Should only infected people be vaccinated?

With biological warfare a distinct possibility, how should health authorities in the most likely target countries - the US and Israel - deal with the threat? Judy Siegel-Itzkovich learns about the options from a visiting expert.

After the disease killed as many as 100 million people and left 200 million blind and scarred victims over the past 3,000 years, the world thought in 1979 that it had said goodbye to smallpox. But despite the success of a heroic effort to eradicate it worldwide, the highly contagious and untreatable viral disease threatens to come back and haunt us via biological warfare. The September 11 attacks last year make the unthinkable a reasonable possibility.

Smallpox is caused by two strains of orthopox virus: variola major, which results in severe symptoms and a death rate of 20%-40% of those infected; and variola minor, which has less severe symptoms and lower mortality (about 1%). After the Spanish invasion of America, 2.5 million Native Americans perished in nine years, and in the early 18th century, 90% of all Native Americans in Massachusetts died from a variola epidemic.

As late as 1966, more than 10 million people died of smallpox, inducing the World Health Organization to launch its World Eradication Program. The US stopped routine smallpox vaccination in 1972, and Israeli health authorities took this step in 1980.

But while variola stocks were kept under lock and key in the US, it is feared that rogue groups in Iraq, Iran or other countries intent on causing
havoc had access to those in the former Soviet
Union.

Spreading variola particles in a crowded place
such as a train station or airport could result in
the virus entering the bodies of thousands of
people by inhalation. Unaware of infection, they
would go on to their destinations, initially
feeling well but then developing visible
symptoms - high fevers around Day 11 and a
rash by Day 14.

If vaccinated against smallpox within four days
of infection, they could be spared from death and
even the disease, and prevented from spreading
it to many others in a chain reaction. But the
smallpox vaccination itself, which uses a live
virus called vaccinia that is a "cousin" of
smallpox, can cause brain damage and has been
known to kill one person out of every one
million vaccinated, especially those with weak
immune systems due to cancer treatment or
AIDS.

So how should health authorities in the most
likely target countries - the US and Israel - deal
with the threat? Even the half of the population
who were vaccinated decades ago as children are
believed to have little immunity left.

Should governments bolster their small available
quantities of vaccine by mass-producing it?
Should they vaccinate the entire population even
if no bioterror attack seems imminent?

In the event of a single localized attack, should
public-health workers be sent to trace all persons
who have been in contact with those infected
and vaccinate them because they can pass it on?
Or should whole populations be vaccinated after
an attack, weighing the risks of delay against the
inherent danger from the vaccine to a tiny
minority of weak individuals?

"Now is the time to decide how to proceed with
vaccination," writes Prof. Dan Michaeli, an
infectious-disease expert and chairman of Clalit
Health Services, in the July 2002 issue of IMAJ,
the Israel Medical Association Journal.
"Revaccination of people who were vaccinated
once or more will enable us to acquire vaccinia-
immune globulin in substantial amounts. This
should be used for people who are prone to
immune deficiencies. Other measures may also
be applied to reduce the risks from vaccination,
although these risks may be acceptable in view
of the risks of smallpox re-introduction [by bioterrorists].

"The time has come," Michaeli concludes in his editorial article, "for governments and health ministries to sit down, prepare plans and implement them without delay, especially in countries already exposed to terrorism and/or heavy international traffic."

"The methods of smallpox outbreak control are known and can be implemented - in fact they were successfully carried out in Israel [to deal with a natural outbreak] in 1949," write Health Ministry chief epidemiologist Dr. Paul Slater and colleagues in the same IMAJ issue.

"The economic cost of preparation is relatively small.... A smallpox outbreak in Israel must not be regarded as a doomsday event. If it occurs, it can and will be overcome.

"If we make the necessary commitment now to vaccine production and stockpiling, laboratory preparation, planning, professional training and public education, the losses - although substantial - can be minimized. Moreover, the reinstitution of routine smallpox vaccination in Israel must be given serious consideration, now and in the future, as improved vaccine [with a lower mortality rate] becomes available."

But the Health Ministry, by order of the Defense Ministry, has remained mum about its actual plans and programs, refusing to say if it already has manufacturing capabilities here and access to enough vaccine for all Israelis, or whether it's planning to reintroduce routine smallpox vaccination or booster shots.

A foreign expert who during the past seven months has created an epidemiological model for coping with smallpox bioterror is Prof. Edward Kaplan, the William N. and Marie A. Beach Professor of Management Science at the Yale School of Management and a professor of public health at Yale Medical School.

Kaplan, who speaks Hebrew, is a frequent visitor to Israel and twice received a Lady Davis Visiting Professorship at the Hebrew University, spent over a week lecturing to experts in the field at the Technion in Haifa, Rafael (Israel Arms Development Authority), Hebrew University-Hadassah Medical School, Sheba Hospital, Weizmann Institute of Science and
He found time during his visit for an interview with The Jerusalem Post on the Hadassah Ein Kerem campus.

Earlier this month, he testified before a panel in Washington to oppose a federal advisory panel plan for for "ring vaccinations," in which health workers isolate infected patients and vaccinate people who have been in close contact with them, forming a "ring of immunization" around an outbreak and a barrier to its spread.

In theory, such a strategy can work because the vaccine, if given within four days of exposure to the virus, protects people from the disease, and is relatively inexpensive. But Kaplan and colleagues argue in a major article in the latest Proceedings of the [US] National Academy of Science that what might begin as 1,000 infections at a train station or airport could spiral out of control over subsequent weeks and months into nearly 100,000 deaths if the outbreak were fought with ring vaccination alone. This would compare with only around 500 deaths resulting from mass vaccinations after an attack.

"Comparing the results to mass vaccination from the moment an attack is recognized, we find that mass vaccination results in both far fewer deaths and much faster epidemic eradication over a wide range of disease and intervention policy parameters, including those believed most likely, and that mass vaccination similarly outperforms the existing policy of starting with traced vaccination and switching to mass vaccination only if required," Kaplan's team wrote.

He explains that it takes time to question people who are known to have been infected.

"If you put a message on TV and radio, asking all people who were at a certain train station at a certain time, will you get all of them and only them, or will you create a panic?"

And those infected, he continues, are likely to be unaware of many people who were in "sneezing or coughing distance" from them. Then you have to find these endangered contacts and vaccinate them, while precious time is wasted.

Initially, the US government planned to vaccinate only a few thousand public-health workers - "early responders" who would deal with any bioterrorism attack - added to the
11,000 American lab workers and scientists who work with the virus and have been vaccinated since 1983. More recently, the US decided to give smallpox shots to as many as half a million health-care and emergency workers to be on the safe side, but it has not abandoned its post-attack strategy of ring vaccination.

But Kaplan suggests the possibility of pre-attack mass vaccination be considered in both the US and Israel. "Some 350 million doses will become available by the end of next year."

Diluting doses to lower strength has been shown not to harm their effectiveness. "There are those who argue that having mass vaccination would deter the terrorists from using smallpox as a weapon, but I argue that they could use it anyway to sow a great deal of panic," he says.

Despite the World Trade Center and Pentagon disasters, Kaplan thinks Americans still remain in the dark about protecting themselves from terrorism.

"Israelis, exposed for decades to actual threats on their lives, would be much more able to cope with a biological-warfare threat," Kaplan said. Not only did they survive the sealed rooms during Saddam Hussein's Scud missile attacks on Israel, the health authorities acquitted themselves well in the 1988 mass vaccination against polio among all adults under the age of 40, which brought an end to an outbreak.

"I don't say that Israel has to mass-vaccinate its population even if a bioterror attack is not clearly on the horizon, but it should be considered - especially as a voluntary effort to raise the population's immunity, which has been greatly reduced in the past two decades.

"It would be great if there were an effective, fast and cheap screening test to see who had immunity and who has been exposed, but I suppose this is impractical."

Kaplan was asked by the US National Institutes of Health to design his model and decide what strategy to use in the event of a bioterror attack.

"I entered the research without having my own preconceived opinion. But now it's clear to me that if such an attack involved quite a number of people, each of whom were in contact with
dozens of others, trying to hold it in control with just ring vaccination would not be enough."

In any case, while most researchers who have created models are eager to see them tried in real life, the Yale scientist declares: "I will be perfectly happy never to see my model on smallpox actually implemented by bioterrorists."

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