Dr. Paul Parkman Interview

Office of NIH History

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Sarah Leavitt: Today's date is Tuesday, June 7th, 2005. This interview is with Dr. Paul Parkman. We are at the Office of NIH History, in Building 31 on the NIH campus in Bethesda, Maryland. Welcome Dr. Parkman! I just want you to acknowledge that the conversation is being recorded.

Paul Parkman: I know the conversation is being recorded and I have already signed a release to this effect.

SL: Great. Why don't we start by having you tell me a little bit about your background and how you got interested in science.

PP: I grew up in upstate New York in the Finger Lakes area, in a town called Weedsport. It was originally a port founded by the Weed brothers on the Erie Canal where you could turn a canal boat end to end. I grew up in this very little town of 1,200 people or so. My father was a post office clerk and he worked very hard to supplement our income—raising turkeys and chickens, being clerk of the board of education, etc. He was very much interested in my career. I remember a conversation with him in the garage there in Weedsport, a notably serious conversation—not often did we talk this seriously! He said, "Well, what do you

want to be?" And I said, "Well, a kid doesn't know what he wants to be." He said, "Maybe you'd like to be a barber." I said, "Oh, I don't think I'd be good at a being a barber." And he said, "Well, maybe you'd like to go into music." I knew that I had no talent, as my music teacher once told him. He didn't believe it, but I knew it. Then he said, "Well, would you like to be a doctor?" And I said, "Yeah, that sounds really good." And that pleased him because I believe he really wanted that answer—I think that's why he put it last.

As I said, he worked very hard to make money to send me to college and medical school. I went to Saint Lawrence University and I was there only three years because I was in a program where, if you did well and delayed getting your B.S. degree until the end of medical school, you could leave undergrad school in three years. So I did. And that's why on my C.V., my B.S. and my M.D. degrees are listed in the same year. People always think it's a mistake but that's right, it was that way.

I did reasonably well at Saint Lawrence. Actually when I went to medical school, I was a better student because I was really interested. I went to the State University of New York College of Medicine at Syracuse, and I really enjoyed my time there. I really liked learning. I graduated first in my class, actually, and

I'm kind of proud of that. I was AOA [Alpha Omega Alpha Honor Medical Society], the medical honorary, and I was off to a good start.

I interned at the Mary Imogene Bassett Hospital in Cooperstown, New York, which is a small hospital. People know of the Baseball Hall of Fame and the Farmer's Museum there better, but the Mary Imogene Bassett Hospital is also a terrific institution in Cooperstown. They are affiliated with Columbia in New York City and it was a great place. It was a wearing place to be an intern, but internships in those days were all wearing, working every other night, every other weekend. I was so exhausted at the end of the year. By then I'd decided I wanted to be a pediatrician. So I went back to Syracuse at the Upstate Medical Center where I knew people. [Dr. Julius B.] Julie Richmond was chair of the department. He was later very important in the institution of the Head Start Program. I was resident and chief resident there for a couple of years and then I had to decide what to do next. That wasn't too much of a question because in those days there was a "doctors draft," so nearly all young physicians went into one or the other of the uniformed services.

SL: What year was this?

PP: This was 1960. This was before my wife had determined that I was not attentive to the paper requirements of anything. Early in your internship they gave you a whole stack of things, and I did a lot of them, but one of the things I missed was the information about the Berry Plan. The Berry Plan allowed a physician to have a shot at getting a position that was parallel to his interests, as opposed say to being a battalion surgeon somewhere. Well, I overlooked that. So most guys had a commitment from the Berry plan and I did not. So I was a free agent.

I had a friend who had gotten an assignment to Walter Reed [Army Medical Center in Washington, D.C.] the year before. Bernie Portnoy was a pediatric resident at Syracuse before me. And so Bernie said, "Well it's really great down here. I'll talk to my boss; maybe you should come down and take a look." So I came to Walter Reed, I went to the main Navy building, which was on the mall, where the Army medical people seemed to be—this was my first introduction to the bureaucracy. I did an interview there and I interviewed with a guy up at Walter Reed and they decided they'd like me to come, and Colonel [Dr. Edward L.] Buescher—actually then Major Buescher—was the head of the virus department and he said if I got a commission he would try and get me assigned to Walter Reed. So I got my commission. Actually, earlier on I tried to get into the Public Health Service to work at the Centers for Disease Control as an epidemiological intelligence service officer. I interviewed with high level people

there, [Drs.] Bruce Dull and [Alexander] Alex Langmuir, and they wanted me to come, but I couldn't pass the physical because I had a history of allergies and asthma from childhood. And so they said, "We can't take you." I appealed that, but "no" was the answer. But the Army didn't care, so I became a captain in the medical corps.

At the Walter Reed Army Institute of Research (WRAIR) I was in the virus laboratory and I was to learn to be a virologist. They were the consulting group for any virus diseases in the military. One of the ways they broke guys in was to assign them to the virus clinical desk where all the specimens wound up that came in for infectious disease diagnosis from anywhere that the Army had servicemen. And it was really a learning experience. I mean, you got to know about the tests you could do—the specimens were accompanied by a little bit of history so you knew what kind of symptoms the patients had and you could try and make diagnoses based on the samples that had been sent in.

SL: So you didn't see patients?

PP: No, they could be thousands of miles away, but their frozen specimens came to us—viruses withstand freezing.

SL: Isn't that interesting.

PP: It was extremely interesting. So that was what I started off doing, and then I got involved in some studies. I isolated a virus from a specimen of a soldier with a respiratory disease. It was an enterovirus and it hemagglutinated. It looked new to me, because this kind of virus seemed different from a lot of the standard enteroviruses. So I thought, "Wow, I've hit the jackpot right from the beginning." Then towards the end of the time I was working it up I found a new paper by [Dr. Robert M.] Bob Chanock. He described, I don't remember, perhaps 100 cases of respiratory disease due to this virus. Gloom, doom! My big discovery is gone, my priority blown to pieces. But all right, that's way it goes.

One of the things I was assigned to do along with several of the young guys who were working at Walter Reed was to study adenovirus disease. There was concern that the vaccine was not working, so they decided to send some of my confreres and myself to do a study on adenovirus disease at Fort Dix, New Jersey, a recruit training post. There was a helicopter ambulance service that wanted to log miles so we went by helicopter from Walter Reed. We had to stop in the middle of the trip to gas up. It was an interesting experience. While we were at Dix, we looked at all these recruits with adenovirus disease and tried to figure out if the vaccine worked or not. It was pretty dull stuff, since it was sort of trying to prove what

other people had already proved. I mean it was useful research, but it wasn't going to get you anywhere professionally.

SL: Right.

PP: So we had some time on our hands. In the mornings we swabbed all the new guys with respiratory disease and runny noses. The problem the army has is, if a guy has a bad cold with a fever, he doesn't have his mother there with chicken soup so he has to go to the hospital. So the hospitals are full of recruits with runny noses and fevers. We would study the new patients who came in for probable adenovirus disease, but by noontime we'd done pretty much all we had to do. So we poked around the hospital to see what else was interesting.

[Dr. Malcom] Mal Artenstein discovered that there was a ward where they put all the recruits who had rashes. Now, rashes are interesting to a doctor—a runny nose isn't too much to look at, but with a rash you've got to decide whether it's something life threatening or whether it's something that doesn't really matter as far as disease is concerned. Most of these recruits seemed to have rubella, clinically. No one had ever isolated the virus. We had the general's permission; he said we could do a study (although not this particular study) so why not? I

mean—that was a long time ago. So we started to work again by taking throat gargles, blood specimens, and urine specimens.

The nice thing about viruses is, if you put them in the freezer you can have them stay alive for years. So you can freeze everything down, put them in sort of a suspended animation. Then when we got back to Walter Reed, at odd times when we were finished working on the respiratory disease study, we started to work up the specimens from rubella patients. Now at that time, nobody knew much about rubella. It was separated from other kinds of rash diseases sometime in the 1800s. German physicians were able to separate, clinically, rubella from measles and scarlet fever. It had not been known before that that it was a separate disease. And that's how it became *German* measles.

From then on until 1941, it was thought to be an innocuous childhood disease. It was only important to know about so you could separate it from measles and scarlet fever which could have more important consequences. During the time that people were gearing up for war in 1941 there were a lot of young military recruits coming together all over the world. In Australia there was a big epidemic of rubella, not only in military recruits but in the civilian population as well.

Norman McAllister Gregg was an ophthalmologist. (He later became Sir Norman). He had referred to him quite a number of babies who had congenital cataracts. He wasn't a big-time ivory tower scientist but he was a curious man so he said, "Why am I having all these babies with congenital cataracts?" It's a very rare thing to have babies with cataracts. He questioned the mothers about what they had in common—actually it might have been the mothers who brought it up to him. There were mothers sitting in his waiting room who said, "Oh yeah, I had German measles." I think it may have been one of the mothers who told him, "A lot of us had German measles." So he went back and looked and actually found that many mothers who had rubella during pregnancy also had babies with congenital cataracts. He said that it must be caused by the virus. Well, who'd ever heard of such a thing? So everybody in the academic establishment said, "Who's this guy, you know, telling us? We're big time, not him." So they did many studies and after a number of years they said, "Well, he's right!"

People thought rubella was caused by a virus because in the '30s there were Japanese investigators—Hiro and Tasaka—who took specimens from rubella patients and put them through a very fine filter and took the filtrate and used it to inoculate other subjects and they got clinical German measles. They said, "It must be a virus to get through those fine filters." That's what we knew in 1960, but nobody had ever isolated the virus. That's why we were really interested. Of

those guys at Fort Dix in the hospital with rashes, maybe 80% of them had German measles rashes. Wow—really surprising! So we have a lot of specimens. We tried everything we could think of to try and isolate the virus.

SL: Who were you working with at this time?

PP: Malcolm Artenstein, who was a year ahead of me as a two-year man in the Army, he was a captain in the Army (as all of us young physicians were), and Major Edward Buescher who was head of the laboratory. He reported to Colonel [Abram Salmon] "Bud" Benenson, who was the head of the Division of Communicable Diseases and Immunology at Walter Reed. All those people were involved. Benenson was the one with eagles on his shoulders who got us to go to Fort Dix. There were several other guys from the laboratory, [Drs.] Phil [Philip K.] Russell, Scott Halstead, Cliff Arrington, and perhaps others, who where involved in the adenovirus part of the study.

We took the specimens and tried everything we could think of to isolate rubella virus. We put it into animals and we put it into a whole variety of cell cultures at different temperatures looking for evidence of cell killing. We used other technical things like roller drums to bathe the cultures intermittently. We tried quite a lot of things. We tried to see if we could detect complement fixing

antibodies, we tried all of these things, but…nothing. It was very discouraging. We didn't have anything—nothing worked.

And then I had an idea. While I was working on the new respiratory virus, and was scooped by Bob Chanock, I had an opportunity to make a whole bunch of enteroviruses to compare with my virus and show that they were different viruses. One of these was ECHO-11 so I'm an expert with working with it—which is not much to brag about. But I read a paper from the common cold research center in England where they had used ECHO-11 to challenge infected cell cultures to try and find common cold viruses. It was hard to do, and at about the same time they found easier ways to show those viruses by other means, so they dropped that idea. I said, "Maybe we ought to see if we can detect rubella virus by using this interference technique." So we added a little ECHO-11 to our cultures—both the rubella specimen and the control cultures which had been incubating for a couple of weeks. I used a dose I knew would produce an effect in about three days, about 1,000 to10,000 infectious doses.

I read them the first day, and of course, not surprisingly, there's nothing there the first day. On the second day it was a little bit strange, there were some ECHO-11 effects in some of the cultures, but in some there weren't: some of the rubella inoculated cultures didn't show any change. I thought, "Well that's odd." But it

was with excitement on the third day that I went to see and "bang!" The ECHO-11 came down and killed all the cells in the cultures used as controls. It killed all of the cultures inoculated with serum from the recruits. It killed all the cultures inoculated with urine from the recruits. But it killed very few of the cultures that had been inoculated with throat washings from the rubella patients—they were as good as new!—and we said, "Wow!" We couldn't get over that.

Mal and I went down to Cameron Station, which was a PX [Post Exchange] here in the Northern Virginia suburbs—it was like a department store. Mal wanted to buy some golf clubs and all the way down in the car we talked about our result and we said, "What could we have done wrong?" But we couldn't think of any way that we could have done something wrong that would make that result. We thought that we had found rubella virus.

When we settled down, we realized of course what you do is see if you can repeat the result. We tried again with additional specimens and we tried further passages, that is, further subcultures from the original cultures, and they all showed the same thing, that those throat washings had something that interfered with ECHO-11 so solidly that you almost couldn't imagine it, you know? So then the thing was to show that the effect is reproducible, you have to show that it isn't produced by any of the other viruses, influenza, for example—so we went through

a long list of viruses, we put them into the cultures to see if they interfered and they didn't interfere. So it was obviously something new. You made anti-sera to our new virus by inoculating rabbits. You took those sera and you could see that they would neutralize this virus and they wouldn't neutralize a whole string of other viruses—influenza, coxsackie, other enteroviruses, common cold viruses—it wouldn't interfere with them. So it was specific for this virus. So bingo —

SL: You found something.

PP: We said, "We've got it." We presented a paper at the spring meetings of the Federated Society. The thing that put it to rest was we had the original specimens. We had specimens from recruits with scarlet fever, others who had a rash and we couldn't figure out for sure what it was, guys who had probable rubella. That is, they had a rash and many of the earmarks of rubella but didn't have enlarged lymph nodes. And then we had a group with classical rubella, who had everything you would want to make that diagnosis. And what you found was the recruits with classic rubella, almost all of them had this virus, those with scarlet fever almost none of them had it—there was actually only one out of the group of guys who had been diagnosed with scarlet fever who had this. And almost all of those with classical clinical rubella had our virus, a few of those with

indeterminate rashes were positive, but almost none of those diagnosed with scarlet fever!

That is what I think really convinced people that we had done it. That was the beginning. After that it's all downhill, because then of course, the first thing we were interested in was a vaccine. I mean, we were doctors, and the first thing was prevention. We were interested in making a vaccine. We were also interested in making something that would allow the diagnosis to be made more easily. It was very cumbersome. If a pregnant woman came into a clinic and wanted to know whether she had German measles or not, I mean there was no way we could deal with the numbers of women who would want to be tested, right? And so we had to develop more simple tests. Am I gassing on too much?

SL: No, you're doing great.

PP: So those were the big things. We had the idea that you might be able to make a vaccine. The first thought was a killed vaccine, because with live vaccines there could be a problem with the virus spreading. The polio vaccine helped get us to the point where there's so little polio. It's been eradicated from this hemisphere, in part because an immunized child could spread the vaccine virus to his playmates, especially if it was not a big hand washing community. There were a

lot of those in America as there are all around the world. While this was good for polio, it could be a problem, a big problem for a live virus vaccine for rubella, where you would be concerned about starting epidemics—with unknown effects in pregnant women.

In those days you didn't have all of these fancy molecular techniques and you didn't know about recombinant DNA, but you knew that measles virus and polio virus had vaccines made based on attenuating them by serial passage in cell cultures. You changed the virus by laboratory manipulation. We decided that was one route to take. So right away we started serially sub-passaging the virus from one set of cultures to the next, to the next, to the next, to the next, with the idea that if you got really high passage virus, it might in fact be changed, might be modified, might be attenuated, so it would produce protection when you gave it to a person, but would not produce disease. The other way of going was to make a killed virus vaccine. This looked simpler, because if it was killed it couldn't spread. It would be easy. You wouldn't have all those worries.

So we tried a killed virus vaccine. We started with monkeys because you couldn't do these kinds of studies in people. We immunized the monkeys with killed rubella virus. We sort of did the Jonas Salk thing, inactivating the virus as he did with polio, and then looked to see if the vaccinees developed protective

substances in their blood called antibodies. A few weeks later we challenged them with unmodified wild rubella virus to see if they were protected.

I was still at Walter Reed during this time, although I was just at the transition of coming to the National Institutes of Health. We challenged with ordinary unmodified rubella virus and they all got laboratory evidence of rubella. They had virus in throats, they had viremia, typical of monkey rubella. So we said, "that doesn't look good." You always have to make choices, but that experiment didn't suggest that there was anything going on in favor of a killed vaccine. So we continued to try to attenuate the live virus and we began to work in monkeys with various passage levels of the virus.

And that was more successful. By then I had moved to work at the National Institutes of Health. The Army was very good to me. I liked my Army time. They gave me the chance to do something significant and so it was a wonderful time, but the Army was not very much interested in German measles. I mean after all it wasn't a debilitating disease—we found a lot of recruit rubella but to them it didn't seem really important enough to continue the rubella program. Also, Mal had decided to go back to Boston.

SL: The Army was not interested because the recruits would recover.

PP: They'd recover, and everything would be fine. So quite understandably the military wasn't much interested in that research. But the NIH was, particularly in the guise of Dr. Joseph E. Smadel. Smadel had once been deputy director for science here. I mean, he was a big time. And he was a straight-forward, outspoken character. He was one of the really strong people. And I don't think he was politic enough for the NIH, you know. Sometimes you have a guy who makes too many enemies and I surmise that the NIH was unhappy with him. And he decided to go back to the laboratory. The Division of Biologics Standards [DBS] was pretty new organization, and they gave Dr. Smadel a virus laboratory there, which he ran with an iron hand. He had also been at Walter Reed earlier; there was a community of people at NIH who had been through Walter Reed. He said something like, "Parkman might be of useful property. He knows about German measles and we think there's very likely to be a German measles vaccine sometime—it'd be good to have somebody on the staff who knew about it." And since I was the main rubella guy, they offered me a job.

SL: Great.

PP: Which was great. So I came over here to DBS, and I continued, really, my work sort of seamlessly for a year between the two organizations, I worked at Reed and

I worked here. Smadel unfortunately became ill very shortly after he made the job offer. He had kidney cancer, which had spread. He died sometime after that, tragically. I think he was a great man.

But anyway, I came over here without a definite laboratory assignment—Dr. [Roderick] Murray, the director of DBS, was undecided as to what to do with me. I had an interview with Dr. Harry Meyer, who was the head of one laboratory to which I might be assigned. After Dr. Smadel's death they split the virus laboratory in two so Dr. Meyer had one of those, and at this time they were trying to decide who was going to go there. So I had an interview. He had some other choices but he selected me. Very good, very good, for me and for him. And Hank Meyer and I then worked as friends and colleagues for a long time. Actually, we followed each other up the chain of bureaucracy for years until he retired in 1987.

He was really sharp. And he was really experienced in the clinical area. He had done clinical trials in West Africa with measles vaccine, so he was very important to have teamed up with. He was really important to the development of the rubella vaccine because for one thing, we had to try and decide how to do clinical studies in people. We had all this data in monkeys that made it look sensational but monkeys are not the end point—we didn't want to immunize monkeys. So he

was important in the design of the initial clinical trial and the subsequent trials. We did it together, but he knew his business in those particular areas and we all learned as we went along, too.

It was in 1965 that we started the first clinical trials. Like the earlier work, they were really successful. Amazingly, as in our monkey studies, the virus didn't spread and the kids developed antibodies.

SL: So where was this? This was in Arkansas?

PP: This was in Arkansas. Hank had a connection in Arkansas. He went to the medical school there [University of Arkansas] and knew the Professor of Pediatrics there, Ted Panos [Dr. Theodore Panos].

SL: Okay.

PP: It was through him that we were able to set up the clinical trials. The trials were done in at the Children's Colony in Arkansas. We needed a place where you could isolate children for a period of weeks because we didn't want to take the risk of spreading rubella if the vaccine was not fully attenuated. We looked at a number of places. There was a hospital in Denver for children with asthma. We

looked at several places to try and find the right one—and this place in Arkansas was ideal. The kids lived in cottages and they had schooling, but the teachers could come in. It was possible to confine the children for a period of, I don't know, three weeks maybe, two and half weeks, I've kind of forgotten the details, but they could be kept there isolated from other people. And the staff who took care of the children, the "house mothers" in the cottages, the people who came in to deliver the food, the janitors, and the people who provided their healthcare could all be tested for immunity to German measles. There was a list on the door of who could come in, and if you weren't on that list you couldn't come in. If you were susceptible to rubella or we didn't know your history, you couldn't come into that cottage. So it was an ideal circumstance.

SL: So you went down there?

PP: Oh yes, we went down there. First you had to convince the NIH that it was a good idea. And that was little bit of a struggle because it wasn't such a common thing for scientists here at NIH to be involved in trials outside of the Clinical Center. And then it was sort of an iffy thing. You could start a rubella epidemic, you know? Things could go wrong. These were retarded children in an institution and that might not be the best thing. Maybe the parents wouldn't understand—a whole lot of things could go wrong. So for the medical board, which approved

protocols in those days, it was a little bit of a struggle. I think we got approval by a narrow margin. But we did. We got approval for the study.

SL: Did you need the parents' approval?

PP: Oh yes, you had informed consent.

SL: So you had to go down there and talk to them?

PP: You had to get informed consent from the parents who were willing. But it all turned out just right, I mean, it was perfect. And people at the Children's Colony and the parents felt like they were doing something that might help prevent mental retardation. Rubella is a cause of mental retardation, and this would be preventable, because if you could keep those mothers from getting German measles then their babies wouldn't get infected *in utero* and come up with mental retardation, congenital cataracts, congenital heart disease, a whole raft of other ailments that are difficult to treat.

I recently went to give a talk at the Helen Keller National Center, which is in Long Island. They're particularly interested in the people who are born blind and deaf. Let me tell you that those people work so hard and it's such a problem.

Helen Keller was amazing. All these kids are amazing and the people who spend all the time helping them, all the effort…and sometimes it doesn't help a lot, you know? But in terms of German measles-associated blindness and retardation we have really thankfully put them out of business. But that's getting ahead of the story.

So the next thing you had to do, you had to publish your successful trial results and persuade people that you were right. So we talked to [Dr. Frederick C.] Fred Robbins, who was a Nobel Laureate, and to [Drs.] John Enders (also a Nobelist) and Sam Katz, who had developed the measles vaccine, about doing confirmatory studies. So they took our virus and our serum and they did studies. By then we were pretty sure it wasn't communicable so the studies were a little easier. They did studies of their own which confirmed that what we'd done was correct. So now you've got something—a possibly useful vaccine. So swell, where are you? Well, then you need to do a lot of things to develop a vaccine. You needed to be really sure that it wasn't communicable. You needed more clinical experience to know how much virus should be in the vaccine, so you needed a study about dosing. You needed to know how long the antibodies would persist. All of this—a long list of things you had to do in clinical trials. So could you make a better vaccine? This vaccine virus was detectable in throat swabs of vaccinees. Could you make a vaccine that wasn't shed in the throat but still produced immunity?

Our original vaccine was at the 77th passage level, 77 passages from that original rubella virus isolate at Walter Reed. Now we went to 120 and then we went to 150 passages and then adapted it to grow in chick embryo cells and made 10 more passages. And what you showed was as you went higher you reduced the ability of the virus to produce antibodies so that you got lower antibody titers. You then failed to immunize some of the children, particularly at 150, but the kids who got antibody with that weakened virus still shed virus in their throats. So we had shown that you could attenuate it further, but in going to these higher passages you weaken it too much, and you needed to stick with the lower passage here. The next step is to show that it's non-communicable in larger studies. So the studies got larger and larger and later, other investigators went on to the point of involving hundreds of kids and hundreds of susceptible contacts and the results were such that you were able to convince people that the vaccine did not spread.

One thing that was important was the question of what would happen in pregnant women if they inadvertantly got the vaccine? We had done some research to look at that in pregnant monkeys. The staff over at the animal facilities here—[Dr. Stephen] Steve Potkay is one name I remember—knew how to time the menstrual cycle of rhesus monkeys. They knew how to do hysterotomies, to look in the uterus and take out the end products of conception. And so that was a magnificent resource. We had shown earlier that if you gave wild virus to a

monkey, virus was everywhere—in many organs and tissues. The attenuated virus only centered in a few places like the throat and lymph nodes. Then in small studies, using maybe five pregnant monkeys or so, in a few of them you could show that the wild virus spread to the products of conception, not to the embryo, but the placentas were positive. That didn't happen with the attenuated virus. So I think that gave people some courage that the vaccine was unlikely to produce birth defects. Eventually you showed that it was okay in pregnant women mistakenly vaccinated…some women got the vaccine who weren't supposed to, who were pregnant. The CDC did a study following up the babies of these women and they didn't get congenital rubella. A very minuscule number got infected but even in these there were no birth defects.

So the chance of that happening is vanishingly small, and it seemed safe to use the vaccine. It was used very cautiously at first. It was used freely to immunize only children between one year and puberty. Its use in women was much more restricted, to avoid pregnant women. Later on, with all the CDC follow-up, it became clear that the big immunization programs stopped rubella epidemics cold. I mean, before, from when the epidemiology of rubella began to be followed in the early 1920s until 1969 there were repeated epidemics. They occurred at 6 to 9-year intervals. There was a major one in 1964, with 50,000 affected pregnancies, perhaps an equal number of therapeutic abortions.

SL: And you were working on the vaccine during that epidemic. What was that like?

PP: We said, "We're going to stop this in time." But we weren't ready to do it. 1964 was too early—I don't think we even had convincing results in monkeys by then. It wasn't 'til '65 that we first tried the vaccine in people. But we were aware of the epidemic. We knew—Lou [Louis] Cooper and Saul Krugman in New York were doing marvelous studies about rubella and its effects on the fetus. A lot of other people were doing those too, to kind of piece out what was important to know. It was a tragic epidemic. I mean, the Helen Keller Institute still sees people blind and deaf from that epidemic. It was a bad time.

SL: Were they doing therapeutic abortions for pregnant women who contracted rubella here in Washington, in this area?

PP: I'm sure they were doing therapeutic abortions everywhere. I mean, a mother had to decide. She was in early pregnancy and she had this little rash disease and she and her doctor had to decide, when presented with the risks, what to do. Depending on the period of pregnancy in which it was detected, if it was in the first trimester a very high percentage of babies born would have congenital rubella. They might be mildly affected, or they might be severely affected. So

the doctor and the mother had to figure out what to do. There were some women, of course, who didn't want to have an abortion. Some women wanted to have an abortion. There were a lot of abortions that were done that didn't—I tried to study some fetuses of women who had rubella and found there were some mothers who had abortions who probably didn't need to. Some did have virus in their fetuses. It was really flip-a-coin time, there was no way to tell which it would be. Those were hard lines to try and draw—that was a wrenching decision for a mother to have to make, really bad.

And there wasn't even a good test. I mean, in the laboratory we knew how to test for antibody which would protect these mothers, but even in a big test, we could test maybe 20 or 30 people in a week. Well, that's not anything, you know? So we tried to find another way of doing an antibody test. We had tried a lot of things before, but we really focused on it then. It was in 1967. Myself, Dr. George Stewart, Hope Hopps, Robert Douglas, Judy Hamilton and Dr. Meyer wrote the paper about our discovery of the rubella virus hemagglutin inhibition test. It was what we had been looking for—a simple test that you could use for rubella diagnosis.

Hemagglutination inhibition was a nice test, and I'd used it a lot before with other viruses, going back to my Walter Reed Days. And so although our initial

experience with rubella was negative we thought well, maybe we ought to focus on that. We tried to concentrate the virus by ultra-centrifugation to try and get material that would have more virus in it. And we used all kinds of different cell lines. We thought maybe the cell line would matter. One of the cell lines we had was called BHK21, baby hamster kidney 21. It was being used for making compliment fixation antigens. And we thought, "Well, from what we hear it makes a lot of virus. Maybe we should try rubella in that." So we put the rubella virus in those cells but the results initially were negative, it didn't produce hemagglutins.

And then finally one experiment showed very low levels of hemagglutin. And we were aware that there were sometimes non-specific hemagglutination inhibitors in sera. And we were using, I think, fetal calf serum to grow these cultures. So one day it occurred to us that maybe if we treated the serum that we used in the medium to remove inhibitors, maybe that would help. So we treated our fetal calf serum with kaolin, which non-specific inhibitors stick to. We used that serum for our cultures. Bingo! All of a sudden we had lots of hemagglutin, which you could do lots of testing with. It was really important to the development of the vaccine because now you didn't have to do these laborious small scale neutralization tests. All of a sudden you could do hundreds of sera in a day with no problem, no problem at all. You could automate procedures to do it. It was really a big help

to everybody, not just to us but everybody in the field. So this paper in 1967 is very important. You might say it doesn't really have to do with vaccines but it did.

So by 1969 we patented the viruses we were working with. I have two patents, one for hemagglutination and one for the virus. I never made a nickel from those patents because we wanted them to be freely available to everybody. No funny business at all. I would be clean as a whistle here at NIH, even today —

SL: Even today. [laughs]

PP: So I sent virus to all the biologics manufacturers and they did various things with them. The people at Merck, along with using their own strains, worked on it and got their own version of the vaccine. Maurice Hilleman at Merck adapted the virus from our 77th passaged virus to duck embryo cell cultures and then he made five additional passages in duck embryo cell culture. He believed that this created a little more attenuation and so he made a vaccine at this cell culture passage level and he got the license approved in 1969 for it to be used commercially. That was the rubella vaccine that was used from 1969 to about 1979. All of the vaccines produced in the United States used our strain, both the Merck duck embryo and the Phillips Roxane canine kidney versions. We also licensed with Smith, Kline

and French, as it was known at those days, for a vaccine made in rabbit kidney using their own strain of virus. So we were involved in the licensing of all the vaccines.

SL: And so you worked with people at the drug companies?

PP: Yes. Well, we didn't work with them closely. We kind of showed them how to do it. We gave them the viruses and they took off and did their own thing. So it wasn't a close collaboration. It was a small collaboration, to get them started, and then they went on to do their own development.

SL: Okay, so it's 1969 and the drug companies have taken over the production of the vaccine. They started distributing it?

PP: They started distributing it. Merck did a really good job. Maurice Hilleman recently died. He was wonderful—he was a great guy, a diamond in the rough, an American original. And he took a lot of people's viruses like ours, and hepatitis viruses, hepatitis A and hepatitis B viruses, and he made them into commercially successful vaccines. He knew how to do that. And that's not something that everybody knows. It's important—when people think of drug manufacturers, everybody thinks of this monolithic thing but the fact is that they're really

important and they know a lot of things that a guy in a laboratory here in Bethesda doesn't know. He made a vaccine of it and it was highly successful. He later incorporated it with measles and mumps to make measles, mumps, rubella vaccine, or MMR. And that is the vaccine that has essentially freed the United States of German measles. I mean, CDC recently announced that, as you know.

SL: Right, I saw that in the paper.

PP: And it really was everybody's effort, but Maurice's effort—the idea of putting three vaccines together—this trail of science has led to the point where there is no indigenous rubella here. I mean, there have been a relatively few cases of imported rubella because other countries have been or are behind, countries like the U.K., countries in Central America or South America, but they're coming along. In the last few years the U.K. has begun to use MMR and there's a lot of use of MMR in South America now.

SL: So what are the advantages of MMR?

PP: If you can give three vaccines in one shot then that's really useful, that's really efficient. And the other thing is that measles was a big driver because people wanted to eradicate measles. They're still trying to eradicate measles which is

very hard to do. But it also helped with rubella, because it virtually eliminated rubella in the United States now; people are still working on measles. What else do I want to tell you?

SL: Well, while we're still on MMR for a second, obviously there's been a lot of controversy recently about rising autism rates being related to MMR. Do you want to comment on that just briefly?

PP: Yes. Now that it's 2005, mothers don't fear polio, they don't close swimming pools in the summer. They let their kids go to the movies; they don't try to quarantine their children. They've forgotten about measles and how sick kids can be with regular measles. They've forgotten about the fear of mothers in the 1960s that were pregnant and got rubella. They've forgotten all of that. That's so long ago, it becomes historic. And the thing about it is that it's historic but it's going to come back if you don't get immunized. That's the first thing, now people are focused on risks of vaccination, forgetting the benefits so that even a theoretical risk is an overriding concern. The second thing is, try to take a rational look, step back and look at the many studies that have been done looking to see, does that vaccine cause autism? And the answer is from each of them no, it doesn't. It isn't associated with autism. There's no evidence that the MMR vaccine is associated with autism.

Now, science has a funny thing about absolutes. I mean, if you ask a scientist, "Can you say for sure"— the scientist will say, "I can't go beyond my data. But my data, which involves these thousands of instances, shows that it's not associated." I believe it's not associated. Some people say, "Oh, it could be a terrible thing if I get my kids immunized, besides there's no rubella and measles around, so I don't need to have my kids immunized." But that's—I hate to be harsh but it is stupid. Yes, maybe the immunization of all the other children in your neighborhood will protect you but if you and the lady next door and the guy down the street decide not to be immunized, you'll have a problem again, sure enough. All of this hubbub about vaccines causing autism—I mean, there are vaccines that occasionally do cause adverse reactions and people have struggled with that. The live polio vaccine did cause a problem. But measles, mumps and rubella are remarkably free of any serious problems. What else would you like?

SL: Can you talk about what it was like to work here at NIH?

PP: I started off at Walter Reed and then left there and I came to NIH and then they moved us to the FDA. So I'm sort of part of three agencies. But I would say the greatest time was at NIH. Walter Reed was wonderful, but being here was wonderful also. I mean, it's really an important place. Where else could you

find a guy who could do surgery on rhesus monkeys and look at the developing embryos? Where else could you find somebody who knew how to time the menstrual cycles of monkeys? Where else could you find people to help in all the different areas?

SL: What building where you in here, and was it all biologics?

PP: All of biologics was in Building 29 first. We were kind of a small outfit. The laboratory maybe had 30 people in it, it wasn't a big lab. Dr. Murray was very supportive of us. I'm sure he had lots of battles with [Dr. G. Burroughs] Bo Mider, who oversaw what was happening here, to protect his science program. We believed and I continue to believe that a basic science program is important at NIH. Not just people who give grants. The intramural program at NIH is a gem and should not be perturbed. I think people should support it and leave their hands off of it, which has not always been the case, and I think the idea of having laboratory scientists in a regulatory organization is an important thing. It was recognized to be important by NIH. It has been recognized for a long time to be important for biologics, even when we got transferred to FDA. I'm very much concerned about it now, though.

SL: From your viewpoint, looking at NIH in the news lately with all the conflict of interest problems…

PP: Well, the new regulations at NIH are much like the ones at FDA, so I'm familiar with them. If I had retired from NIH I could come and go with no problem at all. I could be here, I could be on committees; even though I was retired I could have an office here and so on. But when I retired from FDA, and because I wanted to do consulting, I became a separate person. I can discuss the weather with my colleagues but not much more. I have a folder full of regulations about what I can and can't do. I was director of CBER [Center for Biologics Evaluation and Research] when I retired, so I'm not supposed to have contact with CBER over any issues with which I would have had material input, which was of course everything because I was the director. I think it's too bad that people don't trust you, but it's the way it is. I have done a few things for CBER when they've asked me. When they specifically say, "Could you come and consult with us about this particular matter?" Then I'm free to do so. Otherwise I've decided that it was best to cut all of those ties. And it's been fine. I go to all the open public advisory committee meetings that have to do with vaccines or things I'm interested in like mad cow disease. I'm a member of the NIH Alumni Association. I was on their board for a while and I have some contacts that I keep track of. And of course working with the history office, I was very happy to do that. Vicky

[Dr. Victoria A. Harden, NIH Historian] wanted me to be one of those people who are retired who help you in the history office. But I was busy for a long time with my consulting things. Actually my wife and I were quite busy with nonprofit organizations. You know we got interested in American crafts, especially glass, and I have devoted a lot of time to that. We're very busy now and so I'm not sure I would have the time to do it all—maybe someday. I'm trying to cut down on consulting. Have you seen the Parkman Coupe?

SL: I've seen pictures of it. Please tell me about that.

PP: It's on display at the Renwick.

SL: Vicky actually just saw it last weekend.

PP: We had been involved with the Corning Museum of Glass and we knew that the curator there, Bill [William] Warmus, was going to do a show of the work of Emile Gallé. Gallé was an Art Nouveau period designer. He designed furniture, beautiful things, and he was also interested in glass. He got a commission from the school [École Normale Supérieure of Paris], that Louis Pasteur attended, for a small vase in honor of Pasteur, shortly before he died. It was known as the Pasteur Coupe, and on it was imagery related to Pasteur's career. Bill also had a

translation, fortunately, of an essay that Gallé wrote, to be given to Pasteur at the time of the presentation. He asked me to help him understand the imagery on the vase.

So I knew what Gallé said and Bill had given me pictures of the vase. For example there were some funny little things that Bill couldn't identify. I said, "Those are silk worm larvae," because Pasteur was interested in the French silk industry. And there was a disease of silk worms that he studied, which was killing the larvae so they wouldn't hatch out properly. There was also a culture plate with bacteria growing on it, perhaps because he had isolated the pneumococcus. There was a microscope. There was a dog slavering at the mouth to represent rabies. These things were on one side of the vase, and on the other side were fantastic imaginary creatures—a hydra flying, for example. There were clouds of miasmas. These things exemplified science before Pasteur, all these imaginary things which supposedly caused disease. On the other side was science. And there were quotations from Victor Hugo, a French poet and novelist.

So I helped him with that. I did quite a bit of work on it actually. I told him the percentage chance that what I said was true [laughs]. Some things were very obvious, like pneumococcus, and you know what anthrax looks like under the microscope, you know the microscope, you know the culture plate, but there were

some things you weren't quite sure about. He used that to help him to write his essay and he gave me a tiny bit of credit in the introduction.

So I knew about the Pasteur Coupe. We already had a piece of Dan Dailey's work, and we went to visit him at his studio in Kensington, New Hampshire to talk about a commission and on the way stopped off to see Bill. We went to lunch at a little restaurant near Cornell, the kind of place that has asparagus ferns in the windows, it's vegetarian, you know that kind of place. They have Indian dishes on the menu a lot. This is to set the scene. We were talking with Bill about what kind of things Dan does: the sculptural pieces, large wall panels that have been made from glass. And he makes vessels. We all liked the vessels so we decided we ought to talk to Dan about those. When we got there we described the commission: "I want something to commemorate my discovery of rubella virus and my development of the first experimental vaccine." And he said, "That sounds interesting." He was willing to do it. So I sent him a pile of my papers, and some photographs from when they did a mock up of my laboratory at the Smithsonian's National Museum of American History, it was part of an exhibit they did of Public Health Service accomplishments. I also sent him a letter I got from Lyndon Johnson in 1969. So I sent him all this and after a while he sent back a drawing. He wanted to feature the "eureka!" moment. There's a representation of me holding a big centrifuge flask, Harry Meyer is down below

me. I told Hank if he'd paid for the commission he might have had a higher place on it! Harry is depicted immunizing a child. It has all kinds of laboratory glassware because Dan likes that kind of thing. He included angular Erlenmeyer flasks and graduated cylinders in the frieze around the top, and a quotation from Johnson's letter, "Few men" etc., written in italic because I like to write in italic handwriting. Dan and I decided the coupe should be red for rubella, with a green stem and a red foot. The foot and the stem were cast. The stem was connected by two bronze rings and the bowl was free-blown in layers of yellow and red glass. The imagery was made by a process in which you put a resist cut out to make the image you want and then you sandblast away the glass so then when you remove that you have the image standing out in high relief. There are multiple layers of imagery, it must be really hard to figure that out, since you have to do the resist so it comes out looking lifelike. It's really, I think, a marvelous thing. I paid for it myself and I really was pleased with the result. It took him three years. I gave it, and all the correspondence about it, along with all of our files, to the Smithsonian. They have about 19 linear feet of folders from us, including artist's folders and event folders. We helped start a couple of organizations that had to do with American crafts. The collection also includes correspondence with the curators of American Craft [the American Craft Museum] and Corning [the Corning Museum of Glass]. I kept a journal for a long time, from 1979 to 1993, in leather-bound journals I bought from Jerry Marmelstein up at the Baltimore Winter Market [the

American Craft Council Show at Baltimore]. I was his best customer. I have about 12 of them and they're promised to the museum too, although not in my lifetime because I was a fairly severe critic, actually. I said what I thought and sometimes I said things and I later thought, "Well that's really probably pretty unkind." So I'm going to wait until quite a few years after I'm gone before those go to the Archives. But I was pleased about the donation. We also gave them our library of books that Elmerina and I had collected that relate to American crafts, about a thousand volumes, and several hundred show catalogs and other kinds of things.

SL: Oh, they must have been very pleased.

PP: I think they were very pleased. I hope they were, anyway. But getting back to science. I think NIH can be proud of the fact that they supported my rubella research. Everywhere you go you have to fight hard for science. I don't know about FDA now. I'm worried about the science program at CBER. The thing about it is, it's cheap to hire reviewers because they can sit there and look at papers all day long and make comments and decide what's good or bad. They're right a lot of the time; but sometimes they aren't right. It makes things more complicated and I don't know if it often adds anything positive to the process. Scientists are expensive. So per person, if you want to cut expenses and you want

to cut people, well why not cut the scientists? Because after all, the Center for Drug Evaluation and Research, CDER, has done without laboratory scientists for years, so why not? I think that that's a specious argument. I think to cut the government's ability to do laboratory science is a bad idea. To cut the ability to do science in a facility that's focused on preventing problems with biologics is inappropriate and unnecessary. But what are you going to do? I'm not sure. Things have kind of moved on—the world has moved on from the way it was. I guess old men think things aren't as good as they were when they were young. But sometimes they're right.

SL: What do you think is the most interesting thing going on in vaccine research now?

PP: It's hard to decide. There are a lot of areas where very interesting work is being done. So much has been learned from the AIDS problem. A lot has been learned. It's a really tough problem.

SL: Did you have any involvement with AIDS?

PP: I was on the NIH AIDS advisory committee for a while. I wasn't there too long. I started off because I thought, "Well, yeah, it's a hard problem but we've made a lot of vaccines before and we've always done it and we can do it now." I thought

that a vaccine was the answer, since we only had a handful of therapeutic drugs for virus diseases, I didn't think that was the best option. Well, in a sense, vaccines still are the answer but you haven't got one. And during the time I was on the committee I became quite discouraged about it. Committees are set up to include a range of viewpoints and I think I was the person who was expected to be really pro-vaccines, but by the time I'd heard a lot about the issues I was quite discouraged about vaccines for AIDS. So I really couldn't play that role. Laboratory science is very important. But I think there are a lot of things that are further down the pipeline that are important that people are trying to solve. One of them is how do you get people to trust the medical establishment and get vaccinated. Polio was within a hair's breadth of being eradicated. And then there were some people in Africa who thought that the people in the West were trying to poison them. And now polio is back. It's spread around widely. There are important things we found out about how you use vaccines. That's not test tube research but it's important research none the less, because if you found a way to get to those people early on, maybe you could've helped. Later on I think they did get people who were trusted and who were able to convince them. I think that helped. Now, if you could know about the people and their fears early on, you could get there with your vaccine sooner and distribute it better. And the same is the problem is true with eradicating measles. With all of these vaccines, we have

to learn how to use them better. That's the thing where I think there needs to be more work; there are interesting things to be done.

SL: Do you believe that rubella is eradicated?

PP: No, I don't believe rubella is eradicated. That's the wrong term. They say there's no indigenous rubella in the United States. The CDC is very careful with the terms; it will not say it's eradicated. You still can catch German measles in the United States. If you have a lady who takes care of your kids who's an unvaccinated young woman from, for example, Argentina, or somewhere vaccines have not been used, and she associates with other visiting Argentinians here in town, she could get German measles and if you or your kids aren't immunized they run the risk of getting German measles too. But essentially there is no indigenous rubella. The gene jockeys have figured out where the different strains of rubella are, and there was a U.S. virus strain; it's gone. So if you catch it today the virus will be some strain from South America or some other part of the world.

SL: That's a pretty big accomplishment.

PP: That's a pretty big accomplishment, right?

SL: Yes.

PP: Yes it was. You know, a lot of old people don't sleep well at night. This is a good thing for me to think about when I can't sleep.

SL: So what did I miss? What else would you like people to know?

PP: Let's see, I talked about the people at Walter Reed. Malcolm Artenstein was very important in the discovery of rubella virus. Actually, back in the day when we were trying to figure out how to isolate the virus I had the idea of using interference. But it was Mal who had said, "There's this new kind of cell culture that people haven't used very much, African green monkey kidney." So we included that in the cell cultures we used to try to isolate the virus…and it was important to do this—these cells showed interference very clearly.

SL: Where did he get African green monkeys?

PP: Most of the virus work in the early days was done using the kidneys of rhesus monkeys. You took monkey kidneys, diced them up, treated them with an enzyme to break down the kidney tissue into individual cells, and then you put

them in glass bottles where they grew out in layers, once cell thick. A lot of rhesus monkeys gave their lives for virus science. Most of the monkeys came from India. The monkeys would be put on a plane in their cages and shipped to New York and then they would come to various research labs such as the NIH. NIH used a lot of monkeys in their research. There was some interest in looking at the cells of other monkeys also, besides those from India. Africa was another source of monkeys, which began to be used in the early 1960s. Mal knew about African green monkeys as a cell culture source. They may be cleaner than rhesus; the rhesus tended to have many extraneous viruses in their cells. We tried all sorts of things, at least two kinds of monkey kidney cells, and even human embryo kidney cells.

SL: When I was doing some research on this I found all sorts of statements by religious groups saying that you shouldn't get vaccinated because they used human embryos to make the vaccines. When did they start doing that and what's the reason?

PP: Human embryo kidney cells were interesting—I think common cold viruses grew in them and they were useful for that. They're very nice cell lines, they grow nice flat monolayers, and they're very sensitive to polio viruses and all the enteroviruses. And the rubella virus grew in them too, but we found it didn't

produce very good interference. The African green monkey's cells were the ones that produced really solid interference. So we went with African green monkeys. The human embryos for these cultures were either spontaneous or more likely induced abortions, though at that time there was no big fuss about that. Actually, these early passage human embryo kidney cell cultures were never used for making vaccines.

SL: Really?

PP: Now there's a big fuss about it, as you said. The cell line WI-38 came from lung tissue of an aborted fetus. But, now, there's a distinction that can be made between these human embryo cell cultures and WI-38. WI-38 originally came from an aborted fetus, and then was carried through 25 passages. And those cells have been carried up to quite high passages. Sometime in the lower passages it was found to be very good and stable cell line, it didn't convert to any type of malignant kind of cell line, and was very clean as far as extraneous agents were concerned and so it began to be used a lot, even later on, for vaccine production. We tried rubella virus in it and it grew but not to very high titers and it didn't produce interference so we weren't too much interested. Now, getting back to the cell issue, there is a difference in my mind between WI-38 cells and using cells from a different fetus every time you make a batch of cells. WI-38 is made from a

single abortus from many years ago and has the ability to make cells for 50 or 100 years that are useful for various scientific projects, as well as vaccines. There's a difference between that and getting kidneys from fetuses where every time you have to make a new batch the manufacturer has to get a different fetus. There's a distinction to be made. It's hard for me to imagine that there should be a furor about using WI-38 cells to produce rubella vaccine. But I suppose that some people find it difficult to understand that and would disagree. Perhaps they would have the vaccine maker go back to making vaccines from duck embryo cells.

SL: Less controversial.

PP: Use of human WI-38 cells for vaccines is so far from what the main arena is now, about making new human progeny from skin cells, or fixing people's brains that have Parkinson's disease. I mean, it's so far from that, that it seems silly. But you know, I suppose if you have this kind of mindset…

SL: People get worried.

PP: Yes. There are a lot of people who are conflicted about the use of human stem cells. I can understand that. I mean, I was a doctor, and as an intern I had an

OB/GYN rotation and when I was a resident I saw miscarried fetuses, and I must say….

SL: It's a difficult thing.

PP: So—I understand that. So what else can I tell you? I got off the track. So Malcolm Artenstein was very important because the idea for the African green monkey kidney cells came from him. But I was the one who decided about the interference, and Ed Buescher was the boss who gave us general support. Actually he was nervous about the rubella discovery because he was not a clinician. He had never had an internship. He came out of medical school and got into the virus thing and he was kind of cautious about making clinical diagnoses. He came over to see Joe Smadel and he talked with Chanock and we kept after him. We felt that he wasn't going to make a big mistake in supporting our work—and he did support it. He was good guy. He's gone too.

If you go through all the work we did, there are a lot of names of people that helped. Hope Hopps was a bacteriologist. She was our—it's an unacceptable term now I suppose—but she was our "Girl Friday." She could make any kind of cell culture grow, for example, she developed the BSC-1 cell line, which stands for biologic standards culture one. It is still used for things. I used to come over

from Walter Reed and get a sample. It was a culture made from African green monkey kidney cells and I used to come over and get an 8oz milk dilution bottle and take it back to Walter Reed to make my own cells. And so I would make the cell passages, and then it got all seedy looking and they'd die and they wouldn't grow out. So I'd come over and get another culture. Then the same thing would happen. But she had the magic touch, she could make things grow. And she was very smart. When we were working on the vaccine we tried to get markers that would help us guide what we wanted to do, because deciding where to put things in the clinical trials, that's tricky business. You would prefer not to cause a rubella epidemic! So we developed markers, one depending on the cytopathic effect in rabbit RK13, a rabbit kidney cell line. She developed a marker test that depended on interferon because attenuated virus produced lots of interferon and the wild didn't. As you did your passages you could look at those characteristics, until you took the plunge and decided that this was different enough from the others. The third was, of course, behavior in monkeys. The wild virus caused much more of a German measles-like disease than the vaccine did.

And then we had lots of "two-year men." They came to the NIH to work in our laboratory for two years in part to satisfy their military time commitment. And they did very good work. I won't single any one of them out because there were a

lot of them, but I would like to take a bow to those guys who did a lot of work on rubella.

SL: Is there any particular equipment or laboratory equipment that you used? We do some collecting of old lab equipment, so that's why I ask.

PP: No, it was pretty standard virus stuff. The milk dilution bottle which you used to grow cells and there were also bigger bottles. And just screw-capped tubes. I can send you a picture of the laboratory mock-up they did at the National Museum of American History at the Smithsonian for an exhibit.

SL: Oh, that would be great.

PP: That just shows the microscope, an open notebook, and a big Erlenmeyer suction flask that you used to take off the fluids when you were changing and refreshing the media from the tubes, and little Erlenmeyers on the shelf, and a roller drum. The roller drum looked like a little Ferris wheel. You put your cultures on it and they would roll around, and for part of the time, the liquid nutrient medium was on the cell sheet, and then it wouldn't be, as the drum rolled around. We used that because sometimes with very fastidious viruses it seemed to help them grow better. We tried it for rubella. We didn't find that it did anything helpful.

Anyhow, the picture shows that it just looked like a lab from that era: Things look different now.

SL: Yeah, I guess they do.

PP: Our techniques are still used today. If you want to isolate rubella virus in a laboratory somewhere, despite the fancy technology where you have genes and everything flying around, do you know what you use? Interference and African green monkey kidney cells. I mean, there are other ways to do it but if you really want to know for certain that the virus is there, that's the way you do it.

So it was great ride. The Peter Principle says that in a bureaucracy everyone rises to the level of their incompetence. I was briefly a division director, and then Harry Meyer wanted me to be deputy director of the Bureau of Biologics and then we moved up to be the director and deputy director of the Centers for Drugs and Biologics. And then Harry retired and after looking at me for a long time they decided they wanted me at Biologics so I was I director of Biologics for three years and then I retired. In all that time I did things that were, I think, on the whole useful. And I think that people thought that I did a good job. I mean, I stepped up a lot of times. But the best times, the best times were here [at NIH]. The best times were here, actually, and at Reed too.

SL: You're most proud of that?

PP: Yes. All this other stuff—I mean, what do bureaucrats do? They have meetings. And they try to do things right. Sometimes they do and sometimes they don't, you know?

SL: Yeah.

PP: Swine flu, for example. We were all concerned about the pandemic to come [in 1976]. We thought it had come—we had a couple of soldiers who died at Fort Dix of influenza of a type which hadn't been seen for decades—and caused the great 1918 "Spanish flu" epidemic. That set into motion an enormous effort to produce vaccines for, as [President Gerald] Gerry Ford said, "Every American man, woman and child." We said, "Oh, God, why did he say that?" The thing is, an issue like this goes up to the next level, then the next level, in the chain of command and they want to simplify it and simplify it and finally at the top they want to say something really dramatic, so they say they're going to do the impossible, which was to immunize every American man, woman and child when you couldn't possibly have enough vaccine to immunize 200 million people. Actually, the manufacturers produced 47 million doses before the whole thing

collapsed. Great effort, but we knew that it was going to be a failure for that reason from the start. And it was too bad he said that, but what can you do?

Then, of course, the program came to a bad end, because the CDC discovered that it caused GBS [Guillain-Barré Syndrome]. I don't know whether it caused GBS or not. It's the only time that the two have been associated, and I think the association is pretty weak. The problem is that you could have bias that could create that answer. Could it be that people who got swine flu vaccine and the doctors who were seeing them out there in the country were more inclined to make the diagnosis of GBS if he had a subject who had gotten vaccine? And that bias is impossible to control for. [Dr. Alexander D.] Alex Langmuir defended the CDC position. [Dr. Leonard T.] Len Kurland, a neurologist at Mayo, wasn't convinced, and they had a big debate. I think basically with the data you had at the time, there wasn't any choice really but to say, "Well we'd better pull it." Besides, at that time the swine flu hadn't really spread. Compared with earlier pandemics, when they had disease in the summer and in the fall, we weren't seeing any indication that flu was occurring. So it was a marvelous field day for everybody in the press. The swine flu program was termed a "debacle." I participated in the debacle. What I always said was I want to retire before the next pandemic because there's not going to be enough of the vaccine. If that chicken flu gets roaring, man, you better just play like Poe's "Masque of the Red

Death," and seal yourself in, to better effect, I hope. That was a lively episode I lived through. AIDS was another really tough time. We had to try and decide what to do. It was awful. I mean, on the whole, if you look back you can say that people did their jobs pretty well. [Dr. Robert C.] Bob Gallo and his French colleagues, they isolated the AIDS virus. I guess Gallo now has given up and has said, "Well, I didn't really isolate it. I wasn't the first one. It was the people in France."

SL: After all that.

PP: After all of that. It was generous of him, but I understand the controversy. I think that maybe he didn't do right. Certainly on the outside looking in, I thought he deserved much of the honor because the French were dilly-dallying around in a little laboratory, you know, doing this and doing that and not publishing anything, and maybe you don't want to put this in—

SL: Keep talking!

PP: Well, I thought that they were. I mean, I didn't think they were getting there, and Gallo got there. He had data that convinced the world that there was AIDS virus.

And the French had it, as we know now, too, but the data weren't convincing. I will give Gallo credit for having done it. These things happen in science.

But as I say, I think overall people did their jobs quite well. At the Bureau of Biologics, we were very much concerned about the safety of the blood supply. So we tried to help the companies in trying to develop standards and trying to find a test that could be used to test the blood supply, to ensure the safety of the blood supply. I think that was important work.

SL: But there's been criticism, obviously, that people didn't move fast enough—or as fast as they had with swine flu.

PP: Didn't move fast enough? Between the time when the virus was discovered and when the blood could be tested for HIV was an extraordinarily short time, but it was a period in which a considerable number of people got infected with AIDS virus. That was too bad. I feel bad about that. Could we have done it faster? You know we were going full tilt as fast as we could. We also could've taken all the blood fractionation products off the market, that's the other thing we could've done, but we thought, "That's not a good idea." Blood is really important and the hemophiliac factor is really important—life-saving. The Hemophilia Foundation did not want us to take away their blood products. In retrospect, it might have

been a good idea, but with the information we had, we said we wouldn't do that. And so I think that was too bad, I mean, that we couldn't have done it faster. In looking back I don't see any real way that we could have. I just don't think there was any rational way to do it. If you'd been irrational and taken the blood products off the market, you would have had many people die of other things. Many people might have died who needed blood and blood products.

So I focus on rubella. I think that overall the medical community and Walter Reed and NIH, when we were part of NIH and then when we got to be a part of FDA, I think they all did reasonably well if you take a broad view all along. I think they did a lot of important things and a lot of things that were useful to the American people and their health.

We did some things that were smart. You had the vaccine in 1969, how are you going to use it? Every six to nine years there's a big epidemic, and we'd just had one of those in 1964, it did a lot of damage, created a lot of babies with congenital defects, created a lot of emotional situations for the mothers. We have had that experience. We thought that we ought to have a vaccine and we ought to start using it. Along with CDC we made the decision to use it in children one year of age, the first time when you really could get good antibody responses. Before that the antibody response can be interfered with by maternal antibody if she has it.

So you start immunizing at one year of age up until puberty. That avoids the question of whether the vaccine will affect the fetus. If you really push hard and get all those kids immunized, you're going to stop the epidemics because they're ones who really spread the virus. And we did it. If you look at those epidemic curves, they bumped up and down every 6 to 9 years. After 1969, no more big epidemics.

SL: Can you talk more about the vaccination program?

PP: It was a big vaccine program. It's a problem to get one-year-olds. Five to thirteen-year-olds are okay because they're captive, they go to school. You immunized all the school kids, and you hacked away at it. You started immunizing babies at one year. And you tried as best you can to get the others. Those in that age group between birth and school age it's hard to get, but some of them have regular check-ups with their pediatricians. You get a lot of them—maybe half of them that way. The others are harder to get, you have to do public clinics and try and encourage people to get immunized. That's harder to do. The percentage that was immunized from that age group was not as good, but it was still pretty good. You keep working on it and keep stressing the importance of immunization, and you can do a pretty good job so that you didn't have anymore epidemics. But then that curve bumped along at a low level. There was still

congenital rubella around. Our clinical experience with the vaccine was gradually increasing, and showed that the vaccine didn't spread and thus couldn't cause birth defects, it couldn't infect the fetus. All of those things together along with the increasing experience of use of the vaccine pointed to its safety for pregnant women. A certain number of pregnant women inadvertently got the vaccine. CDC did a follow-up study of their children, and they showed that there were no babies with rubella-induced birth defects. They studied the babies from the standpoint of whether they had rubella antibodies because early in life you can show they'll have a certain type of antibody if they were infected *in utero*. They had blood available and they tested those. So, all of this safety experience put together led people to feel more comfortable about immunizing everybody, although, to be cautious, not to vaccinate women who were, or might be, pregnant. Then, because the disease was still bumping along, the CDC, through their Advisory Committee on Immunization Practices, said, "Well, we ought to immunize adolescents as well." And then they said, "We ought to do prisoners." And, "We ought to do military recruits." Smart. And we ought to do a whole variety of populations at special risk to rubella and important in the spread of rubella. And all of this contributed to the fact we don't have any indigenous German measles anymore here in the U.S. There were other countries that took other tacks. In England they were concerned about the same thing as we were about vaccines and pregnant women. But they said, "It would be safer to

immunize young women at the time of puberty." Another thing people worried about was that the vaccine antibodies wouldn't last long enough. One postulate was that if you vaccinate when they're babies, then when they get up to the young adult years, it's been a long time since they've gotten vaccine, and the vaccine effect wears off, and the antibody is gone. And all of sudden all these women become susceptible, and then they get pregnant. Then they catch German measles because they don't have antibody anymore and you make the situation worse rather than better. Well, we didn't think that was liable to happen because we had data that showed that when you gave the vaccine the antibody titers came up high and they dropped off and then were perfectly level. You have to trust that that's going to happen. We said that will be the way it will go, and besides, if women lose their antibodies they could be immunized again sometime later in childhood. It isn't an irreparable thing, even if that happens.

But the English looked at it and they said, "That's really a risk. So we will immunize all adolescent girls, not boys." I saw their point of view but I thought it was mistake because if you do that, how long will it be before you have any effect on protecting women? 10 years. And during that 10 years rubella will continue merrily along, infecting women, children, boys, and as it turned out, girls. You had a little trouble since it's an odd age to immunize. I mean, a baby is sort of captive, you carry it around. When you get to be that age it's harder for mothers

to remember to get their children immunized. It's harder to set up programs for that even if you do them in schools. So what happened? They had a lot of German measles for years, until finally somebody said, "Well, let's look at the data." In England they had something like eight times the number of congenital rubella syndrome infants than in America. And America is a lot bigger than England. They said maybe we ought to do something about that. So at any rate, now they immunize essentially the same way as in the U.S. They use the MMR and have been very effective now in controlling rubella. We had pretty good control here in the U.S., but the issue of importation of rubella cases has arisen. The countries from which the largest amount of rubella was imported were in Central America and South America, and England. Now, with rubella vaccination increasing in these countries we are much safer.

So I feel like your government did a good job for you. Your government took some risks. But they thought on the whole it was better to immunize. Back when we weren't absolutely 100% sure, they took some risk. They said, "We think that this will be a good thing." And you believe it, it was a good thing and it was an important decision to do that—we did better than other places in the world. Well, I think that's all I have to say. I'm talked out.

SL: Okay. Well thank you so much. This was great. I really appreciate it. Thank you very much for your time.

PP: You're welcome. Well, I enjoyed it. I like to talk about rubella.

End of transcript