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Majority won't have access to antivirals in pandemic but generic drugs could help prevent deaths

Almost 90 per cent of the world's population will not have timely access to affordable supplies of vaccines and antiviral agents in the current influenza pandemic, but it is possible that inexpensive generic drugs that are readily available, even in developing countries, could save millions of lives.

That's the conclusion reached by an extensive review and analysis by immunisation expert Dr David Fedson, published online by *Influenza and Other Respiratory Viruses* within hours of the World Health Organization declaring a pandemic.

Dr Fedson points out that seasonal flu resistance to antiviral drugs like Tamiflu may make them ineffective in the pandemic and maintains that without effective drugs some countries will have to rely on 19th century public health measures to see them through the outbreak.

He is calling for urgent and sharply focused research to determine whether drugs that reduce inflammation or modify the host response - the way that the body responds to infection or injury - could be used to manage the pandemic. And he believes that a lot could be learnt from the work done on these commonly available generic drugs - which include drugs to lower cholesterol and treat diabetes - by scientists not involved in influenza research.

"Despite the best efforts of influenza scientists, pharmaceutical companies and health officials, the stark reality is that although studies of the molecular characteristics of influenza viruses have been enormously informative, they have failed to explain the system-wide effects that flu has on people who contract it.

"For example we still don't understand why so many young adults died in the 1918 pandemic, while the death rate for children was much lower. I believe this is because researchers have focused on studying the actual virus rather than how these particular hosts - the children and young people - responded to the virus.

"Most of the world's population lack realistic alternatives for confronting the next pandemic and urgent research is vital. Otherwise people everywhere might be faced with an unprecedented public health crisis."

Dr Fedson maintains that experiments by non-influenza scientists have defined common cell signalling pathways for acute lung injury caused by different agents, including the inactivated H5N1 influenza virus (bird flu).

"Research suggests that giving patients anti-inflammatory and immunomodulatory agents such as statins, fibrates and glitazones could help to regulate the cell signalling pathways in patients who have suffered acute lung injury, a common problem with influenza" he says. "They can also help to reverse the cellular dysfunction and cell damage that accompanies multi-organ failure.

"Cell signalling pathways play essential roles in the ability of cells to perceive and correctly respond to their microenvironment. They form the basis of development, tissue repair, immunity and normal tissue function.

"Statins are commonly used to lower cholesterol and prevent heart disease - but have also been shown to be effective in reducing hospitalisations and deaths from pneumonia. Fibrates modify fatty acid metabolism and glitazones reduce blood glucose levels in type 2 diabetes. All of these drugs modify the cell signalling pathways involved in acute lung injury and multi-organ failure. Moreover, they are affordable generic drugs that are widely available even in developing countries."

Dr Fedson points out that there is currently no logistical plan to distribute supplies of pandemic vaccines to the non-vaccine producing countries that contain 88 per cent of the world's population.

"In all likelihood, people in these countries won't be able to obtain supplies of pandemic vaccines or they will get them too late" he says.

"Many health officials have placed their hopes on stockpiles of antiviral agents, but resistance to the most widely stockpiled agent, Tamiflu, in seasonal flu outbreaks, has prompted concerns that similar resistance could develop in any pandemic virus.

"It's estimated that countries that do not produce influenza vaccines will only have enough antivirals to treat one per cent of their combined populations.

"At a scientific meeting in 2008 we heard that all of the people who developed bird flu in Indonesia, and did not receive antiviral treatment, died. This observation is terrifying. If this particular virus were to develop efficient human-to-human transmission we could see a global population collapse.

"Swine flu has only recently emerged so we have had less time to study its effects. But any influenza pandemic is cause for great concern regardless of what strain it is."

International influenza expert and journal editor Dr Alan Hampson says that it is essential that the focus on swine flu doesn't distract health professionals from the risk still posed by bird flu, which is continuing to rise, particularly in Egypt.

"Wouldn't it be a terrible irony if bird flu suddenly achieved the ability to transmit readily in humans, possibly aided by widespread infection of swine flu and that fact that most of our resources are focussing on that" he says.

Dr Hampson, who has worked extensively with the World Health Organization and is an influenza advisor to the Australian Government, says that the WHO recommended that all countries should develop pandemic preparedness plans.

"However, web-based evidence suggests that only 45 countries have produced plans so far and these tend to be the more developed countries, who may be less vulnerable" he says.

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Influenza and Other Respiratory Viruses is the first journal to specialise exclusively on influenza and other respiratory viruses. It is the official journal of the International Society for Influenza and Other Respiratory Virus Diseases (www.isirv.org), an independent scientific professional society promoting the prevention, detection, treatment, and control of influenza and other respiratory virus diseases.

The journal is providing all of its content free online at www.influenzajournal.com and fast-tracking the publication of articles to help clinicians stay up-to-date with the latest research and expert commentary.

Notes to editors

Paper: Confronting the next influenza pandemic with anti-inflammatory and immunomodulatory agents: why they are needed and how they might work. Fedson D. *Influenza and Other Respiratory Viruses*. 3.4, 129-142 (June 2009). Editorial: The 'novel' influenza A(H1N1) enigma: is it a pandemic, how should we respond, what should we call it. Hampson A. *Influenza and Other Respiratory Viruses* 3.4, 119-120. (June 2009). Fast-tracked papers will appear in the online early section of the website (www.influenzajournal.com) ahead of publication of the full issue.

Dr David Fedson is the author of more than 160 scientific articles, chapters and reports on his specialist field of adult immunization and the recipient of a prestigious American award for this work in this field. He is the founder and co-ordinator of the Macroepidemiology of Influenza Study Group and has been active in exploring the possibility of using anti-inflammatory and immunomodulatory agents for the treatment and prophylaxis of pandemic influenza.

Dr Alan Hampson is a virologist with over 40 years' experience working in basic research on influenza, vaccine development, WHO surveillance programmes and public health. He is a consultant, advisor to government, chair of an advocacy group for best practice prevention and treatment of influenza and editor-in-chief of *Influenza and Other Respiratory Viruses*.

Influenza and Other Respiratory Viruses is the first journal to specialise exclusively on influenza and other respiratory viruses and strives to play a key role in the dissemination of information in this broad and challenging field. It is aimed at laboratory and clinical scientists, public health professionals, and others around the world involved in a broad range of activities in this field. Topics covered include: surveillance, epidemiology, prevention by vaccines, prevention and treatment by antivirals, clinical studies, public health and pandemic preparedness, basic scientific research and transmission between animals and humans. www.influenzajournal.com

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