



Smallpox Bibliography June 2004

1: Ann Pharmacother. 2004 Mar;38(3):440-7. Epub 2004 Jan 30.

Smallpox: clinical features, prevention, and management.

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OBJECTIVE: To describe a general overview of smallpox, clinical presentation, diagnosis, adverse events, and management of both pre- and postexposure vaccination. **DATA SOURCES:** Literature was identified by search of MEDLINE (1966-June 2003) and International Pharmaceutical Abstracts (1966-May 2003) databases using the key terms smallpox, bioterrorism, biological warfare, and smallpox vaccine. **STUDY SELECTION AND DATA EXTRACTION:** Articles identified from data sources were evaluated, and relevant information was included in this review. **DATA SYNTHESIS:** Smallpox is spread by human-to-human contact with an infected host and therefore can be contagious. The mortality rate for smallpox is approximately 30%. While the disease was completely eradicated by 1980 with successful use of smallpox vaccine, concern has been raised that smallpox may emerge as a tool of bioterrorism. This concern, combined with the reality of current smallpox vaccination programs in the military and selected civilian populations, mandates a clear understanding of vaccination-related adverse events and contraindications by all healthcare professionals. The vaccine may cause moderate to severe adverse events such as eczema vaccinatum, progressive vaccinia, and generalized vaccinia. **CONCLUSIONS:** The balance between the risks and benefits of mass vaccination in prevention of an epidemic is not clear. The Centers for Disease Control and Prevention has established a guideline for appropriate use of smallpox vaccine in the civilian population.

Publication Types:

Review

Review, Academic

PMID: 14755066 [PubMed - indexed for MEDLINE]

2: APA News J Philos Med. 2003 Spring;2(2):209-12.

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Do healthcare professionals have an obligation to be vaccinated against smallpox?

May T, Silverman RD, Aulisio MP.

Medical College of Wisconsin, USA.

PMID: 15040338 [PubMed - indexed for MEDLINE]

3: BMC Public Health. 2003 Aug 11;3(1):26.

Risks of serious complications and death from smallpox vaccination: a systematic review of the United States experience, 1963-1968.

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BACKGROUND: The United States (US) has re-instituted smallpox vaccinations to prepare for an intentional release of the smallpox virus into the civilian population. In an outbreak, people of all ages will be vaccinated. To prepare for the impact of large-scale ring and mass vaccinations, we conducted a systematic review of the complication and mortality risks of smallpox vaccination. We summarized these risks for post-vaccinial encephalitis, vaccinia necrosum (progressive vaccinia), eczema vaccinatum, generalized vaccinia, and accidental infection (inadvertant autoinoculation). **METHODS:** Using a MEDLINE search strategy, we identified 348 articles, of which seven studies met our inclusion criteria (the number of primary vaccinations and re-vaccinations were reported, sufficient data were provided to calculate complication or case-fatality risks, and comparable case definitions were used). For each complication, we estimated of the complication, death, and case-fatality risks. **RESULTS:** The life-threatening complications of post-vaccinial encephalitis and vaccinia necrosum were at least 3 and 1 per million primary vaccinations, respectively. Twenty-nine percent of vaccinees with post-vaccinial encephalitis died and 15% with vaccinia necrosum died. There were no deaths among vaccinees that developed eczema vaccinatum; however, 2.3% of non-vaccinated contacts with eczema vaccinatum died. Among re-vaccinees, the risk of post-vaccinial encephalitis was reduced 26-fold, the risk of generalized vaccinia was reduced 29-fold, and the risk of eczema vaccinatum was reduced 12-fold. However, the risk reductions of accidental infection and vaccinia necrosum were modest (3.8 and 1.5 fold respectively).

Publication Types:

Review

Review, Academic

PMID: 12911836 [PubMed - indexed for MEDLINE]

4: Clin Infect Dis. 2004 May 1;38(9):1320-2. Epub 2004 Apr 14.

Unintended smallpox vaccination of HIV-1-infected individuals in the United States military.

Tasker SA, Schnepf GA, Lim M, Caraviello HE, Armstrong A, Bavaro M, Agan BK, Delmar J, Aronson N, Wallace MR, Grabenstein JD; US Department of Defense Tri-Service AIDS Clinical Consortium.

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We identified 10 individuals who had undiagnosed human immunodeficiency virus type 1 (HIV-1) infection at the time of smallpox vaccination. Mean CD4 cell count was 483 cells/mm³ (range, 286-751 cells/mm³), and mean log₁₀ plasma HIV-1 RNA load was 4.13 copies/cm³ (range, 2.54-5.16 copies/cm³). All vaccinees (3 primary and 7 repeat) had a normal, robust reaction without complications. Smallpox vaccine was well-tolerated in this small series of HIV-1-infected military personnel.

PMID: 15127348 [PubMed - indexed for MEDLINE]

5: Fertil Steril. 2004 Apr;81(4):1172-3.

Society for assisted reproductive technology position statement on donor suitability of recipients of smallpox vaccine (vaccinia virus).

Practice Committee of the American Society for Reproductive Medicine; Society for Assisted Reproductive Technology.

Practice Committee, American Society for Reproductive Medicine, Birmingham, Alabama, USA.

Although there is presently no definitive evidence linking vaccinia virus transmission through reproductive cells, SART/ASRM accordingly recommends that assisted reproductive technology (ART) practitioners consider deferring donors who have recently received smallpox vaccine or contracted symptomatic vaccinia virus infection through close contact with a vaccine recipient (until after the vaccine or infectious scab has spontaneously separated). Good donor practice further suggests that donors who are not in good health, including those with recent complications from smallpox vaccine, should be similarly deferred.

PMID: 15066500 [PubMed - indexed for MEDLINE]

6: Infect Control Hosp Epidemiol. 2004 Feb;25(2):96.

Semipermeable dressing used to cover smallpox vaccination sites as a cause of skin damage.

Crittenton E, Davis A, Hoffmann KK, Rutala WA, Weber DJ.

Publication Types:

Letter

PMID: 14994930 [PubMed - indexed for MEDLINE]

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

Smallpox vaccination and myopericarditis: a clinical review.

Cassimatis DC, Atwood JE, Engler RM, Linz PE, Grabenstein JD, Vernalis MN.

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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]

8: 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.

Nishiura H, Tang IM.

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BACKGROUND: There has been concern that variola virus might be held clandestinely elsewhere. Through constructing mathematical model based on the

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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]

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

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

Benin AL, Dembry L, Shapiro ED, Holmboe ES.

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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]

10: J Gen Virol. 2004 May;85(Pt 5):1291-9.

Interleukin-18 and glycosaminoglycan binding by a protein encoded by Variola virus.

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Poxvirus interleukin (IL)-18 binding proteins (IL-18BPs) are soluble decoys that inhibit the activity of IL-18. The aim of this study was to demonstrate IL-18 binding activity of the Variola virus protein D7L. D7L effectively inhibited the biological activity of IL-18 in a bioassay. We compared the affinity and kinetics of D7L and the Ectromelia virus IL-18BP, p13, for human and murine IL-18 using surface plasmon resonance and no differences were detected, indicating that the differences in amino acid sequence did not affect binding or species specificity. Both proteins had higher affinity for murine than human IL-18. This was similar to human IL-18BP and the Molluscum contagiosum virus IL-18BP, which also demonstrated higher affinity for human IL-18. The host range of Variola virus is limited to humans and thus the affinity of D7L for IL-18 does not correlate with its host range. Furthermore, we demonstrated that D7L is capable of interacting with glycosaminoglycans (GAGs) via the C terminus, while p13 is not. Importantly, D7L interacted with both GAG and IL-18 simultaneously, indicating that the binding sites were distinct.

PMID: 15105546 [PubMed - indexed for MEDLINE]

11: J Infect Dis. 2004 Apr 15;189(8):1401-10. Epub 2004 Apr 05.

Adverse events after smallpox immunizations are associated with alterations in systemic cytokine levels.

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The immunization of healthy adults with vaccinia virus (VV) induces a protective response against smallpox in most individuals but is also reactogenic in a significant number of vaccinees. The immunological mechanisms underlying the protective response or adverse events in humans are not well defined. Although cytokines contribute to antiviral immunity and, in some cases, cause systemic adverse effects, their role in the human response to VV is unknown. We investigated the effect of smallpox immunization on systemic cytokine concentrations in a cohort of VV-naive individuals. We found that smallpox immunization induces an interferon (IFN)- gamma -dominant response in the systemic compartment 1 week after immunization, with concentrations returning to baseline during convalescence. The level of IFN- gamma induced was not affected by the dilution of vaccine used. We also found that particular adverse events correlated with systemic cytokine patterns, which suggests a role for these molecules in the pathogenesis of adverse events.

Publication Types:

Clinical Trial

Randomized Controlled Trial

PMID: 15073677 [PubMed - indexed for MEDLINE]

12: J R Soc Med. 2004 May;97(5):244-7.

The Bradford smallpox outbreak in 1962: a personal account.

Tovey D.

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Publication Types:
Historical Article

PMID: 15121819 [PubMed - indexed for MEDLINE]

13: J Virol. 2004 May;78(9):4433-43.

Smallpox DNA vaccine protects nonhuman primates against lethal monkeypox.

Hooper JW, Thompson E, Wilhelmsen C, Zimmerman M, Ichou MA, Steffen SE, Schmaljohn CS, Schmaljohn AL, Jahrling PB.

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Two decades after a worldwide vaccination campaign was used to successfully eradicate naturally occurring smallpox, the threat of bioterrorism has led to renewed vaccination programs. In addition, sporadic outbreaks of human monkeypox in Africa and a recent outbreak of human monkeypox in the U.S. have made it clear that naturally occurring zoonotic orthopoxvirus diseases remain a public health concern. Much of the threat posed by orthopoxviruses could be eliminated by vaccination; however, because the smallpox vaccine is a live orthopoxvirus vaccine (vaccinia virus) administered to the skin, the vaccine itself can pose a serious health risk. Here, we demonstrate that rhesus macaques vaccinated with a DNA vaccine consisting of four vaccinia virus genes (L1R, A27L, A33R, and B5R) were protected from severe disease after an otherwise lethal challenge with monkeypox virus. Animals vaccinated with a single gene (L1R) which encodes a target of neutralizing antibodies developed severe disease but survived. This is the first demonstration that a subunit vaccine approach to smallpox-monkeypox immunization is feasible.

PMID: 15078924 [PubMed - indexed for MEDLINE]

14: JAMA. 2004 May 19;291(19):2314; author reply 2314-5.

Comment on:

JAMA. 2004 Feb 11;291(6):725-7.

Risk of contact vaccinia from immunization sites.

Weed HG.

Publication Types:

Comment

Letter

PMID: 15150200 [PubMed - indexed for MEDLINE]

15: JAMA. 2004 May 19;291(19):2313-4; author reply 2314-5.

Comment on:

JAMA. 2004 Feb 11;291(6):725-7.

Risk of contact vaccinia from immunization sites.

Lesser D.

Publication Types:

Comment

Letter

PMID: 15150199 [PubMed - indexed for MEDLINE]

16: Lancet. 2004 May 15;363(9421):1566-8.

Dangerous pathogens in the laboratory: from smallpox to today's SARS setbacks and tomorrow's polio-free world.

Heymann DL, Aylward RB, Wolff C.

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PMID: 15145625 [PubMed - indexed for MEDLINE]

17: Nature. 2004 May 13;429(6988):180-4.

Modelling disease outbreaks in realistic urban social networks.

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Most mathematical models for the spread of disease use differential equations based on uniform mixing assumptions or ad hoc models for the contact process. Here we explore the use of dynamic bipartite graphs to model the physical contact patterns that result from movements of individuals between specific locations. The graphs are generated by large-scale individual-based urban traffic simulations built on actual census, land-use and population-mobility data. We find that the contact network among people is a strongly connected small-world-like graph with a well-defined scale for the degree distribution. However, the locations graph is scale-free, which allows highly efficient

outbreak detection by placing sensors in the hubs of the locations network. Within this large-scale simulation framework, we then analyse the relative merits of several proposed mitigation strategies for smallpox spread. Our results suggest that outbreaks can be contained by a strategy of targeted vaccination combined with early detection without resorting to mass vaccination of a population.

PMID: 15141212 [PubMed - indexed for MEDLINE]

18: Ohio Nurses Rev. 2003 Mar;78(3):4-6; quiz 8.

Smallpox: what every nurse should know.

Maier G.

PMID: 15134061 [PubMed - indexed for MEDLINE]

19: Otolaryngol Head Neck Surg. 2004 Mar;130(3):323-33.

Smallpox: what every otolaryngologist should know.

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OBJECTIVE: In light of recent terrorist events and the potential threat of smallpox as a biological agent, we present information concerning smallpox to better inform the otolaryngologist concerning this disease and its prevention. **STUDY DESIGN:** We performed a review of the smallpox and smallpox vaccination literature over the past 200 years using MEDLINE, PREMEDLINE, Centers for Disease Control and Prevention Internet site, World Health Organization Internet site, and references found in previous publications not found in MEDLINE or PREMEDLINE. Our search focused on the pathogenesis, clinical presentation, course, unique manifestations in the head and neck, diagnosis, and treatment of smallpox, as well as the method of smallpox vaccination, vaccination contraindications, and complications. **RESULTS:** Smallpox is a viral disease with a high mortality rate. Its clinical course, manifestations, and methods of prevention are carefully analyzed in light of otolaryngology practice. **CONCLUSION:** Smallpox manifestations in the head and neck often presented as acute airway obstruction and also as long-term sequelae such as ectropion, nasal vestibular stenosis, conductive hearing loss, and blindness. Most chronic sequelae involve the head and neck. Smallpox vaccination is effective but not without potential serious risks.

Publication Types:

Review

Review, Academic

PMID: 15054374 [PubMed - indexed for MEDLINE]

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

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

Everett WW, Zaoutis TL, Halpern SD, Strom BL, Coffin SE.

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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]

21: *Science.* 2004 May 7;304(5672):809.

Biodefense. Smallpox vaccines: looking beyond the next generation.

Enserink M.

Publication Types:
News

PMID: 15131277 [PubMed - indexed for MEDLINE]

22: *South Med J.* 2004 Apr;97(4):375-8.

Smallpox vaccination in the early 19th century using live carriers: the travels of Francisco Xavier de Balmis.

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Realizing that the Spanish colonies were being devastated by epidemics of smallpox resulting in thousands of deaths, Charles IV, King of Spain, sent one of his court's physicians to apply the recently discovered vaccine. Without refrigeration, the vaccine was passed from one child to another (boys taken out of orphanages). Francisco Xavier de Balmis and a team that included three assistants, two surgeons, and three nurses sailed from Spain on November 30, 1803. They vaccinated more than 100,000 people from the Caribbean Islands and South, Central, and North America, reaching up to San Antonio, Texas, and then traveled to the Philippines, Macao, Canton, and Santa Elena Island, landing back in Cadiz on September 7, 1806. During his journey, Balmis instructed local physicians on how to prepare, preserve, and apply the vaccine, while collecting rare biologic specimens. On the 200th anniversary of their sailing, recognition is given to this group for conducting what was the first global vaccination campaign that reached Texas and California.

Publication Types:

Biography
Historical Article

Personal Name as Subject:

Xavier de Balmis F

PMID: 15108831 [PubMed - indexed for MEDLINE]