The University of Texas M. D. Anderson Cancer Center

**Making Cancer History® Voices Project**

**Jordan Gutterman, M.D., Oral History Interview**May 18, 2006

**Interviewer:** Lesley W. Brunet

**Place:** Dr. Gutterman’s Office, Smith Research Building, The University of Texas M.D. Anderson Cancer Center, Houston, Texas

**Chapter 05: Funding Interferon Treatment and Looking towards Future Developments**

**A: The Researcher**

Story Codes:   
D: The History of Health Care, Patient Care

C: Cancer and Disease

A: The Researcher

C: Discovery and Success

A: Professional Values, Ethics, Purpose

B: The Finances and Business of MD Anderson

D: Fiscal Realities in Healthcare

***Lesley W. Brunet***00:07  
This is Lesley W. Brunet, about to record an oral history interview with Dr. Jordan Gutterman. The date is May 18th, 2006. This interview is being recorded in Dr. Gutterman's office on the south campus of MD Anderson. This interview is being recorded for the University of Texas MD Anderson Cancer Center Oral History Project. (break in tape)

***Jordan Gutterman, MD***  
01:08  
-- committed up to a million dollars. So I believe, I think I talked about the trip to Sweden to meet with Strander and Cantell. And went over to the Karolinska and saw a patient, a couple of records, and all that. And then I went to the Pontifical Academy of Sciences in mid-October of 1977 for a meeting on what they called immunotherapy. Very excited. And so, I came back, and I think that's where we left off.

***Lesley W. Brunet***01:35  
Just trying to get my Palm Pilot to stop buzzing. If it does it again, I'll look for it.

***Jordan Gutterman, MD***01:43  
OK. So I think that's where we left off. And we worked out -- at the time, it was very confidential, and the Finnish Red Cross was selling interferon at $50 a million units, so it'd be about $150 for an average dose. Agreed, because it was a foundation, to give us half price, at $25. Which...

***Lesley W. Brunet***02:11  
Because it was the Lasker Foundation.

***Jordan Gutterman, MD***02:13  
Yeah. And I still remember that Dr. Cantell, who was the chief scientist working with the Finnish Red Cross, was very sensitive. Because he was selling small amounts to the NIH for anti-viral studies. They wanted to start small studies. We got a tiny amount from the NCI, but they really -- I sent an application in in the fall of '77 to do some studies on breast cancer, and they just ripped it apart. I remember mentioning to you, to this day I cannot find the records of the review.

***Lesley W. Brunet***02:47  
Would it be among the ones that you gave us?

***Jordan Gutterman, MD***02:49  
It could be. I've never seen it. It's possible. But the review said, reviews things like this will never work, and this is basically a crazy idea, and so forth. And Mrs. Lasker had been trying since 1975 since the Krim meeting to get Dr. DeVita and the NCI thinking about other avenues of research, clinical research other than chemotherapy and surgery and radiation, which eventually we coined the term biological therapy. But, so they made a very trivial effort in this regard. I think the virologists were more interested than the cancer people. Because interferon was clearly identified and recognized and discovered as an anti-viral agent. Hence the name interferon, to interfere with viral replication. So, anyway, she made this financial commitment. And so the Finnish Red Cross and a lot of the correspondents, I'm sure, is in there, from late '77, they began to make the material. And it first arrived -- there are some things that are very, very important, and actually, ironically, historical, that just came out this week, a recognition of some of those early days. I'll tell you about it in a second.

So the material arrived in early February. Meanwhile, I came back and wrote a protocol. Once we had that commitment for a phase I study in cancer, with special emphasis on breast cancer, because that was Mrs. Lasker's interest. She wanted to find some new treatments for breast cancer because of Jane. So we were obligated to focus, initially, on breast cancer. Now, when I was in Stockholm, Strander showed me these data with multiple myeloma cell lines and also lymphoma cell lines and both types of tumors, the so-called B tumors that derived from the B lymphocyte. Were extremely sensitive in the test tube in-vitro. And then he had this one patient with a myeloma that he gave interferon to, three million units a day, and there was just a beautiful remission. There's a serum marker, the M protein they call it, which just went down. And...

***Lesley W. Brunet***05:13  
Three -- three million units?

***Jordan Gutterman, MD***05:15  
Yeah. A day. Three million, yeah. They did it in units.

***Lesley W. Brunet***05:18  
That's a lot, isn't it?

***Jordan Gutterman, MD***05:20  
No, not really.

***Lesley W. Brunet***05:21  
Just sounds like it.

***Jordan Gutterman, MD***05:22  
That's the approved dose for the initial hairy cell leukemia. We're coming up on the 20th anniversary next month. For that. So it's been, now we're sitting in 1978, about 28 years ago. My goodness gracious. (laughter) And I'm even more excited about the new stuff we're going to do. We're doing. But anyway, back to this. So I convinced Mrs. Lasker that breast cancer, we really had very little data to go on. And solid tumors are always more difficult than liquid tumors, hematopoietic. So I convinced her that I'd like to, in addition, once we got the breast cancer study going, is to add patients with both myeloma and a lymphoma. And she agreed with that.

So, we started our first study. It was approved by the surveillance committee and all that. [Redacted]

***Lesley W. Brunet***06:31  
That's OK. But there's a picture of you giving the first dose.

***Jordan Gutterman, MD***06:35  
No, that's the first dose of the synthetic. That's 1981. There are probably pictures around, and I'm must say that we -- it's so difficult. I've had so many different people come through. We've moved four different times, and every time we moved, there's a loss of pictures, and this, and that. [Redacted] The nurse that had worked with me in the breast clinic, Sue Kau, still here at MD Anderson, but I'm going to mention her name because...

***Lesley W. Brunet***07:02  
What's her last name? Cowl?

***Jordan Gutterman, MD***07:03  
Sue Kau, I think. I think it's K-A-U. At least, she was here as of a year ago. She didn't work with me, she worked in the breast clinic. [Redacted]. This is just by memory. And her biggest problem was that she had a big recurrent mass of breast cancer under her right -- under her left arm, under her left arm. She was left handed, so she could barely lift her arm. So she said she had to comb her hair, I remember. [Redacted] So we put her in the hospital. This was the first dose, and we gave her the dose, and we knew -- we anticipated we'd get some fever. And so we started on the 13th of February. And I remembered that I walked on the wards, on the left side, I forget, it was probably on the 10th floor. And she -- I could walk to the room today, because you go down the hall, and I think it was on 10, whatever on the left was. And she had a corner room. And I remember, I was walking there on a Saturday morning, I believe it was. And she was up at the mirror combing her hair -- brushing, brushing her hair. Brushing it.

***Lesley W. Brunet***08:45  
With the left hand.

***Jordan Gutterman, MD***08:45  
With the left arm. And she couldn't lift it the day before.

***Lesley W. Brunet***08:48  
That's pretty good.

***Jordan Gutterman, MD***08:49  
Yeah. Now I have to say in toto with breast cancer, we saw that a lot with lymphomas, where they go very quickly. Doesn't happen too often in breast cancer. But the first one was very successful. And within 24 hours. She had already had enough shrinkage so that the pain was down, and she was able to brush her hair. So I didn't even see her, I already knew we were on to -- I was already off the wall excited. So she went on to have some degree of remission, it was partial and didn't last a few months. And we continued to put some patients on, and I -- it's always my philosophy that, especially a new idea, that new concepts, new drugs, start with patients, that so-called phase I, with very advanced disease, and I try, and I was literally criticized for this, to get the wellest patients I could. To give the concept a chance. First of all, this was in part working through the immune system, and if you had somebody who had ten different regimens, there's nothing left. I mean, it's something we could come back to about my passion about how we really need to change the way we approach cancer. And this is dealing with my current work of earlier intervention, prevention, for example with plant compounds. I -- I don't want to get into this now, but I have a real passion for the fact that we should be treating cancer -- dealing with cancer the way we deal a lot with heart disease. We detect hypertension before we have a problem. You detect, hopefully, heart disease before you have a fatal heart attack. You lower the cholesterol, lower the blood pressure. There should be markers, there are markers. And you need non-toxic drugs by mouth to do that, and that's what we're working on. But, that being said, I still try to go for patients who had somewhat limited disease. Otherwise, and you know, and we had very scarce amount of interferon, it was very expensive, and although it was clear that we needed to find out various things about it, not to be selfish about it, but I just couldn't afford to waste it on patients who are moribund, or terminal. And believe me, I got calls. And interferon was -- there was no publicity on it, so there was no pressure at that -- yet, at that time. There was later, and I'll get to that in a little bit here. Enormous pressure and a lot of criticism where we still had limited amount, very expensive stuff, where we knew it started to work. And I reserved it for people that at least -- it was a difficult choice.

**Chapter 06: Funding Interferon Research through Connections and Industry**

**A: The Clinical Provider**

Story Codes:   
D: Fiscal Realities in Healthcare

D: On Pharmaceutical Companies and Industry

B: The Business of MD Anderson -- C: The Institution and Finances

A: Definitions, Explanations, Translations

C: Cancer and Disease

D: Understanding Cancer, the History of Science, Cancer Research

C: Donations, Gifts, Contributions

B: Fundraising, Philanthropy, Donations, Volunteers

D: On Philanthropy and Volunteerism

***Lesley W. Brunet***11:26  
Why were you criticized?

***Jordan Gutterman, MD***11:29  
Oh, because I didn't do it the way chemotherapists do it. They'll treat...

***Lesley W. Brunet***11:33  
The worst first?

***Jordan Gutterman, MD***

11:34  
Absolutely. And I said no. Because I want this to succeed. I mean, if you treat 20 patients who are terminal, and it doesn't work, it still doesn't mean anything about what it might do in earlier stages of disease. And this -- I knew this idea would die if we didn't see something very soon, because there was no way to raise money. We only had Mary Lasker's money at that point. Yeah. So I'm very proud of how I did it.

***Lesley W. Brunet***12:06  
So, where would you get the criticism from? From within your department, or from the surveillance committee?

***Jordan Gutterman, MD***12:08  
No, not so much within the department, but around the institute, within whatever it was -- the developmental therapeutics, within the division. I mean, I'm jumping way ahead. But much later, I'm just going to mention an example. I still remember this very clearly. We had good evidence. We probably even had a published paper, or close to one, on the activity in breast cancer, but much more significantly in myeloma and lymphoma. And I was called to the clinic to see a patient with chronic lymphocytic leukemia. Walked in, the lady probably -- if she weighed 90 lbs, it would have been lucky. She was gray, she was jaundiced. And this doctor was very, very critical of me. It was a woman doctor who -- and I came out and I said, we still had limited amounts. And I said this patient was not eligible. She said oh, is that because the patient's not rich enough for you? I said no. If we had a patient who we felt comfortable asking that they could pay for the interferons so we could have extra interferon to treat more patients, we would do it. I mean, we had no choice. It was a very -- we should come back to this issue of how I dealt with the money issue, because it was all donations. Because there weren't many wealthy people. Some would give money, some would not.

***Lesley W. Brunet***13:32  
Are you talking about the patients?

***Jordan Gutterman, MD***  
13:33  
The patients, yeah. And I'd get calls from wealthy people. And even there, I would not necessarily accept money. They would say, well, I'll pay for the interferon if you just treat it. And even that, I had to be careful about, simply because...

***Lesley W. Brunet***13:49  
(inaudible)

***Jordan Gutterman, MD***13:50  
Yeah. There's -- you had to be really careful. We should come back to this issue. I don't think this has been discussed at all by anybody, of how those decisions were made. Because it was somewhat of an unusual...

***Lesley W. Brunet***14:02  
That didn't come through to (inaudible).

***Jordan Gutterman, MD***14:06  
No. And I don't want to get distracted, you know, I just -- I'm the one that got off on a tangent, but I won't forget this issue. There's probably multiple subtexts to talk about, if you have the time, I'd like to explore with you, because there's so many facets -- the interferon story is such a prototype, a microcosm for so many issues. Deals with government -- I mean, I don't know many sessions we're going to have, because I got to be a little bit careful getting too detailed with this, because my mind is wandering of all the stuff that is coming here. You know, my tie with Mary Lasker and Washington, and just the whole thing around money.

***Lesley W. Brunet***14:45  
(inaudible) (break in tape)

***Jordan Gutterman, MD***14:47  
Sure. OK. Thanks. All right. So...

***Lesley W. Brunet***14:55  
So you were talking about the...

***Jordan Gutterman, MD***14:56  
So we had these breast cancer patients, and initially, I think we treated about eight patients before we went on to the tumors that I thought were going to be more sensitive. But we needed to do about eight patients. Now. At that stage, Mary Lasker was getting quite excited. I would keep her posted almost on a daily basis of what was going on with the patients, and it was clear that she began to strategize. Because she would think big. How can we move -- assuming that this is -- I mean, she trusted me. She had Strander working on, now, maybe three patients with myeloma, and there was this suggestion that these osteosarcoma patients, bone sarcoma patients, that he had treated post-surgery that he suggested way back in '75 that giving interferon after surgery delayed or prevented the recurrence of sarcoma. That's how the clinical stuff kind of got started. It was not advanced disease, he was using it as a preventative. Which was the logical thing to do. And the irony is no one has attempted to repeat those studies, which it kind of gets back to the whole point of, you know.

So when later people tried to treat advanced terminal osteosarcoma patients, the interferon didn't work. It doesn't mean anything. Doesn't mean anything. It's like trying to treat a hypertensive who's had the disease for 20 years, and the blood pressure now has climbed to 240 over 120, and they have a stroke, and they're sitting there, unable to talk, and now you want to go in there and treat their blood pressure. Well, you need to get it down, but the point is, you can't reverse the damage. Any more you can reverse those mutations, and all the things of osteosarcoma. It's the same principle. So the fact that anti-hypertensive may be able to lower the blood pressure, but would not reverse any of the damage. Mutations and all of the damages that evolve during cancer, once they occur, you're not going to reverse them. If there are too many. So -- but that principle was -- Strander's work has never been appreciated or, for that matter, really, with interferon.

But back to the story. So Mrs. Lasker began to strategize. How can we move this forward. Now, I was new at this, now I -- so, she began to talk to a lot of people. And she had two strategies. She had pretty much given up on the National Cancer Institute, saying they were hostile to the idea of this, which they were. So she felt that the only way we could do this is go directly to Congress to force it down their throats to get more money put in designated for interferon. Number two, the pharmaceutical industry. And number three, the private sector. Other private donors, and then specifically, the American Cancer Society. So she had a three to four pronged approach.

Number one. Private. She called me after hearing about maybe five or six patients. And said, "I had lunch today with Dick Rauscher, Frank Rauscher, who was head of the ACS. A virologist. And being a virologist, being a PhD in virology, he certainly was familiar with interferon. I told him about your results, and he said, for you to write a grant, that they had extra money. They were looking for new avenues for their money, and this sounded like something that would be very attractive to the ACS." I'm sure -- and there's nothing wrong with this, by the way -- I'm sure he was thinking the ACS a unique profile. I'm sure -- in fact, I know that he heard from Mary that the NCI is sitting on their hands or hostile to it, and there were some competition. Rauscher had been the director of NCI, if I'm not mistaken, prior to taking over the ACS job, so there must have been some competition there. And so, I started to put together a grant. And Rauscher's recommendation is, based on the cost of interferon, that I put a grant in for $2 million. To expand -- to confirm, expand these studies in breast cancer, and by the time I start talking to him, we began to get some preliminary results in myeloma and lymphoma as well.

So I began in the spring of '78, began to put a grant together, under the naive thought that -- well, it turned out OK, but under the naive thought that the money was coming to MD Anderson. Mary suggested that we suggest -- that we write it so that the money would be shared with one other institute, which was actually a great idea, so the work would be confirmed, and I suggested a place like Sloan-Kettering. In part, because -- in large part because Mathilde Krim, who had organized that meeting of all those basic scientists that set up a big interferon research laboratory, they had a team of basic scientists, so the environment there, I think, would have been very hospitable -- very favorable towards interferon. I mean, at the time, don't remember when Bob Good was -- I guess he was let go. I don't know if Paul Marks was in president -- but that's not important. The important thing is that the environment there, I think, would have been pretty good.

So, secondly, she called a friend of hers at Hoffmann-La Roche, and I'll get back to the ACS, because it all converged at one time. She suggested that we needed to really get the pharmaceutical industry, because that was explained to her that now recombinant DNA had become a reality. To go back, I mentioned that it was discovered by Cohen and Boyer and Paul Berg all at Stanford -- well, Paul Berg was at Stanford. Stanley Cohen was at Stanford. Not working together directly. And Herb Boyer, in 1976, was the co-founder of Genentech. He was at UC San Francisco, I think.

And then in April the 7th, 1976, Genentech was formed. By the way, I find these dates interesting...

***Lesley W. Brunet***21:34  
Just wondering how you remembered all these dates.

***Jordan Gutterman, MD***21:36  
Well, it's embedded -- and this is not just rote, but the thing is, I do kind of look at things -- I mentioned to you last time, one of my really favorite topics, it's kind of non-scientific. But that my father passed away on April the 7th, 1974, because I went back to the unveiling a year later around the Passover time. I was on the East Coast when Freireich called and Clark called to go to this meeting. Nobody wants to go from here, you're the closest. And so, the same date, again, one year later, April the 7th, is Genentech was formed. Cetus had been formed, that was the first company, and they also were working on interferon, we won't get into that. So, Genentech was formed. So, in 1978, when Mary and I were talking, I told her that the supply problem -- if this was going to continue to work, eventually we're going to get to an insurmountable problem. But, and still, there was no publicity, so there was very little activity outside of the Finnish Red Cross and Mathilde Krim working with the Swiss Red Cross trying to produce interferon in a more economical way.

But I remember talking to her and saying that recombinant DNA may be a ways. So therefore, she said, we got to get into the drug industry. Don't forget now, biotech, in 1978, consisted of Genentech, Cetus which was eventually bought by Chiron, and maybe a couple of other companies.

***Lesley W. Brunet***23:11  
Can you spell that?

***Jordan Gutterman, MD***23:12  
Cetus? C-E-T-U-S. This was a company formed in 1970, and it never really made it, although it was bought out eventually by Chiron. They did work on beta-interferon eventually.

Anyway, so, she called up -- Mary called up her friend in the late spring was I was writing up this grant, at Hoffmann-La Roche, John Burns. She had gone to Burns after hearing a talk on L-DOPA, for Parkinson's disease many years previously, and urged Burns, who was head of research and was one of the co-founders and idea visionaries forming the Institute of Molecular Biology at Hoffmann-La Roche. The only -- as far as I know, the only one of the rarer ones of its kind, they had an institute devoted to the burgeoning science of molecular biology within the drug companies. Pretty -- see, there's no biotech industry, so cloning genes was still kind of a foreign thing for companies. And also, since genes make proteins, proteins outside of insulin really wasn't much part of the big pharmaceutical industry. Proteins come out of biotechnology. But Roche had the vision. There's a guy named Sidney Grunold, I think his name was, or something like that, I could think of it. And John Burns. So anyway. Burns was the head of pharmacologists, and Mary said I have another idea for you. Well it turns out that Dr. Burns, John Burns, who's in the National Academy of Sciences, told Mary that in fact there was an interferon program at Roche already in place, trying to purify interferon. They were having a problem, John told Mary, in getting raw material, i.e. white blood cells, to get enough interferon to try to purify it. Nobody could purify -- nobody knew what the structure was.

So Mary arranged for a meeting, the annual Lasker Awards were, and they still are, in the middle of June. And I was coming up from my first year to be on the jury, which was a great honor. And so we arranged a meeting to go over to Hoffmann-La Roche in Nutley, New Jersey, and I believe -- the dates -- I have the dates at home if they're not in the letters. Around the 15th of June of 1978.

So, to back up just for a second, about two weeks -- no, actually about a month before in May, I finished, completed the application to the American Cancer Society for the treatment of breast cancer, myeloma, lymphoma, asking for $2 million. Sent that off to Rauscher. And it's ironic that the day before the Lasker jury meeting, we went to Roche.

The following day, Rauscher got a group of ten scientists from ten different cancer centers to review the grant and discuss it. So he brought them all into New York. The day we actually were meeting for the Lasker Awards, around the 16th of June. So all of this converged very fast. All of this converged with Mary pushing it.

***Lesley W. Brunet***26:17  
Did you have any trouble getting the grant publication out of MD Anderson? Were things being fed through a research office (inaudible) or through...

***Jordan Gutterman, MD***26:34  
Not that one. I'm trying to remember. Now, this was -- Clark was still here.

***Lesley W. Brunet***26:46  
(inaudible).

***Jordan Gutterman, MD***26:47  
Yeah. Later on, I had big problems. Two separate ones. I can give you names and stuff later. But, I don't think that particularly one had a problem.

Now, I just want to, as an aside, I probably mentioned this, and I fail to do so, but I have extensive notes. Extensive. From 1977, '78, through up to '85, '86. And what is not in your thing -- and I've written this all up, and I have almost like a daily log, because I would drive to work with a Dictaphone, and my secretary at the time would type all this stuff up. I mean, totally uninteresting, but I mean, just random thoughts, you know. The grant went -- I mean, boring things, but you know, it's not boring, because I can read it real fast and get the gist, and really trigger the memory. And I'm finding even today, and I'm -- a point like that, I'm not 100% sure about that one. But there's a lot of things that stand out. I probably, if I had a problem, I would remember it, because there were others with the Clayton Foundation that -- I mean, I'm not going to get into now, but the Clayton Foundation here in Houston came into this within a year, and there was an individual, absolutely blocked my application. The money was already approved to get people too, because the trials were getting bigger. Come back to that later. The guy would deny in the...

***Lesley W. Brunet***28:17  
(inaudible) somebody within the institute?

***Jordan Gutterman, MD***28:20  
Well, he's retired now. I see him from time to time, he's got a lab still up here. And he acts my -- like, for 20 years, my best friend, and he would deny it.

***Lesley W. Brunet***28:30  
[Redacted]

***Jordan Gutterman, MD***28:34  
You got it.

***Lesley W. Brunet***28:35  
(inaudible).

***Jordan Gutterman, MD***28:36  
What's that?

BRUNET: [28:37  
That's what I've (inaudible).

***Jordan Gutterman, MD***28:37  
Yeah. We'll talk about it. Yeah. He put a granite -- he just put my grant in the drawer and [sent a grant in?]behind me to the Clayton Foundation. Of course, they were outraged about it. By that time, LeMaistre was here, and it was all just -- oh, you know. We had a committee that looked at this, and Dr. Gutterman's grant is -- was found to be inferior -- there was no truth to any of it. [Redacted] Stupid. Anyway, it was taken care of, but to me it was just unbelievable. But, on this one, I don't think so. But Clark was still here. (laughter) And, nobody was paying attention (inaudible). After -- these all came later, when all the publicity and -- but right now is all -- that's why, just as an aside, on the work I'm doing now, which is actually, frankly, is potentially much more explosive. I'm...

***Lesley W. Brunet***29:27  
Very quiet.

***Jordan Gutterman, MD***29:28  
Very quiet. So I can get the work done. There'll be a time, and then I can get it out there. But we're not ready yet, because there's no advantage. Yeah, I could probably raise some more money, because, you know, people like to know, and that's -- I've had some problems. But I'm too old for this. (laughter) I don't want to go through this again. It's very exciting. And Mary's not alive, I don't have a fairy godmother here helping me out. OK.

***Lesley W. Brunet***29:53  
Hold on just a minute.

**END OF AUDIO FILE 7**

***Jordan Gutterman, MD***

00:03  
I'll do it again. She knew the foibles of man. She knew that institutes, you know, the higher up, the more problems there are going to be. Including then, you know. The power game. I mean, she always felt that -- there were so many wise things that she said. And one of them -- we'll touch on all of them. The ones I remember. But one is that she always felt that women were much more sensitive to research and healthcare needs, because -- and she said the answer is because most women take care of children -- grow up children, and they're the ones who get up in the middle of the night, in general, don't forget, she lived in a different time. But women are the ones that get up and take care of the colic and the otitis media in the ear, and the screaming and the yelling and all that. And so, they're sensitized to pain. In her mind, certainly up until her death, and again, the prime of her life was at a different time. Men just weren't sensitive to it. It's not maybe they weren't built that way, it's just their roles in life. And she -- and I always found this to be true. And you'll see this as time goes on. Almost always, but not always, we'll find out as we go through this saga, that people who really came up at the bat were women. It's a great -- another subplot. We might even write those subplots...

***Lesley W. Brunet***01:21  
What was the last thing you said?

***Jordan Gutterman, MD***01:22  
About women.

***Lesley W. Brunet***01:24  
Another...

***Jordan Gutterman, MD***01:25  
Another subplot. Yet another subplot. No, I think, as we're talking, I can -- you said something really profoundly exciting to me about -- I hadn't thought about that, of -- besides what I've written, recapitulating it with you, where the memory may not be quite the same, and we're going to have to -- I'll compare notes. I mean, this is all accurate. But I may be forgetting a few things. What I'm telling you, but it's just am I leaving anything out. Probably it's good I'm leaving a few things out, because we could be here forever.

***Lesley W. Brunet***01:59  
And we want to get this to Olson.

***Jordan Gutterman, MD***02:01  
Yeah, I know, so let's get going. But I think there are several -- whether he will do anything with it, it's not the relevant thing, he probably won't, because of this big thing at MD Anderson. But for me to think about these subplots in terms of what are the lessons we learned about how things get done in society, and there are some wonderful stories here. I'm having lunch a week from Tuesday with someone I introduced to her who is a powerhouse of a lady, Sherry Lansing, I don't know if you know the name. She was head of Paramount Studios. [Redacted] And we became good friends. She was very close to Armand Hammer, who's also a friend of Mary's. And Sherry's quite interested in cancer research and health research and stem cells and all that. And she's so typical compared to a man, and Mary recognized in her. She had great possibilities. But almost without exception, women are the ones who came to the forefront.

**Chapter 07: Challenges in Funding and Acquiring Interferon   
A: Obstacles, Challenges, Barriers**

Story Codes:   
D: On Pharmaceutical Companies and Industry

B: Devices, Drugs, Procedures

B: Research

C: Discovery, Creativity and Innovation

D: The History of Health Care, Patient Care

A: Definitions, Explanations, Translations

A: The Researcher

C: Giving Recognition

B: Fundraising, Philanthropy, Donations, Volunteers

C: Collaborations

OK. So, so we continued to treat patients here, and the strategy now was pharmaceutical. And although I had some discussions at times with Merck and a few other companies, the major focus, initially, was on Hoffmann-La Roche. So on the 15th of June in 1978, Mary, her nephew, Jim Fordyce, Dita Blair, Mary's friend, and myself, and Mary, of course, took a limo over to Nutley, New Jersey. And were met there by John Burns, who assembled about eight people, including a guy named Sidney Pestka. P-E-S-T-K-A. Who was and is an MD, but also trained in biochemistry. And he was in charge of the interferon project within the Roche institute, and his whole objective was to try to purify, get a purer form of interferon, so they could do some sequencing of the DNA, and once they had the sequence, they could think about cloning it.

Now, unbeknownst at the time to me, Burns had been having some quiet discussions with Genentech to help out in the potential cloning of the interferon. Because even though Pestka and his group knew the new technology, Genentech, which had been formed, you know, just a little over two years ago, already were renowned for the fact that they were going to be -- based on their name, Genentech, to clone genes. And in '77, they cloned insulin I believe -- no, no, no. I'm sorry. Not them. The first thing they cloned, I think, was somatostatin. That's not even a therapeutic -- it has no health relevance. But even in '78, it was becoming obvious that if there was somebody that could clone interferon, it was probably going to be Genentech. So they were in discussions already when we got there in June.

Big problem was getting enough white cells. They were working with a New York blood center -- I'm going to try to speed this up a little bit. But they just didn't have -- so, I said, well, Pesca said to me, did you know that chronic myeloid leukemia cells are a rich source of interferon? And I did not know that. And I said, well, we have the biggest program in the country, we take off -- at the time, we didn't, you know, interferon was the first real breakthrough, and of course, there was no interferon. So there was nothing to do for these patients. And so what they were doing at MD Anderson under Ken McCredie and Jeane Hester were leukopheresing these people on the blood -- something that Freireich discovered through the cells we're throwing away. I said we have a rich source of natural material. So I came back, and in those days, I don't think we signed any agreement. I'm pretty sure we didn't. I just called Ken up and I said, can we get cells, and we start setting those cells up. That accelerated their research. And in 1979, I believe it was, I'll have to check my notes. Pestka identified the first -- two things. He found out that the natural interferon actually was comprised of several different peaks. Maybe 14 or so subtypes of alpha -- or leukocyte interferon, it was called at the time. And they probably there -- just based on their migrations on gels, they probably differed maybe by one amino acid. But they were able to determine, somewhere around '79 or so, that there were 179, 180 amino acids, and it was -- and now they had material to potentially clone the interferon. So this was a major, major advance, and somewhere in there, they published a paper. I just, as an aside, I just want to say this to you. That MIT has an annual big -- a half million dollar award for an invention. The Lemelson Award, or something like that, it's in Science Magazine. A friend of mine won it a couple of years ago, Robert Langer, who's a chemical engineer at MIT. I did not know, and Goldstein pointed this out to me, that they also give, occasionally at least, a $100,000 lifetime achievement award, and this year it went to Sid Pestka for...

***Lesley W. Brunet***07:20  
(inaudible).

***Jordan Gutterman, MD***07:21  
Just a -- this past week. The ceremony was yesterday at the Contemporary Museum in Chicago, where he was honored for purifying interferon, and leading to the therapeutic use of interferon for the treatments of millions of patients worldwide, including viruses and all. And although very appropriate if they were going to honor one person for that aspect. I mean, obviously, the whole clinical stuff, we led here. I got the white cells for him and -- and it was fine, I mean, it's an appropriate award. Question is, interferon has not been given quite the attention in the award area. I think there's some natural awards for the molecular and chemical people and the clinical side, but that's self-serving, so we won't go into that. But it's nice...

***Lesley W. Brunet***08:07  
That says a lot, that they -- about the importance of getting this story, I think.

***Jordan Gutterman, MD***08:13  
Absolutely, no. In fact, Joe Goldstein, who keeps track of this more than anybody I know, called me yesterday at home, actually, and said, "Jordan, did you know that Sid Pestka" -- because he knows my involvement in interferon. He said this is really -- you know, interferon's been kind of a dormant -- no one's paying much attention to it. I said this is great. That finally, because this was historical. It was historical because this was the first protein in the human body that was -- you could give insulin, because you could make either bovine or porcine insulin. But this was the first protein that you cannot really make enough to do proper testing. Certainly in the pure form, or the amounts. In the whole genetic engineering, recombinant DNA, biotechnology boon, and that's -- they use the word biotechnology. And if you had to pick out one person, depends on what you want to emphasize. Purification, cloning, or clinical. There'd be three people. I mean, I'm not going to say any more about that. But, I mean, it's very exciting. Regardless, awards, you know, I've talked to many of these people who win Lasker Awards, and particularly Nobel Prizes. And they say, you know, the Nobel, the shine of it lasts a little longer than the others. The others, the next day, you just get back to work. They don't last very long. It doesn't create a whole lot of buzz. The Nobel does...

***Lesley W. Brunet***09:33  
You all want the Nobel.

***Jordan Gutterman, MD***09:34  
No doubt about it. No doubt about it. But, and it's nice, it's very nice, the honor, and I think it's good, because it brings publicity in, and it does honor people. Instead of just basketball players and that type of thing. So anyway. Back to Pestka. So, we start sending that -- so, because of those cells, we were able to -- but, you know, what's interesting about that, I mean, they deserve all the credit in the world, Roche, and John Burns, who had the vision for this. And I don't think there was, from patent standpoint or any of those things, we certainly provided -- I suppose, today, it would have taken a year just do the business agreement, to get those cells up there. And in Mary's estimation, I talked to her later about this type of thing -- it didn't -- it didn't bother me. I just want to see things done, and I never have patience for this. To her, let's just get the job done, because the only thing that really counts is to help those patients. But, you know, you got to watch your Ps and Qs and make money for the companies.

***Lesley W. Brunet***10:32  
But Roche holds the patent?

***Jordan Gutterman, MD***10:33  
Oh yeah. Yeah. They -- you know. Yeah. So, that was the meeting. I jumped ahead, what Pestka did with it. But when we left that day, I -- by the way, the brilliance of Mary, and I may -- I got to remember to make the links here. What was brilliant about Mary. She put the money on the table. I got the data with breast cancer. I showed the pictures, and she made sure that every -- and that was another thing. I treated patients primarily with what's called soft tissue recurrence. (inaudible) lymph nodes and skin metastasis. For major -- one reason. They'd be the most logical to respond, because they're not bulky. And you could take great pictures. And you could convince people this was real. Again, if you treat a patient with a tumor this (inaudible) size, could be this size. Huge, I mean, size on the tape like a lemon, or bigger, a grapefruit. They're not going to respond. And then you would say interferon doesn't work. Because it's what Freireich calls the false negative. It's falsely negative. It's much better to have a false positive result; that is, you get eight patients treated with soft tissue disease, and they all respond? That doesn't mean 100% of breast cancer's going to respond. So it's falsely better than it is, but at least you know it works. As opposed to eight patients who have grapefruit-sized lesions, and none respond, and you conclude this stuff doesn't work, and you throw it away. That is a very dangerous situation, false negative. I learned that from Freireich. False negative, as opposed to false positive, which the truth will eventually sort out once you do more patients. You just don't want to miss a lead.

OK. So, they were very impressed with the pictures. This spurred them even further now to solidify the relationship with Genentech, and Pestka was, you know, was -- keep moving. It was very exciting. I used to go to Roche up -- back, all the time. I just loved going over there. It was a brand new -- it was a brave new world for me, because they were talking about purification. I remember in the '75 meeting, a guy who went on to win the Nobel Prize for -- in the Rockefeller in the '80s, blanking on his name. For determining the sequence of a protein -- not insulin. But amino acid sequence, protein sequence, and synthesizing insulin, for example. Chemically. Won a Nobel Prize for a couple of people. And the idea of just estimating what the size of interferon was, it was -- there was no practical way of purifying and synthesizing in the test tube, interferon. Until cloning came about in the mid '70s then. There would have been no way. So, you know, we began to ride the wave with this new technology. And interferon led the way. Led it all the way. Mary's brilliance was that she put the money up, so I could get the data with patients, have pictures, convince Roche to keep putting more money into it, form a relationship with Genentech. So there was this constant thinking-through, and it parallels the ACS story, which I'll tell you in a second.

So. The next day, we left, and I was going to make arrangements to send the material, to back off -- back up a minute. And I remember at the St. Regis Hotel, we had the Lasker jury, I believe it was the 16th of June. And I knew the ACS was meeting about my grant. And about 3:30 -- I was sitting sort of at the end, it was my first meeting, I was kind of scared (inaudible) of all these famous scientists in the room, I was very quiet. And there was a phone call in the outer room, and one of the board members of the Lasker Foundation was called to the phone by Dick Rauscher. And she came over and said they've approved your grant for $2 million. Oh, I was so excited. So in two days, Mary's brilliant strategy, which now I know how to do, of pharmaceutical, of solidifying relationships, but first, getting that clinical data. Then getting the clinical data to put a grant in. But that's just the beginning of the story, of the ACS. She already had ideas about publicizing this, (laughter) and getting more and more, you know, catalyzing more and more things. So two major things are already happening on the 15th and 16th of June. The relationship with Roche, which would spill over to Genentech, and then this ACS approval.

OK. So, and meanwhile, she was talking to other well-to-do people about putting money into this, and we'll maybe come back to that, because I began to meet other wealthy people. But I think the major part of this story for the moment, as we continue to treat more myeloma and lymphoma patients and got more results, was Mary always went to the south of France into Europe for vacation, and this was 1978, and I know she went off to Ireland in a castle someplace, and there was a phone strike over there, and she was really frustrated. So she had to move to Paris, and then on to Venice, and then on to the south of France. And during the time she was there, it was in the summer. I get a call from -- I think his name was Dole. He was the publicity man for the American Cancer Society. Now, I had had some contact with the press during my preceding -- while I was here, with BCG, which was -- and so, I was here at a meeting on melanoma at the Old Shamrock, when a guy with a British accent came up to me, because I -- the work was getting some attention, we had some interesting results. And he asked me a couple of questions, which ended up in the National Enquirer. And Clark had to get the article out, because they were saying BCG is the new cure for cancer. So Clark had to get most of that -- he didn't get the whole article out, but he got it toned down. I remember, and I'm backing up a little bit, I remember calling Lee Clark from a hotel in New York in 1976. Actually, I was -- meet us in New York, then I went to Washington with Mrs. Lasker to do some testimony, and I was panicked. So, I had had some -- I was very sensitized to this. So when this guy calls up and says we want to publicize this $2 million grant, I got really panicky. I didn't want -- I said no. (laughter) No, I don't want anything involved.

Now, I did forget something here. The day after the Lasker -- let me back up a second, I'm -- my memory on this. I promised I was going to do this, and I haven't done it.

***Lesley W. Brunet***17:45  
People don't think in a linear fashion, so...

***Jordan Gutterman, MD***17:48  
Yeah. But I could -- I just need to refresh my notes and try to -- but back, back just for a moment. The day after the Lasker jury, I had lunch with Dick Rauscher at a restaurant in New York, where we discussed the grant. And it was very depressing. (laughter) Here, I'm on a high, right? I've been to Roche, and I've heard this thing. [Redacted]

***Lesley W. Brunet***18:20  
Now this was before you -- before you got the grant?

***Jordan Gutterman, MD***18:23  
No, the day after.

***Lesley W. Brunet***18:24  
Oh, the day after, and it was...

***Jordan Gutterman, MD***18:27  
The grant, I heard from this woman who talked to Rauscher that they approved $2 million.

***Lesley W. Brunet***18:34  
And this is the day after, you're having lunch with him?

***Jordan Gutterman, MD***18:36  
Right.

***Lesley W. Brunet***18:36  
And what was he saying that was...

***Jordan Gutterman, MD***18:38  
OK. So we had lunch. And I'm thinking, you know, how are we going to get the money to MD Anderson, and I probably had to pick a -- because I proposed. So he said, the committee wants to each work with interferon, so we're going to divide this money up among ten institutes.

***Lesley W. Brunet***18:56  
Oh. That wasn't what the grant had said.

***Jordan Gutterman, MD***18:58  
No, no. But I realized immediately of course, everyone wanted part of the pickings -- I mean, the good news, I suppose, is everybody was excited about this. And there were all the major institutes, Roswell Park, Sloan-Kettering, this, that, and the other. And it got a very high rating, I mean, it was like a 1.4 and so forth. But what Rauscher decided to do, he was going to get a committee. The death word, you know. He's going to get a committee of ten people to decide how to use interferon. So there were going to be ten institutes. But I would be the co-chairman, along with a guy named Tom Merigan, who was at Stanford who's a virologist, who had actually treated three patients with Hepatitis B around the same time, and actually had treated a couple of lymphoma patients with success. So, I mean, he had not published this yet, but Merigan is, was, and still is a virologist out at Stanford and had been interested in interferon for many years. And -- but, you know, really not taking this leadership role, which, again, I owe so much to Mary, but -- and so he became the co-chairman. And I never met him, and later I talked to him and I realized this was going to become just a big political football, and it was unclear whether we would get any money.

And so, then a series of meetings, which I will not go into, were called, starting in the fall, where this was going to be organized after the summer vacation, of how the $2 million would be appropriated by the American Cancer Society. And I could just envision this being -- I mean, first of all, you just divide $2 million by ten, that's $200,000. That's very little. And Rauscher said the first thing they want to do is confirm your work.

Well, you know, I wanted to move on. I already knew enough about lymphoma and myeloma. I mean, later on, we found some major things. Just as an aside, we made the major discoveries, besides this, with the money from the interferon foundation. Again, away from the companies, away from any committee, because my intuition took us to hairy cell leukemia and got us approved by the FDA. And that's, again, another subplot of extraordinary importance. There's nothing wrong with committees, I suppose, and all that. But I could see that this was not going to move the ball -- it would, as a matter of fact, because it was -- it was necessary. It's just not my temperament to confirm, (laughter) you know. I wanted to move on. In retrospect, it was probably the right thing to do, because it got everybody talking the same language, instead of everybody, as LBJ used to say, get them inside the tent doing it outwards, instead of outside the tent pissing in, right? (laughter) That's my favorite LBJ line. You know the one, right? So it's true, you know.

There was a lot of stuff going on, but at least everybody was in the same tent when we got together. But I was very upset at this lunch with Dick Rauscher, because he hemmed and he hawed, and I could see he was going to play the political football. I thought the money was going to come to us, and we were just going to keep moving along. I mean, I'm competitive, and I also trust in my creativity and this, that, and the other. And I fully expected one other institute, but not ten. So I'll come back to that later.

But, now, fast forward to late summer, they wanted to publicize $2 million and ten -- they already selected the institutes.

***Lesley W. Brunet***22:21  
So that was -- it went that way, to ten different institutes?

***Jordan Gutterman, MD***22:24  
Yeah. What happened, eventually, is they formed four disease-oriented committees. One on breast cancer, one on myeloma, one on lymphoma, and the fourth was melanoma. And there were members -- I was ad hoc of all four, because of my work. But they took the ten people, ten institutes, and some would be involved with two tumors and three tumors and stuff. And they formed a chairman for each group. One for breast, one for myeloma, one for melanoma, and one for lymphoma. And they would form -- write protocols, and we participated. We got very little amount of money on that, and it was just doing what we already had done.

OK, but the publicity was the key thing. And frankly, I think Mary knew what was going on.

[Redacted]

Don't do this -- this would kill you. This will kill you if you start publicizing it. And I should've -- I mean, that's what I said. And we called Mary, and Mary kind of lukewarmly agreed. I think she said OK, I get it, I think you're right, we shouldn't do this. But it didn't make any difference. They had already decided they were going to publicize this.

So in the fall of September, and the exact dates I'll have to look up. There was a press conference held -- we held -- there was a press conference here in Houston that I went to, and I'm trying to remember if Rauscher came down to Houston for that. I just don't remember. But the press conference and the press release by the American Cancer Society, man did that hit home with the press. I mean, every newspaper -- Time did a big story, Newsweek did a big story. It was just like -- because it was the first that they're going...

***Lesley W. Brunet***25:15  
Did you make the cover on the news?

***Jordan Gutterman, MD***25:16  
Well, eventually. In March 31st, 1980. I'll -- we had a long way to go here. I don't know, sometimes I'm wondering if I'm giving you too much stuff here. But it's just a...

***Lesley W. Brunet***25:26  
I like to hear it.

***Jordan Gutterman, MD***25:27  
OK. What's that?

***Lesley W. Brunet***25:28  
I like it.

***Jordan Gutterman, MD***25:29  
OK. We'll just keep -- I'm just talking.

***Lesley W. Brunet***25:32  
But yeah, what's your schedule?

***Jordan Gutterman, MD***25:33  
No, well, maybe, I'm probably mostly going by fatigue. Where I just wear down, yeah. So, I didn't expect this to happen. I knew there would be some, but you know. It was the first of multiple coverages by the Houston press, and the entire international press. You know, Time did a -- Time did a really interesting piece as well as Newsweek, I believe my picture was in one of them. The Time piece said it was a bold proposal. It started off exactly like that. It was a bold proposal.

So I got a lot of -- tremendous amount of credit for putting in a $2 million grant. And of course, it was the first therapeutic grant for the ACS, and even then, it was a lot of money. Even then, it would be a -- especially for such a conservative organization as the ACS. And so, I think they've given awards out for interferon leadership, but I think I antagonized them, because I was never very enthusiastic. But I never had much to do with them. I don't think -- it's interesting how awards go out, again. They've given awards out for some of those people in that committee for their leadership in interferon. Never went -- I never heard back from them. Kind of a weird thing. But that publicity got the attention of every drug company. Now -- and I think Mary knew this, how this would work. Because now gene cloning was becoming a realistic likelihood, that there may be drugs that could be made by cloning of genes.

***Lesley W. Brunet***27:11  
Going to stop right here just so we could...

**END OF AUDIO FILE 8**

***Jordan Gutterman, MD***00:01  
...maybe.

***Lesley W. Brunet***00:03  
They do wonderful work -- worked with them for a long time. They do all kind of national projects. (inaudible)

***Jordan Gutterman, MD***00:16  
Oh, OK. So, now, I'm trying to remember.

***Lesley W. Brunet***00:26  
Let's see. There's the press conference and the press release...

Chapter **08: Promoting and Publicizing Interferon Research**

**A: Professional Path**

Story Codes:

D: On Pharmaceutical Companies and Industry

A: Definitions, Explanations, Translations

A: The Researcher

B: Devices, Drugs, Procedures

A: The Clinician

C: Patients

C: Cancer and Disease

D: Fiscal Realities in Healthcare

D: Business of Research

D: Understanding Cancer, the History of Science, Cancer Research

C: On Texas and Texans

B: Industry Partnerships

***Jordan Gutterman, MD***00:31  
Now, I've documented all of -- and some of the correspondence in my notes, and I'm not going to go through, you know, CBS coming down, and Nova, and there was just a series of stuff that started then. It's just, the ball started to roll. Meanwhile, now the patients were starting to pile in here. The big benefit, there were many. But the biggest benefit was to happen not until August of -- a year later, August of '79, which was Interferon Foundation. Meanwhile, we continued to see patients, and we still had the same money from Mary, but we had to really be very picky about what we do. A little bit of stuff from the ACS eventually trickled in after all the committees and stuff. But it was just a -- you know, probably treated three breast cancer patients and a couple of other things. I mean, myeloma and stuff. Nothing significant. But we didn't really have any other money. We could get an occasional donation from somebody, but not enough to work. So, I had discussions with other drug companies. I went to SmithKline, got bashed -- I got really beat up a lot.

Meanwhile, I went with Mary to San Francisco to visit Genentech, and in '79, Cetus, this company I mentioned and we really began to pay attention, and Genentech now was getting very excited about cloning the gene, and then in '79, Pestka got these pure things, and they were trying to clone it and also working with Genentech. I'm jumping ahead a little bit. Meanwhile, I was trying to get a (inaudible), I mean, I was writing up all the results. I was really, really busy. Which we finally published in 1980 about the original paper -- responses of these patients, so I was trying to keep my acad...

***Lesley W. Brunet***02:26  
(inaudible) today to see when your publication started.

***Jordan Gutterman, MD***02:31  
The first was in Annals of Internal Medicine, "Tumor Regression" -- "Interferon-induced tumor regression of [least?]breast, myeloma, lymphoma." I think, it was sometime in 1980, I can't remember the month. And that was the first publication. Right before the publication, I get a phone call. There was a press conference being held at the Boston -- what's the name of that hotel. Oh, that's not -- it's downtown. I never stayed there, I've been in it. Anyways, I'll think of it. But the Boston hotel. Charles Weissmann, a scientist in Zurich, Switzerland, working part of Biogen, announced that he had cloned interferon alpha -- well, leukocyte interferon, which they were now calling interferon alpha. Very, very big and exciting news. And it came out of the blue, because Genentech-Roche were doing it. We didn't know it at the time, but sharing -- shortly thereafter, signed a deal with them, Schering-Plough, to co-development. The head of Biogen was a scientist, a future Nobel Laureate -- I guess he had already won the Lasker Prize for DNA sequencing, his name was Wally Gilbert. Walter Gilbert. Very famous scientist. But he left Harvard on a sabbatical to run Biogen. And the way Biogen worked, Biogen, again, was one of the early biotech companies, is that they had labs all over Europe. As well as in the US. One of them was in Zurich under Charles Weissmann, and in part, I think, based on the publicity of interferon in 1978, they -- you know, they were turning to what proteins can we clone, and what are going to be economically important? Well, interferon was the top of everybody's list, you see. And so Biogen -- nobody -- it's like a horse coming out of the blue. Nobody knew about this, that Weissmann was doing this. And he announced this cloning -- and, you know, with all the previous publicity from '78, and the stuff that continued to trickle in, this was huge news.

***Lesley W. Brunet***04:52  
And this happened in '80?

***Jordan Gutterman, MD***04:53  
Yeah. January, around the 15th of January, 1980. 15th, 16th, 14th, something like that. Very historical press conference. I immediately got a call from MacNeil/Lehrer, they wanted to have a full show, 30 minutes at the time. With Gilbert, the head of Biogen, myself, and Dick Rauscher. And Rauscher happened to be in Houston at the time for some reason, I don't know. And so, I went down to -- I went down to channel eight, and we did a 30 minute -- the whole program was devoted to interferon, and that tape was around someplace. I still remember that one question...

***Lesley W. Brunet***05:36  
(inaudible)

***Jordan Gutterman, MD***05:37  
Yeah. I've -- was they asked Gilbert, since it was a Biogen and it was his company, and he was a renowned scientist. I have to check when he won the Nobel Prize, if he was already a Nobel Laureate. I don't recall. But I know he had already won a Lasker Award. "When do you think the interferon will be -- the pure interferon, will be in the clinic?" I mean, this was one day old, you know. I think they found the clones around Christmastime. Weismann wrote an interesting essay called "The Cloning of Interferon and Other Mistakes," because of all the (laughter) -- you know, he was a real pure -- he is a real pure scientist. He's done a lot of work on prions, and it's been 20 years, 25 years since I read that essay. But it was about the fact that -- you know. He wasn't used to -- first of all, he was Swiss, OK. You know how low-key they are. And being in the glare at this hotel in Boston and all that stuff. I think that's what he meant. But Gilbert said I predict in one year. We'll have pure interferon in the clinic. I, just to myself, I just was a little bit dubious, because the technology was so new. The irony is, he was right minus a day. But it wasn't Biogen's interferon, it was Roche-Genentech, because working with Genentech, and the history's a little murky. But Genentech, working with Roche's information and collaboration, cloned interferon like three months later, and I think in large part because of Roche's expertise of scale-up and this, that, and the other, and I think I want to review my notes before going through that whole saga, of the very first patient -- not only with pure interferon, but other than insulin, the first pure recombinant protein ever put into a human being, on January the 16th, I think it was, [Redacted] in 1981. We have the picture. So he was right on, literally almost -- I think he was off by a day -- well, literally, he got it. The irony is, it was not the Biogen, but the Roche-Genentech interferon that got into the clinic.

Now that whole story of...

***Lesley W. Brunet***07:58  
Now, is that a different kind of interferon than the leukocytic...

***Jordan Gutterman, MD***08:06  
Well, leukocyte -- well, OK. So the leukocyte, it comes -- leukocyte is a white cell. And so, what the Finnish Red Cross, who pioneered the technique of partially purifying it, took it from buffy coats. That is the whites -- so they were given the red cells, and they just spun down the white cells. They exposed the white cells in the test tube then to Sendai virus, this was a virus that -- DNA virus that induces -- could be a -- I'm sorry, it's probably an RNA. Well, it's a virus. That induces interferon. And then they would take it and partially purify it. And in retro -- we didn't know at the time we were doing it -- when we were doing the clinical studies, it was approved by the FDA. We had no idea of the purity, nor how many -- we thought it was just one interferon. From Pestka's work, and then from the cloning, it turned out that there were more than a dozen subtypes of leukocyte, which was now changed to alpha. As opposed to another one from the fibroblast, which are from the skin cells, which is called beta interferon, of which they were only one. When they cloned it, there was only one form of beta. That's the one that's been approved for multiple sclerosis many years later.

So -- and alpha, so there's alpha-1, alpha-2, and I think it's -- it's been a while. I think it's alpha-2 that eventually was the most prevalent of the peaks. So both Roche and Schering went after the same type. And eventually, years later, they just co-licensed each other to avoid any patent suits, because they were making the -- the purification techniques varied, and there were some clinical problems with that, which we may or may not get into. Antibodies with the Roche material that is -- formed an allergic reaction. So that's alpha. It's the same. It's just renamed from leukocyte interferon.

Now, I'm going to hold off right now, but the whole lead-up, and I don't want to get into too much detail. It was a very exciting, tense time, putting that first patient -- or maybe I will go ahead. I'm going to jump -- there'll be probably some details I do want to add to this. But I will -- because I remember in December of 1979, we knew we were going to -- nobody wanted to start this over the holidays, but we knew we were going to start the pure interferon in 1980. And -- which we did, and that was a lot of publicity. And naively, I do want to describe that experience. Meanwhile, we had gotten this data, again, on the myeloma, and we were starting to get some leads -- well, I'm sorry, I got to back off.

Let's go back just for a second, let's retrace our steps. We talked about pharmaceutical. Strategy of Mary, starting with Roche. And we've seen, to some extent, how this led -- but it was the ACS strategy which got the publicity that really burned the fires of these biotech -- the few biotech companies there were. And during that period from 1978, in September, when the publicity that I didn't really want to do, there was enormous amount of publicity and flurry of activity of companies starting up, trying to make partially pure interferon. The way Cantell and the Finnish Red Cross was doing it. There was just a mad scramble. Everybody saw a big payoff. A mad scramble of trying to make interferon the old fashioned way. Taking white cells and trying to purify them. There was just companies all over the place being, you know, and we were inundated. And I got to refresh my memory, there's a lot of stories there. Probably they're all -- you know, they're all probably today not terribly important, and I want to kind of review my notes, because there's a lot -- I did a lot of stuff, a lot of it's in the correspondence. There were companies on the East Coast, and I did a lot of trips. I went to Syntex, I mean, that's no longer existing. In the end, it was really Roche -- excuse me, Roche-Genentech and Schering -- Biogen-Schering that really led the way. And cloning just took over. The rest of it just dissipated with time.

So, I mean, I probably will want to read my notes and kind of summarize a lot of activity, because we didn't know in '78, '79. Remember the comment I told you last time about an old high school friend of mine, Bill Carter, at the '75 Krim meeting, said "Jordan, this new technology, we'll be dead in our graves before this becomes commercially viable." So people were really skeptical, you know, in '75.

Now, so, the main lesson here, one of the lessons is Mary Lasker's strategy of ACS -- of first, excuse me. Giving me money, getting clinical results, going to the ACS, getting more results, getting ten institutes, you know, endorsing everything. Getting the publicity, getting the companies going. Simultaneously going to the companies ahead of time saying, look at what you got. See, only Roche had access to my data. Eventually everybody had access to it, so Roche-Genentech had a jump start. Where Biogen exactly started, I don't know, but certainly the publicity in '78 spurred them, and they had all this cloning technique as well. So her strategy was brilliant, you know. Meanwhile, we were also talking to other rich people and so forth and so on.

To me, the biggest payoff from the publicity was the next phase, and that was -- I was getting a lot of phone calls. And I got a phone call one day in August of 1979, two years now, only two years after Mary called me up on a hot August day -- that's redundant. I mean, it's an oxymoron. In Houston, right, an August day in Houston, by definition, is scorching. [Redacted] That one phone call, here's the money, get the patient, do the -- so forth.

[Redacted] And he wanted to come by, he made sure I knew that he ran an oil company. And talked to me about his wife. Well, I said sure. Because I had to filter these phone calls. And I still remember this visit very much, because I was up on the -- what's now the seventh floor, right around the corner from Freireich's office, which is still there, that lab. When you come out of Freireich's office, you kind of go back toward the main hospital. It's not the very first lab that's kind of across from his lab, but it's the first down the hall, just ten feet, there's a lab on the left. And that was my lab. And my office was what is now a tissue culture room. It was probably no bigger than a prison cell, I don't know. It was like 4 feet wide by 12 feet long. And these people came in dressed to kill, and I'm in this teeny little office. Little did I know that was the greatest benefit in the world, because they said if he's doing -- you know, we want to help him out. They had read about me in LIFE Magazine and in Time, but mainly LIFE. [Redacted], who, at the time, for 25 years, wanted to keep this a secret, but she subsequently, it's OK, she had breast cancer. She had some surgery, some radiation, and a couple of positive lymph nodes, I think. She read about interferons, she's a brilliant woman, and she just wanted to get some as an adjunct. Now, we weren't doing that, I mean, without visible disease. And so, they talked, they had read everything, and they brought the medical records, and they said would I treat her? And I said, well, we're not -- you know, there's nothing to measure. So I really don't know what we would be doing. Although it seemed to be the ideal clinical situation, but I told them if we did it, we wouldn't have any way of assessing it. But I said, you know, this is the type of situation eventually I'd like to get to, you know, rather than advanced disease or limited disease.

They had clearly talked about this, and in addition to paying for it, which they clearly could do, and I think no one has to make those judgments. It was clear that -- they were both very compassionate. [Redacted], -- she was the one that talked, and had the real, incredible energy. They said they had this idea of why don't we raise money from the oil industry?

***Lesley W. Brunet***17:34  
What an idea.

GUTTERMAN: 17:36  
Yeah. And this was now, Lesley, in 1979, when -- like today. The situation was not too dissimilar from today. Jimmy Carter was president -- it's always good to remember the historical times when we're talking, and I always try to remember that. Carter was president. I think the Iran crisis was going on. Oil prices, you know, remember, the interest rates were probably -- we'd have to -- we can check on this -- Paul Volcker, probably 17%. Oil prices were up, remember that, the lines. It was that -- during that time. So the oil companies were like today. Not as much, of course, but they were having good times. Houston was booming.

[Redacted]

But if you really wanted a native of Houston, we want you to meet a man named Roy Huffington. HuffCo Oil. Of course, these names didn't mean anything to me.

So I knew these were serious people. And it took me about one nanosecond to realize that this was step number two. After Mary, now we had Houston. All came about because of the publicity. Eventually led to curing patients, which we'll get to. But, I mean, this whole thing of Mary of envisioning this is amazing. We'll probably review the whole thing, just what are the milestones, you know. Mary's decision, this ACS decision, and so forth, we'll put it out there as ten decisions. Because in a book, let's say Olson, for essence. You've got to tell a little bit of the color with it, of course. And whatever.

So, I was very excited about the meeting. I said we would treat her. By the way, it's interesting, as an aside, we did treat her as an outpatient, and she was the only patient that I ever personally treated that, with a first dose, had a horrible reaction. Her liver enzymes went up, she had to be hospitalized, and she's not an easy lady. But -- and to keep...

***Lesley W. Brunet***19:50  
And she had the Roche?

***Jordan Gutterman, MD***19:52  
She -- no. This was 1979. Cantell. We called it -- the Finnish Red Cross material. But that, it turns out, and I'm going to end with that. It turns out that all this -- the toxicity has nothing to do with contamination. It's all interferon. But we didn't know it. We thought it was contamination. Good question. But it wasn't the contaminates. That's the real drama of the first -- it was -- maybe still, one of the most exciting times I've ever had with that first patient, when we realized something really pretty profound. At least it was profound then. It seems obvious today, but I'll get back to that.

But she cleared up, and she went on and took interferon for, god, I don't know, 25 years, 20 years. She's fine today, still.

***Lesley W. Brunet***20:42  
So it...

***Jordan Gutterman, MD***20:45  
We -- the odds...

***Lesley W. Brunet***20:46  
I hate to use the word "cure," but it did...

***Jordan Gutterman, MD***20:48  
Well, she's cured. There's no doubt she's cured of breast cancer. Now, there's no way of knowing...

***Lesley W. Brunet***20:53  
Whether...

***Jordan Gutterman, MD***20:53  
The likelihood is that interferon did save her life, and she credits that, they both do. But -- I mean, you never know for sure. Because, you know, a certain fraction, at her stage, would have -- could have gone on. So she certainly credits the interferon, and I'm not going to (inaudible). (laughter) So that fall, I remember going over to Roy Huffington's house. Tall, lanky guy. I don't know if he's a native of Texas, but -- and the son became a congressman, was it? Yeah, not a senator. A senator from California.

***Lesley W. Brunet***21:35  
The wife Adrianna [sic]

***Jordan Gutterman, MD***21:37  
Yeah, Adrianna [sic] Yeah. That's a whole 'nother issue we won't get into.

So, they decided to form, and this was [Redacted] idea. An entity called the Interferon Foundation. Tax-free entity, with the idea of going to the oil companies to raise money. Now, LeMaistre was in -- now here. And there were some stories early on, which I've forgotten. But we'll come back to that. [Redacted] said, I don't trust big institutes. Why would we even take any chance of overhead, losing the money. Just form the foundation. All monies we raise go to this foundation. You take that money, no overhead. [Redacted] Roy's office will take care of any administrative expenses, and every penny would go to buy interferon, because this was in 1979. We had no idea when this stuff was going to be cloned.

***Lesley W. Brunet***22:40  
Just goes to buy interferon?

***Jordan Gutterman, MD***22:41  
That's all. Period. That's all. Solely, every penny was supposed to go directly to Finland. A little bit to, I think, Switzerland, where Mathilde Krim had a lab. We did give a little bit of money, eventually, to the University of Wisconsin for some -- to buy interferon. We did share a little bit of it. But I told them I had a lot of ideas beyond the tumors we were treating, and the ACS thing was a disaster because they were just confirming the work. And again, I don't want to demean it, because it was -- I mean, without the ACS agreeing to it, without Mary going to Rauscher, Rauscher agreeing to it, you know. Everybody believed in the work now, because it was all confirmed, so it served a purpose. You know. And I had to grow up a little bit and realize this was probably more important than giving it to me. Because if I was a lone wolf, nobody would have ever...

***Lesley W. Brunet***23:36  
(inaudible).

***Jordan Gutterman, MD***23:37  
Oh, absolutely. So my credibility was good, you know. So, I think I'll end with these two stories. The first meeting we had, they decided to go to Shell Oil. John Bookout Sr. And Bookout loved the story. Now, later on, we used as our fundraising, when the announcement of the first clone came out in January of '80 -- see, what's interesting is the foundation was set up in the fall of '79. With the idea that we're going to need this technique of making this very expensive stuff for god knows, five years, ten years? Pestka was just now getting these pure sequences, but I -- you know, we didn't know how long it was going to take to clone it, because cloning was so new. Within two months, (laughter) Biogen announces the cloning of interferon. And I thought, oh my god. That's just going to -- especially with Gilbert's prediction.

***Lesley W. Brunet***24:46  
(inaudible) money?

***Jordan Gutterman, MD***24:47  
Yeah. But it didn't hurt, as a matter of fact, because I think we scrambled over the mixed -- from 1980, when we announced it. But what had turned out to be the best fundraising was the MacNeil/Lehrer tape. So I'd go to all these meetings, and we can kind of go down the list of Pennzoil, and Atlantic Richfield, and so forth and so on. Halliburton, and I got to remember them all. I think [Redated] has a list -- but I think they're probably in the notes too. But, what would happen was, since I was busy, he'd start off with -- always went to the CEO. Not the foundation, we went only to the CEO. And they would have a TV set up -- after the Shell thing. But right after the Shell, I think it was Christmastime, so the next meetings from then on, I was on MacNeil/Lehrer, the middle of January of 1980, and they put that tape on. And that sold everybody. I mean, you know how TV has a mesmerizing power. Particularly MacNeil/Lehrer. PBS...

***Lesley W. Brunet***25:48  
(inaudible)

***Jordan Gutterman, MD***25:49  
Exactly. And here's Nobel Laureate, or soon to be Nobel Laureate, the head of the ACS, and myself, and so, I didn't have to do anything. (laughter) It was just simple. So I'd usually come in halfway through the tape, which was kind of dramatic, and there I was. And I didn't have to do much of anything. It was just zip, zip, zip, zip, zip, you know. A million dollars here, a million dollars there, really. It was really wonderful.

The first one that started it, and that was the key one, was John Bookout. We had a big press conference where they announced it, and I think it was November, December of '79 over at the Houston Academy of Sciences, I still remember that. With a small -- local press conference. I think -- I don't know where exactly LeMaistre began to pay attention to this. So far, I was -- there was very little blockage. (laughter) That was soon to change, I think. But so far, I was kind of a freewheeler. I do know that MD Anderson was not happy about the fact, about this foundation being set up separate from MD Anderson. So, I think, already, I was starting to get into some trouble. This was not my idea...

***Lesley W. Brunet***27:00  
(inaudible) always want the money to come through development.

***Jordan Gutterman, MD***27:02  
Yeah. And this is [Redacted]. "There's no way that greedy organization's going to get a penny. We're putting the money in" -- when you go to an oil company, you have to know -- "[Redacated] when you go to John Bookout or you go to this, that, and the other, they have to know that every penny goes right to the patients." Th ey don't want to get...

***Lesley W. Brunet***27:21  
It does (inaudible).

***Jordan Gutterman, MD***27:22  
Yeah. She was right on. And I'm going to end with the pure -- so a year later, we did raise this. And then we began to think of new diseases, which eventually led to the hairy cell leukemia, which I'm going to save for another time, which was very exciting. But I think you could just follow the path of -- these various paths coming together, all from the original, in my estimation, the original commitment -- really starting with the Krim meeting in '75.

**Chapter 09 : The Ideal Patient**

**A: The Clinical Provider**

Story Codes:

B: Institutional Mission and Values

A: The Clinician

C: Collaborations

D: Politics and Cancer/Science/Care

B: Institutional Politics

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

C: Human Stories

C: Offering Care, Compassion, Help C: Offering Care

We're going to end with '81, and I'll probably pick up a few pieces.

So a year later, we're raising this money. We're starting to think of new -- now we're getting more money, so we're getting more interferons, so I began to think about more diseases. So we start organizing some studies. Meanwhile -- the pure interferons. So it's always more than one track. There's always several tracks coming. We had to prepare for the first pure interferon, which was beyond exciting. And I was thinking this is going to be the great nirvana, because here's pure protein. Pure interferons. It's going to be like insulin. No side effects. All the side effects we were seeing, which was fatigue and fever, you know, exactly what you do as you get the flu, are going to be gone. So, I'll finish with this, and I'm pretty well spent.

So I was in the clinic seeing a patient, her name was [Redacted]. Very public. With lymphoma. Very attractive, what, mid-40s lady with lymphoma in the clinic, and I, in the old station -- near the library. An area you just walk past every day, you know. If you just go straight out of the library, past the elevators, and you get to the first -- not the first corner, by the men's room. Not by the elevator, but the first one, there's an elevator here going there. That area was our clinic. I was there on the -- there's physics offices there. Seeing a patient. And someone said John Burns from -- I actually went upstairs. John Burns is on the phone upstairs, my office called. So actually, somebody ran upstairs to the seventh floor, same little office. And he said we've been approved by the FDA to start clinical studies with pure interferon. So I guess you need to start looking for a patient. And he said, just remember, this is going to get a lot of attention, and I remember Hubert Humphrey was getting -- who I met with Mary -- was getting a lot of publicity with his bald head and stuff. And I said OK.

And I walk back in the [Redacted] room and I think, oh my god. The perfect patient. She's intelligent, well spoken. We were looking for a new therapy. We knew it works in lymphoma. I'm thinking -- so I said, she said, seemed like a call. And I said, yeah, we just got -- and she knew about interferon. In fact, we've been talking about going on interferon, and I said that the FDA has just approved us for the first pure interferon, and she said "Can I be your guinea pig?" And I said you bet you can. So that was it. No, no, excuse me. She didn't say that. "Can I be your poster girl?" That's what she said. Can I be your poster girl. I said yes.

***Lesley W. Brunet***30:42  
And I guess you had permission to use her picture.

***Jordan Gutterman, MD***30:44  
Yeah. And she was attractive in every way. You know, she just was -- photographed well, well spoken.

***Lesley W. Brunet***30:52  
Her picture's in my brochure.

***Jordan Gutterman, MD***30:53  
Yeah. Yeah. And the whole scenario -- now I was beginning to get the vision of Mary. No, you know, you think ahead -- like a chess game? You're at ten steps, you know.

***Lesley W. Brunet***31:04  
I don't play chess, I'm sorry.

***Jordan Gutterman, MD***31:06  
What's that?

***Lesley W. Brunet***31:06  
I don't play chess.

***Jordan Gutterman, MD***31:07  
OK. But you know, in chess, you have to think ahead five steps and six -- you have to have a strategy. These guys can think. I can't do it. I can play the game, but I don't play the game. Or in bridge, and all. You have to know steps ahead. Anyway. So I was beginning to do -- I think I always did this to some extent, I wouldn't be -- have been even where I was or convinced -- impressed Mary, you know. But now I was beginning to play the game too, (laughter) you know. Particularly since I was being beat up about turning down, you know, you don't want the first patient with interferon to be somebody, you know, moribund in bed, bald-headed, jaundiced, you know, that type of thing. And she was the perfect candidate, because she was healthy. She had the right disease. And she was well-spoken and she wanted to be the patient. So, you know, I played the whole game -- I mean, it wasn't a game. Excuse me, I shouldn't say that. But I wanted to choose a patient that would represent a new idea of a non-chemotherapeutic compound. And it was totally legitimate, I mean. We couldn't -- I mean, the protocol -- she fit the protocol, I mean, obviously. This was not a volunteer -- although I was accused, by the way, of hiring a model to get the first (laughter) I had everything happen. Oh yeah. People came down on me. "Hey Gutterman, how'd you hire that model for the patient and lying about her disease?" I mean, people said that stuff in the elevator to me.

***Lesley W. Brunet***32:30  
You said she had lymphoma?

***Jordan Gutterman, MD***32:32  
Nodular -- yeah, nodular lymphoma. Mmhmm. She didn't want -- she had to have some chemo, and didn't respond that well to it. And she just was one of these naturalists who didn't want a whole lot of chemo, or a whole lot of -- she loved the idea of interferon. Which did work on her up to a point.

So I could see that she was going to be the ideal patient. So, without going through the specifics, you know, we did a lot of work in the first two weeks of January. She, in fact, was the first patient, and we injected her. And I had a trip planned to Santa Rosa, California, to a hospital to give a talk, which I didn't do very often. It's just -- it was already scheduled. So my colleague, Dr. Cassada, who was just barely worked with me, it turned out prescient, because he's the one that agreed to work on hairy cell leukemia, because I needed doctors to work on new diseases with the natural stuff.

See, we had these strategies going on. And she was feeling perfect, and she gets the treatment. I didn't expect anything to happen. She was an outpatient. And about two hours after the treatment, I -- we were watching her, monitoring her very carefully. She said -- because FDA was very uptight. She (inaudible) chilly. Got a little headache. And I said, really? And then she really spiked the fever. So I remember calling Dr. Burns, the VP of research, and Pestka, the guy that just got the -- actually, it was Pestka. Both of them, both of them. I was scared out of my mind, I mean, I don't know. Recombinant protein...

***Lesley W. Brunet***34:08  
(overlapping conversation; inaudible)

***Jordan Gutterman, MD***34:10  
Exactly. (laughter) I mean, jeez. And I said, there must be an endotoxin -- an endotoxin is the outside wall of Gram-negative bacteria. Sid, who's been on the arrogant side, he said absolutely not. (inaudible) company, there's no endotoxin, there's no -- you may have contaminated it, but there was none in the vial. So I said, oh my god. Why -- of course, interferon is pyrogenic, it's causing fever. That's what -- when you get a flu, you release interferon, and all the side effects we see is due to interferon. And that was historical for me, personally. I've never written about it, because we were the first to inject a purified protein like this, a cytokine. That, in fact, simulates the side effects of a disease. I mean, that was quite a privilege -- and I recognized it on that afternoon, prior to my trip, that we were seeing history in action, because no one had the technology to ever inject a pure protein outside of insulin, which was synthesized, and it's a hormone, so it didn't cause fever, but this would be classified as a cytokine, a defense hormone, that part of the defense is to induce fever because bacteria and other viruses don't do well in a higher temperature, so evolution created these side effects, which in fact help the host. And we couldn't ever test that before, nor at least did I -- none of us ever talked about that, or did we predict it. So it was not a contaminate. It was, in fact, what pure...

***Lesley W. Brunet***35:47  
How long did it take you to figure that out? Same day?

***Jordan Gutterman, MD***35:50  
Oh yeah, oh yeah. I mean, when they said there was no endotoxin, I finally woke up and I said, well, it's -- oh my god. Of course. I mean, and when you went down to talk to her, she said I just feel achey all over, and I must be getting the flu. And that's what -- when -- I think she said, I think I'm getting the flu, and I'm thinking, oh my god, you are getting the flu, so to speak. You're getting exactly what you do with the flu, you're releasing interferon. (laughter) So we put her in the hospital, and I went to the airport, and I called them at the airport, and when I got to California, she leveled off, and I kept track of her during the night, sort of. But she kind of leveled off. And the protocol was the same dose given twice a week, so we had 72 hours before we had to repeat the dose. And...

**END OF FILE**