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Who is responsible, and why, for the chaotic confusion over the polio inoculations?
A noted medical journalist disentangles the essential facts.

THE PEAK of the polio season usually comes in the second half of August or the first part of September. This year, we might have had substantially fewer cases of polio than usual. As it is, the number we do have will be largely a matter of luck.

We will have whatever number of cases do occur instead of the smaller number we might have had because of the Great Vaccine Mess. During this past spring, the country was made to witness a spectacle without precedent. On April 12, Dr. Thomas Francis, Jr., of the University of Michigan, reported on the largest and most carefully executed field trial of a vaccine product in history, the 1954 test of the Salk polio vaccine. The trial confirmed a major medical discovery.

The Salk vaccine was found to be adequately effective in preventing paralytic poliomyelitis, and remarkably safe. A month later, the hopes the Francis report had aroused, and the vaccine itself, had been very nearly dissolved in an incredible sea of confusion.

How did this come about? Who and what were responsible? It is no doubt too early for anyone to attempt a final assessment of what happened. The principal details, however, can be established.

The Great Vaccine Mess was a tangled compound of many factors. It involved technical questions so abstruse there are scarcely two score men in the United States competent to pass on them, and everyone with a direct part in the situation, or nearly everyone, acted from the best of motives.

But demagogy and political expediency also contributed to the brew. So did over sensationalism by the press, radio, and TV, and a misguided attempt by the Department of Health, Education, and Welfare to withhold from the public for many weeks information the public was entitled to have from the beginning. Also involved were timidity and lack of leadership; a complete failure to educate the public properly on vaccines (despite all the propaganda); the constitutional unwillingness of scientists to give absolute guarantees; and many things more.

The point is, though, that the mess was unnecessary. Even if better planning might not have avoided the accident with Cutter vaccine, many more children than were inoculated could have been immunized *safely* in time for this year's polio season. The vaccination program was perhaps not the best that could have been devised. But it was not a bad program. It could have been kept on the track. All that was necessary was a little judgment and some capacity for decisive action in the right places at the right time.

HOW IT ALL STARTED

THE BEST WAY to unravel the Great Vaccine Mess is to set down, first, a simple chronology of events as they were seen, let's say, by an average newspaper reader or TV viewer. Then we can get on *to* some other things that also happened-though they were **not in the papers-and to an** examination of what went **wrong.**

The place to begin is New York in October 1954. In that month, the National Foundation for Infantile Paralysis, whose office is on downtown Broadway, announced that it was taking a "calculated risk." The Foundation had paid for the development of the Salk vaccine and paid for and arranged the field trial. Now, without waiting for Dr. Francis' report on the trial, it was ordering enough vaccine to immunize nine million children. Its purpose was to get manufacturers into production and to have vaccine on hand as soon as the trial results were announced in the event that these were favorable.

During the March of Dimes in January, Foundation workers and Foundation publicity carried the message of the "calculated risk" into nearly every home in the country. As the date for the Francis report drew near, interest was whipped up still more by advance newspaper stories-like an erroneous New York *World-Telegram & Sun* report that the vaccine had been found 100 per - cent effective.

The date for the Francis report was set by Dr. Francis himself. It could not be later than midApril (otherwise the inoculation of school children could not be completed before the end of the school year). Dr. Francis was pressed by the big news magazines to make it early in the **week (to meet their deadlines).** The University of Michigan, where a special scientific meeting was held to hear the report, asked that the day not be a Monday (to avoid calling out a make-ready crew on a Sunday, at Sunday rates). So it was April 12, the second Tuesday of the month and the tenth anniversary of the death of Franklin D. Roosevelt, the most famous polio victim of all--a circumstance which was to lead to caustic remarks later, but of which Dr. Francis insists he was at the time unaware.

By 9:00 A.M.. of the big day, nearly two hundred newsmen were jammed into a temporary newsroom on the third floor of the Michigan graduate school administration building, awaiting copies of the report. These arrived at 9:15 under the escort of a university press officer and four Ann Arbor policemen. (It took the four policemen to get the press officer and his cargo through the crowd of newsmen and into the newsroom.)

Dr. Francis began reading his report to an audience of five hundred physicians and scientists in the auditorium downstairs an hour later. As the cameras ground, he announced that the vaccine had been between 60 and 90 per cent effective in preventing paralytic polio, and even more effective in avoiding the bulbar form of the disease. Side reactions among the 440,000 children who had received the vaccine had been very few and mild. There was no evidence to connect the vaccine with the cases of polio that did occur among inoculated children; those children simply did not develop immunity or did not develop it in time.

In Syracuse, New York, the success of the Salk vaccine was signaled by airraid sirens, church bells, and the turning of all traffic lights red for one minute. In Washington, late that afternoon, the Secretary of Health, Education, and Welfare signed licenses for manufacture of the vaccine. Parke, Davis & Co., one

of six vaccine firms under contract to the polio foundation, made its first shipment less than four hours after its license was signed. Vaccination of first- and second-graders under the Foundation program got under way, in San Diego, April 16.

Dr. Hart E. Van Riper, medical director of the polio foundation, predicted that there would be enough vaccine to immunize twenty million children by July 1. This was raised to thirty million when the Foundation's medical advisory committee decided on two shots for each child this spring, with the third put off until next winter. (The longer interval between the second and third injections, Dr. Salk reported, would provide more solid, longer-lasting immunity.) Newspapers reraised Dr. Van Riper; they guessed there might be enough vaccine to inoculate forty-five million children before the polio season.

To get some of this vaccine for youngsters not covered by the Foundation program, state and local health departments throughout the country began placing orders with the vaccine manufacturers. The manufacturers said no orders could be accepted until commitments to the Foundation had been fulfilled. It was soon evident that vaccine production was neither so large nor so elastic as expected and that the Foundation contracts would take longer to complete than anticipated. New York and many other communities had to postpone scheduled inoculation clinics repeatedly because the vaccine had failed to arrive. The *World-Telegram* & Sun (Republican) charged that vaccine was being diverted to commercial channels and the "black market." Congressmen (mostly Democratic) charged that the Eisenhower Administration was failing to make adequate plans to meet the demand for the vaccine, and introduced bills to control the vaccine's distribution.

THE CUTTER CRISIS

OVER the next ten days, the vaccine shortage dominated the news. Then, during the night of April 2627, the U. S. Public Health Service received word of six cases of paralytic polio in children inoculated with vaccine manufactured by the Cutter Laboratories of Berkeley, California. This was more than could have been expected to occur by chance, among the comparatively small number who had received Cutter vaccine, in the post-inoculation interval before immunity develops. The Surgeon General of the United States, Dr. Leonard A. Scheele, at once banned the Cutter product and started an investigation to see what, if anything, had gone wrong with it.

Additional cases of post-inoculation polio soon appeared, many involving Cutter vaccine, but also some where the injections had been the product of other manufacturers. The latter almost certainly had nothing to do with the vaccine. Like all other vaccines, polio vaccine takes a period of some weeks to produce immunity. During this interval, the inoculee is still susceptible to the disease, and some inoculees will get it, if there is polio around--as there was in most of the areas where inoculations were taking place. But no one in a responsible position had the wit or courage to make this clear for many weeks, not in the Public Health Service, not in the American Medical Association, not even in the polio foundation itself. So the panic grew.

In the meantime, on April 29, a committee of polio experts met at the National Institutes of Health (the research arm of the U. S. Public Health Service) to consider the problems posed by the Cutter vaccine.

The committee, on April 30, recommended continuation of the polio program with the vaccine of other manufacturers, and the appointment of a smaller committee to see whether more stringent safety standards for polio vaccine were possible.

This second committee met on Thursday, May 5. On Friday, it was joined by representatives of the vaccine firms. At 4:00 A.M. on Saturday, May 7, the Surgeon General ordered a complete halt to the immunization program. He said he had acted because mass immunizations were scheduled in several states over the weekend, and because there had been insufficient time to evaluate the committee's findings.

During the next several weeks, a team of Public Health Service experts and consultants visited the vaccine plants. As a result, vaccine of two manufacturers that had been distributed but not used was "re-cleared" for use. (Vaccine of two other manufacturers was cleared later.) Between trips, the touring experts consulted with more experts at *ad hoc* conferences. These went on at the National Institutes of Health until far into the night.

FINALLY on May 25, Dr. Scheele appointed still another committee. This one, which consisted of two representatives of the Public Health Service and five polio experts (including Dr. Salk), recommended a series of changes in the procedure for testing polio vaccine. After a day of debate, the changes were accepted by the manufacturers.

Meanwhile, it developed that there was live polio virus in some Cutter vaccine. But this information did not come from the Public Health Service; to all questioners (and there were many), PHS was still replying as late as the first week of June that investigation of the Cutter vaccine was not yet completed. The information came from Dr. Louis B. Gebhardt of the University of Utah, via an enter program last fall or winter when the need seemed far less pressing.

More serious, to my mind, is the evidence that there was a notable lack of real planning for the technical aspects of producing vaccine on the part of the Foundation, agencies like the American Medical Association, and-most important, because they have the legal responsibility--the Public Health Service and the Department of Health, Education, and Welfare. No matter how it's sliced, the production of 3,500,000 cc last year was mass production. Any difficulties that turned up this year could and should have been detected last year. Whether or not it could have been avoided, in any event, the Cutter incident was subsequently so mismanaged that it very nearly wrecked the program we had.

In the first place--for reasons that I find hard to understand--the department and the Public Health Service have not been candid with the public. From about the beginning of May through at least the first week of June, a curtain of silence was drawn down around Public Health Service scientific and technical personnel working on the polio vaccine problem. When I visited Washington and Bethesda (the Washington suburb where the National Institutes of Health are located), I was not permitted to see any PHS scientific or technical people. The excuse offered was that all were busy preparing a report for the President on new measures to reassure the safety of the vaccine. But reporters had not been able to obtain information directly from PHS technical people for weeks; and, except for a press conference held by Dr.

James A. Shannon, associate director of the Institutes of Health, the press had seen PHS personnel only casually (mainly in the NIH hospital cafeteria, the only eating place in the sprawling medical research plant). Reporters were forced to submit questions through Department and PHS press officers. Practically all the important questions went unanswered for weeks, though no secrets of state were involved, just the health of the American people.

THREE BIG QUESTIONS

ONE CAN nevertheless establish some of what happened in the Great Vaccine Mess, and much of what the Department and the Health Service did not see fit to tell. I address myself to three questions: What went wrong with the Cutter vaccine? Why did Dr. Scheele call off the immunization program at four o'clock in the morning of May 7? And who finally got the vaccine program "back on the track"?

Let us take up the Cutter affair first. Although the Public Health Service has been at some pains to avoid saying so, there was presumptive evidence of the presence of live virus in some samples of Cutter vaccine from the first dozen polio cases associated with it. First, some cases turned up in areas like Idaho, where polio does not ordinarily occur at that time of year. Second, in most of the first cases, paralysis began in the in jected limb; such an association is not usual, though it may occur once in a while, when there is no connection between vaccine and post-inoculation disease.

By now, of course, the presence of live virus in one sample of Cutter vaccine has been confirmed. (As recently as June 7, however, the Health Service refused to say whether its scientists had found virus in the vaccine or not.) How did it get there?

As Dr. Shannon of NIH points out, this may never be known for certain. The vaccine in involved was shipped from the Cutter plan shortly after April 12. Its defects did not become known until two weeks later. How can one be sure precisely what submicroscopic viruses were where when that vaccine was processed, perhaps months before?

Nonetheless there appear to be only two ways in which live virus could have got into the vaccine. One was somehow to survive the killing treatment and pass undetected through the battery of safety tests to which all polio vaccine is subjected. Recent calculations suggest that this could have happened.

The other possibility is that the virus got in accidentally during bottling or at some other time after the killing agent was neutralized. (The agent employed to kill the polio virus, formaldehyde, is toxic to human tissue as well as virus and must be neutralized before the vaccine can be used.)

In favor of the second possibility is the fact that part of one of the suspect lots was apparently all right; no cases of polio turned up among children injected with a 22,000 cc sublot of one of these lots. This implies (though it by no means proves) that the virus got in after manufacture was completed and before the vials in which the vaccine was packed were sealed. Moreover, Cutter alone among the six vaccine manufacturers bottled in the same building where live virus was handled. Polio virus may well get into the air in such a building. Two considerations would imply this. First, production workers in at least one

other polio vaccine plant have been found to have very high concentrations of anti-polio antibody in their blood, sure evidence of repeated exposure to the virus. Some of this was probably air-borne. Second, accidental polio infections have occurred from time to time in diagnostic laboratories. Some of these are also thought to have been air borne.

It should be emphasized, whatever went wrong or was wrong at Cutter, that the Public Health Service is right in the boat with Cutter. The PHS Laboratory of Biologics Control prescribed the safety tests. PHS regulations permitted bottling in the same building with live virus, provided certain precautions were observed (and they were observed). PHS inspectors visited and approved the Cutter layout before Cutter received its license.

ALMOST NONE of the above was stated or admitted by the Public Health Service. Nor was the Surgeon General telling the whole story when he stated that he had called off the immunization program on May 7--the act that really sent the program into a tailspin--to allow more time to evaluate the findings of the expert committee that had been meeting in Bethesda.

During the ten days between the first Cutter cases and May 6, Secretary Oveta Culp Hobby had evidently made it plain to Dr. Scheele that there must be no more postinoculation polio cases on the Eisenhower Administration's political doorstep. The immunization program was to be stopped unless and until the Surgeon General could give, or obtain from the experts, an ironclad guarantee of no more Cutter incidents.

Dr. Scheele is an experienced public-health man. He knew that there is no medical preparation whatever that is absolutely and unconditionally safe; that some risk is taken when any medicine, even as innocuous as aspirin, is given. He knew also that the product of the other five vaccine manufacturers was (and is) as safe a vaccine as there is; and that the risk of another Cutter incident was very small--especially since other manufacturers began strengthening their safety procedures as soon as word of the Cutter affair got around.

But the Surgeon General is not a specialist in immunology, one of the most highly complex branches of modern medicine and biology; not one physician or public-health officer in a thousand, for that matter, can have a really adequate knowledge of it. Dr. Scheele put the problem to the experts who met on May 5 and 6. Being experts, and therefore men who wouldn't absolutely guarantee anything, the committee would not give him the guarantee he needed. Furthermore, they brought up a variety of technical problems concerning the vaccine which should have been thrashed out prior to April 12 but which were now brand-new to Dr. Scheele. He felt he had no choice but to close down the program.

The person who finally started the program back on the track was none other than Dr Jonas Salk. In the two weeks after the shut-down order, Dr. Scheele called platoons of additional tional experts to Washington. ("I've had more calls to the Washington airport in the past two weeks than in the last twenty years," said a Bethesda cab driver.) The experts now met in "ad *hoc"* conferences. This meant that anyone could say whatever he wanted to, at any time he desired, and no one had authority to anything.

The "ad *hoc"* conferences stretched on and on into futility until one man decided he had had enough.

On Friday night, May 20, Dr. Salk went home to Pittsburgh. On Saturday night, he sent Dr. Scheele a wire informing him that he would attend no more "ad *hoc"* conferences and calling upon the Surgeon General to appoint a committee with power to act and get the program going again. A wire from Basil O'Connor, president of the polio foundation, seconded Salk's proposal. The committee (a larger one than Salk had suggested) was appointed May 25; Salk was named a member (though he had not proposed himself). In two days, this committee--given different titles in different Public Health Service releases--drew up and secured acceptance for a new set of safety standards. At last, the wheels slowly began to turn again.

LOOKING BACK

THE NEW safety standards, which were announced May 27, make three matieral changes in the procedure for testing polio vaccine.First, larger samples of each lot
must be tested to make more certain that any live virus present is picked up. Second, the killing process is somewhat lengthened and two successive negative tests for live virus instead of one are required at the end of the killing process. Third, the vaccine must be tested for live polio virus after bottling.

The new standards invite two comments. To begin with, there is no requirement for duplicate testing of all lots of vaccine (although the Public Health Service is increasing the number of lots on which it is running tests). The reasons why PHS has not asked for full duplicate testing are that the Health Service hasn't the manpower or facilities to perform them, and doesn't believe duplicate tests are necessary. Last year, the vaccine used in the field trial was triplicate-tested because few laboratories were experienced in performing the tests, and as a test of the reliability of the safety tests themselves. The tests (especially the tissue culture tests) were found sufficiently reliable so that no purpose would be served by holding up immunizations this year until all lots of vaccine could be duplicate-tested.

THE OTHER comment is that the new testing procedures, as Dr. Scheele has said, make a safe vaccine safer. They lock up all the doors through which live virus could have got into the Cutter vaccine, or might get into other vaccine. However, they could *and should* have been developed before the Cutter incident. Failing that, they could and should have been developed without putting the immunization program into reverse.

In saying this, I am aware, of course, that I have the benefit of hindsight. Also, I am urging someone else to have shown courage I, for one, might have lacked, had I been in the kitchen when the heat was on.

It seems to me that the Surgeon General should have announced, as soon as he realized that some of the Cutter vaccine had gone sour, that Cutter's Polio vaccine production unit had been shut down and would not be reopened until it had been entirely rebuilt under the most severe safeguards. Simultaneously, he should have directed other manufacturers to perform a final afterbottling live virus test on a sample of adequate size. This would have provided immediate protection against live virus in the final product (however it got there), and enabled the immunization program to proceed. Any other needed changes in

safety standards could then have been made later.

The Surgeon General must or should have recognized almost immediately the probability that he was dealing with live virus, and that how it got there was likely never to be settled for sure. Instead of first conducting a "scientific experiment" to settle largely unanswerable questions, he should have been busy putting out the forest fire that the Cutter accident had started.

If he had paid attention to putting out the fire, much less damage would have been done to the immunization program, to the Public Health Service, to public confidence in the Salk vaccine, to the dignity of the medical profession in general, and, incidentally, to Cutter Laboratories. An ironical feature of the policy the Surgeon General and his superiors actually followed-ironical because this is a Republican, pro-business administration--is that it has served only to deepen Cutter's difficulties. If the Surgeon General had announced that the Cutter polio-vaccine unit would have to be rebuilt--which it will have to be anyhow, if the Berkeley firm again expects to sell the vaccine-Cutter's name would soon have dropped out of the headlines. The Health Service's prolonged refusal to say what the situation was at Cutter and what was being done only kept reporters asking questions and thus kept Cutter's name in the newspapers.

Perhaps the misguided silence on Cutter was merely one more manifestation of a failing that has plagued the Health Service and the Department of Health, Education, and Welfare throughout the vaccine mess. The Health Service and the Department not only hurt the polio program and themselves by doing the wrong things. They did it through plainly avoidable public-relations ineptness, typified by Dr. Scheele's penchant for announcements in the small hours of the morning and by Secretary Hobby's classic fatuity: "No one could have foreseen the public demand for the vaccine."

Shortly before I left Washington, I stopped by for a chat with a friend in the Public Health Service who has nothing to do with polio or vaccines. "The only good thing this mess has shown," he said, "is that people are more discriminating than we think. Most of the kids who missed out on their shots will be back, though perhaps not as soon as they should be. But I don't know how our service will come out. I asked a housewife who withdrew her youngster from the program at his school whether she'd lost confidence in the vaccine. 'No,' she replied, I'm just waiting for the Public Health Service to get itself squared away.' "