hard it was to infect the second cell type, and how much virus it went on to produce.

The investigation revealed that in the case of severe infections Tamiflu can be beneficial to patients several days after the initial 48-hour infection window; as long as the drug is taken before the infection's peak, the medication will substantially shorten the infection's duration.

The study's mathematical model is the first of its kind to reproduce both an uncomplicated infection, and a long-lasting, serious virus similar to the bird flu or some of the severe types of swine flu. Now, instead of relying solely on clinical trials—which place limitations on drug-dosage experimentation to protect patients' health— the mathematical model provides flu researchers with another, more flexible, option for testing the effectiveness of various drug-treatment protocols.

"Severe influenza causes pandemics, so it's important that we create models for these worst-case scenarios and prepare strategies to deal with them," Beauchemin says. In the future, findings from Beauchemin's study may help reduce the flu virus' impact and improve our use of flu-fighting drugs.

More information: Scheduled to be published in the January 2011 edition of the *Journal of Theoretical Biology* (currently available ahead of print on the journal's website), Beauchemin's "Neuraminidase

inhibitors for treatment of human and avian strain influenza: A comparative study" and its sister study titled "Exploring cell tropism as a possible contributor to influenza infection severity" published in the November 2010 edition of *PLoS ONE*, were funded by the Natural Sciences and Engineering Research Council of Canada and by F. Hoffmann-La Roche, Ltd.

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