



DEPARTMENT OF DEFENSE
ARMED FORCES EPIDEMIOLOGICAL BOARD
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Armed Forces Epidemiological Board

APR 16 2004

MEMORANDUM FOR

Assistant Secretary of Defense (Health Affairs)
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force

SUBJECT: Multiple Concurrent Immunizations and Safety Concerns 2004 - 04

1. References:

(a) Memorandum, Deputy Assistant Secretary of Defense, Force Health Protection and Readiness, 7 October 2003, Multiple Concurrent Immunizations and Safety Concerns.

(b) Military Vaccine Agency, An Incomplete Bibliography of Simultaneous Vaccinations, 22 January 2004.

2. On 7 October 2003, the Assistant Secretary of Defense for Health Affairs (ASD(HA)) requested that the Armed Forces Epidemiological Board (AFEB) consider the scientific evidence regarding multiple simultaneous vaccinations including combination vaccines, and whether there are potential combinations of vaccines that together might be cause for safety concern when administered to adults. This review was initiated to ensure current DoD policy on vaccine administration meets our national obligation to protect and preserve the health of the men and women who serve our Nation.

3. On 17 February 2004, the Board devoted most of its meeting to reviewing the data on multiple concurrent immunizations, and heard presentations from a variety of immunology, epidemiology, and vaccine content experts. In addition, members of the Infectious Disease Prevention and Control subcommittee reviewed the Institute of Medicine (IOM) Immunization Safety Review Committee publications prior to the meeting and a pre-meeting teleconference was held. COL John D. Grabenstein, RPh, PhD, Deputy Director for Clinical Operations, Military Vaccine Agency, U.S. Army Medical Command, provided an overview of current DoD immunization practices and reviewed the published medical literature on simultaneous vaccinations (reference b). The Board also received a brief from COL Renata J.M. Engler, MD, MC, Director, Vaccine Healthcare Centers Network, Allergy-Immunology Consultant, Army Office of The Surgeon General, on "The DoD Vaccine Healthcare Centers (VHC) Network and the surveillance and care of adverse events." The VHC Network has become an integral component of the referral and consultation services available on vaccine adverse event issues for the DoD and can play an important role in the study and evaluation of cases or clusters of possible rare vaccine-induced adverse events. In addition, members of the

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Infectious Disease Prevention and Control subcommittee reviewed the IOM Immunization Safety Review Committee publications before the meeting and held a pre-meeting teleconference.

4. A number of recognized scientific entities, including the Centers for Disease Control and Prevention (CDC), the IOM, professional specialty societies, and individual investigators have assessed this issue. These entities have consistently concluded that available scientific evidence has not documented any known serious health risk from receipt of concurrent immunizations. Therefore, they continue to routinely recommend the use of combination vaccines when available, and concurrent multiple immunizations when combinations are not available. The Board is cognizant of data demonstrating an additive effect in the incidence of transient, spontaneously resolving local and systemic reactions from receipt of multiple concurrent immunizations. Further, the Board acknowledges that this leads to short-lived discomfort, pain, mild systemic symptoms, and potential lost work time, although these studies did not consider the effect of a specified number of vaccinations divided over multiple immunization encounters.
5. All combination vaccines utilized within the DoD are vaccines licensed by the Food & Drug Administration that have undergone rigorous scientific and safety evaluation, ensuring that the combined antigens can safely be administered together.
6. The Board is unaware of any scientific data suggesting either that a “threshold of safety” exists for the number of vaccines that can be concurrently given, or that receipt of concurrent vaccinations has been conclusively associated with serious or long-term adverse health effects. It is likely that concurrent vaccination simply mimics simultaneous encounters with multiple viruses and bacteria in the natural environment. In addition, there are no scientific data available demonstrating that multiple or concurrent immunizations can “uncover” or “trigger” rare and serious illnesses in genetically predisposed persons, although the Board acknowledges published case reports including a recent report where this possibility could not be excluded. While it appears that there may be theoretical biologic mechanisms by which this could occur, no scientific data currently exist to support this hypothesis in humans.
7. Data derived from electronic immunization tracking systems operated by the US Army and US Air Force indicates that service members could receive between one and eleven vaccines in a given day. However, according to current data, 93% of service members receive three or fewer vaccines on a given day, and only 7% receive more than four vaccines on a given day. A published report examining 99 men who received total career cumulative vaccine doses of between 52 – 134 mL and who were followed over 25 years demonstrated no unusual diseases or unexplained symptoms, and no observed increase in mortality compared to actuarial expectations.
8. The Board makes the following findings and recommendations concerning the issue of multiple concurrent immunizations and safety concerns:

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At the current time, decades of experience and extant data do not demonstrate serious or long-term adverse health effects causally related to multiple, concurrent immunizations, and there is no reason to deviate from current consensus guidelines for adult immunization. Standard clinical practice and the recommendations of multiple scientific and professional medical societies currently support the practice of concurrent immunization. For these reasons, and the demonstrated positive health effects of widespread immunity to infectious diseases that can seriously impair readiness, the current practice of multiple, concurrent immunizations should be continued in the Armed Services. The recommendations below outline suggested strategies to decrease concurrent vaccinations and minimize discomfort to vaccinated personnel without sacrificing the individual and population benefits of widespread vaccine-induced immunity to infectious diseases.

(a) Where possible, it seems prudent to spread immunizations out over time. For example, at the start of initial recruit training, administer vaccines with immediate potential for preserving health (such as adenovirus, meningococcal, MMR, influenza, varicella, and pneumococcal). At the end of initial entry training (or during advanced individual training or at first duty station), administer the remainder of needed vaccines (e.g., yellow fever, tetanus-diphtheria, hepatitis A, hepatitis B, and poliovirus). This would reduce the number of concurrently administered vaccines in the recruit setting.

(b) Several opportunities exist where vaccine use could be reduced without any increase in disease risk. For diseases where immunity is likely to be high due to naturally occurring infection or routine vaccination prior to enlistment, it is prudent and often cost-saving to screen for serologic evidence of immunity and vaccinate only susceptible individuals. For example, immunity to measles-mumps-rubella (MMR) is likely to exceed 90% in people now entering basic training due to routine childhood vaccination and over time immunity against hepatitis B will become common due to advent of childhood vaccination against hepatitis B. Similarly, immunity to varicella is high due to natural infection. Serological evidence of immunity in this setting is also preferred, as immunization and/or disease history has been shown to be inadequate. The choice of specific strategies will need to take into account the prevalence of immunity against specific diseases; the feasibility and costs of selective vs. universal vaccination; and the likelihood and risks of missing susceptible persons. For diseases where risk is limited to specific geographic areas, vaccination can be limited to those likely to travel to those areas. A risk-based approach is strongly recommended for vaccines such as yellow fever. The Air Force reduced its use of yellow fever vaccine by 81 percent with a change in policy requiring a risk-based requirement before vaccination.

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(c) After basic training, standard clinical practice considering past immunization history should be better utilized by the Services, including a threshold for presuming vaccination. For example, individuals who have gone through recruit training should be presumed immune to the standard diseases for which vaccines are administered in this setting (e.g., measles, rubella, and polio). Personnel should be required to bring immunization records with them at the time of mobility processing or for the annual review of individual medical readiness requirements, and these records should be used to individually determine the need for any given vaccine. Recognizing the difficulties of integration, electronic immunization registries and databases should enhance tracking and documentation of vaccination, but lack of documentation in an electronic records database should not be used as the sole determinant of vaccine need. An algorithmic or “order of merit” approach is more appropriate.

(d) Data were presented demonstrating that the Reserve Component forces may more commonly receive multiple concurrent vaccines with higher numbers of vaccine doses than the Active Component. DoD procedures should minimize just-in-time delivery of preparatory countermeasures. An increase in the frequency of medical-readiness reviews would serve to “spread out” the number of vaccines needed for Force Protection. Implementation of an annual individual medical readiness requirement for Reserve Component forces would further decrease just-in-time delivery of preparatory countermeasures including vaccines.

(e) The Board considers risk communication an integral component of DoD’s vaccination program and supports development of risk communication materials and training provided by the Vaccine Health Care Network, Military Vaccine Agency and the DoD Clinical Center for Deployment Health.

(f) The Board was briefed on current DoD and United Kingdom Ministry of Defence studies and a proposed study looking at immunological changes associated with multiple concurrent vaccine receipt at Marine Corps Recruit Depot San Diego. These studies address issues as diverse as determining the most common simultaneous combinations being administered, immunologic, behavioral, cognitive and health effects over time of multiple concurrent immunizations (in a non-human primate model), and possible adverse effects of

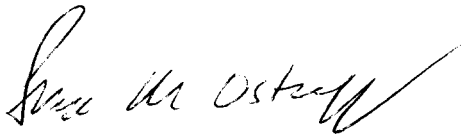
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multiple concurrent immunizations. The Board will review and comment on these data, as well as any additional information relevant to this topic, as they become available.

9. The above recommendations were unanimously approved.

FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD:



STEPHEN M. OSTROFF, MD
Assistant Surgeon General,
US Public Health Service
President, AFEB



GREGORY A. POLAND, MD
Mary Lowell Leary Professor of Medicine
Director, Mayo Vaccine Research Group
Associate Chair for Research, Dept of Medicine
Subcommittee on Infectious Disease, AFEB

Enclosure

Memorandum, Deputy Assistant Secretary of Defense, Force Health Protection and Readiness, 7
October 2003, Multiple Concurrent Immunizations and Safety Concerns



HEALTH AFFAIRS

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007 7 2003

MEMORANDUM FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD

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In 2000, the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) asked the Institute of Medicine (IOM) to establish an independent expert committee to review hypotheses about existing immunization safety concerns. On February 20, 2002, the IOM released its third report that addressed multiple immunizations and immune dysfunction. The IOM Immunization Safety Review Committee found that the available scientific evidence did not indicate that the infant immune system is inherently incapable of handling the number of antigens that children are exposed to during routine immunizations or that a causal relationship between multiple immunizations and increased risk for infections exists. The Committee recommended limited but continued public health attention to this issue in the form of policy analysis, research and communication strategy development.

Multiple simultaneous immunization has been a long-standing practice in military medicine, even though less published information is available regarding this practice in adults than in children. A number of vaccines have been combined in a single dose for simplicity of administration. These have undergone rigorous evaluation to make sure that the combined products do not interact with each other and can be given together safely. To ensure current DoD policy on vaccine administration meets our obligation to protect and preserve the health of the men and women who serve our Nation, I request the Armed Forces Epidemiological Board to consider the scientific evidence regarding receipt of multiple simultaneous vaccinations including combination vaccines, and whether there are potential combinations of vaccines that together might be cause for safety concern when administered to adults.

I would like the Board to address this issue at the February 2004 meeting and provide any pertinent recommendations as appropriate.

Ellen P. Embrey
Deputy Assistant Secretary of Defense
(Force Health Protection and Readiness)

cc:
DASD, Clinical and Program Policy