AVIAN INFLUENZA — WHY ALL THE HYPE?

We are now 6+ months into discussions about avian “bird” flu that began last fall with interest in the White House that has permeated all levels of government and medicine. What we know thus far is that since 2003 the current avian influenza virus H5N1 has infected >170 persons of whom over 50% have died. The virus has been identified in birds in 13 countries in Asia, Europe, the Middle East and Africa (Figure 1). It has likely spread through the long distance travel of migratory birds. This is still very much an avian virus which has only affected persons with close contact with infected birds and poultry. It is not well adapted to people and in only a couple cases has it spread from an ill person exposed to ill poultry to another person not exposed to poultry.

For influenza to spread worldwide and cause increases in

AN EMERGING STRAIN OF CLOSTRIDIUM DIFFICILE TIME TO PAY ATTENTION

An emerging strain of Clostridium difficile (a spore-forming, gram-positive bacillus that produces exotoxins A and B) has been associated with outbreaks of severe disease in North America and Europe. This variant strain is resistant to fluoroquinolones and is reported to produce toxin levels 16 – 23 times higher than other strains. As of November 15, 2005, sixteen states, predominately in the Eastern United States, have reported outbreaks associated with this new strain of C. difficile. The strain has not yet been identified in Tennessee; however many States surrounding Tennessee have identified this strain.

Most individuals exposed to C. difficile develop asymptomatic colonization and develop protective antibodies against the toxins. It is the toxins produced by C. difficile, and not the organism itself that causes the clinical symptoms. Symptoms may include watery diarrhea, cramping, fever, abdominal pain/tenderness and nausea. CDAD can result in diarrhea, pseudomembranous colitis, toxic megacolon, colonic perforation and death.

Important control measures include judicious antimicrobial use (in particular decreasing use of quinolones), a higher index of suspicion for CDAD, and infection control. Use contact isolation precautions (gown and gloves), and place the patient in a single room, preferably with dedicated bathroom. Use dedicated patient equipment. Avoid use of rectal thermometers; if used, ensure proper cleaning between patients. Ensure that bed-pan flushers are working properly. Strict adherence to hand washing with soap and water is critical. Alcohol does not kill spores; therefore, soap and water scrubs are preferred over alcohol-based hand gels. Frequent, thorough environmental cleaning with a hypochlorite (bleach)-based solution is extremely important.

For influenza to spread worldwide and cause increases in

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AVIAN INFLUENZA — WHY ALL THE HYPE? (CONTINUED)

(Continued from page 1)

mortality and morbidity such as that seen in a pandemic, the virus must be a new strain, not previously seen in the human population, and it must mutate to allow easy transmission from person to person. This is what happened in previous pandemics in 1918, 1957, and 1968. The severity of pandemics varies substantially based on the ease of transmission and the virulence of the pandemic strain (Table 1). The historical experience with pandemics in the last century has been helpful in spelling out expectations for the next pandemic. Because the population has no preexisting immunity to a pandemic strain it is expected that up to 35% of the U.S. population could become infected. Mortality rates in the past have varied between 0.2% and 2%. As with annual influenza epidemics, infection can be spread up to 24 hours before symptoms develop. On average each ill person will infect two to three others. Typically pandemics occur in 2-3 waves of 6-8 weeks each over a 1 to 2 year period. After immunity develops in the community the pandemic stops and the new strain can become a routine annual strain and months after that to produce enough for the entire U.S. population. Likewise, antiviral agents such as oseltamivir are in short supply and will be available only for the sickest patients and not for prophylaxis. Relying on either vaccine or antivirals is not wise until such time as vaccine manufacturing is streamlined with increased capacity and more antivirals are manufactured.

If you would like more information about pandemic influenza to http://www.pandemicflu.gov or http://www2.state.tn.us/health/CEDS/panmdemic.htm.

<table>
<thead>
<tr>
<th>Year</th>
<th>U.S. deaths</th>
<th>Global deaths</th>
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<tbody>
<tr>
<td>1918</td>
<td>500,000-675,000</td>
<td>20-50 million</td>
</tr>
<tr>
<td>1957</td>
<td>70,000</td>
<td>1-4 million</td>
</tr>
<tr>
<td>1968</td>
<td>34,000</td>
<td>1-4 million</td>
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Table 2. Pandemics of the 20th Century: Estimated U.S. and Global Mortality

PANDEMIC PLANNING IN TENNESSEE

On December 12, 2005 Dr. Kenneth Robinson, Commissioner of Health, convened the first meeting of a newly formed Pandemic Influenza Coordinating Committee to discuss newly updated federal guideline for pandemic planning. This diverse group of leaders in health care, law enforcement, business, homeland security and government sectors will be utilized to provide valuable input into the state pandemic influenza plan which is currently being drafted. Since the initial meeting many small work groups have met to discuss varying aspects of the plan. Some of the major challenges facing the planners are 1) providing adequate surge capacity for what may be a 25% increase in hospital admissions, 2) prioritizing the use of a limited vaccine supply that will likely be delivered over many weeks as it is produced, 3) preparing schools and businesses for a major outbreak and potential disruption in staffing, and 4) prioritizing use of scarce antivirals for treat of severe influenza cases.

It is anticipated that a draft plan will be sent to the committee for review in late March and that a final plan will be available later in the spring. On April 10th a pandemic influenza summit is planned to highlight the threat and response to a pandemic with participation by senior state and federal officials.

CLOSTRIDIUM DIFFICILE TIME TO PAY ATTENTION (CONTINUED)

(Continued from page 1)

Not all disinfectants are effective against spore-forming bacteria; use of an EPA-registered hypochlorite-based disinfectant for environmental surface disinfection after cleaning is advised.

The Tennessee Department of Health is requesting that healthcare providers contact their health department if they see patients who have (1) community associated C. difficile associated disease [CDAD] (no contact with acute or longterm healthcare facilities and no antibiotic exposure in preceding 3 months) or (2) severe CDAD. Severe CDAD is defined as any case of symptomatic CDAD that results in (a) megacolon, (b) admission to intensive care [ICU] (or is the cause of continued stay in the ICU), or (c) in death or requires (d) colectomy. You can obtain case report forms from your local health department.

Most laboratories look for evidence of Toxin A and/or Toxin B in the stool to confirm the diagnosis of CDAD. Until recently, most laboratories have not been performing cultures of C. difficile. However, to further characterize the strain of C. difficile it is important to have culture isolates. A protocol on culture methods for C. difficile has been sent to infection control professionals and microbiology laboratory staff in Tennessee. If you have a case of severe...
**Clostridium difficile** Time to Pay Attention (continued)

(Continued from page 2)

CDAD or community-associated CDAD, and your laboratory does NOT perform cultures of *C. difficile*, the TDH State laboratory is willing to perform these cultures. Please ensure that the laboratory request form specifically states: “*C. difficile* culture”, fill out the case report form and fax to your local health department.

As of March 2, 2006, the TDH has received 15 reports of and 11 completed case-report forms on patients fitting the case-definition of severe disease. In only two cases was an isolate obtained; the main reason given was that the original specimen was discarded before the laboratory was notified that the patient had “severe” CDAD. In all but one of these cases, the patient died from *C. difficile*, and it was impossible to obtain a specimen. To prevent this from occurring in the future we urge laboratories to not discard *C. difficile* toxin positive stools for 14 days. If the patient develops severe CDAD in that time-frame, the specimen will then still be available. The stool specimen may be frozen, kept in the refrigerator or mixed with alcohol (1 ml stool, 1 ml 95% ethanol).

**Letter: Revised Immunization Recommendations Regarding Hepatitis B Virus (January 18, 2006)**

Dear Colleague:

We would like to bring to your attention revised immunization recommendations from the Advisory Committee on Immunization Practices (ACIP) to ensure that newborn infants are protected from hepatitis B virus (HBV) infection, a major cause of cirrhosis and liver cancer in the United States. The ACIP now recommends that, except on a case-by-case basis and only in rare circumstances, universal infant hepatitis B vaccination should begin at birth. Previously, the ACIP noted a preference for giving the first dose at birth, but also recommended that infants born to uninfected mothers could receive the first dose at age 1-2 months. To prevent HBV transmission among children at greatest risk for HBV infection, the ACIP also recommends that prenatal care providers, delivery hospitals, and health departments implement policies and procedures to identify and manage children born to infected mothers and mothers with unknown HBV infection status. The ACIP statement, including all of the revised recommendations, is available from CDC in the Morbidity and Mortality Weekly Report (http://www.cdc.gov/mmwr/PDF/rr/rr5416.pdf). A synopsis of the updated recommendations is provided below.

**Recommendations for Prenatal Care Providers**

Management of all pregnant women:
- Test all pregnant women for hepatitis B surface antigen (HBsAg) during each pregnancy.
- Transfer a copy of the original laboratory report of the pregnant woman’s HBsAg test result to the patient’s medical record in the delivery hospital.
- Inform pregnant women of the importance of newborn hepatitis B vaccination.
- Vaccinate pregnant women who are at risk for HBV infection.

Management of pregnant women with chronic HBV infection:
- Inform HBsAg-positive women of HBV transmission risks and ways to prevent HBV infection, including the importance of postexposure prophylaxis for newborn infants and hepatitis B vaccination of household, sexual, and needle-sharing contacts.
- Refer HBsAg-positive women to an appropriate case-management program to ensure that their newborn infants receive timely postexposure prophylaxis and follow-up.
- Provide or refer HBsAg-positive women for appropriate medical management of their chronic HBV infection.

**Recommendations for Delivery Hospitals**

- Implement standing orders to ensure that, except in rare circumstances (see statement for additional details), all newborns with birth weights of >2 kilograms receive hepatitis B vaccine before discharge.
- Implement policies and procedures to ensure that all infants born to HBsAg-positive mothers and all infants born to mothers with unknown HBsAg status are identified and receive appropriate immunoprophylaxis. These policies and procedures should include the following standing orders:
  - Review HBsAg test results for all pregnant women at the time of admission for labor and delivery.
  - Conduct HBsAg testing as soon as possible after admission for pregnant women who do not have a documented HBsAg result and for pregnant women identified as being at risk for HBV infection during pregnancy (e.g., >1 sex partner in the previous 6 months, evaluation or treatment for a sexually transmitted disease, recent or current injection-drug use, HBsAg-positive sex partner).
  - Administer hepatitis B vaccine and hepatitis B immune globulin within 12 hours of birth to all infants born to HBsAg-positive mothers.
  - Administer hepatitis B vaccine within 12 hours of birth to all infants born to mothers with unknown HBsAg status.
  - Document on the infant’s medical record the maternal HBsAg test results and the infant’s hepatitis B immunization.

**Recommendations for Health Departments**

- Provide or assure case-management services to ensure that 1) all pregnant women are tested for HBsAg during each pregnancy, and 2) infants born to HBsAg-positive women and infants born to women with unknown HBsAg status receive recommended immunoprophylaxis.

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Before hepatitis B vaccination became routine in the United States, transmission of HBV infection perinatally and during early childhood caused an estimated 30%-40% of chronic HBV infections. Approximately 25% of chronically infected children die prematurely from cirrhosis or liver cancer. The majority of chronically infected persons remain asymptomatic until the onset of cirrhosis or end-stage liver disease.

These recommendations update the ACIP strategy to eliminate HBV transmission in the United States. This strategy has been implemented with considerable success and has resulted in a substantial decline in hepatitis B incidence in the United States. However, challenges remain to eliminate perinatal and childhood HBV transmission. In particular, CDC estimates that only about half of expected births to HBsAg-positive mothers are identified for case management, which is needed to maximize on-time delivery of postexposure immunoprophylaxis. In addition, errors in management of infants born to HBsAg-positive mothers and infants born to mothers with unknown HBsAg status have kept many of these infants from receiving appropriate immunoprophylaxis to prevent HBV infection.

On February 2, 2006, from 12:00 pm to 1:00 pm Eastern Standard Time, CDC will host an Internet conference to discuss the new ACIP recommendations. This conference is intended for physicians, nurses, administrators, and other medical professionals, particularly hospital obstetrical and neonatal staff, prenatal care providers, professional organizations involved in perinatal care, and public health staff. The one-hour program will combine a telephone audio conference with online visual content. The session will allow for a question-and-answer segment by telephone and via the Internet. Internet access and a separate phone line are needed to participate. Please visit the following website before January 31, 2006, to register: http://www.cdc.gov/nip/ed/ciinc/hepatitisb.htm. If you cannot view this conference on February 2, you will be able to visit the following website for replay and viewing of the slides: http://www.cdc.gov/nip/ed/ciinc/#archive.

Additional resources may be found at the following website: http://www.cdc.gov/ncidod/diseases/hepatitis/b/acip.htm. Thank you in advance for your efforts to eliminate HBV transmission in the United States.

Sincerely,

John Ward, MD, Director
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