



This Week in the Journal

April 25, 2002

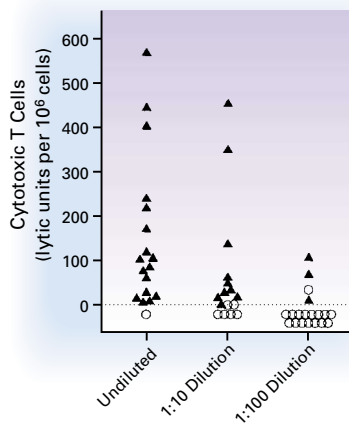
Responses to Dilutions of Smallpox Vaccine



In a randomized, single-blind study, 680 healthy, previously unvaccinated adults were inoculated intradermally with undiluted vaccinia virus vaccine, a 1:5 dilution, or a 1:10 dilution. The success rates were similarly high in all three groups: 97.2 percent, 99.1 percent, and 97.1 percent, respectively. Local and systemic symptoms were common, and 14 percent of subjects had rash at another site, including erythema multiforme in two subjects.

The data from this large study show that the limited supply of smallpox vaccine can be diluted 1:10 and still induce an immune response in about 97 percent of healthy, younger adults. Of the 15 subjects who had no response to the initial vaccination, 6 had pre-existing neutralizing antibodies, suggesting previous exposure to vaccinia virus.

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Dose Effects of Smallpox Vaccine

The administration of undiluted vaccinia vaccine led to vesicle formation in 19 of 20 healthy volunteers. With a 1:10 dilution, the success rate was 70 percent. With a 1:100 dilution the success rate was only 15 percent. The appearance of vaccinia vesicles correlated well with vigorous cytotoxic T-cell responses and with interferon- γ T-cell responses.

This study documents that the vaccinia vaccine produced in 1982 still has excellent potency but that dilution decreases the success rate. The formation of a vesicular skin lesion is an excellent indicator of the development of a protective immune response.

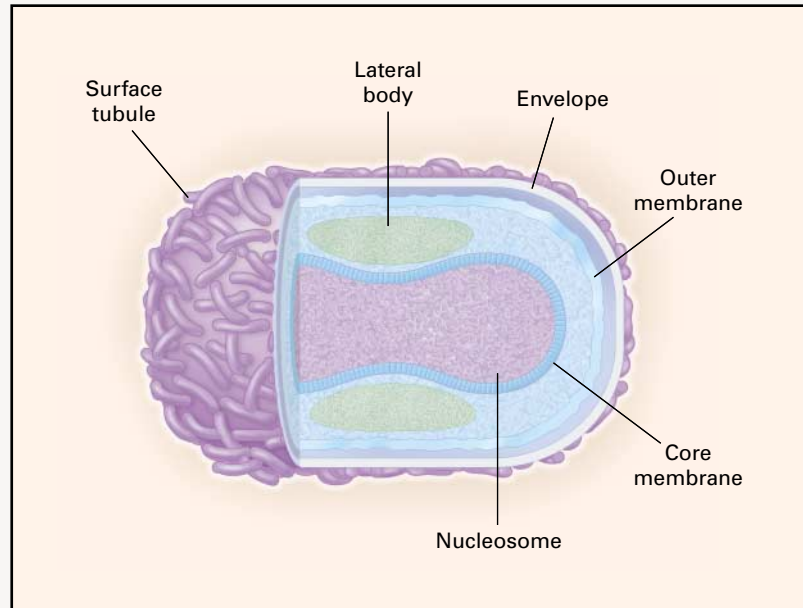
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PERSPECTIVE

Smallpox and Bioterrorism

This issue of the *Journal* contains more information about smallpox than I hope you will ever need. Smallpox was eradicated as a naturally occurring disease over 20 years ago. Thus, any new case of smallpox would have to be the result of human misadventure, either planned or unplanned, involving the laboratory stocks of the virus that were retained in the United States and the former Soviet Union when the disease was contained. Is smallpox a threat to our health? At the present time, there is no way to know. If smallpox virus is in the hands of bioterrorists, then it could be a threat. If all the infective virus is securely held by responsible authorities, then it is not a threat. Since virus stocks cannot be tracked with accuracy, it is impossible to know the answer to this important question. This issue of the *Journal* brings you a considerable amount of information about a killer disease that we can no longer ignore. The goal is to educate and inform.

Two Original Articles in this issue demonstrate that our current stocks of smallpox vaccine can be diluted 5-to-10-fold without substantial loss of efficacy. Immunity comes at a cost. Even in these well-controlled trials involving healthy young adult volunteers there was considerable morbidity, including both systemic effects and substantial local reactions. A Review Article about smallpox provides additional information to help medical professionals recognize and treat this condition when and if it occurs. Unfortunately, even if we all



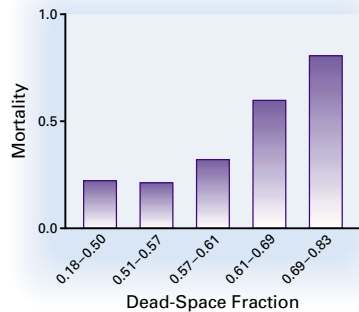
The Smallpox Virus.

become well acquainted with the clinical presentation of smallpox, by the time the disease is recognizable, it will probably be too late to prevent hundreds or thousands of deaths. Thus, the most pressing question is whether we need a preemptive vaccination campaign against smallpox. The decision on such a plan depends on the likelihood that terrorists will use smallpox as a weapon. A year ago it seemed unthinkable. Recent events, however, have raised the possibility that such an attack could conceivably occur. In an editorial in this issue, Fauci frames the critical issues about smallpox vaccination and calls for an open and thorough debate on this subject. I strongly agree.

To open the debate, Bicknell, in a Sounding Board article, outlines the case for mass vaccination. He provides realistic estimates of the incidence of deleterious side effects and the number of deaths that

might occur if we immunize the entire population. One such hazard, disseminated vaccinia, is illustrated in the Image in Clinical Medicine. The risk of this complication is especially great in persons with undiagnosed immunodeficiency syndromes. Bicknell also outlines what might ensue if we do not immunize the population and a coordinated smallpox attack occurs. A letter to the editor from Dworetzky provides a firsthand account of managing a reasonably contained smallpox epidemic. It is clear from his description that as a U.S. Army physician during World War II, he felt personally threatened in dealing with smallpox even though it was a disease to which he was immune.

The final decision on the best course of action for the country should be made after all the potential risks and benefits have been carefully weighed. We need to hear from those with the greatest knowl-



Pulmonary Dead Space and Mortality in the Acute Respiratory Distress Syndrome

Pulmonary dead space, the fraction of ventilation that is wasted, is greater than normal in patients with the acute respiratory distress syndrome who are undergoing mechanical ventilation. This study found that when the dead-space fraction was measured early in the course of the syndrome, higher values were independently associated with an increased risk of death.

The cause of the elevated dead-space fraction in these patients is unknown, but it may reflect pulmonary vascular injury. The dead-space fraction, which can be measured at the bedside, could be used to identify patients at a particularly high risk of death.

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“Among enrollees in for-profit HMOs, sick enrollees gave significantly lower ratings than healthy enrollees for half of the outcome measures we studied.”

Special Article: For-Profit and Nonprofit Health Maintenance Organizations

There is some concern about whether medical care of similar quality is offered by for-profit and nonprofit health maintenance organizations (HMOs). This study analyzed assessments of medical care by enrollees in for-profit and nonprofit HMOs. It found that although there were few overall differences, for-profit HMOs were rated less favorably than nonprofit HMOs by patients with self-reported fair or poor health.

In large part, these findings reflect differences in the perceptions of care. The study did not include objective indicators of clinical quality or patient outcomes. Thus, it cannot provide information about whether patients who are in poor health are actually more or less likely to receive good medical care through nonprofit or for-profit HMOs.

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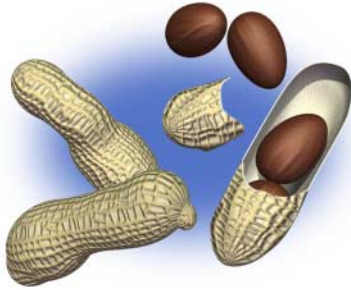
edge of the subject, and we need to consider what operational plans might be workable. If we do proceed with large-scale vaccination, we need to consider who should be immunized, when they should be immunized, and how to reduce unintended sequelae. Although medical facts frame the decision-making process, the choice in the end will

be in the hands of our government officials.

In my opinion the people of the United States have made it clear since September 11 that they are willing to make sacrifices for the common good. The debate on preemptive vaccination cannot go on indefinitely; we need to make a decision. I believe that if the deci-

sion calls for widespread vaccination, despite its attendant risks, we will accept those risks bravely, with our sleeves rolled up, ready for action.

JEFFREY M. DRAZEN, M.D.



Clinical Practice: **Peanut Allergy**

A 19-year-old woman is brought to the emergency room because of the acute onset of dyspnea, wheezing, vomiting, and generalized flushing. She has well-controlled asthma as well as a history of atopic dermatitis as an infant and urticaria after ingesting peanut butter at the age of five years. According to friends she ate a chocolate-chip cookie from a vending machine just before her symptoms developed. The ingredients listed on the cookie wrapper do not include peanuts. Nevertheless, how should this patient's condition be treated?

This article reviews the diagnosis and management of peanut allergy, which accounts for the majority of fatal and near-fatal anaphylactic reactions in the United States.

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“If given very early in the incubation period, vaccination can markedly attenuate or even prevent clinical manifestations of smallpox.”

Current Concepts: **Diagnosis and Management of Smallpox**

In 1980, smallpox was declared to have been eradicated, but some laboratories retained the variola virus. Because of the possibility of bioterrorism or even an accidental release, physicians need to be aware of the essential clinical facts about this highly infectious viral disease. Two experts summarize the clinical manifestations, epidemiologic features, and treatment of smallpox, including guidelines for use of the vaccine.

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“We do not have to sacrifice civil liberties for an effective public health response to a bioterrorist attack.”

Legal Issues in Medicine: **Bioterrorism, Public Health, and Civil Liberties**

In the wake of the September 11, 2001, terrorist attacks, the Centers for Disease Control and Prevention proposed a model act for the states that specifies steps to be taken to contain an epidemic resulting from a bioterrorist attack. The act would grant broad powers to the states in the event of public health emergencies arising from bioterrorism. Annas discusses the trade-off between civil liberties and the need to protect the health of the public in the event of bioterrorism. His underlying premise is that the model act, despite being revised in December 2001, goes too far.

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