Q At this point, I would like you to search your memory and to tell me about the progression of your work with arthritis after you came to Cincinnati.

A It progressed along two lines: One was to still continue in the attempts to isolate directly from human lesions, particularly in children with rheumatoid arthritis and Still's disease, to isolate the pleuropneumonia like organisms. That continued until about 1941. I gave it up. The other one was to use this model of arthritis which was so similar to human rheumatoid arthritis in its progression, development, promisity, pathology, as a model for the human disease to study potential chemo-therapy. This is again where Joel Warren and I worked together. We, he is a Ph.D. so he had very little conception or familiarity with what was being done clinically. But I established my contacts with the people in the field of rheumatoid arthritis before I left New York and continued later.

First of all, we wanted to see whether of the various drugs that had been tried and used on patients with the rheumatoid arthritis, what they would do in mice. With a disease that we could control, could we have this organism, it would grow, we could produce certain a course of events. We knew that 100% of the mice would develop joints that would progress. Then we carried out this study, and interestingly enough found that the
only compounds which were claimed to have any effect on rheumatoid arthritis at all in man also had an effect on this disease. This experimental disease, namely gold compounds. And that the forms of gold which were considered, whatever to be ineffective in man were also ineffective in mice. So we had two perhaps.

One of the great problems with gold therapy at that time, and it is still being used, because that was discovered that cortisone has only a temporary effect in relieving the inflammation. People are still going back to gold. Now one of the great drawbacks to the use of gold therapy was that even in the forms in which it was better tolerated, knows a very high frequency of side effects, toxicia organs, dermatitis, . So, we tried to determine whether there was any way in which we could, now by quantitative methods, alter the relationships between the toxic dose of gold--this is in mice--some experimental models--and the therapeutic dose. Because with a clean-cut model, we could measure the quantitative. Then we found that when we took the best compound that was being used, sodium aurothiomalate, and made it insoluble by substituting calcium for the sodium, that interestingly enough, it lost all toxicity in mice. All toxicity. The largest amount we could innoculate--we could put in--and you had to put it in as an insoluble suspension per subject--was non-toxic, and yet miligram for miligram of gold, even though there was some delay, it was as effective as the other. The question obviously was, would it work in man? I am not one of those people who does something in model system and
then stops and says, well, if anybody's interested, they can pick it up." So, in addition to the work on polio, and toxoplasmosis and all the other things, I went out and gathered a group of foremost clinical investigators in rheumatoid arthritis in the United States. And convinced Merck, Sharpe and Dhome to prepare this in a way that would be acceptable as an investigational drug, developed a protocol with those people—that all would use the same way, decisions on what kind of patients to use—mind you, this is just before our involvement in World War II.

Incidentally, on the recommendation—because it had eventual commercial exploitation—this work, it was decided that the Children's Hospital Research Foundation trustees would take out a patent on it, and if anything came of it, it would benefit the Research Foundation. Well it turned out to be very interesting. The effects that were obtained were the same as those that were obtained with gold. 70%, 5%, at least it was no different. But the complete absence of toxicia that was observed in mice was not quite in man. Now what was lacking in man was the life threatening toxicity of visceral toxicity—the toxicity for the liver, the kidneys and the other things—but the dermititis continued to be a complication—not as much as in the other. I ultimately brought the thing together—because I went off to War. Others went off to War, and it was left in that state, of not being pursued further. I think that with the return to gold therapy now, because nothing else has been found, it is a great mistake not to go back to calcium.
aurothiomalate instead of using the other gold compounds. I've not had time to get into this field again, because I've been involved in many other things. But, shortly after the War, since we published it in science and journals, I discovered that a Swedish compound with an invasion of the patent had produced it commercially and was selling it. I never followed through. I believe also that further work along these lines perhaps could have also found some way to overcome the skin complications. But, the culture that was used in all of those experiments on experimental chemo-therapy in this model disease was lost during the War when I went off, when I left the country. Nobody has taken the trouble to find another one like it because other strains of mouse, mice, as I myself had shown in the microplasma do not have the capacity to produce this very typical disease and so nothing more has been done about it.

Q In looking through your correspondence, I discovered a vast correspondence with Merck Sharpe and Dhome, and it is clear that even sending you myochrisine which was one of the gold compounds, was a very expensive business for the drug companies. My problem is, what kind of pressure do drug companies put on investigators when they supply out of the goodness of their hearts—so to speak—materials to work with.

A Let me say that the research arm of the large pharmaceutical industries in the United States is guided, not all, but many by very wise people with considerable research experience. And research experience shows that as in other kinds of investment, you have a
multiplicity of investments, something may pay off, something may not. They never do anything out of the goodness of their heart. They do something as a gamble, yes—goodness of their heart, no. I do not say this in a derogatory manner because they make certain investments in something that has a potential. Because they will gain by it. So, in the case of Merck, Sharpe and Dhome, I have had several relations with them. First this, they saw in it a distinct possibility that here was the most prestidigious group of investigators around the United States engaged in a study with material that they had prepared and processed according to our directions. If something significant would come out, they'd have something to sell. Even though, although we had a patent, hell, they could make a profit out of it because the number of people with rheumatoid arthritis and around the world, this would be a very significant item. So they didn't do it out of the goodness of their heart.

Finally, things came to no definitive conclusion, they didn't lose very much. In other occasions, some years later, it was Merck, Sharpe and Dhome who were trying to develop on the side their own inactivated polio vaccine to market while they were doing that, they actually set up a unit to prepare the two million doses of type I, type II, and type III that were used in the big world wide field trials. And they did it for nothing, as their contribution. This was again diversified investment. They ultimately did not go into production of oral polio vaccine. They did other things, and as I get it now,
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Pfizer which broke the ice, built a new facility in England, broke the ice, I mean in the non-communist world and began production of the oral polio vaccine in England before the United States. It is now going out of the total business of vaccine production, trying to sell their know-how to Merck, Sharpe and Dhome--this is not generally known yet--and maybe Merck, Sharpe and Dhome will go in and take that over.

Q Now I have one other question to ask about the arthritis. There was such tremendous interest, really, you know for example, you were offered a post to come and do work in arthritis in New York in 1942. Some doctors in New York either offered you a post to come back to New York to work on it

A Really? Where did you find that?

Q That's in the Oletsky correspondence.

A Here?

Q Yes. I can point it out to you later. There is tremendous interest, and yet that interest is allowed to die in essence. No one, for example, picks up with the therapeutic idea of working.

A But I just gave you an explanation. If that culture had been maintained, and if it were available to start the work up again as we did, any number of pharmaceutical companies would have grabbed it and gone off to do other things with it. I have had correspondence where I am asked for this culture "please, please do you have this culture?" I said "I'm very sorry, it was one of those things that was lost but if you want to really go ahead, you do what I did." Now maybe this particular strain is unique
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to the Swiss mice at the Rockefeller Institute. Get some of those mice. I got it, I had taken ten brains and out of one brain, I'd get it out. Isolate it and test it. It's very simple. Test the different--. But nobody did it. If I would be able to present this to them on a silver platter and they'd be able then to go off and inoculate mice and produce this beautiful model disease, then some more work would have been done. But the hard job of going out and doing all the things that I did was not done.

Q So the disappearance of the strain was not--

A I think in my judgement the loss of the strain was responsible up until this time for not pursuing this further.

Q Well, then, at this point, what I would like to do is to turn to the work that you do in polio at Cincinnati. But before you do that, I would really like for you to make some comments on where polio research had arrived, say 1938, 1939 and '40. Here I would like you to make comment about particular people who were working in the field and particular types of work, and let us begin by the contributions of John Paul and James Trask.

A My dear Saul, Now whenever I start something like that--if I am going to take the time to give an evaluation of the wonderful contributions of the many people who have worked in the field, I am going to write a book that would be a sequel to John Paul's book on poliomyelitis. I cannot do it here. I cannot do it here because what I can do is to answer the first part of your question. You ask me that question--what was the status of knowledge of polio which was the result of many contributions of many workers in this country and abroad at the time of about 1939 when I was faced with
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the transmission leaving the Rockefeller Institute, and going and starting over again on a tack which was somewhat different from what others had.

That I can undertake to do. But I cannot do it in this minutia--

Q Alright, do it in any way that you want.

A Now, it so happens that as I was already--I had made the decision in the middle of 1939 to leave the Institute. I was asked to write a summary for the International Bulletin. I actually summarized the situation of where it was. If you want to stop this a moment--

I would say that about 1939, one of the most significant, challenging problems in poliomyelitis was the pathogenesis of the disease in man. Just where did the virus first attack? How did it invade the nervous system? Because the concept that was so deeply impressed upon the scientific community in the previous decade, or less than previous, really five eight years. First traceable to Simon Flexner, who had a simple vision that the virus came in by way of the nose, a little bit like meningococci, and just invaded the central nervous system. That was discarded in favor of the work done, again with the horrible unfortunately laboratory modified strains like MV, which led to the beautiful demonstration in experimental models which turned out to be utterly misleading—that polio virus comes in by the olfactory neuronal pathway and spreads in the central nervous system that way.
The first direct practical consequence of that, and I am talking not just of bringing to 1939—the first consequence of that of course was all the work on trying to block the portal of entry at the nose with chemicals. The work that was done in Oletsky's department. I became involved in it, and by Armstrong and Schultz which finally led to the field trial carried out by Armstrong and his associates. During an epidemic they were putting picric acid up the nose of children, people, it worked in monkeys, and it turned out it just didn't work in humans.

So there were all kinds of questions: Why didn't it work in humans? when it worked in animals. You know, you have to consider all sorts of possibilities. It was that experience plus my, and I am going to talk from my personal publications—plus my personal experience of working on methods of tracing the pathways of viruses through the nervous system. And the demonstration in monkeys that by examining olfactory bulbs of monkeys that developed paralysis after putting the virus in the tonsillar area, that it was free—this is even using the MV virus, the highly modified one, and that when you put it intranasally, you always had those beautiful footprints in the olfactory bulb. That led me to ask the question: Are we correct in our assumption that the olfactory pathway is the way the virus gets in in human beings? Having developed this technology based on examination of the olfactory bulbs, some work in literature that was fragmentary I embarked on the systematic analysis of olfactory bulbs. I think that by the time I left the Rockefeller Institute—I'm going to refresh my memory—
I had already examined enough, and based on more specific identification of lesions, not just perivascular infiltration, which led some other people to say that there weren't any. I came to the conclusion that in human beings, the thing doesn't look at all like that in monkeys.

Now, in an article that I prepared for a publication called International Bulletin, I am curious now to see what I wrote. The first line was published 1939-1940. This is an article on portal of entry and transmission of polio virus. It shows that our understanding of the natural history of poliomyelitis virus infection in man was very inadequate at that stage. I start this article by saying

It is necessary to admit that the very beginning that we have still little or no direct data upon which to construct the picture of how the virus of poliomyelitis enters the human body, from what site it invades the central nervous system, and in what peripheral site it either multiplies or is liberated in sufficient quantities to permit the continued transmission and existence of the disease in nature. What is the change by which it maintains itself?

Of course, Paul and Trask had already demonstrated the presence of virus in stools and we knew that it somehow got in the stools, but even for years after 1939, at meetings that were gotten together by the National Foundation for Infantile Paralysis, there were those who held for "Well, obviously it multiplies in the nose, and it is swallowed. That's why it is in the stools."
Now, I go on to say that furthermore, as far as our present knowledge goes, the human being is the only known reservoir of the virus and it is therefore necessary to find an explanation for the entire cycle. That is, from the moment of entry to that of egress and dissemination within the human body itself. An analysis of this phase of the problem must draw upon and integrate information derived from a) our knowledge of viruses with neurotropic affinities; b) the behavior of poliomyelitis virus in the only known experimental animal, the monkey and c) the limited studies on human beings.

Then I go on to analyze this and I will not read the whole thing. I analyze for example, the available work on the gastrointestinal tract as the portal of entry. I will add here that it has been one of the interesting facets in the history of poliomyelitis how certain people in Europe would feed polio to monkeys, and they would say that on feeding, the monkeys developed, some monkeys developed paralysis, particularly—not rhesis monkeys, Santa Monica monkeys. This was so contrary to Dr. Flexner's concept that he would immediately and do exactly the same thing with that wonderful strain of virus he had--MV--he said, I fed the same strain of virus. I did exactly what you did and I got nothing." And so this went back and forth. Then after a while, other people put the virus, other strains of virus in, and fed them, and sure enough, they did get paralysis. Simon
Flexner was wrong. There was something that had to do with the strain. But, very easy. That when you feed it to them, it regurgitates and it goes in by way of the nose, and it is still the olfactory pathway. So, what did he do? Several people did it. I did some work in which I examined olfactory bulbs, because Robbie Ward and engaged in two studies after we started in Cincinnati. First, the natural history of the infection in monkeys, especially cynomolgous monkeys, not using the MV strain, using freshly isolated strains that we ourselves would isolate.

Q So already you suspected that--

A Oh, by the time I got to Cincinnati, I was convinced that the olfactory pathway was wrong, even though most people used to come to the Symposium of the National Foundation held out for the other. Well, a number of people became involved. We showed in the first place that after feeding, there were no lesions in the olfactory bulbs. Other people cut the olfactory tracts and this I think was done in the Baltimore laboratory, cut the olfactory tracts and fed chimpanzees, monkeys, had no effect. They had the olfactory pathways cut and still they would come down with polio. Then it became the real issue was, what happens in man? The old hoped for—you see, the proper study of mankind is man. I think that's the quotation, and so we followed that with polio and I decided that in addition to studying the model systems that were quite different from the ones we studied before, particularly what happens after feeding, that would be necessary to study human beings. Other people were studying feces
and all that. Well, ad infinitum. What do you learn? You find it in the feces. So you have it in the feces. But where is it all over the body?

I decided again to follow the pattern of chasing a virus around a whole body that I used with vesicular stomatitis virus, with encephalomyelitis, with equine encephalomyelitis virus with pseudo rabies and so on. We decided to do in man what we were doing in monkeys. For that we had to set up a system of getting to fatal cases of polio myelitis as soon as possible after death and to do the autopsy ourselves. Because there was no question that there was plenty of virus in the stool. Then when you see a patient lying on a slab in the morgue, and the possibilities of contamination with stools and the way the autopsy is done, it would be absolutely meaningless that if you found virus in certain places. As a matter of fact, when I searched the literature, I found that somebody had gotten one bottle, a piece of intestine, a piece of brain, a piece of this—all in one bottle. Probably taken out with the same instruments. It was meaningless.

We developed a special system of work. In the first place, we had a tremendous number of sterile instruments so that everything would be done with aseptic instruments. We will do the autopsies ourselves. Before we would take out, open up the intestine or do anything on the rest of the body, we would take out the central nervous system with aseptic precautions. We would get off the hair, we would clean down, we would do it as surgical as possible, make incisions with sterile instrument,
and take out the central nervous system aseptically. Then cut
different parts with separate instruments and put it in a
separate bottle. In other words, we came with a terrific
chest of instruments and bottles. We set up the system of
being called to do autopsies within a four hundred mile radius
of Cincinnati.

The way it worked was this: Of course we got everything
that came in to Cincinnati. But if something happened in
Louisville, in those days, the frequency of flights was very
low, but Robbie Ward had a big Buick, a convertible Buick.
We'd get into that and boy, it did 90 miles an hour on the
road like nothing. Even to Cleveland, we would drive the 250
miles, and in that convertible, it was mostly in the summer.
And because, excuse the asides, here, because Robbie Ward was
an outdoor man. He used to drive a motorcycle. He taught me.
He showed me how to put a lot of newspapers under your coat,
and provide insulation to keep warm. At any rate, we used to
drive or fly out. If it was as far as Vanderbilt, because we
were called there too, we would take the plane. So, we would
drive or fly. We went to Indianapolis, Columbus, Cleveland,
Huntington, West Virginia. We went within the four hundred
mile radius, and we accumulated a certain number of human materials
which we then proceeded to innoculate in monkeys. We could to
that only because we got sufficient money from the National
Foundation for Infantile Paralysis. The monkeys cost about
$7.00 apiece, and I had already established a big monkey
facility at the Children's Hospital Research Foundation to house about 300 monkeys. We went into the big business of studying the growth of the natural history of the disease in monkeys after experimental infection with different strains of polio virus. And in locating the virus in man. From this came out a pattern. That pattern pointed to. I am not speaking with—I never speak with absolute certainty, but it was a meaningful pattern of very high probability that a) that the primary portal of entry in human poliomyelitis was the intestinal tract itself or alimentary tract. The posteaal pharyngeal wall was included in that. But it wasn't necessarily the one because the washed intestinal tract by itself—it wasn't merely swallowing—as you, which you couldn't rule out. And that then the invasion was difficult just from the autopsies to say whether it followed entirely a neural route or whether there may have been also a hematogenous route because we did find virus in lymph nodes taken out and different things, but it was difficult to pin point the time when one occurred or when the other occurred.

In the monkeys, we could. In chimpanzees which we studied, we could. I have a number of publications in which this very meticulous was carefully analyzed. To bring it to a point of conclusion. By the time I left Cincinnati to go into uniform, to go into the army, which was February, 1943, we had arrived at a conclusion, had a working conclusion about the nature of infection in human poliomyelitis, the one that I just described. The primary portal of entry is the intestinal tract. Subsequent
invasion of the central nervous system. The other data pointed to the fact to the pattern that was responsible for the very manifestations, depending on the number of neurons that are involved, which

Then, there was the War. When the work was resumed. Of course, we also did other things. Like Paul and Trask, who also did work on flies.

Q Alright. Now talk about the work on flies.

A Well, because it became evident that the natural history of polio involved the virus coming in by way of the mouth and multiplying in the intestinal tract and then going out by way of the feces, the question naturally arose whether or not, even though the human being was the source of the virus.

Q I am afraid I am recording the knocking.

A The question was whether flies, for example, or roaches, others have raised the question of roaches, which can become contaminated with human feces, and there are special flies that feed on human feces, you can see it. Whether they can a) just mechanically pick up enough virus to let us say then be able to transmit it so that you would not really depend on human contact alone for transmission of the disease. Therefore, we went out to epidemic areas, and some of them in very nice neighborhoods, and you wondered where there would be a fly, because there was no horse manure for them to breed in or there were no garbage cans in which to breed. We went out to Atlanta, and we went to Cleveland, and other places. I
don't remember now all the places. We had special traps which we baited. We collected the flies. We demonstrated that in flies that we caught in epidemic areas you could by inoculation of monkeys, demonstrate the presence of virus. Now all it meant was, that somewhere these were homes with flush toilets, mind you, that we looked around. We couldn't see. These were not open privys. We asked ourselves the question, where in heaven's name were these flies picking up the virus. The answer wasn't obvious. But there must have been somewhere in the area, and they have only a flight range of not more than one or two miles.

Well, we didn't discover it. We demonstrated that flies carried the virus, and there were endless discussions, I remember during various seminars, symposiums I did on this, does it mean anything? How do you know that--alright, they have it, how do you know this wasn't on the outside of the fly? You have to ask the question whether it is possible that it multiplies in the fly. Well, there were some very elegant experiments that were done by others. I think Melnick and his group did some very nice experiments in which they actually suspended flies with some parafin, and then had it feed on a solution with naturally occurring polio virus, and then sacrificed the flies at different times. I think the evidence was yes, it did persist inside, but there was no evidence of multiplication.

Personally, when I look back on this, the many interesting heated discussions, there is no question now that person to person transmission is the most important mode of maintenance
of the virus. The most significant experiment, in my judgement, to indicate the possible role of flies was the one, direct experiment, was the one done by Robbie Ward later in which he fed bananas on which flies from an epidemic area had fed, not artificially infected flies, because that would be an artificial experiment. As I recall it now, it was a completely natural experiment. Flies that were actually caught, whether it was caught with the bananas, or they were subsequently allowed to feed on bananas, flies from epidemic areas were fed to chimpanzees and evidence of infection in those chimpanzees was established. I think by excretion of virus. I forget what mechanics were involved.

My own epidemiologic approach to this was interestingly enough, in a very large epidemic that I was called upon to study in Berlin in 1947. Then I had a publication on that in which I particularly tried to study the role of flies. And the extent to which the higher incidence of polio in the Soviet sector of Berlin, because things were not cut off. People were moving back and forth. Could be traced to the fact that in the non-Soviet parts of Berlin, this includes the American occupational forces, French, and British, before the outbreak of polio they were spraying actually against mosquitoes because they were afraid of transmission of malaria from returned prisoners. This also greatly reduced the number of flies in the area. When I compared, and I worked very hard on this in Berlin to get the precise data, the prevalence, the incidence per month and the
time around the week of that, of polio cases in the Soviet sector and the other sectors. And at that time all Berlin was in rubble. There was more in the Soviet sector. Now the Soviet sector, the Soviets said "You don't spray our part of Berlin. You spray your part." Berlin is a big area. You spray and there are plenty of flies. Moreover, the things that interested me was that I went out and examined the sewage disposals systems, and another thing, in '47, when times were hard for the German people in Berlin, and many of them used human feces. They had flower boxes, which they used to fertilize with human feces, and grow tomatoes in it and other things, just increase their crops. And also, there were areas immediately around Berlin which was enclosed, by a ring, again the fields were fertilized with human feces, as in China. This was a sort of round about epidemiologic possibility in circumstantial evidence that under certain circumstances in which flies have a very special opportunity to pick up polio virus, which was wide spread at the time, they could be an additional factor.

Q There are two things I don't understand. The first thing is that as early as 1912 Kling, Wernstedt, and Peterson report that they find polio virus in intestinal washings. I can't understand why this observation, in a sense, went to

A Intestinal washings of human beings--

Q Yes. Intestinal washings of human beings, why this observation, which is a pregnant observation then takes on a long sleep.
A Let me explain some of the factors--yes. Number one, Kling turned out to be a very uncritical investigator when it came to interpreting the positivity in monkeys. When Robbie Ward and I understood the work during World War II, we had no contact with Kling. I very carefully studied his things, and there is an analysis of it in my first report on that. It is evident that Kling would make a positive diagnosis of polio if he looked at sections of a monkey whether he developed anything or not, and he found some perivascular infiltration. Then we were able to show that perivascular infiltration occurs spontaneously in any monkeys and that his conclusions were such a mixed bag that you couldn't do anything. This was one factor.

The second factor was the authority of Flexner. Basically, the studies, the careful studies on human excretion. I may be wrong, but I think that it was Paul and Trask who started anew without prejudice, on human feces and really demonstrated without any question of a doubt that polio virus was being excreted in human feces. But do you know what it meant?

Years of bickering at scientific seminars. What the hell does it mean John? Jim? It just means that some virus which went down from the throat into the intestinal tract is excreted. In other words, it didn't mean anything until it could be shown that it wasn't just swallowed virus, that in our autopsies of human material, never mind monkeys, never mind chimpanzees, that washed intestinal tissue, thoroughly washed, had the virus in it. Now, there is an interesting side light that I'll mention.
It was during the course of such experiments that we had a lot of washing of autopsies, intestines, human intestinal material. That one of my technical assistants, Barbara Johnson, who at that time had already stopped working with me on PPLO in the human material and came on to help with the work in polio, that she committed the error of something that was being washed, somehow or other, the water came too strong and it, the tissue came off. She picked it up with her fingers. Within a matter of less than ten days, there was no polio around anywhere. We can't be absolutely certain that that is what she got it from. The probability was very high that she was infected by handling this, and she develops a very crippling case of poliomyelitis that made it impossible for her to go on. At any rate, this is the--let me tell you an anecdote. In connection with Kling, because you mentioned Kling.

My first direct encounter with Kling was in 1947 in Copenhagen when after World War II, the first international microbiological congress was held in Copenhagen. Kling who at that time already had the hairdo of Beethoven, you see, now everybody has it, approached me. He said, "You know, the things you said about my work from the interpretation of polio in an article War, that's all wrong. You are wrong." He says, "You come to me. You come to Stockholm with me after the Conference and I'll show you. I'll prove it to you." I said, "Professor Kling, I would be delighted." These are the dividends of the scientific life, the overtones, you know.
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So after the Conference, I arrived at Stockholm, he waits for me, we start off with a luncheon at the Hotel. No hurry, we'll get to my lab soon enough. Let's have a regular Swedish lunch. One aqua vite after another. One aqua vite after another. It was a three hour luncheon. It was terrific. We were so happy, by the time we started out for his lab that it really didn't matter very much one way or the other. So we get to his lab at the Bacteriologus Collaboratorium and he begins to show me the work on--he has tanks, no sewage water, just a little bit here, just a little bit there, he was glancing virus then, to be able to test with mice. He says, "Look, it multiplies." I said, "What's your criterion that it multiplies?" And he shows me mice with lesions, the same sort of things he saw--and I said "Professor Kling, I am sorry, I like you so much, we feel so happy, I hate to say it." He said, "What is the evidence that these infiltrations which I've seen in any number of innoculated mice, that this means that you've passed polio." He says, "You know, that's the trouble with you people in America, you are always in such a hurry. I've only worked on it for three years. It's a long, long to Tipperraree."

And so, we ended up by singing songs, and the argument was not resolved, but it was quite obvious to me that Dr. Kling lived in a world of his own, and the criteria that he used for polio virus multiplication, or in fact, either in mice or monkeys or criteria that were not acceptable to anybody.
I have a load of questions, and I don't want to miss one. I have one that--Dr. Sabin, could you give me your memories of the development of the laboratory infection in Barbara Johnson.

Barbara Johnson, who was working as a technical assistant to Dr. Ward and myself, in the search for polio virus in various tissues of cynomolgous monkeys after they had been fed human virus, virus of recent human origin. She developed paralytic poliomyelitis after washing tissues of the cynomolgous monkey that had developed paralysis after feeding, washing intestinal tract, postenal pharyngeal wall, etc. Under circumstances which made us conclude that the balance of probability was that she had acquired the infection as a result of her work. The reasons for that, quite, perhaps special. They were at that time.

This occurred in 1940. During the thirty years preceding that, the work of poliomyelitis, 1910 to 1940, there was not really an instance that we were aware of anybody acquiring polio by working with it in a laboratory. Many people had worked.

One of the factors that might have contributed to that was that most of the work, not all the work, but most of the work had been done with laboratory adapted strains which perhaps do not have the capacity to infect by any more. Or at least sufficiently so. The other is that most adults already have immunity. Well, in the case of Barbara Johnson, at age 35, she was one of those adults in the United States, who lacked immunity and it occurred during a period when, in Cincinnati, up to the time that, of this event, there had been
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no cases of poliomyelitis here. She went off on her vacation and ultimately to Buffalo, also in areas where there had been no polio. Then she comes down with the paralytic disease, isolated the virus from her stools, and proved that it was polio. It was for that reason we thought the balance of probability was that she had acquired it. We published this report in order to warn other people who are now beginning to work more and more with human material and with strains of recent human origin, that was a potential danger. We couldn't absolutely prove because we had no particular markers in those days such as we have now by which we might have been able to at least establish a closer relationship between the strain of polio virus we isolated from her and the strain that we isolated in the monkeys, in the tissues that she handled. I did elicit a story from her which is not included in our report that during the washing of the tissues, she broke the laboratory discipline and apparently handled some of this infected tissue with her hands. It was a tragic case because she was very severely paralyzed, and she got back to work quite after it--I think a couple of years. She was unable to work in the laboratory any more because of her paralysis. She had a remarkable spirit. She turned to statistics, and then many years, she continued to work in statistics, adapting to the problems.

Q I think one of the interesting side roads of this infection--was it regarded then, as an occupational disease?

A It certainly regarded as an occupational disease because it hadn't happened, as I mentioned before. The possibility of
being infected by handling such tissue was only just coming to the foreground. But my own conclusion was that it was an occupational disease, or occupational hazard, particularly if one did not observe the precautions that should be observed with such material.

Q Were you ever able to get her insurance for her?

A Well, she, as an employee of the Children's Hospital Research Foundation, she carried workman's compensation in the State of Ohio. We submitted a request for compensation and I was prepared to defend the conclusion that she acquired this disease as a result of her work. I was called to testify in Columbus before a special commission. I was prepared to explain what I meant by the balance of probability. But interestingly enough, there must have been so much compassion among the members of the committee, that they did not ask me to prove the balance of probability that she was entitled to compensation, but because I think they were all Republicans, and very much concerned about Franklin Delanore Roosevelt, they asked me only one question. It was, "Doctor, tell me, does polio affect the brain?" I had to answer, "I don't know whether to say that I am sorry or that I am glad to say that there is no evidence that it has any effect on the brain. I only affects the motor cells."

Q I wanted to raise one question about the flies, and then we'll let is ride. When one looks back on the literature on flies, one almost gets the feeling that the problem of flies had been settled very early, in 1912, 1913. At that time,
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Milton Rosenau, AU of Harvard had published an interesting paper on the transmission of polio through the biting fly, stomyx calcitrans, and as a matter of fact, Anderson and Frost had also published a paper confirming that, and they could not really confirm it, they just withdrew that paper.

Flexner attacked Rosenau, noting that while sometimes polio virus did appear in the blood, it didn't appear in sufficient quantity to--

A  Is that what Flexner said?
Q  Yes. He did say that.
A  I don't know what evidence that he had.
Q  He had found from time to time he would find polio virus in the blood.
A  No. Those records.
Q  Yes. It would disturb him but he would never truly--
A  Big little men who know that I'd like the references to that.
Q  Yes. okay. and he would. It would bother him for a little bit, but he never truly troubled to find out more about why this phenomenon occurred. He didn't believe that a biting fly could transmit polio. The fly experiments that he did with Clark with flies and mosquitoes suggested only that the fly or mosquito might carry the polio virus, but there certainly was no evidence of multiplication of virus using the fly or mosquito. So in a sense, that question almost seems to be answered circa 1913. And comes 1940, '41, and I find that you and Ward are
again working on the problem of the fly, and transmission and this type of thing. I wondered what the reasons were for getting into this.

A There were two totally different reasons for the approaches within two or three years after polio had been established as a virus disease, and for the work that started again in 1940 by Paul and Trask and by ourselves. The early work was done because one was really in the dark about pathogenesis of poliomyelitis. I am not aware of any acceptable evidence at that time by anybody, Flexner or anybody else, and I want to stress the word acceptable because there were reports of polio in everything under the sun based on improper criteria. But it was a reasonable experiment to perform. Apparently, these were blood sucking flies to determine flies which had sucked the blood of a monkey with polio would be able to transmit it to another. I must confess I have not read the details of what it was that was transmitted in the experiments of Rosenau and Brewer's and then the others.

Whether it was actually paralytic poliomyelitis that was transmitted, how good was the histological evidence of transmission, whether a second passage was established. I don't know. Certainly, if I would have to seriously analyze this situation, I would not want to say anything more about those experiments until I satisfied myself that they really transmitted polio, and not some lesions which were not polio. But, it is conceivable that they may have had a human strain, because they were all freshly isolated strains then. Which had produced enough virema
in the monkeys at the time they put on these flies, and I don't know how many flies they had to feed on them. I don't have the stuff in front of me, that it is conceivable that it might have been transmitted, and that the reasons that they themselves and others subsequently could not repeat the experiment was that they may have already used virus that had been passed too much in the monkey brain.

Q I have to change the tape here.