

INFORMATION PAPER

Military Vaccine Agency
1 March 2007

SUBJECT: Adenovirus Infections and Adenovirus Vaccines

1. Purpose: To describe adenoviral disease and the vaccines to prevent it.

2. Facts.

a. Microbiology. Adenoviruses are a group of 49 distinct virus types that infect the linings of the respiratory tract, the eyes, the intestines, and the urinary tract. Adenoviruses account for about 10% of acute respiratory infections in children and are a frequent cause of diarrhea. In adults, adenoviruses can cause an acute respiratory disease. These viruses are unusually resistant to chemical or physical agents and pH conditions, allowing prolonged survival outside of the body.

b. Epidemiology. Adenoviruses vary somewhat, but all are transmitted by direct contact, fecal-oral transmission, and occasionally water-borne transmission. Some types can establish persistent asymptomatic infections in tonsils, adenoids, and intestines of infected people, who can shed these viruses for months or years. In the United States, acute respiratory disease (ARD) is often associated with adenovirus types 4 and 7. Adenovirus type 7 infection acquired by inhalation can cause severe lower respiratory tract disease, whereas infection acquired orally usually causes no or mild disease. Outbreaks of adenovirus-associated respiratory disease are more common in the late winter, spring, and early summer. However, adenovirus infections can occur throughout the year.

c. Vaccines. Adenovirus vaccines are not currently available in the United States. The Food & Drug Administration (FDA) licensed Wyeth Pharmaceuticals to manufacture live attenuated adenovirus vaccines against either type 4 or type 7 in 1980. Unfortunately, manufacturing ceased in 1996, and the last of these lots expired in late 1998. These vaccines were noteworthy for taking the form of oral tablets (type 4—white tablet, type 7—yellow tablet). Adenovirus vaccination of military trainees dramatically reduced infections and training disruptions in this group. The Department of Defense contracted with Barr Laboratories to resume manufacturing these vaccines. FDA licensing for these vaccines may occur in 2007 or 2008.

d. Immunization. The vaccine consisted of two enteric-coated tablets that contained live attenuated adenovirus; one contained type 4 virus and the other type 7. The tablets could be administered simultaneously, but had to be swallowed quickly without chewing. Oral adenovirus vaccine recipients shed virus in their feces for 4 days after vaccination, and could continue to do so for an additional 7 days, and possibly up to 6 weeks.

e. Cautions. The following people should not receive the vaccine: people with known severe allergic reactions to the vaccine or any of its components, including gentamicin, neomycin, and amphotericin B. Defer vaccination to people with moderate to severe acute illness. Vomiting and diarrhea could interfere with vaccine effectiveness. Vaccinating pregnant women was not recommended, because the possible effects on fetal development had not been studied.

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f. Adverse Events. In 1973, a Navy trainee was hospitalized with fever, malaise, and dyspnea for 11 days after receiving the adenovirus type 4 and type 7 vaccines. The patient died on the 10th hospital day with the diagnosis of adenovirus type-7 pneumonia, based on cell culture. It was not possible to determine whether his infection was caused by a wild-type 7 adenovirus infection present before developing vaccine-induced immunity or to a vaccine strain. Adverse reactions caused by type 4 and type 7 vaccination have not been reported.

g. DoD Policy. Once the vaccine is available, adenovirus types 4 and 7 vaccines will be administered in a single dose to recruits shortly after arriving at training sites.

h. Special Considerations. Adenovirus vaccines were recommended for use in military populations at risk of developing ARD caused by adenovirus. Use of these vaccines was not recommended for other populations. The development of adenovirus vaccine for children would likely require dosage forms other than enteric-coated tablets or the use of further attenuated virus strains.

3. References.

a. CDC. Two fatal cases of adenovirus-related illness in previously healthy young adults-- Illinois, 2000. *MMWR* 2001; 50:553-5. www.cdc.gov/mmwr/preview/mmwrhtml/mm5026a1.htm

b. CDC disease information. www.cdc.gov/ncidod/dvrd/revb/respiratory/eadfeat.htm

c. Adenovirus. In: Plotkin SA, Orenstein WA. *Vaccines*, 4th ed. 2004; 863-879.

d. Gaydos CA, Gaydos JC. Adenovirus vaccines in the U.S. military. *Military Medicine*. 1995;160(6):300-4.

e. Multiple resources assembled by the Military Vaccine Agency:
www.vaccines.mil/adenovirus

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