DEFENSE HEALTH BOARD
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MEMORANDUM FOR: GEORGE PEACH TAYLOR, JR., M.D., DEPUTY ASSISTANT SECRETARY OF DEFENSE (FORCE HEALTH PROTECTION AND READINESS), PERFORMING THE DUTIES OF THE ASSISTANT SECRETARY OF DEFENSE FOR HEALTH AFFAIRS

SUBJECT: Recommendations Regarding the Department of Defense Routine Smallpox and Anthrax Immunizations Policies 2010-05

BACKGROUND

1. The Department of Defense (DoD) Directive 6205.3, "DoD Immunization Program for Biological Warfare Defense", instructs the Defense Health Board (DHB) to recommend appropriate immunization protocols to the Department and identify vaccines available to protect against biological threat agents.

2. The DHB Infectious Disease Control Subcommittee formed a Vaccine Safety and Effectiveness Workgroup within its membership to examine the following:

   a. Operationally significant infectious disease surveillance data

   b. Data from DoD researchers evaluating the safety and effectiveness of vaccines currently in use by DoD

   c. Future vaccine safety, effectiveness, and disease surveillance studies in DoD

3. The DHB Vaccine Safety and Effectiveness Workgroup met on September 17, 2009, June 9, 2010, and July 14, 2010 and received briefings on smallpox and anthrax vaccines from the Military Vaccine Agency (MILVAX), U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), the Naval Health Research Center (NHRC), and the Vaccine Healthcare Centers (VHC) Network. On June 9, 2010, the Infectious Disease Subcommittee also received briefings from the Joint Staff and Department of Homeland Security (DHS) on the Chairman's Biological Agent Threat List and corresponding DHS domestic threat list. Among the issues examined were: determining which infectious agents pose a continued threat, the availability of alternative countermeasures, as well as vaccine-associated adverse events and safety data.

INTRODUCTION

4. The Anthrax Vaccine Immunization Program (AVIP) was signed into effect in December 1997, with implementation for the Total Force on May 18, 1998. In October 2004, the mandatory program was suspended due to a federally imposed injunction that prompted a review of vaccine safety data and the vaccine's applicability to prevent inhalational anthrax. Following a comprehensive examination of scientific evidence, the Food and Drug

Administration (FDA) issued a Final Rule and Final Order on December 15, 2005, stating that anthrax vaccine adsorbed (AVA) is licensed for the prevention of anthrax infection, regardless of route of exposure to *Bacillus anthracis*. Following the submission of data from the FDA and DoD, the court found in favor of reinstituting the AVIP program.

5 On October 12, 2006, the Deputy Secretary of Defense directed that the mandatory AVIP program be resumed. Mandatory immunization against anthrax is required for DoD Service members, designated DoD civilians and contractor personnel performing mission-essential services assigned to United States Central Command (CENTCOM), the Korean Peninsula or the Horn of Africa for a minimum of 15 days. Additional groups include special units with biowarfare or bioterrorism missions and specialty units with approved exception to policy. Immunization is voluntary for DoD service members who are not in the mandatory group and have received at least one dose of AVA during or after 1998. The vaccine is also voluntary for DoD civilians and contractors and their adult family members if they are residing in CENTCOM, the Korean Peninsula or the Horn of Africa for a minimum of 15 days.

6. The Smallpox Vaccine Immunization Program (SVIP) was implemented in 2002 to protect DoD personnel following the intentional or unintentional release of smallpox. The SVIP has been conducted in adherence to Advisory Committee on Immunization Practices (ACIP) guidelines.

7. Immunization against smallpox or variola is accomplished by the use of a vaccine against cowpox or vaccinia. Because the two viruses are closely related, immunization against cowpox confers immunity against smallpox.

8. Immunizations and Chemoprophylaxis Joint Regulation, issued in the 2006 DoD Directive 6205.02E, synchronized the military Service immunization programs.

FINDINGS

Anthrax Vaccine Adsorbed

9. The Centers for Disease Control and Prevention (CDC) has not reported any elevated risk of serious adverse events attributed to the anthrax vaccine in the context of a large, prospective, placebo-controlled clinical trial.

10. The anthrax agent is a continued bioterrorism and biowarfare threat due to recent intentional releases and the ease with which it could be acquired and formulated for widespread dispersal.

11. Defense Medical Surveillance System (DMSS) data have not yielded evidence indicating that possible adverse health events are associated with AVA. Study results have suggested that concurrent vaccinations, that include AVA, are not associated with an increased risk of hospitalization. When compared with other vaccines, AVA is not associated with an increase in life-threatening or permanently disabling vaccine-related adverse events.

12. Available data indicate that AVA is both safe and effective in conferring protection against *Bacillus anthracis* infection, consistent with the Board's findings and recommendations issued in 2005, following a review of issues pertaining to anthrax vaccine and AVIP.

Smallpox Vaccine: ACAM2000®

13. Enhanced ACAM 2000® vaccine safety and adverse event surveillance is in place through internal collaboration between MILVAX, Armed Forces Health Surveillance Center (AFHSC) and the NHRC and external collaboration between DoD and the FDA. Vaccine related adverse event data are collected passively through the Vaccine Adverse Event Reporting System (VAERS), Reportable Medical Events, and the VHC Network.

14. The FDA requested that DoD pursue the following five post-licensure requirements in order to ensure the safety of ACAM2000®:

    a. Implementation of an ACAM2000® Phase IV enhanced safety surveillance study;

    b. Implementation of a study to assess the effectiveness of DoD adverse event screening procedures;

    c. Utilization of the DMSS Database to identify symptomatic cases of myopericarditis;

    d. Establishment of an ACAM2000® myopericarditis registry to monitor cases over a five year period;

    e. Annual evaluation of DoD risk management initiatives and protocols.

15. As of July 10, 2010, 1,968,071 U.S. military personnel received the smallpox vaccine. Among these recipients, relatively few experienced a vaccine-related adverse event.

    a. Adverse events identified through passive surveillance were: eczema vaccinatum, progressive vaccinia, autoinoculation, and contact transfer vaccinia.

    b. Approximately 228 potential and confirmed myopericarditis cases were identified through the ACAM2000 registry®; of these cases, 191 are probable, 31 are suspected, and six have been confirmed. Among these, one fatality has been possibly linked to this vaccine following lupus-like illness.

16. The SVIP includes considerable attention focused on education and training initiatives targeting both staff and vaccine recipients to prevent the secondary transmission of vaccinia.

17. Vaccinia Immune Globulin (VIG) is used to treat serious complications following vaccinia vaccine administration. VIG is stockpiled by the CDC. The time for delivery of VIG within the continental United States (CONUS) is between 24 and 48 hours. Delivery to locations outside CONUS (OCONUS) may require 72 hours, which may not permit optimal initiation of treatment.

18. Two antiviral medications are currently available to treat vaccinia virus: cidofovir and an investigational drug, ST-246. ST-246 has been administered twice in CONUS and delivered within 24 hours. Cidofovir could be delivered in the continental U.S. (CONUS) within 48 hours, and OCONUS shipments would require an additional 48 to 72 hours. Treatment of exposed individuals within 72 hours improves patient outcomes.

19. To prevent disease, smallpox vaccine should be given within three days of exposure and ideally within the first 24 hours. The smallpox vaccine could be delivered to in-theater locations within 72 hours following exposure among vaccine-naïve subjects. Moreover, DoD is able to alter the number and locations of smallpox vaccine stockpiles as appropriate to facilitate timely delivery of vaccine.

20. Continuation of this program in the light of a questionable threat, vaccine related adverse events, the ability to deliver vaccine if required and the overall cost of the SVIP represents a burden to DoD.

RECOMMENDATIONS

21. The Board deliberated the proposed recommendations of the Vaccine Safety and Effectiveness Workgroup on August 17, 2010. Based on the available evidence, the Board recommends the Department pursue the following:

a. Suspend the current smallpox routine immunization program absent an immediate or credible threat. However, the Board recognizes that special circumstances might arise under which the administration of the vaccine would be necessary and should continue following a decision rendered by DoD (i.e. potential use in Special Operations teams, lab workers, etc.).

b. Consider altering antiviral and vaccine stockpile locations to be configured at the "ready level".

c. Extend surveillance window beyond the current five-year follow-up required by the FDA for ACAM2000® vaccine recipients who have incurred specific smallpox vaccine-related adverse events in order to capture late-onset cases.

d. Maintain current DoD anthrax immunization policy without amendment.

e. Continue current safety monitoring and reporting of AVA-associated adverse events.

22. The above recommendations were approved unanimously.

SUBJECT: Recommendations Pertaining to Department of Defense (DoD) Policy Pertaining to Routine Smallpox and Anthrax Immunizations 2010-05

FOR THE DEFENSE HEALTH BOARD:

Wayne M. Lednar, MD, PhD
DHB Co-Vice President

Gregory A. Poland, MD
DHB Co-Vice President
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Infectious Disease Control Subcommittee

REFERENCES

1. Presentation, Smallpox and Anthrax Vaccine Policy, to the DHB Infectious Disease Control Subcommittee, July 14, 2010, by COL Krukar, Director, Military Vaccine Agency.

2. Military Vaccine Agency, Smallpox Vaccine Immunization Program Information Paper, July 13, 2010.

3. Presentation, Update on Military Vaccination Programs: Providing a Continuum of Care in Immunizations, to the DHB Infectious Disease Control Subcommittee, June 9, 2010, by COL Michael J. Krukar, Director, Military Vaccine Agency.

4. Presentation, ACAM2000® Vaccinia Vaccine Study, to the DHB Infectious Disease Control Subcommittee, September 17, 2009, by COL Phillip R. Pittman, Director, Vaccine Clinical Research Center, U.S. Army Medical Research Institute of Infectious Diseases.

5. Presentation, Vaccine Analytic Unit (VAU): An Infrastructure in Transition, to the DHB Infectious Disease Control Subcommittee, September 17, 2009, by Dr. Michael M. McNeil, Vaccine Analytic Unit, National Center for Prevention, Detection, and Control of Infectious Diseases.

6. Presentation, ACAM2000® Smallpox Post-Marketing Phase IV Case/Control Surveillance, to the DHB Infectious Disease Control Subcommittee, September 17, 2009, by Dr. Dennis J. Faix, Naval Health Research Center.

7. Presentation, Phase IV Enhanced Safety Surveillance Study of ACAM2000® in Military Personnel, to the DHB Infectious Disease Control Subcommittee, September 17, 2009, by LTC Patrick Garman, Deputy Director, Military Vaccine Agency.

8. Presentation, ACAM2000® Myopericarditis Registry, to the DHB Infectious Disease Control Subcommittee, September 17, 2009, by Dr. Ava Marie S. Conlin, ACAM2000® Myopericarditis Registry Team, Naval Health Research Center.

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11. Centers for Disease Control and Prevention (2007) Morbidity and Mortality Weekly Report 56(19):478-481.

12. Department of Defense Directive Number 6205.02E, Policy and Program for Immunizations to Protect the Health of Service Members and Military Beneficiaries, September 19, 2006.

13. Memorandum, Under Secretary of Defense for Personnel and Readiness, Implementation of the Anthrax Vaccine Immunization Program, December 6, 2006.

14. Memorandum, Deputy Secretary of Defense, Anthrax Vaccine Immunization Program, October 12, 2006.

15. Memorandum, Assistant Secretary of Defense for Health Affairs, Continuation of the Anthrax Vaccine Immunization Program, December 22, 2005.

16. Memorandum, Armed Forces Epidemiological Board, DoD Immunization Program for Biological Warfare Defense, August 22, 2005.

17. Memorandum, Secretary of Defense, Anthrax vaccine Immunization Program Pause, October 27, 2004.

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20. Memorandum, Deputy Assistant Secretary of Defense, Smallpox Vaccination Program, September 30, 2002.

21. Memorandum, Secretary of Defense, Implementation of the Anthrax Vaccination Program for the Total Force, May 18, 1998.

22. Department of Defense Directive Number 6205.3, DoD Immunization Program for Biological Warfare Defense, November 26, 1993.