Dr. Benison: I'd like to come back to a point you made last time. You indicated last time when we stopped the characteristics that you look for in people who come to your laboratory. Let me throw a curve ball at you. If someone showed up in your laboratory today and said, "I want to work by myself. Perhaps I don't have much training, but I'd like room in the laboratory to work." How would you react to it?

Dr. Sabin: Of course, today I have only an improvised laboratory, which I improvised for myself, but it will hold four people. But in the old days, which goes back...let's say the end of 1969 going backward...my work was very programatic, and at that time, I did not have a great deal of space. I had a certain number of rooms; I had a floor which was the Children's Hospital Research Foundation of the Department of Pediatrics. So frankly, I was not in a position of a head of a department...let's say, Microbiology...in which there are numerous activities to be fostered. As a research professor, and as I said in these later years, I was definitely dedicated to certain programs and I had no room for people who would come and say I don't know what to do, or what I would do, but I just want a place to do it. I just didn't have that luxury. So that kind of a person would get no where. People did come; some were students and some were persons who, let's say who may have just gotten their degree, and said I would like to see what you're doing and mind if I could be here and learn some of the techniques, and those I did accept. And some of them turned out to be extraordinarily good people. I don't know if this is the time to mention them. If I recall, the person that comes most to my mind and I would regard as probably the best of my scientific sons is
Robert Channock who was a resident in Pediatrics at the University of Chicago and I think it was immediately after World War II (1948 or so), and his boss had worked on the same floor as I did in different departments at the Rockefeller Institute. And he said, "I've got a very smart young fellow who would like to go into studying infectious diseases as a pediatrician. Would you take him?" I was impressed with the solidity of this man, even though it was obvious that he didn't have any experience in virology or hadn't done really anything very much. Well, he came to work with me and joined me in a project on which I already was well along and that had to do with hema agglutination of anthropod borne encephaletic viruses. And he worked with me and it was very quickly apparent that he was a person of very great ability and tremendous litigation. Then he worked with me for a number of years on different things and finally because of the great regard I had for him and I realized that it was wrong for his future constantly to be working on things I had initiated, I suggested to him that the time had come that he should go off by himself and start working in a field which he could develop and with which his name would become identified. And I said it would have to be a field in which I was not working at all, that he would have to start on his own in the lab. And after a discussion of what fields one might regard as specially important, it was decided that the role of viruses in human respiratory disease was something with which many people had become involved in and worked—that it was a wide open field. And there we were; we had clinics with babies who were coming in all the time with all sorts of things that were not understood. Here was he, who already had good experience in virology, and, sure enough, he immediately discovered a new virus. Subsequently it became
para-influenza virus and he showed that this was responsible for a form of virus called infantile __________. (incomplete sentence) To make a very long story in short, it's now 25 years since then; he has not only/my judgment, but the judgment of many people become the most outstanding contributor to our knowledge of viral respiratory disease. And only this year, I was very happy to see him elected a member of the National Academy of Sciences. He's received many kinds of awards.

There were other people who came to work with me that way and have made important achievements. One of the earliest ones in Cincinnati was Dr. Robert Ward. He was a resident in pediatrics at Johns Hopkins and the same way; a professor, named Park, who was a famous pediatrician. I just left the Rockefeller Institute and he thought he ought to come to me. Frankly, Robert Ward— one might call him a _______________ because he was a very unique, suave person. (incomplete sentence) But with a very excellent mind and it was with Robert Ward that I began the studies on human poliomyelitis, which led to our understanding of the nature of the disease and subsequently, during the war years went to Yale and New York University as a professor, and for many years he's been the head of the Department of Pediatrics at the University of Southern California.

There were a number of others with me. Another one who was in the laboratory about the same time that Bob Channock came was Ed Buscher. He had just gotten out of medical school at the University of Cincinnati. And when he came, he said, "I don't know anything." And I had just become involved in a study of hema glutins of anthropod borne viruses and Japanese encephalitis, and he joined me in this study.
Again, it was obvious that again here was a man who had the ability, took off, so that the formula that I applied to myself really didn't work very well in my laboratory, but it goes to show that it's not the only formula. That some people who start really without knowing their direction, be given an opportunity to learn the tools of the game. He can then very quickly find out if they have something on their own. Well, Ed Buscher then joined the Army and he did very excellent research and right now he's the Commandant of the Walter Reed Medical School. There were a number of others. This is the immediate post-war period. There was Harry Feldman and then there were people who came from Germany, Hans Agars, who was a very important professor in Germany now, and a number of others who came through the lab who did not fulfill the formula of saying 'give me a place to work'. But supposing that I were head of a department of microbiology where the work was more or less divided into specific targetive objectives, and also who has a responsibility for developing new investigators, I would certainly look for those who knew what they wanted to do. But I must confess, I would never give a job to anyone like me. And the way I got it. In other words, if somebody came to me the way I came to first Professor Charles Krumwiede in the Department of Bacteriology in New York University, he turned me down. He said, "What do you know?" Go back and learn some more." Instead, I didn't accept his refusal and I went to the Chairman of the department, over his head, William H. Park, as I think I mentioned before, and he was soft-hearted. Maybe he was taken with my enthusiasm and desire to learn things by myself. And even though the facilities of the Department of Bacteriology at Bellevue at the New York School of Medicine were not very great, and I think he gave me a spot—a corner—to the annoyance of people who needed space; I don't think if I were in Park's place
I would have done it. You see, I was lucky that Park was not like me.

Dr. Benison: Let me put another question to you in the sense that I put this question to you before. Who did you work with, or who did you work for?

Dr. Sabin: I think I've never worked for anybody in my life. Because it was contrary to my basic constitution to work on problems that did not arise within me. But the very first publication, which appeared in the Journal of American Chemical Society in 1928, which was less than a year after I entered medical school, shows how I looked for help when I needed it.

Dr. Benison: Would you discuss that paper?

Dr. Sabin: Well, it has a bearing, in part, on the subsequent work that I did. It's probably the most sophisticated paper on which my name appears.

Dr. Benison: I'll take that with a grain of salt!

Dr. Sabin: The reason for that is the following: As a student when I came to work in the lab, I observed others. You see, I'd observe what was going on. This was in 1926; I wasn't yet admitted to medical school. And there an assistant professor in the laboratory, Professor Klosterman, was going some work with bacteriophage. And mind you in 1926, that's 47 years ago, the question of bacteriophage as a living
thing was not among the significant hypotheses, and the current hypotheses was that some special substance that was liberated by certain bacteria, and I was intrigued. It was a question of intrigue. The problems that I worked on always rose out of some experience that I had. And it's not very sophisticated because I did not develop hypotheses from reading and theories and then went to work, because frankly, I was a very poorly trained person when I started to do research. But when I observed something and my curiosity was aroused sufficiently, I went to work on it. So here I observed, or had pointed out to me (I don't remember now if it was pointed out to me--I'm not sure whether Klosterman was even concerned), when he showed me the clear zones, which represented the action of bacteriophage on plated bacteria, and you saw the individual plaques, the individual clear zones. It was evident some were big and some were small, and so on. And my curiosity was aroused. I think I asked him why do you think this one is small? And this other phage you are working with is big? He didn't know. Well, in my simplistic way of looking at things, I asked a question, I said, "Is it possible for a different bacteriophage to diffuse at a different rate in agar jelly because the bacteria grown on agar?" So since I didn't then have the technique for working with bacteriophage, I developed, and nobody had time to teach me. Instead of asking the question directly with bacteriophage which may have been difficult to answer, I went to do some simple experiments which wouldn't cost anything and I wouldn't need more room and I wouldn't need any budget. I wanted to learn about the diffusion of dyes, of simple substances into agar jelly. First, before going to the more complicated (and frankly I didn't know the literature of long ago but some basic curiosity led me to set up an experiment in which I added dyes like ____________, tubes of agar carefully
made so it would diffuse in the aga and not run down the sides, etc. But I was again curious to know whether it would diffuse differently going against gravity, that is the diffusing down of the ordinary way the jute stands, the agas on the bottom; you put the dye on top and then measure how fast it diffuses. The curiosity was, would it diffuse differently without the help of gravity because this is not solutionless, its solid gel. And I had studied pathoidal caloidal chemistry at the time I was studying caloidal chemistry at Washington Square College. The various hypothesis on how it would gel were constituted. But I did the experiment by putting methylene blue to the tubes of aga gel and to one set of this I added vasoline on top and turned it up side down. So one set of tubes was diffusing down with gravity and the other set of tubes was diffusing up against gravity. Because there were books written at the time about the nature of gels. Gels are so called conviction currents which means currents that are set up when two solutions of different concentrations need each other do not play it off because it happens when they're gelling. Well, much to my surprise, it turned out that with the set up that I had used, the dye was diffusing more rapidly day by day, against gravity when it had to diffuse up than when it had to diffuse down. I carried out a number of studies with other substances and there was this peculiar phenomena, which I didn't understand. And, frankly, I didn't have the training of how to begin to approach to study this in a sophisticated manner except that it seemed unreasonable. Now just at that time, a young chemist by the name of Harry Sobottka, who had just received his Ph.D. in chemistry in Munich with the great Willstatter. This Willstatter especially became known at the time for his contribution on the purification of enzymes, the different aluminate gels; it was quite obvious that Harry Sobottka was a sophisticated young chemist trained in
a way that I just wouldn't even approach, and I came to him with this problem. I said if you have an explanation you know, it shouldn't happen according to the books. So I said, could you help me find a way out of this? And out of this came my first paper in which Dr. Sobottka was senior author for a very good reason, because the sophisticated experiments which led to an important discovery on the diffusion of gels was called baraphoresis in gels was his. Mine were merely the basic observation which he didn't make, which nobody else made, but I made, but I needed help. He was the one who gave it meaning, you see. I only made the observation. But to me that was a lesson. It was a lesson on the way to plan experiments and the way to work things out to an end point. And while I worked like the devil getting the data, he was the one who designed the protocols for the sophisticated experiments. And out of that came a demonstration that the books were wrong about what they said about gels. But in effect, when you have an aga jelly, you have a fluid in between what I called ma-cells of the gel. And that fluid has a very definite specific gravity. It's not just that there's no fluid; it's just solid jelly all the way. And depending on the specific gravity of the intramacellular fluid in the gel, the way another liquid diffuses into it, either against or either with gravity down or against gravity when it has to diffuse up or sideways which happens when you have an aga plate of diffusion going on in a gel is the terms of a specific gravity of the diffusing fluid and the specific gravity of the intramacellular fluid. For example, if the specific gravity of the intramacellular fluid is low, and the diffusing fluid going down is high, then it turns you see. If you have a juncture, at the juncture you have the greater concentration on the top, the lower concentration on the bottom and it sort of creates these swirls, which are known as convection currents. And these swirls help to bring
the stuff up or prevent it actually from going down, but supposing it's the reverse. Supposing that the fluid below is heavier than the fluid above. Then they don't. You see, it's like a lighter sugar solution sitting on a heavy sugar solution. You don't get convection currents. Convection currents you get when something is heavier on top than on the bottom. Now supposing you turn it upside down. You turn it upside down and then everything changes, because if the stuff is heavier in the fluid than the jelly, and lighter than the fluid that is diffusing, it carries it up. Well, I don't know if I've become involved here, but the point is not the thing itself, and, frankly, I don't know if it's ever been referred to, there are so many activities now--gel electrofaresis and other things, and I'm not sure whether or not this paper published in 1928 by Sobottka and myself has ever been really given proper consideration--the control phenomena of diffusion. But, nevertheless, it was a lesson to me. So this man helped me. I didn't work for him. Because the idea, the observation was mine, but he helped me make something out of it because I wasn't able. But then came the next one--another example, which was a little difficult. Because it wasn't so much sophistication as it was opportunity. I think shortly after I entered medical school in order to be able to support myself and have somewhere to live, I went to work at Harlem Hospital in New York after hours in medical school. I lived there and in order to earn my keep at the hospital and my food. Well, this was through Dr. Jesse Bullowa, a person who had been doing a lot of work in serum treatment in pneumonia. Pneumonia in those years was a very serious disease, particularly in the winter time. There were hundreds of people dying. The only thing that was available that had some effect was serum treatment. Dr. Bullowa worked very closely with Dr. William H. Bach who was then the Director of the Bureau of Laboratories for the City of New York, and it
was there at that anti-neuococcal serum was produced, also concentrated and purified, so there was a close liaison between Dr. William H. Bach and Dr. Jesse Bullowa. Bullowa was a clinician, a very good clinician, and actually because I didn't have money to support myself, and I forget now what the tuition was, I think Dr. Bach was influential in two things: first, I was the first recipient of a Jesse G. Bullowa Scholarship. It was a very interesting story. Littauer was a very rich man who was a relative of Dr. Bullowa. I think there's also a Littauer professorship at Harvard and so on. He's a glove manufacturer somewhere. And actually there's a special laboratory in the Department of Bacteriology at New York University where Dr. Sobbotka was working that was called the Littauer Research Laboratory, which was just on the ground floor as a separate little building, and it was called the Lucius N. Littauer Fund for Pneumonia Research. This was a chemical laboratory of the Lucius M. Littauer Fund for Pneumonia Research. And actually Dr. Sobottka was working there on soluble substances, specific soluble substances, of pneumococci. So there was a time, you see, Bullowa was a relative of Littauer; Littauer had provided a fund for research in pneumonia, and so there I was. So first I received the scholarship, and then Bullowa gave me a job to work at Harlem Hospital for which I had to do the following. When I arrived from medical school (it was quite a distance from Harlem Hospital—go by subway and so forth), my job was to sputum type. Because everyday these patients with severe pneumonia would come in and the sputum had to be typed to know which type of anti-serum to give. So that was my job to do—a routine job, a routine procedure to type pneumococci, grind up the sputum, you inoculated it into the peritoneal cavity of mice and then the next day, you see, they were either dead, or just before, you could open the peritoneal cavity and wash out the fluid and the peritoneal cavity
really eliminated the other bacteria and selectively allowed the pneumococci to grow out and then you could set up a regular serological test to determine which ______. (incomplete sentence) This is the work that I was doing and the other thing that I had to do was to help the resident with the patients who were admitted to administer the serums. So I would stand by. Sometimes he would even let me give the intravenous injection--I was just a first year medical student. Well, this led again to three research projects, which I was doing throughout the period that I was in medical school. Perhaps I should digress here how I could do that. In the first place, the two years that I had in dental school had given me a basic training in anatomy, body chemistry, physiology, embryology, pharmacology, pathology--the pre-clinical sciences were to a very large extent the same. Now maybe there were a little heavier and more concentrated and so on, but I didn't study very hard and because I went into medicine, not because I wanted to become a practitioner in medicine, which I do not regard as unimportant (I believe it's most important), but at any rate because I wanted to do research, I didn't do much studying. Besides, it was easy. I was the second time for me--it was the second dose. So whatever free time I had, I would get away--sometimes I would cut classes and I would study, but I organized a research program and then I had to work. So in the course of this work, my curiosity was aroused. Why? I would come in late in the afternoon and evening and innoculate the sputum of a number of patients were admitted, and until then you couldn't give them serum--there was no use giving them the wrong serum, and I would come in the next day to determine the type of pneumococcus so they could get the proper serum. And very often the patients were already dead the next day. And I said, "Look, I don't like the existing method. Wouldn't it be very helpful if when I come in the afternoon, let's say 5 o'clock or thereabouts, I innoculate the mice with
the sputum or somebody else there innoculates it before me, and then if that same evening I could determine what is the type of pneumococcus and give it to the patient right away." Because there was correlation between time after the onset of the disease and the administration of serum as regards the effectiveness of the serum. So I set about fooling around to see if I couldn't get the answers to this thing. And out of this came my first publication, which was my own. I didn't have to go and ask anybody—it was very simple bacteriology and immunology. I developed a test which could give me an answer the same evening, because instead of doing it macroscopically, I did it microscopically. Instead of waiting until the pneumococci multiplied to a very heavy extent in the peritoneal cavity of the mouse, I punctured the mouse and put in a little glass capillary down through the abdominal wall, got out a little fluid because there wasn't very much in two or three hours, and I would smear it out on a slide, mix it with the different reagents, like 1 anti-serum, dye 2, dye 3 and so on, stain it quickly, and look at it. And to my amazement, there was enough pneumococci by then so they would agglutinate in very nice form and characteristic form depending on the type they were, so I could say it was either Type 1, Type 2 or Type 3. Those are types for which we used anti-serum most. So pretty soon I did it routinely. I did this, then it was double-checked the following day because I didn't kill the mouse because the mouse from which I got a little bit of fluid through the capillary tube continued to live the next day, you see; it was either dead and then I could show there was perfect correlation. (Incomplete sentence) So, immediately there was a practical thing to apply and, you see, I was involved. First in the comparative study to make sure that my three-hour test, so to speak, was as good as the regular 12-24 hour test and to give the serum quickly to the patient. Now
another part of this test was the following. Again, you see, my studies rose from practical needs and this almost remained one of the dominant features in my selection of subjects for investigation—some arose from sheer curiosity, like the very first piece of work I did, but the predominant part arose out of problems in medicine to which I was exposed. So let me follow through. In order for serum therapy pneumonia to be effective, you had to be sure you gave a large enough dose so there was an excess of antibody and how to know there was an excess of antibody. So using the same technique as I used for sputum typing, I developed a technique of taking a drop of blood from a patient's finger and mixing it up with cultures of Type 1, Type 2, Type 3 pneumococcus, whichever it was, so see whether there was an excess. And if after a couple of hours after administration it was given intravenously, you didn't have to wait. If there was not an excess, in other words you had to wait a couple of hours depending upon how much of a lesion you had in the lung because if you had a big consolidated lung and took out all of the antibodies as it went through and there wasn't anything left, then obviously that wasn't enough. So it wasn't merely a question of dilution because that you can calculate. But the question of how much infection there was which was combining with the antibody. So there was another test that I'd found. And then the resident receiver became involved. I was doing the research and he was following orders. I was a first year medical student. So the research was again accidentally published in another publication. It greatly appealed to Dr. Bach, my boss. He felt that what he did against his better judgment seemed to have been repaid. And because he had to lecture a great deal in the country on pneumococcus infection and pneumonia, he immediately popularized it was the Sabin Test Pneumococcus Typing. Well, as I watched the patients getting the serum and as I was giving them
serum myself, I saw how often, and in definitely different lots, about half an hour to 40 minutes after we got the serum intravenously, they would go into a shaking chill. And their temperature would go up sometimes to 106-107°F, and you'd think that the man was going to die.

Dr. Benison: Not quite an emaphalactic reaction?

Dr. Sabin: No, no, this was an immediate thing and apparently it had no relationship to the effectiveness. So it was obvious that there was some substances that produced fever and chills in patients who were getting certain lots, and this was usually by then they were getting purified globulin, not the straight horse serum, and not in others. My curiosity was aroused. How can you find out ahead of time—it was deadly, I mean, you'd think that man was going to die. Could you find out ahead of time which lots had it and which didn't and what was the reason for it. So I was then a studying medical student, but I had a little lab in the Department of Bacteriology and on the floor above, the Department of Pharmacology. The Department of Pharmacology was headed by a very remarkable man, Professor George B. Wallace. And one of the women working in the department was Mrs. Kidd. I think she had a crush on him. She used to go down and they used to make lunch there and have sandwiches. So one day, I went down there and said, "Here's a problem—a chill producing fact which I see in my work in the afternoon when I leave school"—I'm not sure whether I had already started taking pharmacology (this was in 1928) and I said I would like to try it out on some other animals. The experimental animal that was almost exclusively used in pharmacology as in physiology in those days was the dog. And I said could you please let me have some dogs, and I would like to give them some lots of anti-pneumococcal purified globulin, which is used
on the patient, which I have saved at Harlem Hospital. Some of them it gave chills almost uniformly, and others didn't. Even with much larger doses. I would like to see whether dogs would get chills and whether the stuff that gave chills in human beings would also give them in dogs and whether those that didn't, wouldn't. So again, a decision. It wasn't a big department. They were working on all sorts of things, interesting problems there. They had two very good people on the staff and to give me a place to work with dogs and to give me dogs, was a big thing. But again there must have been something. He said all right. Now there's a little side room there and you can have four dogs. And they were in cages. What did I want to do? I said I wanted to innoculate them in the jugular vein. Well, here's how we innoculate dogs into the jugular and then I said I wanted to take their temperature every 20 minutes to see first of all what their base line is and see whether it will shoot up, whether or not they then shiver, could I please have some short haired dogs? If there's something in their vascular mechanism that I could see if they would chill or not, they couldn't have a lot of hair. All right, you can have short-haired dogs. Well, the first test that I did remarkably enough worked out. It turned out that the dog that got the chills developed a rise in temperature and he shook and then it went away as when in human beings, and then another dog which got the other stuff didn't, and then they recovered, the same dog would be used again. And that started a study. Now I was doing two things: I was working at Harlem Hospital at night, and during the day when I was goofing off from other courses, I would go to the Pharmacology Department and sit there and innoculate dogs and take temperatures every 20 minutes. I had four dogs; I would put this one down, then it was ready; the thermometer went in the same distance, same thermometer, and I would record. I will never forget one thing about George
Wallace, which taught me a beautiful lesson: Dogs deficate and they particularly deficate more after they got this intravenous innoculation--something would begin working, something we learned later. But there was I sitting on a chair with a dog on my lap taking his temperature, surrounded by dog crap all over the place. One day, Dr. Wallace walked in and didn't say anything to me. He took a dust pan and he went around by himself and cleaned up the dog crap, put it in a can, and walked out. Now nothing he could have done could have impressed more upon me my lack of discipline, of care of proper way of working. If he'd said, "Look, Albert, for God's sake, why don't you clean up all that crap around you....", but when he just did it himself, I never forgot. And he never had to do it again. So that in between taking temperatures there, I would clean up dog crap. Well, that was the beginning of a very fine relationship because once I established a correlation for which I didn't need his help, because it was a simple thing, the next stage came---what was it that was doing it? What was the nature of the factor? How does it happen? And then we discovered there came a joint study between Dr. Wallace and myself, and he helped me because he knew pharmacology more; he helped me a great deal with determining the factors and this resulted in a publication which was called "On the Nature of the Chill Producing Principle in Anti-Pneumococcus Serum". Now I'm the senior author because basically I was asking the questions and he was helping me with citing which drugs to use in order to study mechanism and interpretation.

Dr. Benison: But you did a number of very interesting things in that paper. For example, there was a therapeutic problem involved in the chill producing factor and there have been a whole series of methods used by physicians to treat the chill producing
factor. Some of them used morphine, but the thing that impresses one in the paper is a meticulous use of certain material either to eliminate whether it is effective or not effective. That's one part of the paper that's interesting, but more interesting part of the paper is the search for the factor. And I wonder if you would discuss the problem of searching for the factor.

Dr. Sabin: The search for the factor was again a very practical problem. Because the serum that was given to patients, as I said, was a globulin. And the globulin was being concentrated by chemists in the Bureau of Laboratories of the City of New York. And so they were using because the antibody was salted out with ammonium sulphate at a certain fraction, I wanted to see which way the chill producing factor went. You see, we now had a method of assay in dogs, and first we wanted to know how did it get in there? First, there were several possibilities. The chemist could be working dirty. Don't forget, there were no antibiotics then and a lot of bacteria could have been multiplying in it and I think now this is an important factor because subsequent studies on endotoxin which were transferred to rabbits actually were preceded by these studies on dogs with chill producing factors. Some of it unquestionably was due to the contamination with bacteria during the chemical process of separation of the globulin. The bacteria were then filtered out, but the endotoxin remained so depending on how well they worked—you see, sometimes you had a lot that had a great deal of it and sometimes very little and probably depended on whether or not they kept their stuff very cold and how it became contaminated because chemists didn't use antiseptic procedures. So that was the reason for salting out, using different proceedings.
Another one was to not to assume that it was due only to bacterial contamination, but maybe there was something in the clotting mechanism. How you got the blood from the horse. So experiments to determine whether if you just could take blood from a dog a certain way and not get chill producing factor and take it another way and get chill producing factor, which would have nothing to do with contamination. And that's why I set up the direct transfusion. I had dogs set up, took the blood out and without any anti-coagulant or anything else, immediately gave it to other dogs in large quantities and there was never a chill producing factor. So it was evident that when you transmitted blood from one dog to another without coagulation, there was no chill producing factor, but if you did the same thing and allowed it to clot, that during the process of clotting, it was possible for a chill producing substance to appear. Well, all of this was worked out, at first, as an aid to purification—practical problem, preparing the serum. Secondly, there was the question of the mechanism of the chill producing factor. And this is where Dr. Wallace's advice came in, a very helpful way, by studying for example the effect of morphine which showed very definitely that morphine, then a very definite concentration, could completely eliminate the chill factor. Now it was not just antipyretics. I mean we studied it in patients, blood pressure and rectal temperature were automatically recorded, then we studied different drugs which were carried over to patients, and morphine and (incomplete sentence). And the recommendation of which drugs to study came actually from Dr. Wallace because he then interpreted the effect of drugs on this phenomenon of what probably was involved—central nervous system mechanisms, peripheral vascular mechanisms, and so on. At any rate, subsequent to this, it became standard procedure
for some years later to test everything to be used for intravenous inoculation, particularly fluids, had to be inoculated into rabbits. Dogs were much more difficult to work with so the thing was standardized on rabbits and the pyretic effect was an indication of antitoxins....at any rate, the point is that it was really detailed study involving in depth what the phenomenon were. I mean, while it had a practical objective, it nevertheless was as much my way of thinking, basic sciences, as if I were trying to determine these physiological phenomenon without reference to practical means. But this case, the problem was dictated by a practical need and in pursuing and trying to get an answer in depth, there came out findings which were somewhat helpful practically, but also illuminated physiological phenomenon.

Dr. Benison: There are a number of interesting things in this paper. You didn't only work with Wallace, you looked for help from a number of people. One, of course, was Banzhof, who in a sense....

Dr. Sabin: Dr. Banzhof...the reason I turned to Banzhof was he was purifying the globulin; he was getting the globulin out of the horse serum, so I had to learn from him what procedures to use in trying to sort out. I reached his cooperation by asking him to give me certain factions which would ordinarily throw away, if I remember correctly. So that's why I engaged his help.

Dr. Benison: Then there was another man named H. C. Falk, who was essentially a gynecologist, who did pathological gynecology and he was interested in the effect of ___________________ (incomplete sentence).
Dr. Sabin: You know, I don't remember Dr. Falk at all, but obviously as I was....

Dr. Benison: Because one of the reasons I raise Falk is that almost one of the tools that comes out of this is really a greater concern with biochemical problems.

Dr. Sabin: Well, you see, my association was across the board and since I didn't have too much training in biochemistry except as I was really getting trained by Sobottka and by Banzhof, I had to use their expertise to help with my problems. Now I think the reason I turned to Dr. Falk, now as I see it, was that at the time there was no lifelization in which you could dry things from the frozen state. But Dr. Falk had evaporated antibody solutions to dryness and vacular temperatures under 40°C. And then with subsequent heating to 80°, etc., etc., and so he had done that and he apparently was able to achieve this without any appreciable effect on antibody clunkling. So mind you, we are not dealing with living things. At least he did not in any way destroy the antibody, so we got some of his preparations for study and the chill producing activity was not destroyed by this method of heating. So it appeared that heating serum at 56°C for one hour or heating the evaporated serum at 80° did not destroy the chill principle. But then there's a question that again we studied the desication and vacual...I don't remember all the details now.

Dr. Benison: Well, the interesting thing is that you finally locate the chill producing factor and the acitraction rather than the alkaline fraction.
Dr. Sabin: Well, at this time this is of historic interest, but I think as I look back on my work as a student, mind you, I had to do all this while I was still studying, while I was working nights, while I was doing research and writing papers, because these things were being published and...

Dr. Benison: You say published. There's one other thing about the publication that is very interesting. This particular paper is published in the Journal of Experimental Medicine.

Dr. Sabin: Well, I began to visit the Rockefeller Institute while I was still a student because some of the very basic studies on pneumonia, which was started by Avery during World War I, continued on in the Rockefeller Hospital where obviously work was carried on. So I began to visit the Rockefeller Institute and for me there was only one journal, so that some of the things were published first as was the custom then, a quick report and the proceedings of an experiment in biology and medicine, you would give the paper at a meeting in New York, but basically Dr. Park said to me, you get that published so it can become quickly available because this is not just a theoretical thing. I want to have laboratories around the country using it. As a matter of fact, I don't know whether I mentioned it to you before, when I came to take my examination for life insurance in the State of New York in 1931 after I got out of medical school, one of the questions on the examination was to describe the test that I had developed as a student! I think maybe that was the edge between my passing and flunking because the extent of the negligence
of some of the subjects was something that I probably wouldn't stand for in any person.

Dr. Benison: Well, this becomes enormously interesting. You really had your heart on becoming a bacteriologist, very very early.

Dr. Sabin: Infectious disease...

Dr. Benison: And medical school seems almost like an afterthought.

Dr. Sabin: Well, it was a means of making a doctor out of me because if I had wanted to be a bacteriologist, maybe I would have gone and studied for a Ph.D. because even then they were having Ph.D.'s in bacteriology. But I wanted to be primarily a doctor. I wanted to understand disease problems myself and not get it from somebody else. I wanted especially to be a complete clinical investigator; I wanted to be my own doctor, my own microbiologist, my own pathologist. I wanted to be able to really have a broad comprehension of disease and one or two tools of sophistication with which to carry out the studies. And that's why even though my objective was not to make the best possible grades in all subjects in medical school, I did want to be a doctor. And that is why I didn't go from medical school directly to research. I set my heart on having an internship...and a rounded internship...an internship in pathology, an internship in surgery, an internship in internal medicine, which was very good.
Dr. Benison: Before we jump to that, I do have one question. On the typing of pneumococcus serum by the rabbit method, especially by microscopic means, am I mistaken...didn't Neufeld have such a technique worked out in 1902 and then it was discarded and no one paid....

Dr. Sabin: No, he discarded it, as I remember. He discarded it because he didn't find it practical. And, as a matter of fact, when I was an intern at Bellevue Hospital, I went back to Neufeld's theory and then was able to show how by technical modification you could use the Neufeld technique and then that superseded the microscopic stain method that I had developed in 1927 because later then I published on this and showed how it could be done. I did it while I was in the hospital doing research, sometimes instead of attending to my duties as a junior/senior intern and then that had become, since and still is, the standard method of typing pneumocci...not the one I developed originally, but my modification and practical utilization of the original Neufeld phenomenon. But I developed the technique for making it a practical, useful simple test...so you could get the answer immediately.

Dr. Benison: I was just wondering, you know, at the fact that it was discarded.

Dr. Sabin: Well, it was discarded, as a matter of fact I think, in my very first publication on that the more extensive one which followed the preliminary publication and the proceeding for the ___________ in experimental biology and medicine was while it/just 2 pages, a publication in the Journal of Infectious Diseases, I referred
to Neufeld. I think I said that as far back as 1902 Neufeld observed that when a suspension of pneumococci...mind you, suspension... was mixed with immoluous serum on a slide a reaction occurred which was characterized not by glutination but by swelling of the capsules. And then he attempted to apply this method to typing of pneumococci and he used again a drop of perintoneal obtained from a mouses peritoneum, you could type organisms, but he felt that the lack of drying and other things in the hands of technicians, it wouldn't work. And Type 3 the way he was doing it, didn't work and he himself abandoned the procedure for the macroscopic methods. In 1902 there was no anti-serum, and it didn't make much difference. It was a matter ultimately to know...I don't think they were even typing pneumococci in patients...so it was abandoned and nobody bothered. During World War I they re-established a macroscopic method which was used but then when the urgency of giving the right kind of serum when that became available, combined with the accident of this curious mind of mine, which I wanted to be helpful, I first used the other technique and finally went back to Neufeld and showed how it could be used. I have in front of me a collection of my publications, and I wanted to see here just when that was published because I did that while I was in Bellevue Hospital as an intern. "Immediately pneumococcus typing directly from the sputum by the Neufeld reaction"...and that was published in the Journal of the American Medical Association, 1933, and if you'll permit me, I'd like to look up what I said because I don't remember. You see my mistake was that I fixed it. And then in 1932, which was several years after I developed the other method, Armstrong and then Logan & Smeel in England reported simultaneously that when sputum is mixed with immune serum and examined in a fresh state, one can observe the specific swelling described by Neufeld and the pneumococcus typing could thus frequently be performed within a few
minutes. Now several competent bacteriologists in the United States attempted to
use their method in which sputum and serum are mixed on a slide, covered with cover
slip and examined with a high powered lens, so the oil immersion lens but with little
success. Some of the difficulties that were encountered were: the absence of small
number of pneumococci in the preparations, as well as the difficulty to find them,
and the rapid drying and frequent lack of specificity. Now recently, Dr. Kenneth Goodner
of the Hospital of the Rockefeller Institute for Medical Research in New York observed
the method as it is carried out in Professor's Neufeld's laboratory of the Robert Falk
Institute in Berlin. He used it successfully himself...then he was at the Rockefeller
Hospital...and several cases and kindly demonstrated it to me. The technique differed
from that of Armstrong and Logan & Smeel in that the mixture was stained with methylene
blue to facilitate the detection of microorganisms and it was examined in a hanging drop
instead of spread out in a cover slip. So I'm giving credit to Dr. Kenneth Goodner and
we became very good friends subsequently, for showing me the technique as he learned to
himself from Neufeld. After several trials in the laboratories in Bellevue Hospital
had been successfully performed, this study was undertaken to investigate the factors
that would make the procedure more uniformly reliable and practical. Preliminary tests
reveal that the following considerations were of great importance: the horse pneumo-
coccus serum commonly used for typing were unsuitable for this method, because they
frequently gave non-specific reactions. That's why many people discarded it. These
non-specific reactions could not be eliminated by dilution of the serum since the
quelling phenomenon occurs basically with undiluted serum. Secondly, carefully prepared
rabbit serum gives absolutely specific reactions. Here was the real entre...it wasn't
merely a trick of putting it as a hanging drop on a special slide. And then whereas
crystal violet or ice stain fails to stain the pneumococci in this preparation, alkaline
methylene blue gives excellent results. And the use of this alkaline methylene blue years later (16 years later), I used it to develop toxoplasma tests. See how one thing leads to another. The sputum should be typed no later than one or two hours after it is coughed up because the pneumococci very rapidly (incomplete sentence).

Now this is a beautiful example, I think, on which I might take off. Here's a basic observation made in 1902--the original investigator tries it and says it's no good; he abandones it. Then some people go back to it in England 30 years later--they try it, they report it, they say it works sometimes, but then other people in the United States repeat it and it doesn't work. They discard it again. Now, as a result of my visits to the Rockefeller Hospital, this was already after I had finished medical school and my developing friendship with Dr. Goodner, who was five years my senior, demonstrates to me how to do it. But the problem is still there. The sera that are being put out for common typing turns out to give so many non-specific results that it is no good. Other headaches, no good. But my business is not to try to give up what somebody else had done. I studied the factors that made a difference and finally found that if I did it a certain way, that if I used it very fresh (that doesn't come as a revelation--I sweated hours as an intern at nights working at Bellevue Hospital to work these things out) that when you use very fresh sputum, when you use rabbit sputum instead of horse sputum, when you use an alkaline methylene blue, sometimes it worked and sometimes it didn't. Then it works out that alkaline methylene blue works, then the procedure works. With these considerations in mind, the method was applied to 100 patients with -pneumonia in the medical wards at Bellevue Hospital. The sputum was obtained from the patient by me in each instance. I didn't rely (this is
another one of my compulsive neurotic characteristics in all work--on something that
is decisive, I do not want to rely on anybody who may make the different between
success and failure by some stupid negligence) so it was obtained by me in each in-
stance and the typing was performed almost immediately thereafter. And, in view of
the fact that from the therapeutic standpoint, it is essential to know chiefly whether
or not the cases were Type 1 or Type 2 pneumococcus pneumonias, and also because
rabbit serum for these two only were available at the time, this is another thing be-
cause before we had only horse sera. When I began to work in 1927, there weren't any
rabbits there. Then only for these two types, these were the only ones for which the
sputums were examined. The results were checked with those obtained by the mouse
methods and bacteriology laboratory at Bellevue Hospital, and, of course, it worked
very well, but became the standard method.

Dr. Benison: You've talked about the Neufeld thing. Now there's another thing that's
sort of striking about pneumonia. Avery & Chickering, as early as 1917, are able to
demonstrate that if you have typed specific sera it is very useful in treatment of
pneumonia, and yet as late as 1928 or 1929, Bullowa is complaining that physicians
don't like serum treatment of pneumonia. They won't use serum treatment of pneumonia.
Was it because of the problems in typing?

Dr. Sabin: Those patients had no way of knowing. What they complained about was
this horrible chill reaction because they thought they were going to die. It was a
horrible experience to go through. Serum treatment was the best that was available
at the time. Used properly and early it did make a difference of life and death in thousands of patients, but it wasn't the absolute. So actually, what happened was that at the Rockefeller Hospital they, they came along with more potent, better developed rabbit sera and they carried out a lot of studies on rabbit sera until selphanilite came in and then penicillin came in....

Dr. Benison: And then you forgot about the rabbits. As a matter of fact, Goodner and __________ developed a very....

Dr. Sabin: It worked with the rabbit serum for years. I'm looking now at the publication of the Journal of the American Medical Association, in which there are two illustrations that were made—one of my classmates, Dr. Jack W. Kahn— I notice he signed it. He was sort of an artist, and he made a beautiful illustration of what you see in the sputum in the negative and positive test which I used to illustrate this, but I notice that I wasn't satisfied merely to study 100 patients with this new phenomenon, but I also studied sputum of patients successfully treated with serum. I studied the nature and biologic significance of this phenomenon. And I was always interested in the basic problems that really underly the phenomenon that have to be used in the practical way to achieve practical problems.

Dr. Benison: Let me take you back....

Dr. Sabin: Are you going to take me away from pneumonia? Because there's another thing that interests me.
Dr. Benison: All right, speak your piece on pneumonia.

Dr. Sabin: One of the things that intrigued me, again as a student while watching patients treated at the Harlem Hospital, was that, of course, at the time one of the things that were done diagnostically were not only typing the sputum but you take blood cultures, and many of the patients had many organisms, many bacteria, in their blood. And I often saw patients who were treated with the proper serum in the proper amount and their blood stream was cleared of bacteria, but they went on and died anyway. So I asked myself the question, to me this was a challenge. I said, why do they die? Is it only because that surely that one load that's consolidated, they have three other loads with which to breathe, three, four, or even if one whole side is consolidated, they still have another lung. So why do they die and what do they die so quickly? And so I was very curious to know whether or not something was given off in the lesion; whether or not there was some sort of toxin that was liberated that might be killing without the multiplication of the bacteria. And I carried out a certain number of studies while I was a medical student and these studies were published also in the Journal of Experimental Medicine. I must make another digression here...you say it was a prestigious journal, as it still is, and I have a certain debt of gratitude to pay the editor. The first papers that I wrote were so lousy that it was simply incredible. The first paper published by Sobottka and Sabin was written by him. It was damn good; it was a marvel by a good Munich Ph.D. It was good, but I didn't write it. I had all the data there. I did all the step work, but he wrote it. But from then on, I wrote. And I remember the first one I did with Dr. Park, and he read it,
he began to criticize it all over the place, and my face was beginning to get redder and redder and he could see that I was emotionally upset—that my ego was hurt. He's a very kindly man. He said, "Albert, I see you are ready to pop a blood vessel because of the criticisms I just made. Please remember, it happens to everybody." When I was a young fellow, I was working with the Department of Pathology at Columbia University and I took my first paper, I think to Prudin who was a great American pathologist, and I showed to him. Let me tell you, he wasn't as kind to you as I am to you. He just ripped me to bits. And I was getting so red and he said to me, 'Bill Parks, now why did you bring me this paper you just wrote? Did you want me to tell you you're a nice fellow? You brought it to me for criticism. Right? You're getting it, aren't you? Yes, well, then what the hell are you made about? What are you getting red about? Criticism is good for you". So Dr. Park taught me how to write some papers. But that was the beginning. Park was a very busy man. I didn't have much contact with him. So from then on, you see, what I brought to Park, the first one was for the Proceedings for the Society of Experimental Medicine, but the very next paper then goes into the Journal of Infectious Diseases and there also Park helped and Bullowa helped with criticism, but the very next paper, I had some help from Wallace in writing on the nature of the chill producing principle which was published. That was later. But the first paper in the Journal of Experimental Medicine was on the presence of antipneumococcus serum of types specific protected antibody not neutralized by immologous specific soluble solutions. This was an important thing because I was looking for other factors. Now, it was not written well, and Dr. Peyton Rous who is the editor really. He was a very kind man, a busy man, but he was a very conscientious editor. He turned down a great many papers. He rejected a great number of papers, but he
never rejected one of my papers from the very beginning. Somewhere in my archives I think there should be the manuscript which I cherished and kept with his marginal notes. He taught me how to write a paper. He performed a function that few editors these day perform. I tried to perform during my days as editor. He taught me how to write; instead of rejecting, he would say when I would say so and so claimed that...and I remember as if it were now, he put down in the margin, "Claim is an unfortunate use of the word. Science is not argument. You can say reported..." He went into details like that so that the criterion that he used was...are the data worth reporting. If the data were worth reporting, he helped me. And this went on for a long time because you don't get educated overnight. And this went on paper after paper that I published in those years, and subsequently in the *Journal of Experimental Medicine* because I published almost everything after I came to work at the Rockefeller Institute. And he taught me how to write papers. So now, let's get back....

Dr. Benison: This paper is a very interesting one...the one about the specific soluble substance not neutralizing.

Dr. Sabin: Well, I start out my discussion there by saying that the mechanism whereby anti-pneumococcus serum averts death of a pneumococcus infected animal is not understood. And then I went on and then I tried other things, you see. There was another paper for example in which I infected mice with tremendous amounts of bacteria and I gave them enough serum to cover it so they didn't get any bacterium, but nevertheless, they died. And then I used another procedure that I learned from my friend, Kenneth
Goodner, because he at that time already had moved from the Rockefeller Institute and he produced infection in rabbits by innoculating a little bit of verelin culture in the skin so that instead of getting a big lesion and consolidation in the lung, you got it in the rabbits skin where you could see it. And then I used this to give lots of serum and still the rabbits would die. I prevented the bacteremia but the rabbits would die and I tried to allucidate the phenomenon of the mechanism of action of anti-pneumococcal serum and other factors involved because I just wasn't happy to stand by and not understand how things worked. But then, of course, and now, I let you have the break because a big change in my life occurred after I graduated from medical school. I continued these investigations on mechanisms of action of anti-pneumococcal serum with the mechanism of death and pneumococcal infection--something that we still don't understand completely now...all these years...when along came the big polio epidemic in New York City in July of 1931, and I was just one month out of medical school when my boss again, my beloved William H. Park turned me to investigating some problems in polio, and my contact with Sobottka again led me to some very important interests.

Dr. Benison: Well, I don't want to jump ahead. I did want you to cast back into your mind for one thing...I'm very interested in what the laboratory was like--the bacteriology laboratory and the kind of people who worked in it. For example, the armamentarium of laboratories was quite different....
Dr. Sabin: It was a very old-fashioned, straight-forward bacteriological laboratory. Remember this was 1926...47 years ago. Now there were already many more sophisticated bacteriological laboratories in the United States, but not too many, because after all, Dr. Park was the umbilical cord between the great advances and the development of the sciences of bacteriological in Europe and its developed in the United States. And students were taught how to identify bacteria so that it was a rather ancient laboratory with the smell of the media kitchen and burned cotton and all the attributes really of almost early 19th century laboratories in Germany and France where the science of bacteriology was being developed. The people who really were doing the most of the teaching were people who were on the firing line. As a matter of fact, a few of them in bacteriology were actually working in the medical school department itself--Dr. Park, Dr. Krumwiede, a number of others, Dr. Williamson, many, many others. They were working in the New York City Department of Health Laboratories because that's where the action was. They were dealing with epidemic disease, with problems of sanitation... with all sorts of problems. That's where they were doing their work and they would just come in and give their lectures and go out. So there's not much research going on in the laboratory at the time. As a matter of fact, during my days at least, the research that was being done in the laboratory...Klosterman who had a master of science, and I don't know if he's published anything ever, he was fiddling around with bacteriophage which was an intriguing problem at the time. Some of the best work dealing with again problems of make up of the pneumococcus was being done by Sobottka was in a special laboratory attached to the department, and I would say he was undoubtedly the most sophisticated person, but he was a chemist; he was in very close touch with Heidleberger
and so on... he was as capable as Heidleberger and Goebel at the Rockefeller and actually he provided me, now that I remember it, with the entre to the Rockefeller Hospital.

Dr. Benison: There are certain things if you look at the laboratory of William H. Park, it almost seems like a matriarchy. Every other worker in the laboratory seems to be a woman. Lucy Michelo....

Dr. Sabin: Mind you, these people were not working in the medical school, as I said. The medical school was a place for them to come and lecture. They were working hard in the New York City Department of Public Health Laboratories. And women, why? As a matter of fact, this was a little bit like the status of medicine in the Soviet Union now... it was not considered to be a bacteriologist.... this was not a very manly kind of occupation, and so many women went into it.

Dr. Benison: You worked closely with some--Georgia Cooper.

Dr. Sabin: Well, I mean they were all involved, you see, with Park and the pneumonia problem... pneumococcus. I really didn't work closely with them. When I was studying problems, I tried to utilize their special knowledge in certain fields that I needed, so I would go to them for advice, but I never worked with any of them.

Dr. Benison: Now, you know one of the legends in New York... it's not legend... is that Parks laboratory and the Flexner laboratories of the Rockefeller Institute, were
really not on very good terms. How did Park react, for example, if he learned that you had gone up to the Rockefeller to see Goodner?

Dr. Sabin: Well, I mean actually there was no such...you see one must distinguish between the relationship of Dr. Park who was a very kindly man, in the field of pneumonia which was really under the leadership of Dr. Cole, first medical director of the Rockefeller Hospital, and Dr. Avery, and actually this was a continuation of the World War I group...Dr. Blake who was then, or subsequent, professor of medicine at Yale, and so on...and I think the relations were very closely. They were not in any way competitive at all. On the other hand, the business that I think you refer to between Dr. Flexner and Dr. Park is something that began when Dr. Park entered the field of poliomyelitis, with that big epidemic in 1931. And not until later, let's say around 1935, when he associated himself with an unfortunate set of experiments by Dr. Brodie, the first vaccine, that there was a sort of confrontation with Dr. Flexner. But I think that during the years prior to the polio... Dr. Park's cross-reaction with people at the Rockefeller Hospital was chiefly in relation with pneumonia. That was the number one health problem, there's no question about it then.

Dr. Benison: Dr. Sabin, one last question on pneumonia. These years between 1928 and 1931, there were really two extraordinary developments at least in pneumonia work. One is Griffith's classic paper in 1928 on transformation of Avery... and Dubois' work with Avery on use of bacterial enzymes to dissolve the capsules polysaccharide. Were you aware of that work at the time?

Dr. Sabin: Well, actually, during the period of 1928-31, I had no time to go and attend meetings or do a helluva lot of reading. I tried to read because I was a
medical student; I had to work for a living at Harlem Hospital, I was trying to carry on a research program, and I think very few people who had more leisure and more understanding than I did paid too much attention to Griffith's important work. It was only in subsequent years and I think it came up...I used to attend rather religiously the meetings of the Society for Experimental Biology in Medicine which met at the New York Academy of Medicine when I was a student. And out of the thousands of people working in New York City, there were rarely more than 40 or 50 people. It was not a league. It was just a neglected society and I think it still is from the point of view of actual need. So that I can't recall now that there were not discussions, but I was not personally involved in this until a later period because the business of Duboses enzyme studies came much later actually.

Dr. Benison:

Dr. Sabin: But at that time I was already on the staff of the Rockefeller Hospital. And I remember in 1935 at one of the staff meetings on which were reported, his concluding remark that if this substance were not so remarkable for the effect it has on pneumococci it would be remarkable for its toxicity. In other words, it's a very interesting thing, and it was really not until other people took up penicillin, not as a curiosity because to me it was interesting because I had just come back from a year in England where I attended regulisouly the ______________________ Royal society and remember hearing Fleming describing what subsequently turned out to be penicillin, with his nice clear areas on blood araclates and really maybe I'm wrong now in my recollection, but I had the feeling in subsequent years that Fleming did not really appreciate the true significance or potential significance of this discovery. I remember the first meeting in which he described it in 1934, or the first meeting at
least that I attended, he saw it as a potentially useful tool in diagnostic purposes where so many bacteria taken from the mouth and throat overgrow other organisms...to me it has always had a very important lesson. This limited view of Fleming, the almost deadend reached with the remarkable studies of Dubose of the fact that the initial investigator isn't always the person who necessarily carries through a fundamental discovery to its ultimate significance. And without carrying it through to the ultimate significance, the initial discovery would have interesting curiosity. Therefore, I regard both as very important and I think it is for very good reason that the Nobel prize for penicillin was given not just to Fleming, but given to also Florey and Chain. Chain thinks he made a basic discovery. I don't think he made any kind. He happened to be working with Florey, who was a good experimental pathologist, and as an experimental pathologist, I think Florey supplied the vision and the approach which Fleming as a bacteriologist, as an aga plate bacteriologist, lacked. Chain provided the know-how that made it possible to get at least the initial concentrations of penicillin with which to establish something. And, then, of course, was the subsequent developmental work in the United States that really made penicillin something that was widely available. So to go back to Griffith, Avery was impressed with him. And, of course, Avery's follow-up, Avery and people who were working with him, because this became the problem at the Rockefeller Hospital laboratory under Avery. And I think that he really directed when young fellow's jsut out of medical school, you know, bright, came to work with him, he put them to work on these things. And it was Dawson in those years, and later on McCloud, and still later, Macklin McCarty, until the whole thing came through and it was developed. But I think Avery, probably more than any other, was the person who appreciated the great potential significance of Griffith's observation.