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WHAT ABOUT SMALLPOX?

In 1980, the World Health Organization certified that smallpox had been eradicated and recommended the cessation of smallpox vaccination worldwide.[1] Routine vaccination ceased in the United States in 1972 (the last case had occurred in Texas in 1949), and vaccination of U.S. military personnel stopped in 1990. Variola survived at only two facilities—viz., the Centers for Disease Control (CDC) in Atlanta and the Russian State Research Center of Virology and Biotechnology in Koltsovo, Novosibirsk Region, Russian Soviet Federated Socialist Republic.[2] But 6 years following the disintegration of the Soviet Union, a visit to Koltsovo found "a half-empty facility protected by a handful of guards who had not been paid for months. No one can say where the scientists have gone, nor is there confidence now that this is the only storage site for smallpox virus outside the Centers for Disease Control and Prevention."[3] Aggressive experimentation with other biological agents by well funded terrorists[4] fuels concern that like-minded individuals might get (have gotten?) their hands on the variola virus.

Preventing the re-introduction of smallpox is the job of intelligence and law-enforcement officials. Should it once again be seen in our midst, recognizing it and dealing with it is our challenge.* We hope to forearm you in this issue of the *CD Summary*. There are two strains of the virus—variola minor, which causes a generally mild disease with case-fatality rates of <1%; and variola major, which causes the more severe illness. This article focuses on the latter.

THE CLINICAL PICTURE

After an incubation period of about 12 (range, 7–19) days, fever, malaise, backache, and a splitting headache ensue. Patients appear ill at this stage; about half vomit, and some develop delirium or convulsions. By day 2 or 3, the temperature generally falls, and the patient feels better. The rash appears at this time.[1]

An early maculopapular rash may be seen in fair-skinned persons, and mucosal lesions may be observed at this early stage. Cutaneous papules appear 1–2 days later. Unlike chickenpox, where crops of vesicles occur over several days, the cutaneous lesions of smallpox are "synchronized," erupting at about the same time or in quick succession; they appear on all parts of the body within 24 hours, and all are generally present by day 4 of the rash. Another distinguishing feature is that the distribution of the smallpox rash is roughly centrifugal—i.e., more pronounced on the face and (especially distal) extremities than on the trunk, and it is more pronounced on the extensor surfaces than on the flexor. Lesions may be seen on the palms and soles as well. The lesions become vesicular on day 4 or 5, and they soon become pustular and umbilicate. Smallpox skin lesions are deeply embedded in the dermis and feel like firm, round objects embedded in the skin; they have usually been described as "shotty." Scabs begin to form on about the 14th day of the rash, and with healing of the lesions, the scabs separate over the ensuing 2 weeks.[1, 5]

The above describes *ordinary* smallpox, which accounted for 89% of cases in unvaccinated persons in one large series. The much more serious *hemorrhagic* form accounted for 2% of cases. Other types, not further elaborated here, include *modified* (usually seen in vaccinated persons) and *flat*. The overall case fatality among unvaccinated persons in this series, which involved hospitalized patients in Madras, India, was 35%.

A differential diagnosis for smallpox includes chickenpox, erythema multiforme, allergic dermatitis, drug rash, syphilis, impetigo, vaccinia, and other skin diseases.[1] Most likely to be confused with smallpox is chickenpox; distinguishing features of these two exanthems are listed in the table (below).

TRANSMISSION

Although airborne transmission of smallpox is possible, it is fortunately not the rule. Rather, contact with respiratory droplets is usually required, which means that closer contact is needed and that a given case is likely to spread the infection to fewer susceptible persons. In contradistinction to chickenpox, smallpox is generally not contagious before the rash appears; and once it does, afflicted persons are likely to limit their exposure of others outside their homes. Transmission is possible until all scabs have separated (usually 3–4 weeks after rash onset). No animal or insect reservoirs or vectors of smallpox exist: we have "only" to worry about transmission from our fellow human beings.

THE VACCINE

The cowpox (vaccinia) virus made the worldwide eradication of smallpox possible, and in the process saw its name become a generic word, nearly synonymous with "immunization." It is this virus that makes up the current smallpox vaccine. (The formulation now in the hands of the feds was prepared from calf lymph; a vaccine using virus grown in cell culture is currently under development.[5]) More than 95% of primary vaccinees develop neutralizing or hemagglutination-inhibition antibodies at titers of 1:10. Epidemiologic studies have demonstrated that although some immunity persists, it wanes after 10

Differentiation of smallpox from chickenpox

Feature	Smallpox	Chickenpox
Incubation	7-17 days	14-21 days
Prodrome	2-4 days	minimal/none
Distribution	centrifugal	centripetal
Progression	synchronous	asynchronous
Scab formation	10-14 d post rash	4-7 days post rash
Scab separation	14-28 d post rash	<14 days post rash

* yes, this means you, gentle reader

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years, and persons vaccinated before 1972 cannot be considered immune today.[5, 6] More than 75% of persons will have antibody titers of 1:10 more than 10 years after receiving a second dose, and for as long as 30 years after a third dose.

MULTIPLE PUNCTURES

The vaccine is not administered by the usual hypodermic needle. Rather, a special, pre-sterilized, bifurcated needle is inserted vertically into the vaccine vial, and a droplet of vaccine is recovered between the two prongs. With the bifurcated needle held perpendicularly to the skin over the triceps or the insertion of the deltoid muscle, 15 punctures are made rapidly and with vigorous strokes. How vigorous? You should see a trace of blood 15–20 seconds after the procedure. Any remaining vaccine should be wiped off the skin with dry, sterile gauze, which should then be put in a biohazard waste container.

The vaccination site should be inspected 6–8 days later to assess the reaction. A "major" reaction is defined as a vesicular or pustular lesion or an area of definite or palpable induration or congestion surrounding a central crust or ulcer. A "major" reaction is good: it indicates that the vaccine has "taken." Less pronounced reactions may occur after re-vaccination.[5]

Why don't we vaccinate the whole country right now? Well, even if we had enough vaccine (we don't), the side effects associated with primary vaccination (table, right) would have to be considered. Although for most medications a death rate of 1 per million would be accepted, this figure means that a nationwide smallpox vaccination campaign would kill about 280 persons, with thousands more suffering non-fatal but severe side effects. This side-effect profile is momentous—especially when weighed against the complete lack of any cases of smallpox in the world since 1978.

THE PLAN

The director of CDC will authorize release of smallpox vaccine based on confirmation of a case of smallpox; credible reports of clinically compatible cases, once an outbreak of smallpox has already been identified; a large outbreak of a clinically compatible illness, pending laboratory confirmation; or confirmation of smallpox virus in an environmental sample associated with potential human exposure. Although planning is still in progress, the basic strategy to contain a case of smallpox would be isolation and "ring" vaccination. This means that, rather than resorting immediately to mass vaccination, we would endeavor to isolate the case and to vaccinate and monitor a ring of people to form a barrier against transmission. These would include household members; face-to-face close contacts and members of *their* households; those involved in the direct medical care, public-health evaluation, transportation, quarantine, or law-enforcement interviewing of suspected cases; laboratory personnel involved in processing specimens from suspected cases; anyone permitted to enter facilities designated for confirmed or suspected smallpox cases; and anyone else known to have been exposed to the same release of the virus as the case. In addition, we would institute aggressive surveillance for additional cases, and the police and FBI would mount an intensive investigation to identify the perpetrator.

Rates of reported complications associated with primary vaccinia vaccination[5]

Complication	Cases/million
Inadvertent inoculation	529
Generalized vaccinia	242
Eczema vaccinatum	38
Progressive vaccinia	1.5
Postvaccinial encephalitis	12
Death	1

Detection of smallpox depends upon alert clinicians. If you see a patient with a rash that looks like smallpox, call your local health department immediately, as you would for any public-health emergency. Be assured that we and the rest of the government will get involved from there. In the meantime, visit our web site, *http://www.oshd.org/acd/bioterr/home.htm* for more information.

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