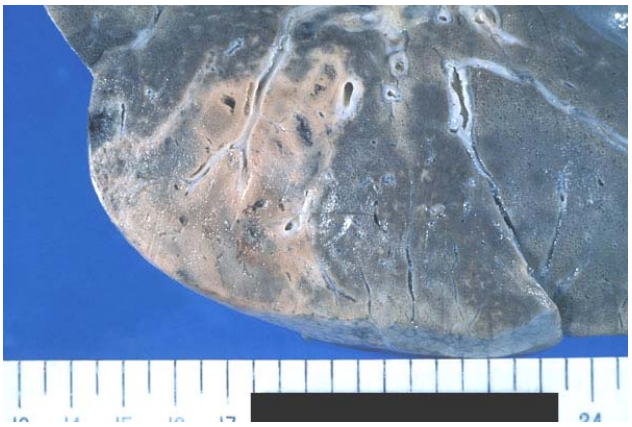
Adenovirus Vaccine Information Paper

A licensed vaccine developed by DoD and its partners

Product name: Adenovirus vaccine
Commercial name:
Adenovirus Vaccine live oral type 4
Adenovirus Vaccine live oral type 7
Date of U.S. licensure: 1980 (out of production 1995; not available after 1998 [adenovirus 4 vaccine] and 1999 [adenovirus 7 vaccine]).
Type of product: live viral vaccine tablet for oral administration
Company of manufacture: Wyeth (1980-1995)

Target microorganism/associated disease: Adenoviruses are DNA viruses that are usually transmitted via respiratory (aggravated by crowding) or ocular (spread via swimming pools, physician offices with inadequate sterilization and handwashing practices) routes. Asymptomatic infection and a prolonged carrier state contribute to spread. Diseases associated with adenoviral infections include febrile respiratory illness (bronchitis or pneumonia), eye infections (conjunctivitis), sore throat, and diarrhea. Complications of adenovirus include acute bacterial ear and lung infections, and death.

Reasons for development: Adenovirus -- a frequent cause of epidemic acute respiratory disease (ARD) associated with pneumonia, hospitalizations and some deaths especially among military recruits -- is a proven threat to military readiness. Adenovirus infections also cause illness among deployed troops and civilians. There is no effective antiviral treatment for adenovirus. During World War II, epidemics of respiratory disease in new recruits disrupted training and greatly increased the burden on medical staff and facilities. Before vaccines were available, adenovirus was consistently isolated in 30-70% of trainees with ARD, and adenoviruses were associated with 90% of the cases of pneumonia among trainees in basic combat training (BCT). The vast majority of all adenovirus infections in BCT are caused by serotypes 4 and 7. In prospective studies in the 1950's of ARD in BCT recruits, Hilleman and his co-workers established that 20% of recruits were hospitalized with febrile ARD, another 20% sought evaluation at an outpatient facility, 40% had mild or inapparent infections, and the remaining 20% (probably immune) were not infected. In a similar subsequent study of an ARD outbreak in BCT recruits at Fort Dix in the 1960s, Buescher and his co-workers observed that 37% were hospitalized with febrile ARD, and an additional 48% were also ill with less severe infections. Since termination of Wyeth vaccine production in 1995, the burden of adenovirus disease in recruits has increased to that of the pre-vaccine era.



Massive congestion and focal necrosis are seen in the left lung. Adenovirus was proven from the lung tissue obtained at autopsy. Photo from www.yamagiku.co.jp/pathology/image/093/1.jpg.

Role of Department of Defense in product development: A commission on ARD was established at FT Bragg, NC from 1942 to 1945 to undertake epidemiologic studies. The viral nature of these infections was established when bacteria-free filtrates were shown to transmit the infection to volunteers. In the 1950s, Hilleman and Werner at the Walter Reed Army Institute of Research (WRAIR) identified adenovirus types 4 and 7, and established the importance of neutralizing antibody as a marker of immunity for these infections. Effective formalin-inactivated type 4 and 7 vaccines were developed in the 1950's and licensed by the FDA but subsequently withdrawn because of variable potency and concerns (later established as unfounded) regarding potential oncogenicity due to contamination with SV-40. Because ARD epidemics caused by adenovirus type 7 continued, Top and co-workers at WRAIR developed a similar safe, highly antigenic live oral adenovirus type 7 vaccine. After extensive testing, these vaccines were approved for distribution by Wyeth Laboratories in 1980. The Wyeth adenovirus vaccines were effective in preventing ARD in recruits without producing adverse effects. In 1995, Wyeth -- the sole manufacturer of adenovirus vaccines -- elected to cease production when faced with the requirement for costly updated manufacturing facilities for the vaccine; DoD supplies were depleted by 1999. Because of the subsequent surge of adenovirus cases in recruits, DoD contracted with Barr Laboratories in September 2001 to develop replacement live adenovirus vaccines. The first clinical study of the new adenovirus types 4 and 7 vaccines has been successfully completed by investigators at Fort Sam Houston.

Adenovirus vaccine references:

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