



**California Association
for
Medical Laboratory Technology
Distance Learning Program**

SMALLPOX

Course # DL-050

by

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Approved for 2.0 CE/Contact Hours

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SMALLPOX

Objectives

After studying this course the participant will be able to

- Describe the variola virus
- List the symptoms of smallpox
- Outline the history of smallpox
- Compare variolation to vaccination
- Describe the vaccinia virus and the present-day vaccination procedure
- Summarize the eradication of smallpox
- State the Soviet smallpox weaponization program and its impact on the present day world situation
- List the complications of vaccination
- State the pros and cons of the U.S. vaccination program

Introduction

Smallpox, once called “The most terrible of all the ministers of death” (Macaulay) was declared eradicated in 1980 by the World Health Organization (WHO). The last case of person to person transmission had occurred in Oct., 1977. However, stocks of the smallpox virus were still held by several countries. By the mid 1980s only the Centers for Disease Control in Atlanta and the Ivanovsky Institute of Virology in Moscow still had smallpox stock. Who would have imagined that smallpox now is a bioweapon threat? How has this terrible specter come about?

In this course we will look at the

- a. causative agent and disease
- b. history
- c. era of vaccination
- d. eradication
- e. re-emergence as a biowarfare threat
- f. present day debate about vaccination.

Causative Agent and Disease

Smallpox is caused by the variola virus, an orthopoxvirus,

Family: Poxviridae

Subfamily: Chordopoxvirinae

Genus: Orthopoxvirus

Strains: variola major
variola minor

The virus is large, biscuit-shaped, the size of a small bacterium. It contains double stranded DNA which potentially codes for 200 proteins. The virus can survive outside the body. Survival in air can be 24 hours but the time is decreased by exposure to sunlight and heat. The virus is related to a number of orthopoxviruses found in animals and usually named for the primary host. Chickenpox, however, is misnamed. It is not caused by a poxvirus but a herpesvirus.

The most common transmission of smallpox is by airborne droplets from saliva or other bodily fluids, although it can be transferred by contaminated objects. The incubation period is 7 to 17 days (average time is 12 to 14 days) during which time the person is asymptomatic and non-contagious.

The initial symptoms of the disease last from 2 to 4 days and are characterized by high fever, chills, head and body aches, especially lower back pain and sometimes vomiting. After this time the fever declines and a rash begins in the mouth and throat. The sores break open and the person is most contagious, spreading virus into the air with every breath or cough. The rash then spreads to the face, then arms and legs to hands and feet. The early rash appears as raised bumps which become filled with thick, opaque fluid and have a center depression. The fever rises. After 5 days the rash becomes pustular, followed by crusting and scabbing. During this time the person remains contagious with the virus present in the pustules and scabs. Within about 3 weeks the scabs fall off and leave pitted scars. After the scabs are gone the person is no longer contagious.

The fatality rate of variola major averages 30% in the non-vaccinated population. Most of these fatalities have mucocutaneous hemorrhages or confluent pox on the face and limbs. Most surviving victims have permanent damage. Nearly all are disfigured with pocks - ugly pitted scars - and 10% are partially or completely blind as a consequence of pox in the eyes.

HISTORY

Variola virus seems to have evolved from an animal poxvirus 10,000 or more years ago in tropical forests in central Africa. About 9000 BC agricultural settlements grew in northeast Africa - in Egypt and Mesopotamia - thus bringing people together and allowing constant transmission of the disease from person to person. It was spread by traders into India, then to Asia and into Europe by around 400 BC. The earliest evidence of skin lesions resembling smallpox is found on the faces of mummies in Egypt from about 1500 BC. The mummy of Ramses V who died as a young man in 1157 BC shows these lesions. (1) In 1350 BC the first recorded smallpox epidemic occurred during the Egyptian-Hittite war. The Hittite King Suppiluliumas I and his heir, Arnuwandas, were victims, thereby causing their civilization to fall into a steep decline. (2)

Smallpox was called variola in 570 AD by Bishop Marius of Avenches, Switzerland. The word derives from Latin, *varius*, meaning spotted, speckled or *varus*, pimple. In England the name, smallpox, came from small pockes (meaning sac) to distinguish the illness from syphilis which was then known as great pockes.

Smallpox affected the development of western civilization. It has been one of the greatest scourges, surpassing plague, cholera and yellow fever in its impact. It was called Variola Rex because it caused the fall of empires.

Some of the significant incidents include a large epidemic in 180 AD, coinciding with the decline of the Roman Empire. The Arab expansion carried the disease across North Africa into Spain. The Crusades continuously brought the disease to Europe. Silk Route traders dispersed it over large areas from China. It was unknown in the New World until introduced by the Spanish and Portuguese. It was instrumental in the fall of the Aztec and Inca empires.

A population which has never encountered an infectious agent is particularly susceptible, due to lack of immunity and to no genetic resistance. For example, when the Spanish arrived in 1518 Mexico had about 25 million inhabitants. By 1620 the population was reduced to 1.6 million. In North America the disease, introduced by both Europeans and the slave trade, swept through the native population. In 1616-1619 an epidemic wiped out 90% of the Indians in the Massachusetts Bay area shortly before the arrival of the Pilgrims.

Some of the historical figures killed by smallpox include Marcus Aurelius in 180 AD. In the period from the late 1500s to the late 1700s the list includes: King and Queen of Ceylon and all of their sons, William II of Orange and his wife in, Emperor Ferdinand IV of Austria, Emperor Gokomyo of Japan, Emperor Fu-lin of China, Queen Mary II of England,

Emperor Joseph I of Austria, King Louis I of Spain, Tsar Peter II of Russia, Queen Ulrika Elenora of Sweden, King Louis XV of France. (2)

The general population was also greatly affected. By the 18th century smallpox replaced bubonic plague as Europe's most devastating disease. In the late 18th century in Europe 400,000 people died of smallpox each year and one third of the survivors went blind. As recently as the late 1960s there were at least 10 million to 12 million cases in 31 countries with 2 million deaths annually.

VARIOLATION

Thucydides, in 430 BC, noted that those who survived the disease were later immune to it. Rhazes, about 910 AD, not only gave the first medical description of the disease and how it was transmitted, but also stated the first theory of acquired immunity in his explanation of why survivors do not develop the disease. (2)

A milder form of smallpox, variola minor, also known as alastrim and Kaffir-pox, led to the first efforts at prevention. These efforts began with physicians and others intentionally infecting healthy persons with smallpox in the hope that the resulting infections would be less severe than the naturally transmitted disease and confer immunity. Various materials obtained from pus or scabs from individuals with mild forms of the disease were introduced through the nose or the skin. This procedure was called variolation.

This method was evidently first practiced in India before 1000 BC and spread to Tibet and then China by 1000 AD. Caravaners brought this knowledge to Arabia, Africa and Persia by 1700. Variolation was practiced widely throughout the Ottoman Empire. Travelers from Constantinople (Istanbul) introduced this method into Europe. Although variolation was communicated to the Royal Society of London in 1714 and 1716, the conservative English physicians did not try it.

Lady Mary Montague had survived smallpox in 1715 at age 26 but her lovely face was left with ugly scars and her brother died of the disease. When her husband was appointed Ambassador to Turkey in 1717 she learned about the procedure. She was so impressed by the Turkish method that she ordered the embassy surgeon, Charles Maitland to inoculate her 5 year old son in 1718. When she returned to London she had Maitland inoculate her 4 year old daughter in the presence of the physicians of the court, including the President of the Royal Society. The Royal family granted Maitland license to perform variolation on six prisoners. All the prisoners survived and were shown to be immune. The Princess of Wales was so impressed by this experiment she had her two young daughters variolated.

Variolation then gained favor in England. Although 2 to 3 percent of variolated persons died of smallpox, this was demonstrably better than the 30 percent fatality rate. Some side effects included transmitting other diseases such as tuberculosis or syphilis from the pus of the donor. Improved methods reduced the possibility of these diseases. Another problem was that variolated persons were infectious and could occasionally transmit smallpox. Some epidemics were triggered this way.

Variolation also spread throughout Europe including many of the crowned heads and their families. Frederick II of Prussia inoculated his soldiers.

During the 1721 smallpox epidemic in Boston Cotton Mather persuaded a physician to use the technique to stop the epidemic. In another Boston epidemic in 1753-54 Benjamin Franklin (whose son died of smallpox in 1736) analyzed the survival rate of inoculated versus uninoculated persons and he became an enthusiastic supporter. Variolation became so popular in the colonies that it contributed to the growth in population during the last half of the 18th century by reducing smallpox deaths.

The devastating effect of smallpox gave rise to one of the first examples of biological warfare. In the aftermath of the French and Indian war, most of the victorious British army returned home. Rebellious Indians overran the lightly defended British forts in western

Pennsylvania and laid siege to Fort Pitt. The British were desperate to control the Indians. In 1763 Sir Jeffrey Amherst, commander-in-chief of British forces in North America, wrote a letter to Colonel Henry Bouquet, suggesting that the defenders of Fort Pitt should contrive to send the smallpox among the disaffected tribes. Bouquet replied that he would try to grind smallpox scabs into some blankets that were to be distributed among the Indians. (1)

Evidently smallpox again was used as a biowarfare weapon in 1775-76. The Continental Army had taken Montreal and was about to conquer Quebec City when the British fort commander reportedly had people variolated and sent them to mingle with the Continental troops. In two weeks a smallpox epidemic spread through the troops and their numbers were so reduced they were unable to take Quebec from the English, leading Thomas Jefferson to lament that were it not for the epidemic Canada might be part of the U.S. General Washington, who had survived smallpox when he was 19, said smallpox was his “most dangerous enemy.” He learned his lesson from the Quebec defeat and had his Revolutionary War soldiers variolated.

VACCINATION HISTORY

It was well known in England and European countries that milkmaids became immune to smallpox after developing cowpox. Cowpox appears as irregular pustules on cows’ udders, with no signs of systemic disease except slight decrease in milk production. Milkmaids developed similar pustules on their fingers. Various physicians as well as others noted that people who had had cowpox did not develop smallpox and showed no reaction to variolation. A farmer in Dorset, Benjamin Jesty, observed that two of his milkmaids who had had cowpox were able to care for children with smallpox without getting the disease. He decided to take material from cowpox pustules and introduce it into the skin of members of his family. A similar scenario occurred in Holland where Peter Plett did the procedure on the children of a family he was tutoring, but inflammation of the arm or hand of several of the recipients dissuaded both Jesty and Plett from continuing. (2)

Dr. Edward Jenner knew this common lore that cowpox offered protection against smallpox. As a teen-age apprentice to a surgeon near Bristol he heard a milkmaid say, “I shall never have smallpox for I have had cowpox. I shall never have an ugly pockmarked face.” The connection between cowpox and smallpox continued to intrigue Dr. Jenner. He had an opportunity to test his belief in 1796 when a milkmaid he knew developed cowpox. He took fluid from a pustule on the milkmaid’s hand and inoculated it into incisions in the arm of an 8 year old boy, James Phipps. Six weeks later Jenner variolated the boy, but there was no reaction. He later repeated the variolation with the same result.

Jenner sent an article to the Royal Society describing his observation that 13 people who had had cowpox did not react to variolation. He also described Phipps. The Royal Society castigated Jenner because he was “in variance with established knowledge and he had better not promulgate such a wild idea if he valued his reputation.” (2)

Because of lack of cowpox cases several years passed before Jenner was able to continue his investigations. Once cowpox appeared again locally Jenner vaccinated more children and challenged them with variolation. He also conducted a nationwide survey that substantiated his belief that cowpox conferred resistance to smallpox. He revised his article and, on the advice of friends, published it himself. The title, “an inquiry into the causes and effects of the variolae vaccinae, a disease discovered in some of the western counties of England...and known by the name of the cow pox” introduced the word vaccinae. This word was from the Latin, vaca, meaning “cow.”

Other physicians in London, impressed with his publication, started vaccinating without attribution to Jenner. Dr. Woodville, the chief of London’s Small Pox and Inoculation Hospital, obtained cowpox material from a local outbreak. Unfortunately some of the cowpox vaccine became contaminated with smallpox. These mistakes in the early

vaccination programs also included contamination of the lancets used for vaccination with the smallpox virus and confusing smallpox rashes with cowpox, resulting in using smallpox material for vaccination. Jenner published another pamphlet warning against contamination and also the importance of using the vaccine before its protective potential was lost.

Vaccination using pustule fluid from cowpox spread rapidly. It reached most European countries by 1800 and about 100,000 persons had been vaccinated in Great Britain. The procedure soon spread to the United States. The problem of supplying the demand was that the inoculation material was hard to obtain. Cowpox occurred sporadically and was found only in England and Europe. The cowpox material also deteriorated over time, especially when exposed to high temperatures or exposure to sunlight.

Jenner had shown that the cowpox virus could be transmitted from person to person. This “arm to arm” procedure became prevalent. One person was vaccinated and material from the vaccination site was used to vaccinate another. This transfer could keep the vaccine active over distances or in areas where it was hard to obtain. The first mass overseas vaccination program, the Expedición de la Vacuna was sent by King Charles of Spain to dominions in North and South America and Asia. The vaccine was kept active across the Atlantic by 22 orphans who were vaccinated in pairs during the long sea voyage.

The demonstrated value of vaccination was so great that Napoleon insisted that all his troops should be vaccinated and then French civilians a year later. Vaccination programs were extended to many European countries as well as the United States. Resistance to the procedure, however, was still prevalent, particularly in poorer classes. In the United States, Congress repealed the vaccination law in the 1820s and the incidence of smallpox rose.

Jenner realized the importance of his work. In 1802 he wrote, “It now becomes too manifest to admit of controversy, that the annihilation of the small pox, the dreadful scourge of the human species, must be the final result of this practice.” This prediction took almost 200 years to accomplish.

VACCINIA VIRUS AND MODERN VACCINATION

Smallpox vaccine is made from live vaccinia virus and protects against the disease smallpox. The vaccinia virus is antigenically similar to smallpox (variola) virus and its appearance is similar. At some time cowpox virus was superceded by vaccinia virus. In 1939, much to everyone’s surprise, Allan Downie of the University of Liverpool determined that the virus then in use around the world to immunize was genetically distinct from cowpox. It is an orthopoxvirus that did not exist in nature. Over the years vaccinators had been selecting vaccine strains that had fewer side effects and gave smaller skin lesions. Where the vaccinia virus came from and when it became the primary vaccination virus remains a mystery.

“Worldwide, different vaccinia strains have been used for production of smallpox vaccine, but all U.S. vaccine formulations contain the New York City Board of Health (NYCBOH) vaccinia strain. This strain has been reported to be less reactogenic (i.e., it causes fewer adverse events) than other strains. U.S. National Pharmaceutical Stockpile (NPS) stores of smallpox vaccine include two previously manufactured calf-lymph--derived vaccines, Dryvax® (Wyeth Laboratories Inc., Marietta, Pennsylvania), and Aventis Pasteur vaccine (Swiftwater, Pennsylvania). Acambis/Baxter Pharmaceuticals (Cambridge, Massachusetts) has developed two new vaccines: ACAM1000, which is grown in human embryonic lung cell culture (MRC-5), and ACAM2000, which is grown in African green monkey cells (VERO cells) (CDC Drug Services, unpublished data, 2002). Prospective studies are under way to determine the reactogenicity of the newer cell culture vaccines. Dryvax is the vaccine currently used in the U.S. smallpox vaccination effort. CDC is holding other vaccines in reserve.” (3)

Normal Vaccination Procedure and Progression

Smallpox vaccine is administered with a bifurcated needle that is dipped into the vaccine solution. When removed, the needle retains a droplet of the vaccine. The needle is then used to prick the skin a number of times in a few seconds. The pricking is not deep, but will cause a sore spot. The vaccine is usually given in the upper arm. The vaccinia virus replicates in the dermis of the skin. Three to five days later a papule forms at the vaccination site of immunocompetent vaccine-naïve persons (also referred to as first-time or primary vaccinees). The papule becomes vesicular (approximately day 5-8), then pustular, and usually enlarges to reach maximum size in 8--10 days. The pustule dries from the center outward and forms a scab that separates 14-21 days after vaccination, usually leaving a pitted scar.

Formation by days 6-8 postvaccination of a papule, vesicle, ulcer, or crusted lesion, surrounded by an area of induration signifies a response to vaccination. This event is referred to as a major reaction or a “take”, and usually results in a scar.

Vaccination-site reactions are classified into two categories: major reactions and equivocal reactions. A major reaction indicates a successful vaccine take and is characterized by a pustular lesion or an area of definite induration or congestion surrounding a central lesion, which can be a scab or an ulcer. All other responses are equivocal reactions and are called “nontakes.” Equivocal reactions can be caused by suboptimal vaccination technique, use of subpotent vaccine, or residual vaccinia immunity among previously vaccinated persons.

Persons with equivocal reactions cannot be presumed to be immune to smallpox, and revaccination is recommended. (3)

The World Health Organization has recommended that response to vaccination be evaluated on postvaccination day 6, 7, or 8. These are the days of peak viral replication, and the period during which take should be assessed for both first-time vaccinees and revaccinees.

Routine vaccination of the American public against smallpox was stopped in 1972 after the eradication of the disease in the United States in the mid 1940s. In 1946 and 1947 there were imported cases of smallpox caused by infected people coming to the U.S. One occurrence was in San Francisco where several infections resulted from an imported case and was promptly contained by vaccination of contacts. Medical personnel in the area were also vaccinated. I was one of them.

ERADICATION OF SMALLPOX

By the late 1950s many countries had eradicated smallpox: Sweden in 1895, Austria in the 1920s, England, the Soviet Union and the Philippines in the 1930s, the U.S. and Canada in the 1940s, Central and South America with the exception of Brazil in the late 1950s. In 1953 Dr. Brock Chisholm, the first WHO director, proposed the idea of eradicating smallpox but a number of industrialized countries felt this too ambitious and costly and WHO opted instead for a program to eradicate malaria.

At the annual World Health Assembly meeting in Minneapolis in 1958 the Soviets proposed a 5 year plan for the worldwide eradication of smallpox. Their arguments were based on the threat of imported smallpox to the countries where it had been eradicated as well as the cost of maintaining vaccination programs. Although this met with lukewarm support, WHO adopted the Soviet proposal in 1959 but gave little money to the program.

By the mid 1960s the expensive malaria eradication program had made little headway and the U.S. began to endorse the smallpox program which the Soviets had continued to promote. In 1966 a vote to monetarily support the smallpox eradication program narrowly passed at the World Health Assembly meeting. WHO launched a program to eradicate smallpox. This required the elimination of the causative organism from all natural sources.

Dr. Donald A. Henderson of the United States Public Health Service (USPHS) and CDC was appointed to head the program. Smallpox was an ideal target for global eradication because

- a. humans are the only known reservoir
- b. the variola virus has a single unchanging antigenic type that induces solid immunity.
- c. the susceptible population is readily reduced by vaccination and individuals recovered from the disease are also immune.
- d. smallpox vaccine induces immunity rapidly, providing nearly total protection in 10-12 days. Thus those exposed to smallpox could be protected during the incubation period if vaccinated in 3-5 days after exposure.
- e. supplies of freeze-dried smallpox vaccine were available. The vaccine was easy to manufacture, relatively stable and cost about a penny a dose.
- f. smallpox rarely causes inapparent cases and does not result in the carrier state.
- g. presumably no viruses are shed in the prodromal state so communicability begins only after symptoms appear.

At the beginning of the eradication campaign smallpox was still prevalent in Africa, the Indian subcontinent, Brazil, and Indonesia. The initial strategy was to prioritize the areas to begin the campaign. A West Africa program was already underway. Brazil and Indonesia were initially selected because after smallpox had been eliminated there were no contiguous countries to re-seed the disease.

Many felt the wholesale vaccination of populations was not feasible because of cost, personnel and inability to reach every person in remote villages over hazardous terrain. As the program developed general vaccination was combined with identification of any case, the isolation of the person, identification of all the people in the family or in contact with the person and vaccination of all these contacts. In actuality this immunization was expanded to vaccinate all the people in a ring around the case. This might include an entire village. This strategy was called “surveillance-containment” or “isolation, contact tracing and ring vaccination.” It was a very successful strategy and as cases became sporadic, was the procedure used during the final stages of eradication.

During the program the Soviets kept their promise to provide large quantities of vaccine. Other countries also supplied vaccine and some of the target countries began to produce their own. The vaccination project was aided by the development of the bifurcated needle which was cheap, easy to use and economical of vaccine.

By April, 1971 there was no more smallpox in Brazil, thus the disease was eradicated from the Western Hemisphere. There had been unbelievably rapid progress in eradicating the disease, leading to the United States halting mandatory vaccination for schoolchildren but still requiring it for travelers.

Smallpox could still be contracted by travelers or brought in by citizens of countries where it was still endemic. An epidemic in Iran in 1971 brought by pilgrims to Mashhad in Afghanistan eventually spread to neighboring countries and involved many thousands of people. A large vaccination campaign was required to halt the epidemic and again make the area free of smallpox.

There were still trouble spots in the Indian Subcontinent and Ethiopia and Somalia. India accounted for nearly 60% of the reported cases. The strains there at this time, 1971, were especially deadly. India’s large, dense, mobile population required a dogged approach involving many people and many discouraging set-backs. Finally by January 1975 the number of smallpox cases diminished so that the surveillance-containment technique combined with a 1000 rupee reward for reporting cases was used. By May 1975 smallpox was finally eliminated in India.

Ethiopia and Somalia became the last stronghold. Just when it was thought that smallpox was eliminated, there were reports of an outbreak in Somalia. The epidemic peaked in June, 1977. An international team helped contain the new cases. Finally the cases were restricted to one nomadic tribe. In October 1977 several of the children exposed a hospital worker, Maow Maalin. In Oct, 1977 he was the last individual to have a case of person to person transmitted smallpox. By 1980 when no cases had appeared for 3 years, WHO announced the eradication of smallpox as a clinical disease.

Variola Virus in Laboratories

Although smallpox was declared eradicated as a human disease, in 1980 samples of variola virus were still stored in 18 laboratories in the world and WHO was attempting to restrict the number of these laboratories. Some institutions still did research on the virus. One regrettable incident occurred at the University of Birmingham in England. Inadequate safety guidelines led to spread through the air to Janet Parker, a photographer in the Dept. of Anatomy. She developed fatal smallpox and spread the disease to her mother, who recovered. Dr. Henry Bedson, director of the research laboratory, overcome by guilt, committed suicide. (1)

Gradually laboratories either destroyed their specimens or sent them to one of the remaining labs. By 1984 WHO authorized only two laboratories (the CDC in Atlanta and the Research Institute for Viral Preparations in Moscow) to retain samples of variola virus.

Weaponization of Smallpox

In 1992 Kenneth Alibek, (Kanatjan Alibekov) the former deputy director of the Soviet Bioweapons Program, defected to the United States. In his book, "Biohazard," (4) he states that the Soviet Union had been working since 1947 with smallpox as a possible biowarfare agent. He wrote, "Soon after the WHO announcement that smallpox had been eradicated...the Kremlin perceived a military opportunity where other governments saw a medical victory. A world no longer protected from smallpox was a world newly vulnerable to the disease. In 1981, Soviet researchers began to explore... a better version of a smallpox weapon that had been in our arsenal for decades. "In 1967 they had obtained a virulent, heat stable strain from India. "In December 1987... I was assigned to supervise plans to create a new smallpox weapon...In December 1990 we tested a smallpox weapon in aerosol form. It performed well. We calculated that the production line ...was capable of manufacturing between eighty and one hundred tons of smallpox a year." During his debriefing in the U.S. he said he believed the twenty-ton stockpile of smallpox virus had been destroyed in the late 1980s, but the seed cultures of the virus were not only at the Moscow site but also at several laboratories that had been working with weaponization. He brought up the possibility that unemployed former Soviet bioweapons scientists could have smuggled samples of the variola virus to other countries that were hoping to develop a biowarfare program. It is particularly ironic that the Soviet Union, which was so instrumental in promoting the eradication program, has been the nidus for the possible re-introduction of smallpox to the world's people.

Now, faced with the possibility that the virus is held by other countries that might use it as a biowarfare or bioterrorist agent, the United States is starting a smallpox immunization program.

Present Vaccination Program

The world's population has become extremely vulnerable to smallpox. Routine vaccination of civilians was stopped in the U.S. in 1972 and in other parts of the world by 1984. Since the protective immunity produced by the vaccine lasts only about 3 - 5 years in first time vaccinees and about 7 - 10 years in repeat vaccinees, those who were previously

vaccinated have become vulnerable. In the aftermath of the events of September and October, 2001 and the possibility that unfriendly governments have the variola virus, the U.S. government began stockpiling smallpox vaccine. At present the United State has sufficient Dryvax vaccine to vaccinate every person in the country in an emergency.

In Dec. 2002 the president announced a plan to better protect the people against the threat of smallpox attack. The plan included creating smallpox healthcare teams that would respond to a smallpox emergency. Members of these teams would be voluntarily vaccinated, as would certain military and civilian personnel who are or may be deployed in high threat areas. The government did not recommend vaccination for the general public. (5)

The response to the vaccination program has been disappointing. The government hoped to vaccinate 500,000 initially and as many as 10,000,000 eventually. As of the middle of April, 2003, slightly fewer than 33,000 civilian health care and public health personnel have been vaccinated. Over 200,000 members of the armed forces have received the vaccine. Much of the civilian resistance is due to the perceived risk of the vaccine itself.

Statistics from the vaccination program in the 1960s and early 1970s showed that vaccination caused 1 or 2 deaths and several dozen cases of serious adverse events per 1 million recipients. The deaths weren't evenly spread throughout the population, but were most common in those with certain skin conditions such as eczema and those with suppressed immune systems. (3)

Adverse events include (3)

- Eczema vaccinatum
- Erythema multiforme major
- Fetal vaccinia
- Generalized vaccinia
- Inadvertent inoculation
- Myocarditis/pericarditis
- Ocular vaccinia
- Postvaccinia encephalitis or encephalomyelitis
- Pyogenic infection of the vaccination site.

In the present program those at risk for serious side effects (those with skin lesions, immunodeficiency, pregnancy or anticipated pregnancy) are screened out. However there are increased numbers in the risk categories. Wholesale vaccination might result in a higher death rate than extrapolated from the 1960-1970 program. It is estimated that if the entire U.S. population were vaccinated, there would be at least 125 deaths.

In the present program there have been few cases of confirmed side effects - one case of vaccinia, two inadvertent inoculation, 2 ocular vaccinia. Additional problems have been reported but not yet confirmed. Non-serious side effects (mild expected reactions) such as fever, rash, headache, pruritis) have been reported in fewer than 350 people to date. The heart attacks which were reported in the media were not due to vaccination.

Another concern is that since the vaccine contains a live virus, it can be transmitted by the vaccinated person to others, a condition called contact vaccinia. A number of health care workers have not agreed to vaccination because they believe they might transmit vaccinia to patients, many of whom have risk factors for complications.

Any vaccination campaign would need to continue indefinitely because of the turnover of health care workers and the waning of immunity after 3-7 years. The question of whether to push for fulfilling the government's objective of vaccinating 500,000 or more is difficult to answer. It depends on how great the threat of smallpox bioterrorism is compared to the risks of vaccination. (6)

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Review Questions

Course #036-950

Select the **one** best answer

1. Variola major is
 - a. a herpesvirus
 - b. an orthopox virus
 - c. the causative agent of chickenpox
 - d. an orthomyxovirus
2. Historically smallpox originated in
 - a. South Africa
 - b. India
 - c. China
 - d. tropical Africa
3. Smallpox is contagious
 - a. from the beginning of the rash until the scabs fall off
 - b. only during the prodromal period
 - c. during the latter part of the incubation period
 - d. only when the rash is filled with pus
4. The smallpox virus
 - a. is an RNA virus
 - b. can occur in certain animals
 - c. is killed after short contact with the air
 - d. is a DNA virus
5. Permanent sequelae of smallpox include
 - a. pain in the lumbar region
 - b. blindness
 - c. loss of the sense of smell
 - d. enlarged joints
6. the person to have first tried vaccination was
 - a. Dr. Maitland
 - b. Dr. Jenner
 - c. Lady Montague
 - d. Benjamin Jesty
7. Vaccinia virus
 - a. was first known as cowpox virus
 - b. can transmit smallpox to immunodeficient persons
 - c. is heat killed before use as a vaccination agent
 - d. is a herpes virus
8. Which of the following is not a contraindication to vaccination?
 - a. eczema
 - b. pregnancy
 - c. previous vaccination
 - d. immune deficiency

9. WHO declared smallpox eradicated in
 - a. 1977
 - b. 1980
 - c. 1972
 - d. 1984

10. After the initial vaccination “take” the protection against smallpox is about
 - a. 3-5 years
 - b. 7-10 years
 - c. life long
 - d. 10-20 years

11. Which of the following exceeded smallpox in devastating effects on the population?
 - a. cholera
 - b. plague
 - c. yellow fever
 - d. none of the above

12. Minor reactions to vaccination include all but
 - a. headache
 - b. ocular vaccinia
 - c. rash
 - d. fever

13. Smallpox was an ideal candidate for global eradication because
 - a. it occurs only in monkeys and humans
 - b. the virus cannot survive outside the body
 - c. it has a single unchanging antigenic type
 - d. it is transmitted only by touching secretions of diseased individuals

14. Participation in the present vaccination program is less than expected partly due to
 - a. health care workers are concerned about transmitting vaccinia to patients
 - b. not enough vaccine is available
 - c. there have been more serious side effects than anticipated
 - d. the government has decided not to advocate vaccination

15. Variolation
 - a. is another name for vaccination
 - b. was practiced first in China
 - c. reduced the fatality rate of smallpox from 30% to 2-3%
 - d. was not adopted in the United States

16. In the global smallpox eradication program Brazil and Indonesia were initially focused on because
 - a. it was easier to get around the countries
 - b. there were no close countries to reinfect the populations
 - c. the governments were more friendly to the vaccinators
 - d. there was sufficient vaccine already in the countries

17. The eradication of smallpox depended on
 - a. vaccination of the entire population
 - b. isolation, contact tracing and vaccination of all contacts
 - c. developing a newer, more potent vaccine
 - d. isolation of the last case in India

18. The earliest record of the use of smallpox as a biowarfare weapon in North America was in the
 - a. Revolutionary War
 - b. Civil War
 - c. French and Indian War
 - d. War of 1812

19. By 1984 the WHO had restricted the variola virus to which of the following 2 labs?
 - a. Univ. of Birmingham and CDC
 - b. WHO and Moscow's Institute for Viral Preparations
 - c. Moscow's Institute for Viral Preparations and CDC
 - d. WHO and the Royal Society in London

20. All but which of the following have probably led to the initiation of the United States present vaccination program?
 - a. the reported research on variola virus by the Univ. of Birmingham
 - b. the reported development of the Soviet bioweapons program
 - c. the lack of immunity in the general population
 - d. the possible smuggling of the variola virus from Russia to other countries.

**Course #DL-950 - Smallpox
Registration/Answersheet - 2.0 CE Credit**

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Please circle the one best answer for each question.

- | | | | | | | | | | |
|-----|---|---|---|---|----|---|---|---|---|
| 1. | a | b | c | d | 11 | a | b | c | d |
| 2. | a | b | c | d | 12 | a | b | c | d |
| 3. | a | b | c | d | 13 | a | b | c | d |
| 4. | a | b | c | d | 14 | a | b | c | d |
| 5. | a | b | c | d | 15 | a | b | c | d |
| 6. | a | b | c | d | 16 | a | b | c | d |
| 7. | a | b | c | d | 17 | a | b | c | d |
| 8. | a | b | c | d | 18 | a | b | c | d |
| 9. | a | b | c | d | 19 | a | b | c | d |
| 10. | a | b | c | d | 20 | a | b | c | d |

Distance Learning Evaluation Form

According to state regulations, this evaluation must be completed and returned in order to receive CE hours. Your comments help us to provide you with better continuing education materials in the distance learning format. Please circle the number that agrees with your assessment.

1. Overall, I was satisfied with the quality of this Distance Learning course.

(strongly agree) 5 4 3 2 1 (strongly disagree)

2. The objectives of this Distance Learning course were met.

(strongly agree) 5 4 3 2 1 (strongly disagree)

3. The difficulty of this Distance Learning course was consistent with the number of CE hours.

(strongly agree) 5 4 3 2 1 (strongly disagree)

4. I will use what I learned from this Distance Learning course.

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5. The time to complete this Distance Learning course was: _____ hours

6. What did you like or dislike about this Distance Learning course ?