Polio: Salk Challenges Safety of Sabin's Live-Virus Vaccine

Back in the early 1960's Jonas Salk, the famed developer of a killed-virus vaccine against polio, suffered a crushing reversal of fortune at the hands of his medical colleagues. Although Salk's vaccine had provided the first spectacular gains against polio during the 1950's, the nation's top health authorities recommended that it be replaced by a live-virus vaccine that had since been developed by Albert B. Sabin and others.

The rationale for the change was that the live-virus vaccine was thought, for a variety of reasons, to offer better protection against the disease that still sent tremors of dread through parents anxious to protect their children from the crippling effects of the polio virus. Authorities concluded that the live-virus vaccine would be more acceptable to the public (because it is given orally on a sugar cube rather than by injection); would produce longer-lasting immunity; and would even immunize many people who had not bothered to get vaccinated but who came into contact with those who had and caught a generally harmless infection from them. They also felt that the live-virus vaccine would do a better job of eradicating the wild polio virus from the environment because the live-virus vaccine suppresses the wild virus from the intestinal tract, thereby interfering with the spread of polio through fecal matter and sewage, whereas the killed-virus vaccine does not.

The switch in vaccines was recommended by such authoritative bodies as the U.S. Public Health Service, the American Medical Association, and the American Academy of Pediatrics, among others. Salk and his adherents did not give up without a fight. They argued that there was no real evidence that the live-virus vaccine would provide greater immunity or do a better job of eradicating the disease than would the Salk vaccine. And some warned, Cassandra-like, that the Sabin vaccine—containing live viruses, although in attenuated form—would probably *cause* some cases of polio whereas a killed-virus vaccine would probably not. But the advice of the medical establishment prevailed. Within a few years, the Salk vaccine had largely disappeared from this country. None has been manufactured here since 1968, although a small amount continues to be imported. The Sabin vaccine has become the weapon of choice in the fight against polio, not only in this country but in most foreign countries as well.

The battle inflicted lasting scars. Proponents of the competing vaccines occasionally vilified each other and, even today, organizers of scientific meetings often take pains to seat Salk and Sabin at opposite ends of a room to lessen the presumed antagonism that exists between them. But the issue of public policy toward polio immunization seemed to have been settled. While the lay public continues to venerate Salk as the folk hero who conquered polio, the medical authorities routinely dispense the vaccine developed by his rival.

That's where matters stood until a few years ago when Salk launched a campaign to reopen the question. His interest was aroused, he says, by a court case (Reyes *v.* Wyeth Laboratories) in which an 8-month-old girl contracted paralytic polio shortly after receiving a dose of Sabin vaccine. Both a federal district court and an appeals court found the manufacturer liable for failing to provide adequate warning that the vaccine might cause polio in a small proportion of recipients. The appeals court specifically noted that such warnings are important because an individual who is aware of the small risk in the Sabin vaccine might well choose to be inoculated with the Salk vaccine instead, or refuse inoculation.

Salk has since been arguing that his killed-virus vaccine should be reinstated to favor. He contends that experience abroad over the past decade and a half indicates that his killed-virus vaccine is more effective than was generally believed when it was rejected here in the early 1960's, while experience in this country and elsewhere reveals that the live-virus vaccine is less safe than was originally believed. In fact, the live-virus vaccine is now "associated with" most of the handful of paralytic polio cases that now occur each year in this country. As a result of this changed situation, Salk argues, the killed-virus vaccine should now be recommended for routine immunization for persons of all ages, while the live-virus vaccine should be reserved for combating outbreaks that might arise in communities with low vaccination rates. Even Salk acknowledges that the Sabin vaccine is superior for suppressing outbreaks. But for routine immunization, Salk seeks nothing less than a reversal of the decision that went against him in 1961–62.

Salk has presented his case vigorously in a variety of forums. He has met with, and submitted voluminous documents to, three expert committees that have enormous influence over vaccine policy—the Committee on Infectious Diseases of the American Academy of Pediatrics, the Panel on Viral Vaccines and Rickettsial Vaccines of the federal Bureau of Biologics, and the Advisory Committee on Immunization Practices of the U.S. Public Health Service. He has testified before two key congressional committees—the Senate subcommittee on health and the House subcommittee on health and environment. And he has spoken at scientific conferences, written articles (including one in the 4 March issue of *Science*), and granted newspaper interviews.

His warmest reception seems to have been before the Senate health subcommittee. After hearing Salk's testimony and that of another witness—Harold S. Ginsberg, professor of microbiology at Columbia University—who called it "ill-advised" to continue use of the Sabin vaccine, the committee's ranking Republican, Senator Jacob Javits of New York, said he found it "amazing" that the government had not "reversed its field" and reinstated the Salk vaccine. The views of organized medical groups, Javits suggested, are now "outdated." Similarly, the subcommittee's chairman, Senator Edward M. Kennedy (D–Mass.), pushed hard on the theme that parents should be given a choice and enough information to decide whether they wanted their children to take the killed- or live-virus vaccine. Kennedy had little doubt that parents would opt for a vaccine that carried "virtually no chance of being able to contract polio" rather than a vaccine that might cause one case of polio in every few million people vaccinated.

But none of the expert groups that have reviewed the data seems ready to jump on Salk's bandwagon. The American Academy of Pediatrics committee concluded that the live-virus vaccine remains the preferred choice for routine immunization. The two government panels—the Advisory Committee on Immunization Practices and the Panel on Viral Vaccines and Rickettsial Vaccines—have both completed draft reports that have not yet been released; persons familiar with the drafts say that, while the reports find mer-

it in Salk's vaccine, they do not recommend that it become the preferred weapon against polio. The latest expert group to consider the issue is a committee of the Institute of Medicine of the National Academy of Sciences, which was asked to review the matter by the Public Health Service because of inquiries from Senators Kennedy and Javits. That group met for 3 days in mid-March and is due to issue a report to a national immunization conference on 6 April. Again, many participants in the Institute study indicated to *Science* that they are reluctant to recommend a switch back to the Salk vaccine.

There is general agreement that both vaccines are highly effective. The Salk vaccine has virtually eradicated polio from Finland—there have been no cases of polio and no isolations of polio virus in that country since 1964. The record has been almost as impressive in Sweden, another country which uses only the Salk vaccine. Sweden just recently reported its first case of paralytic polio in some 15 years (excluding cases imported from abroad); the victim had not been vaccinated. Meanwhile, the Sabin vaccine has achieved impressive results in the much larger and more diverse population of the United States. Polio victims numbered in the tens of thousands per year in this country before the Salk vaccine was introduced, and they still numbered in the thousands per year during the Salk era. (The Salk vaccine used then was less potent than that used today.) But the record has improved steadily in subsequent years. For each of the past 4 years, there have been fewer than ten cases reported in this country (1976 data provisional).

As for safety, there is general agreement that the Sabin vaccine is indeed the source of, or at least is "associated with," a small number of polio cases. According to the federal Center for Disease Control, there were 44 cases of paralytic polio associated with the Sabin vaccine in this country between 1969 and 1976, a period in which some 114.5 million people were vaccinated. Ten of these cases occurred in recipients of the vaccine—making the odds about 1 in 11.5 million that an individual who takes the live-virus vaccine will get polio from it. The other 34 cases occurred in parents, friends, and others who came into contact with vaccine recipients and apparently caught the live virus from them. The Sabin vaccine has been so successful at suppressing the wild polio virus that most cases now occurring in this country are those associated with the vaccine.

The Salk killed-virus vaccine, on the other hand, is generally exonerated from causing polio. The vaccine caused a number of polio cases back in 1955 when improper inactivation procedures failed to kill the virus, but since then it has generally been deemed safe. (Sabin challenges this view but has little support.) Thus, if one considers only the question of polio induction, the Salk vaccine appears safer, although many scientists consider the risk of getting polio from the Sabin vaccine so vanishingly small that the difference is marginal.

How the two vaccines compare in other safety respects is unclear. There seems to be little hard data on the extent to which either vaccine is associated with such rare disorders of the central nervous system as Guillain-Barré syndrome, the disease that brought the swine flu immunization campaign to a halt. The countries where the Salk vaccine is now used are too small for such rare problems to be detectable. Thus scientists who have been reviewing the data have no firm idea whether a switch from Sabin vaccine back to Salk vaccine would produce more, or fewer, complications. Both vaccines in the past have been shown to be contaminated with the SV40 virus, which causes cancer in hamsters but is not known to harm humans. That problem seems to have been eliminated.

The Problems of Switching

Most experts agree that the Salk vaccine is well suited for special categories of people, including children with immune deficiences, who are particularly susceptible to infection from live-virus vaccines, and adults who have had no previous polio immunization and plan travel to polio-infected areas. But they foresee problems if this nation tries to switch to the Salk vaccine for routine inoculation of infants and children, the core of our immunization effort against polio.

Some problems are of a practical nature. It would, for example, be costly for a drug company to develop new manufacturing facilities and train people to make the Salk vaccine. Eli Lilly & Co., which used to make Salk vaccine, estimates that a $30 to $50 million investment would be required over 3 years time. There is also some doubt that there would be an adequate supply of monkey kidney cells, which are used to grow the viruses for both vaccines but which are needed, some say, in greater quantity for the Salk vaccine than for the Sabin vaccine.

Such practical problems could presumably be solved if a switch were deemed desirable. The chief question that is troubling many experts is whether, if a switch were made, the Salk vaccine would really prove as effective in this country as the Sabin vaccine has been. Salk interprets the data from abroad as evidence that his vaccine provides long-lasting immunity to the individual and solid protection to the community as a whole (witness the apparent eradication of the wild polio virus from Finland). Some experts are inclined to agree with him; others question the significance of the findings.

Both Finland and Sweden are small, homogenous countries with highly effective vaccine-delivery systems that reach better than 90 percent of the target population, often with as many as seven separate shots of Salk vaccine. In this country, with its larger, more diverse, and highly mobile population, the delivery system reaches only about 70 percent of the target population with multiple doses; many individuals drop out after getting only one dose in a planned series of three or more. In those circumstances, some say, the Sabin vaccine is apt to provide better protection, partly because a single dose of Sabin vaccine is more effective than a single dose of Salk vaccine, and partly because recipients of the Sabin vaccine seem to infect, and thus immunize, large numbers of the unvaccinated, thereby making up for the failures of the delivery system. (That such infection occurs on a large scale is widely believed but not absolutely proved.)

If this country did switch to the Salk vaccine and the level of protection declined, then an outbreak of polio might occur that could be far more damaging than the few cases of the disease that have been associated with the Sabin vaccine. "Why rock the boat," says one expert who is pondering the issue. "We're doing so well that to shift now would make me nervous."

Whether the public and its political leaders will agree with that reasoning is uncertain. The debate over polio vaccine has raised troubling issues of informed consent. Senator Kennedy believes that people should have the right to choose which vaccine they want on the basis of adequate disclosure of the risks involved. If so, then it is always possible that the public might choose the Salk vaccine regardless of what the experts recommend as best for community-wide protection. There is also the disturbing likelihood that the Sabin vaccine is infecting some people who have not even been vaccinated, making it a two-edged sword that increases community protection but may cause polio in a few unlucky contacts. Who has the right to decide that these "contacts"—some of whom may have shunned vaccination to avoid the risks—will nevertheless be infected surreptitiously for the good of the nation? These are knotty questions that are seldom even considered.—PHILIP M. BOFFEY