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Flaws in Disease Data

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Science and Man

THE VIRTUAL CONQUEST of polio by immunization of most of the population with the Salk and Sabin vaccines is a cardinal achievement of public health. Fifteen years ago, there were more than 50,000 cases of polio a year. In 1964, there were only 121 cases reported and most of those afflicted had not received the immunization.

Yet for all its proved value, mass immunization has potential dangers that need to be explored more fully. We must improve our techniques of collecting large-scale data on the safety and efficacy of mass immunization programs. Despite uncertainties, however, no one should be deterred from seeking immunization against polio. At this point, the danger of polio greatly exceeds any danger likely to be discovered by future research.

The uncertainties exist nevertheless and it is the job of science to remove them. They were emphasized when a new virus, SV-40, was discovered as a contaminant of seedstocks and production batches of the polio vaccines. SV-40 occurs in rhesus monkeys, whose tissues are used for polio-virus cultivation.

The virus has no obvious effect on the tissues of the monkeys, but it has been discovered to cause tumors in hamsters injected with it shortly after birth. There has been no evidence that the same result can be expected in humans, there has been no huge increase in cancer since the polio immunization program began in 1955 and there is no positive proof of any human diseases that can be associated with SV-40.

WE MUST, however, ask how sensitive our surveys are. How many cases of a new disease would have to be associated with SV-40 before we realized the relationship?

Dr. M. R. Hilleman, virologist at the Merck Institute for Therapeutic Research, who discovered SV-40 in 1960, wrote in 1964, "Careful followup in persons who receive such vaccine has failed, to date, to reveal any adverse effect attributable to the vaccine."

He refers to a paper by Dr. J. F. Fraumeni Jr., and colleagues at the National Cancer Institute, published in the American Medical Association Journal Aug. 30, 1963. The study appears to be the main foundation of prevalent attitudes about SV-40.

Dr. Fraumeni found that during the introduction of Salk vaccine, batches used in different states contained varying levels of SV-40 contamination. A study was made of mortality statistics compiled in 1959 for children born in 1948 and who received the vaccine in 1955. If SV-40 was associated with cancer, there should have been a higher incidence in children living in states which received the vaccine containing the greatest amount of SV-40. But no significant differences were found.

As Dr. Fraumeni points out, however, a latent period of longer than four years between inoculation and contraction of a disease would have frustrated this research.

Now, it so happened that in 1952, three years BEFORE the immunization began, the incidence of leukemia was 60 per cent higher in the states that later proved to be areas of high exposure to SV-40. Any association between the two situations would be illogical and obviously spurious, but nevertheless, under our present systems of reporting diseases and with the crudeness of our vital statistics procedures, such a connection would be possible.

THE HIGHER incidence of leukemia in those areas can reasonably be attributed to variations in diagnosis and reporting of disease. That this conclusion is possible in itself gives some idea of the poor precision that can be expected from present procedures.

The sad fact is that there has been no large-scale followup of specific individuals exposed to SV-40 because of the lack of adequate records. And now that SV-40 is a recognized potential contaminant, it would be ethically questionable, and in fact it is currently forbidden by government regulation, to administer Salk or Sabin vaccine that is not proven to be free of SV-40.

Unhappily, it would be quite possible for SV-40 to induce many thousands of cases of childhood diseases, or, on the other hand, to immunize against many others, all unbeknownst to anyone because of the inadequacy of present investigative techniques.

The only technique that would give us information of any real value would be explicit registration of exposures to specific batches of vaccines on a record that identifies each recipient for later followup.

This implies a much more meticulous and individual approach to vaccination than we have been accustomed to, and it certainly would be more expensive. So would other measures that must be elaborated if we are to achieve the same assurance of safety and efficacy of vaccines that we now demand from other drugs.