H5N1 Avian Influenza Virus Can Cross Placenta

BY JONATHAN GARDNER
London Bureau

In humans, the highly pathogenic H5N1 avian influenza virus can spread beyond the lungs and also can cross the placenta to the fetus, according to research published in the Lancet.

Chinese researchers examined the postmortem tissues of two adults, a 35-year-old man from Jiangxi province and a 24-year-old woman from Anhui province who was 4 months pregnant. Both individuals were confirmed as infected with H5N1 by the Chinese Centre for Disease Control and Prevention (Lancet 2007;370:1137-45).

Examination of tissues from the respiratory, digestive, and central nervous systems, and from other organs found viral genetic material and antigens to the virus. In the respiratory system, the researchers found signs that H5N1 had affected, among other tissues, the alveoli, in contrast to human influenza, which mainly targets the upper respiratory tract.

In the pregnant woman, the researchers found infected cells in the placenta and, in the fetus, they found viral sequences in the lungs, circulating mononuclear cells, and the liver.

The woman had been admitted after 6 days of fever, cough, and shortness of breath. She had handled ill birds 2 weeks before admission and died 2.5 days after, despite treatment with antibiotics and corticosteroids. No antivirals were given, the investigators noted. The man died 27 days after developing fever and productive cough. Admitted to hospital with a 6-day history of symptoms, he was first administered corticosteroids, followed by an antiviral, and then antifungal treatments.

The researchers said their findings help shed light on how H5N1 infections progress, which will be important for public-health officials to watch because that strain of virus is feared as the most likely to result in a pandemic.

"Little is known about the specific effects in organs and cells targeted by the virus," wrote the researchers, led by Dr. Jiang Gu of Peking University in Beijing. "The infection initially seemed to be restricted to the lungs, but later reports have suggested that influenza A H5N1 could disseminate beyond the lungs. ... These newly obtained data are important in the clinical, pathological, and epidemiological investigation of human H5N1 infection and have implications for public health and health care providers."

In all, the researchers found viral genetic material and antigens in epithelial cells of the lungs and trachea, T cells of the lymph nodes, neurons of the brain, and Hofbauer cells and cytotrophoblasts of the placenta. They found viral genomic sequences but no antigens in the intestinal mucosa.

The route of infection for the central nervous system could be through the blood-brain barrier or through respiratory system nerves after replicating in tissues there, the researchers write. For the intestines, the virus could be bloodborne but could occur through the ingestion of respiratory secretions, they added.

How the vertical infection of the fetus would affect the fetus is unclear. Human influenza strains infecting a pregnant female have not been shown to affect the fetus, but since H5N1 also has effects on humans not seen from human strains, such as viremia, “the likelihood of virus reaching the uterus and placenta is probably higher in avian influenza than in human influenza,” they wrote.

In an accompanying commentary, Dr. Wai Fu Ng of Princess Margaret Hospital in Hong Kong and Prof. Ka Fai To of Chinese University of Hong Kong raise questions about the effects of the vertical infection route.

“The absence of pathological changes in the immunologically incompetent fetus is taken as evidence that viral replication itself is not pathogenic,” they wrote. "Speculation about the fate of the fetus if the mother survived the infection is interesting. With the development of antibodies in the mother and their transplacental crossing into the fetus, pathological lesions in the fetus may result.”