Pat Merz Interview

Office of NIH History
Oral History Program

Interviewer: Maya Ponte

Interviewee: Pat Merz

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National Capitol Captioning, LLC

Interviewer: [beginning of interview] From Staten Island and how you ended up here.

PM: Graduated from Mount Saint Vincent's in 1963, Bachelor of Science, chemistry, with a math and physics minor. Went to work at Shiva Pharmaceutical in Summit and worked in their macrobiology section, which was basically metabolism, using tritium C14 pathways and I was in the results, testing whether a drug did something or did not do something.

Interviewer: Did you like working in industry? Was it a good experience?

PM: It was fine, I mean the environment was good. This was in the heyday though when you had money, and the only thing I didn't like was the spin always put on how great the company was. It was at the time when they were moving into that "Mary Ann Antibiotics" and how great that was.

Interviewer: Interesting.

PM: Did a lot of cholesterol metabolism, left there to go to grad school down at the University of Pennsylvania. Met my husband down there, left grad school came up here, Staten Island.

Interviewer: And you came here together?

PM: Came to the institute and we worked together in the lab for a while but it was a situation in which if you didn't have a PhD you were considered to be a technician -- you were considered a technician that meant you could not think, that meant that you had to be told what to do everything, which I rebelled against, and so George and I –

Interviewer: But you had gone to graduate school, but you just got a Masters?

PM: No.

Interviewer: Was that – no you didn't.

PM: No I spent six months there and left.

Interviewer: Okay I see.

PM: So we kind of split. He stayed with cell biology and we were in the same lab and I was doing metabolic studies on the animals with scrapie and that.

Interviewer: So he was working on scrapie too?

PM: Yes.

Interviewer: You were both working on scrapie.

PM: Yes, a different aspect. Then in the '70s some time, Margaret Somerville [spelled phonetically] came over and I was starting to learn E.M. because I got fascinated with the aspect that you could diagnose hepatitis by AA particles in the blood. And the AA particles are not the virus but the Ames particles. So I got fascinated with that wondering if you could detect something in the blood with scrapie because that had not been done, but in order to that I had to learn negative stain electron microscopy, I had to learn electron microscopy, I had to learn how to do carbon grids, I had to learn to do all the stuff.

Interviewer: And you learned all of that here?

PM: Yes.

Interviewer: So there were people at the Institute who could do that, who trained you?

PM: No.

Interviewer: No. You taught yourself?

PM: Basically I taught – yeah, there was one person who would say, "Here is an evaporator, these are the grids, this is how you do it," and that was it. So I would go into the microscope – and I would have to learn the microscope. We had a little Hitachi 8 then. I had to learn the microscope.

Interviewer: And how difficult was that?

PM: People did think I was crazy.

Interviewer: Or what were the challenges in learning how to work with the microscope and prepare the samples?

PM: There were many challenges. One, if at the time you would put – the recommended way to negative stain was to put a form bar coat on the grid and if you put the form bar coat you are putting a layer of acrylic underneath the carbon coat. If you did that then it took more energy for the beam to penetrate the sample to reveal what was there. We had a very weak, small microscope, or the only access we had been to that one. So I learned to do carbon coats by ourselves. If you held a carbon coat, you made it, you would float a layer of carbon, you'd rinse through, drop it down – many ways, you had to learn not to put them in any form of draft.

I used to do it underneath – started to do it underneath a hood because I was dealing with scrapie; it's infectious. The airways of the hood would just blow the carbon part apart. So you had to learn all of this by trial and error. You had to learn what good negative staining is versus what's called positive staining, and negative staining outlines what you're interested in, lets it stand out from a darker background. Positive staining stains it darkly and it doesn't stand out, it doesn't reveal anything and things are kind of dehydrated and pulled together so you can't determine what it is. So you had to learn all of that. That's trial and error – that's – you don't even know what you're looking at. You're learning all of the artifacts.

Interviewer: How did you figure out – I mean at that stage sort of teaching yourself and going through this, how do you learn how to distinguish artifacts from something real? How to optimize the samples so that you can tell you're detecting something –

PM: Something real?

Interviewer: That's not background.

PM: It's trial and error and it's going to books to look at any – what negative stain microscopy looks like, going to books to see what a virus looks like, going to – flipping through, looking at the magnifications and the blood center gave us some hepatitis positive blood so I used that, I could work on that. And then started to look at samples of blood that I would extract and stuff like that. Couldn't find anything. Saw a lot lipoprotein material, but what this did was you're now building – pathology of any type that's visual is building references within your head. It is not – the book does not tell you but you build references within your head. You know when you look at this an artifact. You know when you look at this this is real. You may not know what it is yet, but you can go to books to find – to see what other people have reported. And you have a mind that knows what you have extracted from, reasonable conclusions. So that took two, three years. Robert came in and was trying to find the agent. He thought the agent was postsynaptic – in the postsynaptic density. So he was looking to isolate in postsynaptic densities from the brain. I was interested in maybe I would see something. So we struck up collaboration.

Interviewer: So how – had he applied to come here? Like it was his idea to come here and do that work?

PM: He came over from Edinburgh.

Interviewer: Why did he come?

Interviewer: Not from Edinburgh –

Interviewer: Was he invited?

PM: He came from Compton I think it was, and he came over because Dickinson and Kimberlin recommend he come over and he had just gotten his Ph.D. and he was looking to do a postdoc type thing, and so he came over to work with Dick Clark in his laboratory.

Interviewer: And Carp had previously worked in the UK, right? Or do you know?

PM: I'm not sure he worked there. I know that he and Dickinson are very close friends and he and Kimberlin are very close friends, and there had been big exchange between Dickinson, Kimberlin and Dick Clark on samples, strains of agent, and things like that. We replicated some of the work that Compton had done -- didn't publish it, we replicated it. He got the VM mice from Dickinson much later, things like that. So there was a long-standing collaboration and it was kind of a new lab.

Interviewer: The lab here?

PM: Yeah.

Interviewer: At the time, yeah.

PM: This was set up, basically, in '69, '68 / '69. It didn't get off of its feet, probably, until '72 really. So I said I would look at his samples. He was following – oh, I can't remember his name – a procedure that someone at Compton worked on, which is basically using detergents and everybody knew that the agent was membrane associated, old, old work and [unintelligible] the detergents and I would look. So from the very first time I was already used to looking at brain samples from other things that we were doing, we were doing some M.S. work. So I was already used to looking at brain samples so I'd already had some –

Interviewer: Were you looking for viral particles in M.S.?

PM: Yeah.

Interviewer: Okay.

PM: I already had frameworks of some brain structures.

Interviewer: So you could differentiate. You were already used to differentiating the usual backgrounds and –

PM: The usual artifacts – I mean the usual artifacts you could do. There is – people say do random looking when you're doing – take a sample, you have grid, put a sample under and do random looking. What does random mean? Random means that I have the grid there, I have it at a certain magnification. I can see or cannot see whether it is covered with carbon and the beam hits it and there's no carbon coat, does that mean I count it as a square or do I do it random in the sense of I find the square that has a coat and then say yes or no? I'll go up in it, etc., etc. So what does random mean? You still decide what the randomness is.

Interviewer: You have to make that decision?

PM: You have to make those decisions. You have to make decisions like that all the way along the line. Similar to what we were talking about earlier when people say if you show me the data I can make a decision, but you have to make decisions without having the data.

Interviewer: You have to make decisions about what counts as data and how it counts as data.

PM: Right, right. But from the very first time that Robert gave me a sample of what he considered – to look at [laughs] I was looking for what were known as Baringer particles [spelled phonetically]. They had been reported in one of the papers, Baringer had seen them in the E.M. and this is on cross section E.M. and I was looking what he called Baringer particles in that. And I snapped pictures and developed the negatives and then was printing them. And when I printed them there were these [unintelligible] picture from the very first sample that Robert ever gave me. And I asked around to everybody, I had not seen them on the grid, it shows how blind you are, how you are prejudiced about what you see that's there and –

Interviewer: So you had not seen them on the grid?

PM: No, I had not seen them on the square I was looking at. And I was looking at the square – they didn't register on my eye. I was looking at, let's see, there was 18,000, the bionocks were 10, so 180,000. As you scan across up and down on the grid square. And they weren't in the normals, because you take pictures – you have normals in scrapie and you take pictures – you take pictures of the normal – scrapie. Try to make them comparable. So they were there. Nobody knew what it was. I asked around a number of people, "Have you ever seen anything like this?" "No, no. No, no."

Interviewer: So when you said you asked people you asked other people –

PM: There were a lot of E.M. people in the building but they're cross-section people. There were very few negative stain people. One was David Soufer [spelled phonetically] who had done a lot of microtubule work. Microtubules are polymerized and the best way to see them is negative stain, because they depolymerize when you fix them for cross-

section work unless you use tannic [spelled phonetically] or something. So I asked people like that. At the same time there was a lot of interest in Alzheimer and Alzheimer amyloid. So amyloid – there were some amyloid were around so there were some books on amyloid. So I went through a number of those books, looking to see what they were, and well first – that was later. First, it was something that was observed. Then came the question, is it related to scrapie or is it not? So you do a ton more experiments in which you look at it from how many times do you see it in this strain of agent and this strain of mouse. It came out 100%, none in normals. Well, maybe it's just related to this strain because you're always determining between pathological byproduct and something that is actually related to the agent. That's the question that is always there. So then it was different strains of agent, different strains of mice. Well my god –

Interviewer: So here is working with Robert? Robert would isolate…?

PM: Right, and we would have discussions and by this time we had worked out a system that we could use which was simpler, which didn't require three different centrifugations. It was basically a mitochondrial preparation and they would be in there so we would use that for quick work. So we – they were also in the hamster scrapie, 263K. So then we maybe – it's only seen when you have clinical disease. So you back it up because if it's related to the agent it should be there before you have clinical disease, that means it is not necessarily a pathological byproduct. So we did that. Yes it did appear before – meanwhile, all the samples I would get would be blind. They would be coded. I couldn't know about what that were because that would influence everything. I could ignore the normals and deal with the scrapies. We did those. We did a ton – bye, bye.

OMSpeaker: No I'm just going over mom's. I don't know if you will be here when I get back or not so…have a good weekend if you're not here when I get back.

PM: Same to you.

OMSpeaker: Thank you.

PM: We did – I mean, I went through gradients, it must have been 10 gradients I looked at normal and scrapie documenting it. That was based in the first paper. At the same time, I tried to look at every bit of brain material that I could get my hands on that had been put through any isolation procedure. That meant – there was a lot of Alzheimer work going on, so that meant getting ahold of Alzheimer material, amyloid and PHF. It meant getting ahold of – there was some work going on in polymerizing neural filaments. You looked at that. You scanned the whole – they were glial filaments. So you looked at the whole range of any filamentous material you could possibly see: actin, myosin -- anything at all. Worked out the procedures. Take a look at a sample, if it didn't stain well how does – work out the procedures again and again for making – getting good stain, working out the procedures for that which will give you good negatively stained preparations of the material of interest. And low and behold, it was -- it just held and held and held and there were differences. You could tell by the structure of how the

same procedure, you could tell what they were by what they looked like on the grid. You could recognize where they were from.

So that led to – by this time Robert and I are not getting along very well, because he was interested in postsynaptic densities and I thought we had handle on the agent and he didn't think we had a handle on the agent. So we went to – I went down to – there was a meeting in – I think it was in neurology, maybe a neurology meeting. I was doing neural filaments with [unintelligible] and I went down with him to the meeting and he said I should talk to – Sam was doing some interesting things on scrapie at San Francisco. So I met I think it was Mike McKinley or Stan, I'm not sure which. I can't remember now. And I said we had found some things in scrapie and he said that they had found some things in scrapie, I said, "Well how about you? We can exchange pictures." We exchanged addresses, then I said, "Okay." Came home about two weeks later I got a letter, "No, we don't have anything really so I don't think we should exchange anything." All right. Meanwhile I was tracking amyloids and the rest of it. By this time we had accumulated over 100 experiments. It had held true the entire time. I had been told to stop the research here at some point during here because it wasn't going to amount to anything.

Interviewer: Really? Here you were told to stop?

PM: Yeah it was [unintelligible], Boyd, David Soufer [spelled phonetically] and Henry went to a meeting with Robert and I and they told me that it wasn't going to go anywhere. So I should stop.

Interviewer: So a meeting – like a meeting here at the institute?

PM: Yes, so I should stop, I should stop. There was no interest. So I listened, I said, "That's because you are the experts and you are telling me that it doesn't have any meaning?" I said, "I want to be clear on this." They said, "Yes." I said, "Okay." So Robert and I came back down from the meeting, this is before any publication or anything. He said, "What are we going to do?" And we went – we continued – we said, "We'll just go ahead," just continue it, continue it and continue it.

Interviewer: Yeah, so you just kept going even though they told you not to.

PM: We just kept going. So it was when I heard that Stan may have something – I came back from that meeting and I said, "Robert we have to do spleens because if this is related to the agent and it's not related to brain pathology and it's not related to anything to do with the brain or the inoculum or anything like that it has to be in spleens." It has to be. Oh God no – yeah all this stuff. So anyway we find it in spleens and sure enough –

Interviewer: Okay, you convinced him to do spleens?

PM: Sure enough it was in spleens. So then we had them branch out from scrapie in animals to CJD. So meanwhile we were drafting the paper. We wrote the paper and it

went over to *Acta Neural Pathology – Neuropathologica*. We were continuing going. There was an international meeting of virology at Strasburg, '81. Robert and I both went. I had a poster because nobody knew anything about this because we hadn't been to any meetings about it. Oh no, we had been to one meeting and that was the cell biology meeting before that I think, or just after. So up front my poster and the paper had been accepted and it was going to published, so maybe it was '82 / '83 – '82 maybe, and cell biology was '81. Yes that's right because I put up my poster in cell biology, it was on – what I had to get the SAF in cross-section embedded and be able to recognize them and presenting staining problems and things like that and my poster went up. I had one or two questions from some virology type people, plant virology / animal virology people and that was it. Mike McKinley was giving a talk, 10-minute session. He arrived the day he was giving his session. He spent time with Robert and I, never asked a word about what we were doing and was busy telling us about what he was doing. Hadn't been in there for the whole meeting, just flew in for that one day. So then was the -- the paper was published in this –

Interviewer: So when you said he was busy telling you about what he was doing, was he talking about were they doing any work on similar work to what you were doing like on – or what was he talking about then at that time?

PM: Oh they were doing biologic – doing purifications. And Robert at this time was getting very worried about Stan.

Interviewer: What was he worried about? Like how – how did his anxieties sort of come out?

PM: The anxieties were because when you are purifying you're going for dropping out a lot of things and increasing infectivity and dropping out everything else and that which is left is usually considered to be the agent. And Robert was going for postsynaptic densities and McKinley -- Stan were going for purification of the agent and using various detergents to do this. Robert was very knowledgeable about detergents and he was afraid that they were getting along fast – getting further in the purification than he was and getting further in infectivity yields. At this time, Stan's papers were the same as everybody else's. It was, "We tried this, we tried that, we have a purification of – we've got a 10^{th} increase in infectivity," things like that. We couldn't inactivate the agent, we couldn't do this, we'd get it back – you know we couldn't do it. Nothing that would give you handles to lead to anything. So then I had just gotten the prints from the publication in -- so I figured what did I know? This is the only second time ever giving a talk in front of any – or being anywhere talking. So I grabbed a bunch of them and brought them with me to Strasburg. We put up our posters, had this -- you know, and we were – that's the first time I actually saw Stan in operation.

Interviewer: In Strasburg?

PM: Yeah. And that was illustrative because he was running around telling everybody about what great progress he was making. You know, "I've got to tell you about this, this

is what I've been doing, this is how great it is, look at this!" When I put up my poster I had streams of people come through. I said, "Would you like a copy of the paper?" They took the paper, took the paper. I ran out of papers. I thought this was usual. I had no idea what was going on, and other people would come up and you know I talked to Dick Clark about how great progress is on scrapie and I said, "What do you mean progress on scrapie?" There was an attention all of a sudden that I hadn't expected, but people knew me and accepted the work.

Interviewer: What did you think was going on? I mean all of a sudden –

PM: I had no idea. I mean, I'm kind of dense, innocent, all of this stuff. So then we had – by this time we had – Robert and I arranged with Laura Mandalevis [spelled phonetically] to do CJD in the animals. That we did. Laura's view was that if we were doing this type – we could see this -- that we should be able to increase infectivity. The sample, the way that it was designed was to go for the structures, we didn't care about infectivity at that time, we were going for purification. And I couldn't talk Robert into a purification system for SAF and infectivity. That took a long time. That was the breaking point between us.

Interviewer: Why?

PM: Because Robert was in love with PSDs. It was his viewpoint that that's where the agent was.

Interviewer: And so you were moving away from PSDs at this point? You were purifying them –

PM: I was asking them to purify SAF.

Interviewer: Okay, and that was moving away from what he wanted to do?

PM: From moving away from what –

Interviewer: -- what he thought was going on.

PM: Right, right. I couldn't talk him into it. I couldn't –

Interviewer: But I thought the SAF was first isolated from the postsynaptic densities.

PM: That's right. And the system that we worked out to do a quick test was basically synaptosomal mitochondria prep in suspension. It also contained microsomal material, and it also contained some –

Interviewer: So that's why he didn't like it, was because it was starting to include things that weren't just strictly PSDs?

PM: No, no, no. We used this just a spot check of did it have SAF or not. And he didn't want to leave his PSDs. I couldn't talk him into it. I was not a biochemist in isolation. He was. I was a very good microscopist, could get it, could use my brains, could do all that type of stuff. So he went to Laura Mandaleves and she thought that when we were doing – her view was that we should be able to get isolated infectivity here. That was not the set-up for the protocol. I mean, the protocol was not set-up for that, it was set-up just to see if SAF were there, were they not there. So yes they were in the hamster -- in the guinea pig CJD, they were in the animal models of CJD. There was no great increase in infectivity, that's what she tested, which led her basically to think they were pathological byproducts.

Interviewer: This is what Laura tested?

PM: Yeah Laura –

Interviewer: She looked for an increase in infectivity and purified in biochemically purified –

PM: Right, in this material, which was mitochondrial synaptosomal microsomal preparations, she used this as an element for saying it was the infectivity, how increased was the infectivity. And she came to the conclusion that it didn't enrich for infectivity, so therefore they were not related necessarily to agent. It's one of the points at which she later goes on to I wouldn't say prove, she has never proven it, nobody has ever proven it, but it's one of the backbones of her research and her thinking processes and the way in which she approaches it. So then I was asking Henry about – "We should go down to NIH. We should really go down to NIH." "Oh no…later."

Interviewer: Henry?

PM: He was the director of the institute.

Interviewer: Okay, got it.

PM: So Robert and I set it up with Laura. Henry didn't even know we were going down. At that point Robert was fed up, absolutely fed up. I don't know – I'm not – I think I know why he was fed up -- I think, I'm not sure. I think it had to do with it was SAF and Robert's work on infectivity. I think it had to do with the split there. I'm not 100% sure of that. I know he's – anyway, he left in the middle while I was down there going on [inaudible]. And I think, basically, it's that. I think he thought all he was doing was doing it for me, not for himself.

Interviewer: Wait, this was Robert Rower [spelled phonetically] or --

PM: No, this Robert Summerville.

Interviewer: So Robert Summerville, you guys went down to go see Robert Rower [spelled phonetically] and at that point Robert Summerville got fed up with – he felt like it was going off in a direction…

PM: Well he – I think he felt – I'm trying to give you the feel of it, so I'm not holding my words. I think he felt that I didn't have a PhD, I was getting recognition for this work, we were now writing papers, we were asked to meetings, stuff like that. I was the one getting the recognition, he wasn't. If anybody had realized the significance of the work at the time it was done other than Robert and I, I would never have been the first author on that paper. It would have been taken over by the upper echelon of science, shall we say, good word.

Interviewer: At the institute here?

PM: Mmm-hmm.

Interviewer: You mean other people would have…

PM: Mmm-hmm. Oh yeah, yeah – no, they would have made sure their name was first. Oh absolutely, [laughs] not question about it. It's been done a million times here. Robert, I think Robert was getting annoyed that he was not getting recognition and I was, and of course I'm stumbling along. I don't know anything about this. What do I know about? And that we went to Laura's and – to NIH, and Laura and Robert were doing the samples and I was putting my grids and I was going to go look at them and I spent a long time looking at these grids, they were all double blind. I knew the importance of this experiment. And in the middle of it Robert walked out, left. He was not going to wait to the end of it. And he – I think he was mad about that. I think he was mad at me for all the attention. I did not have a PhD, he did. I think that's what was behind it, I'm not 100% sure about it. I was a woman, he was a man. There was a number of things associated with it. So we broke the code, and lo and behold everyone was correct.

Interviewer: So now it was just you and Robert Rower [laughs] in the lab because Summerville had walked out, but you continued working? You continued to –

PM: Oh absolutely.

Interviewer: -- looking at the samples they had prepared, and then when you went back and looked at the code…?

PM: When the code was broken it was with Gibbs, Robert Rower and myself. And it was correct all the way through, which meant now that this was a marker. Now, you have to understand up to this point you had no markers in scrapie, you had nothing! You had nothing except clinical science. So now we had a biochemical marker, I mean it's made up of biochemicals. We had a structure, we had a marker. And so this – my God, what can we do with it? [laughs]

So then it shifted to [unintelligible], basically. We had a meeting – I've got to try to get the – all right, I submitted a paper to *Nature* the [unintelligible] work. They held it for a year and a half. Stan published a paper in *Biochemistry* I think it was at this time stating that they had seen some strange things in their scrapie samples that they had also seen in normals, that was aimed at – I can't remember the date. I think it was '82.

Interviewer: But that was aimed at discrediting…

PM: That was aimed at discrediting me, our work.

Interviewer: Why was your paper held at *Nature* for a year and a half?

PM: They were [laughs] Bob Rower had called me and told me that he had reviewed the paper in *Nature,* and he said, "I gave it a very good positive review." I said, "Thank you." And they sent it up to Gajdusek. Gajdusek and [unintelligible] don't get along. So the review was never sent over. So I tried to get it through to Nature to try to find out what happened to it. I couldn't get anything because "our reviews are sacrosanct, our reviews are this, we have our own experts," blah, blah, blah. You may want to turn this off for a second.

[break in audio]

PM: I'm trying to get the timeframe right. After the virology meeting, meanwhile we had been through a lot of amyloids and a lot of this and a lot of that. After the virology meeting I was asked to give a talk at – the French have a meeting every couple of years on TSEs, and that was the first time that this material basically came out in the TSE world. And that was the first time I had ever given a 10-minute presentation.

Interviewer: So this was in Paris?

PM: This was in Paris.

Interviewer: Okay.

PM: And everybody loved it. So now it has to be '82 maybe –

Interviewer: Was Prusiner at that meeting?

PM: Yes.

Interviewer: Did he say anything at the time?

PM: No.

Interviewer: We had no interactions. The interactions occurred – I think there was a Rocky Mountain meeting around '83 and Hino Daringer [spelled phonetically] had

worked – the dates are, you know, so far gone. There was a Rocky Mountain meeting, Cheuseburg [spelled phonetically] had set it up and Dina was there. Meanwhile, we had a lot of information. We knew that we had a marker. We knew it was real for the TSEs. Almost anything you went to with TSEs would have this. We knew that Stan was working very hard. We hadn't purified it. We didn't have a protein. Hino Daringer came to the United States just before the meeting at Rocky Mountain.

Interviewer: Did you know who he was?

PM: No, we just – I think Kimberlain had recommended he come up because Kimberlain had been advising him on his research. So he came over, we replicated what he was doing. Now what he had done was he had purified the agent -- or he had purified to the point that he had proteins by silver stain, and he had high infectivity and he had the same – he was wondering whether he had SAF there. So he came over to replicate that just before the Rocky Mountain meeting and so he spent two weeks here and we replicated it, and he did have SAF. So we were feeling pretty good. He had put in a paper – just submitted a paper to *Nature*. He had submitted for the Japanese virology meeting, he had submitted an abstract. In that abstract he talked about what he had done and the person who reviewed the abstracts was Stan. He was in charge of the workshop. At this point Stan had nothing.

Oh, there's one other point you have to know. At the time that it might be amyloid, the strain of agent that this material was seen in was one that had never, ever, ever been associated with depositions of amyloid, had never in its entire life – and I mean it had a long, long history of no amyloid.

Interviewer: And which strain was this?

PM: This was 139A in Compton wide source C57 blacks, never, ever produced any type of amyloid. So I wrote to and sent pictures to the leading people in amyloid and I said, "Can you identify this material that you see here? Is it an amyloid? Would say that this is like an amyloid you have seen?" One persons that I sent it to was Glenner [spelled phonetically]. And so they all wrote back – two out of the four of them wrote back and said, "It doesn't look like anything I've ever seen." One of them was Glenner. So Hino had sent over his abstract and Stan had read it and we went to the Rocky Mountain and we heard that they might have – they had a protein I think by this time. I'm not a 100% sure – I think it is, yes. They had a protein by this time, Dave Bolton had a protein, and they were just releasing – was the prion hypothesis out at this point? I can't remember.

Interviewer: '82 right? It was the early, early '80s –

PM: We are in the – yeah, it gets fuzzy as to where it was. I think this first – it was this first one in *Science* that he was proposing, everybody was poo-pooing it. I think that's correct. I'm not 100% sure of that, and we already knew that what he did was he went to the editors. He went to the higher-ups, he went and talked about his work to everybody. Meanwhile, people in the field are busy working, they're not spreading up to

the higher levels. Oh, and Lawrence Altman, yeah, Lawrence Altman was caught up in that which he later regretted.

Interviewer: What was he doing? What was his role?

PM: Lawrence Altman was a medical doctor at the New York Times. He covered science. He was caught up in all that stuff and he fell for it.

Interviewer: In to promoting…?

PM: Yeah, and later, if you go back over his stuff that he writes later he's very toned down, he doesn't take a stand, he was similar to Gary Toms, he had been burned. So then was – so we went out to –

Interviewer: Did you want to know the status of…

Off-Mic Speaker: Yeah I don't if you're recording or what you're doing.

Interviewer: Yeah.

[break in audio]

Off-Mic Speaker: That's after a lot of –

Interviewer: Other stuff, yeah.

Off-Mic Speaker: -- the other stuff. So whatever you want to do Maya, I'm you know…

Interviewer: Okay.

Off-Mic Speaker: …whatever.

Interviewer: [laughs] Thank you.

Off-Mic Speaker: I'll talk to you later.

Interviewer: I'll come find maybe in a little bit if we reach a good point…

Off-Mic Speaker: I don't know if you saw this but I made a copy –

[break in audio]

Interviewer: Go ahead.

PM: At this time Robert has left the institute, he's gone back to England.

Interviewer: And did he leave – were you on poor terms when he left?

PM: We were on poor terms when he left. I was devastated. Henry said, "Just get another biochemist." But biochemistry and isolation, and that is not something you just say, "Hey, follow this procedure, it's the same as EM." You need expertise. You need a sense of it and Robert had that. Robert had that very much. Anyway, these are expertises you build up in your fingertips like a good cook, like a good gardener – anything that's an art. So Hino –

Interviewer: So you were devastated to lose Robert Summerville?

PM: I was.

Interviewer: Because you lost your source in a sense of all the –

PM: I lost a companion –

[end of transcript]

PM: …I'm a pipsqueak and this is going on. Who am I? "Why should I listen to you?" "Who are you to ask a question?" "Who are you to think?" "Who are you to be anybody?" and we're talking about PhDs / PhD MDs, etc. So no, I was not. Go outside of the institute, loved the work. Inside the institute there was no interest in it, no anything. So Hino came over and we replicated the work and we did all of –

Interviewer: And where did you replicate the work? Here –

PM: Here.

Interviewer: -- at the institute?

PM: At the institute. That was, I think it was Rick Kazat [spelled phonetically] did that. So we went out to the meeting and I think Stan had the protein at that time. I'm pretty sure he didn't – yeah, because Dave Bolton was there. And so he presented the work that it was protein only and that – and was going on about what he was doing. There was somebody from NIH who was there and we had had one other exchange to exchange photographs and Stan had said no, that it wasn't worthwhile."

Interviewer: Oh okay wait, but there was something critical that we were talking about that I wanted to ask you more about. So you said that you had actually taken the initiative and sent out these photographs –

PM: No, I didn't send them.

Interviewer: -- to the amyloid people.

PM: Oh I sent them out to the amyloid people.

Interviewer: Yeah.

PM: Oh yes.

Interviewer: This is critical though, so you had actually sent them to Glenner –

PM: Oh yes.

Interviewer: You had sent them to the big people in the amyloid field and they looked at them and said this is not anything we recognize as amyloid.

PM: Absolutely, otherwise I would have named them – I would have called them just an amyloid. It becomes important later, '83. So anyway, we replicated Hino's [unintelligible] when we were out there. I think Stan presented the protein. I had never presented the full wealth of evidence that we had on the SAF. So I did that, it was Dick Clark and myself. And meanwhile we heard about how much Stan was using 10,000 hamsters to do purifications and we are a little state-run institution, how in God's name could we compete on this? We could do Hino's procedure so should we enter this? Should we go on with it? Can we do it? I said, "Yes, we can. We can go ahead and do it." We're doing all right. We're even. So I presented everything and people asked me questions, people wanted some information on that, and we seemed to be even. Williamson presented the CWD for the first time. We had conversation with Chesebrough [spelled phonetically], tried to get Chesebrough. He didn't know anything about what was going on really. He knew Stan's side but he didn't know anything about us, and tried to enlist him to look for RNA because he's a nucleic acid person. He didn't really know what we were talking about because we were into expression. We weren't nucleic acid people. [laughs] Since then, of course, he's changed. It was just very interesting. He was caught in the middle.

Interviewer: Chesebrough?

PM: Yeah, because he was being used by Stan. His facility was being used by Stan. His expertise was being used. The relationship with Hadlow was being used, and this is what Stan does. He uses the names and then he drops them. He uses, supposedly, their expertise, but these people don't necessarily know how he's going to use the expertise, how he's going to present it. Anyway…

Interviewer: So you had been – you'd gone to Rocky Mountain.

PM: Right, we tried to enlist Chesebrough –

Interviewer: -- enlist Chesebrough to look for RNA.

PM: We failed. Came back and set up a program doing Hino Danringer's procedure once a week. It was a four-day procedure. It meant we had to have somebody on it. We put in a grant for it. They gave it to us.

Interviewer: And did Hino's procedure involve ultra-centrifugation –

PM: Yeah, four-day procedure. High sonication rates but the material is cleanest that you ever want to see. It's contaminated with feratin, it's contaminated with a little bit of nuclear protein, but SAF quantities are superb. It's treated with protease and high detergents and high salt.

Interviewer: Did any of that change the composition of the SAF?

PM: No you could still recognize it.

[phone ringing]

Interviewer: Should I answer it?

PM: Go ahead.

Interviewer: Hello. Hi, yes, hold on just a moment.

PM: Hi George.

[break in audio]

Interviewer: Okay, we're back on. Sorry about all the interruptions.

PM: Oh, while we were out at Rocky Mountain, Mike McKinley showed me some photographs that he had taken, I'm fairly sure it was there, it may have been a different meeting. But he showed me some pictures he had and sitting in that picture besides SAF is a long strand of material, which was nucleic acid. And I said, "Do you know what this is?" I said, "No," because I had also done a lot of viruses. And in the virus preparations you would have cracked viruses and nucleic acid comes out. Some coat, some not, depending on the virus, depending on what we are dealing with. So we set up work here.

So now we were starting to go off to virology meetings, and there was one up in Ithaca. Oh this is when – fall of '83 I think it was. Our papers were accepted in *Nature* with Hino's, and out comes Stan with a big splash in *Cell* that they had –

Interviewer: Before you were published? I mean, they had been accepted?

PM: It was around the same time, it was around the same time -- with a paper with Glenner in which amyloid was shown to be present within infectivity. And this is the same Glenner that I had sent the photographs to.

Interviewer: So what did you think was going on there?

PM: I spoke to Glenner about that. I went up to him at the neuropath meeting. I went up to him and I said, "I sent you pictures, I sent you material, you wrote me back." I said, "Do you retract that? What do you say now?" He didn't answer. He had a daughter that, if I remember rightly -- I may be wrong -- he had a daughter that had Down syndrome. He was working on an Alzheimer amyloid from that, he needed money and [unintelligible]. And this is also around the time you see that Hino had – there was a lot of stuff that went on right in there, that there have been questions about whether it was true or not. It's another story.

Interviewer: Was Hino still here at that time?

PM: No, he had left. He had gone back. Then – so we were going to meetings and Mike would present material – this was one of the arguments. Yeah, I'm fairly strict, I'm fairly straightforward, I'm very practical and I'm very able to put 1 and 1 makes 2. 1 and 1 ½ does not make 2, and 1 + 2 does not make 2. So they would present something and they would talk about quantifying it and they'd show an aggregate of fibrils and say there were 10 fibrils in there and –

Off-Mic Speaker: She's not here?

PM: She may be back, she may not. I would say, "But how could you do that?" You can't do that.

Interviewer: Right, how can you count them –

PM: You can't count them. You don't know if there are two underneath this one and ten underneath another one, you don't know how high they are, you don't know anything about them. They thought I was crazy. They could do it. I was the one who was crazy. So that was beginning. So Stan and I didn't get along.

Interviewer: So that was the beginning of meetings where they would present something and you, at the meeting, would raise –

PM: You would say – yeah.

Interviewer: -- questions about the data and they way that they were interpreting it.

PM: Right, right. They didn't like that. Now, maybe I was wrong but no one else was doing it. No one else was saying a word. No one else was and I didn't think that was science.

Interviewer: Why do you think no one else -- at this point why do think that no one else was –

PM: I'd like to – wait a minute, I'll ask you another question. How many meetings have you been and nobody asked questions?

Interviewer: Oh people ask questions. I've even heard people shout out that things are wrong. [laughs]

PM: It depends on the meetings and it depends on what is going on. Neuropathology meetings are classic for full-blooded arguments. Virology meetings are not. You don't – people don't ask very much. They may ask about how to extend it, they may ask – actually questioning how you're counting our how you're doing something doesn't – that actually led to several problems. It led to – that was part of what went on at the Abbey in Edinburgh. Actually, Dickinson did not want me there because I was not a scientist.

Interviewer: You weren't a PhD?

PM: Right. So I should not be there. Stan – supposedly Dickinson set up something with – again it was an accounting issue if I remember rightly, again, and Dickinson set up to be friends. I just sat there and basically Stan said how kind he is to all his technicians. He puts them on the paper. He likes them very much and he made clear that whatever I said or whatever I did, he didn't consider worth anything. The other one was –

Interviewer: So you're saying he was insinuating –

PM: He was condescending.

Interviewer: He was treating you as though you were just a technician or you were basically making comments to insinuate that you couldn't analyze the data because you were just a technician, and he would say these things in front of everybody at the conference.

PM: No, it was just the two of us. We were patching things up.

Interviewer: At the Abbey?

PM: Yeah, we were patching things up. We are patching things up. Now, I'm not sure how we are patching what up because he doesn't acknowledge any of the work and the paper. They don't answer the scientific questions that you ask, but I'm the bad person either because I asked the questions and had no right to ask them or I hated them. I mean, that's what comes across. Or I was too outspoken, that's another definite one, but I was not being female. Now, you look at how many females are in the field in that time, I think there was only one other and that was Mendelevez.

There was that. There was the international virology meeting in which he lambasted Hino in an arrogant, snotty, contemptuous –

Interviewer: What was the discussion about or did he…?

PM: It was scrapie, and I can't remember the exact words but he was the know it all expert on amyloids, which he didn't know anything about and hadn't spent any time working on them, and worked on them for 10 and 15 years, could look at histopathology section and recognize amyloid, could work with it in our hands, could isolate it, could do a lot of work with it, and he was telling us that we didn't know anything about it. And so Hino ignored him. Oh, I know it was, he was implying again that all the structures were totally amyloid and that all amyloids were made up of mutations in the genetic code which changed the amino acids, which therefore led to a mutant protein, which therefore led to misfolding, which therefore led to deposition of amyloid, and that was not true. I knew it was not true because I had been reading up a lot on amyloid and there was a pre-albumin case, Portuguese pre-albumin case in which they had analyzed the amyloid that was deposited and it was a normal fold – normal pre-albumin, no mutation in any amino acid, nothing. And so he made that statement. So when I got up to talk I said, "You're wrong, there are cases." "No I'm not." I got complements for doing that from a number of people, but a number of people probably hated me for doing it. But the other thing there that it is, is I'm not someone who likes to come out of the stand. I liked it back here. So you're forced.

Interviewer: Either you stand up for yourself or no one does, because the other thing is it's not like – I mean, here's Robert Summerville who had been doing all this work with you and he wasn't standing up and defending it. I mean, you were the only one who was going to…

PM: Right. I don't like to stand out like that. I'd rather write a paper, fine, I'm back here. Personally, yes, six of us together, two of us together, four of us together argue out a case – oh yeah okay, okay yeah your right, I'm wrong. Let's take it from another angle. Argue it out, throw it on the ground, tear it apart. I'll put my two cents in, you put your two cents in and out of that should come some good ideas. That's what we were doing at that time and we had some really good times. That was gone. Stan has basically taken that away.

What was the other one? There were several. The only place in which we actually were competitive with him, we were competitive with him on the science for a long period of time through the message, through the alleles, at that point we lost it because we couldn't keep up anymore. We couldn't. We didn't have the expertise, we didn't have the people, we didn't have – because you're asking other people to move in on something. Stan worked very well through getting the grants. We had difficulty getting grants.

[background comments]

Off-Mic Speaker: It's doing fine.

[break in audio]

PM: We got – I mean Gary Tobbs [spelled phonetically] came out during all of this and turned around on Stan, basically. No one knew that he had already interviewed him and was turning around. No one knew what the story was going to [unintelligible]. Michael Stone came, Johnson came out for "Six Killers of the Brain," something like that, but in the sense of spreading what was going on the field? No, because we didn't go to neurology meetings, we didn't go to – we went to virology meetings, we went to TSE meetings, we didn't spread out among a lot of them. Oh the other incident was McKinley was mad, probably rightfully so, and he went to the virology meeting after the Tokyo meeting and basically --

Interviewer: He was mad about what?

PM: About whatever had happened at the international meeting in Japan.

Interviewer: And that's one that you weren't at, so you're not sure --

PM: I was. He basically spent 20 minutes lambasting our work, and everybody said – I didn't say a word.

Interviewer: Michael McKinley did?

PM: Yeah. And everybody said, "Don't do it." I didn't, I just – I didn't care. I care about what the science says, if you're interpreting it I want to know you're interpreting it. If you're not interpreting it – I mean, I don't take interpretations as fact, I take interpretations as interpretations that may or may not be right. That western blot is a fact. That EM is a fact. What I say about that EM is interpretation.

So the only other one was one of the, again, virology meetings [unintelligible] -- oh God, I can't remember his name right now – stood up and put up two SAS pictures, one from Stan and one from me. He said, "Can you tell the difference for this? I can't tell the difference on these. Can you tell the difference on these? I can't tell the difference" – about ready to go to the chair somewhere. So Stan's ignoring it and everything else in many ways hurt him, in some ways he survived on it. When the Nobel Prize was given out --

Interviewer: Why do you think he didn't just recognize it and say, "Okay, we found the same thing they did and then we took it a step further," because like you were saying, eventually with his ability to get grants and stuff…

PM: Really you want to know?

Interviewer: Mmm-hmm.

PM: Pure ego. There is a tale the people have said about when he was out in USC, USC [unintelligible], ran across a case of CJD when he was a doctor – you may have heard this already. And he said, "That's what I'm going to hit my homerun with." Now,

what is he? He's just become a doctor. This is -- [laughs] this is he's a doctor, he's an MD! It's not about caring for people, it's what I have gone over and over in my mind whether or not the MVPSD program and the way the medical schools are geared now, you're pulling in the most competitive people possible. Where's the caring? How can they possibly care about the disease? How can they devote time to people and mechanisms and have a – no, they're too concerned with their own selves, and money. And it's ruining science, ruining science. I think, that's my own personal opinion. But that's basically it.

Interviewer: So at the Abbey -- [laughs]

PM: They? See, you made a much more information than I can recollect at the moment but I won't pick up anything I can.

Interviewer: I'm just curious because people recollect that as this is Dickinson who's trying to get together a small group from the field and bring the field together and instead it fractured --

PM: It fractured, it fractured more, he was trying to bring everybody together, he was trying to – because Dickinson had the strains of animals. He had all this pathological work that had gone on -- incubation period studies, all of the things that Stan – and he did use incubation period but he used incubation period in a very, very different way than Stan does. He had put all this time and effort into it. Now, Dickinson had been in his own battle in Washington in '67 in which he saw the fracturing going on and had been the cause of one of the fractures. So he was trying to resurrect that. I didn't know that at the time, no idea about it. And basically, it fractured but nobody talked to me about it. I know – yeah, I can talk, I can read, I can understand body language, I can understand words. But yes, it did fracture. It's cost a lot of people their jobs, it's cost a lot of people things.

Interviewer: And since then, what's happened to the field since that time? The researchers, the people who are actually doing the work on TSEs?

PM: I'm not sure I know what you mean. Dickinson's out. Gajdusek's out. Gibbs is out. Brown's out. Laura Mendelevez is still doing it. I tried for a while but I'm up to certain other things that have to be done. And you need a support system.

Interviewer: What do you mean by support system? Like what do you need to be able to take this on and sort of --

PM: Well, you need money, you need people and you need people who believe that it can be done and have energy and enthusiasm. If you don't have that, the work dies because they don't – nothing lights it up, mentally or physically. And in one sense that's probably what's happened here. I went to graduate school – because I had reached the end on EM, I went to graduate school to learn molecular biology, worked on Q-beta RNA, the [unintelligible], learned a lot. Didn't get the PhD because in the middle of it I

finished all the coursework, did all the work, realized that the professor didn't actually know the virus – knew molecular biology, didn't know the virus. Wanted me in a position of serving coffee, was not willing to discuss things, and I learned that basically scrapie would have an RNA because of the mutation rate – tremendous [unintelligible] mutation rate.

Interviewer: But can you talk about that a little bit more too? The idea of – strains and strain adaptation and why --

PM: You have to think about…you have to think about how does something get in there, how does it get out, how does it grow? And those are all different questions. So it's very reasonable that PrPn or c is the access point into a cell, it's very reasonable because when you remove PrP you remove access, or ability for the agent to get in. Work it out. You don't have any residual infectivity, you don't have any. So that protein is very important for exit and probably entry.

All right, so if it comes in how does it get in? All right, it's in a little vacuole. What happens to that little vacuole? Where does it go? Does the protein allow it to go through the vacuole and deposit something? Does it circulate in that little vacuole and not go to the lysosomal compartment? Because that's the truth, that's where that vacuole's got to go. If it doesn't do that then it's going right back out. So how is it making more of itself? It's never come in contact with the protein. It's not in the ER. How's it going to do it? All right, so something else is there. Something else is needed, then it has to get into the cytoplasm. Then it has to either get into the nucleus or stay in the cytoplasm. Still not gonna make the protein.

So you start thinking along those lines, you think about that you have two strains of mice and they're very different mice. And you have this one agent that has a name that you have passaged and passaged and passaged the way you would any virus, never seen anything different with them. Always does the same thing, you can count on it, it's clockwork. You take this virus and you put it into another strain of animals.

Interviewer: Is that – let me just stop, is that common for if you're passaging like a regular virus in the same strain, like inbred strain of mouse or something, would it stay the same or would you expect to see adaptation occurring? I mean, not adaptation --

PM: One, would you recognize the adaptation? That's the wrong question. You ought to get adaptation and recognize adaptation when you bring it outside its normal environment. You wouldn't know you have six strains in one passage unless you had other means of detecting it. But 139A is a classic example of the staple agent. ME7 was thought to be a staple. But ME7 had a history of depositing amyloid plaques and not depositing them depending on what the strain of animal it went into. ME7's the one that broke out, ME7 mutated. And what does mutation mean? It didn't change the protein. It's in the same strain of animal, that amino acid didn't change, something else changed. So that something else is moving along with the agent. You can take DNA – everybody loves the story of Paul Brown burying scrapie. What are spores? Spores exist in the air;

they're dehydrated. What is dehydrated? That's usually a beta sheet around it. Repels water. That's what a beta sheet's for. What's an amyloid strand? What's an SAF? What's any of them? They repel water.

All right, so. You can explain its properties, you can – the only thing that explains its mutation, the only thing that explains the tremendous number of strains of agent is the ability to mutate. The ability to mutate is an inherent property of RNA. It is not an inherent property of DNA, it is an inherent natural property of RNA, it's the – if you want to say the lifeblood of the – I mean, just think about it. Phages to bacteria, bacteria to bacteria, they all pass nucleic acid. Bacteria to humans, we pick up their nucleic acid. Viruses in humans were passed back and forth, and the one that mutates is not the DNA, it's the RNA. The one that changes, the one that has different properties. So you're not looking – you are looking at a different type of agent, you are looking at an agent that will probably in its life [unintelligible], once you understand this agent, be a model for Alzheimer's, be a model for Parkinson's, be a model for what everybody hoped it would be a model because if it does have the little piece of RNA you have a hope of stopping it, you have a hope of identifying it, you have a hope of saying yes you have it and you have a means of getting rid of it, a means of finding where it comes from. Because the protein's too late.

Interviewer: And why is it that if it's a protein you don't have that hope?

PM: If it's your own natural protein, change it. There's almost no drug you could take that could stop that change. You have to get it in the central nervous system, blood brain barrier, you have to be able to attack only that protein and no other and not interfere with the [unintelligible]. So that means the drug has to bind to it. If the drug has to bind to it, then is it interfering with this normal drug or not? Actually, the way the protein is in the cell, it still has its PLP – PLC linkage. You only detect it free by splitting it off, with protease. There's all sorts of questions like that. You either have to put somebody in that grabs it up and soaks it and then you excrete it, or you've got to put a drug in that sits there. Membrane proteins are not made to be destroyed, if you look at all of the biochemistry. They may recycle, some of them go to lysosomal pathways, but outside that they're either cut off somewhere outside the cell, they don't come back in, they don't mix again with the cytoplasmic [unintelligible]. But people don't talk about that.

Interviewer: So then – okay, so your – what do you think then, or how do you respond to what Prusiner would say or others would say about strains being the product of multiple confirmations of a protein that then self-catalyzed the production of – what do you have to say about that?

PM: It's ad-lib. It's an excuse. I mean, [laughs] if that's the case it doesn't matter what shape the protein's in, it'll be diseased. It doesn't matter.

Interviewer: Why?

PM: Because there's nothing regulating.

Interviewer: So in other words, a protein should --

PM: I mean, a body is regulated. Every cell in your body is regulated, whether we're talking about an individual organ, an individual cell, an individual body, it's regulated. If you – where does it do this [unintelligible]? There are cells to take care of all this. I mean not cells, [laughs] there are enzymes and proteins to take care of this, there are enzymes that go bring a protein back into the cell – oh God, remember those compartments, I'm trying to remember the compartments [unintelligible] in this folder. Which is the EM picture?

Interviewer: Not the lysosomes, [unintelligible].

PM: No, not the lysosomes. It's a pathway you have ubiquinous – ubiquination machinery [spelled phonetically] ubiquitin, and shown to be associated with the proteins at all. You bring it back [unintelligible]. If it's a way in which when it replicates [unintelligible], some RNA or [unintelligible] RNA, very reasonable to go out to the cytoplasm with the messenger RNA machinery. Very easy to meet a protein that's going through. Very easy to meet it, very easy to attach.

Interviewer: Right, so you don't see – otherwise you think we'd be having these kinds of build-ups of negatively conformed proteins all over the place if we didn't have this machinery which --

PM: Right, right, right. You don't see those big aggregates of material and scrapie, you don't see them stacked up in the cell, [unintelligible] all those, you see that one a lot, but you don't see any of that. You don't see any indicating machinery that's been blocked. You don't see PrPsc on the membrane, blocked.

Interviewer: But then, basically, at a certain point after --

PM: Which means something's coming out from the cell, something that's not supposed to be there is coming out of the cell. Not something that I inoculated or ate and it came in the cell and went to the ER compartment and contaminated it. It doesn't work. None of it works.

Interviewer: But then – so you kind of left the field then after about ’84 or so?

PM: ’87. ’87 / ’88 I did two things. Well one, ’84 my mother died, she had been in my house for a while and my aunt died. I had to take care of my aunt. I was tracking nucleic acid and I had pictures of what would be a nucleic acid coming out of SAF, removable with RNAse, but you need to some form of an infectivity study to show the requirement for that, and that’s extremely difficult.

Interviewer: Why? What are the challenges to doing that?

PM: Because you are also doing – I've had three experiments that worked, two that didn't. You have to denature a lot. When you denature you lose infectivity. You have to show that what happens on a grid is what happened in an animal, that's not necessarily so because of snapbacks. When you have material in a concentrated form and treat it with something, some things happen but then when you're going to inoculate it into the animal you are not going to keep it in that form because you are going kill the animal. You have to dilute it and you have to add something that under these conditions now things snap back. So there's a number of problems with that.

So the end result was no nucleic acid, demonstrable nucleic acid, identifiable nucleic acid. The interfering RNAs, the small RNAs is what caught everybody's attention, that's a good possibility, a very good possibility. We were working with Q-β, one of the interesting things on that was if you just followed LD50s in the cells, bacteria, you wouldn't realize necessarily how many non-infected particles you had. All you would detect are those that lyse, you wouldn't detect this amount that didn't lyse. This amount that carried 50 million different copies of an RNA that is not infectious. They had polio. Polio has the – the plasma for polio has a promoter on it that releases polio. So just think about people when they were growing polio – growing the plasma in the bacteria and growing up the bacteria. What happened during there was that it was releasing polio into the medium. That polio was infectious for one round in human cells. One round, then it was done, then it was noninfectious.

So this is human polio came out of a plasmid in a bacteria, excreted, infectious for one round. Now, what round was that in the human? Was it a child? Was it an adult? Was it MS? Was it – I mean there were all sorts of things like that but you wouldn't know about it. You never think about it. That's all things like that. Well anyway, I'm branching out too much.

Interviewer: Well, should I go up and meet –

PM: Go.

Interviewer: -- this seems like a good breaking point, at least.

End of transcript