Submission to the Royal Society and Academy of Medical Sciences' call for evidence on Pandemic Influenza.

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I believe that an influenza pandemic will occur at some time in the future. These have occurred at irregular intervals in the past, and I know of no new information that says a flu pandemic won't happen again.

The current "bird flu" H5N1 virus, however, might not be the cause of the next pandemic. During the past 10 years this virus seems to have had every chance to acquire human transmissibility and the fact that it has not, may mean it will be unlikely to do so in the future. But, of course, it is impossible to predict what might eventuate.

Many of the measures Governments are proposing to control a pandemic, if one should suddenly erupt, are unlikely to succeed. Closing schools might create more problems than it solves, fever clinics seem to be a waste of time and thermal imaging devices at airports would not detect recently infected people who show no symptoms and have no fever but are shedding virus in large amounts. It is true that there is no evidence that such people are also good transmitters, but it would be safe to assume this is the case.

I believe that the British Government will install thermal imaging devices at airports, not because it is thought they will be effective at detecting flu-infected incoming passengers, but rather to alleviate public fears that the Government is not doing enough to keep the country safe.

My concerns are, however, restricted to two issues. Vaccines and anti-viral drugs..

VACCINES.

Many countries are preparing and testing H5N1 vaccines, with the realization that they may never be used. It is well recognized that the more the pandemic virus differs antigenically from the vaccine virus, the less effective the vaccine will be. And, of course, if the pandemic is caused by a virus of a different subtype, the vaccine will be no good at all. So far there has been no solution to this problem. Universal flu vaccines have been proposed, but none exists.

My concern is that many manufacturers are making a split H5N1 influenza virus or "subunit" vaccine, when they should be making a whole, inactivated virus vaccine. At low doses, the whole virus vaccine is very much better at inducing an antibody response than the split virus vaccine (1). At high doses, there is little difference between the two . The whole virus vaccine can cause some very nasty side reactions, worse in some people than in others, but it is unlikely that any H5N1 vaccine would be used for mass immunization before a pandemic. If an H5N1 pandemic did occur, and people started dying, some toxicity in the vaccine would be tolerated. The advantage of making a whole virus vaccine is, of course, that in an emergency the lower dose required means there would be much more vaccine to go around for everyone.

ANTI-VIRAL DRUGS

The neuraminidase inhibitors are the only drugs available to combat the deadly H5N1 virus, and of the six created, only Zanamivir (Relenza) and Oseltamivir (Tamiflu) have so far been approved for use.

Tamiflu is orally bioavailable and is swallowed, while Relenza is a powder that is puffed into the lungs. Thus, Tamiflu is a systemic drug and Relenza is restricted to the respiratory tract.

Although only a few human H5N1 infections have been treated with Tamiflu, some mutant viruses resistant to the drug have been found. These mutants were still sensitive to Relenza. So Tamiflu might not be the drug of choice in a “bird flu” pandemic. On the other hand, there is some evidence that the H5N1 virus might replicate in organs other than in the respiratory system. In this case, Relenza might be less effective than Tamiflu.

Governments around the world are stockpiling Tamiflu in huge amounts. The Australian Government has 3.9 million treatment courses. But the strategy to use this stockpile is wrong. If used correctly, there would already be enough Tamiflu in the stockpile for everyone in Australia who might need it in a pandemic situation.

The plan was to use the stockpile to give Tamiflu to “essential workers ” to be used prophylactically for a period of 6 weeks. This is, of course, a complete waste of a valuable drug. What happens, after 6 weeks when the stockpile is used up and the pandemic is still raging ? What about people in the community, not on the essential worker’s list who fall ill or whose children fall ill ? Knowing there is a drug out there that might save then, but is locked up so they can’t get it, will cause panic, civil unrest and feelings of anger against the Government. It is possible that this plan has now been changed so that early treatment of “ essential workers ”is proposed. How would early treatment be achieved ?

The best idea, it seems, would be to have Tamiflu available in every pharmacy in the country where people who needed it , essential workers and others not on the list, could get the drug quickly. To get Tamiflu in Australia, flu victims must first get a doctor’s prescription. Tamiflu is most effective when given very soon (6 to 12 hours) after the first symptoms are experienced (2) and the time taken to get a prescription renders Tamiflu ineffective. There is no reason to need a

prescription. If Tamiflu is taken inappropriately, for the common cold or an RSV infection for example, no harm will be done, the influenza virus will not develop resistance, but, of course, the drug will be wasted. To prevent this, a rapid, sensitive and accurate point-of-care diagnostic test for influenza should be available in the pharmacy.

So people who think they might have caught the flu, can go immediately to the pharmacy, be rapidly tested, and if positive be given Tamiflu, if negative be denied the drug. As a bonus, people who do have flu, take Tamiflu quickly and recover, should then be immune to re-infection with the same virus for the rest of the epidemic or pandemic (3). This simple procedure of "test and treat " should be adopted world-wide for both seasonal and pandemic influenza.

The Australian Government will not allow OTC sales of Tamiflu without a prescription, but give no reason. As a result many people are now getting prescriptions and creating their own personal stockpiles of Tamiflu. This also is wrong. It is wrong on two accounts. First, nothing might happen and their stockpiles will be wasted. Second, if it is used, it will be on the basis of self-diagnosis and this is not a good idea.

SUMMARY

Influenza H5N1 inactivated virus vaccines for use in a pandemic should contain whole virus particles, not split virus or virus subunits.

Tamiflu (and possibly Relenza) should be rapidly available to everyone who needs it OTC in pharmacies, without a doctor's prescription, but in conjunction with a rapid flu diagnostic test.

REFERENCES

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DECLARATION OF INTERESTS

I have no financial interests in Tamiflu, in Gilead Sciences who created Tamiflu, or in Hoffman La Roche, who market the drug.

I do, however, have strong personal interests in having Tamiflu available in the local pharmacy where I can get it quickly if I ever suddenly experience high fever, shivering attacks, muscular pains, headache and a dry cough. That is, when I have caught the flu and may be at risk of dying. And there are many thousands of others in a similar situation.