Emergence of Adenovirus Type 14 in US Military Recruits—A New Challenge

Leonard N. Binn,1 Jose L. Sanchez,2 and Joel C. Gaydos2

1Division of Viral Diseases, Walter Reed Army Institute of Research, and 2Department of Defense Global Emerging Infections Surveillance and Response System, Silver Spring, Maryland

In this issue of the Journal, Metzgar et al. [1] report a significant addition to the adenovirus (Ad) types infecting US military recruits with acute respiratory disease (ARD). Their ongoing epidemiological studies, which use rapid molecular diagnostic procedures, enabled the detection and identification of a species B2 Ad, type 14 (Ad14), that had not been previously observed in US military recruits. This virus was originally recovered >50 years ago from Dutch recruits [2], with only 2 subsequent reports of ARD associated with Ad14 [1, 3]. In contrast to the B1 Ads (i.e., types 3, 7, and 21) that often infect the respiratory tract, Ad14 respiratory infections have been very rarely observed in adult military and civilian populations [4].

At present, studies are under way at military training centers to field test replacements for the live oral Ad4 and Ad7 vaccines that had been used for >25 years but were lost when production ceased in the 1990s [5–7]. The recent recovery of Ad14 raises new questions as to whether Ad14 will take hold as a respiratory disease agent in civilian and military populations and whether the candidate Ad4 and Ad7 vaccines will protect against Ad14. The absence of identified Ad14 respiratory infections in the United States suggests that we have highly susceptible civilian and military populations.

Review of past experience with the live oral Ad vaccines may be of value in assessing the long-term threat of Ad14 to recruits. Previous observation of responses to the Ad4 and Ad7 vaccines indicated that they were highly effective against homologous viruses and Ad3 [6, 7]. Vaccines responses to Ad3 were attributed to some level of Ad3 occurring naturally and to Ad3 being antigenically related to Ad7, both being species B1 viruses. Therefore, after exposure to the Ad7 vaccine virus, heterotypic responses to Ad3 occurred [8]. In contrast to Ad3, naturally occurring background infections with Ad21, also a species B1 virus, have been considered rare. Recent studies of recruits with ARD found only small numbers infected with Ad21 [1]. Only a few additional Ad21 infections were identified via antibody testing, suggesting that the virus currently is not highly communicable [9, 10]. However, in 1975–1976, Ad21 was recovered from large numbers of recruits with ARD who had been vaccinated against Ad4 and Ad7. ARD-associated Ad21 infections continued for months at most training facilities, resulting in the testing of an experimental live oral vaccine [11, 12]. However, long-term observation revealed that Ad21 did not persist as a significant cause of ARD, even though outbreaks occurred in the 1970s and again in 1985 [13]. Thus, there has been no interest in renewing studies of an Ad21 vaccine.

It is possible that Ad14 and other Ads could cause significant ARD morbidity among military recruits for a limited period and then disappear as an important cause of respiratory disease. It is also possible that some protection against emerging Ads could be provided as a result of heterotypic antibody responses to other viruses, including the Ad7 vaccine virus. Past studies in The Netherlands found that Ad14-associated ARD did not persist in their recruits [2, 14]. Additionally, the development of heterotypic antibody to Ad14 after Ad7 immunization was reported in 1960 [15].

Contemporary serologic surveys of new US military recruits will provide important information on their susceptibility. Testing archival serum-bank specimens from recruits vaccinated against Ad4 and Ad7 and from recruits with ARD who had laboratory confirmation of a specific Ad type could provide data on the occurrence of heterotypic antibody re-
responses to Ad14. Additionally, measurement of Ad14-associated ARD during the current Ad4 and Ad7 vaccine trials will be important, as will measurement of immunity to Ad14 associated with immunization. Molecular studies should be conducted to characterize recovered Ad14 isolates and to determine whether changes may have occurred in the genome that could affect communicability and pathogenicity, a situation that was described in Spanish recruits in 1976 [16].

The events described by Metzgar et al. provide strong support for ongoing, laboratory-based surveillance in military training populations. Because little is known about the dynamics involved in the emergence of important acute febrile respiratory disease pathogens in military populations, studies describing agent persistence and transmission within military communities and surveillance of associated civilian communities should be continued. Whether Ad14 will persist as a significant cause of ARD in recruits cannot be predicted. Therefore, it is advisable to preserve candidate specimens of Ad14 for passage in suitable cells for vaccine seed virus and molecular studies.

After the licensure of the Ad4 and Ad7 vaccines currently being tested, complacency regarding the control of acute febrile respiratory diseases in military populations cannot occur. Continued surveillance will be necessary to assess the effectiveness of the new vaccines and to detect the presence of emergent Ads, influenza viruses, and other respiratory agents that cause morbidity and interfere with military training. The application of the modern tools of molecular biology should greatly enhance our understanding of these agents and the dynamics of acute febrile respiratory diseases in the unique environment of military recruits undergoing their initial entry (i.e., basic) military training.

References