A Communicate how many different strains with plaque purified this way and tested intraspinally in monkeys but that is all in the published reports and also in my semiannual reports but there are a large number. And I must say that finally we selected three and they were in effect derived from the strains that we had already tested in human beings. Namely the strains that I designated LSC and that became 2-ab for type 1 and then the strain that was called P-712 and the Leon because when all the tests in the other strains that had been screened intraspinally were done, certain plaques derived from these were the ones that were selected. Now when this had been achieved they were the selected plaques based on optimum spinal neural virulence performance. They were fed to chimpanzees. Would it be possible that when I have selected those they would—because if they wouldn't multiply in the intestinal tract of chimpanzees even though there is a differential between the chimpanzees and the human I would know that I would be in trouble. Well I want to make an aside here that when I did that of course what was also studied was the neural virulence of the virus excreted by those chimpanzees. They multiplied, these selected special spinal neural virulence selected strains. But in, with the type 2 when I tested the excreted virus chimpanzees that were fed type 2 there was one stool specimen which virus had multiplied very extensively and I could find no change at all. So I thought ah, maybe the intestinal tract of the chimpanzee had done a job for us. It had selected a virus
particle with greater stability than the others. So I plaqued
the virus that came out in the stool of that chimpanzee triply
purified it and did that you see, used that as a strain. That
is why in the designation of the type 2 strain it's P-712-ch.
The ch stands for chimpanzee. Now we were reach to go ahead
after all of these studies to go ahead and see what they did
in human volunteers without antibody. But I do not remember
the sequence now whether I did it concurrently or whether at
the same time it became necessary to determine by the same
techniques that I used for determining neural virulence what
was the relative neural virulence of strains that let's say
Dr. Cox. Not let's say Dr. Cox of Lederly who was pushing
because he had not selected and yet a certain number of strains
type 1, type 2, type 3 and Dr. Koprowski who was basically
working with the same strain. He got the type 2 from me
December 12. But you know the moment--it was not purified
by the plaques or selected this way, because I don't want to
stress it here to assume that I was the only person working
and that there was no so called scientific and public competition
for a vaccine for strains that would be incorporated in a
vaccine would be certainly not portraying the situation, the
very dramatic situation that actually came at the time. But
it was necessary to determine what by one person, well I knew
Dr. Cox from long ago because he and I worked in adjacent
rooms at the Rockefeller Institute in 1935 and so I asked Dr.
Cox to come to my laboratory, bring his strain. I would
inoculate them because he said by the techniques he had they
had no neural virulence that they were excellent etc., etc.
I said let me inoculate. And so he came. He brought his strains were inoculated it and it turned out that when the inoculum was properly placed either for intracerebral by putting it directly in the thalamus because there it also makes a difference where you put it, and there is a histologic check. You don't have to take things on faith of one person inoculating. And when the inoculum was properly placed in the anterior horn that the strains that he was working with were very much more highly virulent even by the intracerebral route and on spinal inoculation they were strains that didn't even approach even the earlier ones. So whether I convinced him or not doesn't matter. So then the same thing was done with the strains that Dr. Koprowski was working actually the type I was the same as Dr. Cox was working with. Those also came out quite different and much more highly neural virulent. But the point is that I was the one who did it. I made the sections to show the inoculation. It was evident that the way they were doing it, for example, when Dr. Koprowski said oh these strains that I am working with have no virulence by the spinal route in a monkey that they were not being inoculated in the anterior horn. So it was necessary for somebody else to make an independent evaluation. I don't remember at what stage that independent evaluation came but ultimately it was the Bureau of Biologics I guess it was called something else. It was the Division of Biologic Standards or something. The Division of Biologic Standards realized that ultimately some decision would be required so they--it was Dr. Melnick who was selected
to make an independent evaluation. He got material from me. He got material from Lederly, Cox, he got material from Koprowski and he was supposed to have been independent. Well there was a problem there also because Dr. Melnick's technique of inoculating virus intraspinally he would blow. He would put it in in such a way that he would blow most of the anterior, the grey matter out of the spinal cord and it was very easy to get the virus spread all over the place. At any rate, even using by this technique which I subsequently showed how how unsuitable it was for determining the capacity of a virus to spread from cell to cell not by jet injection into the grey matter. And other people did studies on this subsequently because this also became a subject of controversy. But when he himself did it by the same technique, the verdict was that the strains that I had selected by triple plaque purification were much less neural virulent by whatever way you measure them than the others.

Alright. So now we had reached the point and I think I also received a strain from Holland. I had one from France. I don't recall. It's in the record. But I did not select the three strains that I said these are the ones now that are the best that I can do, until I had tested a whole lot of virus. So now the decision was made. Here are the three strains. And then we went first of all back to Chillicothe to see how they would behave in human volunteers by comparison with the parent material that we had tested before this plaque purification and selection by spinal inoculation. Well they multiplied just as well in the intestinal tract and when we tested the progeny of this material. Mind you this is in 1956 now as I was saying
when we tested the progeny in the excreted virus there really wasn't all that difference.

Q In '56 or '57?

A '56. '56. Because as I wrote in my letter to Dr. Janney that in April '56 we were getting ready to do this in the volunteers. But as we as we had approached that let's see now. My train.

Q Okay. I'm sorry.

A The thought was broken here now. It was in '56. It behaved properly with the doses that were fed. It multiplied alright. There was no question. The crux of the issue was the tests on virus excreted and here again I must convey the complexity and amount of work done on the stools of every volunteer. It was not just a question of taking one specimen of stool and testing it directly depending on the amount of virus that was in the stool, making an extract, putting it into monkeys, and then also growing out a culture from it. But it was testing it at different intervals after feeding. Because it was necessary to test the stool, the progeny at three days, five days, seven days, ten days, fourteen days, 21 days, 28 days. There was no other laboratory that did work like that with any other strain. But I felt it was necessary because as I subsequently learned something that will happen much later in the period of multiplication when you had more generations of virus progeny and you have the selective action of the human intestinal tract by itself we even found examples where certain variants that could be detected at two weeks were no longer
detected at 28 days or four weeks or five weeks showing we were what we the reason we were doing this is to see if it had a selective advantage. In other words, supposing at seven fourteen days the peak of viral multiplication we found certain variants that had greater neural virulence than the stuff we had put in. So the question is, that if those virus particles had an advantage in multiplying in the human intestinal tract there should be more of them later. So you test the virus excreted. Three weeks, four weeks, etc., etc. and they should increase later. But they didn't. They very often disappeared, showing that even though such mutants may appear they didn't--there was no selective advantage for them. And it was only by such studies that it was possible. This involved a tremendous amount of work on the virus excreted by each volunteer. Because it involved inoculating monkeys intracerebrally with multiple doses and so on and so on. A tremendous job. But what we learned then was that the virus that came out and that didn't become apparent until later on in '56 was that--I am trying to think now of the time that things were done. Could you shut this off a moment?

Q  Yes.

A  I would like now to read into the record a portion of the report for the period of July 1, 1956 to June 30, 1957 under the heading of Summary of Significant Findings and Developments during that Period. Some of this will be a repetition of what I said before but there has been an orderly progression.
Most of the period between July and November 1956—this was July November 1956—was devoted to the task of selecting the optimum single plaque progeny strains for use in the oral vaccine studies. The strains that were finally selected LSC,2ab for type 1; P-712-ch,2ab for type 2; and Leon 12a1b for type 3 were the results of many laborious tests on large numbers of single plaque progeny strains that are described in more detail in the paper submitted for publication in the Journal of the American Medical Association. In the case of the type 1 virus this involved the testing of large numbers of individual triply purified plaques derived from various attenuated strains. Plaque size was found to be of no help in guiding the selection of strains with the least residual neurotropism for the monkey and only spinal tests in large numbers of monkeys could be used as a basis for final selection. The special problem here was the finding of a strain that did not exhibit the zone phenomenon because quite a number of strains were found which upon inoculation of the maximal doses, one million or more tissue culture doses in large numbers of monkeys produced no paralysis while inoculation of ten times or a hundred times less virus did produce paralysis in 20 to 60% of the monkeys.

Q Could you take a minute and explain what a zone phenomenon is?

A A zone phenomenon means that if with the largest concentration, highest concentration we get zero for whatever it is you are looking for and when you use a smaller concentration you get something that is a zone phenomenon because logically you expect whatever effect you are looking for to get with the
highest concentration and to have that effect disappear this is so called the dose-related thing. But when you get the unexpected things where the largest dose doesn't do anything and ten times or a hundred times less does something, that is a zone phenomenon.

Q Fine. Go ahead.

A Alright. Now after extensive spinal tests in monkeys of 37 different plaques the strain finally selected LSC,2ab was the only one that not only had the least residual spinal neurotropism but also did not exhibit the zone phenomenon. The zone phenomenon digressing here is something that suggests the possibility of a mixed population. So that with the larger dose virus particles may protect or prevent the effect of others that have a different capability. You dilute those out and then the others come through. That is the importance of the zone phenomenon. In the case of the type 2 strain the optimum plaque derived from the attenuated P-712 was fed to three chimpanzees and the excreted virus was tested for neurotropism in monkeys. In one of these chimpanzees it was evident that some increase in neurotropism had occurred. Accordingly the cultures of the stools from other chimpanzees which exhibited no paralytogenic effect with the maximal dose inoculated intraspinaly in monkeys not just intra-cerebrally was used to obtain new plaques for further study. One of these plaques yielded the strain designated P-712,ch,2ab that was selected as the optimum. In the case of the type 3 virus we had two single plaque progeny strains to choose from.
Both of them being nonparalytogenic in maximal doses inoculated intraspinally in monkeys. Cultures of each had been fed to chimpanzees and tests on neurotropism of the excreted virus indicated that the one that was selected, namely Leon 12-a₁b yielded little or no change in neurotropism of the virus that had multiplied in the chimpanzee. I want to digress here to say that what happens in chimpanzees is not quite what happens in man because there is less viral multiplication. But at least that is our first screen, you see, and it is important to stress here again of the system of our work. We never went to man until we tested things in chimpanzees.

Now during the course of these studies it was also found that the best way to grow these attenuated strains in tissue culture in order to obtain both the highest yield of virus and I want to digress here. That is a very important thing because if you can get a yield that is a hundred times more when you grow it one way than when you grow it another way it makes the difference between being able to have a hundred million doses or a million doses. And that is 99 million doses and from a practical point of view that is a most important thing for a virologist in the lab it is only two logs. And too many virologists in the labs think in logs as if it were nothing. But if they would think in terms of a hundred million dollars and one million dollars it would make a terrific difference. And that is why as a practical person thinking always not only of what I can find in the lab or this but ultimately what will matter in the field that is why I have this here. And I am glad. I am going to start
over again now. During the course of these studies it was also found that the best way to grow these attenuated tissue strains in tissue culture in order to obtain both the highest yield of virus and to maintain the attenuated characteristics of the strain was to make certain that during the period following inoculation of virus into the cultures the pH did not drop below about 7.2. Now, let me digress again. When I finally finish and say to the manufacturer, This is how you must do it, an observation of this sort is the most important. Many other operations that I can think of up to the present time even with live influenza virus vaccine fall down when you get into the manufacturing stages because you don't know how to tell them how to just exactly how to do it. So to be able to say that to give these specifications is a very important preliminary job in the laboratory. After repeated tests with cultures grown in small volumes indicated that reproducible results were obtainable in the spinal tests in monkeys an arrangement was made with the Merk Sharp Dome Research Laboratories to grow 25 liter lots of each of the selected strains. I want to digress here that this was approximately October 10, or thereabouts 1956. The reason for that, the reason I am digressing here is this. That when a portion of this material that had been grown in cynamologous monkey kidney cultures incidentally was given to Merk Sharp and Dome and a portion was frozen down presumably for posterity that date is on there and recently I will come later to the fact that the whole responsibility was turned over to the World Health Organization recently 20 years later. Actually it was done at the end of
1975 so it is nineteen years later. The World Health Organization was interested in developing new seed lots for posterity or for new work. And they went. They asked the Bureau of Biologics which was holding in a minus 70° refrigerator some of the original stuff that I prepared then from the triply purified plaques from 19 years at -70. They titrated it and they found it had exactly the same titer that I had obtained nineteen years before in October 1956. And when the committee was sitting in session and the call came in from Washington because it was being done while we were sitting in session last I think it was October or early November in Geneva in 1975. Applause. They applauded because it was really quite remarkable that 19 years later these original seeds were there and had the same potency.

Q  The choice of Merk, Sharp and Dome. There are all sorts of drug companies.

A  Why was Merk, Sharp and Dome chosen? Well I had a--they prepared previously large lots that were used on previous strains. They had a very good tissue culture setup much better than other laboratories. I don't know what my particular relations had been with them but they offered to do it for nothing you see as a service so, and this was a big job, even though they subsequently decided against making this vaccine. Now, these large lots were prepared at Merk, Sharp and Dome. There is another story for posterity which is of interest here. That obviously they made it at that time the monkeys that were most readily available because they were making Salk vaccine.
You see at that time please remember in 1956 there were already many companies making monkey kidney tissue culture for Salk vaccine and what was used were rhesus kidneys from rhesus monkeys. What we did not know at that time was the existence in rhesus monkey kidney of a virus that was subsequently cymnuo virus number 40 or SV40 that was rarely if ever present in cynamologous monkey kidney tissue culture so that the seed that I provided to Merk Sharp and Dome didn't have this contaminating virus which was discovered only later whereas the rhesus monkey kidney culture that were being used for mass production of Salk vaccine and which they used for production of these twenty five liter lots did have this virus. So that became a subsequent problem. But let's go on.

These large lots after size filtration yielded virus of good potency about 40 million plaque forming units per milliliter. The test for neurotropism by intracerebral and intraspinal inoculation in monkeys was comparable to those previously obtained in the tests on the smaller lots. This to me, a digression, was wonderful because it showed the stability at least. On multiplication in vitro under controlled conditions in large quantity not in small quantity. So this was a necessary precondition. Now each lot was inoculated intraspinally into each of three chimpanzees now in doses of about eight million plaque forming units and no polio lesions were found at the site of inoculation or anywhere else in the spinal cord. These again these are all the things
that were done on these large lots that were to become not only the source of tests on volunteers in Chillicothe and then on children and then on increasingly large numbers of people around the world ending up in almost 50 million people altogether. These are all the tests that were carried out before anything was done. All three strains had no effect on spinal inoculation in mice. The usual safety tests for "B" virus, cubical bacilli and other contaminating organisms, at least that we knew of, were negative. No scitopathogenic agents other than the polio virus could be demonstrated in these large lots at least by the procedures that we were using then. Aliquots. These large lots were then fed to a total of one hundred volunteers at the Federal Reformatory in Chillicothe Ohio. Because this was really the final test. This is the material now that we'll either use of throw away and stop. We were reaching, we were going down the line to the end point of decision so that aliquots of these lots were fed to a hundred volunteers at the Federal Reformatory in Chillicothe as well as to ten individuals including five children aged five to eleven years in two families. This I will discuss later.

Q Yes.

A Some of the details of these tests are mentioned in a paper submitted for presentation at the International Poliomyelitis Congress and for publication in the JMA. That's in 1957. The main findings were as follows: in a dose of about 100,000 plaque forming units and mind you that means that there were in the tissue culture fluid type of filtration after all everything that means that there were
250 such doses in each milliliter of the 25 thousand ml that we had prepared you see because we fed only a dose of ten to the 5, a hundred thousand whereas the undiluted material had 25 million plaque forming units per ml. In a dose then of about 100,000 plaque forming units these new strains indicated their capacity to multiply in the alimentary tract and to produce antibody in individuals without homotypic antibody both by the pH and scitopathogenic tests. This is an aside here. There had been developed methods for doing tests for polio antibody that were much more sensitive than we had before and that measured different kinds of antibody because there were higher avidity antibody and low avidity antibody that comes but that is another point. But that is the significance of this statement.

The only failure was encountered in three adults who received the type 1 virus and there is reason to believe that these may be individuals who had previously experienced a natural type 1 infection and accordingly have a resistant alimentary tract but with residual antibody below the level of detection by the most sensitive test. As an aside, this was subsequently proven to be the case and among them was my own wife, Sylvia. And she was at that time--she was born in 1910--she was at that time 47 years old. And she had resistance of the alimentary tract had no demonstrable antibody. We were able to prove by other studies that I made later.

Point number 2. A considerable number of adults were encountered who exhibited no antibody by the scitopathogenic tests but possessed variable low levels of low avidity antibody
demonstrable by the pH test. When type 1 virus was fed to such individuals the virus multiplied in the vast majority although generally for a shorter period than in the volunteers without antibody. While in a certain proportion, three out of 17 there was neither detectable multiplication nor any boost in antibody which means that it just didn't multiply at all. And this as an aside. I would say subsequently we learned that in the spectrum of response you have a certain number of individuals who do lose their antibody or never developed it. Even though they develop resistance of the intestinal tract. And this became very important guideline to understanding many phenomena. I continue now. When type 2 and type 3 virus was fed to such individuals. That is individuals with such low avidity antibody detectable only by the pH test, the virus multiplied in all but again very often for a more limited period than in controls indicating previous exposure. There is reason to believe that the majority of these individuals these variable low levels of low avidity antibody may have been the result of infection with heterotypic polio virus. Number 3. Each type of virus was also fed in the same dose to groups of six volunteers who possessed high avidity antibody for all three types. We wanted to know what would happen in people who had a previous natural infection. And here is what happened. Neither virus multiplication nor boost in antibody was demonstrable in the twelve volunteers who received type 1 or type 2 virus however, in three of the six volunteers who were fed the type 3 virus limited viral multiplication as well
as a boost in antibody were demonstrable. This was furthermore increased on larger numbers. A very important observation. That resistance to infection in the intestinal tract may be quantitative.

Number 4. These viruses were also fed to a total of 23 volunteers who had been immunized eight to fifteen months earlier by ingestion of the other attenuated strain. Among the ten volunteers who received the type 1 virus nine had no demonstrable virus multiplication. While one showed a limited multiplication for a short period of time. The resistance of the alimentary tract in these individuals was without preference to the residual antibody titers. As an aside. Absolutely these are fundamental observations. Showing the difference between local resistance at the site. That is in the intestinal tract and levels of antibody in the circulation. The one individual who was reinfected had exhibited only a limited infection of the alimentary tract when the virus was fed to him eight months earlier. The importance of that statement is that subsequent observation showed that if the initial viral multiplication on first exposure goes on for a long time the resistance to the subsequent infection is very much greater. But if for one reason or another it multiplies only for a short time there isn't as much resistance to multiplication. But after another exposure the resistance becomes greater and you can reach a point where it is absolute no matter how much virus you feed. I am going to continue to read now.
Q Go ahead.

A In the group of seven volunteers who received the type 2 virus only one showed multiplication of a very low level for a limited period of time and this was an individual who fifteen months earlier had been fed a mixture of type 1 and type 2 viruses with both of them multiplying simultaneously in this intestinal tract. The significance of that statement again is that there may not have been maximum multiplication of type 2. Accordingly there is reason to believe that part of his alimentary tract that previously had no experience with the type 2 virus. In a group of six volunteers who were fed the type 3 virus only one, only one exhibited a trace of virus on a single day. The resistance of the alimentary tract in these individuals have no relationship to the level of their residual antibody. The high resistance of the alimentary tract encountered in the volunteers that were immunized by previous ingestion of attenuated type 3 virus than that found in volunteers with naturally acquired antibody is of special interest. It may either be a reflection of some natural antigenic variation among type 3 strains since the same strain of virus was used for both the initial and challenge feeding in the volunteers or it may mean that under natural conditions infection with type 3 strains may frequently be of a more limited character. So that portions of the alimentary tract that previously had been unaffected by the virus despite the presence of good levels of high avidity antibody. These are absolutely fundamental observations to understand the modus operandi of behavior of virus multiplication of the human intestinal
tract and resistance and information necessary for what you have to achieve to get a break in the chain of transmission in not one individual but in a community.

Number 5. Tests for possible interference resulting from a feeding of mixtures of various combinations of the three types of virus were carried out in nine individuals. These tests show that while occasionally all three types of virus may multiply simultaneously there was nevertheless clear evidence that the Type 2 virus was the dominant one. And greatly interfered with the multiplication of the others in the intestinal tract when all three were given together.

Six. The efficacy of feeding the three types of virus one at a time at three week intervals which had been demonstrated previously using the same strains prior to the selection of the optimum plaque progeny was again demonstrated for the present strains in five children who lacked all three types of antibody. Each virus multiplied in turn for a period of at least three weeks, and a good antibody response was obtained for all three types. I want to digress here to say that subsequent experience has shown that while three weeks is an interval that prevents interference of one type of polio virus with another that that was not a good interval because if you allow the virus one type to multiply as long as it can, initially, let's say a minimum, give it a minimum of eight weeks, you get a much better intestinal resistance. And then you give this next type and let it multiply for at least eight weeks, not three weeks, and the last one to multiply as long as it can, that
ideally in my judgment now and on the basis, based on my recommendations in certain areas where it is important to achieve intestinal resistance the optimal interval between each two types that are fed is eight weeks, not three weeks. Okay. Number 7. An additional opportunity was presented to test the effect of feeding the type 1 virus to an individual who had previously received Salk vaccine. One of the medical officers at the Chillicothe Reformatory had had a second dose of Salk vaccine three months prior to the test during this period his type 1 antibody which initially was low had dropped to less than eight by the pH test. That is the most sensitive test. And was negative in undiluted serum by the scitopathogenic test. The type 1 virus multiplied in this individual and the antibody rose to a level of 1024 although the time of first appearance of antibody was no faster in this man than in other volunteers who had no demonstrable antibody to begin with. That is another point of theoretical interest and potential practical importance which however, also on further studies did not hold up. But that is why it was stressed. Then I continue. Extensive studies on hundreds of monkeys were carried out for the neurotropism of excreted virus. Using cultures of stools obtained both early and late after ingestion of the attenuated strains from children as well as from adults the details of these tests already shown in the paper submitted for publication clearly indicated that in a certain number, not all of the individuals a definite increase in the neurotropism had occurred especially the spinal test in monkeys. The intra-cerebral test on the same culture showed that an excreted that
excreted viruses were still in the highly attenuated range of the neurotropic spectrum. Small aliquots of these large lots not in excess of 100 ml of each type have been distributed to several qualified investigators for the performance of varying types of studies under different conditions varying with the individual plans of the individual investigator. Now this is the beginning of my international collaborations. Having selected these three strains as the best I could do. Having prepared large lots from which all studies would be carried out so there would be no variation in the material used. Here is a listing of the people who then requested and received 100 ml or what would be the equivalent here of let's say 250 that would be 25,000 doses you might say, of each type.

Q Now this is the beginning of '57.
A This is still in '57 because this report ends for the period of June 30, 1957.

Q So it is the early part of '57.
A Alright. Thus far Dr. M. Romulus Alvarez and Dr. F. Gomez of Mexico City; Professor Verlinda of the Institute of Preventive Medicine in Leiden, Holland. Incidentally I am going to mention the purpose that each one had. Dr. Romulus Alvarez had spent four years with me, had just gone back to Mexico and had his own laboratory in '57 and the point of studying this in Mexico was that there were children, very young children who were living practically in a sea of other enteric viruses. And the question of interference and what the response would be there was being, could be studied by him.
Dr. Verlinda on the other hand wanted to carry out a study among the faculty and their family of Leiden. University of Leiden in Holland which would be a family setting in an area in which a large number of persons had little or not previous exposure to polio viruses. Professor Joe Vernardy of the Institute of Hygiene in Milan again wanted to study it in children in certain institutions, let's say in Italy. Professor Chumakov in Moscow and incidentally we will come back to this in another chapter. Wanted to study these final strains or aliquots of that because wanted it for various purposes. He wanted to use it in actual tests on children and let's say day care centers in Moscow and as it subsequently turned out he also used this as seed virus for preparing millions and millions of doses of vaccine himself. Professor Smoradinso in Leningrad. Now Professor Chumakov and Professor Smoradinso in the Soviet Union were certainly competitors to put it mildly but at this state they were both working in different groups. Professor Chumakov had primary responsibility for making Salk vaccine as an inthrop(?) but he was also interested in this. On the other hand Professor Smoradinso in Leningrad was in a position to carry out studies in orphanages and again day care centers with thousands of young children. Dr. James Gear in Johannesburg South Africa again had opportunities to study it in different population groups. Dr. Professor James Hale then of the University of Malaya of Singapore to study it in Singapore. It is very interesting because subsequently Singapore I think it was in 1957 had a terrific epidemic of polio in which at least the effect of using mass vaccination only with type 2 vaccine.
Some of this material was used for determining the effect on an epidemic. Dr. John Fox at Tulane University was working with Gelfain. Dr. John Paul with Dorothy Horstman at Yale University. So here were nine different groups already who entered into the field to make independent observations, independent of me to see not to do all the tests that I carried out but to feed it, test for excretion of virus and do all the things that, antibody development and so on.

Q  Now before you go on there is one thing I don't understand. These tests that you've done in this period between July 1 and let us say the middle of '57 seem to be very remarkably good. Where did the period of depressions come in?
A  Let me come to that later.
Q  Yes.
A  I am going to skip one chapter because it has to do with a line of so called rabbit kidney cells in which polio virus multiplied but it turned out they were helo cells contaminants. I am going to skip that. We did a lot of work on that because we thought that if we could grow this virus in a stable line of rabbit cells that were susceptible how wonderful it would be instead of having to use monkeys. But it turned out to be no good. So I go on further.

Comparative tests on the usefulness of the optimum attenuated strains for routine neutralization tests showed that the titers obtained with these were as high or higher than those obtained with other strains of polio virus both
in the pH and scitopathogenic tests. I am going to skip that also.

The next paragraph. The definitive study carried out in 1956 on a hundred children with summer diarrhea. That is another thing. Echo types, and other things.

I think this brings up to the middle of 1957 basically where we stood with aliquots of the three large lots of vaccine on which a decision would have to be made will this become the basis of live virus polio vaccine or not. Now the crux of the situation were the feelings of some of the people about the significance of the fact that some of the, in some individuals and this happened in my own children also. Some of the virus excreted had by certain tests in monkeys a higher level of neurotropism than the virus they were fed. It didn't happen in the cultures themselves but in the intestinal tract it happened. And the question is, is it safe to use such a vaccine. This was an important issue for decision. The National Foundation for Infantile Paralysis in 1957 was at the peak of its activity of trying to get as many people as possible vaccinated with the Salk vaccine. The period of the unhappy Cutter incident had passed. A very traumatic period. And it was engaged in convincing the American people because it was a harder job because of the Cutter incident that everybody should be vaccinated because that was the way polio would be wiped out. The encouragement of that moment of the possibility of testing a quite different kind of vaccine, a revolutionary vaccine from the point of view of its not only acting on the
individual but setting up a chain of transmission because subsequently we learned and family studies that in little children it spreads. Those were very serious, a very serious question. I sensed the tendency that while the National Foundation was quite happy to support me up to the point of final decision that when however it came to the point of final decision that somewhere in this world a decision would have to be made between the use of killed virus vaccine and live virus vaccine and field trials with live virus vaccine with increasingly larger would have to be made. So this was not a happy situation for that trial. That Dr. certainly Mr. O'Connor didn't want Dr. Rivers I think also at that stage wanted every possible excuse for just not proceeding along these lines and so he picked on the fact that there was no so called genetic stability on multiplication of the virus in the intestinal tract and that such changes could constitute an imponderable danger if let loose in the population. So that on the basis of these quite valid assumptions however these are assumptions without actual scientific fact or trial but assumptions were also needed. He made perhaps the most traumatic statement to me at that time that anybody had made. He said Albert we were pretty good and old friends in 1957 we had already known each other for at least almost 25 years and we were very close because he tried to do all sorts of things for my career. He said Albert my advice to you is for you to throw it down the drain and forget about it. You've done a good job. We've got a
good vaccine on our hands. We must convince the American people that despite the Cutter accident it is safe. It is effective and it will wipe out polio. I think at this point I should like to take an opportunity to give my reactions to the repeated statements that during those years were made not only by the National Foundation of the Communicable Disease Center, the Public Health Service were working very close in order to get the maximum possible number of people to be vaccinated which was the desirable objective they kept saying it is safe it is effective it is absolutely safe. It is killed. We have learned our lesson in the Cutter incident. It's safe; it's safe; it's killed because it is killed it is safe. But there was a problem there in that in the surveyanance every month within thirty days after inoculation of Salk vaccine there were not only: some hundreds of persons who developed paralysis during the period regardless of the time of the year when it was given. But also a considerable proportion would develop their paralysis first in the inoculated extremity. And this by some epidemiologists including myself presented a very good reason for suspecting that some residual virus and because very virulent virus was used for formal and inactivation in the Salk vaccine. That some virus that escaped inactivation was actually causing paralysis. And in effect this continued up until 1959 yet at no time did the public health service consider the possibility that when you test the safety of the vaccine in ten monkeys by inoculation as they did, by cerebral inoculation and you find no residual virus that is quite another thing to
inject it in one million persons and there were millions that were being injected. My interpretation of all the data that had been accumulated is that the statement a killed vaccine is safe is safe period because it is killed is an absurdity. Because it depends (a) on the virulence of the virus that you use for inactivation and on a curve of inactivation which always can leave a certain number no matter what you do virus particles uninactivated and when you inoculate it in hundreds of thousands and millions you can still get it. Nevertheless if that had been done as the public health service was doing in the initial mass vaccination trials with live vaccine in the United States the number of people they would be able to vaccinate would be very much less. So certainly we were working then in an atmosphere in which the intrusion of another vaccine was not a good idea. Particularly a vaccine that had certain uncertainties. When I repeated the statement to some of my colleagues like John Fox and John Paul of what my very good friend Tom Rivers told me and Tom Rivers had his ups and downs. Sometimes he would make the wild statement that he later regretted. He told me later on that he shouldn't have made that statement to me.

Q  But it did affect you.

A  We were very close but I mean, after all, to me it was traumatic. And they advised me no, no, no, don't throw the stuff away. And as a matter of fact they said let us have some of that stuff. They studied it in families and in other ways.

Q  Did you have to go to the Foundation to get permission to distribute this stuff?
A I notified them but they didn't tell me don't do it. And if they did I would tell them to--

Q Well the reason I raised this question is in the middle of '57 you in fact did ask them whether you could distribute the stuff and they said they wanted to wait until you had completed the tests at Chillicothe before they would--

A That was earlier. I did not distribute my material until I had completed the test at Chillicothe, until the tests were finished on my own children and the children of my neighbors and all the other things. It was not distributed before then.

Q Did you think that Rivers had a point when he said--

A Well I think he had a point for consideration, but the statement to throw it down the drain and forget it was most irresponsible and if I had done that we wouldn't have had a live virus vaccine, at least not in my judgment and in the judgment of many others. Certainly it has altered the picture very considerably. But what happened then. There I was in the middle of 1957 I had done all the tests I could myself I will describe later the family situation. Other people were having samples of it, studies were going on in many different countries and along comes an international poliomyelitis congress at which I presented this material and presented all the facts. I you will stop at this point I would like to read my own frame of mind--Alright.

In the light of what I have just said I would like to read into the record the two concluding paragraphs of my
presentation at the International Poliomyelitis Congress in July of 1957 in Copenhagen. I presented my paper on July 9, and I said,

Our own previous studies in a hundred and thirty three volunteers and the test of Koprowski and of Dick on many hundreds of individuals with strains of different degrees of attenuation as well as our present tests in 110 individuals with a very highly attenuated strains were without any harmful effects. However, it would probably require tests on tens of thousands of people to establish whether the theoretical expectations of safety are confirmed in actual practice. Simultaneous feeding of such a vaccine to entire families and communities during seasons of the year when polio viruses naturally disseminate poorly or in communities where polio viruses of varying degrees of virulence are known to be spreading extensively already might be the best way to conduct such tests. But where and under what circumstances would tests on increasingly larger numbers of people be justified. The definite reduction in the incidence of paralytic poliomyelitis achieved thus far by killed virus vaccine may naturally incline to a decision that in countries where mass application of killed virus vaccine is feasible it be given an opportunity to show what can be achieved over a period of years. If the passage of time should prove that immunity resulting from the killed virus vaccine--

END OF TAPE