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Pregnancy and H1N1 infection

Denise Jamieson and colleagues (Aug 8, p 451) highlight the risk of infection with pandemic influenza A virus (H1N1) in pregnant women, documenting high rates of hospital admission and complications. Notably, six deaths in H1N1-infected pregnant women were reported between April 15 and June 16, 2009, in the USA.

These observations suggest that antivirals ought to be used to prevent and treat H1N1 infection in high-risk pregnant women. Indeed, the US Centers for Disease Control and Prevention recommend chemoprophylaxis with either oseltamivir or zanamivir against H1N1 influenza for people at risk of complications, including pregnant women. However, a survey has shown that oseltamivir has important side-effects (including gastrointestinal and neuropsychiatric symptoms) in more than half of treated children, raising serious questions about the wide use of this compound, not only in children, but also in pregnancy.

This side-effect profile, together with the detection of oseltamivir-resistant strains, suggests that novel safe compounds are necessary for the treatment of H1N1 infection in pregnancy. Two human anti-influenza A H5N1 monoclonal antibodies (hMAbs) have been cloned, and their H5N1-neutralising potential has been assessed against highly pathogenic avian strains, indicating that powerful and safe treatment of influenza H5N1 infections with hMAbs is possible. From this point of view, a strategy for the treatment and prevention of H1N1 infection in pregnancy based on neutralising human monoclonal antibodies should be planned in the future, being also aware of the efficient protection of the fetus by circulating IgGs.

We declare that we have no conflicts of interest.

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Denise Jamieson and colleagues highlight high morbidity and mortality rates in pregnant women infected with the H1N1 influenza virus. Admission rates were 41% and the median time from symptom onset to receipt of antiviral therapy was 9 days. Could earlier initiation of antiviral therapy have resulted in a better outcome?

In 2003, Singapore was notably infected with the H1N1 influenza virus. Admission rates were 41% and the median time from symptom onset to initiation of antiviral treatment was a median of 2 days. Three women were admitted for observation, and one developed pneumonia; initiation of treatment was 4 days after symptom onset in this woman. No deaths have been reported nationwide in pregnant women thus far.

Our experience suggests that timely medical attention with early recourse to antiviral therapy is associated with a better outcome in H1N1-affected pregnant women.

We declare that we have no conflicts of interest.

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Authors’ reply

We agree with Roberto Burioni and colleagues that novel treatment approaches for influenza virus infection such as use of anti-influenza monoclonal antibodies might hold promise and are certainly worth pursuing. However, most investigations have used animals, and treatment in human beings has mainly focused on the most severe cases. Treatment with anti-influenza virus antibodies has not yet been shown safe and effective for use in non-pregnant people. It will probably be even longer before such treatment options would be considered for pregnant women since additional Submissions should be made via our electronic submission system at http://ees.elsevier.com/thelancet/.
safety studies would need to be done, and pregnant women and their health-care providers might be reluctant to use new treatments, even if proven safe and effective.

Therefore, it is important to promote a strategy of vaccination and basic hygienic prevention, and prompt antiviral treatment of pregnant women who develop influenza illness. Frequent hand washing, covering mouth and nose when coughing or sneezing, staying home and away from others when sick, and avoiding contact with people sick with influenza-like illness are basic steps that can help decrease the likelihood of influenza and other respiratory illnesses. Owing to the increased risk of severe disease and death, once influenza is suspected in a pregnant woman, appropriate antiviral therapy should be started promptly, ideally within 48 h when the benefit is expected to be the greatest. Although there are known side-effects of antiviral therapy, as pointed out by Burioni and colleagues, the benefits of antiviral therapy outweigh potential risks for pregnant women.

We were pleased to learn of the experience in Singapore as reported by Lin Lin Su and colleagues. Singapore should be applauded for its remarkable achievement in providing antivirals to 28 pregnant women promptly, with a median of 2 days from symptom onset to receipt of antiviral drugs. We agree that experience with managing pregnant women during the outbreak of severe acute respiratory syndrome probably helped prepare them and others for this current influenza pandemic and that there is much for us to learn from the experiences and successes of others.

Finally, the very promising news about the 2009 pandemic influenza A (H1N1) monovalent vaccine highlights the potential role that vaccination efforts can have in preventing morbidity and mortality. It is essential that all pregnant women are encouraged to be vaccinated, as reflected in current US guidance that places pregnant women in a high-priority group for vaccination with 2009 H1N1 vaccine.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. We declare that we have no conflicts of interest.

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Artemisinin resistance on the Thai–Cambodian border

Your Special Report (July 25, p 277)1 provides a timely and balanced account of ongoing efforts to contain the spread of artemisinin-resistant falciparum malaria on the Thai–Cambodian border. One of the most urgent and challenging priorities is to replace the use of artemisinin monotherapy in Cambodia with a fixed-dose combina-

tion such as artemunate–mefloquine or dihydroartemisinin–piperaquine. Dihydroartemisinin–piperaquine is safe and effective in Cambodia 2 and elsewhere.3 However, there is still no quality-approved product on WHO’s list of prequalified drugs, making it almost impossible to procure with donor funds.

The continued availability of artemisinins as separate tablets threatens the entire class of combination drugs. Why does this happen? Partly because of skewed incentives in the pharmaceutical industry, and partly through bureaucracy. Many manufacturers of new combination therapies are small-scale industries and lack the resources to clear the final hurdles of stringent international drug regulatory requirements. And why should they, when they can market their products in the thriving and often poorly regulated private sector in malaria-endemic countries? They will need extra incentives if they are to meet the necessarily exacting quality, safety, and efficacy standards required for WHO approval.

We need to be able to fast-track drugs that are of major global health significance by creating incentives to invest in fast approval and large-scale generic production. Lessons can be learned from the vaccine field, where the pilot advanced market commitment has encouraged drug companies to invest in pneumococcal vaccines suitable for developing countries.

Where public health emergencies such as artemisinin resistance loom, we cannot allow our most useful tools to get stuck in the pipeline.

We declare that we have no conflicts of interest.

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