Medical News

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Droplet Spread of Ebola Virus

Secondary transmission of Ebola virus infection in humans is known to be caused by direct contact with infected patients or body fluids. Dr. N. Jaax and colleagues from the United States Army Medical Research Institute of Infectious Disease in Frederick, Maryland, recently reported the transmission of Ebola virus (Zaire strain) to two of three control rhesus monkeys (Macaca mulatta) that did not have direct contact with experimentally inoculated monkeys held in the same room. The two control monkeys died from Ebola virus infections at 10 and 11 days after the last experimentally inoculated monkey had died.

The monkeys were housed in cages in the biocontainment laboratory, and strict procedures were followed to prevent unintended transmission of the virus from the experimentally inoculated animals to the control animals, eg, all medical procedures and cage cleaning procedures were performed first on the control animals.

Virologic and histopathologic examinations of lung tissue found virus titers and lesion patterns consistent with those previously reported in monkeys exposed to aerosolized Ebola virus. The researchers believe that the most likely route of infection of the control monkeys was aerosol, oral, or conjunctival exposure to virus-laden droplets secreted or excreted from the experimentally inoculated monkeys. They advise at-risk personnel to use precautions to protect against ocular, oral, and nasopharyngeal exposure to the virus. The CDC incorporated recommendations for eye and mucous membrane protection in its updated guidelines for the management of viral hemorrhagic fever patients.

FROM: Jaax N, Jahrling P, Geisbert T, et al. Transmission of Ebola virus (Zaire strain) to uninfected control monkeys in a biocontainment laboratory. *Lancet* 1995;346:1669-1671.

Inactivated Polio Vaccine Recommended

The US Immunization Practices Advisory Committee (ACIP) recently voted to change the basic infant immunization series and supplement the long-standard oral polio vaccine. The new series would begin with two doses of enhanced-potency inactivated vaccine, given at ages 2 and 4 months, followed by two doses of oral live-attenuated polio vaccine, given at 6 months and 12 to 18 months of age.

The transmission of natural polio virus from person to person has been eradicated in the Western Hemisphere since 1991. But eight to 10 cases of polio are diagnosed in the United States each year as a result of the live-attenuated oral vaccine itself. One half of the cases occur in children who received the vaccine and the rest in people having close contact with vaccine recipients. No cases have been associated with the inactivated vaccine.

Experts agree that the new sequential schedule, with use of inactivated vaccine followed by oral vaccine, probably would reduce the cases of vaccine-associated polio. The inactivated vaccine is unlikely to cause paralytic polio, and giving that vaccine ahead of the oral polio vaccine probably would provide a level of immunity sufficient to examine the risk of contracting polio from the oral vaccine.

ACIP announced that this was only an intermediate step toward entirely replacing the oral vaccine with the inactivated vaccine. One rationale for this approach is that the oral vaccine is considered the most effective against wild polio, which, although eradicated in the United States, continues elsewhere in the world, particularly in India, and could be brought in by visitors. It is expected that this transition will take approximately 1 year.

FROM: Discussion at the US Public Health Service Advisory Committee on Immunization Practices, October 18-19, 1996; and US Panel calls for change in mix of polio immunization. *New York Times* October 19, 1996, p A8.

Hepatitis A Linked to Clotting Factor Concentrates

Three cases of hepatitis A occurring between September and November 1995 in recipients of factor VIII concentrates recently were reported by the CDC. The lot factor of VIII concentrate implicated in these cases (Alphanate TM, lot number AP5014A Alpha Therapeutic Corp, Los Angeles, CA) was removed from the market voluntarily by the manufacturer on December 8, 1995. In addition, one case of hepatitis A in a recipient of factor IX concentrate (AlphaNine S-D TM, also from Alpha Therapeutic Corp) is under investigation. On January 11, 1996, the manufacturer voluntarily withheld four lots (CA5410A CA5412A, CA5413A, and CA5421A) of this product.

Hepatitis A outbreaks associated with receipt of clotting factor concentrates have been reported previously in Europe but not in the United States. This is the first time hepatitis A virus (HAV) transmission has been documented through clotting factor concentrates in the United States. Most cases of hepatitis A in the United States occur in communitywide outbreaks through person-to-person transmission by the fecal-oral route. However, because viremia occurs during the prodromal phase of the illness, asymptomatic blood donors have been the source of HAV infection transmitted by transfusion.

In Europe, investigations of hepatitis A outbreaks among recipients of factor VIII concentrates implicated products prepared by a manufacturing method that included a solvent detergent (S-D) viral inactivation step. The largest outbreak occurred in Italy, involving 52 patients

with hemophilia. The factor concentrates used by the case patients in the US outbreak also were prepared using the S-D method of viral inactivation. Although this method inactivates enveloped viruses such as hepatitis B virus, hepatitis C virus, and HIV, nonenveloped viruses such as HAV and parvovirus B19 are resistant to inactivation by this method. Clotting factor concentrates manufactured by recombinant technology, which now are available, have not been shown to transmit infectious agents.

Officials of both the US Food and Drug Administration and the National Hemophilia Foundation renewed suggestions that hemophiliacs be tested for hepatitis A and that those who are susceptible be vaccinated. The CDC recommends that practitioners should consider vaccinating susceptible patients that receive clotting factor with the inactivated hepatitis A vaccine (HAVRIX R, SmithKline Beecham, Inc, Pittsburgh, PA) licensed in 1995. Additional information about this investigation of hepatitis A related to factor VIII or factor IX is available from the CDC's Hematologic Diseases Branch, and information about hepatitis A vaccine is available from CDC's Hepatitis Branch, Division of Viral and Rickettsial Diseases, NCI, telephone (404) 639-3048.

FROM: Centers for Disease Control and Prevention. Hepatitis A among persons with hemophilia who received clotting factor concentrate—United States, September-December 1995. *MMWR* 1996;45(2):29-32; and Altman L. Hepatitis virus passed to hemophiliacs by clotting therapy. *New York Times* January 19, 1996.

Staphylococcus aureus Genome Mapped

Scientists at Human Genome Science, Inc, in Rockville, Maryland, recently reported the identification of a chemical sequence of 99% of the genome of *Staphylococcus aureus.* The company believes that knowledge of the full genetic sequence will assist with the development of vaccines.

One conventional method of making bacterial vaccines is to use killed bacteria to stimulate the body's immune system. The immune system then attacks major proteins on the bacterium's coat. However, these proteins often change to evade the immune attack. With the bacterium's full genome, scientists can seek out rare coat proteins that the bacterium cannot modify. This method already has been used to identify vaccine candidate proteins from *Haemophilus influenzae,* which was sequenced a year ago by Dr. Craig Venter and colleagues from the Institute for Genome Science, Gaithersburg, Maryland.

Dr. William Haseltine, Human Genome Science's chief executive, said the company would not release specific information about the sequence of the genome until it was patented. The sequence contains 2.8 million chemical units, coding for some 3,000 genes. Dr. Haseltine said it probably would be approximately 18 months before a patent was issued and the results of the study published.

Researchers also are developing a vaccine for toxic shock syndrome. Dr. Philippa Marrack and colleagues of the National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado, in collaboration with scientists at NeXtar Pharmaceuticals Inc, Boulder, Colorado, have prepared and tested a vaccine against the staphylococcal toxin that causes toxic shock syndrome. The researchers say that development costs for this vaccine could hit $50 million before the drug is on the market. As a result, it may never become available to the public because of the cost.

FROM: Wade N. Company reports unlocking gene code of harmful germ. *New York Times* January 19, 1996, p A12.

Guidelines for Xenotransplants

An increasingly critical shortage of human donors has limited the availability and benefit of organ and tissue transplantation. This chronic shortage, combined with recent scientific and biotechnical advances, has resulted in new therapeutic approaches directed at using animal tissue in humans. Concerns have been raised about the use of xenogeneic tissues and organs for transplantation or perfusion, and the potential of both recognized zoonotic pathogens and unknown xenogeneic agents to infect individual human recipients and then spread within the human population.

Public health guidelines intended to minimize the risk for transmission of known pathogens through human-to-human transplantation do exist. Similar guidelines addressing the issue of infectious agents that may be associated with xenotransplantation are being developed by Public Health Service working groups at the CDC, FDA, and NIH. A provisional draft of these guidelines will be published in the *Federal Register* for public comment. Publication of a final version of these guidelines in *MMWR* is planned for spring 1996.

In a commentary in a recent issue of *Nature Medicine,* Jonathan Allen, a member of the FDA panel that considered the guidelines, voiced his concerns about the risk of infectious diseases related to baboon transplants. Allan notes that baboons carry viruses that can infect humans and argues that the animals should not be used as donors for humans. Allan argued that pigs should be the only outside species used for human transplants and that federal regulations should be strict, including licensing and inspections.

FROM: Chapman LE. Guidelines on the risk for transmission of infectious agents during xenotransplants. *Emerging Infectious Diseases* 1995;1(4):156; and Allan J. Commentary: xenotransplantation at a crossroads: prevention versus progress *Nature Medicine* 1996;2(1):18.

Block Grants May Weaken State Public Health Programs

The Clinton Administration is seeking to consolidate several categorical programs into Performance Partnership Grants (PPGs). Three new PPGs would be created for CDC: for immunization; HIV/AIDS, STD, and TB; and