National Institute of Allergy and Infectious Diseases
Oral History Interview Project
Interview #3 with Dr. Robert Chanock,
Conducted on February 23, 2001, by Peggy Dillon
at the National Institutes of Health, Bethesda, Maryland

PD: Good morning. Today, I'd like to continue our conversation about your time at the National Institutes of Allergy and Infectious Diseases . . .

RC: Oh, so that's the name of the place.

PD: You didn't know?

RC: No, I just come to work. I don't look up.

PD: There was a study published in 1980 that said that you and your colleagues performed the first description of RNA splicing of transcripts from an RNA genome. Could you talk about how knowledge of the viral genome have helped in development of vaccines over the last two decades?

RC: Well, that was an discovery that was made by Chin Chu Lai of this lab together with Robert Lamb, who was at the Rockefeller Institute at that time and who was in the laboratory, working in the laboratory of Purnell Choppin, who later became the President of the Hughes Medical Research Institute. And he had been, Bob Lamb had been studying influenza and other similar viruses for many years, well,

five or ten years anyway, following his Ph.D. studies at Cambridge, actually. So, he had predicted that there were several more proteins in the influenza virus than other investigators would agree to and, of course, he was absolutely right. Bob Lamb was almost always right. He was a superb fellow.

And so he collaborated with Chin Chu, who had sequenced—he had determined the DNA sequence of the various RNA segments of this virus. The genome was broken up into very, a collection of RNAs. It's not a big, long linear RNA, but each gene is handled separately in the infected cell, produced separately and operating separately. So when they were comparing the RNA sequence with what was known about the various proteins, there were eight RNAs, but there were ten proteins. And they found that two of the RNA coded for two proteins by a protein that was represented linear or an RNA structure, RNA sequence.

And the second one was another protein which started in the same way that the unit-long sequence did and then it was interrupted and there was splicing and when it finally was copied into protein, the sequence of the protein was at the very end, so that you had an RNA that was linear and a linear total sequence was expressed as a long protein. And then there was another protein that was produced by the viral polymerase moving along the RNA and then suddenly stopping. There was a signal there and then reattaching at a distant site and producing a smaller protein which had a different sequence than the full-length.

So this has never been described before. Splicing was thought to be the province of RNA that is transcribed from DNA.

Many of the genes are transcribed using the splicing mechanism in the eukariotic cell. However, this was an instance where the splicing occurred from a template of RNA rather than from a template of DNA. DNA is the genetic material of most, in most instances, but in viruses, the genetic material can be RNA. Many viruses have RNA as their genome rather than, have an RNA genome rather than a DNA genome. So this was the first description of splicing of an RNA transcript from an RNA template. The standard accepted strategies splicing of RNA from a DNA template. So this meant that it was possible, in RNA viruses, it was possible for one gene to code from more than one protein. And this was, this was sort of a revolutionary concept and discovery as well.

We did a lot of work, he did a lot of work in terms of sequencing the various, the genes of the influenza virus and so forth, but after about eight or ten years, the, he wasn't able to achieve the goal that had been set for that program which was, mainly, to be able to set up a system in which you, the genome of influenza could be manipulated in DNA form and then the mutations that were produced would then be, would then be recovered in an infectious virus. The RNA genes, the proposed strategy was to make DNA copies of the RNA genes and then to introduce mutations into them and then make RNA transcripts from the DNA and

introduce those back into the cell to then produce an infectious virus. In other words, this is rescue of virus from a CDNA copy of the viral genome.

It has not been possible to date to introduce mutations into specific sites into the RNA genome. You can hit the genome with chemical mutagens and do all sorts of things, but you can't make, you can't produce the mutation of your design. You just have to take what comes and recognize mutations and use them if they're helpful. But when you have a copy of the genome in DNA form, you can put mutations anywhere you choose, you see. So you are in charge. It's not the process where you do something that's very drastic and then you look for mutants. Here you can produce them to your specifications. So if you have a virus that's quite large, you can cut a piece of it out to see whether the virus will still function. If you're interested in vaccines, the intent would be to slow the virus down, in other words, to attenuate it so that it would grow well enough to induce immunity, but not well enough to produce disease.

So, we didn't succeed with flu. The person who succeeded was Peter Palesse, who is at Mount Sinai Hospital. P-A-L-E-S-S-E, Peter Palesse. Many people were competing at that time to do it. So, not being able to do, to achieve this specific goal of rescuing viruses from viral CDNA, I told a lie that we ought to re-orient the program and work with viruses where we could be more certain or more likely to be successful in developing a rescue strategy. And what we did

was we, I chose dengue because I was interested in dengue and it's a very important virus. And to date, there is not, a vaccine has not been produced to date. There are a lot of candidates, but nothing has been licensed. Nothing, there is no such vaccine in general use.

The virus was discussed, dengue viruses, viruses have two to four different stereotypes. The first two, the first dengue viruses were discovered by Albert Sabin during World War II. It was one of the major health problems for the military in the Pacific. Dengue just, you know, incapacitated an awful lot of soldiers in the Pacific. And this happened under conditions which were inopportune to the military. A large island assault was being prepared and the mother ship was loading Marines onto assault boats and so forth, you know, to travel to the beach and disengorge the Marines and then come back for others and so forth.

And on three different occasions, dengue was recognized just as this process was in, just as the Marines were being loaded onto these salt ships. They recognized dengue, and of course, it's a mosquito-borne virus. The few cases that occurred, that were evident at that time would assuredly be followed by many more later on. That's exactly what happened. So there were three major island invasions that were aborted at the very last minute because of dengue, so the military had dengue as one of their prime targets for vaccine development.

Albert spent half of his time working on dengue and half on sandfly fever, which was the major problem in the Mediterranean area during World War II. He succeeded in both of them. He isolated the virus of sandfly fever and he isolated the first two serotypes of dengue, characterized them with studies in volunteers, recovered the virus in mice, and prepared an experimental vaccine that worked, that could not be used because the virus was grown in mouse brain. And it, that's a no-no, except in wartime. And also, this, the vaccine strains they developed didn't grow well in tissue culture so they couldn't be used, they couldn't be produced economically.

Anyway, so then the tissue culture era arrived in the '50s and many attempts have been made to attenuate dengue, but not successfully. You can attenuate it, but the vaccine strains that have been produced to date are either too attenuated or still too virulent. So it's just, it's a just-so proposition. You can't attenuate it too much because it won't infect or it won't induce immunity or if you don't attenuate it enough, it produces disease symptoms. It's got to be just so, very delicate, very difficult balance must be achieve. Now, dengue is an RNA virus. Its genome is made up of a long, linear stretch of RNA. It doesn't have separate RNAs for each of the, of the genes. Influenza has that sort of a genome. The rotaviruses have many RNA segments, each one coding for a protein and so

forth, but dengue has just a single linear molecule of RNA and about 11,000 nucleotides.

Now, after the War, scientists in Australia demonstrated that purified RNA from dengue virus will infect mice if inoculated directly into the brain. All of the mouse-adapted strains are also neurovirulent. In other words, they kill following inoculation into the brain. So, this was done by Gordon Ada, A-D-A, who was with McFarland Vernette in Melbourne, Australia, a very famous virology lab. So it was clear that the RNA of dengue was infectious if you could get it into cells. So we set about to construct a full-length DNA copy of the RNA genome that could be manipulated to produce mutations, you know, anywhere you wanted and then copied the DNA, the complementary DNA is then transcribed into RNA and introduced into cells by a process called transfection. You just add the RNA and some of it goes into the cells.

Well, it took about four years to do it, but it finally happened. A rescue system had been developed and this allowed us now for the first time, to manipulate the genome, this long, 11,000-kilobase genome. We could now manipulate it in its DNA form, get the transcribed RNA back into cells and infectious virus. So, by mutational analysis, by analyzing various mutants, it's then possible to learn an awful lot about how the virus functions and where it can sustain a mutation that doesn't kill it, but slows it down because many mutations are lethal. In other

words, if you put that mutation in, you can't recover infectious virus. It's just, you know, it's like creating a person and not having a heart, you know. They can't, I mean, they can't live.

So there are certain things that you can do to slow it down or to make it do this or that sort of thing. But, many mutations are not acceptable. I mean, they will, the resulting mutant is not viable. You can't recover it. It will not grow because it's missing something that has to be present, you see. So when you, when you use rescue, the rescue strategy, you only recover viable virus. I mean, whatever you don't recover is not viable. So it was possible then to do a mutational analysis of dengue. What's permissible, what's not permissible? And it turns out that a single deletion in the very far end of the dengue genome in a region that doesn't coat for protein, it's a regulatory region. It starts here and at the very end it's, is a region called the three prime, noncoating region.

It doesn't coat for proteins, but it's involved in the regulation of the replication of the virus and so forth. A 30-base, 30-nucleotide deletion was created and this attenuated the virus. And the way that we knew that it was attenuated was we inoculated Rhesus monkeys with the parent virus and the monkeys sustained a, developed what is called a viremia. That means there's, blood is present, virus is present in the blood. It's produced in other parts of the body and then there's so much of it that it then spills over into the blood system, blood stream. And

viremia, that is, presence of virus in blood is an indication that the monkeys have been infected and the duration of viremia and the height of viremia, that is, the amount of virus that is recovered in blood indicate the level of replication in the body.

So, if you have a very attenuated virus, you may not find any virus in the blood or a very low level. And the parent virus produces a very high level of viremia. So we were able to show that this three-prime non-coating region deletion, 30 of 30 nucleotides attenuated dengue virus so that the level of viremia that it attained in monkeys was about a hundred fold lower than the parent virus. However, this virus, even though it was attenuated was still able to induce a high level of antibody and to protect the monkeys against challenge with a, with a parent virus at a later date.

So, this virus was then prepared for use for study in people and that's a whole other world because everything has to, every move, every material, every manipulation has to satisfy the requirements that have been set down by the FDA. So, this took about a year, to prepare virus that could be tested ethically and legally in human volunteers. So we had to use a specific type of cell, media, everything had to be annotated and signed in a book, you know, that we did this and other people would come in and say, "Yes, that was the case," and so forth. And all of the ingredients, all of the manipulations, everything that was used, the

conditions, the area in which the virus was grown, everything that we did in those various manipulations and so forth met the standards set by the FDA.

So we were ready, we tested this three-prime deletion mutant in volunteers at Johns Hopkins and it was beautifully attenuated and it didn't produce any symptoms other than a very mild rash on the chest. And most of the volunteers didn't know that they had this rash. It was just very mild. And actually, Albert Sabin had noted this with his vaccine and I had actually seen it because he did studies in medical students while I was in Cincinnati in 1950 to '52. And he would see them at lunchtime, they would come in and he would look at them, and I knew what the rash looked like. So it was a very, very satisfying result for us. It meant that we may not have had the ultimate vaccine strain, but we were on the way.

The volunteers developed a high level of neutralizing antibody in their serum. So, clearly, they would be protected against dengue, type 4. This was the Dengue Type 4 virus that we were. So, now we're looking at the, we're looking at the feasibility of introducing additional mutations into this just to sort of nail down the attenuations so that if something fails in the three-prime, then we'll have another mutation and another place that will make the virus attenuated. And this work is in progress. But in the meantime, the original mutant is proceeding down the pathway towards ultimately large field trials and another 19

volunteers have been inoculated. And by dropping the dose, we've been able to show that it's even more attenuated.

So, this is very satisfying, very fulfilling. It's a long road. And Sabin [nicely] the virus in '44 and here we are, what is it, 57 years later. Now the other point is that there are four different serotypes of dengue. You know, like there's influenza A and influenza B; there's dengue type 1, dengue type 2, type 3, type 4. And since there are four types of dengue, we have to have all four types in the vaccine. So the strategy that's being used is to produce a chimeric virus. A chimeric virus is a hybrid virus deriving some of its parts from one parent and the rest of its parts from another parent. It's a hybrid. What we've done is we've made the decision that we would use the dengue type 4 virus mutant, remove the two genes that code for the protective antigens, that is the two genes that code for the proteins that reduce immunity, remove them from the 4-type virus and replace them with the corresponding genes of type 1 or type 2 or type 3.

You can only do this with a rescue strategy. You cut out two of the ten genes and replace them with the corresponding genes and now you have a type 1, a type 2 or a type 3 virus on a backbone of type 4. So we have a constant, it's actually the second and third genes. We have a backbone of eight other genes and these come from type 4. And that's where the replicate, that contains the genes that are involved in replicating the virus and making it grow and do various

things in the cell. The two genes that code for the protective proteins don't have any of those functions. So, we'll have a constant background in the protective genes of type 1, type 2, type 3, and type 4 for a quadrivalent vaccine.

PD: I would like to talk about the process of discovery in your work on the rotavirus. It happened over about a quarter century?

RC: Well, yes, it started in '73, actually. Dr. Kapikian has been the leader in this, as you know. And Chin Chu Lai had been the leader in dengue, but now it's shifted to Brian Murphy because we have another standard to meet here and that is, we have to, you know, be compliant. We have to comply with all of the regulations set down by the FDA, and with the institutional review boards and so forth. And Brian has been doing studies with influenza and ROS and so forth in volunteers. So he has taken over the more recent studies and laboratory manipulations of the dengue viruses because he's a molecular biologist. Also, he is a clinical investigator and Lai is not a clinical investigator. He's strictly a molecular biologist.

The story of rotavirus I told you about, I think, last time, namely, Kapikian discovered the Norwalk virus by Immune Electron Microscopy and he set out to look for similar viruses in young infants with severe diarrhea, which is a major problem. In the wintertime, the pediatric wards of pediatric hospitals fill up with

two kinds of patients—patients with severe respiratory tract disease, which is RS and paraflu, for the most part, and flu during the flu outbreaks. But RS together and then the three paras together are as important as RS. And that covers about 40 to 50 percent of all hospital admissions for respiratory disease. The other half of the admissions to hospital are for severe diarrhea for young infants.

So he looked in those and he found these big particles which were 70 nanometers. The Norwalk was only 27 nanometers, much larger virus, much easier to see. And just at the time he discovered these viruses here in Washington, Ruth Bishop in Australia had described it by taking biopsies, by putting a tube down, and cutting out a little piece of intestinal tissue from children with severe diarrhea and she saw 70 nanometer particles. And Al Kapikian saw them in stool, which made it, that's a much easier way to look for particles. So from that point on, we, and it was clear that about 50 percent of all infants admitted to hospital for serious diarrhea during the wintertime, this is not summertime, wintertime, that 50 percent are infected by rotavirus. And in developing countries, where the mortality for infantile diarrhea is about two million—two million infants died worldwide every year, half of those are rotavirus.

PD: The reason I brought it up again is that I was, that we had talked about it in the early stages and I was curious about the process of discovery in the '80s, when you came out with first, a monovalent vaccine trial.

RC: Oh, that was . . .

PD: Is that a fairly classic procedure where you try [a monovalent vaccine]?

RC: No, I don't think anybody's ever done anything quite like it. What we needed, we were looking for evidence of attenuation. And we were looking for an attenuated virus and the serotype plan of Rotavirus wasn't known at that time. We really didn't know how many serotypes there were. We didn't know which ones were important in people. This was something that was discovered and refined concurrently. In the beginning, we chose the strategy that had been used by Edward Jenner, the man who formulated the first vaccine. He was the man who developed the first smallpox vaccine.

PD: In the late 1700s?

RC: It was, it was 203 years ago or something like that. And he made a very important observation. Smallpox was one of the major health problems in England at that time. And he made the observation that milkmaids who milked cows, who had cowpox, the cowpox-like disease, their udders, you know, were just filled with these pox, that looked very much like the pox that developed in

people who had smallpox and died, you see. It's a big, cycular, it's a bleb, containing fluid and all sorts of . . .

PD: Like a blister?

RC: Yes, but hundreds and thousands of them. And smallpox patients were often disfigured because they had so many on their face, that when they healed, they were pits. And so, he observed that milkmaids who had been infected with cowpox from milking cows were spared when smallpox came through the community.

PD: They weren't getting it when everybody else was getting it?

RC: That's right. You've got it. So, he said, "Why not use cowpox to prevent smallpox?" And he did and that was the beginning of the smallpox vaccine. Now, what this involves is using an animal virus which is closely related to a virulent human virus for immunization. You substitute an animal virus, which is attenuated in people to protect against the virulent human form, the human virus.

PD: That's assuming they both exist in nature for a given disease.

RC: Well, cowpox doesn't kill. It's a rather mild disease in cows so nobody thought much about it, you know. Milking and then, oh, look at this. They developed lesions, but they weren't sick. So Jenner substitute a virus closely related to smallpox derived from an animal for the prevention of smallpox. So we coined the phrase Jennerian immunization—Edward Jenner. Now Edward Jenner had a terrible time convincing people in the scientific community that this was a seasonable and safe approach, an effective approach to immunization. But he ultimately did, but there was still a lot of resistance. Terrible cartoons of a huge cow with lots of pox and so forth being brought into a room to immunize small children and all this sort of thing.

It wasn't anything that the scientific community and the community at large weren't prepared for this. But ultimately Jenner prevailed. And a very interesting historical side note is Jenner was elected to the Royal Society in England. The Royal Society is the progenitor of the National Academy of Sciences. It was the first august and highly esteemed assembly of scientists in England. Newton was a member and so forth. I mean this is really the scientific elite of England. And from what I learned, Jenner was elected for the discovery of a number of important bird songs. He was an ornithologist.

PD: But they wouldn't elect him for what he did . . .

RC: Not for what he did in the development of Jennerian immunization, but he was elected because of his prowess in ornithology.

PD: So you were comparing his techniques to what you used in the discovery process.

RC: Well, what we did was we sought an animal rotavirus that was attenuated in people that was related antigenically to human rotavirus and we settled on the, we had two candidates. One was a bovine rotavirus and the other was a monkey rotavirus. And that would make it fully Jennerian using a bovine virus. But anyway we tested the Rhesus rotavirus first and it was very attenuated, but it stimulated a high level of antibody. And it turned out that when we finally had the serotype scheme system, we finally understood it, the Rhesus rotavirus was serotype 3 and that is one of the human serotypes. There are four, there are 15 different serotypes and four of them are found very, the most, 95 percent of the viruses from infants with serious diarrhea are included in the first four serotypes. Serotypes 1 through 4 account for 95 percent of all serious rotavirus disease.

So, with Rhesus, we said that we thought that, well, there might be some, we thought that it was likely that there might be enough antigenic similarity or relationship between the Rhesus rotavirus and the other humans that we could just use one strain and so we did a study in Venezuela and it worked beautifully.

And we found out that later that the epidemic virus was serotype 3 and after that, it didn't work. We tested it in a number of situations. So then we decided to use a modified Jennerian approach, which was to substitute a gene for the major protective antigen of serotype 1, serotype 2 or serotype 4 to add that to the rotavirus to replace the major protective protein of serotypes, well, of the Rhesus rotavirus major antigen.

In other words, the Rhesus rotavirus has a type 3 protective antigen and we substituted a type 1 human, a type 2 human or a type 4 human for the type 3 serotype protective antigen of Rhesus. So we had ten genes from Rhesus rotavirus and then with an added, or with a replacement, serotype 1, serotype 2 or serotype 4 major protective antigen. So all of the four rhesus rotavirus strains have ten genes in common and the protective antigen is type 3 so we didn't have to make, we didn't have to modify it, but the others we modified through the process of gene reassortment.

And gene reassortment occurs in viruses that have multiple independent genes, like influenza and there are a whole series of other viruses that have each of its genes packaged separately. They're not lined up in a linear array of a single stretch of verheyenii. There are 11, it has a segmented genome, 11 separate genes. And the way we were able to replace the gene was by what is called gene reassortment. If you coinfect the cell with two viruses, which have each,

which have a segmented genome, all of the genes are produced, but they're packaged randomly, so you have all the possible combinations. And what you have to do is select from all of these combinations, the one you want and this is the same with influenza.

Influenza has eight genes and Ed Kilbourne a number of years ago developed a strategy for very rapidly moving a new virus that was producing an epidemic or possibly a pandemic by moving this virus into vaccine production. Before he discovered his strategy, viruses were discovered from an outbreak somewhere else in the world and brought here. And the manufacturer had to then modify the virus because generally these viruses didn't grow well in eggs. And they'd work and work and work and they'd lose a lot of time adapting the new virus to grow in eggs so that enough virus could be produced, you know, to have an inactivated vaccine. It had to be economically feasible. There's not an infinite source of eggs in the world, you know.

So what Ed did was to take a, to use an influenza virus which was well adapted to eggs and by gene reassortment replace the two protective proteins, the genes for the two protective proteins of influenza, replace them with a pandemic strain. In other words, he created a virus which had six genes that were involved in replication and all sorts of intracellular events and he replaced the hemagglutinin and the two protective antigens of flu with the corresponding genes of the new

pandemic virus or epidemic virus. So six genes have been constant over the years in inactivated influenza virus.

These are the genes that make the virus grow well in eggs and then you by certain manipulations you select for the 6:2 combinations, six genes from the well adapted influenza virus that grows well in eggs and the other two genes from the new virus that you're making the vaccine for.

PD: Hold that thought. I just want to turn the tape over.

[End Tape 1, Side A]

[Begin Tape 1, Side B]

PD: Okay.

RC: So what you have is, you have in rotavirus, you have a constant in the vaccine strains, 10 strains from the rhesus rotavirus, which confer attenuation and one gene from a human rotavirus, which confers the antigenic specificity that you're . . . so that virus will protect against human viruses varying that antigenic specific. And in flu, for the inactivated vaccine, there are six genes that are conserved in all strains that are used for the preparation of inactivated vaccine. And then

there are two more genes that come from the new epidemic strain and they are the protective antigens.

PD: Okay.

RC: So all, everything has to do with replication and adaptation. It's constant and you just have, you introduce new protective antigens into the vaccine. Now, in the next year or two, we will, we will most likely, very probably have an inactivate, a live attenuated vaccine for influenza and it's produced in the same way. An attenuated virus was produced by John Maassab at the University—it's M-double A-double S-A-B. John Maassab. He developed an attenuated virus by growing it at very low temperature and selected for highly, and then in the end, he had selected a highly attenuated virus.

This virus was studied by Brian Murphy here and really prepared for use in people. What the strategy for the use of this attenuated virus, which we will now call the donor virus, this virus donates its six genes, the genes that are involved in replication and also to things that happen in the cell and the other two genes are the protective, the genes that coat for the protective antigens of the new epidemic or pandemic virus. So it is exactly the same maneuver that Ed Kilbourne used for the inactivated vaccine. If you have a virus that has six genes that will attenuate or do all sorts of things that are very beneficial and beneficent

in terms of public health, all you have to do is update it when new strains come in and you do it by reassortment.

PD: And you're able to keep up with the new strains?

RC: Very quickly . . . but the point is that the attenuated vaccine is, I think, more effective than the inactivated vaccine and it can be produced in response to an epidemic or pandemic threat much quicker. And it produces a broader and a more durable immunity. So the company called Aviron has licensed this from John Maassab and from our Institute. And they did a big field trial two years ago and it was very successful. And they tested it in adults. And in children, it was 95 percent protective and it protected against otitis media, relayed that this induced by influenza. Do you have small children?

PD: No.

RC: Are you an aunt?

PD: Yes.

RC: Okay. Do you know how often your nieces or nephews have ear infections?

PD: Yes.

RC: And they have to go to the doctor and sometimes they have to pierce the eardrum and that sort of thing?

PD: Yes.

RC: Well, that's otitis media. It's otitis in the middle ear. Now, most of the otitis media is caused by a virus, which sets the scene allowing the bacteria to enter the middle ear. If you prevent influenza or paraflu or RS, you prevent otitis media. And in this big trial, they showed that influenza-related otitis media was reduced 95 percent. So mothers and fathers are going to be in a very good position soon where otitis media, which is the bane of their life. Some children have it three and four times a year for the first few years of their life. They're very sick and they scream at night and they have great pain and they have to be on antibiotics for a long time. And they have to sometimes drain the fluid and the middle ear and that sort of thing. Ultimately when effective viral vaccines are available, this disease will fade into the distance.

PD: Is this vaccine work being done in anticipation of another flu pandemic?

RC: Oh, absolutely, yes. One of the plans that we have here that Brian Murphy is working on is to prepare live virus suspensions that can be used as seed virus for

any virus that comes along. There are only 15 hemoagglutinins so, and only three to this time, only three of the subtypes, 1, 2, and 3 have been involved in human influenza. But a very ominous thing has happened in the last few years, avian viruses have been able to move into people in Hong Kong, type 5 and type 9. And so the plan is to prepare experimental vaccines for type 1, 2, 3, 4, 5, up to 15, have them all ready and test them in animals and maybe even in people so that you just push the button and vaccine production starts with material that's already certified.

PD: And it could ramp up pretty quickly?

RC: Yes. So that's the strategy for pandemic preparedness. But also, in terms of pandemic preparedness, there is other good news and that is that there are two or three antivirals that target the neuromiticides which is one of the two protective antigens and this has been done in drug companies in England and here as well and it's based on structural studies from Australia that define the structure of this neuromiticides and it's really, it's what's come out of this is a designer drug, knowing the structure of the neuromiticides drugs were fashioned so that they would fit into some parts of the neuromiticides and prevent it from doing its job.

And now they're licensed. And it's been shown, well, they've been used in therapy. Flu can be very severe and used in therapy, they're reasonably

protective, but they've also been used in families where there's a contact for the or there's, where one of the family members introduces, is infected with flu and this would ordinarily be transmitted to other members of the family with great facility. The giving the drug to family members for a period of several weeks very markedly reduced the occurrence of contact infection and disease in the family.

PD: Interesting.

RC: Yes, how do you like that?

PD: I like that.

RC: Yes. So the problem is who's going to make a warehouse full of this stuff and who's going to pay for it because it'll just be there on the ready, you see. It's going to be a difficult thing, but that's what should be done.

PD: But that's not likely to occur?

RC: Well, companies are not beneficent, you know, and the government has to do this and I don't think that they've thought that far ahead. But that would be the ideal situation. You would have a huge, huge storage area and you would have drug being taken from the facility and used during that year and then replaced at

the other end and just having it moving through at the rate that is determined by the amount of flu disease that is occurring, but have the material that is being stored there sufficient to prevent a pandemic in the United States. But that also, it's expensive, but it also would present tremendous political problems. We would be the only country in the world not to have a flu pandemic and there would be calls on us, "Oh, please release this." I don't know how that would, we have it within our power to really take the edge off of a pandemic now.

PD: But there are all these other considerations—financial and political and [inaudible] possibility.

RC: Yes.

PD: We had moved away from the discussion of the rotavirus vaccine. I mean, I had asked you sort of about the steps during the 1980s when you . . .

RC: Well, we tested with type 3 first and it worked in Venezuela and it worked. It was terrific. But then we saw the need for a modification in the Jennerian approach and that was by replacing the major protective antigen of the rhesus rotavirus with the corresponding antigen of type1, type 2 or type 4. Type 3 wasn't required because the rhesus was already a type 3.

PD: This is all in the late '80s, when you did this modification?

RC: Yes. And, and we did many, many trials and the vaccine was licensed in '98 and then it was dealt an almost mortal blow by CDC [the Centers for Disease Control].

PD: A few months later, correct?

RC: No, no, it was about nine months later. And they had done, they had analyzed the occurrence of intussusception to the vaccine. and we think that they did a faulty job. And we have now taken another approach which is to study a large population for a study of any increase in intussusception and we can't find it. So now, it's, we're sort of butting heads with CDC. And we think we know why they have miscalculated, misestimated, but they don't listen to us at all.

PD: So the current status of the vaccine is it's off the market with the possibility of it coming back on or?

RC: It's not off the market. I was in a meeting recently downtown, a meeting of the national vaccine program and we had a discussion similar to the one we're having here now and the CDC people said, "We took it off the market." And the FDA representative said, "You did not take it off the market. It is still licensed."

What they did was they removed the recommendation of their CDC Advisory Committee that the vaccine be used.

PD: What was the effective result of their doing so? Did parents stop?

RC: It's dead. The manufacturer retrieved all the vaccine that hadn't been used and so forth. They were worried about litigation and all this other sort of thing. So we think that, there's an ongoing study now to include more and more and more people for this analysis where you actually analyze that, this is work being done by Lone Simonsen in the Deputy Director's office. We've analyzed . . . she has analyzed six states, the six states that received the most vaccine. And the birth cohort, that is, the children who were one year of age during that year represents about 600,000 infants.

And our analysis shows, her analysis shows actually, that the amount of intussusception was the same as the year before, before the vaccine was used. And he, actually, two years before, three years before, four years, five. And now she's analyzing the year after the year of use, the year before and the year after being analyzed in every possible way. And there's no evidence of increased risk.

And we think that there's an explanation for this and that is that the vaccine might cause as very small number of cases in children who are just ready to become intussuscepted. Intussusception is the telescoping of the small bowel into the large bowel.

And there are many thoughts about the etiology. Nobody knows for sure what is the exciting cause, but it's thought that it's most likely an enlargement of the lymph glands in the intestine, which creates sort of a leading edge when the intestine is moving, when things are moving along the intestine, which is called peristalsis. The regions that have these big lymph nodes are sort of pulled along and then they're pushed into the large intestine and stoppage occurs at that point, but it can be reduced without surgery.

Most of the cases are being reduced now without surgery, but in the old days, they just would go in and pull apart and there were no deaths at all among these 600,000 kids. Now, if this highly attenuated vaccine produces intussusception, the virulent wild type virus which is circling in communities should do it even more often and there's no real agreement that rotaviruses are an important cause. They may be a minor cause of intussusception and what Lone found was that among the young infants, there was a very small increase, but over a period of a year, there was actually a ten percent reduction and we think what happens is that it may, the vaccine may identify children who are about to become in inception cases so it telescopes these events to a period just after immunization.

However, it's protective effect over the next eight months is sufficient to produce an overall reductions of 10 percent, so that the small number of initial cases, of

vaccine-initiated cases is subsumed in to a much larger group where there's a big reduction.

PD: So, NIAID is actively working to improve that vaccine?

RC: We are busy little beavers, I'll tell you. It's been very hard because CDC has been very uncollegial . . . noncollegial . . . not collegial.

PD: But you are continuing to go back and forth in terms of?

RC: Well, we can't. Al Kapikian e-mails them almost every day and they never write, they don't answer, they never miss it. You know, that's the plaint of a Jewish mother. "My son never comes, never visits, never calls, never writes, you know?" You know what I mean? I'm sure it's true for every other ethnic group, too—never writes, never calls, never visits. So we just, we can't reach these people and they just think that what we're saying is nonsense. They are focusing on this one small window and that's the way they work—the little window after immunization. This is a dynamic system. All these things are happening, you know, and what we like to emphasize is it's the total attributable risk.

PD: If you take all the children who are in the group that received vaccine and you study them for a year—this is the time when most intussusception occurs, is there any increase?

RC: No. There's a 10 percent decrease.

PD: So what other audience are you speaking to to make this . . .

RC: Well, the National Vaccine Program, which is separate from the CDC, but unfortunately folded into it, but they're listening and then there are going to be other things happening. There was a paper that was submitted to *Lancet* that will be published soon. But the CDC people just don't understand. They're slow learners. They should be in the room, what do they call the room?

PD: The remedial class?

RC: No, the uneducable or whatever it's called. There's a special name for that room, you know, children who can't be educated. They just don't understand. This is a small part of CDC. It's not, we're not out to trash all of CDC. We just feel very uncomfortable with this group that deals with the recommendations. They just don't understand and they won't talk about it and they wouldn't share data with us at all.

PD: But you are continuing to . . .

RC: We're generating our own data. Yeah. We're doing to ultimately end up with 22 states, 80 percent of the birth cohort. That's three million infants. And there's a system called HCUP.

PD: Hiccup, as in h-i-c-c-u-p?

RC: It's H-C-U-P. It's Health Care Utilization Program and they receive all of the discharge summaries from all individuals hospitalized in, in the state. So we're looking for that we use that as a way of tracking intussusception. It doesn't account for all the cases because in many cases, the condition is reduced when the x-ray man gives the barium enema, the intestine gets pushed back up to where it belongs. But the point is that the intussusception that we're studying represents the children who go to hospital and leave with that diagnosis. But it's the same for vaccinees and non-vaccinees. It's not selective. We haven't introduced any sort of fudge factors or anything like that. So that, that's the way it's being done.

PD: Well, I want to ask you a number of other questions. One of them, looking at the bigger picture is to discuss your accomplishment in the broader context of this

laboratory and its legacy as the most direct descendant of the Marine Hospital Service Research Laboratory?

RC: At Staten Island.

PD: Yes.

RC: Yes. Dr. Kenyon's.

PD: He started in 1887, I believe.

RC: That's right.

PD: So you've been here at LID and NIAID almost the entire span of the Institute since it was established in '48 as the National Microbial Institute.

RC: Yes.

PD: What are the changes you've seen here?

RC: Well, I thought you were going to ask me why did I stay so long, because I . . .

PD: Well, you can answer that, too.

RC: I have no imagination. (LAUGHTER) No, it's been just such a scientist-friendly environment. We've been supported and supported, you know, royally, regally. And we've never lacked for support. Our limitation has really been our, our ability to formulate, or to recognize problems before they become too large or after they become too large and develop a strategy for understanding what's happening and intervening and this sort of thing. And we've never lacked for support. I mean the limiting factor is our imagination, our ability to understand, analyze, project, and so forth.

PD: When you say you've never lacked for support, do you mean financial, logistical?

RC: Financial. We don't have the world's greatest space here but we've worked in it for forty some years and unfortunately, we're going to a new laboratory, which may be more sumptuous, but I'm not sure it will be any better than what we have here.

PD: When are you moving and where are you going?

RC: In a couple of months. Building 50, right down the road.

PD: What are some of the major changes you've seen in the time you've been here?

RC: Well, the Institute has grown significantly and I think the AIDS epidemic certainly played a significant role, but we've been able within the laboratory, you know, to obtain support that doesn't come from appropriate funds. Manufacturers, pharmaceutical companies, we have a number of interactions with pharmaceutical companies, which are called CRADAS.

PD: Craddas?

RC: C-R-A-D-A. Cooperative Research And Development Agreement. And we actually collaborate with them after we have established, after we have prepared a CRADA agreement that is acceptable to NIH and to the manufacturer. And we state in this, we state the scientific plan, the plan for research and then the apportionment of responsibilities. In the CRADA, we state, we will do this, we will do that, we will do this, we will that. And then the manufacturer agrees, we will do this, we will do that and so forth. So everything is spelled out ahead of time.

There are no surprises. Monies flow from the pharmaceutical companies to the laboratory, but not in the other direction. So they provide us with additional funds to support the clinical research where the various vaccines, the candidate vaccines are subjected to clinical trial and all that sort of thing. And we actually have more people now who are supported by CRADA. We have scientists who

are paid through the CRADA mechanism—technicians, equipment. So we have sort of leveraged what we do here through the CRADA mechanism.

PD: Is the CRADA mechanism ubiquitous throughout NIH or is it just in your area?

RC: Well, anybody can play if they have something that is of interest to the pharmaceutical companies.

PD: How has that worked out, then? Has it turned out that this laboratory . . .

RC: Well, many other labs are doing the same thing. But what we do is we advertise, we advertise for a CRADA partner and we, we announce what we've done and what we can't, what we plan to do, and we look for a partner.

PD: And you've had several.

RC: Wyeth, Smith Kline for the hepatitis studies. Bob Purcell upstairs. So we've had, we've been very successful. And it's a considerable amount of money. It's maybe a third of our appropriated funds. It's equivalent to a third of the money that Congress appropriates.

PD: What are some of the other major changes you've seen in the time you're been here?

RC: Well, a deep concern and involvement and understanding of technology transfer. So, for example, we've, we have patented many of the things that we have done here because we are enjoined to do this. There was a law passed, oh, gosh, maybe twenty years ago called the Bayh-Dole Act.

PD: Bayh-Dole?

RC: Birch Bayh and Robert Dole. And this law said that we were not to be encouraged to collaborate with industry. We are directed to do this to facilitate the transfer of basic research results into the clinic. So if we sat here with a wonderful vaccine candidate and didn't do something about it, we would go to jail, or something similar to that. We have to do that. And I believe that was very far-seeing on their part, because there's been a tremendous increase in collaboration. Before that the people in the pharmaceutical industry just didn't want to talk to us and see us because there was no way in which they could benefit, you know. Inherent in this, in the CRADA system, or at least understood by the pharmaceutical industry is that if they perform well and we interact successfully, they will obtain a preferential license for the use of the product, not for the use, but for the manufacture and use of the product.

PD: So, are CRADAs spelled out in the Bayh-Dole Act? Are they linked?

RC: No, they came later.

PD: Which came after? The CRADA's came after the Bayh-Dole Act?

RC: Well, there was how do you do it? Then the CRADAs came along.

PD: Okay, and when was the Bayh-Dole Act passed?

RC: Oh, gosh, it was probably around 1980 or something like that.

PD: So that's a major change.

RC: Oh, yes, before, we couldn't do anything with industry. They didn't want to know us and we couldn't know them. There was no way we could interact, you see.

PD: But in many ways, it seems as if this arrangement sort of . . . it helped you fulfill your mandate. I mean, this is the original public health system.

RC: We're in the public health system, exactly.

PD: So it's a modern-day facilitator in carrying out your mission.

RC: Yeah. That's right. So things moved much faster from bench to the bedside.

PD: Okay.

RC: It's interesting. Congress has increased the budget of NIH again this year and I think over a period of five years, we will have doubled our budget. But they've also provided, they've also asked us to do things that we haven't done in the past. Do you take any medical journals or anything?

PD: I don't.

RC: Well, *Nature Medicine* has a description of this just this last month. And Congress has instructed NIH to summarize their success in various areas, mainly in areas where cooperation is involved. And they want to have a report next year before the appropriations are being, will be considered. What has been done by this Institute or that Institute in terms of moving products beneficial to health through the system and into the clinic. And they want to know about, they want to know in detail about products that are, that represent, let's see, products that have an economic value to the manufacturer greater than a half a billion dollars.

PD: Half a billion.

RC: Yes. They want to know how many of those products are coming from each Institute.

PD: This is a first-time request?

RC: Yes, that's right. They must, each Institute must report before the next appropriations hearing. That's, you know, in the next, before the next fiscal year and they have to tote up their successes and maybe describe their failures and all this sort of thing. It's interesting. So this is one step beyond Bayh-Dole. You don't just say, "This is what you have to do." They're going to check now, very specifically.

PD: It's, they're formalizing that procedure.

RC: Yes, in other words, you guys want to have your budget doubled in, and, you know, within this five-year period, next year, you're going to have to tell us about this, this and this. How do you like that?

PD: Well, it's holding everybody accountable.

RC: It's very explicit, very explicit. And we actually have a, from this lab here, we have a license, we have licensed a product, or a product of research to a company which, this year, I think will sell, will have sales of 427 million. They're just a little ways from half a billion. Next year they'll be like 600 million dollars. This is the monoclonal antibody that's used for prevention of RS virus disease in high-risk infants, Synagis™, the Medimmune product.

PD: And so you won't have to report that until it reaches the half billion mark?

RC: Well, no, we don't report it, the Institute, but next year, we're going to have one because the projected sales to Synagis™, six to eight hundred million dollars last year.

PD: Wow! I wanted to also ask you about some of the people you've trained. You're the leader of the nation's largest program for developing new vaccines. You've trained a number of other leaders. Who would you say are the most notable? Talk about where they are now, what have they accomplished?

RC: Oh, this is for attribution.

PD: It is for attribution.

RC: I'd really rather not rank people.

PD: Okay.

RC: I'd say we've had some really outstanding people. The people who have remained in the lab are outstanding. Al Kapikian is the father of viral gastroenteritis as well as being an outstanding world, world renowned epidemiologist. He was President of the Epidemiologist Society two years ago. This is an organization that is so elite, arcane that most people don't even know it exists. But he's terrific. He's a very humble person. If you asked him this, he would blush. So don't.

Bob Purcell is probably the most important person in viral hepatitis. Let's see, A, B, C, D—there are five hepatitis viruses and he was responsible, together with Al Kapikian were responsible for identifying hepatitis A. Bob developed the first experimental vaccine that showed it was possible to protect against hepatitis B by immunization with the surface antigen of hepatitis B, by studies in chimps. He and Al Kapikian discovered the hepatitis C virus, the non-A, non, first called non-A, non-B. It was by exclusion. Bob discovered the nature of hepatitis D and he identified the syndrome of hepatitis E. It now has a vaccine that is going through clinical trial that will probably be put, but this is a very important cause of hepatitis

in other parts of the world, not in the United States, but it's very important. So, that's a lot.

And then Brian Murphy is head of the respiratory virus program now and he, actually, is the person responsible, I think, for the development of the live attenuated flu virus.

PD: He led that charge?

RC: Yes, because there were laboratory studies. He did the appropriate clinical studies that answered the questions that had to be answered. It's an incredible job. He is now in charge of the RS and the paraflu vaccine efforts.

PD: Okay.

RC: And then Peter Collins is the molecular biologist, who is probably at the top of his field. We worked on respiratory syncytial virus. And he's the person who after ten years succeeded in developing the rescue system for RS. The things I was telling you before, you know, it sounded so easy. It took him ten years. No one else was able to do it. So now we have all kinds of mutants made to order. We have paraflu mutants made to order because we can, these viruses are fifteen thousand basis nucleotide small. And he has developed the strategy for using complete CD&A copy to rescue a virus or mutants of the virus. And he's got

mutants coming out of his ears. We have a big CRADA with Wyeth and this, he's producing them faster than they can make them or test them.

PD: Interesting.

RC: Yeah, and Brian is working on paraflu and actually using paraflu as a vector. The other thing you can do now—I didn't go into this—with these long RNA viruses that are not segmented, you can introduce additional sequence. You can put other genes in. Just open it up and put them in. It's a bigger virus, but it is viable. It works well. And he has, he has introduced the measles hemagglutinin, the protective antigen of measles into, into paraflu, paraflu 3. And the reason for doing that is measles eradication is going to be a little more difficult to achieve than polio because the attenuated measles vaccine can't be given until 15 months of age because the antibodies that the mother passes to the infant, there are still enough of those antibodies around that the attenuated vaccine can't replicate.

You can't immunize until after about 15 months. But, if you go into the upper respiratory tract, the effective passive antibodies is diminished considerably. They don't protect up here very well. So, his strategy is to use para three as a vector, something that it'll be a virus that carries another gene and that would be the measles gene, the measles protective antigen. And he's able to immunize

monkeys so they develop a very high level of antibody to paraflu and measles at the same time.

PD: A double vaccine.

RC: It's like Doublemint gum, it doubles your pleasure.

PD: That's interesting. And that was Dr.?

RC: Murphy.

PD: Murphy. So you've named Drs. Kapikian, Murphy, Purcell and Collins. Are those the notable ones still in house?

RC: Yes. We've had really wonderful people who didn't stay. For example, John Mills, the person, he came from Harvard, actually, took a year off while he was in medical school and worked in the laboratory and Bernie, Bernard Davis, the Chairman of Microbiology at Harvard. And he came almost fully armed. I mean, he knew how to do research. Most people come here not armed at all. You know, you learn on the job. John was here for a couple of years and then when he left, Brian replaced him. John is now the Director of the McFarland Burnett Center in Melbourne, Australia. McFarland Burnett is one of the most famous scientists ever produced in Australia. He won a Nobel Prize and he was one of

the great virologists-immunologists and this research institute is named after him and John is in charge of that now, so he's doing very good work.

One of the . . . Doug Richman was here. Douglas Richman, who is in San Diego. He's one of the leaders in AIDS research. He was here, he came at the same time Brian came and then he went back to California. He came from Stanford originally. He's an absolutely outstanding guy. He's probably one of the most credible people in clinical investigation in AIDS. Douglas Richman.

Harry Greenberg was here about that time, too and he, he left, oh, actually, he left and went to Stanford and then came back here and was very active in the early rotavirus studies. In fact, he was the first to demonstrate the use of gene reassortment to make viruses to order, you know, the way I described to you. He described that. That was the basis of the patent for the reassortment virus vaccines. Then he went back to, after, he was here about eight years, I think, and then he went back to Stanford and a couple of years ago, he was appointed the Dean for Basic Research at Stanford Medical School. Now, he's on leave and he's on leave and he's the Vice President for Research at Aviron. That's the company that's developing the live attenuated flu vaccine for commercial use.

PD: Do you have a CRADA with them?

RC: No, no, no we don't.

PD: You don't. So, any others?

RC: I'm just trying to think, well, those were the first to pop into mind. Oh, interesting, very interesting little diversion here.

PD: Okay.

RC: A couple of weeks ago, my wife and I went up, a couple of months ago, my wife and I went up to Boston, or Baston.

PD: Careful, I'm from there.

RC: So's my wife. She's from Lexington.

PD: I'm from Swampscott.

RC: But anyway. Ken McIntosh is one of our outstanding people, Kenneth McIntosh. He was the Chief of Infectious Diseases at Boston Children's Hospital, which is the pediatric division of the Harvard Medical School. And Ken's study was here. He started his career here and then he went to Boston and he was chairman of . . . chief of Infectious Diseases and he retired.

He was retiring and the person that I sat next to was one of our great alums, Ray Dolin. Raf Rayfield. Ray Dolin, D-O-L-I-N, who was involved in the Norwalk studies. He was involved in the volunteer studies that we did that showed that the Norwalk, the material from the Norwalk outbreak, when filtered through a bacterial-type filter produced a, produced the Norwalk disease in volunteers and that was the start of gastroenteritis research. Ray was here and he, then when he left, he went up to Boston and did some more clinical training and then he went to University of Vermont as Chairman of the Department of Medicine in Burlington. Then he went to Rochester and he was Chairman there until just a few months ago.

PD: I hate to cut you off, but I think we're going to run out of tape. I'll make a note and we'll pick up where we left off.

[End Tape 1, Side B]

[Begin Tape 2, Side A]

PD: All right, this is Tape 2, Side 1 of an interview between Peggy Dillon of History Associates and Dr. Robert Chanock of the National Institute of Allergy and

Infectious Diseases. This interview is being conducted February 23, 2001, in Dr. Chanock's office at NIH.

RC: You should say "luxurious office." (LAUGHTER)

PD: Luxurious office.

RC: Watch out, that shelf is going to come down on you. (LAUGHTER)

PD: Well, you were talking about Ray Dolan.

RC: Dr. Ray Dolan. So Ray left the University of Rochester in just the last couple of months and is now the Dean for Clinical Affairs at Harvard Medical School. He's the second ranking dean there.

PD: Pretty good.

RC: So we have friends in high places. And while we were having dinner, he said, "And by the way, do you know who the new Director of Admissions is, the Dean for Admissions?" Dienstag, an alumnus of the laboratory.

PD: Really.

PD: D-I-E-N-S-T-A-G. Jules Dienstag. And he worked in hepatitis. And he worked with Bob Purcell and he was here for two years and he published twenty-two papers. He wrote so many papers that the secretaries couldn't keep up with him. He had to stay over at night and type his own papers. Wonderful fellow and he went back, he went to the Massachusetts General, which is one of the prized of Harvard hospitals, as you know, and he's now the Dean for Admissions. So two of the three deans at Harvard came through this laboratory.

PD: Are alums. Wow! So you've sent them out into the world.

RC: Oh, yes, someday they will all rise together and take over the biomedical staff issues.

PD: Sounds as if they are already.

RC: Yes.

PD: Which of your mentors made the biggest impression on you and why?

RC: Well, I had two mentors, obviously, Albert Sabin and Bob Huebner, and they were diametrically opposites. You know, I mentioned this before.

PD: You did, some.

RC: Albert Sabin, the solitary scientific giant, and Bob Huebner, the first of the great entrepreneurial scientists in biomedicine. And they taught me an awful lot. And they were both, they both inspired. There's just no question. Albert inspired, you know, by the rigor of his, of his research and by his ability to analyze and project and to move against great odds and so forth. And Bob Huebner inspired so many people, people who were just sort of doing things halfway. He galvanized them, excited them, raised them to a very high level of energy, so they became leaders. He was just an incredible man. And he did it without threatening or pressuring. He just did it by the sheer force of his intellect and of his enthusiasm.

PD: You've been here at the Laboratory of Infectious Diseases long enough to have become its institutional memory. I'm curious as to whether you worked with other scientists here or at NIH to talk about things that you hear about that remind you of some development that happened years ago. I mean, do you hear of work being done that makes you want to contribute something from years ago?

RC: Well, we've worked with, with Bernie Moss, Bernard Moss, who is the father of the vaccinia vector approach to immunization, probably the world's authority, the world's leading scientist in the area of pox virus research. And he's helped us tremendously and we've worked with him using various genes from various

viruses that were vaccine targets, thinking, using vaccinia vectors to express these. And we've really done a lot of work with him, but it hasn't led to any final solution, but he's a prince of a person, extraordinarily effective mentor. He has about 40 people that he's mentoring simultaneously.

PD: Where is he?

RC: In Building 4, Bernard Moss, he's wonderful. He's a member of the National Academy also and he's absolutely outstanding. There are a lot of other wonderful people here, not necessarily in our Institute. There's John Robbins, who's the father of more bacterial vaccines than I think anybody else in the world today. And he's in the Child Health Institute. And we talk a lot and we interact. We don't, we haven't worked on anything together, but he's a delightful, reverent, right-on-target person who has an extraordinarily high success rate. And we talk a lot. He calls me and we talk a lot. He's interested in our problems. I'm interested in his problems. And we haven't done anything together, but we just sort of have bonded.

We have Lou Miller, who is the Chief of the Laboratory of Parasitic Diseases, Tropical Diseases, and he's a malariologist and he's also a very valued colleague. And then his predecessor, who's still in the lab, Frank Neva, is a very old friend. Frank was Director of the, Chief of the Laboratory of Tropical

Medicine for many, many years. And he sort of reversed the flow when people were leaving here to go to medical schools—Harvard and so forth—he left a chair position at Harvard to come here. So, our Institute is probably the best-positioned institute now in terms of achievement and, you know, the prospects for, you know, future achievement. It's a very all-star group.

The immunologists I can't, I can't speak for their proficiency, but they're highly regarded by other people. They live in a different world than their own. We've had magnificent scientific directors, that is, directors of intramural research, just wonderful. John Seal was the first one. He was a Navy captain who retired and he had actually established the Naval Medical Research Unit, NMRU unit in Cairo for the Navy. And during the three-day war when the Egyptians broke off diplomatic relations with the United States and maintained that position for a long time. But NMRU, his NMRU unit just continued on. They just wore civilian clothes, because they were doing such wonderful things for the Egyptians, you know, and for the United States.

And John actually came from, and he was just wonderful. He was the, he became the deputy director, I think, under Richard Krause, who was the Director of the Institute before Tony Fauci. And then he, John Seal was followed by another retired Navy captain. John Seal was followed by Kenneth Sell, who was also a Navy captain, who retired. And he retired from the position of director of

the Naval Medical Research Institute, across the street, NMRI, it's called, I think. And Ken was here for, for a number of years and very supportive.

We never lacked for money, for equipment, and so forth. We just, sometimes we lacked imagination and intuition and ability to think, you know, to think a problem through, but that's where the limiting, those were the limiting factors, you see. And then Ken left when Tony Fauci became, when Tony Fauci became Director, Ken Sell went to Emory as the Chairman of the Pathology Department. He died about a year and a half ago. He was a super guy. And then he was followed by John Gallin, G-A-L-L-I-N, who also, was totally supportive. John was from the, came from our Intramural Program. He was a Lab Chief, Chief of the Laboratory of Host Defenses. He was a sort of a clinical immunologist. And presently, he is the director of the Clinical Center. John Gallin.

And then followed, when John left to become the director of the Clinical Center, Tom Kindt, Thomas Kindt, K-I-N-D-T, was appointed the scientific director or directorate. He's called Scientific Director by some people and by others Director of Intramural Research. He was a lab chief, an immunologist, immunogeneticist. He's been totally supportive. We've never had any pressure from, or we've never, there's never been any substantive disagreement or, or difference of opinion. We don't worry about moving in the direction opposite of that that would

be, you know, accepted by the, or approved by the, or disapproved by the scientific director. We've always thought as one and it's, never had a problem.

PD: So it sounds as, as if in terms of resources and direction from above, it's been almost a Golden Age.

RC: That's right.

PD: Do you think that's a function of the era in which you've, I mean, the post-War era or the luck of bringing people in?

RC: Well, I think our Institute is fortunate in that the directors and the scientific directors have not attempted to direct research at the laboratory level. We've been given sort of free reign to choose our topics of interest, the topics of research and so forth. But when we do, when we go into here, they support us and it's wonderful. It has been wonderful. So I've never felt any pressure to go to the outside. There was a brief moment when I thought I might go to Yale.

PD: When was that?

RC: This would be 1980. They wanted me to come to Yale to be the Director of the Institute, their Department of Epidemiology, which was really a School of Public

Health. They wanted me to be the Director of the School of Public Health. And it was very appealing. I mean, I had been here enough, long enough time to be able to retire from the Public Health Service and it would have been advantageous in terms of salary and all that sort of thing, but I'm glad I didn't go.

PD: What made you decide to stay?

RC: I don't know. My wife and I came back from several trips up there and every time we came into the house, we said, "We can't leave." And my son was just starting medical school and he came and joined us when we, you know, went around, we were, we spent a number of days up in New Haven. The man who was the, the head of the School of Public Health was Bob McCollum, who was a very close friend of mine. We were, we were together in Japan during the Korean War. And he was a protege of John Paul, who was the, sort of one of the ranking virologists in the world, who really, was one of the most highly respected people. He wrote the history of poliomyelitis.

He was a very important figure in poliomyelitis research and when John retired, they appointed Bob McCollum to be the director and Bob was director for about ten years or so. And then he was invited to come to Dartmouth and he was the, he was recruited to be the chief of the, the Dean of the Medical School. In fact, it was his wife who discovered those . . . two faculty members who were killed,

they were neighbors of the McCollum's. You remember the doctor and so on, that was Bob McCollum.

PD: Well, how about that.

RC: So one of the things that happened, I, well, the man who was the vice president of Yale was Bob Berliner, who was the Director of Intramural Research for the entire NIH for many years and he wanted me to be the Director of the School of Public Health. So we went up and I, I knew they were serious when I received a call from New Haven. I went with Bob Berliner several times to the various facilities, the gym, the gymnasiums and so forth—wonderful facilities there. They have huge, I think it's the Vanderbilt gym or something like that, named after some very rich person.

PD: A Vanderbilt!

RC: A Vanderbilt, or an equivalent, and they had three pools, but the major pool was a huge swimming pool and it had about twelve lanes, but there were four or five people in each lane. And each time we went, I said, I said to Bob, "I can't swim like that. I need a whole lane to myself. I swim backstroke." So we came back from that trip and I got a call from New Haven. It was the swim coach at Yale. He said, Dr. Berliner has talked to me and I guarantee you that you'll have an

open lane designated for your use exclusively if you come. That was the thing that really ruined it.

PD: They wanted you.

RC: Yes. They have a powerhouse swimming program. You know, they've had a great history of Olympic swimmers, and it's one of the great places for swimming. And my wife knew about it because she went to a camp in Maine, where Bob Kippith, who came very often. Bob Kippith was the legendary swim coach at Yale for about thirty years.

PD: They really wanted you, Dr. Chanock.

RC: I sort of figured that out. I agree with you. That was, well, that we pretty tough to turn down.

PD: Your own lane?

RC: And this gym, my God, can you imagine how strong the foundation had to be to have this. This was on the third floor, the largest pool. Twelve lanes and five, six people in each lane churning away. So I would have had to go in early, but I

would have done it. I swim early now, anyway. So, but that was very tough to give up at the time.

PD: I just want to talk a little bit more about the heritage of this lab. It represents the oldest continuous link, the original lab. How do you think its mission to improve public has changed, stayed the same? Talk about how that evolved over time.

RC: The goals are the same. The technology changes and the opportunities are increased. I mean, now that we can rescue viruses from [seed], complimentary DNA, we can do anything with a virus. It's just, it's incredible. Paste pieces of two different viruses together, which is what the chimeras are. We can substitute. We can add to, we can take away from. Before we had to take what we, what we received, what value, by putting viruses in very drastic, treating them to very drastic, in a very drastic way so that [abuse] that would be favored by that sort of selection would pop out and then we could identify them and use them. But now, we're in charge. We're in charge.

PD: And you said that the goals had remained the same. If you would just summarize them . . .

RC: That is to study infectious, identify the etiologic agents of the etiology of diseases that have not been understood before, to learn how the agent, to bring the agent into the laboratory, characterize it as best we can, and then determine what, what

is important in protecting against that and then doing it and testing it and then going on to something else. We, we just started a program at West Nile and the plan is to actually, we've, Dr. Plentev, P-L-E-N-T-E-V, has succeeded in producing a viable West Nile dengue chimera. It's, the virus is dengue except for the two protective antigens and it's West Nile. So we will be going into a vaccine in a moment here. We're going to shift gears and evaluate this as a potential vaccine for West Nile.

PD: So the goals are the same, the technology has changed. Is there a central thread that you would say has held this lab together over the years?

RC: Well, it's the ability of scientists to carry out long-term research and to start the program and finish it. Sometimes it takes 10, 20, 30 years and it's very hard to maintain that sort of continuity in academia because you're scratching for money all the time.

PD: You were saying earlier that sometimes the limitations here were those imposed by your imagination . . .

RC: Yes.

PD: And yet, the lab's had a lot of accomplishment, so . . .

RC: Well, the point is you don't bat a thousand, usually. You bat two to three hundred if you're really good. Albert Sabin must have batted eight hundred or nine hundred, really. He was incredible. Whatever he set out to do, he did and he found a lot of things along the way.

PD: Well, to the degree that you have been successful in this lab, what do you think accounts for that?

RC: Oh, I think it's a mix of people. It's a mix of, in the mix, you have to obviously identify the fact that we operate without pressure from above. We're free to choose our goals as long as they're within the limits of an important health, as long as they're within the limits that are defined as "public health"—major problems, situations in public health—have to be involved in some way in the, in the equation. What we're doing has to be directed towards the major solution of a public health problem. We don't just sit here and sort of contemplate and diddle around. We use everything we have to solve major public health problems, no matter what the, what is required.

PD: Which development would you say has had the most significant impact on public health in the time that you have been here?

RC: Well, the discovery of mycoplasma pneumoniae and the identification of, well, and the demonstration that the organism was not a virus. It was a mycoplasma that could be treated by tetracycline therapy, that was very important. The development of the live adenovirus vaccine was very important in terms of military medicine and the potential applications of that strategy to prevent adenovirus diseases in the civilian populations, which has not been exploited by the pharmaceutical companies. They want a billion dollar product every day, you see, and I don't think that, they don't think about how much disease can we prevent or anything. Can we ultimately, at sales of a billion dollars or whatever.

But the military has found that to be extremely important in their control of, in their, in the maintenance of a healthy recruit population. The RS virus program when it finally comes to fruition, the vaccine program will be extremely important. The rotavirus vaccine was extraordinarily important, not as much in the United States as in other countries, but in the developing countries, a million infants can be protected. Hepatitis, hepatitis vaccine developed by Bob Purcell with Smith Kline, CRADA with Smith Kline. The, the RS monoclone, which was, had sales of 427 million dollars last year and it's just in the United States. They're licensed in Europe, but they haven't started selling there. Make a big difference. RS, the RS virus is a very important virus and it particularly picks out infants who are compromised, premature, who are born too early so their lungs are not fully mature and all that sort of thing.

PD: You've been extremely vocal about talking about a number of public health issues outside of the Institute. Can you talk about some of these issues that you find unduly neglected.

RC: Well, pandemic preparedness is something that I think has been neglected very seriously. It's a very serious problem. It's a potentially very serious problem. It could be devastating. If we had a repetition of 1918, we could have, there would be a million and a half people die within a period of a few months. There were six hundred thousand who died in the 1918 outbreak when we had only a hundred million people in the United States. If strains similar to the H-5, hemagglutinin-5, subtype 5, from Hong Kong ever really developed wings, that is, developed the ability to spread from infected people to contacts, to their contacts—people taking care of them in the hospital, family members and so forth, this could be devastating because that virus, which came from birds directly into man was the first time, that spread directly from birds to man could occur and that virus in birds has a 95 percent mortality.

And it if really, if it just continued to mutate so that it became better adapted to humans, was able to, and could be transmitted, it would just be the biggest disaster in the history of the universe. So pandemic preparedness is extraordinarily important. And we've talked about it with people in other parts of

the institute, that is, you know, in the extramural program. They just have meetings, but nothing happens.

PD: Is there a groundswell of activity to prepare or are you . . .

RC: Well, we're actually supporting, one of our graduates, Kanta Subbarao, who is just, he's a wonderful laboratory scientist, certified pediatrician and so forth, worked with Brian on the live attenuated vaccine. She's now at CDC and we are providing her with money to do this out of our budget. And Aviron is also interested in this, so we're going to make the effort to prepare experimental lots of live attenuated vaccine representing the various hemagglutinin serotypes.

PD: So you'll make them available?

RC: Oh, of course we will. We'll make them and test them and then we'll, then it's up to the pharmaceutical industry. And they won't respond. But the point is if we have them and they can be activated quickly, accessed quickly and amplified into, you know, the process of vaccine manufacture, we will have done something.

PD: So, influenza pandemic preparedness is one.

RC: That's outside, yes.

PD: Haven't you also spoken out about ways to deal with the West Nile virus?

RC: No.

PD: You haven't been involved in that at all?

RC: No. I don't speak out. I just speak. (LAUGHTER)

PD: Okay.

RC: The other thing that I've been involved in that's not in the province of this Institute is the problem of viral terrorism and bacterial, and microbiological warfare, bacterial, biological warfare. I'm a member of a subcommittee of the National Academy and we've spent a lot of time meeting with the Russian scientists from the Soviet Academy. And we've had a lot of talk, but nothing much has happened. I know more about what's happening there now from reading the newspapers than I do by attending meetings in which we have discussions. Think about it, you read *The New York Times* everyday, you'll see an article once a week that, you know, mentions this. Sometimes it features biological warfare and that's a very serious, very serious problem.

PD: Across the board or with certain kinds of organisms, smallpox or?

RC: Well, anthrax and smallpox seem to be the two leaders, right, I mean, the two most likely possibilities. And I went to a meeting of a group who said they were going to talk about this. And there were a lot of people there and we talked about this and then none of, just a lot of discussion and nobody summed up the meeting and now they want me to come to another meeting in a month and I'm not going to go. It's just, I don't want to sit around and talk. I think we ought to establish a strategy for assuring that enough of smallpox vaccine is made that if anybody unleashes it, nobody will be protected, we can be protected. It's a terrible prospect. The man who eradicated smallpox, D.A. Henderson, Donald A. Henderson, was with the Public Health Service at CDC and he was secunded to WHO and, in 15 years.

This was a junior person and after 15 years there, he finished, but he was responsible, the program had finished when the eradication of small pox was certified. And he came back to the United States and he was Dean of the School of Public Health at Johns Hopkins. He's retired from that and he's now set up a Center for Bio-Preparedness, Biodefense.

PD: Wow!

RC: And he's presented a number of scenarios that, which are reasonable and certainly represent things that could happen if a terrorist group introduced a few patients who, a few people who, were experimentally or purposely infected with smallpox and they went to hospital and weren't recognized. That's happened. Just before the eradication was certified, there were two outbreaks in Europe—one in Yugoslavia and one in Germany. Somebody came back from the Far East. It was Bangladesh in one case and Saudi Arabia in the other case. These two individuals were, had been immunized with smallpox vaccine 20, 30 years before and they had an atypical case of smallpox.

They didn't have florid smallpox, but they were infected and they were hospitalized in Germany and in Zagreb and their disease was not recognized. They were in hospital. They were isolated. And the cases then, two weeks later that occurred in other parts of the hospital. One lady who just poked her head into the, onto the ward and asked a question and then closed the door came down with smallpox and died. And there were people then spread out all over the country. And in Yugoslavia, they had to immunize 12 million people. Everybody was immunized and the adjoining countries closed their borders. And if you had five or six people like that in the United States, the country would just come to a standstill.

PD: And Yugoslavia could do it because they . . .

RC: There was vaccine then.

PD: There was vaccine, but there was also the political, the autocratic political world that says “shut down the borders.”

RC: Well, I think if you have a public health imperative like that, the National Guard, the FBI, everybody would jump in and say, “You’ve got to do this. Everybody has to be vaccinated.” Well, fortunately the Government has contracted for 40 million doses, which is not enough.

PD: Forty million is an eighth of the population of the United States.

RC: Yeah, that’s right, but it’s better than zero. You see, the vaccine that was left over from the eradication program has been outdated and most of it isn’t usable anymore. It’s been sitting around a long time.

PD: It wouldn’t be helpful?

RC: No. You know, it had, it was distributed in little glass vials with a sort of a rubber top to it and there’s been enough seepage that the color of the fluid has changed and a lot of it is not usable. But the problem is it’s going to be ‘04 before this

vaccine is delivered. It should have been done, it should have started five, six years ago. This is what D.A. Henderson was saying and he knows.

PD: Wow!

RC: So anthrax is the other problem, obviously. That doesn't travel. It infects, if you inhale it, you develop pneumonia and you die.

PD: And that's it.

RC: Yes, unless you're treated with antibiotics within the first few hours. Who knows, it's a silent killer. Somebody releases it from the top of the Washington Monument and it's blown through the, you know, by air currents through this area, a lot of people will die, tremendous number.

PD: So do you see your role as a scientist here as also being one as . . .

RC: A person who sounds the alarms?

PD: Yes, in the greater scheme of public health. I mean, your advocacy has included the Vice Chair of the [Production] Development Committee here.

RC: Yeah.

PD: A member of the NIH Clinical Research Committee, head of the World Health Organization International Reference Laboratory for Respiratory Viruses. I mean, you do see yourself as somebody who should speak out.

RC: Well, you see, all of these activities were things that we would have done anyway and we did it, in the WHO setting, we did it in collaboration with a lot of other people. We actually extended our influence way beyond the boundaries of the laboratory and found that what we had established for the respiratory viruses here was the same everyplace in the world—viruses that moved among, from one individual to another generally have the same, the same natural history. When you have something like dengue, you depend on a mosquito to transmit and there, if you don't have the mosquito, you don't have dengue, that sort of thing. Like West Nile, you, you have to have mosquitos of a certain type, and so forth.

PD: In a 1984 *U.S. News & World Report* article, you said that NIAID went after "diseases that are most important medically and where technology now makes it possible to produce a vaccine."

RC: Yes.

PD: How do you determine which diseases are most important medically?

RC: Well, the incidences, mortality, hospitalization, after-effects of infection, and so forth. There are a lot of important viruses that don't kill people. They just make them very sick and they bring the economy to a standstill. You have viruses like smallpox, which, if they get loose, will kill 20 percent of those infected. RS virus causes maybe 4,000 deaths a year in the United States, but it also, it causes, it's responsible for about 20-25% of all hospitalizations of small infants. So, I mean, that's a problem.

PD: Yes. Yes. So there are a number of factors, not just the mortality factor.

RC: Right, sure. That's right. In the United States, rotavirus is a cause of serious diarrhea. In developing countries, that's a serious cause of mortality.

PD: Okay, another question broadly speaking. What do you think are the qualities essential to being a good scientist?

RC: Well, well, there are probably, it depends on the problem. There are, the requirements are really determined by the nature of the problem. If you have a problem that requires one person to develop monocular vision and just look straight down the tube towards the goal of understanding and eradication and

that person is not deflected, just, you know, works and studies with a sort of a laser-like intensity. That takes a certain kind of person and also somebody who doesn't want to work with other people. Albert Sabin had that, you see. He had that monocular vision and he wasn't, you couldn't deflect him once he got onto it.

But there are other people who's interested in everything and is willing to take a chance and jumps high and falls on his face very often, but many times, he lands on his feet. It's completely different. There isn't any one job description that fits, that fits everybody, no job requirements, it just depends on the problem. You know, there are people who can't work with other people, but do brilliant work. There are those that have to work with other people. My son, Stephen, is like this. He has to have personal contact. That's why he still does clinical work, too. He can't, when he went to Princeton, he went as a math major. He'd already taken all the math courses in the university. When he went there, when he arrived, he was put into the post-graduate course, schedule.

PD: Really?

RC: Yes, and after the first semester, he opted out because he was in the big math tower there and mathematicians sat in their offices and they never talked to anybody else. They just sat there and did their work and he had nobody to talk to. He had to be with people, so that's why he did music instead.

PD: But then he went back to medicine.

RC: Afterward, yes. But the point is, he was in pediatrics and he still has contact with lots of people and once a year, he's in charge of the pediatric cancer ward.

PD: So there's no single quality that is essential for a good scientist.

RC: No, I think it varies very significantly. There are people, for example, structural biologists, people who determine the structure of a virus at the atomic level. They can see things in their head three dimensionally. I look at the diagrams they draw and I can't see anything. I don't have that facility.

PD: So it all depends on your perception.

RC: Well, not only perception, but the way your brain is wired.

PD: Okay. You've talked about a number of vaccines that may be coming out in the last couple of years. Are there other major health issues that you're allowed to specifically working on in the millennium?

RC: No, we stay, and this is a very big area. We limit ourselves to infectious diseases; it's the Laboratory of Infectious Diseases.

PD: So that you've pretty much covered all the things that you're working on?

RC: Well, we chose very big problems, requiring a long time for the solution. The fastest, the fastest wrap-up occurred with the live adeno vaccine. Everything just went together so fast, that it was incredible. But, more often, it's 10 years, 20 years. Think in terms of decades.

PD: Okay. Well, I'd like to talk to you about some of your interests outside of work. I was encouraged to do so. Swimming . . .

RC: Music.

PD: Music and movies.

RC: I love classical music. My mother was trained as a pianist.

PD: Well, let me just turn the tape over and you can tell me about that.

[End Tape 2, Side A]

[Begin Tape 2, Side B]

PD: Okay.

RC: Okay, my mother was trained as a pianist and during her high school period, she competed for the opportunity to play with the Chicago Symphony, which is one of the great symphonies in the world. And she won the competition in her junior and her senior year in high school and played with the Chicago Symphony. Frederick Stock was the very famous conductor and then she married just after graduation and my father said, "You can't play in public anymore." And that was it, she stopped.

PD: Why did he say that?

RC: This was 1922. (LAUGHTER)

PD: And she stopped.

RC: Well, she played for her own enjoyment, but not as much as she should have. But anyway, she loved music and she took me to concerts and especially piano recitals and I saw Rachmaninoff every time he came to Chicago.

PD: You did?

RC: Yes. And I saw Rubinstein and Circon and I developed a love for piano music, but then also orchestral music, good orchestral music played by great orchestra, great thrill.

PD: She took you when you were very young?

RC: Yes.

PD: Did you play yourself?

RC: It's interesting. I tried. I took piano lessons. I am totally illiterate. I am not able to coordinate my eye, my eyes and my hand. I don't have eye, . . .

PD: Hand/eye coordination.

RC: I just couldn't play, you know, looking at the music and reading it. But it skipped a generation. My son's a good pianist. (LAUGHTER)

PD: Music major.

RC: Yes.

PD: But you have a voracious interest.

RC: In music.

PD: Yes.

RC: I just love it. And when we do on vacation, we seek out, you know, opportunities to go to Salzburg and Vienna, and England. Actually, two years ago, three years ago, we went to England and we were able to go to Glyndebourne. Glyndebourne is the home of summer opera in England and it's a magnificent estate that was owned by a very rich man and he married, his wife was a singer. He built an opera house for her. Glyndebourne is maybe 10, 15 miles north of the Channel. It's just due south from London and it's about 10 or 15 miles from, you know, from the Channel, from the coast.

And he built this wonderful, wonderful opera house for his wife and it became a center. And a lot of the German ex-patriots who left Germany, you know, just before the War ended up there. And it was, it's been a great place, historic. The problem is, and it still is, the problem is that you can't get tickets. It's a small opera house and all the tickets are spoken for. They're sort of hereditary. They're passed on from generation to generation and we've always wanted to go there and we've tried so many times and we've never been able to get tickets.

So we went to England, we went to England and Ireland—it was two years ago, her 70th birthday and she said, "I want to go to Ireland and I want to, I want to see the children in the castle." I'll show you the castle.

PD: Oh, you're calling it up on your computer.

RC: Yes. My son's wife's stepfather owns a castle in Ireland. There it is. This is right off of . . . it's part of Galway Bay in County Clare in Ireland. It's in the West Coast and if you look hard in the distance, you can see the Arran Islands from the castle. It's a turret castle five stories, built in the 13th Century. Look at that.

PD: And it's in the family sort of.

RC: Well, it's owned by my daughter-in-law's stepfather and he is willing it to Steven and Lizette's brother. So every year they go and spend a week or two there. And the castle has a very narrow, winding staircase so it could be defended. In other words, 15 people couldn't rush in, one at a time, very narrow and if someone's coming down and someone's coming up, one of them has to go, has to stop at that landing so the other one can pass.

PD: That's narrow.

RC: Yes.

PD: What is that insignia on the bottom right?

RC: Oh, this came from a catalog. It was a Norm Thompson catalog. It was on the cover so I scanned it and that's what it looks like.

PD: So you went over there for your wife's 70th birthday.

RC: Well, she wanted, every year the whole family has gone there—son, daughter-in-law and four children—but we had never been there. So she insisted that we go and see them in the, at the castle. They lived in the castle. There are five stories. Each one is a big room. So we went and we stayed at an Inn, which is over here. Now, the Cliffs of Moher, very famous . . .

PD: I've been there.

RC: That's where it is. You've seen it.

PD: Yes, I was trying to place this castle, but, yes, I was there in 1980.

RC: The Cliffs of Moher are right over here and the Arran Islands are here. And we stayed at a motel, at a hotel called the Arran View Hotel. It was about two or

three blocks away, straight up, and all of the windows in the hotel look out on the Arran Islands. So we go there and we were there for a week. We had a wonderful time. Every night we went to Doolin's tavern in the little town . . . and they have Irish music and they play it every night. And they, Steve and Lizette know the people who sing and play the instruments and all this sort of thing. And the kids go and they dance on the tabletop and when the family goes into the city, the people who say, "That's the little fellow who was dancing on the tabletop at Doolin's Tavern last night." So, and they climb all over the place. Anyway, we decided that we would go. It was her birthday. So, I, I looked at a magazine I had, the *BBC*, *British Broadcasting Music Magazine*, and it has a schedule of events in Europe and all throughout the world, all the major concerts are listed every month.

I saw the schedule of Glyndebourne and the one night that we were going to be in England, we went back to England after another four or five days after that and then came home. So the one night that hadn't been spoken for, the Glyndebourne Opera Company was going to present "Capriccio," the last opera of Ricard Strauss, finished just during the end of, at the time of the end of World War II. And we had seen that the year before at the Metropolitan with Kiri Te Kanawa. Do you know who she is? Great singer, Kiri Te Kanawa. And we just absolutely had been bowled over by "Capriccio," it was a glorious opera. So, the, the magazine schedule, the schedule of the magazine indicated that either Kiri

Te Kanawa, Dame Kiri Te Kanawa or Dame Felicity Lott would sing on that night and there were twelve performances and there were six by Kiri Te Kanawa and six by Felicity Lott.

So immediately, we decided we were going to try to get tickets. We were going to go all out. So, we called a friend of ours who is a good friend of my son Steven's. He's a Solicitor and his father was Yehudi Menuhin's physician. You know who Yehudi Menuhin is? The violinist of the century, great violinist, Yehudi Menuhin. I can't believe it. You don't know, there was a famous comedian who used to say, "Who is Yehudi?" That was his standard line. Anyway, Yehudi Menuhin, he was an American citizen, actually, he was born in the United States, but he became Sir Yehudi Menuhin, and I think Lord Menuhin before he, before he died. He died a couple of years ago.

Anyway, so this friend of Stephen's was pretty well situated in terms of the music scene in London. So he tried to buy tickets for us. The tickets were all sold out because this was "Capriccio," and it was either Felicity Lott or Kiri Te Kanawa. He called the scalpers. They didn't have any tickets. He worked with a number of big companies. He tried to find out if there were corporate seats, you know, boxes or individual blocks of seats that he might be able to get them. Couldn't do it. Then, he knew the man who was the son of the, the son of the man who built the Opera House for his wife. This was the son. That man had died and he had

inherited the Opera House and they'd actually torn it down three or four years before and built a new, better, larger Opera House.

He called him, "Sir George, please help me." So George says, "I've had two thousand requests for this performance," because most people thought that Kiri Te Kanawa was going to retire right after the, right after the season. He called him again and he said, "I just don't have a single seat. Everybody wants to come. I can't do it. Gideon, I can't help you." So Gideon said, "Okay, thank you." He wrote him a letter, which I've never seen.

PD: This other person.

RC: Gideon, Stephen's friend, the Solicitor wrote to Sir George. I don't know what was in the letter. Two days later, he got a call and he said, "Your friends can have my box at the performance." We had the Royal Box at Glyndebourne. It was magic. Everything was magical. What happened was, when you go to Glyndebourne, you take a train from Victoria Station and you take a picnic box, a picnic hamper or whatever you call it, provisioned, where the provisions come from, Fortnum & Mason in London. Do you know London very well?

PD: I've not been there.

RC: Fortnum & Mason is the top place for, for picnic ingredients. So, we got to Victoria Square and you must wear formal attire. I had to wear, I took a tuxedo with me when I found out that we were going to be able to go, and my wife had a formal dress and we got to the station. How are we going to find the right train and I could tell right away. There was this parade of people with, with Fortnum & Mason. And in formal attire, we just got on the train. It was the right train. The train stopped at a town called Lewes and we, we took a, the bus was waiting for us when we arrived and it was just, it's a huge estate and there's sheep grazing in one portion and cows in another portion and there are statues by Henry Moore. Do you know about modern art?

PD: Yes.

RC: He was the great sculptor of the middle 20th Century, the greatest in England. Statues by Henry Moore. Everybody's all dressed up and some of the people bring candelabras. It's discouraged, though. It's considered gauche. And we saw and then we entered the box right in the, the boxes are numbered and then the middle box has nothing on it. It's Sir George's box. We sat there and people were looking up at us, you know, and figuring out who we were, and going like this, you know, please sit down. (LAUGHTER) I didn't do anything, but it was, and then at the interval, at the intermission, we went out onto the grass and had our picnic.

PD: It must have been like your dream performance.

RC: Yes.

PD: Wow! When was this?

RC: It was two years ago in the summer.

PD: That was the highlight in your music appreciation in your lifetime?

RC: Well, actually, we had seen Kiri Te Kanawa the year before at the Met. And we had also seen two other operas and a play, the [Mammoth] Play and the New York City Ballet, and Lincoln Center Chamber Players. When we go up there, we really concentrate. We focus.

PD: You do!

RC: There wasn't a minute wasted. Anyway, those are, those are great times.

PD: Don't you also collect a lot of music? Some of your colleagues were telling me how many, many CDs . . .

RC: Yes, I have about ten thousand CDs.

PD: Ten thousand?

RC: Yes, no rock. Just classical. I like jazz a lot, too, so we have a lot of jazz.

PD: So tell me about some of your other passions. I understand you have a home movie theatre?

RC: No. We show. I tape movies on the VH-VCR and I show them on the grandchildren on the weekend so that my son and daughter-in-law have a free Saturday night and they're generally out somewhere with the other young folk and we have the four children. It's not all of the four children, it's three children because Nicholas is 17 going on 18 very soon. He's going to college and he has his own car and . . .

PD: Oh, he's mobile.

RC: He's totally mobile and he's absent most of the time. He's with his compadres.

PD: But you have something of an encyclopedic knowledge of movies as well?

RC: Yes my grandfather built the two theaters in the mammoth part of South Chicago that I was telling you about. And during the, when the stock market crashed, he lost everything. So, he lost these theaters and he had a big, condominium-like building and so forth. But my father supported him from that point on. So he was given a life-time pass to these two theaters which were close to where we lived and he would go almost every night to the movies. He loved it. So I would go with him three or four times a week. I saw more movies than anybody. This would be from 1930 on. Lots of movies, I saw an unbelievable number of other movies. And, of course, they had these little two-reelers. They didn't have double features early on. They had a two-reeler, you know, a twenty-minute movie, comedy. Buster Keaton or the Three Stooges sort of thing, so it was a feature film and then a two-reeler. So it got to, I saw a lot of movies.

PD: And it stayed with you through the years.

RC: Oh, yes well, I love good movies.

PD: Do you have a collection of them?

RC: No, well, I have this, I have maybe five, six hundred films now on VHS for the grandchildren.

PD: Okay.

RC: But we film a lot of foreign films that you can't see very easily like Fitz Coraldo by Verner Herzog, "No Sweat Ought To," by Verner Herzog. These are wonderful, wonderful foreign films.

PD: So you don't have a theater at home.

RC: No, we just have a 32-inch television and a VCR and pretty soon, we'll get a DVD when they finally perfect it.

PD: Ah!

RC: But I like, I love, I love good movies. I just love a good movie.

PD: Any particular director?

RC: Well, Werner Herzog and Hitchcock and, you know, Orson Welles. When I was, just the summer before I entered college, I served, I was an usher at one of the large movie houses in Chicago. And I was there for a month and they showed only one movie, Orson Welles, "Citizen Kane," which I loved. I watched it

everyday during my lunch hour. I watched it when I was within the theater, you know, patrolling up and back. I could recite every line in that movie. I still love it. It's a masterpiece. Orson Welles. Have you seen "Citizen Kane"?

PD: I have, but a long time ago.

RC: It is a masterpiece.

PD: It is.

RC: I saw it over and over and over again and I didn't get tired of it. It's just an incredible movie.

PD: Again, one of your staff suggested I ask you about your "Three Stooges" telegram.

RC: Oh, God, that came about, we were cleaning out something the other day. We were cleaning out some papers and I came across this telegraph, telegram and it was, I had won a, I had been given a medal or something in the Public Health Service. In other words, if you're in so many years, they give, they have to decide who's going to get the medals, you know. They have to distribute them

around and I was given some sort of a Public Health Service Award that was presented by Elliott Richardson, who was the . . .

PD: HEW [head of the Department of Health, Education, and Welfare].

RC: Yes, he was the HEW, he was the Cabinet Minister, he was—oh, what do you call the people of the, oh, let's see, he was . . .

PD: Was he Secretary?

RC: Secretary. It was HEW at the time.

PD: Yes.

RC: And I had been down there and made some presentation before him and so forth. So, I one thing that happened that was very interesting before we get to the Three Stooges. I never had a complete Public Health Service uniform. I only had a hat. I bought a hat. Al Kapikian had a coat. Somebody else had pants. You put them all together. But I only wore a uniform maybe three times in 31 years. But at that time, I had to wear that uniform. And Al has much shorter arms than I do and the best I could do when I, was like this! The sleeve came about half way up my arm and there was no way I could cover it. (LAUGHTER) I have

pictures of it, too. So anyway, I apparently received a telegram which was in a file here and I didn't, I didn't remember receiving it when I saw it, but it was from Mo Howard from the Center . . .

PD: With the black hair?

RC: Yes. And he was a friend of my parents in Los Angeles. (LAUGHTER)

PD: And what did he say in the telegram?

RC: Well, he said, "Congratulations, we're all proud of you," and this sort of thing. (LAUGHTER) It's hysterical.

PD: You should frame it and put it up in your office among all the awards.

RC: Well, I've got it around here, I think, someplace. Sandra has it. We filed it somewhere. (LAUGHTER) Everybody around here was pretty impressed with that, you know.

PD: I don't think too many people in this lab have a telegram from Mo Howard.

RC: Yes.

PD: Well, . . .

RC: He was not Mo Howard in real life.

PD: But it was the same guy?

RC: Oh, yes, no, he was a very fine fellow, very wonderful. He was a vaudevillian, you know.

PD: That's how he came up in television?

RC: Yeah, and movies. But two-reelers, the twenty-minute movies.

PD: Yeah, another anecdote that somebody suggested I ask you about was visiting your mother at the Bel Air, she was staying at the Howard Hughes suite?

RC: No, well, actually, my father was a part owner of the Bel Air Hotel for a long time.

PD: Okay.

RC: When I interned in California, I interned in the Bay Area, he and my mother decided they were going to leave Chicago. He'd put together a munitions factory for the Navy during World War II. They made, they made munitions shells and all

this, he had a, he had a large lamp factory which he closed down and he converted it to the production of munitions for the, for the Navy. And he won, he was awarded the Navy E, which is the flag that flies above the factory. So he decided that he was going to retire and not, you know, go back to making lamps.

PD: Making lamps.

RC: He retired to California and they built a home in Bel Air and my mother didn't like it because it was too big and too much trouble. So they moved into the Bel Air Hotel and he was half to a third owner, depending on the time, of the Bel Air. So they lived in a suite, a five or six-room suite in the Bel Air. And my mother lived there for almost 44 years. She died two years ago. She was in this suite. And I have something around here—I don't know where it is—but *Fortune* Magazine had a special, I don't know what you would call it, but a special called "How Do you Go All Out When You're in Los Angeles?" "How Do you Go All Out When You're in New York?" If money is no object, what can you do if money is no object? So in L.A., they picked out the Bel Air Hotel and the suite that was occupied by Mrs. Theodore Chanock for, for 44 years, four thousand dollars a night or something.

PD: And it was the Howard Hughes connection?

RC: Well, what happened was the apartment was on a, was on a quadrangle. It was one side of a quadrangle, okay? And there was a six-room apartment here, a six-room apartment here and a four-room apartment here and there was a courtyard in the center. Howard Hughes moved into the apartment on the other side of the Courtyard and he lived there for about four or five years. And his wife—her name was Peters, Jean Peters—she was a movie star. And my parents never saw him. You know, he only, he did business at night by telephone, but he was never, no one ever saw him. You know, he was totally reclusive, a recluse. He had three male Mormon caretakers, three, there were three Mormons who took care of him. And they wore gloves, you know, he had this germ fetish and all this thing.

He had two refrigerators—one for his wife and one for himself. She couldn't touch his food and they touched it with gloves, you see. So, my parents never saw him. Then he moved out and he moved somewhere else. And I, we, I was on a trip with Albert Sabin and we came to the hotel. My father put us up in this apartment. And I said to Albert, "Albert, let's look at the couches right away, take the pillows out and see if any address books had dropped out."

PD: Had they?

RC: No, God, I, I never made it. It was incredible. (LAUGHTER) Because he was one of the great womanizers of the century, as you know. You know that?

PD: Yes.

RC: So Albert enjoyed that very, that thought. So we actually stayed there for a few days, then we came back. And a man who was the, who owned a major share of the hotel, was a very rich guy and he bought the summer home that William Randolph Hearst bought for his paramour. He had a wife and family.

PD: This wasn't the castle?

RC: No, this was on Santa Monica.

PD: Okay.

RC: It's on the coast, it's on the Pacific Ocean. It's about, it takes about 20 minutes from the Bel-Air Hotel to go there, down to Santa Monica. So he built this 60-room house for Marion Davies and then, as an afterthought, he built a 15-room house adjoining it for Marion Davies' mother and they had, they, he had a large swimming pool. It had been built many centuries before in, in Florence, made of Florentine marble. He bought things, disassembled them, reassembled them.

This huge pool was in front, was part of the establishment. It was about a 30, 40-yard pool with two bridges crossing over in the first third and the second third of the pool, Florentine marble and I swam in that everyday. So we, my parents put us up there because we had two children and they didn't want children running around the Bel Air Hotel. So we stayed in the, in Marion Davies' mother's digs.

PD: Gee!

RC: And at that time, I thought, I can't think of her name now, very famous female movie star, was a very good friend of a man who did all the, who built this place or who bought it. I can't remember her name right now, but I thought she as just the most beautiful woman I'd ever seen on the screen and she was staying there because she was a friend. She was not acting in the movies. She was sort of over the hill, she was like 37 or 38 or something like that.

PD: Right. She was no longer the starlet.

RC: Well, I mean, no, she was maybe 45 years old and just a gorgeous woman. And when I say this to my wife, she really blushes. When I say, "But you're much more beautiful that she was," and she really is, really was. (LAUGHTER)

PD: Some of the other interests I want to ask you about.

RC: Oh, we can close the castle [on the computer sources].

PD: We can close the castle now.

RC: Okay.

PD: You swim daily, this has been of your regimen for about how many years?

RC: For about 40 years.

PD: And you have your own pool.

RC: Yes.

PD: Seventy-five foot pool?

RC: Twenty-five yards. Yes, it's a regulation short course pool. The long course is fifty meters, the short course is twenty-five yards. When they, when the college, when they have the AAU or college, national competitions, they have two. One is long course, one is short course.

PD: Yours is short course?

RC: Yes, it's challenging.

PD: And then, finally, family, . . .

RC: Yes.

PD: Lots and lots of pictures.

RC: Yes, well, actually, I have four times as many, but it's based on falling down and my wife hasn't fixed them up again. But you can see what a happy grandmother she is.

PD: Yes.

RC: And that one over there is my favorite with Sabrina, the only granddaughter.

PD: Very little.

RC: Oh, she's little. She looked like a little bird about to sing. She is 98 percentile in height. She is the tallest girl in her class.

PD: Very interesting. I see a picture of her over there.

RC: Yeah, she's very short there. But that was three years ago. She's sprung up a lot. Nicholas is 6 foot 2 now.

PD: The one on the, the oldest, the one with his own car now.

RC: Yeah. Yeah.

PD: I did want to ask you a few more questions about your research. Anything else about your outside interests that you'd like to talk about?

RC: No, I think that exhausts my outside interests. But, you know, there's a very famous story about Francis Crick, who was the co-discoverer of the structure of DNA with James Watson. And he was profiled in some British magazine. They asked him a lot of questions. They asked him, "What is your main hobby?" And his response was, "Girl-watching."

PD: He said that!

RC: Yes. (LAUGHTER) He's a very witty guy. James, Jim Watson is witty, but he's very, he's very, he can be very painful. He can inflict pain and he does often. His friend, his collaborator is very [fey] sort of a person, with a twinkle in his eyes

and thoughtful. And he's not, he doesn't want to excite or to, or to injure anybody. He's just a nice, wonderful person. Watson can be very destructive, as you know, reading the newspaper.

PD: All right, I'll ask, what's you favorite hobby?

RC: Girl-watching. No, they've got me in this office here and I can't . . .

PD: You can't girl-watch.

RC: I have an open door, but they don't, they go by too fast for me, so.

PD: Well, to try to lock up our conversations, what accomplishment in your scientific career are you proudest of?

RC: Well, it's, my longevity, my ability to sustain myself over a long period of time, staying with rough problems and solving them and having wonderful friends and colleagues that make it possible to do this. To blend entrepreneurial and solitary giant, giantism, not giant, but melding, you know, the entrepreneurial approach and the solitary scientific giant approach.

PD: The best of your mentors?

RC: Well, yeah and there are different strokes for different problems.

PD: Are there aspects of your career that have been especially enjoyable?

RC: Well, I've had some real highs, you know, when we cracked the atypical pneumonia problem, adenovirus vaccine problem and the coming very close now with RS and paraflu and rotavirus, the use and acceptance of and usefulness of the rotavirus vaccine are extraordinarily gratifying and we will prevail.

PD: You're working on it.

RC: Yeah, diligently and extensively.

PD: Are you, overall, are you satisfied with the work you've done or are there things you wish you'd done differently?

RC: No, I just wish there'd been more hours in the day, like it's when three times a day and do more science. I've tried hard, but nobody can, nobody can make that happen. I've gone all the way up to The White House.

PD: They won't put more hours in the day for you?

RC: Declare a 26-hour day. They just refuse to listen to me.

PD: Were there any setbacks that you found particularly discouraging?

RC: Well, when the inactivated RS virus vaccine potentiated disease, that was a horrendous setback. And it's resonated through the entire program for a couple of years. Then we said, "Well, we're going to have to figure out why this happened, how it happened and make sure it doesn't happen again. And then move into alternate, develop alternate strategies, which we have with live attenuated virus vaccine approach, which has been very successful.

PD: If we were to continue this interview series, who would you suggest that I speak with?

RC: Oh, you want to speak with Al Kapikian and Bob Purcell and Brian [Murphy].

PD: Okay.

RC: Yes.

PD: That would be the big three?

RC: If you want to get the real story, talk to my wife.

PD: The off-the-record story?

RC: Yes.

PD: Do you have any plans to retire at any particular time?

RC: No, I think, I want to see the rotavirus vaccine back in the fold and also be assured that the dengue, the dengue program is going beautifully, the dengue vaccine program. I plan to retire in another year or two.

PD: Oh, you do?

RC: Yes.

PD: So you want to wrap up these things?

RC: I'll be 78 or 79. That's going to be long enough. I have served my term, I think, at this point.

PD: I can't remember if I asked you this. Have you put your papers somewhere in particular? Do you have any plans to donate them to a particular institution?

RC: No, maybe to the incinerator, the shredder.

PD: Oh, you want to talk to [NIH Historian] Vicky Harden before you do that.

RC: Yes.

PD: Any other thoughts?

RC: No.

PD: No, all right.

RC: As they say in the restaurants, enjoy.

PD: This is you? [Looking at photograph]

RC: And Tony Fauci, yes [head of NIAID].

PD: And this was taken just a few weeks ago?

RC: Yes.

PD: For, what was the reason?

RC: Well, it was, "you have been appointed a," . . . Let me read this: "The President of the United States of America does confer on Robert M. Chanock, the rank of Meritorious Executive in the Senior Executive Service for sustained superior accomplishment in management of programs for the United States Government and for noteworthy achievement of quality and efficiency in the public service." What's funny, I brought this home and my wife said, "You've got one upstairs just like that."

PD: You do?

RC: Yes. It's signed by Clinton. I was given this in 1993 and she was right. I said, "Oh, it can't be." It's the same one. I have two of them now.

PD: May I pass these on to Dr. Harden?

RC: Yes. But the date is different, you see. This is dated somewhere. My wife said, "You've got one of those already." Yes, let's see where is it? Yes, it's 2000 down here.

PD: Well, I'll take those and thank you very much.

[End of Interview]