



## Smallpox Bibliography July 2004

1: BMC Public Health. 2003 Jun 11;3(1):20.

Attitudes of healthcare workers in U.S. hospitals regarding smallpox vaccination.

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**BACKGROUND:** The United States is implementing plans to immunize 500,000 hospital-based healthcare workers against smallpox. Vaccination is voluntary, and it is unknown what factors drive vaccine acceptance. This study's aims were to estimate the proportion of workers willing to accept vaccination and to identify factors likely to influence their decisions. **METHODS:** The survey was conducted among physicians, nurses, and others working primarily in emergency departments or intensive care units at 21 acute-care hospitals in 10 states during the two weeks before the U.S. national immunization program for healthcare workers was announced in December 2002. Of the questionnaires distributed, 1,165 were returned, for a response rate of 81%. The data were analyzed by logistic regression and were adjusted for clustering within hospital and for different number of responses per hospital, using generalized linear mixed models and SAS's NL MIXED procedure. **RESULTS:** Sixty-one percent of respondents said they would definitely or probably be vaccinated, while 39% were undecided or inclined against it. Fifty-three percent rated the risk of a bioterrorist attack using smallpox in the United States in the next two years as either intermediate or high. Forty-seven percent did not feel well-informed about the risks and benefits of vaccination. Principal concerns were adverse reactions and the risk of transmitting vaccinia. In multivariate analysis, four variables were associated with willingness to be vaccinated: perceived risk of an attack, self-assessed knowledge about smallpox vaccination, self-assessed previous smallpox vaccination status, and gender. **CONCLUSIONS:** The success of smallpox vaccination efforts will ultimately depend on the relative weight in people's minds of the risk of vaccine adverse events compared with the risk of being exposed to the disease. Although more than half of the respondents thought the likelihood of a bioterrorist smallpox attack was intermediate or high, less than 10% of the group slated for vaccination has actually accepted it at this time. Unless new information about the threat of a smallpox attack becomes available, healthcare workers' perceptions of the vaccine's risks will likely continue to drive their ongoing decisions about smallpox vaccination.

PMID: 12801426 [PubMed - indexed for MEDLINE]

2: FDA Consum. 2004 May-Jun; 38(3):3.

Side effects of smallpox vaccine.

[No authors listed]

Publication Types:  
News

PMID: 15218825 [PubMed - indexed for MEDLINE]

3: J Am Coll Cardiol. 2004 May 5; 43(9):1503-10.

Smallpox vaccination and myopericarditis: a clinical review.

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Smallpox is a devastating viral illness that was eradicated after an aggressive, widespread vaccination campaign. Routine U.S. childhood vaccinations ended in 1972, and routine military vaccinations ended in 1990. Recently, the threat of bioterrorist use of smallpox has revived the need for vaccination. Over 450,000 U.S. military personnel received the vaccination between December 2002 and June 2003, with rates of non-cardiac complications at or below historical levels. The rate of cardiac complications, however, has been higher than expected, with two confirmed cases and over 50 probable cases of myopericarditis after vaccination reported to the Department of Defense Smallpox Vaccination Program. The practicing physician should use the history and physical, electrocardiogram, and cardiac biomarkers in the initial evaluation of a post-vaccination patient with chest pain. Echocardiogram, cardiac catheterization, magnetic resonance imaging, nuclear imaging, and cardiac biopsy may be of use in further workup. Treatment is with non-steroidal anti-inflammatory agents, four to six weeks of limited exertion, and conventional heart failure treatment as necessary. Immune suppressant therapy with steroids may be uniquely beneficial in myopericarditis related to smallpox vaccination, compared with other types of myopericarditis. If a widespread vaccination program is undertaken in the future, many more cases of post-vaccinial myopericarditis could be seen. Practicing physicians should be aware that smallpox vaccine-associated myopericarditis is a real entity, and symptoms after vaccination should be appropriately evaluated, treated if necessary, and reported to the Vaccine Adverse Events Reporting System.

Publication Types:  
Review  
Review Literature

PMID: 15120802 [PubMed - indexed for MEDLINE]

4: J Biol Chem. 2004 Jun 11;279(24):25838-48. Epub 2004 Apr 07.

Biochemical and functional analysis of smallpox growth factor (SPGF) and anti-SPGF monoclonal antibodies.

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Variola, the causative agent of smallpox, is a highly infectious double-stranded DNA virus of the orthopox genus that replicates within the cytoplasm of infected cells. For unknown reasons prominent skin manifestations, including "pox," mark the course of this systemic human disease. Here we characterized smallpox growth factor (SPGF), a protein containing an epidermal growth factor (EGF)-like domain that is conserved among orthopox viral genomes, and investigated its possible mechanistic link. We show that after recombinant expression, refolding, and purification, the EGF domain of SPGF binds exclusively to the broadly expressed cellular receptor, erb-B1 (EGF receptor), with subnanomolar affinity, stimulating the growth of primary human keratinocytes and fibroblasts. High affinity monoclonal antibodies specific for SPGF reveal in vivo immunoprotection in a murine vaccinia pneumonia model by a mechanism distinct from viral neutralization. These findings suggest that blockade of pathogenic factor actions, in general, may be advantageous to the infected host.

PMID: 15070899 [PubMed - indexed for MEDLINE]

5: J Epidemiol. 2004 Mar;14(2):41-50.

Modeling for a smallpox-vaccination policy against possible bioterrorism in Japan: the impact of long-lasting vaccinal immunity.

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**BACKGROUND:** There has been concern that variola virus might be held clandestinely elsewhere. Through constructing mathematical model based on the detailed epidemiologic data, we focused on simulating the various possible scenarios arising from a bioterrorist attack whereby smallpox virus was introduced into Japan, and sought to develop the most effective way of nationwide vaccination policy based on the theory of residual immunity. **METHOD:** The analysis is based on a deterministic mathematical model which predicted the epidemiologic outcome while simultaneously evaluating the effect of any specified control strategy of the smallpox epidemic. To clarify the required amount of vaccines, we performed mathematical analysis for hypothetical population to acquire herd immunity based on long-lasting vaccinal immunity. **RESULTS:** It is demonstrated that the crude size of the potential epidemic could be greatly affected by possible level of residual immunity. The results also suggest the possibility to develop optimal distribution of nationwide vaccination according to the immune status. The prevalence at 50th day among

population without immunity in our simulation would be approximately 405 times greater than expected population with residual immunity, and required amount of vaccines for equal distribution would be 3.13 times more than optimal distribution. CONCLUSION: The mathematical model formulated could determine the vaccination priority based on the real status of immunity which required much less amount of vaccinations than would be calculated using an equal distribution program. It is therefore crucial to determine the real immunity status of the population via epidemiologic studies.

PMID: 15162977 [PubMed - indexed for MEDLINE]

6: J Epidemiol Community Health. 2004 Apr;58(4):279.

Is smallpox "in" again?

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PMID: 15026436 [PubMed - indexed for MEDLINE]

7: J Gen Intern Med. 2004 Jan;19(1):85-9.

Reasons physicians accepted or declined smallpox vaccine, February through April, 2003.

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From February to April 2003, we performed an e-mail-based survey to assess responses of physicians at Yale University to being offered smallpox vaccine. Of 58 respondents, 3 (5%) had been or intended to be vaccinated. Reasons cited for declining vaccination included: belief that benefits did not outweigh risks (55%), belief that the vaccination program was unnecessary (18%), desire to wait and see what side effects occurred in vaccinees (11%), and worries about compensation or liability (7%). Most (94%) considered risks to themselves, family, or patients in their decision. Only 3% thought a smallpox attack in the next 5 years was likely or very likely. Physicians did not accept the smallpox vaccine because they did not believe the potential benefits were sufficient.

PMID: 14748865 [PubMed - indexed for MEDLINE]

8: Mol Interv. 2003 Aug;3(5):242-7.

D.A. Henderson: acting globally, thinking locally.

Henderson DA.

They had said that it couldn't be done—the worldwide eradication of smallpox. To hear D.A. Henderson tell it, the job of leading the World Health Organization's initiative to conquer the disease in the 1960s and 1970s rather fell into his lap. In fact, he describes each of the posts that he has held with great modesty, beginning with his military service at the Centers for Disease Control and Prevention all the way through his assignments as Dean of Public Health at Johns Hopkins, Associate Director of the Office of Science and Technology Policy in the Executive Office of the President, and more recently as Director of the Office of Public Health Preparedness under Secretary Thompson at the Department of Health and Human Services. Confronted with enormous challenges in terms of public health initiatives, Henderson describes each assignment as a matter of communicating with the people he works with and the people that he serves, and drawing on their insights to devise strategies for accomplishing the task at hand. With bioterrorism posing one of the major public health concerns to face the United States and the world, it's gratifying to know that someone with Henderson's track record and wide-ranging expertise is paying attention and making sure that medical and government officials are preparing to respond to the threat. Again and again, Henderson appears to have the knack for showing up in the right place at the right time with just the right idea.

Publication Types:

Interview

PMID: 14993437 [PubMed - indexed for MEDLINE]

9: *Pediatr Infect Dis J.* 2004 Apr;23(4):332-7.

Preevent vaccination against smallpox: a survey of pediatric emergency health care providers.

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**BACKGROUND:** In January 2003, smallpox vaccinations were offered to health care workers to create hospital-based teams prepared to care for patients with smallpox as part of national bioterrorism preparedness activities. **METHODS:** An anonymous survey of pediatric emergency health care workers was conducted in November and December 2002. Two mailings were sent to physicians, nurses and ancillary staff at five academic pediatric emergency departments in major US cities. We assessed the willingness to receive preevent smallpox vaccine. In addition we measured the prevalence of vaccine contraindications, perceived likelihoods of a local smallpox outbreak or a vaccine-related adverse event and reasons for or against wanting to receive the vaccine. **RESULTS:** Overall 72% of respondents were willing to receive the smallpox vaccine. Individuals who were willing to receive the smallpox vaccine, compared with those not willing, believed a local outbreak was more likely to occur (odds ratio, 1.29; 95% confidence interval, 1.16 to 1.44). One-fifth of respondents reported a contraindication to smallpox vaccine; however, more than half indicated they would still be willing to receive vaccine. Individuals who perceived themselves at high risk for vaccine-related adverse events were less willing to receive the

preevent smallpox vaccine. Self-protection was the most common reason cited for wanting to receive the vaccine. CONCLUSIONS: A majority of pediatric healthcare workers were willing to receive preevent smallpox vaccine before the onset of Phase I of the CDC Smallpox Vaccination Program. A greater understanding of the knowledge, attitudes and beliefs of pediatric health care workers toward preevent smallpox vaccination will assist in the development of future bioterrorism preparedness programs.

PMID: 15071288 [PubMed - indexed for MEDLINE]

10: Vaccine. 2004 Mar 29;22(11-12):1486-93.

Mouse neurotoxicity test for vaccinia-based smallpox vaccines.

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The only US FDA licensed smallpox vaccine, Dryvax, was associated with rare but serious neurological adverse events. After smallpox was eradicated in the United States, mass vaccination ceased in 1971. As counter-bioterrorism/biowarfare measures, new smallpox vaccines are now being investigated. However, there are no established pre-clinical neurotoxicity assays with which to evaluate these new vaccines prior to licensure. Here we report the development and initial characterization of a small animal neurotoxicity assay for vaccinia-based smallpox vaccines using Dryvax virus as a reference vaccine strain and the neuroadapted Western Reserve (WR) strain as a neurotoxic positive control. In neonatally inoculated mice, the WR strain produced significantly greater and more rapid onset of mortality than the Dryvax vaccine reference. Expression of virus antigen in neural cells and infectious virus replication in the brain was also significantly different between the two strains. In addition, the appearance of high titer virus antibody correlated with the clearance of virus from brain. With further validation, this assay incorporating a licensed vaccine reference standard and positive control strain may provide important pre-clinical neurotoxicity data on new vaccinia-based smallpox vaccine strains.

PMID: 15063573 [PubMed - indexed for MEDLINE]