

SMALLPOX: SPREAD, CONTROL AND COUNTERINTUITION

THE LAST CASE of smallpox occurred in Oregon in 1946,¹ and the world celebrated the eradication of the disease in 1980.² Even so, we are awash with concern about new epidemics of bioterrorism-related smallpox. On the heels of the atrocities of September 11th, and with the security of remaining Russian stocks of smallpox virus in doubt (see *CD Summary* 12/4/01), a review of the largely forgotten lessons learned during the eradication era might aid us in rational planning. Some of the more intriguing lessons to be covered in this article are:

- smallpox is a wily bug but not usually as contagious as we modern humans believe;
- mass vaccination for smallpox is not the miracle control that we intuitively believe it to be; and
- quarantine is an ineffective can o' worms (but we do it anyway).

STANDARD TRANSMISSION

"In his delirium, WP twice 'escaped' from the hospital and in his wanderings about the streets, a mass of pus and crusts, he perhaps infected others."³

In days of yore, when smallpox still occurred naturally, it was most commonly acquired not by inhalation of airborne aerosols, but through mucosal contact with respiratory droplets. As lesions of smallpox in the mouth and throat ulcerated and burst, they released large amounts of virus. Spread was then facilitated through sneezing, coughing and even singing. Once introduced into a household, smallpox transmission was likely to occur among its members. However, even within a household, smallpox was not highly contagious and usually required prolonged or close contact for spread.²

The most severe cases were the most infectious. However, the most severe cases were also most likely to be confined to bed and therefore less likely to spread infection beyond their own households. Conversely, mild cases excreted less virus but were often well enough to move about and come in contact with many more people. Mild cases were frequently not recognized as smallpox, leading to transmission of disease before it could be correctly diagnosed. The most notable outbreak of this kind occurred in 1972 in Yugoslavia. There, two people with mild disease produced 27 secondary cases between them while a correct diagnosis was still pending.⁴

UNUSUAL TRANSMISSION

"The versatile virus apparently also spread in this one outbreak from a corpse, from laundry of another case-patient, and by remote airborne exposure (on an airplane) ..."⁴

Smallpox was transmitted occasionally without face-to-face contact, leading to fears of uncontrollable epidemics. While the overwhelming majority of spread occurred in close family contacts of overt cases of smallpox, extensive transmission from a single case did occasionally occur. Patients with severe disease could generate infective aerosols, as in measles, and infect others over long distances and/or during very brief contact.²

One of the most noteworthy examples of such transmission occurred in 1970. A German electrician acquired smallpox in Pakistan and was hospitalized upon his return home. From this single case, smallpox spread to 19 people in the hospital on 3 different floors, including to a person who visited the hospital for less than 15 minutes and never came in contact with the electrician.

The unusually widespread nature of these cases occurred because of airborne, rather than droplet spread of the virus. Airborne transmission was facilitated due to the unfortunate coincidence of wintertime low humidity* and cool temperatures, conditions under which the virus prefers to spread. Additionally, the electrician had severe respiratory disease, and the hospital heating system forced dry air throughout the building, making an ideal transport system for the large quantities of virus expelled by the patient.²

THE MYTH OF MASS VAX

Mass vaccination is often the first disease control measure that comes to mind when we are confronted with an epidemic of communicable disease. It seems intuitive that rapid and extensive vaccination would halt an epidemic of smallpox. This may not, however, be true. One of the last mass vaccination campaigns in the U.S. (and touted to be the most successful) was mounted in 1947, after a businessman returning from Mexico brought smallpox to New York City. The index case was admitted to two hospitals with varying diagnoses over the course of 5 days and was eventually diagnosed with smallpox at autopsy. He had given smallpox to 3 people while still alive; the diagnosis of smallpox in the secondary cases was not made until well after his death—not soon enough to prevent transmission to 8 more people. Several weeks later, the NYC Dept. of Health mounted an enormous vaccination campaign. Vaccination clinics ran night and day at 179 sites for a month, vaccinating 6,350,000 people.⁵ At the time, mass vaccination was credited with halting the New York outbreak. Today there is well-founded doubt that it really worked: the number of cases in New York was already in decline by the time the campaign was initiated.⁵

*We should be so lucky.

In the last U.S. outbreak in 1949, Texas public health officials were surprised at the small number of cases (8), “particularly in view of the delay in starting the mass vaccination campaign.”³ Similarly, in the 1901–03 smallpox outbreak in Boston, house-to-house and forced vaccination of the homeless and voluntary vaccination of 400,000 of Boston’s 560,900 residents, failed to contain the two-year epidemic.⁶

According to Fenner, vaccination coverage of 80%—once thought to provide enough herd immunity to interrupt the transmission of smallpox—“may leave a population density of 100 unvaccinated subjects per square kilometer...”² Indeed, in Indonesia, a very densely populated country, smallpox transmission was sustained over a two-year period even with a vaccination rate of 90%. On a larger scale, the incidence of smallpox during the eradication era did not decline dramatically until focus was shifted from mass vaccination to search-and-containment or ring vaccination,⁷ the so-called “sheet anchor” of the eradication era.² Rapid identification and vaccination of cases, contacts and contacts of contacts (the “ring”) during disease incubation is far more effective in curbing disease spread than large scale, indiscriminate vaccination. The decline in disease with the implementation of ring vaccination is clearly seen from experiences in West and Central Africa where improvements in population-wide vaccination failed to affect significantly the number of cases. When search, containment and ring vaccination were implemented, case counts plummeted dramatically (see Figure). Ring vaccination was effective because it:

- 1) provided protection for the exposed but uninfected,
- 2) served as prophylactic or disease-modifying treatment for the exposed and already infected, and
- 3) prevented 3rd generation cases in contacts of #(2).

QUARNATI GIORNI

The *trentini giorni*, or 30-day quarantine, was first instituted to prevent disease spreading from plague-ridden ships in Venice in 1377. It was subsequently expanded to 40 days (*quarnati giorni*), because 30 didn’t prevent spread.⁸ Like mass vaccination, quarantine is another intuitive measure regarded fondly by nostalgic public-health practitioners. Barbera et al. mention a “striking example of the inclination to resort to quarantine” in the recent national terrorism exercise TOPOFF 2000.⁹

Considering the severity of the disease and the rare but noteworthy instances of airborne transmission of smallpox, it may at first blush seem reasonable to invoke large-scale quarantine should an outbreak occur. However, several problems demonstrate this dramatic response to be less than effective, not terribly feasible, and sometimes unethical.

The 2-week incubation period for smallpox ensures that many infected people will have moved away from the source of their exposure by the time their symptoms develop. Second- and third-generation cases can then occur at substantial distance from the “indigenous” case. Consequently, there is no contained population or identifiable geographic “scene” to quarantine effectively.

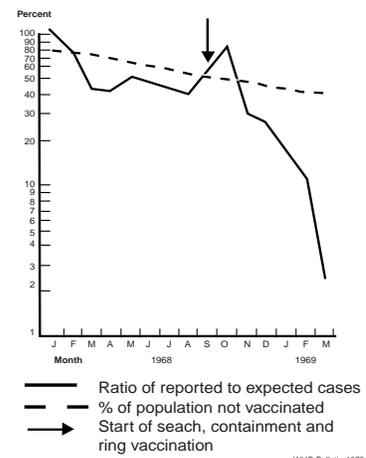
If quarantine is imposed, detainees must be sequestered from exposure through incubation and illness, a period of several weeks. Housing, food, hygiene, medical care, laundry facilities, custodial arrangements for dependents, etc., would need to be provided for many months on a large scale, with attendant staffing, maintenance and security.

Medical care must also be provided to all detainees during quarantine. However, in a large outbreak, medical resources will be stretched to the breaking point providing hospital care, vaccination clinics, disease investigation and follow-up. Scarce medical resources will likely be used up in the devotion of targeted care and not available for long-term, large-scale care of institutionalized detainees.

Quarantining the ill with the well (or even the incubating) is unethical but continues to occur. Similarly, quarantining of “lower classes” or selected ethnic groups is another common but unethical pitfall that ensures that quarantine will be less than effective.⁹

More precisely targeted measures are likely to curb disease transmission more effectively than quarantine—and without unduly harming the ill or the well. Enlisting the public in population-based measures, such as eliminating large gatherings, closing public transportation, and distributing health information, are reasonable approaches to limiting the spread of smallpox. Cohort isolation of willing family members with cases after vaccination avoids disruption of families and the

Smallpox eradication in West and Central Africa
January 1968–March 1969



attendant need for care of dependents.⁹

CONFUSION, CONCLUSION AND COUNTERINTUITION IN THE POST-ERADICATION ERA

In conclusion, it seems that several of our intuitive beliefs about communicable disease and its control are not sustained based on experience from the smallpox era. Smallpox can spread in dramatic and unusual ways, but does not often do so. Mass vaccination didn’t control the disease the way we believed it would. Quarantine is not an efficient, cost-effective or humane way to contain a disease that can spread widely before its symptoms are manifest. While clinicians scurry to re-learn the differential diagnosis for a bygone disease and public health officials concoct emergency plans for managing the unthinkable, it is important to recall the lessons of history and to avoid reverting to practices which, while they might have been intuitively satisfying, didn’t work.

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NB: In the event of a bioterrorism-related smallpox outbreak, **vaccinated clinicians** will be needed to care for the ill and exposed. However, due to the vaccine shortage and adverse effects profile, vaccine will not be released in advance of an outbreak. CDC believes that people who were vaccinated multiple times are probably still immune and could safely care for smallpox victims.

If you have been vaccinated and are willing to volunteer in the event of an outbreak, please fill out and return the survey at the end of this issue.

Influenza Update

HERE IN OREGON the current season has been rather un-newsworthy due to the very low level of transmission to date. Type A viruses have predominated; no type B virus has been detected in cell cultures of effluvia taken from Oregonians. Through the week ending February 9, reports of 40 cell cultures were A-positive compared with 99 by the same period last season. Other recovered viruses posing as influenza have included RSV, rhinovirus, adenovirus, parainfluenza, and coxsackie B.

H1N2

Elsewhere, WHO and the Public Health Laboratory Service (PHLS) in the United Kingdom reported the recent identification of a new influenza virus strain, influenza A(H1N2), isolated from humans in England, Israel, and Egypt. In addition, the Centers for Disease Control and Prevention (CDC) and the Wisconsin Division of Public Health have identified an influenza A(H1N2) virus from a patient specimen collected during December

2001 in Wisconsin. Influenza A(H1N2) viruses have been identified in the past. Between December 1988 and March 1989, 19 influenza A(H1N2) viruses were identified in 6 cities in China, but they did not spread further.

Another finding of perhaps greater concern was reported by the National Microbiology Laboratory in Canada, which has antigenically characterized 103 influenza isolates to date this season: 76 were A(H3N2); 2 were A(H1N1); 3 were B/Sichuan/379/99-like, and 22 were B/Hong Kong/22/01-like. The A(H3N2), A(H1N1) and the B/Sichuan/379/99-like viruses are similar to the current vaccine strains. However, the B/Hong Kong/22/01-like viruses belong to the B/Victoria/02/87 lineage of influenza B viruses (first characterized in Victoria, Australia in 1987) which last circulated in Canada during the 1988–1989 season. The B/Hong Kong/22/01-like viruses are **antigenically different** from the vaccine strain, and the current vaccine is expected to provide limited cross-protection against these viruses.

Subtyping of influenza type A viruses is done on the basis of two proteins, hemagglutinin (H) and neuraminidase (N), on the surface of the virus. Since 1977, two influenza A virus subtypes, A(H1N1) and A(H3N2), have circulated widely among humans. The new H1N2 strain appears to have resulted from the reassortment of the genes of the currently circulating influenza A(H1N1) and A(H3N2) subtypes. The hemagglutinin protein of the A(H1N2) virus is similar to that of the currently

circulating A(H1N1) viruses, and the neuraminidase protein is similar to that of the current A(H3N2) viruses. Because the current influenza vaccine contains strains with H1 and N2 proteins similar to those in the new strain, the current vaccine should provide good protection against the new A(H1N2) virus. No unusual levels of disease have been associated with this virus and, at this time, it is uncertain whether the A(H1N2) virus will persist and circulate widely.

In the United States as of the end of January, 99% of the subtyped influenza A viruses reported through the U.S. WHO and the National Respiratory and Enteric Virus Surveillance System (NREVSS) collaborating laboratories have been H3 viruses and 1% have been H1 viruses. CDC has received 6 influenza A H1 viruses (2 collected in September and 4 collected in October) for further antigenic characterization. These isolates include the A(H1N2) virus from Wisconsin. The neuraminidase type of the other H1 viruses has not yet been determined, but testing is underway. International influenza surveillance conducted through WHO and U.S. surveillance conducted by CDC will continue to track the sightings of A(H1N2) viruses.

Last but not least, WHO has recommended that vaccines to be used in the 2002–2003 season (northern hemisphere winter) contain the following:

- an A/New Caledonia/20/99(H1N1)-like virus;
- an A/Moscow/10/99(H3N2)-like virus;*
- a B/Hong Kong/330/2001-like virus.

* The widely used vaccine strain is A/Panama/2007/99

SMALLPOX VACCINE QUESTIONNAIRE

Oregon Health Services is developing an emergency plan for use in the event of a bioterrorism-related smallpox outbreak. Previously vaccinated healthcare workers who have experience with the disease will be vital to preventing disability and loss of life. If you are willing to volunteer in the event of a smallpox outbreak, and you have been vaccinated against smallpox, please take a moment to complete the following questionnaire and return it to us at your earliest convenience. For questions, please call Maria Gilson Sstrom at 503/731-4024. Thank you for your time.

1. Were you ever involved in administering smallpox vaccine, caring for smallpox patients or the WHO smallpox eradication campaign? Yes No
2. How many times have you been vaccinated for smallpox?
 one two three more than three
3. Are you a Physician PA NP
 Other _____

Comments? _____

Please print legibly

Name _____
 Address _____

 Phone _____
 Fax _____
 County of residence _____
 E-mail _____

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