



Vaccine Safety Surveillance

Experiences and Lessons Learned

Supporting the Military Health System (MHS)

Mandatory Immunization Programs

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2007 Updates



Immunization Healthcare

An Evolving Mission





Challenges: Current & Future Vaccine Safety Surveillance



- **Biodefense: from preventive health to terrorism & pandemic preparedness – immune modulators**
 - Mandatory active or passive vaccine programs
 - Service members AD/Reserve: 2,400,000
 - DoD employees > 2,000,000
 - Beneficiaries > 6,000,000
 - Homeland defense support Millions++
- **Adverse vaccine side effects/reactions management**
 - Serious AE, exemption management? 1-2%
 - Individual causality assessments → new skills required
 - For service members alone 24-48,000
 - *Multiple vaccines, drugs + vaccines → clinical questions*
- **Implications for disability clarification ?**
 - Complex case evaluation, documentation, causality?



Department of Defense Largest Adult Immunization Program



- **Most complex immunization exposures**
 - Usual recommended ACIP vaccines: ever expanding in number
 - Travel vaccines mixed in new ways: safety data?
 - Biodefense vaccines: anthrax and smallpox with potential expansion
- **Mandatory employment requirement**
 - Medical and administrative exemption process
 - Demand for clinical competencies that represent “new specialty”
 - Complex new questions for which there is no literature, guidelines
 - *When to exempt and when not*
 - *How to optimize care of adverse events → guidelines*
 - *Need for clinical research to validate “opinion” guidelines*
- **Unique challenges in delivery system: ongoing training**
 - Traditional and non-traditional sites with personnel turnover, global
 - Working towards NVAC minimum standards MMWR Mar 2000



DoD Requirements Immunizations As “Operational Drugs”



More Vaccines – increasing safety and efficacy concerns

- **↑ Immunization complexity, standards, clinical ?’s**
- **↓ Trust in vaccines: risk communication complexity**
- **Anthrax Vaccine Immunization Program AVIP**
 - Complex clinical problems arise – how best to assess
 - Epidemiological safety versus individual responses
- **Smallpox vaccination program**
 - Increase in clinical needs & educational support
 - ↑↑ requirement for clinical expertise & consultation
- **Identify & manage adverse reactions over time**
 - New case definitions: critical to future genetic research

VHC Network = Response to Clinical Concerns

Start Working to Address the Unanswered Questions, Diversity



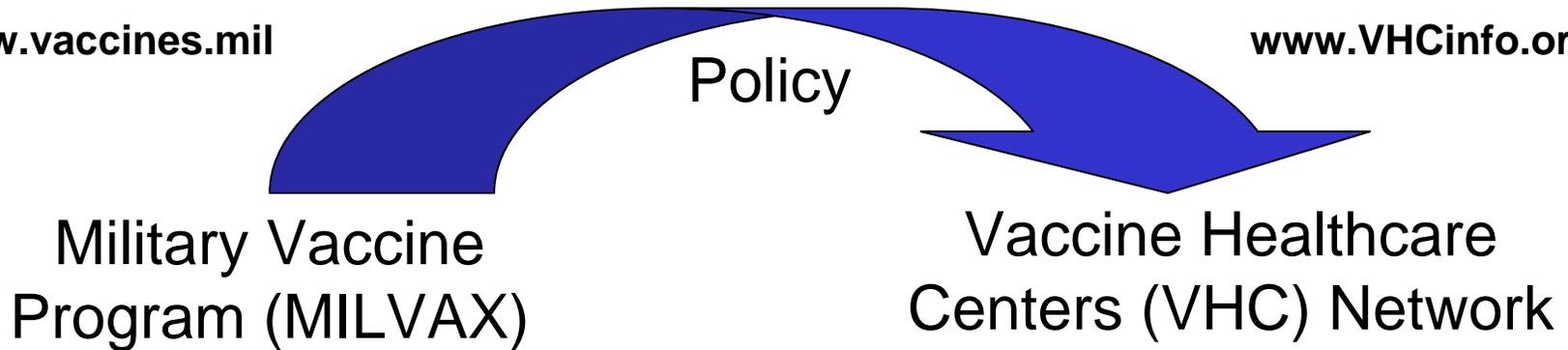
DoD Vaccine Program

Science – Quality – Confidence – Care



www.vaccines.mil

www.VHCinfo.org



Policy

Military Vaccine Program (MILVAX)

Vaccine Healthcare Centers (VHC) Network

Policy & Clinical Practice Improvements

Clinical Consultations, Investigations, Advocacy,

VAERS Support

Clinical

- Centralized location
- Policy
- Program administration
- Program logistics
- Regional sites w/dense Active Duty
- Vaccine safety surveillance/research
- Patient/provider advocate
- Clinical consultant, registry support



DoD Service Members Beneficiaries and Employees



- Receiving mandatory vaccines as part of employment
- Eligibility for National Vaccine Injury Compensation Program
www.hrsa.gov/vaccinecompensation/
 - **IF, vaccine is part of childhood mandatory vaccine schedule**
 - Information about this program included in new Joint Regulations
 - Support needs: preparation of comprehensive clinical summaries needed for VICP applications if requested? What are competencies?
- **Challenges for such evaluations**
 - How to sort out question of multiple vaccines: usual in DoD
 - *EXAMPLE of New Clinical Immunology Concerns: vaccinia is a powerful TH1 immune adjuvant – what are the dangers of early diphtheria-tetanus immunization with pertussis in the context of vaccinia adjuvant effects? Should they be mixed?*
 - Recognition of possible rare adverse events
 - *Example: thrombocytopenia after MMR – does it occur in adults?*



MILVAX with Regional Analysts

VHC Network with Regional Sites

Global Outreach Logistic & Clinical Services



- **Develop the needed infrastructure for global support of mandatory vaccine programs:** education, consultation, availability, problem solving
 - New program launch and implementation of policy
 - Multi-site rare adverse events surveillance & definitions assistance
 - Supports future clinical vaccine safety research; phenotype → genotype
- **VAERS education, program quality improvement**
 - Facilitate needed health care worker culture changes
 - Standards for minimum quality: outreach education
- **Regional lines of referral for complex VAERS**
 - Multidisciplinary case management and education support services coordination, feedback to front lines for care quality improvements, ↓ practice variances
- **Facilitate mass immunization programs as needed**
 - Rapid feedback infrastructure on lessons learned, issues in need of resolution, dissemination of changes
 - Evolving clinical guidelines rapidly based on lessons learned



Challenges in Vaccines Military Allergy-Immunology



- **Restart of mandatory anthrax vaccine immunizations**
 - Limited to those deploying to high threat areas
 - Package insert 2002 version – awaiting reanalysis of data regarding dose reduction route change study → example of evolving data post marketing-licensure: “knowledge changing as science evolves”
 - Pregnancy and anthrax vaccine exposure question in MILVAX trifold
 - Systemic prolonged side effects/adverse events still being defined
 - Long term complications of large local reactions: neuropathy
 - Additional data regarding gender differences
 - *Not just for local but also systemic reactions*
 - *How do we best support high responder-low responder differences*
- **New Vaccines**
 - Tdap for adults: caution with high responders, neurologic AEs?
 - Human papilloma virus vaccine: new mixtures



Educational Products at www.anthrax.mil

Trifold

- 1. Powerpoint Briefing Slides
- 2. Watch On-line Multi-Media Briefings
<http://anthrax.digiscript.com/anthrax/index.html>
- 3. Questions and Answers
- 4. Service Messages

WHAT YOU NEED TO KNOW ABOUT ANTHRAX VACCINE



For more information:

www.anthrax.mil

www.vaccines.mil

vaccines@amedd.army.mil

877-GET-VACC,

DSN 761-4245

VHC: Ongoing Commitment to Life-Cycle Vaccine Safety Surveillance

Evolving Case Definitions for More Severe Side Effects

2007
> 1.5 million Vaccinated
> 5.9 million Doses



Vaccinia Safety Enhancement With Increased Surveillance



- **1.1 million vaccinees**
- **Screening standardized**
 - Eczema vaccinatum risk, etc.
- **Outcomes of program**
 - Significant reduction in historically predicted serious adverse events
 - Progressive vaccinia: 0
 - Eczema vaccinatum: 1

(10-15/million historically)
- **“New-Old” Myopericarditis**
 - Anticipated in pre-launch training program, added chest pain to diary
 - Centralized case management
 - Registry process evolved for longer clinical follow-up and support-consultation services
 - Quality improvement to VAERS

Triservice/DOD
Expert Consensus
**Clinical Guidelines
For Post Vaccinia
Myopericarditis**

Coordinated by VHC Network
Based On
In-Depth Case Investigations &
Causality Assessments
Access www.VHCinfo.org for
complete tables plus
algorithm documents
Iterative Updates With Case Reviews
2007 Revision underway



Smallpox Vaccine Myopericarditis & Beyond



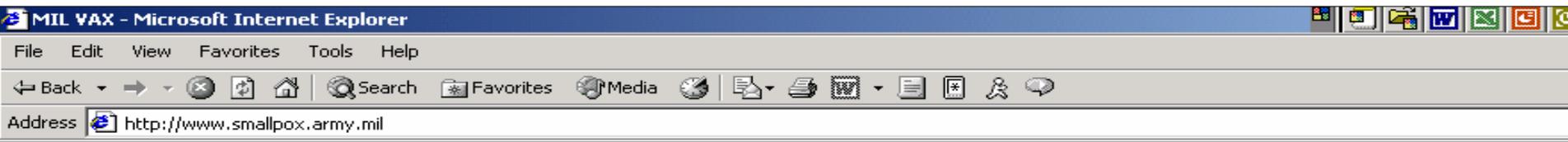
- **> 1.1 million vaccinated**
 - Myopericarditis risk at ~1:6-7K but actual risk may be higher
 - *Recurrence spontaneously: cases under investigation*
 - *Deaths: 2 “possible” associations both with evidence of eosinophilic myopericarditis on autopsy*
 - *Evolving clinical guidelines for diagnosis and treatment based on ongoing review of case based clinical experience*
- **Other new adverse events case definitions in progress**
 - Example: new onset acute urticaria, angioedema evolving to chronic disease after live virus vaccines
 - Labor intensive, slow process of in depth causality assessments with
 - *Outcomes follow up*
 - *Assistance with diagnosis and treatment*
 - *Iterative case review to refine case definitions (WHO criteria)*



Military Immunization Leaders' Course Executive Overview



DoD Smallpox Website – www.smallpox.mil



<p>THE DANGER</p> <p>THE VACCINE</p> <p>THE PRIORITY</p> <p>THE STRATEGY</p>		<h2>SMALLPOX VACCINATION PROGRAM</h2>		contact us
		<p>adverse event info</p>		
		<p>education toolkit</p>		
		<p>resource center</p>		

- Smallpox is contagious, deadly, and would disrupt military missions.
- Smallpox vaccine prevents smallpox and we will use it carefully.
- Preserving the health and safety of our people is our top concern.
- The Defense Department's smallpox vaccination program is part of our national strategy to safeguard Americans against smallpox attack.

[DoD Begins Smallpox Vaccination Program](#) [SVP Online Proficiency Training](#) [DoD's Smallpox Vaccination Lessons Learned](#) [MM](#)

[http:// www.smallpox.mil](http://www.smallpox.mil)
[http:// www.vaccines.mil](http://www.vaccines.mil)

Last Updated 01/24/2003



Immunization Tool Kit Learning Management System (LMS): www.VHCINFO.org

Supporting
Immunization University

www.vaccines.mil

Meeting Requirements
Competency &
Quality STDs
New Joint Regulations



Adult, Military
and Childhood
Immunizations

IMMUNE READINESS LMS

Version 1.3

Wednesday, September 22

Welcome

John D. Grabenstein
Learner

Logout

- Welcome
- About Immune Readiness
- Goals and Objectives
- Target Audience

Courses

- Other Resources Under Development
- Credit Information
- Transcripts
- Profile
- Change Password
- Acknowledgements
- Disclaimer
- VHC (Vaccine Healthcare Center)
- Privacy

[Back](#) [Contact](#)

AVAILABLE COURSES

Anthrax	Haemophilus Influenzae type b (HIB)	Hepatitis A
Hepatitis B - Advanced	Hepatitis B - General	Influenza
Introduction to Vaccination	Japanese Encephalitis	Measles
Meningococcal	Mumps	Pneumococcal
Polio	Rabies	Rubella
Smallpox Disease	Smallpox Administration	Smallpox Vaccine
Typhoid	Vaccine Storage and Handling	Varicella
Yellow Fever		

Take a Course

Requests for
Biodefense Modules



Annual Updates
DEVELOPED AND DISTRIBUTED BY



2007
Edition
Pending

VETER REED NATIONAL
HEALTHCARE CENTER
REVISED OCTOBER 2003





Address <http://www.vaccines.mil/>

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MIL VAX Search

Friday, January 13, 2006 2:05:29 PM ET quick reference | contact us | site map

- Vaccines - Diseases
- Resource Center
- Education Toolkit
- Adverse Events
- Imz University

FDA Issues Final Order - AVA Safe and Effective, Protects Individuals at High Risk for Anthrax Disease

On 15 December 2005, The Food and Drug Administration (FDA) issued a Final Order with respect to anthrax vaccine adsorbed (AVA).

After review of the comments and finding no additional scientific evidence to alter the proposed categorization, FDA accepts the Panel's recommendation and adopts Category I as the final category for AVA and determines AVA to be safe and effective and not misbranded.

In light of the final order, the department will review program options. The military services will continue anthrax vaccinations as they have since April 2005 on a voluntary basis for eligible servicemembers with the option to refuse.

[more ...](#)

President Announces National Strategy for Pandemic Influenza

ACIP Offers Immunization Strategy to Eliminate Hep B Transmission

The report provides updated recommendations to improve prevention of perinatal and early childhood HBV transmission, including implementation of universal infant vaccination beginning at birth, and to increase vaccine coverage among previously unvaccinated children and adolescents.

[more...](#)

Recommended Adult Immunization Schedule -- United States, October 2005--September 2006

The Advisory Committee on Immunization Practices (ACIP) annually reviews the recommended Adult Immunization Schedule to ensure that the schedule reflects current recommendations for the use of licensed vaccines. In June 2005, ACIP approved the Adult Immunization Schedule for October 2005--September 2006. This schedule has also been approved by the American Academy of Family Physicians and the American College of Obstetricians and Gynecologists.

All About Japanese Encephalitis

Have fun learning about vaccines and vaccine preventable diseases with our monthly crossword puzzle, brought to you by Immunization University.

[more...](#)

DoD Pandemic Influenza Resources

Pandemic influenza is a global outbreak of disease that occurs when a new influenza A virus appears in humans, causes





Quality Improvement



- **Educational outreach to enhance understanding of vaccine adverse events reporting system submissions**
 - Immunization University with emphasis on VAERS
 - Training materials distributed at time of immunization
 - Support services to complete VAERS with causality assessments
- **Ongoing challenges**
 - Medical school and residency training limited beyond vaccine schedules
 - During outreach training, misconceptions and reasons for reporting frequently confused by providers and healthcare workers
- **Awareness of Vaccine Injury Compensation Program**
 - Limited among most health care workers and vaccinees
 - Causality assessments and documentation critical to process



Defense Medical Surveillance System (DMSS)



- **Highlighted by IOM as a valuable resource**
 - Hospitalizations and outpatient visit diagnostic codes since ~2000
 - *Earlier years: coding quality and use of system variable*
 - Immunization registry
 - *Comprehensive for anthrax and smallpox vaccines, then influenza*
 - *In future: anticipated improvements in comprehensive vaccine recording for all services*
 - *Air Force more comprehensive since 2000*
- **Resource for epidemiological studies**
 - Limited ability to validate diagnostic codes
 - Methodologies with healthy warrior effects raise questions
 - *Gender, ethnic differences have not been adequately considered in past analyses and require further consideration*
- **Does the MHS need a VSD equivalent?**
 - Improve safety surveillance for new complex vaccine mixtures



Vaccine Safety Questions

DoD Clinical Vaccine Call Center

ASKVHC Written Inquires, Case Reviews



Rare Adverse Events Questions

- Hair loss & hepatitis B/vaccines
- Bleeding disorder
- Diabetes
- Chronic fatigue syndrome
- Neuropathy
- Arthritis
- Autoimmunity
- Type 1 adult onset diabetes
- Chest pain after influenza
- Pemphigus & vaccines
- Immediate hypersensitivity
- Thrombocytopenia

- Headaches, new onset, reproducible
- Muscle and joint pains that persist
- Autoimmune hepatitis

Risk factors?

- Multiple vaccines
- Genetic risk
- Gender
- Ethnicity
- Atopy
- Others

Clinicians as well as patients seeking clinical not epidemiological information with frequently complex scenarios.

Challenge: rapidly evolving clinical guidelines, evidence to validate the guidelines.

Relative/Absolute Contraindications

- Management strategies?

Side Effects/Adverse Events

- Strategies for treatment & prophylaxis



VHC Network Goals

*“Caring for Those Who Serve:
Before & After Immunizations”*



- **Vaccine Clinical Support & Consultation Services**
 - Adverse events & efficacy case management, medical exemptions
- **Vaccine Safety**
 - Surveillance, reporting & adverse events registry, long term follow-up
- **Immunization Education**
 - For Health Care Workers & Service Members, Beneficiaries, DoD, etc.
 - Integrate with Immunization University
- **Support for Research**
 - Clinical focus, post-licensure, to “enhances vaccine safety, efficacy & acceptability”
 - Adult military vaccine related gaps

- **Advocacy**

- For quality immunization healthcare delivery
- For care of complex AE’s



Network of MTF-linked Sites
NOT service specific but regional

Outreach & Support 24/7
Clinical Call Center
Secure Consultative E-mail



Research Commitments (Partial List)

Built on VHC Network Platform



Protocols* <i>Partial Listing</i>	Collaborators <i>WRAMC/NARMC+</i>	Funding <i>Extramural</i>
Smallpox Vaccine Myopericarditis Immunogenetics*	CDC-CISA/Kaiser U of Washington Molecular Immunology	CDC-CISA NIAID/NIH
Anthrax Vaccine Adverse Events - Immunogenetics*	U of Oklahoma Rheum-Immunology	NIAID/NIH
Anthrax Vaccine & Pemphigus Antibodies*	U of Pennsylvania Immunodermatology	NIAID/NIH
Anthrax Vaccine Side Effects Tripler Data Review*	MRMC/Ft Detrick	MRMC
Half Dose Flu Vaccine Study* (To be finalized this year)	CDC/Civ Academic/ NIAID/ USAMMDA	AMEDD/CDC/ NIAID/USAMMDA
Vaccine Telemedicine Technology Development*	VHC-Allergy-Immunol Department, WRAMC	P8 Grants, MRMC
VAERS KAB Survey*	VHC-CDC	CDC-NIP
Exercise Exacerbated Prolonged Myalgia/Arthralgia/Fatigue	VHC-Georgetown-U of MD Collaborative Grant Applic	Extramural to USAMRIID May 2007

*IRB/HUC Approved



MILVAX Mission



Joe Raedle / Getty Images

1-1

What have you done for them today?





End of Briefing

The views expressed in this presentation are those of the author and do not reflect the official policy of the Department of Army, Department of Defense, or US Government.

Questions?



References Based on VHC Network Enhanced VAERS



1. Arness MK, Eckart RE, Love SS, Atwood JE, Wells TS, Engler RJ, Collins LC, Ludwig SL, Riddle JR, Grabenstein JD, Tornberg DN. Myopericarditis following smallpox vaccination. *Am J Epidemiol.* 2004 Oct 1;160(7):642-51.
2. Wollenberg A, Engler R. Smallpox, vaccination and adverse reactions to smallpox vaccine. *Curr Opin Allergy Clin Immunol.* 2004 Aug;4(4):271-5. Review.
3. Eckart RE, Love SS, Atwood JE, Arness MK, Cassimatis DC, Campbell CL, Boyd SY, Murphy JG, Swerdlow DL, Collins LC, Riddle JR, Tornberg DN, Grabenstein JD, Engler RJ; Department of Defense Smallpox Vaccination Clinical Evaluation Team. Incidence and follow-up of inflammatory cardiac complications after smallpox vaccination. *J Am Coll Cardiol.* 2004 Jul 7;44(1):201-5. Review.
4. Cassimatis DC, Atwood JE, Engler RM, Linz PE, Grabenstein JD, Vernalis MN. Smallpox vaccination and myopericarditis: a clinical review. *J Am Coll Cardiol.* 2004 May 5;43(9):1503-10. Review.

NOTE: Myopericarditis is an autoimmune phenomenon with an undefined future risk from revaccination or other environmental exposures; unanswered research questions require LONG TERM follow up – ongoing challenge to manage organizational barriers