

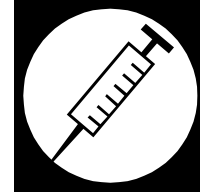
Smallpox: Will Vaccination Avert a Bioterrorism Threat?

A curriculum activity to complement the December 1999 HHMI Holiday Lecture “2000 and Beyond: Confronting the Microbe Menace”.

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Learning Objectives

1. To learn about smallpox and its infection.
2. To learn how vaccinations protect against disease.
3. To learn the risks of immunization.
4. To gain practice using the scientific literature.



Exercise

1. Watch the lecture “Emerging Infections: How epidemics Arise” by Donald E. Ganem on the HHMI Holiday Lecture DVD “2000 and Beyond: Confronting the Microbe Menace”. The specific chapters about Smallpox are Chapters 24 and 25.
2. I have provided some background information below:

The first background information came from the Mayo Clinic website www.mayoclinic.com

What is Smallpox?

Smallpox (variola) is a contagious, disfiguring and often-deadly disease caused by the variola virus. It's believed to have first appeared in northeastern Africa or the Indus Valley of south-central Asia nearly 12,000 years ago. Since then, few other illnesses have had such a profound effect on human health and history. Naturally occurring smallpox was eradicated worldwide by immunization programs that were then discontinued in the late 1970s. But its potential for use as an agent in biological warfare poses a new and serious threat.

Smallpox occurs in humans and in some circumstances in monkeys. Particles containing the virus are released into the air when an infected person coughs, sneezes or simply talks. They also may spread through direct contact such as kissing or through contaminated bed linen and clothing. Inhaling a single virus particle may be enough to cause infection.

Because it's highly contagious, smallpox has the potential to spread rapidly. Unlike anthrax, which is not transmitted from person to person, a smallpox epidemic could conceivably start with a single infected individual.

Smallpox causes pus-filled blisters (pustules) on your skin that leave severe, pitted scars. Historically, about one-third of infected people die. There's no known cure, but a vaccine can protect against the disease. In addition, antiviral drugs that have been developed since smallpox was eradicated are now being tested to see if any are effective against the smallpox virus.

The United States discontinued smallpox vaccinations in 1972 because the disease had virtually been eliminated in this country and because the vaccine itself carries potential health risks. In 1980, the World Health Organization (WHO) recommended that all countries discontinue vaccinations.

Nevertheless, stocks of the virus remain. Officially they're stored in only two high-security WHO labs — one in the United States and one in Siberia. But throughout the 1980s, the Soviets carried on a clandestine biological program. Virulent smallpox strains — intended for use as biological weapons — were manufactured in secret labs. Since the collapse of the Soviet Union, some of this stock may have fallen into other hands.

This possibility is especially alarming because few health workers in the United States have seen or treated smallpox. Yet a great deal is known about variola. Scientists affiliated with the Centers for Disease Control and Prevention (CDC) in Atlanta and the WHO are among the world's leading experts on the disease.

The next information was obtained from the American Medical Association website. We have wiped out smallpox virus from the face of the earth through a very thorough vaccination process. However, if smallpox virus were found again today (through an act of bioterrorism?) we would most certainly be at risk. This following information will begin to explain why old vaccinations may not help us now.

The article came from the Journal of the American Medical Association Volume 281 No.22 June 9, 1999

Smallpox as a Biological Weapon

Medical and Public Health Management

PREEXPOSURE PREVENTIVE VACCINATION

Before 1972, smallpox vaccination was recommended for all US children at age 1 year. Most states required that each child be vaccinated before school entry. The only other requirement for vaccination was for military recruits and tourists visiting foreign countries. Most countries required that the individual be successfully vaccinated within a 3-year period prior to entering the country. Routine vaccination in the United States stopped in 1972 and since then, few persons younger than 27 years have been vaccinated. The US Census Bureau reported that in 1998, approximately 114 million persons, or 42% of the US population, were aged 29 years or younger.³⁰

In addition, the immune status of those who were vaccinated more than 27 years ago is not clear. The duration of immunity, based on the experience of naturally exposed susceptible persons, has never been satisfactorily measured. Neutralizing antibodies are reported to reflect levels of protection, although this has not been validated in the field. These antibodies have been shown to decline substantially during a 5- to 10-year period.²⁴ Thus, even those who received the recommended single-dose vaccination as children do not have lifelong immunity. However, among a group who had been vaccinated at birth and at ages 8 and 18 years as part of a study, neutralizing antibody levels remained stable during a 30-year period.³¹ Because comparatively few persons today have been successfully vaccinated on more than 1 occasion, it must be assumed that the population at large is highly susceptible to infection.

In the United States, a limited reserve supply of vaccine that was produced by Wyeth Laboratories, Lancaster, Pa, in the 1970s is in storage. This supply is believed to be sufficient to vaccinate between 6 and 7 million persons. This vaccine, now under the control of the CDC, consists of vaccine virus (New York Board of Health strain) grown on scarified calves. After purification, it was freeze-dried in rubber-stoppered vials that contain sufficient vaccine for at least 50 doses when a bifurcated needle is used. It is stored at -20°C (James LeDuc, PhD, oral communication, 1998). Although quantities of vaccine have also been retained by a number of other countries, none have reserves large enough to meet more than their own potential emergency needs. WHO has 500,000 doses.³²

There are no manufacturers now equipped to produce smallpox vaccine in large quantities. The development and licensure of a tissue cell culture vaccine and the

establishment of a new vaccine production facility is estimated to require at least 36 months (Thomas Monath, MD, unpublished data, 1999).

Because of the small amounts of vaccine available, a preventive vaccination program to protect individuals such as emergency and health care personnel is not an option at this time. When additional supplies of vaccine are procured, a decision to undertake preventive vaccination of some portion of the population will have to weigh the relative risk of vaccination complications against the threat of contracting smallpox.

A further deterrent to extensive vaccination is the fact that presently available supplies of vaccinia immune globulin (VIG), also maintained by the CDC, are very limited in quantity. The working group recommends VIG for the treatment of severe cutaneous reactions occurring as a complication of vaccination.^{33, 34} Vaccinia immune globulin has also been given along with vaccination to protect those who needed vaccination but who were at risk of experiencing vaccine-related complications.³³ It has been estimated that if 1 million persons were vaccinated, as many as 250 persons would experience adverse reactions of a type that would require administration of VIG (James LeDuc, PhD, oral communication, 1998). How much VIG would be needed to administer with vaccine to those at risk is unknown.

Some other information I found valuable and good starting websites for your students to begin their research:

A Website for the exhibit "Smallpox - Inocuation, Vaccination, and Eradication", at the Louise M. Darling Biomedical Library at UCLA.

<http://www.library.ucla.edu/libraries/biomed/smallpox/>

The MedLine Plus website at the National Library of Health in Bethesda, Maryland is an excellent and complete resource. This website has many useful links.

<http://www.nlm.nih.gov/medlineplus/smallpox.html>

Assignment

1. It has been suggested that several governments around the world may have studied the smallpox virus as a possible biological weapon. In fact, the CIA has informed the President that stockpiles of weapons-grade smallpox exist in several foreign countries. Current international tensions and the technical expertise of radical terrorism groups create an even greater amount of concern about possible smallpox outbreaks. The students in your class will participate in a role-playing exercise concerning possible smallpox threats.
2. Tell the students that they have been selected to serve as student interns in the Office of the Surgeon General of the United States. The President of the United States is worried about the risk of an intentional release of smallpox virus and has asked the Surgeon General to prepare a plan to handle the smallpox threat. The Surgeon General is considering the use of vaccination against smallpox to decrease the threat imposed by intentional release of smallpox virus by an enemy or terrorist group.
3. Suggest the Surgeon General has assigned the student interns to investigate the use of vaccination to address the smallpox threat. He has asked the students to provide presentation/reports that outline the arguments for and against vaccination. The reports/presentations will be given to the President and his cabinet.
4. The presentations/reports could be accomplished in several ways:
 - ?? Have the students write written reports
 - ?? Have the students make presentations (a good exercise to improve their skills in PowerPoint)
 - ?? Have the students debate the issue (prophylactic vaccination vs. vaccination only after an outbreak)
5. I suggest dividing the class into groups to work on developing the reports/presentations. This will solve the problem of limited time and resources. Also, we have noted that interactive group learning is very successful with this type of assignment. Students will assist each other and provide pointers on research and presentation techniques.
6. Remind the students that the scientific knowledge of President Bush and his cabinet may be limited. A strong argument should provide scientific background material so that the cabinet members can understand the issues completely. The final paper (presentation) should have references.
7. Give the students access to the library and/or computer lab to research the topic. This emphasizes the value you place on the exercise, and allows students to utilize the school's resources in developing strong research skills.