

Deaths from Adenovirus in the US Military

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Mike Miller] Hi, I'm Mike Miller and today I'm talking with Dr. Robert Potter, a research associate for the Armed Forces Medical Examiner System, and Dr. Joel Gaydos, science advisor for the Armed Forces Health Surveillance Center. Our conversation is based on their paper about deaths from adenovirus in the US military, which appears in CDC's journal, Emerging Infectious Diseases. So, Dr. Potter and Dr. Gaydos, welcome.

[Dr. Potter] Thank you for having us.

[Dr. Gaydos] Thank you for the opportunity to be here.

[Mike Miller] So, Dr. Potter, let's begin with you. What is adenovirus?

[Dr. Potter] Adenoviruses are respiratory DNA viruses that primarily cause respiratory infections, but they can also cause gastrointestinal infections and conjunctivitis. Most infections result in non-serious illness in otherwise healthy people. Adenoviruses can also result in serious illness and death. Some infections actually produce no symptoms in people, yet these same people can spread the virus to other people. There are dozens of different strains of this virus, called serotypes. Those at greatest risk for infection are infants and young children. Because of this, day care facilities can be affected. Also very susceptible are immunocompromised patients, such as those with HIV, cancer treatment patients, and organ transplant recipients. Also affected are military training facilities, such as our military basic training sites.

[Mike Miller] Why is it prevalent in the military?

[Dr. Potter] Well, close crowding seems to promote easier spread of the virus. The theory is that these common viruses are brought to the training facilities by a mildly ill or asymptomatic person. At these facilities, thousands of young adults from all over the country are brought into close contact for weeks, allowing for easy spread from person-to-person. The physical and psychological stress of training also increases susceptibility. Also, this virus is very hardy and can survive on common surfaces, allowing a new group of trainees to be infected by the previous group. There is also mixing of trainees from one group to another, also promoting spread of the virus. Other countries have documented problems with adenovirus infections in their military populations.

[Mike Miller] Okay, Dr. Gaydos. Why was vaccinating military personnel stopped?

[Dr. Gaydos] In the 1950s, the adenoviruses were shown to be the most important cause of acute, febrile respiratory disease in military trainees, and almost all of this morbidity was caused by two types: Adenovirus Type 4 and Adenovirus Type 7. Live virus, enteric coated vaccine tablets, one for the Type 4 and one for the Type 7 were developed and tested, and routine administration of these vaccines to the trainees started in 1971. During the 1970s, rigorous surveillance of military training facilities was conducted to monitor adenovirus vaccine safety and effectiveness. Based on the data accumulated, the US Food and Drug Administration, the FDA, gave approval for use of the vaccines in military populations. This occurred in 1980. With the FDA approval, the surveillance efforts were relaxed.

Now since only the US military used these vaccines, there was not a great demand. Therefore, there was only one manufacturer. These vaccines were found to be very safe and very successful in controlling the acute, febrile respiratory disease that was occurring in the training camps. So successful that few people remain sensitive, to the large numbers of people who had been ill because of adenoviruses in the pre-vaccine era.

In 1984, the sole manufacturer of the vaccines notified the Department of Defense, otherwise known as the DoD, that they needed to revise their agreement with the DoD. Perhaps because many considered adenovirus-associated disease in the military a problem of the past, this notification and the possible loss of these critical vaccines was not widely appreciated. The DoD made attempts to address this problem, but none were successful. The manufacturer continued to produce the vaccines, but on a yearly basis, until 1994 when it announced that it had stopped vaccine production and that when the existing bulk vaccine had all been placed in tablets and sent to the DoD, there would be no more vaccine from the company. The last shipments of vaccine occurred in 1996.

The military had been using these vaccines year round. In an attempt to extend the remaining supply, vaccine administration was changed so that vaccines were given only in the colder months. The Global Emerging Infections Surveillance & Response System of the Armed Forces Health Surveillance Center partnered with other DoD organizations, like the Naval Health Research Center in San Diego, to upgrade and intensify surveillance at the military training centers. During the time the vaccine was being rationed, outbreaks occurred and these were documented when the vaccine was not being given. Finally, in 1999, all existing vaccine supplies were depleted and the return of adenovirus-associated acute respiratory disease to military training centers in the winter, when it tended to be more severe, and at other times during the year, again became a major problem for the US military.

[Mike Miller] But why did the company stop making the vaccine?

[Dr. Gaydos] The company's vaccine facilities were aging and the company was very concerned about worker safety and environmental protection and felt strongly that they needed to modernize their production facilities.

[Mike Miller] Well, college dorms seem to have a lot of outbreak in diseases, such as measles and meningitis. Is adenovirus one that strikes college students, too?

[Dr. Potter] Well, outbreaks have been described in college-type settings and in a Job Corps training facility. It is likely that adenovirus outbreaks in these settings are going undetected. Routine testing for specific adenoviruses is not usually performed in college settings, as is done in military facilities. Also, the symptoms of an adenovirus respiratory infection are not specific and could be attributed to other common respiratory viruses, such as the cold virus or a case of mild flu.

[Mike Miller] Well, how much of a problem is adenovirus in the general population?

[Dr. Potter] The prevalence of specific serotypes seems to vary from country to country and over time. There are documented adenovirus outbreaks in child care centers, boarding schools, and chronic care facilities. It has been reported that up to 10 percent of all febrile illnesses in infants and young children are caused by adenoviruses. Even though many young children are exposed to some adenovirus types and develop antibodies, they remain susceptible to later infections by other serotypes. One study of entrants from the civilian population into a military training facility showed that only 34 percent had antibodies to Adenovirus Type 4, therefore most, 66 percent, were at risk for getting this virus, which is one of the virus vaccines. Even more new trainees, 73 percent, were susceptible to Adenovirus Type 7, the other virus in the vaccine combination.

[Mike Miller] I see. Is there a new vaccine in the works?

[Dr. Potter] A new vaccine for military recruits was approved by the FDA in 2011 and is now in production. Like the original vaccines, it is a live, enteric-coated, oral vaccine consisting of two tablets, one for serotype 4 and one for type 7, which were the same serotypes used in the original adenovirus vaccine. Since November 2011, the new vaccine combination has been administered at all military training facilities. Preliminary data shows that the new vaccine has been associated with a dramatic reduction in acute, febrile respiratory illness among military recruits.

[Mike Miller] If the vaccine is so effective and young children are so susceptible, why don't we vaccinate children, too?

[Dr. Potter] The military was fortunate in being able to have a vaccine program based on only two of the many different adenovirus serotypes. The cost-effectiveness of the military vaccines has been studied and evaluated on several occasions. The current adenovirus vaccines were tested only in the military and were approved by the FDA for use in that population only.

A vaccine program for civilian pediatric use would depend upon scientists being able to develop a vaccine or vaccines that covered enough important disease-causing adenovirus types in that population. It would also depend on recognition of a market large enough for vaccine manufacturers to become interested in producing such a vaccine. Finally, testing and evaluation of the vaccine in the intended population, to the satisfaction of the FDA would be required.

[Mike Miller] Well, thanks, to both of you, Dr. Potter and Dr. Gaydos. I've been talking with Drs. Robert Potter and Joel Gaydos about their paper, *Adenovirus-associated Deaths in US Military during Postvaccination Period, 1999–2010*, which appears in the March 2012 issue of CDC's journal, *Emerging Infectious Diseases*. You can see the entire article online at www.cdc.gov/eid.

If you'd like to comment on this podcast, send an email to eideditor@cdc.gov. That's e-i-d-editor - one word - at c-d-c-dot-gov. I'm Mike Miller, for *Emerging Infectious Diseases*.

[Announcer] For the most accurate health information, visit www.cdc.gov or call 1-800-CDC-INFO.