



Smallpox Bibliography September 2004

1: Am J Emerg Med. 2004 Jul;22(4):267-9.

Mass smallpox immunization program in a deployed military setting.

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A prospective, observational study of immunizing over 6,000 active-duty troops against smallpox in a 4-week time period was conducted. It focused on the complications of the vaccine and lost workdays. Comparison is made to the complication rates of earlier smallpox immunization programs. In direct response to elevated bioterrorism concerns, the United States military and civilian first-responders have begun a mass smallpox immunization program. This article reviews the experience with implementing such a program in a forward-deployed location while maintaining military readiness. The objectives were to assess the impact of a mass smallpox immunization program on operations in a forward-deployed military setting and to comment on lessons learned in the screening and immunization process. From January 16, 2003 through February 11, 2003 6,002 members of the United States military were immunized in a forward-deployed location. Information was obtained using data from the Air Force Complete Information Tracking Application (AFCITA) and the Global Expeditionary Medical System (GEMS) we plan to calculate the following Main Outcome Measures data: (1)Percentage of individuals eligible to receive the vaccine, (2) Vaccine take rate by CDC criteria, (3) Number of serious complications, (4) Number of life-threatening complications, and (5) Number of manpower days lost as a complication of the vaccine. A total of 6,739 individuals were screened for vaccination with 6,348 (94%) remaining eligible for the vaccine. The "take" rate for the vaccine was 98.6% as per Centers for Disease Control and Prevention (CDC) criteria. The immunization program produced an additional 156 medical visits (2.6% of patients required one visit). A total of 0.55% of immunized individuals lost one or more work days. In conclusion, a mass smallpox vaccination program can be effectively administered in a forward-deployed military setting despite high tempo military operations with minimal operational impact.

PMID: 15258865 [PubMed - indexed for MEDLINE]

2: Commun Dis Public Health. 2004 Jun; 7(2): 145-50.

Why, which, how, who, when? A personal view of smallpox vaccination for the 2000s.

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The uncertainty about the extent of proliferation of smallpox virus holdings since the early 1990s, and particularly whether terrorist groups or so-called rogue states might now hold the virus, confronts potential target countries with a continuing dilemma. An increasingly large majority of their populations have never been vaccinated, and those who have been vaccinated may have become susceptible to smallpox again. Yet recent attempts by the United States and other governments to persuade large numbers of key personnel and others to accept vaccination have at least partially failed and a different long-term strategy is needed. This strategy should be based on surveillance of rash illnesses, improved public education, more refined contingency planning and a new approach to smallpox vaccination. The last should if possible be based on cell-grown, less reactogenic vaccines, even though it may be some years before these can become available. Meanwhile this article examines other expedients including the use of existing lymph vaccines.

Publication Types:

Review
Review, Tutorial

PMID: 15259419 [PubMed - indexed for MEDLINE]

3: Dermatol Clin. 2004 Jul; 22(3): 275-89, vi.

Smallpox: vaccine reactions and contraindications.

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Concern regarding the use of smallpox for bioterrorism has led to the reintroduction of smallpox vaccination. The historic background leading to protective methods against smallpox disease, the adverse reactions and contraindications associated with vaccination, and the ongoing development of potentially safer smallpox vaccines are reviewed here.

Publication Types:

Review
Review, Tutorial

PMID: 15207309 [PubMed - indexed for MEDLINE]

Library Program Office
Office of Information
Veterans Health Administration

4: Dermatol Clin. 2004 Jul;22(3):263-74, vi.

Smallpox: the basics.

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Variola major is the causative agent of smallpox, a severe disease that was arguably one of the most serious human pathogens in recorded history. Humans are the only known reservoir of variola major; no known animal or insect reservoirs have been identified. Thus, after eradication of smallpox through a global immunization effort, this incredibly lethal scourge was eliminated from all corners of the globe. Despite the total eradication of naturally occurring smallpox, there are still stockpiles of smallpox virus maintained in the United States and the former Soviet Union. Unfortunately, it is impossible to know if all smallpox stocks have been accounted for or whether unknown or unreported stocks of smallpox may still exist. In the age of genetic engineering, these viruses could theoretically be modified to increase their virulence to the levels associated with smallpox itself.

Publication Types:

Review

Review, Tutorial

PMID: 15207308 [PubMed - indexed for MEDLINE]

5: Emerg Infect Dis. 2004 May;10(5):961-2; discussion 962.

Smallpox vaccination and adverse cardiac events.

Upfal MJ, Cinti S.

Publication Types:

Historical Article

Letter

PMID: 15216847 [PubMed - indexed for MEDLINE]

6: Emerg Infect Dis. 2004 May;10(5):960-1.

The 1947 smallpox vaccination campaign in New York City, revisited.

Sepkowitz KA.

Publication Types:

Historical Article

Letter

PMID: 15216846 [PubMed - indexed for MEDLINE]

7: Emerg Infect Dis. 2004 May;10(5):917-20.

Mass smallpox vaccination and cardiac deaths, New York City, 1947.

Thorpe LE, Mostashari F, Karpati AM, Schwartz SP, Manning SE, Marx MA, Frieden TR.

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In April 1947, during a smallpox outbreak in New York City (NYC), more than 6 million people were vaccinated. To determine whether vaccination increased cardiac death, we reviewed NYC death certificates for comparable periods in 1946, 1947, and 1948 (N = 81,529) and calculated adjusted relative death rates for the postvaccination period. No increases in cardiac deaths were observed.

Publication Types:
Historical Article

PMID: 15200831 [PubMed - indexed for MEDLINE]

8: Emerg Infect Dis. 2004 May;10(5):832-41.

Ring vaccination and smallpox control.

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We present a stochastic model for the spread of smallpox after a small number of index cases are introduced into a susceptible population. The model describes a branching process for the spread of the infection and the effects of intervention measures. We discuss scenarios in which ring vaccination of direct contacts of infected persons is sufficient to contain an epidemic. Ring vaccination can be successful if infectious cases are rapidly diagnosed. However, because of the inherent stochastic nature of epidemic outbreaks, both the size and duration of contained outbreaks are highly variable. Intervention requirements depend on the basic reproduction number (R_0), for which different estimates exist. When faced with the decision of whether to rely on ring vaccination, the public health community should be aware that an epidemic might take time to subside even for an eventually successful intervention strategy.

PMID: 15200816 [PubMed - indexed for MEDLINE]

9: J Clin Microbiol. 2004 May;42(5):1940-6.

Real-time PCR system for detection of orthopoxviruses and simultaneous identification of smallpox virus.

Olson VA, Laue T, Laker MT, Babkin IV, Drosten C, Shchelkunov SN, Niedrig M, Damon IK, Meyer H.

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A screening assay for real-time LightCycler (Roche Applied Science, Mannheim, Germany) PCR identification of smallpox virus DNA was developed and compiled in a kit system under good manufacturing practice conditions with standardized reagents. In search of a sequence region unique to smallpox virus, the nucleotide sequence of the 14-kDa fusion protein gene of each of 14 variola virus isolates of the Russian World Health Organization smallpox virus repository was determined and compared to published sequences. PCR primers were designed to detect all Eurasian-African species of the genus ORTHOPOXVIRUS: A single nucleotide mismatch resulting in a unique amino acid substitution in smallpox virus was used to design a hybridization probe pair with a specific sensor probe that allows reliable differentiation of smallpox virus from other orthopoxviruses by melting-curve analysis. The applicability was demonstrated by successful amplification of 120 strains belonging to the orthopoxvirus species variola, vaccinia, camelpox, mousepox, cowpox, and monkeypox virus. The melting temperatures (T(m)s) determined for 46 strains of variola virus (T(m)s, 55.9 to 57.8 degrees C) differed significantly (P = 0.005) from those obtained for 11 strains of vaccinia virus (T(m)s, 61.7 to 62.7 degrees C), 15 strains of monkeypox virus (T(m)s, 61.9 to 62.2 degrees C), 40 strains of cowpox virus (T(m)s, 61.3 to 63.7 degrees C), 8 strains of mousepox virus (T(m), 61.9 degrees C), and 8 strains of camelpox virus (T(m)s, 64.0 to 65.0 degrees C). As most of the smallpox virus samples were derived from infected cell cultures and tissues, smallpox virus DNA could be detected in a background of human DNA. By applying probit regression analysis, the analytical sensitivity was determined to be 4 copies of smallpox virus target DNA per sample. The DNAs of several human herpesviruses as well as poxviruses other than orthopoxviruses were not detected by this method. The assay proved to be a reliable technique for the detection of orthopoxviruses, with the advantage that it can simultaneously identify variola virus.

Publication Types:
Evaluation Studies

PMID: 15131152 [PubMed - indexed for MEDLINE]

10: J Exp Med. 2004 Jun 7;199(11):1585-93.

Distinct time effects of vaccination on long-term proliferative and IFN-gamma-producing T cell memory to smallpox in humans.

Combadiere B, Boissonnas A, Carcelain G, Lefranc E, Samri A, Bricaire F, Debre P, Autran B.

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Residual immunity to the smallpox virus raises key questions about the persistence of long-term immune memory in the absence of antigen, since vaccination ended in 1980. IFN-gamma-producing effector-memory and proliferative memory T cells were compared in 79 vaccinees 13-25 yr after their last immunization and in unvaccinated individuals. Only 20% of the vaccinees displayed both immediate IFN-gamma-producing effector-memory responses and proliferative memory responses at 6 d; 52.5% showed only proliferative responses; and 27.5% had no detectable vaccinia-specific responses at all. Both responses were mediated by CD4 and CD8 T cells. The vaccinia-specific IFN-gamma-producing cells were composed mainly of CD4Pos CD45RANeg CD11aHi CD27Pos and CCR7Neg T cells. Their frequency was low but could be expanded in vitro within 7 d. Time since first immunization affected their persistence: they vanished 45 yr after priming, but proliferative responses remained detectable. The number of recalls did not affect the persistence of residual effector-memory T cells. Programmed revaccination boosted both IFN-gamma and proliferative responses within 2 mo of recall, even in vaccinees with previously undetectable residual effector-memory cells. Such long-term maintenance of vaccinia-specific immune memory in the absence of smallpox virus modifies our understanding of the mechanism of persistence of long-term memory to poxviruses and challenges vaccination strategies.

PMID: 15184506 [PubMed - indexed for MEDLINE]

11: Methods Mol Biol. 2004;269:243-66.

Monitoring of human immunological responses to vaccinia virus.

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For the last 30 yr, interest in vaccinia virus immune monitoring has focused on the use of the vaccinia virus as a recombinant vaccine vector and the potential detrimental effect of antivector immunity on subsequent vaccination with a recombinant vaccinia virus. However, interest in this area has intensified after the publication of reports suggesting that smallpox may be a major pathogen selected for bioterrorist activities. Owing to the unacceptably high incidence of complications induced by previous effective smallpox vaccine strains, alternative safer strains (e.g., modified vaccinia Ankara [MVA]) are being assessed for their antigenicity in clinical trials. The exact immune effector mechanism responsible for vaccine-induced protection to smallpox infection has not been fully elucidated, although it is believed that neutralizing antibody plays a major role. This chapter describes a simple enzyme-linked immunosorbent assay (ELISA) to quantify vaccinia virus antibody titer. Additionally, to define serum-neutralizing activity, both a classical plaque reduction assay and a high-throughput 96-well plate method based on reduction of recombinant vaccinia virus expressed beta-galactosidase is described. Furthermore, details are given for a T-cell proliferation assay, primarily for monitoring T-helper CD4 activity and an enzyme-linked immunospot (ELISPOT) assay for CD8 analysis. The use of reliable immunological assays is vital in assessing the potential efficacy of new vaccines to protect against smallpox infection.

Publication Types:

Review

Review, Tutorial

PMID: 15114020 [PubMed - indexed for MEDLINE]

12: Mil Med. 2004 Jun;169(6):455-60.

Implementing a smallpox vaccination program aboard an aircraft carrier.

Apple J, Hare P, Crerar C, Walker E, Wilson J, Brown C, Moses K, Hendrickson T, Field D, Hoffman F, Pedrus P, Miller J, Smith B.

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OBJECTIVE: To determine the feasibility of implementing a smallpox vaccination program aboard an aircraft carrier in conjunction with anthrax vaccination.
METHODS: Retrospective review of smallpox vaccination program conducted from January 17, 2003 to February 19, 2003. Morbidity and loss of manpower were the major endpoints. **RESULTS:** There were 5,204 sailors available for vaccination. There were 243 (4.7%) medical exemptions and 24 administrative exemptions. During the program, 4,931 sailors were vaccinated. There were five reportable complications. Three sailors had autoinoculation, one sailor had localized cellulitis, and one patient had a positive beta human chorionic gonadotropin during vaccination. None of the complications required medical evacuation. Only two sailors required time off from duty. **CONCLUSIONS:** Smallpox vaccination can be accomplished rapidly and safely aboard an aircraft carrier. There was not an increase in adverse events compared to historical data despite the close-quarter conditions. Smallpox and anthrax vaccinations can be completed simultaneously with minimal morbidity.

PMID: 15281676 [PubMed - indexed for MEDLINE]

13: Prehospital Disaster Med. 2003 Oct-Dec;18(4):313-20.

Standardized emergency management system and response to a smallpox emergency.

Kim-Farley RJ, Celentano JT, Gunter C, Jones JW, Stone RA, Aller RD, Mascola L, Grigsby SF, Fielding JE.

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The smallpox virus is a high-priority, Category-A agent that poses a global, terrorism security risk because it: (1) easily can be disseminated and transmitted from person to person; (2) results in high mortality rates and has the potential for a major public health impact; (3) might cause public panic and social disruption; and (4) requires special action for public health preparedness. In recognition of this risk, the Los Angeles County Department of Health Services (LAC-DHS) developed the Smallpox Preparedness, Response, and Recovery Plan for LAC to prepare for the possibility of an outbreak of smallpox. A unique feature of the LAC-DHS plan is its explicit use of the Standardized

Emergency Management System (SEMS) framework for detailing the functions needed to respond to a smallpox emergency. The SEMS includes the Incident Command System (ICS) structure (management, operations, planning/intelligence, logistics, and finance/administration), the mutual-aid system, and the multi/interagency coordination required during a smallpox emergency. Management for incident command includes setting objectives and priorities, information (risk communications), safety, and liaison. Operations includes control and containment of a smallpox outbreak including ring vaccination, mass vaccination, adverse events monitoring and assessment, management of confirmed and suspected smallpox cases, contact tracing, active surveillance teams and enhanced hospital-based surveillance, and decontamination. Planning/intelligence functions include developing the incident action plan, epidemiological investigation and analysis of smallpox cases, and epidemiological assessment of the vaccination coverage status of populations at risk. Logistics functions include receiving, handling, inventorying, and distributing smallpox vaccine and vaccination clinic supplies; personnel; transportation; communications; and health care of personnel. Finally, finance/administration functions include monitoring costs related to the smallpox emergency, procurement, and administrative aspects that are not handled by other functional divisions of incident command systems. The plan was developed and is under frequent review by the LAC-DHS Smallpox Planning Working Group, and is reviewed periodically by the LAC Bioterrorism Advisory Committee, and draws upon the Smallpox Response Plan and Guidelines of the Centers for Disease Control and Prevention (CDC) and recommendations of the Advisory Committee on Immunization Practices (ACIP). The Smallpox Preparedness, Response, and Recovery Plan, with its SEMS framework and ICS structure, now is serving as a model for the development of LAC-DHS plans for responses to other terrorist or natural-outbreak responses.

PMID: 15310043 [PubMed - indexed for MEDLINE]

14: Proc Natl Acad Sci U S A. 2004 Aug 3;101(31):11178-92. Epub 2004 Jul 12.

Comment in:

Proc Natl Acad Sci U S A. 2004 Aug 3;101(31):11177.

Discovery of antivirals against smallpox.

Harrison SC, Alberts B, Ehrenfeld E, Enquist L, Fineberg H, McKnight SL, Moss B, O'Donnell M, Ploegh H, Schmid SL, Walter KP, Theriot J.

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Publication Types:

Review

Review Literature

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