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The ABCs of Smallpox

Which methods of treatment make sense and why

BY MARC SIEGEL

MEDICINE DEPENDS ON probability: the probability of a disease occurring, the likelihood that it will spread or can be prevented, the odds of a side effect resulting from a tool of treatment or prevention. A risk-benefit analysis evaluates the risk of a disease versus what doctors can do to prevent or treat it. With smallpox, the greatest problem recently has been an exaggerated perception of its risk. The public is divided into two camps: those who are afraid of smallpox and those who are afraid of the vaccine.

Smallpox is a debilitating disease that leaves behind disfiguring scars. But it is containable by public health measures that have been in place for more than 100 years. When untreated, it has a 30 per-

cent mortality rate. It spreads by airborne saliva when a person already has a fever as well as obvious skin lesions, so it's easily quarantined. Furthermore, giving the live virus vaccine to victims after infection can reduce the mortality rate to less than 10 percent. And a new oral form of cidofovir, an anti-viral drug that's proven somewhat effective at treating and preventing the spread of smallpox, shows great promise.

For people over 30, some residual immunity probably remains from vaccination in early childhood. According to Dr. Douglas Zeiger, an infectious-disease expert at the New York University School of Medicine, this lingering "herd immunity"—the idea that when a large portion of a group is immune to a disease, it's less likely that an infected person will come into contact with a susceptible victim—"may well slow down the spread of smallpox if it were to occur" in the United States.

Though it is likely that smallpox has spread from its "secure" place in a Russian laboratory to rogue states such as Iraq, it presents a remote threat. If smallpox were to occur at all, it would probably be in isolated cases that could be limited by containment. However, as David Goldston, the House Committee on Science's chief of staff, points out, the danger hasn't been clarified yet. "It's difficult to weigh the risks versus the benefits since the government hasn't given out information about the risks, even to the panel advising it on vaccination policy," he says.

Dr. Martin Blaser, an infectious-disease specialist and chief of medicine at the NYU School of Medicine, notes, "The old smallpox vaccine offers excellent protection. It is the reason why smallpox is no longer circulating in the world." This vaccine uses a related virus (vaccinia) that is much weaker than smallpox but that may cause or exacerbate skin conditions or brain swelling, or be spread if the vaccinated spot is touched. Furthermore, any vaccine using a live virus is not safe for someone who is pregnant or has a compromised immune system. These groups constitute a significant percentage of our population and must be protected. Unfortunately, many of those who are newly pregnant or immuno-compromised aren't aware of their condition.

Still, the old vaccine is useful in certain populations. Those in the military, especially soldiers going into Iraq, are a reasonable group to vaccinate because their risk of exposure outweighs the risk of the vaccine. The same is true for first responders, the emergency medical personnel who would be first on the scene if a smallpox outbreak occurred in the United States.

Hospitals are at the center of the controversy. Some want the old vaccine; others are refusing it. Though the risks of the old vaccine are small, many reluctant hospitals and their employees appear to be scared by the possible side effects, which publicity has magnified. They also may be bolstered by the reasonable belief that there would still be time to vaccinate hospital personnel if a case of smallpox occurred.

At the same time, the public is riddled with unrealistic ideas concerning smallpox. In mid-December, the

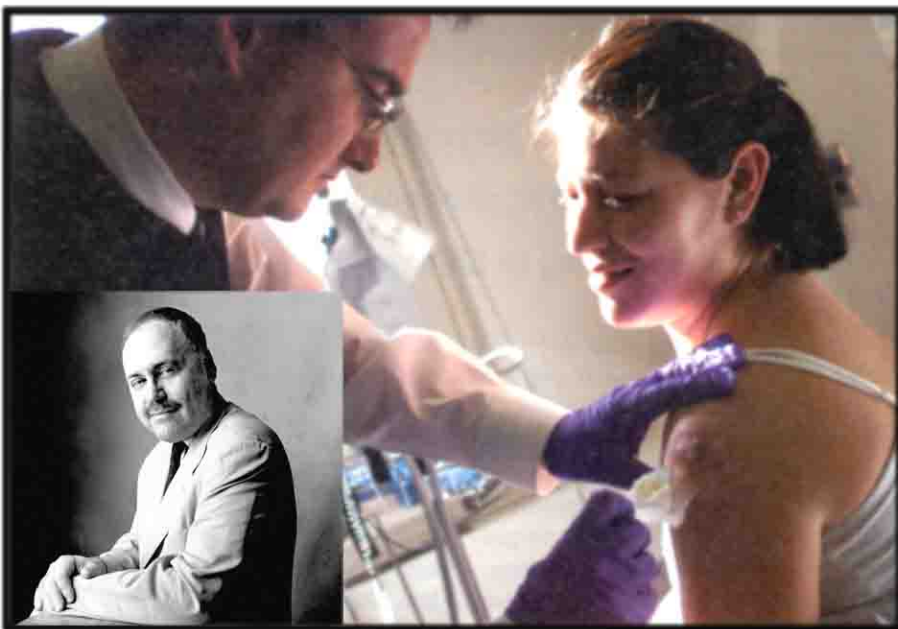
New England Journal of Medicine released a survey showing that 65 percent of Americans believe that everyone should be vaccinated now. Fears drive those numbers, but the fact is that smallpox is containable by public health measures and vaccination, and has never become as widespread as, say, influenza. Nor has smallpox been endemic to a region the way polio and influenza were in New York City in the early 20th century. Still, smallpox is disfiguring and potentially deadly. When 1,600 cases broke out in Boston between 1901 and 1903, 270 people died. It is not a disease to be taken lightly.

Almost entirely lost in the debate has been the newer inactivated virus vaccines, in which the virus doesn't cause side effects. One of these has been given safely to more than 300,000 people in Japan. Another has been given to 100,000 people in Turkey. The National Institutes of Health has 100 people enrolled in a clinical trial of this type of vaccine; that study should be completed within a year. Interestingly, the Centers for Disease Control and Prevention's Web site lists these facts, but then goes on to call this vaccine untested, as though the only tests that matter involve Americans. But there is no reason to believe that this vaccine couldn't be used, at least in low-risk populations.

At the same time, work is proceeding on a recombinant vaccine in which viral DNA is piggybacked onto user-friendly bacteria. Recombinant vaccines are generally the safest and are used for hepatitis and other viruses. It is likely that one will be developed for smallpox, further altering the probabilistic equations that public health officials use when determining if a population should be vaccinated.

Accurate information and an informed perspective could bring the public's fear of smallpox more in line with its real risk. Exaggerating the side effects of a largely safe and effective vaccine is not the best way to treat the fear of the virus. But immunizing everyone just to manage the public's panic would be even worse. ♦

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Getting ready for smallpox, both the vaccine and the disease