

Edmund A. Gehan, PhD, Oral History Interview
Interview Session 1: March 28, 2003

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Chapter 01: Early Life and Education in Brooklyn, New York

A: Personal Background;

Story Codes

A: Character, Values, Beliefs, Talents;

A: Professional Path

B: Personal Background; Influences from People and Life Experiences

C: Formative Experiences;

Tape 1 of 3, Side A

Lesley W. Brunet:

You said you had spent an hour getting ready for this interview.

Edmund A. Gehan, PhD:

Approximately. I don't know how you do this, but I guess one way to say it is my name is Edmund (Ed) Gehan. I first came to M. D. Anderson July 1, 1967, and I left in March 1994. I started out in the Department of Biomathematics, that was then under Lee Cady [M.D.], this is July 1967. Basically I followed Tom Frei [Emil Frei III] and J Freireich [Emil J Freireich] here.

As we will hear later, I started at the National Cancer Institute (NCI) in biostatistics working for someone who has since become very well known in statistics, Nathan Mantel, who I can talk about later. He was my first boss. Shortly after getting to NCI, I came in contact with Tom Frei

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and J Freireich. Tom Frei was, I believe, head of the medicine branch, and J Freireich was head of the leukemia section within the medicine branch. They were in the Clinical Center at NCI.

I guess one of the themes that I would mention is that biostatistics has a very rich history at NIH, which would almost take another time to talk about. It was sort of a birthplace of biostatistics in medical research, so I felt very fortunate to go there.

I had finished my Ph.D. in Chapel Hill, North Carolina. I went to the University of North Carolina, but as you'll see in my biography, it says NC State. Almost every line here is a different story. (Laughter) I don't know how far back one wants to go here.

Lesley W. Brunet:

Actually, I am interested, depending on how much time you have.

Edmund A. Gehan, PhD:

The only thing I am really interested in is to go to the Gottlieb [Memorial Award] lecture, so I could stay this afternoon. Actually my wife and I are scheduled to meet our daughter and her two kids for dinner, so depending on your time, I would like to go to the Gottlieb lecture at noontime, but I could come back in the afternoon.

You would like to hear some more of the background?

Lesley W. Brunet:

Do you have time to ... (?) (Counter53)

Edmund A. Gehan, PhD:

Well, I was born in Brooklyn, New York in 1929. I am 73 now. I went to Catholic School, St. Augustine's High School. I got good academic training there and then ended up at Manhattan College in New York City in the Bronx of New York, which is at 242nd Street and Broadway—a thirty-two stop subway ride from Brooklyn. (Laughter)

At that time they didn't have so many advisors. My father died when I was thirteen. If he hadn't, I probably would have gone into real estate and insurance, which he was in. But, unfortunately he died when I was thirteen. My mother did take me to the Johnson O'Connor Research Foundation. They sort of advise on how you should study. I guess I was kind of on track to go into perhaps a business school. I took various tests there. (Laughter) I did very well on two tests and very badly on one other. One very well was a number memory test, where they flash six digits on the screen for about five or ten seconds and then they do eight of these. Then after that they say, "OK, what are the numbers?" The first time through I got about five of the eight right.

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The second time through I got them all right. The third time through, of course, I still had them all right. So I did very well at that. So what does that mean? They don't know what it means exactly. That means I did a lot of my work by studying the night before the exam. (Laughter) Short-term memory.

Another one that I did very well on is I have always been interested in track and field, and you might be interested in this because they said, "This is your creative writing background." They said, "Supposing you could run two hundred miles an hour. How would this affect your life?" I am running on the track team at St. Augustine's High School. Well, I did non-stop writing for ten minutes. I broke every world record that existed. Then they just counted the words. "How many words did you write?" I was more than the ninety-fifth percentile. So what does that mean? Well, it doesn't mean anything, I guess, as far as creative writing skills. It was just a reflection on the exam.

The one that I did very badly on was the Wiggley Block Test. They still give this Wiggley Block Test. It is a rectangular solid and it is black. There are nine pieces to this rectangular solid. I guess if you think of the one in the very middle—the two ends of that one are black and everything else is a natural color. So they show it to you and then they go, "OK. Put it back together again."

It was a random thing for me. I don't know, I got it together in several minutes and I [said], "Well, I'm done with that."

"Nope, you're not done with that. Do it again."

I was slower the second time than the first. OK. So what does that mean? That means structural visualization you are very bad at. So don't go into engineering. (Laughter)

But actually I was among the worst in that, but then they said, "Well, structural is sort of a complement of abstract." (Laughter) So without giving a test, you are better at the abstract. Well anyway, at least I knew I wasn't good at engineering.

Also, I think one of the positive things coming from that, and you may appreciate this. You know, what is a mark of a successful person? One mark is having a good vocabulary—knowing words. Reader's Digest always had words that increase your power. I used to like to read them. I still need improvement. In the end they said, "No, don't go to business school. Go to an art's school—go to Liberal Arts." So I did that. OK, so that gets me to Manhattan College. Maybe it is longer than we thought we would be.

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Chapter 02: Choosing An Educational Background Focusing on Statistics

A: Educational Path

Story Codes:

A: Professional Path;

A: Influences from People and Life Experiences;

A: Professional Path;

C: Giving Recognition;

Edmund A. Gehan, PhD:

00:10:11

I started Manhattan College in the Bronx in September 1947. A lot of veterans were coming back from the war. Probably half my class was veterans. But I had just graduated from high school. The first year was kind of a repeat of what I had in high school. They were bringing the veterans back into the picture of things. I didn't work very hard at all. They had A, B, C, D—I guess the floor index was perfect, and so on. My first semester, I still remember, I got about a 2.7. I was bored. Well, I had better knuckle down the second semester, which I did, and I got a 3.4, which is an average of 3.1. That is what I graduated with four years later.

In the second year, this may be of some interest to you. Which department are you in?

James S. Olson, PhD:

I am a historian.

Edmund A. Gehan, PhD:

Oh, OK. But I am sure you had a lot of background in English, too.

James S. Olson, PhD:

Yes.

Edmund A. Gehan, PhD:

So I finished my sophomore year, and I did pretty well in English and I did pretty well in mathematics. I still remember to this day walking—again, not having an advisor. You know, what are you going to major in? You have to decide in your junior year. So I walked back and forth—major in English, major in mathematics. What should I do?

Then I said, “What do the English majors do at Christmas time? They write book reports. What do the math majors do? They don't do anything. I think I am going to major in mathematics.” (Laughter) So I majored in mathematics, but I was always reasonably good at English. I think

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that has helped me later in my career to have at least an interest in background in English. But mathematics, I mean I was good at it, and was studying differential equations and complex variables and algebra and advanced calculus and so on. But in my senior year I took a course in statistics. Statistics to me was mathematics applied to life's problems—mathematics applied to research. This really turned me on.

I graduated in 1951 and I asked my professor... Well, I never have served in the army or the military. A lot of my schoolmates were going into the Korean War, but I can honestly say I wasn't trying to avoid that. But I was kind of interested in statistics. So I said [to the professor] where can you go with statistics? He said there were three places you could go. You could go to Columbia University in New York, you can go to University of California Berkeley, or you can go to University of North Carolina in Chapel Hill.

Well, I told you it was thirty-two stops from Brooklyn to Manhattan College. I don't know the exact number, but Columbia is at 116th Street and Broadway. I would have been riding the subway a lot more. I had enough of that so I didn't want to go to Columbia.

I wrote a letter to UC Berkeley, and I should have saved the response I got because it was from Jersey Neymann (?), who is a giant in statistical theory and so on. I asked him, "Can you get a master's degree in one year?" because Berkeley was the other side of the world from Brooklyn and New York. You couldn't get a master's degree in one year, and I guess I was from a middle class family and it just didn't seem feasible. So by that logic, I ended up at the University of North Carolina in Chapel Hill, which in retrospect was the best of the three to go to because North Carolina had a theoretical department and an applied department. Whereas the others were more theoretical, which I didn't know at the time.

So I went to Chapel Hill in the theoretical department, the Department of Statistics. People in that department are giants—Harold Hotelling (?), Herbert Robbins in probability, R. C. Bowes, S. M. Roy. These were all giants in statistics. I guess one thing may be sighted. Two of them were Indians from India. I would say if you took the students from New York City and India that was more than half of the department. There was nobody from North Carolina at that time. I studied for one year in that department.

The applied department, under another great woman statistician, Gertrude Cox, was in Raleigh. So I was spending part of the time commuting from Chapel Hill to Raleigh.

James S. Olson, PhD:

Was less than thirty-two stops?

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Edmund A. Gehan, PhD:

It was thirty miles. (Laughter) And I didn't have a car, but I was fortunate to meet some friends that had a car. Well, I could see some of the theoretical stuff was beyond me and I enjoyed playing cards.

There weren't many books in statistics then. The first class I took from Herbert Robbins, I still remember, he talked some about the binomial distribution and what is the probability that the better team wins the World Series—certain probability things that are straightforward. Then at the end he said, “By the way, do the problems at the end of the first three chapters in [William] Feller's book (Place book title here?).” This wasn't homework. He just said, “do this.” Well, there may have been a hundred and twenty problems in those three [chapters], and if you did them you really would have learned a lot, but I didn't do them. Anyway, I wasn't doing particularly well, and I could see that more of my work was toward the applied so I switched my major to experimental statistics where the major was at North Carolina State, but I was living in Chapel Hill. I loved Chapel Hill. It is a beautiful town and I had already formed a number of things there.

Lesley W. Brunet:

Things?

Edmund A. Gehan, PhD:

Friendships and so on. Well, this is a sidetrack. It may come up later, I don't know, but it is something in relation to this sort of thing.

One of the aspects of my career was that I worked at a summer resort in New Jersey. It was a hotel for young people, but they put on shows during the weekend. The closest I could come to it is they would have shows like Saturday Night Live up there. They had a whole sequence of skits there, and I was smart enough—I don't know whether that is the right word, but when I went to Chapel Hill, I brought copies of about six or seven of these skits. Again, this was a long time ago. It wasn't so easy to meet girls on a campus. In the Fall they would have a party where the girls were invited and they were down there. I was in a graduate dormitory. So they had some entertainment. A guy played the guitar or something, and somewhere in the middle of the dance they said, “OK, so and so is going to play the guitar.” It didn't work. Everybody was standing around. It didn't work.

So I said, “I think I can do better than that—I've got all these skits.” The second semester, or the second year, I said I would put on the show. We got a carpet from somewhere where the people could sit down on it. We put on some of these skits, which went over extremely well and became popular and so on. The other thing is that I eventually became the dorm advisor because I was

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known to some of the people. I was the dormitory advisor of the graduate dorm in Chapel Hill. One of my claims to fame is while I was a graduate student at North Carolina State I was a dormitory advisor at Chapel Hill. So, in all of my affiliations, I spent perhaps two nights in Raleigh. I mean, I don't have anything against Raleigh. Anyway, that is kind of a sidetrack. Yes, I graduated from North Carolina State, but all my work was at Chapel Hill.

The Department of Statistics there started in 1949 under Bernard [Bernie] Greenberg, and when I got my master's degree in 1953, Bernie Greenberg, also from New York City, invited me to study for my doctorate and paid me the grand sum of \$250 a month, which was fantastic—tax free.

James S. Olson, PhD:

Not bad.

Edmund A. Gehan, PhD:

Not bad, not bad at all.

Since that time, if today one did what I did, your degree would be from Chapel Hill. Biostatistics was a part of experimental statistics in Raleigh then.

When I left Chapel Hill in early 1958—I think there it shows that I was an Instructor, 1955-57 because I didn't have my Ph.D. But they didn't have so many people in biostatistics, so when a student named Harry Smith graduated and went off, Greenberg put me on the junior faculty even without my degree. So from 1955-57 really is when I began consulting with medical investigators. That is almost fifty years ago—forty-eight years ago. I'd better retire.

In 1957 I got my Ph.D. Chapel Hill was beautiful, but you know, there was ivy on the walls. I don't know. I didn't want to see my fortune go up or down with how basketball or football... It was great while it lasted, but I was interested in moving on.

I moved to Washington, D.C. and to NCI in January 1958.

James S. Olson, PhD:

Where on the diploma is your Ph.D.?

Edmund A. Gehan, PhD:

N.C. State, in experimental statistics and public health because biostatistics was a part of the School of Public Health. That's kind of another story. I was never very interested in public health. I was much more interested in medical statistics.

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Chapter 03: Work at NCI/NIH, the Role of Statistics in Medical Research, and its Application in Sequential and Combination Cancer Treatment Evaluation

A: Professional Path;

Story Codes:

A: The Researcher;

D: On Research and Researchers;

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

B: MD Anderson Culture;

A: Personal Background;

A: Professional Path;

C: Funny Stories;

D: On Research and Researchers;

Edmund A. Gehan, PhD:

Anyway, I started in 1958 [NCI] working with Nathan Mantel, who died last summer, actually. He comes into the story later. I worked for him for about a year.

I think of all of these different stories...

Nathan was a tremendously intuitive statistician. He was the one who first taught me about consulting because when I first got to NIH [National Institutes of Health], Jerry [Jerome] Cornfield, who also will come in later, was the head statistician. NIH has the Cancer Institute, the Heart Institute—about eight institutes. Jerry was the senior leader. He would tell me about certain investigators, “Go see so and so.” Well, so and so would transfer all the data on his desk to me to me [and say], “You take this away and try to make some sense out of it.”

Nathan was my boss. Nathan was always walking around—he never seemed to have anything to do, and I couldn’t understand this. Then I went with him on one of his (?) and he taught the investigators to do their own statistics. He didn’t take anything away. I can tell a number of stories about shortcut methods that he used where he taught them to use their own data. I have come in that direction.

Anyway, we are still not to M. D. Anderson.

James S. Olson, PhD:

May I ask you a question?

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Edmund A. Gehan, PhD:

Sure, any time.

James S. Olson, PhD:

Was there any resentment among the physicians at NCI to having a mathematician or statistician come in and start looking at the data, or did they welcome it?

Edmund A. Gehan, PhD:

They welcomed it. I guess one of the things I had to do back at Chapel Hill is to teach statistics to the medical students, the dental students, and the nursing students. There must have been a hundred or so medical students in the class, but the ones interested in research are the ones that you could talk to. I mean, you don't get a paper in the New England Journal of Medicine or the good journals unless it has solid analytical support. Some of the students would read the paper. The ones at NIH, particularly Tom Frei and J Freireich, and there are specific examples of this. I guess one particular example is not really on this list, but one of the first studies I worked on was the 6MP and methotrexate study. They studied 6MP treatment and methotrexate treatment, and the combination. Well, 6MP had a certain response rate and so did methotrexate have a certain response rate. You can find a write-up in the paper about what is the predicted response rate of the combination. The analogy I drew was in the paper, if you shoot an arrow at a target, the patient, with a certain probability of a hit with 6MP and you shoot another arrow at it with a certain probability of a hit with methotrexate, you can calculate from that. You don't need both of them to hit to be a success. You only need one. That is a successful treatment. It is one minus the probability that neither one hits, is the probability that one or the other hits. What we were able to show in this particular paper is that the actual response rate of 6MP plus methotrexate was very close to what you would predict by shooting arrows at the target. You'd have to ask Tom Frei and J Freireich where the idea would come from to study multiple drugs given at the same time that didn't have additive toxicity. If you are adding the toxicity, you are in trouble. That is one example within a paper that is in my curriculum vitae. Frei was the first author, "Studies of sequential and combination treatment in leukemia."

I helped to provide the analytical support to some of the ideas—both at NCI and later here—sort of in a broad sense. Both Tom and J were research-oriented people that realized that someone like myself could help them.

Tape 1, Side B

Edmund A. Gehan, PhD:

In a way, they should have invited to all to come to that [7th Foundations of Clinical Cancer Research Symposium].

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Lesley W. Brunet:

We don't get invited to those things.

Edmund A. Gehan, PhD:

I talked some with Thomas (?) and he said to me that he is going to send you up to Michigan to see Dr. Hickey. Oh, you didn't know that?

Lesley W. Brunet:

I am glad it is getting to be Spring.

Edmund A. Gehan, PhD:

Time to go.

Lesley W. Brunet:

That's good.

Edmund A. Gehan, PhD:

Freireich is great. How many people did they have at that dinner? Fifty? Something like that. I don't know, but different tables. Somewhere along the line, Freireich gets up and says, "The cost of your coming to this dinner is to get to give a speech." He sort of presses people to give some kind of a talk, so people do. Of the people last night, Tom Frei gave a nice talk and told a very good joke. I gave a talk. Michael Keating and Freireich were kind of co-MC's [Master of Ceremonies]. They got Dr. Levy [Robert], a very fine man, and of course a lot of the talks were in reference to Gottlieb [Jeffery A.], but this is the 28th [Annual Award]. My talk was more about Frei and Freireich last night. Rowinsky [Eric], a younger guy, getting the Freireich Award, he talked later. Was it about they are all honored to be with Frei and Freireich? What is it about them? And he mentioned the passion—the passion. And he was right. There was a certain amount of camaraderie, but also passion for doing better.

This is part of the theme. You know, mathematics is really kind of dry, but statistics is... I have always turned on by sort of being a member of the team where the statistical part is an important part of the progress. You are a member of the team and this is the part that you are contributing to.

I have just given you a statistical example. You could say, "I don't really think that Gehan has showed that... and therefore we can give..." It was broader than that. I certainly wouldn't claim that certain mathematical arguments would suggest that combination chemotherapy was better. But, it can be seen as part of the justification anyway.

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Lesley W. Brunet:

When did you first join that Frei/Freireich team at NCI?

Edmund A. Gehan, PhD:

Well, I started in January 1958. I worked some with Freireich. I would have to review the larger curriculum vitae. I remember working with Freireich, in particular, on several projects. It was in 1958. But, you know Freireich was kind of a bear to people. He would tend to put people down. I guess I can be thankful that I was in a different field. He wasn't going to put me down in my field, and I think he could see that I could help him. I basically started working with both of them then, where it says [curriculum vitae] "Acting Head" and then "Head of the Biometrics Section, Cancer Chemotherapy National Service Center.

Another good man at NCI was a guy named Marvin Schneiderman. He left to get his Ph.D. in England, so they needed somebody to replace him. In 1959, I am 30 years old then, a youngster, they appoint me Acting Head and then later Head of this Biometrics Section. Well I am sure you have heard of these cooperative groups, including the Southwest [Oncology] Group and the Eastern [Oncology] Group. This section kind of oversaw all of those statistical groups. Some of the groups, in particular the Acute Leukemia Group B, I was the statistician for that group, and we had a statistical clerk that worked on that. Tom Frei was the chairman of the group and J Freireich was one of the members, so beginning then I worked very closely with them as part of the Acute Leukemia Group B, which is now the Cancer and Leukemia Group B, which is still in existence.

I told a couple of stories even last night. In some ways it was more fun. I remember a particular meeting at Mt. Sinai in New York. Maybe the conference table was bigger than this, maybe one and a half times [bigger]. But the whole group is around the table. One of the stories I told... (Laughter) Tom is just an amazing guy. He is the chairman, so he was making certain announcements at the beginning. He has an index card and he starts, "This is what we are going to do in the meeting," and this and that. As he talks he keeps referring to this index card and saying something about the meeting and what's going to happen. How in the hell did he have all that stuff on this index card? So I looked at it later. The index card was blank. (Laughter) He didn't have anything on the index card.

The other thing about it was that how were ideas for clinical studies developed? They were developed at the blackboard. Dr. X (?) was offering Dr. Freireich, "I think the treatment should be this." Then they would write it out. Then the other group should be this. At that time, Frei was the moderator. He is a fantastic moderator—great, I think. And J was very outspoken. On one side, Jim [James] Holland, I am sure you have heard that name before, was very outspoken.

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By the time all of the arguments [were presented] for this or that approach, everybody had a pretty good understanding of what it is we are finally agreeing to. What would happen in the course of the discussion, somebody would go to the blackboard and erase, “No, it shouldn’t be that—it should be this.” Then various ideas would be put forward. Eventually it would be agreed to, and Tom was the one for bringing people to agreement. Then they would say, “OK, well let’s do this group for the next three months and see how things go.” [There was] no written protocol, no IRB, no approval mechanisms; it was just done. There was a certain level of excitement in what was being done. One of my analogies is it was more fun back then.

I haven’t been to a Southwest Oncology Group meeting for a long time, but one of my statistical theories... Everyone is trying to find the cure for cancer. What is the chance that you will find the cure for cancer if you are a member of a team and you don’t even know all of the people on this team. (Laughter) It’s just gotten so big. It was more fun back then. Is it better now? In many ways it is better, but I think it was more fun [back then]. I became good friends of them there.

For myself, from 1962 to 1964, I was a special fellow at Birkbeck College of London [England]. Perhaps one of the most famous people in statistics is Sir David R. Cox. In 1956, he was a visiting professor in Chapel Hill, so I first met him in 1956. He is now Sir David Cox, but I could see that he was a brilliant man. I was immersed a lot in data, but an important decision for me—I was kind of interested in doing some research work on things that came up at NIH, so I applied for this fellowship to go to London and I was fortunate enough to get this fellowship. So I was working in Professor Cox’s department, which at that time was at Birkbeck College of London. Birkbeck College is a night school of the University of London. It is not one of the better colleges. He is at Oxford University now though. He eventually became the Warden at Meffield (?) College, which is a very prestigious position, and he is still at Oxford. I’ll think of the other school in London.

I worked with Professor Cox for two years. I married my wife Brenda in part because we were going to have to go to London, and you have to either fish or cut bait at that point, you know, in terms of personal relationships.

I came back to NIH, but I wasn’t too happy for reasons that I don’t want to [talk about]. It just would take too long to talk about.

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**Chapter 04: Strengthening Medical Oncology at MD Anderson with the Aid of NCI
Researchers in the Department of Biostatistics
B: An Institutional Unit**

Story Codes:

B: Building/Transforming the Institution;

A: Professional Path;

C: Giving Recognition;

D: On Research and Researchers;

Edmund A. Gehan, PhD:

00:44:28.850

It was around 1966 that Frei moved here. Have you ever heard this story of how he moved here?

James S. Olson, PhD:

All I have is a letter from Kenneth Endicott I came across to Dr. Clark about 1965-66, when Frei and Freireich had made the decision to come and Endicott was just absolutely heartbroken about it. He was happy for Dr. Clark in a way, but he just thought it was a real blow to him and the program.

Lesley W. Brunet:

But Frei came down in 1964.

Edmund A. Gehan, PhD:

Who?

Lesley W. Brunet:

Frei came down in 1964.

Edmund A. Gehan, PhD:

1964?

Edmund A. Gehan, PhD:

Late in the year.

Edmund A. Gehan, PhD:

Well, it was around 1964-65. But do you know why he came?

Where was Houston in 1964?

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Well, I can tell a very brief story, which I mentioned. I first came to Houston in the late fifties, early sixties. It was probably in the 1961-62 time. I was sort of a member of an NCI group visiting Dr. Clark. Dr. Clark had applied for some money for a project that I don't remember, but he took the following tack. There was a committee of seven or eight people, and head of that particular biometric section was actually in some ways was still the best job that I have had in terms of administratively. But Dr. Clark spoke to the group and said, "We know we are well behind down here. We are trying to catch up with you there at NIH. We need some more excellence in our research people and better capabilities than we have. If you give us this money, that will help us along the road." Well, he got that money. That was a very successful approach to dealing with people.

And I later followed Frei and Freireich [here]. I have asked Tom and you should ask him, too. "Why did you ever move here?" He is from St. Louis and he was doing well in Washington. He had a very senior position. The answer is a personal matter.

Tom has five kids. He has four girls and a boy. We do, too. We have four girls and a boy. Tom's wife was Liz Frei, a wonderful woman. Liz had a sister, Lil, who had seven or eight kids and was married to a postman, who died at age 39 or 40, something like that. Tom is the only potential source of income for these, so Tom is responsible for thirteen kids. Some of them were old enough to take care [of themselves]. It might have been eleven or twelve, I don't know, but he basically moved here because he couldn't afford to support that size family on a government salary, and so that's why he came. I am quite sure of that.

Lesley W. Brunet:

Yes, that is true.

Edmund A. Gehan, PhD:

When I first came here for an interview, I guess I'll never forget this part either. Tom says, "Why don't you come for dinner?" You know it was part of the recruitment. "Oh, OK." But he didn't have a car, so Liz was going to come and pick him up. So Liz came. [I thought] Who is taking care of these twelve or thirteen kids? (Laughter)

Well, you get to the house. Liz took care of all that. Tom is oblivious to things. It was like a picnic table. And the dinner was kind of thrown together. I guess one of the things about Tom is that his professional life is tremendously well organized, but his home life is chaos—absolute chaos. I can expand on that.

I came here in 1967. It started out that Lee Cady was head of the Department of Biomathematics, although he was an M.D. I guess one of the others have probably told you stories about this, too.

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In the final stages of the negotiations with Clark, I get to see Dr. Clark. I had already got a good background. I had already been to London and I had a number of published papers, and so on, so I had a pretty good background in statistics. Lee Cady, as I said, was an M.D., but he was a Professor of Biomathematics. So we came down [after] talking to Dr. Clark. "What level of appointment do you think you should have?" I said, "Well, if Lee Cady is a Professor, I should be a Professor, too." Done. That's taken care of. [There were] no committees, nothing. Then we came to discussing salary. I was making about \$14,000 with the government. I was a GS14, which is actually a reasonably high level. It was something like \$15,000 that he was going to offer me, something like that. I said, "Well, I was really hoping to get something more, maybe \$16,000," a thousand or two more than he said. (Sound of a hand hitting the table) Done. (Laughter) I mean, Dr. Clark was autocratic, but he was a good autocrat, and in the end that is kind of the reason that we came here.

I would regard the letter that you had from Endicott that they really brought M. D. Anderson into the modern era. There were a number of good old boys here, and they certainly were good old boys.

Lesley W. Brunet:

I'd like to hear about that.

Edmund A. Gehan, PhD:

I was one of the younger people. Somebody could say, "What were the research accomplishments at M. D. Anderson prior to their coming?" They were the headquarters of the Southwest Oncology Group under Dr. Grant Taylor, who was the chairman.

James S. Olson, PhD:

There is controversy about that though, isn't there? A problem with Taylor?

Edmund A. Gehan, PhD:

No, not at the beginning. The mid-fifties are when these cooperative groups got started. Gordon Zubrod went around the country with Marvin Schneiderman, the statistician, so right from the start there was always a clinical chairman and a statistician. Houston, even though it wasn't such a great place, was a major spot here. I guess Clark assigned Grant Taylor to the chairmanship of the Southwest Group. A woman named Eleanor Macdonald, who Clark had run into, was at the Connecticut Tumor Registry. She was more epidemiologist and a tumor registry person than a statistician. And then a fellow named Ken Griffith was the statistician. That started in 1957-1958, around there. There was a Dr. [Roy C.] Heflebower. Joe Boyd was on the business side. Others could tell you, Clark certainly was loyal to the people closely around him. But I wasn't a part of that mix.

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James S. Olson, PhD:

That is kind of interesting because he had that team he started off with, and as the place really grew, he had to start marginalizing some of those people. He was loyal to them, but some of them were kind of out of touch with what had happened in the disciplines so you start seeing them getting pushed to the side a little bit.

Edmund A. Gehan, PhD:

Yes, a little bit. I guess one personal part of this, as I said, I became a professor in biomathematics, but within six months of coming here, Lee Cady left and went to California. OK. Who is going to be head of biomathematics now? I have a reasonably good background. I am not picked. Stu [Stuart] Zimmerman is picked. Where is Stu Zimmerman? Stu Zimmerman is actually more in the Dental School. He is an associate professor and he doesn't have a primary appointment here, but he gets one. To this day, I think that Clark didn't want to give too much power to Frei and Freireich. Frei is the head of Developmental Therapeutics. I think, and we'll never exactly know, by any objective standard I was far ahead of Zimmerman, who wasn't really in biostatistics anyway, he was in biomathematics. Part of the crosses I have had to bear is that Stu Zimmerman became chairman in 1967, and I was very disappointed in not being chosen. Stu did not step down as chair until, what, last year?

Lesley W. Brunet:

Yes.

Edmund A. Gehan, PhD:

I think he was the longest serving chair in that particular department. I don't know whether you have spent time with him, but you should go through some of the same things [with him]. He was not particularly supportive of me. I guess, in part, I'm sure he perhaps detected some resentment on my part, but he kept a fairly tight lid on me and the [other] people.

One other small story is I said we have five kids, and a number of them are in the Houston area, so I had this opportunity to go to Georgetown to be head of a small group. My wife really didn't want to leave. I did go to see Dr. LeMaistre and I did go to see Dr. Fred Becker. Becker and Zimmerman got along very well, and Becker was head of research. One of the things I went to Becker about was biostatistics has been a part of biomathematics for a long time. I think it's time that it could be a separate group. Becker said, "Well it may become a separate group some day, but it won't happen for you."

It has happened since. For two years they tried to find a replacement for me. They found Don [Donald A.] Berry, who was a terrific biostatistician, and now there is a Department of

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Biostatistics, but biostatistics is four or five times the size. Biostatistics, when I was here, was a section in the Department of Biomathematics. Now it is its own department. You'll have to look it up on the web site. It is four or five times what it was. Biomathematics has gone down to this. They recently had a site visit. What are we going to do with Biomathematics?

James S. Olson, PhD:

Is that a trend?

Edmund A. Gehan, PhD:

I would just say that I have heard Mendelsohn say this, which I agree with, "Biomathematics is a luxury; biostatistics is a necessity." You're not going to solve cancer with mathematics. It's much more statistical modeling and computer modeling, not strictly mathematical modeling. Is that a trend? Yes. I guess the trend since my coming into the field is much more in the direction of computer modeling and computer-intensive methods.

I guess one of the things I had to deal with, towards the end, people wanted more expansion in the area of biostatistics. OK, we're going to set up a new section. I was head of the section of biometrics. We're going to form a new section, I think it's section of clinical biostatistics. So if we're going to form this new section, we're going to have to find a new head. However, all of the people in biometrics will be invited to be part. So, in other words (tape ends)...

Tape 2, Side A

Lesley W. Brunet:

Is that what you mean when you say Zimmerman was not supportive?

Edmund A. Gehan, PhD:

Things started a lot before that. I really want to be positive, but I can't be positive about Zimmerman. Get him here and say, "OK, what were the things that happened in your tenure as head of the department from 1967 to 2001, or whatever it was, something like that."

There are still some good people. Terry Smith is someone I've mentioned to you, Peter Thall is excellent, and [J.] Jack Lee [Ph.D.] are three people that I recruited to come here that are still key parts of that group. We have had other people that were there.

I guess I would like to say that Zimmerman was not at all helpful to me over the years, but I wasn't working with him. I was in his department, and so on, but he didn't mentor my work or the people's work under me. I may not have gotten the recognition here that I might have

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otherwise, or at least had more control of things. Everything I wanted to do had to go through his office. I am not a negative person; I don't think [I am].

What were the main influences here? I would say for me it would be providing the analytical support to the Frei/Freireich team. They build up people in clinical pharmacology, immunology. I mean they broadened out the whole the medical oncology work.

James S. Olson, PhD:

By design?

Edmund A. Gehan, PhD:

Oh, yes. Oh, yes. I think some of it was an analogy to what was at NIH, and that you had a lot of capabilities there and they weren't here. Now how they actually got the money to do all this, that I don't know. You'd have to ask Freireich more about that.

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Chapter 05: The Leadership Styles of Dr. Frei and Dr. Freireich and Working with the Southwest Oncology Group (SWOG)

B: An Institutional Unit;

Story Codes:

B: Institutional Politics;

B: Controversy;

C: Funny Stories;

D: On Research and Researchers;

Edmund A. Gehan, PhD:

01:02:52.960

I guess [I have] one other kind of personal story. Tom Frei has been a friend since 1958 or 1959. He is also the godfather of one of my children. So he has been a good personal friend over the years. Back when I first came here, if we needed another computer programmer, we needed something. I would go to Tom. "We need somebody at the computer." "Oh Ed, no problem. Yes. Fine." Nothing ever happened. He never disagreed with anything, but I guess that's one of the things that have amazed me and you should probably check this out. Tom is a terrible administrator. He has always had high administrative positions. He was head of the medicine branch here. Then you went to Freireich, who was the deputy head. "J, listen, I talked to Tom some weeks ago about this. Nothing has happened." (Sound of fist hitting the table) "I'll take care of it." And he did.

Lesley W. Brunet:

He has admitted that he did most of the administrative work.

Edmund A. Gehan, PhD:

He did. He did a lot of things for Tom. They were an excellent team.

I guess going back to one of the things about when Tom came here, the Southwest Group had an adult division and a pediatric division. Pediatricians were scared stiff of Freireich. He was aggressive. As I understand it, when Tom came here, they were going to run oncology for the adults and children—both of them. But Freireich was going to be the one handling the kids. Margaret Sullivan was a person here.

Watsuto (?). If you haven't gotten his story, I could certainly tell parts of it. He was a great man. He died about 1981 or 1982, but he was a key part of pediatrics. [He was] A very gentle soul. He was one of the good people here in the sense of having really done research.

Lesley W. Brunet:

He did service with you?

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Edmund A. Gehan, PhD:

Yes. Yes. But one of the things they didn't get was that Freireich didn't run the clinical studies in pediatrics, either as part of M. D. Anderson or in the Southwest Oncology group.

For me was being part of the team, but I also became the statistician for the Southwest Oncology group around 1968 or 1969. As I said, I used to oversee these when I was back at NCI. And when you talked about what are the offices, we had four groups—

Acute Leukemia B, Eastern Group, Veteran's Prostate Group and there was a Breast Group, and I would take people on a tour. Here is our office for Acute Leukemia Group B, meet Joy Schwartz (?). It was me and a clerk—that was the whole team.

The grants for these groups were about a million dollars. You might have thirty or forty people working on these groups. Then when the Southwest Group became bigger, our grant got up in the neighborhood of a million dollars, so you could control the money. I was bringing in a lot of money through the statistical center. Frei became chairman of the Southwest Group around 1970?

Lesley W. Brunet:

The notes I have say 1969.

Edmund A. Gehan, PhD:

OK. I'm going from memory. Frei became chair in 1969, and then he left in 1972. Who is going to replace him as chair? Freireich is a candidate. There is a Freireich candidate and a non-Freireich candidate. You either voted for or against Freireich. The against Freireich candidate was Barth [Kenneth R.] Hogstrom who was from Kansas. This happened around 1972. There was a vote in New Orleans, and I guess the statistical center kept track of the vote. The vote is seventeen to sixteen in favor of Hogstrom. All the pediatricians hated Freireich. The precise numbers I don't have, but it was something like fifteen or so votes in pediatrics and seventeen or eighteen votes adult. The adults are like sixteen to two for Freireich. The pediatricians are the other way around for Hogstrom. Hogstrom ends up seventeen to sixteen as a winner. I mean it was a total split. And later the pediatric group splits off anyway, but the outcome of that election is that Hogstrom is elected chair. He was very difficult for us—he was a very autocratic person. It became very difficult, and I guess ultimately M. D. Anderson drops out of the Southwest Group. I don't know year you have that for, but M. D. Anderson drops out of the Southwest Group.

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Actually Freireich didn't want to just resign from the group. He wanted to be voted out. There was a requirement that you enter fifty patients a year? I don't know, some number. M. D. Anderson, big as it is, didn't meet the patient entry requirements of the group, deliberately. The executive committee votes them out. I guess this happened around 1980 maybe, something like that.

We still have the statistical office here. My loyalty then starts coming into question. By this time, a new chairman is picked, Chuck [Charles A.] Coltman from San Antonio, and my loyalty to them, should the statistical office remain at M. D. Anderson, when M. D. Anderson is not a member? I was forced in continuing because it was a source of a lot of my support. We had twenty-twenty five people, something like that, working as part of this.

I do remember one story. We were getting ready for a site visit. You know, when people become chairmen, they wanted people to be aware of that. So from now on, all the forms, instead of being sent directly to Houston, will be sent directly to San Antonio and San Antonio will then ship them here to be analyzed. They had on a blackboard a box San Antonio – Houston. And I still remember being at the rehearsal when they were describing this process. Somebody said. That line between San Antonio and Houston, that doesn't look strong enough. "Oh, OK. Let's darken it more." And they did. (Laughter) The line didn't last long and we lost the statistical center to the Southwest Oncology Group. I could say more, but M. D. Anderson was not a member of the group at that time. There were some criticisms at what we were doing in the office.

Lesley W. Brunet:

Did it move to Seattle?

Edmund A. Gehan, PhD:

Yes, it moved to Seattle. You see Seattle didn't have to be approved by an NCI group and I happened to know one of the site visitors that went to Seattle. They have an excellent biostatistical team up there, but they said they almost weren't approved. Things weren't well set-up up there. They were approved.

Right now, the Southwest Oncology Group is still flourishing with Coltman in San Antonio as the chair and their statistical center is in Washington [State], and I am sure it's a very good group up there.

One of the things I did, as I said, was to bring this two-page biographical sketch, and I think in another twenty minutes or so, could mention some of the key papers in it. My secretary typed it out. I think it would take maybe about twenty minutes to do that.

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Lesley W. Brunet:

Should we do that? Do you want to do that or would you prefer asking him a couple questions?

Edmund A. Gehan, PhD:

What I am proposing is... Well, I didn't know how to prepare for this meeting.

Lesley W. Brunet:

You didn't have to prepare, but it is wonderful that you did.

Edmund A. Gehan, PhD:

I guess what I would like to do...

Lesley W. Brunet:

Would you like to go over this? We can always figure out what we have to talk about this afternoon.

Edmund A. Gehan, PhD:

Yes. This is the two page biographical sketch that you have to have. I have picked out a number of papers that I thought have had some impact. As I say, I actually did bring along copies of all these papers, but then you have to read them maybe.

Lesley W. Brunet:

We will put your sketch with your interview so it will be very clear.

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Chapter 06: Dr. Gehan's Research and Publishing Impact

A: The Researcher

Story Codes: A: The Researcher;

B: Research;

C: Human Stories;

C: Funny Stories;

C: Collaborations;

C: Giving Recognition;

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

Edmund A. Gehan, PhD:

01:16:35.350

I will just try to give you a little bit of the background.

This reference one (Reference #1?) is how many patients to you need in a Phase II trial? There was a big search at NCI before coming to M. D. Anderson, you know. There was a whole pipeline, studies in animals, pharmacology, and so on. I would be at meetings like this: the physician would study five patients; they were all toxic; the treatment is worthless, let's stop. So I addressed the question of what is the minimum number of patients you should study, that if they all fail, then you can stop. One answer to that question is fourteen, which is justified in the paper. Fourteen has become almost a magic number in Phase II trials. As I say, I have a copy of this paper.

Reference two (Reference #2) is a test for survival data, and it arose directly from the clinical trial that I did with Frei and Freireich. This is perhaps the most theoretical paper that I have written. Well, then I guess in a way it is some justification of "why do you need a statistician working in a clinical trial?" It's a way to compare two survival distributions. A lot of the patients are still alive in both groups, so there is no average survival time. I worked on this paper in London, working with Professor Cox, and both of these are citation classics.

Somehow if you are going to have a test named after you, you'd have it made. (Laughter)

Lesley W. Brunet:

Yes.

Edmund A. Gehan, PhD:

These are some pages from the *Encyclopedia of Biostatistics* [References 1 and 2]. So there were games designed for Phase II trials. I called it a generalization of Wilcoxin test, but since then people have called it the Gehan test. My proposals were basically the first ones in both of these

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fields. People have gone on further with a lot, obviously a lot further. And that is spelled out in the write-up that is in the *Encyclopedia [of Biostatistics]*. Well, I am proud of those parts.

Believe it or not, in statistics, there is a book called *Data*. What they said is, "It's not always easy to find a good example that you can work with." Agnes Hertzberg is a good friend of mine. Her own handicap is that her father won the Nobel Prize and she will never live up to her father, but she is a very fine woman. Anyway, she asked me to use this leukemia data, and actually this is a very readable thing, but it shows how the data that got into that Wilcoxin test. This not only got into the Wilcoxin test, but I said I worked with David Cox in London. The most famous paper published in the twentieth century was Cox's paper on regression models and life tables. In that paper he uses this data as an example. By the way, if I was smart enough, I would have developed that test, but I didn't. (Laughter) Anyway, this is a readable thing as to how this clinical trial of cancer lead to my work on comparing survival distributions, and also to Cox' work. If he is asked, "Where did you get the idea for that?" He doesn't say, "I got it from Gehan." He doesn't say that. There were several other influences, too. And as I said, he was brilliant.

This is a paper that I wrote at M. D. Anderson [Reference 3]. People don't do things like this anymore. An important aspect of survival functions is estimating the hazard function, the risk of death per unit of time. Actually Cox's work is based upon dealing with hazard function. If you group all of the survival into intervals, it tells you how to plot the hazard function. Here is the hazard function. You can see the risk was high here, then it was flattened out then it went up. I think this was a nice paper. But people don't do this anymore because [with] computers, you don't have to group the data.

This paper, "Non-randomized Controls in Cancer Clinical Trials" (Reference #) is a special article in the *New England Journal [of Medicine]*. This study is one of the most quoted sets of data. This study was the first prospective, randomized, double blind, placebo-controlled, sequential analysis theory. It was the first study of this type to be done and Freireich was the co-author. His was the main idea for the clinical study. Freireich's proposal since then said, "Well, I've been there, done that and now I don't need to do that anymore." All the combination therapy, they didn't randomize, they didn't randomize. I guess you'd have to ask him something about randomization; there were certain things on the skid about that.

Lesley W. Brunet:

Yes.

Edmund A. Gehan, PhD:

There was a paper published before this by Tom Chalmers, "Controls in Clinical Investigations"

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in which he said, “There was a good argument for randomizing the very first patient in a new therapy. And if the study wasn’t randomized, it wasn’t controlled.” Well, I didn’t believe that. Dr. Ingelfinger was then the Editor of *the New England Journal [of Medicine]*. We said we wanted to comment on Chalmers’ paper, and he said to his credit, “I don’t want anything saying that Chalmers is full of bologna. Give me a positive paper of why non-randomized controls are good.” So we did. I basically wrote the paper. This was a key justification for why you might want to consider non-randomizing. I know you have been treated for cancer, but not many people want to have their treatment decided by the flip of a coin. Although I statistically support randomized trials when there is equipoise.

One of the stories is that Dr. ...I’ll have to think of his name again now. He was in pediatrics and he had to deal with parents that had a child with cancer.

Lesley W. Brunet:

Was he here?

Edmund A. Gehan, PhD:

No, he wasn’t [here]. He was in Philadelphia. He was trying to persuade the parents to enter their child on this randomized trial. The parents said, “Which one do you think is better, doctor?” He said, “I don’t know which one is better, that’s why we want to do the randomized trial. We’ll find out which one is better.” “Yes, doctor, I know that you don’t know, but which one do you think is better?” And with that he had to say, “Well, this one may be better.” “Well, that’s the one I want for my kid.” Logically there are many reasons for randomized trials and theoretically I am for them. Freireich I think goes too far the other way, that you never have to randomize.

This is another rational basis for historical controls, the logic for doing it. These were all written when I was here. (Ref ?)

There is one statistical evaluation of therapies and historical controls (Ref ?). One of the points this makes is, “Let’s look at the progress in cancer.” There is a table here. What new treatments were found by randomized versus non-randomized trials? Here is a list that came out of historical control studies. Some of them weren’t well historically controlled, and one of them was by Watsuto in osteosarcoma.

This may not be a great paper, but “The Training of Statisticians for Cooperative Clinical Trials” I did write while I was here (Ref ?). As you get older, how do you teach somebody coming into the field? This is a series of thoughts about that, some of which came from Mantel. It said, “Beware of people that say I only need five minutes of your time to handle my [problem].”

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They've been thinking about it for years maybe, and they only need five minutes of your time to solve their problem. Beware of such people; they need more than five minutes.

This is an article also written here, "A Strategy for Evaluation of New Treatments in Untreated Patients: Application to a Clinical Trial of AMSA for Acute Leukemia" [Reference 10]. It was Freireich's basic idea. We all want to evaluate new treatments, but there are already treatments available for all kinds of cancer. So if a new patient comes in, and those are the ones that you really want most, how do you try to evaluate a new treatment in that patient? The standard way of doing it is administer all the known things and then when things are toward the end of the line, then give the new [treatment]. Well, that is the biggest hurdle for the new treatment. Maybe you'd be better giving it closer up front. This was an idea that Freireich had, but we implemented, which said, "Use a statistical regression model based upon—in this case—their age, their temperature, antecedent hematologic disorder, BUN, hemoglobin, liver size." We can use this model based on past data and get out of it a probability that you are going to respond to the treatment, given the standard. Some of the patients are going to have a high probability, and those you give the standard. Those that have a low probability, you give them the new [treatment].

Tape 2, Side B

Edmund A. Gehan, PhD:

As I say, administering the new treatment to those with lower probability of response. Actually, it turned out they did pretty well, and the criteria were gradually moved up. I think it's a good idea that hasn't adequately been followed.

This is "Historical and Methodological Developments in Clinical Trials at the National Cancer Institute" (Reference ?). This paper was written here in 1989, and this is somewhat of an historical paper. How do the cooperative groups develop? You take the cooperative groups program in 1960, and at that time [in] the Southwest Group, Dr. Grant Taylor was the chairman and Eleanor Macdonald was the statistician. This takes all the groups. Frei was acute leukemia. He was the chair of that one and Schneiderman was the statistician. I am not listed on any of these, but a year later I had taken Schneiderman's place. This gives a pretty good historical review of the clinical trials program as it evolved at NCI and spread out.

James S. Olson, PhD:

Was Eleanor Macdonald a statistician?

Edmund A. Gehan, PhD:

No. I guess she has died now.

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Lesley W. Brunet:

No, she is living.

James S. Olson, PhD:

Yes, still alive.

Edmund A. Gehan, PhD:

Good for her. I think she would consider herself an epidemiologist. She was one of the old buddies of Dr. Clark, and she worked for the Connecticut Tumor Registry. She wasn't trained in mathematics or statistics. I think she certainly knew some statistics, but a lot of hospitals have tumor registries, and that was the background from which she came.

James S. Olson, PhD:

Right.

Edmund A. Gehan, PhD:

I think she had passed over the statistical part of the group to Ken Griffith, even by the time that I came here. We were always pretty good friends although we didn't work very closely together. If you didn't have any proprietary interest in maintaining the head of the statistical (trails off).

James S. Olson, PhD:

Who replaced her in epidemiology?

Lesley W. Brunet:

(?) (Counter 48)

Edmund A. Gehan, PhD:

He came well after she was out of the picture, I think. I think there was an interval. You'd have to ask Genet [Louis]. I am sure he is still around. He is retired. Who replaced her [Eleanor Macdonald]? Genet eventually did, but I think there was an interval there. I don't know what it was.

Lesley W. Brunet:

Do you need to run?

Edmund A. Gehan, PhD:

No. Well, I guess in five minutes.

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This is the article I wrote for that encyclopedia on nonrandomized trials. It gives arguments against and for, “Under what conditions might you really do it?”

As I said, a couple of years ago they had “The Role of the Biostatistician in Cancer Research.” I gave this talk at M. D. Anderson [2000] about “Triumphs and Challenges in Oncology.” This was a review statistics and the development of statistics in one slide. This was abstracted from another publication (Ref?). The key people at NIH, and this is a whole story by itself. This is a group of consultants, Sam Greenhouse, who died two years ago, Nathan Mantel, who died last summer, Jerry [Jerome] Cornfield, who was treated the last few months of his life here at M. D. Anderson, Max Halperin, Marvin Schneiderman, and Harold Dorn. Harold Dorn was the head of this group. Greenhouse was from New York, Mantel, Leiberman, Cornfield, Marvin Schneiderman; Max Halperin was from Omaha, Nebraska. Anyway, they were in this room and somebody would call up and one of them would take on whatever the project was. This sort of gives some of the ideas of their philosophy.

Jerry Cornfield was the first one to support the ideas of relative risk. In the lung cancer/smoking studies, what’s easy to do is to look at a group of people with lung cancer, another group without lung cancer, and ask them whether they smoke. But that is not the question you want answered. The question you want answered is, “If you smoke, what is your risk of getting lung cancer?” He developed and justified the first relative risk estimate. There is a book on *Breakthroughs in Biostatistics* that I refer to here, and he was a great guy who died of pancreatic cancer here in 1979. And that is almost another story because he was treated here by J [Emil J] Freireich three of the last four weeks of his life.

The other one was Mantel, who I learned a lot from, and as I say he was my first boss. There is a Mantel and Hensell (?) paper that is a citation classic that he wrote in 1959.

The third one is David Cox. He was knighted in 1985. People don’t talk about the Cox model now, but where are we going to go from here? This was some effort at saying, “What is going to happen to biostatistics in the new millenium?”

I mentioned before that I worked at this resort in New Jersey, but I have always been interested in humorous things, too. (Alarm sounds)

Lesley W. Brunet:

Is that your alarm?

Edmund A. Gehan, PhD:

One of my papers (trails off).

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Lesley W. Brunet:

I haven't seen that one.

Edmund A. Gehan, PhD:

You haven't seen this? "How to Find the Cure for Cancer"? You want to go directly to the problem, right? How to find the cure for cancer. So I have a paper that is published on that (Ref ?). We [the Southwest Oncology Group] were doing pretty well and we were meeting in Las Vegas. Usually I gave a lecture on some statistical topic. [I thought] I'll have to do something different in this meeting in Las Vegas, "How to Find the Cure for Cancer." Well, I can tell you the answer is statistics is the cure for cancer. If you manipulate your statistics properly, you can cure cancer. (Laughter) I am proud of this article. This was a lead article in the *Journal of Irreproducible Results*.

Lesley W. Brunet:

Was that the name of the journal actually?

Edmund A. Gehan, PhD:

It was a real journal. There is a copy of every one of those reprints.

Lesley W. Brunet:

After your luncheon, do you want to come back?

Edmund A. Gehan, PhD:

Yes, I'd be glad to. I kind of enjoy this, as you might have gathered here. I have done a lot of the talking here.

Lesley W. Brunet:

Why don't we interrupt this for now—we'll stop this for now, and we'll talk about it (? Counter 133).

[Session Resumes]

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**Chapter 07 The Relationship Between the Department of Developmental Therapeutics and
Department of Medicine at MD Anderson**

B: Institutional Processes

Story Codes

B: Institutional Politics;

Lesley W. Brunet:

01:41:50.560

Do you mind if we back up and go over a few things?

Edmund A. Gehan, PhD:

Yes. I might have an extra copy of that, but I don't have an extra copy of that memo. Did I give you two copies?

Lesley W. Brunet:

No. Do you mind if we back up and go over a few other things?

Edmund A. Gehan, PhD:

Now what is that you have there?

Lesley W. Brunet:

This is the chronology of Developmental Therapeutics. As we go through the documents, make notes and (?) a time line.

Edmund A. Gehan, PhD:

Yes. Is it being taped right now?

Lesley W. Brunet:

Yes, but I edit the tapes.

Edmund A. Gehan, PhD:

Maybe we should say that this is the afternoon of Friday, March 28, about 2 p.m. and Ed Gehan is continuing the some of the historical discussions.

Lesley W. Brunet:

I'm trying to clear up some little things and get some additional information.

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I'd like to talk about the relationship between DT and Medicine from your perspective. Obviously it is complicated.

Edmund A. Gehan, PhD:

Oh you mean to comment on that?

Lesley W. Brunet:

To comment on that. I know there was tension and I wondered if you could see if from your end or a number of things that occurred at the time.

Edmund A. Gehan, PhD:

I didn't see much of it. I guess Dr. Cliff Howe (?) was head of the Department of Medicine, I believe, and I guess Dr. Schulenberger (?) was in that department who took care of chronic leukemias. I think you would have to check with the clinicians.

My impression is roughly the following: We have talked a lot about Frei and Freireich coming in and going into the modern area of therapy for cancer. But if a patient just came to M. D.

Anderson with breast cancer or leukemia or whatever, they went on a track to be taken care of by the Department of Medicine, I believe. However, Drs. Frei and Freireich were very well known, so other times patients would be referred specifically to Dr. Frei or Freireich or maybe people on their team. So my general impression is that [the Department of] Medicine sort of controlled the entry of patients that weren't referred to any particular doctor. This kind of limited the ones that would come specifically to Developmental Therapeutics, and I think that was a source of tension.

Lesley W. Brunet:

Especially in the early years it seemed to be the repeated reference is to not getting a sufficient number of patients because they would come in through a diagnostic clinic and not to DT.

Edmund A. Gehan, PhD:

I had no direct connection with that, but I told you what I thought. I think it may have sorted out in different ways. I know Dr. [Raymond] Alexanian in multiple myeloma, I think he is the longest serving physician here. He dealt with multiple myeloma. I think that was not in competition with things that Frei and Freireich were doing. I think they worked together with Ray Alexanian as part of the Southwest Oncology Group. I think Dr. Schulenberger, who I think is still around here.

Lesley W. Brunet:

Yes.

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Edmund A. Gehan, PhD:

I believe he dealt with chronic leukemia and maybe some acute leukemia. And I think that there might have been some competition, but you know, it would be better to talk to others on this subject.

Lesley W. Brunet:

I have some (? Counter 220) (Dr. Gehan talks over you.)

Edmund A. Gehan, PhD:

In fact, I don't know, was what I said somewhat consistent with what you have heard?

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Chapter 08: Working as Adjunct Faculty at Rice University and The University of Texas School of Public Health; Consulting Work with the Southwest Oncology Group (SWOG)
A: The Educator

Story Codes:

A: The Educator;

A: The Mentor;

A: Critical Perspectives;

A: Contributions;

A: Activities Outside Institution;

Lesley W. Brunet:

01:46:30.130

Yes, but I always like to get a supporting opinion. You were here when the medical school was opened in 1971.

Edmund A. Gehan, PhD:

When did that open?

Lesley W. Brunet:

1971.

Edmund A. Gehan, PhD:

1981?

Lesley W. Brunet:

1971

Edmund A. Gehan, PhD:

1971?

Lesley W. Brunet:

I don't think they had the school back then, but that was the year it started.

Edmund A. Gehan, PhD:

Yes.

Lesley W. Brunet:

You taught at the medical school in later years, or was that the graduate school?

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Edmund A. Gehan, PhD:

No, I never really taught in the medical school.

Lesley W. Brunet:

At the School of Public Health?

Edmund A. Gehan, PhD:

I gave lectures there from time to time. I had an adjunct appointment at Rice University, and I think that may be on there. They have a Department of Statistics there; it's a small department. Dr. Jim Thompson, who was the head, rotated headships, but I think they were interested in expanding the department, so they asked me if I would have an adjunct appointment there, which was fine, but it was mainly a name to be in the catalogue. I did teach one course there on survival analysis in one year, and attended their seminars and went there from time to time. But they didn't have any real demands upon me. Similarly, I had an adjunct appointment at the School of Public Health, in the Department of Biometry, which I still have. You know, I guess some of these places like to have names in their catalogue, but I never taught a full course there. I gave lectures there and I supervised at least one student, someone named Lena Asmollar (?), through her Master's Degree. I suggested a thesis topic and monitored that. And, I was also part of her Ph.D. Committee.

There was plenty to do here at M. D. Anderson, so these others were kind of side activities that didn't really take much time.

Lesley W. Brunet:

You said you had plenty to do here. You worked with DT, but you worked with other groups, right?

Edmund A. Gehan, PhD:

Yes.

Lesley W. Brunet:

It sounded like when you were at NCI, when you were developing your protocol, you were at the table. Is that the way it occurred here?

Edmund A. Gehan, PhD:

Here? Well, yes. We tended to work with people who wanted to work with us. Biostatistics was not specifically a consulting group to Developmental Therapeutics. I mean, it was to whomever at M. D. Anderson called upon us. In particular, Dr. Alexanian, was not part of Developmental

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Therapeutics. He was, I believe, always in medicine, but I and Terry Smith (?) worked quite a bit with him over the years. We tended to work with people that were in research, so we were doing clinical research, and a lot of that was through the Developmental Therapeutics group.

And, as I said, I was the head statistician for the Southwest Oncology Group, so in the early years, from 1971 until about 1982, a lot of the M. D. Anderson studies were also Southwest Oncology Group studies. We did a lot of work through the Southwest Oncology Group, where sometimes the principal investigator would be from here, so I would mention Michael Keating, in particular, on a number of protocols, and Dr. Ken McCredie, who I guess died some years ago now, as being involved in studies. I worked closely with Dr. Watsuto (?). I have a number of papers with him, and he was in pediatrics. We did work with Dr. Margaret Sullivan on studies in intergroup Hodgkin's disease. And, I guess one of the things that your group should have come across is a book by Grant Taylor on *Pioneers in Pediatric Oncology*.

Lesley W. Brunet:

I have read that.

Edmund A. Gehan, PhD:

Well, believe it or not, I am one of the people listed in that book. I think there is a brief chapter. I think maybe not enough people read that book.

When I first came, Grant Taylor was the head of the Southwest [Oncology] Group, and as I say, I became the statistician so I was working with him through there. He was the chairman; I was the statistician. He was more of an administrative chair; in other words, he wasn't like Frei where Frei would be throwing ideas to be studied. Taylor was much more on the administrative side, and I guess one of his claims to fame, and I think it is, well I don't know, but he was one of Clark's old buddies. One of the things I heard he did was say that we really should buy that Main Building—that was the Prudential Building and later became the Main Building. I don't know any of the details of this, but my understanding is that Grant Taylor was instrumental in somehow seeing that the Prudential Main Building became part of M. D. Anderson's empire. I see there is a new building going up in the garden of the Main Building. I don't know what's going to happen, but Prudential—you may not remember, "Solid as a rock," right?

Lesley W. Brunet:

I do remember.

Edmund A. Gehan, PhD:

You do remember that. OK. Well, the building is solid as a rock.

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Lesley W. Brunet:

It was one of the first high-rises in this part of the city.

Edmund A. Gehan, PhD:

I don't know what's going to happen to that building, but it's an older building now.

Lesley W. Brunet:

It is going to come down.

Edmund A. Gehan, PhD:

It is going to come down? I wouldn't be surprised, but on the other hand, they have the property that goes around that building, too. My understanding is that he [Grant Taylor] deserves the credit for that, and in his later years he could be seen going around picking up trash. He was very interested in recycling and making sure that things were clean. He was very dedicated in that way.

Lesley W. Brunet:

Did you know him very well personally?

Edmund A. Gehan, PhD:

He put me in the book, so I guess he had respect for my work. He was of a somewhat different generation and we were professional. Even though I worked with Frei and Freireich, he didn't see me as an enemy of pediatrics whereas he did, I think, see Freireich that way. I didn't have enemies of that type here, at least through Taylor.

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Chapter 09: Luminaries in the Department of Pediatrics and Evolution in the Field of Cancer Research

B: An Institutional Unit;

Story Codes:

B: Building/Transforming the Institution;

C: Giving Recognition;

D: On Research and Researchers;

Edmund A. Gehan, PhD:

01:56:11.830

I did quite a bit of work with the Department of Pediatrics. I would mention in particular, Dr. Watsuto, who died in 1981 or 1982—1981, I think.

Lesley W. Brunet:

I know his wife just passed away last summer.

Edmund A. Gehan, PhD:

Really?

Lesley W. Brunet:

I have been talking to his daughter about some things still at the family home.

Edmund A. Gehan, PhD:

He was a very gentle man—a very, very fine man.

I think that some of that group first met in Japan. I think Dr. Taylor was head of a group concerned with the effects of atomic radiation and Watsuto was in that group and so was Pat Sullivan. The three of them, I don't know the exact story of how they came here, but they did. Perhaps it was between the relationship Taylor and Clark. I think they were close.

Lesley W. Brunet:

They really did chemotherapy research in Pediatrics?

Edmund A. Gehan, PhD:

In Pediatrics?

Lesley W. Brunet:

Yes, Pediatrics. I don't know that it compared to the amount they did in Developmental Therapeutics, but it was substantial (voice over)...

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Edmund A. Gehan, PhD:

I think that the distinction between them and Developmental Therapeutics, I think Developmental Therapeutics was a broader program. They were interested in clinical pharmacology, immunology—kind of the whole spectrum of the development of cancer drugs. Whereas pediatrics was more, you know, as drugs came along they would apply them to the pediatric patients. Well, cancer is tragic for children, but it is not a major problem for pediatric [patients]. Cancer still is mostly an older population. Statistically, there are smaller numbers of pediatric patients.

I think they had a good group, and I think they did have kind of an inferiority complex, I don't know. They always felt that they were sort of the weaker sisters of the Southwest Oncology Group. Initially it was just one group, but then there was an adult division and a pediatric division, and I don't remember exactly—that came in the 1970's sometime. They wanted more control to do their own thing, so to speak. Before that there were protocols. The children and adults were entered into the study, but the entries would tend to be dominated by the adult entries, so pediatrics was smaller.

Tape 3, Side A

Edmund A. Gehan, PhD:

This is Dr. Ed Gehan again at 2:40 p.m. It may be easier to track it down; March 28, 2002.

So I think the pediatric group has always been concerned about their image and having control of their own destiny, so eventually they did have their own division within the Southwest Oncology Group, and eventually they left the Southwest Oncology Group.

Lesley W. Brunet:

Do you know why they left?

Edmund A. Gehan, PhD:

I think it may have been that there wasn't enough of a critical mass. I think there has been further consolidation since then. There used to be, well again you'd have to talk to some other people here, but I think there was a pediatric division in cancer in leukemia group B Southwest Group and others. I think now there is only one pediatric group. There was a notion of consolidation and I think that when they left Southwest Oncology they consolidated with some other entity. Archie Bleyer [M.D.] is still around here, right? He would know more about how those things took place. Now there is just one large pediatric group. Georgetown is not a member of that as

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far as I know. Well, they do enter some patients on those studies, but I haven't been part of the statistical aspects of those studies.

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Chapter 10: Dr. Jan VanEys and the Development of MD Anderson's Code of Ethics; Working with Pharmaceutical Industry

B: An Institutional Unit

Story Codes:

B: Building/Transforming the Institution;

B: Ethics;

B: The Business of MD Anderson;

C: Critical Perspectives;

C: The Professional at Work;

D: On Research and Researchers;

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

D: Ethics;

B: Industry Partnerships;

D: On Pharmaceutical Companies and Industry;

Lesley W. Brunet:

02:02:47.640

I notice you didn't mention Dr. VanEyes.

Edmund A. Gehan, PhD:

I didn't mention Dr. VanEyes. He is the ethicist, right?

Lesley W. Brunet:

He was a pediatrician.

Edmund A. Gehan, PhD:

His research interests were in ethics, and I think it may well be that there is still sort of the ethical guidelines at M. D. Anderson. I believe that may be so. He formulated them or I think he was very instrumental in that.

Lesley W. Brunet:

He and Dr. Bowman (?)

Edmund A. Gehan, PhD:

I am one hundred percent for ethics. Who is against it? But I would be hard-put to say how the headship of pediatrics helped in the prevention or treatment of pediatric cancer patients. I think he had a certain special area, which he pursued. I guess one point that I would make, not in relation to Dr. VanEyes, is that statistics have helped to provide quantitative ways of dealing with

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ethical problems, this notion of a sequential trial comparing treatment A to treatment B. You begin randomizing patients and the study goes on, and you start to accumulate data and the data will tend to favor one group or the other. I think we mentioned briefly this morning, when is it ethical to randomize patients? I think the ethical argument is when there is clinical equipoise, when the chance for benefit, as far as is known, is equal on both treatments. We really don't know which of these treatments is better. We have some previous data. We want to do this study to find out. OK, we do this study and I think I can show you that data problem. Things like this have happened.

[I have] a pretty good friend here, Don Berry, who is now head of Biostatistics. I have heard that he gives a talk something along the following lines. It is a randomized double blind clinical trial. The data have started to come in. Here are the first four patients. Three of them favor 6MP in terms of length of remission. Do we still have clinical equipoise? They are three to one. We are still randomizing patients, we are still saying the next patient has a fifty-fifty chance for 6MP or placebo. Let's keep going. Oop. Placebo. We keep on. I have heard people give a talk to the audience and say, OK, well now it's eight to two. Shall we keep going? Would you be willing to be randomized? Now it's ten to two. Oop. There is a lot of evidence in favor of 6MP. Don Berry is a Bayesian, which we haven't really talked too much about.

Lesley W. Brunet:

Bayesian?

Edmund A. Gehan, PhD:

Bayesian. It gets into a philosophy. This study was planned from a sequential viewpoint, but it was using the frequentist philosophy, and I don't think we'll have enough time to explore that, but this study was planned and it was based upon the number of preferences for 6MP minus the number on placebo. The way the actual trial ended, but it was planned from the beginning this way, was at the eighteenth one. At that time there were fifteen preferences for 6MP and three for placebo. Now if one takes a different philosophical approach, this Bayesian approach, and if you want to learn more about that...

Lesley W. Brunet:

I'm going to look it up.

Edmund A. Gehan, PhD:

You could ask Don Berry to come over here and tell you. I have never actually heard him give this talk, but there would be a way of incorporating [this]. Suppose you said at the beginning, "I think 6MP and placebo are equal." You don't have any prior preference. But the Bayesian incorporates the evidence so with each successive pair of patients, what is the evidence now that

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6MP is better than placebo? Using the Bayesian approach, you would have stopped earlier than here, but we didn't use the Bayesian approach. This was planned in 1959 (Reference ?), something like that. The general point that I was making is sequential analysis provides a way of giving quantitative weight to the evidence favoring treatments. Yes, it was ethical at the beginning to randomize, but as data are accumulated the statistical idea of sequential analysis is to permit you to stop the study and declare one treatment significantly better than another based upon the evidence. In a way, I think that statistics is a way of quantifying ethical statements.

Lesley W. Brunet:

(Inaudible)

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The Statistical Department's Work at MD Anderson, NIH Versus Pharmaceutical Company-Funded Cancer Research, Data Management and Drug Testing/Reporting

?: An

Story Codes

?: Building/Trans

Edmund A. Gehan, PhD:

02:11:19.480

I didn't work with Dr. VanEyes. As I said, we did not tend to go out and knock on people's door [saying] do you have anything that needs statistical help? We were responsive. I did work with Dr. Balch when he was head of surgery. They had a research committee within surgery and I guess this was after Dr. White was here. I think he was interested in research, and he had come from, I believe, the Southeast Group in Birmingham. I was on a committee and went to certain meetings, but it didn't develop as far as it might have. Our group in biostatistics collaborated with people who called upon us.

Lesley W. Brunet:

02:12:43.970

At one point in 1980, I saw a letter where Dr. LeMaistre was recommending that all grants, contracts, and arrangements with pharmaceutical companies be required to have a solution overhead to support data collection process. Is that the statistical side?

Edmund A. Gehan, PhD:

Support the data collection process... All protocols?

Lesley W. Brunet:

Just that the grants, contracts and arrangements with pharmaceutical companies (? Counter 171) external support for the data process. Was that your work?

Edmund A. Gehan, PhD:

Do you have a precise quote on that?

Lesley W. Brunet:

I just had a note (Dr. Gehan talked over you...)

Edmund A. Gehan, PhD:

He was not talking about statistics. I think he is talking about data management. A lot of the pharmaceutical companies, and this is a trend that has taken place, is that more of the pharmaceutical company "X" comes not only at M. D. Anderson but to many other places. We would like this drug tested in certain kinds of patients, and we are willing to pay you "X" dollars

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per patient to get this done. They may want to submit the results of this trial for registration at the FDA [Food and Drug Administration]. So there are fairly rigid reporting requirements for this. They really need a lot of detail data to accomplish that, and I think my reading between the lines of that is that before this, we are going to give you maybe \$1,000 a patient, which sounds like a lot of money. On the other hand, when they say, here are the forms that you have to fill out, then there would be the follow-up of the patient after they leave. This is quite an expense, too. It looks to me like a reaction saying that, "Look it should be more than \$1,000 a patient," roughly speaking.

Lesley W. Brunet:

Yes.

Edmund A. Gehan, PhD:

But it would have nothing to do with statistics. Those trials are planned by the pharmaceutical companies. M. D. Anderson is big enough so that they may try to do the whole trial at M. D. Anderson. Georgetown is not as big as M. D. Anderson. (? Counter 213) does say, we're going to do this study at ten sites, of which M. D. Anderson might be one and nine others. They are more or less drug testing, for which they should make enough money to make it worthwhile. They are working for the pharmaceutical companies. If you can get a copy of Dr. Rowinsky's slides, he had let's say before 1980, a lot of the therapeutic research is sponsored by NIH and the government, but now the pharmaceutical companies are doing most of it. I think that was a reaction saying M. D. Anderson should be sufficiently well paid to do this kind of work from the data reporting sense.

Lesley W. Brunet:

There did seem to be sort of a reduction in some of the contracts in 1980, for example the protective environment federal contract was reduced and then ended in 1981 and I didn't know why. (Dr. Gehan coughed) Was that part of the events in 1981?

Edmund A. Gehan, PhD:

One of the things I did was re-read this (Reference ?). It was easy to do at the time. One of the references is to the protected environment study. I guess what I have heard... Have you interviewed Dr. Bodey?

Lesley W. Brunet:

I am interviewing him on Monday so that's why I am pumping you now.

Edmund A. Gehan, PhD:

Well, you ask him about this, but protected environments are tremendously expensive. They are

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very expensive. I think the story you are going to hear from Dr. Bodey is that the administration here was never enthusiastic about studies of this type because it was simply too expensive.

Lesley W. Brunet:

Was this the Clark administration or the LeMaistre?

Edmund A. Gehan, PhD:

I think it was LeMaistre. Actually what I remember re-reading here is a statistical approach to dealing with a protected environment study. We did publish a paper with Dr. Bodey, “Protected environment, prophylactic antibiotic program in the chemotherapy of acute leukemia” (Reference ?) Dr. Bodey had been entering patients. I think there were thirty-three patients entered into the protected environment, and was this good for the patients or bad? It wasn’t a randomized study, and actually I argued before that some of the studies shouldn’t be necessarily be randomized. This wasn’t done conscientiously in this way, but I think there are good arguments for not doing a randomized study. One of the arguments being these environments are tremendously expensive. If are going to randomize a patient, fifty percent, this patient goes into the environment or he doesn’t. If he doesn’t, then that room is empty. (Laughter) That’s costing us a lot of money, even if it’s empty. So it is in our financial interest to keep that room like the airplanes—keep them in the air. But that’s what he did, he just entered patients. He worked closely with Terry Smith and myself and we found a group of patients that didn’t go into the protected environment around the same time, and we found ways of finding for this patient that went in, a potential pair-mate for that patient with certain characteristics such as age, sex, infection status, white blood count, platelet count, time from diagnosis to therapy, and previous therapy. All of those features would affect your subsequent outcome. We found possible pair-mates from among each of the thirty-three patients that went in. Then in a double-blind way, [we] said to Bodey, here is a list of six patients. We’re not going to tell you which one actually went into the [protected] environment. You rank these patients in whatever way you think, which one has the best chance, and so he might rank the protected environment patient number three. Then we would pick number two as the pair-mate, the more favorable one. This is a way of finding comparable patients, as comparable as we could find them. In the end, analysis was done of the thirty-three that went into the environment versus—actually we did sixty-six. We found two pair-mates, and this was kind of a statistical argument. We said, well Bodey’s hypothesis is the protected environment is good, so the protected environment patients should be doing better than the ones that didn’t go in. However, we’re going to put two pair-mates and neither one of those will have gone into the [protected environment]. One way of justifying this study is if the protected environment patient did better, but that the other two pair-mates did the same, that there was essentially no difference between them and that is exactly what happened. The protected environment patients did ten to fifteen percent better in various measures. The pair-mates,

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choosing two controls for each patient, weren't different from each other. I think one could argue that if it's ten to fifteen percent better in terms of survival rate in various measures, is it worth it?

Lesley W. Brunet:

(Dr. Gehan talks over your question.)

Edmund A. Gehan, PhD:

We were just concerned with what is the weight of the evidence in favor of one or the other.

Bringing the cost into play, that's another whole issue. I think they thought it was too expensive.

If you're interviewing Bodey...

Lesley W. Brunet:

I'll ask him about that. (Dr. G talks over you).

Edmund A. Gehan, PhD:

There can be psychological problems for the patients, too, if you're completely isolated.

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Chapter 11: The Differing Leadership Styles of Drs. Clark and LeMaistre

B: Key MD Anderson Figures

Story Codes:

B: MD Anderson History;

B: Controversy;

B: MD Anderson Culture;

B: Institutional Politics;

C: MD Anderson Past;

C: Leadership;

C: Portraits

D: On Leadership;

D: On Nature of Institutions;

Lesley W. Brunet:

02:25:20.120

We were talking about Dr. LeMaistre. I want to know and Dr. Olson also wanted me to ask you to compare and contrast Clark and LeMaistre.

Edmund A. Gehan, PhD:

Clark had more passion. I guess one of the points I made this morning is that he didn't pick me to be head of the Biostatistics or Biomathematics Department, so I was certainly very disappointed in that, but I didn't let that affect my work. I liked Dr. Clark. He put in a very good benefits program here, and he also made sure that the Ph.D.'s got these benefits as well [as the M.D.'s], but not quite as many. We didn't have cars, but it was a very good benefits program for the Ph.D.'s as well as the M.D.'s. He was a very human man in that we had this annual dinner dance that was often held over at the Warwick Hotel in June. It was an elaborate dinner and dance.

Lesley W. Brunet:

It's not the one from (Dr. Gehan talked over you).

Edmund A. Gehan, PhD:

I don't know if they still have the Rogue's Gallery here with all the pictures.

Lesley W. Brunet:

Yes.

Edmund A. Gehan, PhD:

As people started—I couldn't say what year—it started in the late 1960's early 1970's, but I mean

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an elaborate dinner dance, which was very nice. But Clark was the Master of Ceremonies. Whoever was retiring, and of course they really had to be old timers then, you could talk as long as you wanted. Some of them were drunk when they got up to speak. Even Dr. Clark had often somewhat too much to drink, but it was very human. We didn't always listen to all the talks, but I think Clark was a passionate man, a believer in trying to do what was best for cancer, but he had his own flaws.

LeMaistre was much more the organization man. He would never be drunk at these events. You would have five minutes to give your talk. He was much more the organization man, and I guess one could say that as the organization gets bigger, you need someone, you can't just do it like you did it in the old days. There certainly was need for them, but I would be closer philosophically and emotionally to Clark than to LeMaistre. That's just my view. I think both kinds are needed, and perhaps in their own way each of them was the right one to have at the time.

I guess one of the things, and I guess this relates to Freireich, too, that LeMaistre is the one that finished Developmental Therapeutics. I think they were trying to find a leader. The precise administrative part of this I don't know, but they were trying to find a head of medical oncology, so they formed a search committee and they recommended Freireich. Dr. LeMaistre said, "Go back to the drawing boards. Look again. See what else you can come with." Well, we still recommended Freireich. I'm not sure just exactly how this process took place. Freireich didn't get the job. LeMaistre had the chance to make the decision. Irv Krakoff (?) got the job. Freireich would have been a lot better choice. Again, I think LeMaistre was, I don't know, you'd have to ask him. He's still around.

Lesley W. Brunet:

Excuse me. Just a minute.

Tape 3, Side B

Lesley W. Brunet:

I want to tell you that Dr. Freireich and I have discussed this at length.

Edmund A. Gehan, PhD:

You have discussed this at length?

Am I close to being right?

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Lesley W. Brunet:

(Dr. Gehan talks over your answer.) I just wanted hear it from you, to get your impression of Dr. LeMaistre.

Edmund A. Gehan, PhD:

I don't see him as a bold decision-maker. He kept himself very well; he dressed very well. I think of him as kind of the organization man, but without much passion, which I think you do need to have to really make progress, and not being willing to make bold decisions. I think he would tend to make the decisions that created the least waves, and I don't think that's the way you make real progress. In terms of putting up buildings and so on, I think he certainly did make progress there. Overall I think perhaps he was helpful, but maybe we would have made more progress in the fight against cancer if some of the decisions hadn't been that way. As anybody in a situation like that, would tend to support people that they could work with closely, and I think maybe he felt that he couldn't work with Freireich very closely, but I don't think Krakoff's tenure here was particularly successful. As a matter of fact, I had known Krakoff. He used to be at Sloan Kettering in New York, then he went to Vermont. And he is still around, too.

Lesley W. Brunet:

Right.

Edmund A. Gehan, PhD:

After he got the job, I went over and said, "I just want to let you know that our group here is in biostatistics. We have worked closely in research. I welcome you here and would be glad to work on research projects." Nothing really much developed after that. He didn't take advantage of that.

Lesley W. Brunet:

(Inaudible question.) (Counter 46)

Edmund A. Gehan, PhD:

I guess he had his own vision. Again, I don't think he was all that interested in research. I don't think so. As head of the research program, that's one thing that should be a requirement for the job. (Laughter) I don't think if you asked him to do exactly what I did, show me your curriculum vitae, go over the highlights in your career that might have had some impact on the treatment of cancer patients. I think he did some things back when he was at Sloan Kettering. Ask him what was the main progress made in the fight against cancer while you were here at M. D. Anderson, and how did your tenure here influence that. I don't know the answer to that. Others might be better at that, but I suspect that not much came out of that. I'm giving impressions here, but I will stand behind more of what I have presented than I have written.

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Chapter 12: The Contributions of Colleagues to MD Anderson's Legacy

B: Key MD Anderson Figures

Story Codes:

B: MD Anderson History;

B: Insitutional Politics;

C: MD Anderson Past;

C: Portraits;

Lesley W. Brunet:

Using that same methodology, Dr. Olson had wanted me to ask to have you evaluate other people or rather the history of oncology (Dr. Gehan interrupts you).

Edmund A. Gehan, PhD:

On a score of one to ten? (Laughter)

Lesley W. Brunet:

What would be their contributions and why? There are a number of names we have already talked about.

Edmund A. Gehan, PhD:

Maybe I'll score them on a one to ten basis. Ten is high and one is low.

Lesley W. Brunet:

Obviously, Dr. Frei.

Edmund A. Gehan, PhD:

I'd give him a ten. And as you saw, he is the first Icon [in Oncology] Award. Of course, Freireich was on the committee.

Lesley W. Brunet:

I was very impressed by him.

Edmund A. Gehan, PhD:

Who, Frei?

Lesley W. Brunet:

Frei. He seemed a wonderful person.

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Edmund A. Gehan, PhD:

He is a very fine man. I had dinner sitting next to him last night and he said, "You know, I'm almost going to be eighty." I hope he makes it to eighty, which will be early next year I think. We lived a block apart in Meyerland. When we came here in 1967 Freireich said, "You've got to live in Memorial. You've got to live in Memorial." I don't like long commutes. Ever since Brooklyn, New York, I don't like long commutes. So we looked around, and in the end we didn't end up in Memorial, we ended up in Meyerland, a block away from Frei. He's a pretty big guy. He has pretty big hands. He's about 6'4".

Lesley W. Brunet:

(Dr. Gehan talked over you.)

Edmund A. Gehan, PhD:

Even then we used to go out and play touch football. On Sunday we'd find much younger guys and pick up games, and we more than held our own. He's pretty tall. I think of myself as originally a good athlete, too. In fact he even told me. We used to do a lot of jogging around Godwin Park. He did something that I never did. He always came in sweaty and then he would go and hug one of his daughters. (Laughter)

My kids think of Tom as Santa Claus because, strange as it seems, he used to dress up as Santa Claus. I mean this thin, scraggily scarecrow-type guy dressed up as Santa Claus. And they used to go Christmas caroling, he and his family. His daughters were babysitters for our daughters, so they always came to our house. We have been very good personal friends over the years, but it's more than that. He has a ten record in his research, too, and he just doesn't administer drugs to patients. He is interested in the pharmacology and all the arguments for it. Parkinson's has slowed him tremendously now.

Lesley W. Brunet:

How about Freireich?

Edmund A. Gehan, PhD:

I'd say he is a ten. I would rate him up at the top, too. He is much more into education now. How are people keeping up with the latest work in micro (? Counter 121) studies, biological therapy, the very latest things in the forefront of research. He probably isn't there. Based on the moment, he probably isn't [there], but in terms of his career, I think there is no question about that.

Lesley W. Brunet:

Some other people in Developmental Therapeutics, perhaps Dr. Bodey?

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Edmund A. Gehan, PhD:

Bodey I would rate very highly, a seven or eight maybe. He is a specialist in infectious diseases and that is a reflection of the breadth that they were looking for. The major cause of death in cancer is infection, and he was a specialist in infections, but some of it is kind of routine work. He is very well organized and he really turned out a lot of very good work, and I think that he was close to the top of the field in dealing with infectious diseases. If I had any serious infection, he's the person I would call. I would rate him very highly, but maybe not a ten. You can't rate everybody a ten. (Laughter)

Lesley W. Brunet:

You can drop that number again if you want to.

Edmund A. Gehan, PhD:

No.

Lesley W. Brunet:

What about Dr. Gutterman? We haven't really talked very much about him.

Edmund A. Gehan, PhD:

I wouldn't rate him that high, five or six maybe. I think he's been kind of up and down. I think he has done some good work, but he hasn't shown the consistency. He was at that dinner last night. I think he did some very good work, I think in interferon, but he's not a good team player. He tended to go off in his own directions. He did call upon us from time to time and we did work with him. Some of my ratings are based upon how much the folks worked with Biostatistics and some parts of that. I think he has done some good work, but he probably didn't live up to his full potential.

Lesley W. Brunet:

He's still around quite a bit.

Edmund A. Gehan, PhD:

Yes. He's still here.

Lesley W. Brunet:

He's in the library every day.

Edmund A. Gehan, PhD:

Every day? I think he's a real bright guy. Maybe he should have had more impact I think.

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Lesley W. Brunet:

What about Keating?

Edmund A. Gehan, PhD:

I'd rate Keating very highly. Maybe a seven or eight up there. He's not as well organized as some of the others. I think he's an idea man and a great guy. I'd always want him on my team whatever the game was. He has been mentored by Freireich and I think he came over here as a fellow from Australia, but he stayed. His life and career are here. I think he has done some very very good work, especially in chronic leukemia. And again, he did work closely with us. That paper on this method of dealing with untreated patients, he was the one who shepherded that through, so I would rate him very very highly.

Lesley W. Brunet:

What about Dr. Hersh?

Edmund A. Gehan, PhD:

I would rate him very highly, too, probably a seven or eight. He is in immunology. Again, he is a very good personal friend. He is from the Bronx, New York. None of the other people that you have mentioned are from New York City, but Hersh is. I think people from there, you have to have a pragmatic attitude. You find a way to get the job done by whatever means it can be done.

Lesley W. Brunet:

You have that characteristic because you're from the Bronx?

Edmund A. Gehan, PhD:

I'm not from the Bronx. I'm from New York.

What do I mean? I mean that you're used to dealing with all kinds of people. Some of the people that I played with as a teenager have gone to jail, others went to longshoremens. There used to be street vendors and others would commit crimes by stealing from the street vendors. Yet others would go on and do very well in school. You get a picture of all sides of life.

Where were you brought up?

Lesley W. Brunet:

Several different places. Maryland (Dr. Gehan talks over you.)

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Edmund A. Gehan, PhD:

Oh, Maryland? I guess the theme was, I have yet to speak to a person. I say, somebody is from the country. [They would say,] I wouldn't change anything. I grew up on a farm. It was great and I learned animals and all this stuff. Most people, unless they had terrible parents in one way or the other, their childhood was fine. I'll say the same about how my parents treated me well, except that my father died when I was thirteen, so that wasn't so good for the family. Number one, being able to deal with all kinds of people, including getting into bar fights occasionally, was good. And also a feeling of independence. You could take subways or busses anywhere. We could go to the beach. You just dealt with things as they came. I think that's kind of stayed with me. How did we get on to this?

I said Hersh and I were both from New York. I have heard him lecture a number of times. He is very sharp. He is a very good immunologist. I think one of the reasons Hersh left here was because of Krakoff. I think he and Krakoff didn't [get along]. Hersh is still active in Arizona. One reason I can't rate Krakoff highly because I think this place would be better if Hersh were still here. But he has made a good career for himself in Arizona. I think M. D. Anderson would have been better off if he had stayed. He has done very good work in immunological and biological aspects of cancer trials.

Lesley W. Brunet:

One other person who left, and I wonder if he comes in that same group, Blumenschein, the head of the breast program?

Edmund A. Gehan, PhD:

Blumenschein. Yes. Well, he's up in Dallas or somewhere near there. I believe he more or less went into private practice. I think he's a fine man. He didn't do much in cancer research, but I think he's a good guy. I think he's more a private practice type physician than one that would be successful in sort of research. I think he was more of a follower in that respect and I think he got along well with administration. I don't know exactly why he left, but he is more on the private practice side of things.

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Chapter 13: Transitions at the Department of Developmental Therapeutics
B: Institutional Change

Story Codes:

B: MD Anderson History;

B: Growth and/or Change;

B: Controversy;

B: Research, Care, and Education in Transition;

B: Institutional Politics

D: On Research and Researchers;

D: On the Nature of Institutions

Lesley W. Brunet:

I'd like to talk to you about the closing of DT. And Dr. Olson wanted to talk about also what you remembered about that. Was it part of a national (?) trend to decentralize chemotherapy and to spread it out?

Edmund A. Gehan, PhD:

As part of the closing of DT?

Lesley W. Brunet:

Yes, he wondered that.

Edmund A. Gehan, PhD:

I don't know whether you've talked to LeMaistre, have you?

Lesley W. Brunet:

Not yet, but he has at length.

Edmund A. Gehan, PhD:

At length?

Lesley W. Brunet:

Yes.

Edmund A. Gehan, PhD:

You'll have to ask him. I know J was very disappointed in this.

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I have given you this article, “M. D. Anderson and Freireich (?): The first fifteen years.” (Reference ?). They knew the handwriting was on the wall that DT was going to be closed then. At the time, July 1980, I gave this talk. Part of the idea of having that one day conference was not so much a last hurrah as, “Let’s try to put together the work that we have done over the years,” but the winds of change were already there that this might be the last meeting we ever have as a Developmental Therapeutics group, so let’s celebrate our time. That was kind of the theme of this “M. D. Anderson and Emil J: The first fifteen years. They knew at the time it might not go to sixteen or seventeen [years]. I never say down with J and said, “J exactly what happened? Why did all that take place the way that it did?” I’m not that kind of a person, so I can only look at what actually ended up happening, not why it happened. But LeMaistre should be able to say. Why, when it closed, and the first couple of search committees said, “We want Freireich.” He said, “Send me somebody else.”

Lesley W. Brunet:

You said the shape for the future, what were the signs? What made them think that it was going to close?

Edmund A. Gehan, PhD:

I don’t know. I think obviously senior administration had some discussion with J about some kind of a break up of the department. The department was getting perhaps too big and too strong, and too dominating in the institution. Maybe by breaking off certain parts of it, that part could become its own department. Things of that sort.

Someone you should probably talk with, if you haven’t, is Bill Plunkett. Have you ever talked with him?

Lesley W. Brunet:

No.

Edmund A. Gehan, PhD:

He is still here. In fact, he was at the dinner last night. I guess one of the things I know is true, he came here to work for Freireich. He’s a pharmacologist. He came here to work in Developmental Therapeutics, Friereich’s group. I said to him, “Where are you now?” He then listed off the group of his bosses. I’m sure I can’t repeat [it exactly], but Freireich was the first, then I think Krakoff was one, then Bast I think was one, and I think Marty Raber (?) was one. Who else? I think now he said he’s in a group that has an interim chairman. Again, this was at a dinner party.

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Lesley W. Brunet:

(Dr. Gehan talked over you.)

Edmund A. Gehan, PhD:

He is one example of someone who was in Freireich's group. The clinical pharmacology part evolved, and maybe in a way it's better for pharmacology by having broken it off from DT. I wouldn't rule that out. I guess Freireich and Frei built all that up and then to see it break up has got to be disappointing. But Plunkett was someone and Hersh was somebody else. He was in that group and then he ended up leaving.

Lesley W. Brunet:

Yes.

Edmund A. Gehan, PhD:

I guess Gutterman is not in that group anymore either.

If Olson has already spoken to LeMaistre and Freireich, they were at the table, I wasn't.

Lesley W. Brunet:

(inaudible)

I just have a little bit of tape left. Do you mind repeating what we talked about before I started the tape about Rowinsky's comments today?

Edmund A. Gehan, PhD:

His comments today built on the theme he talked about first, last night, when they had this dinner. And as I say, I think you should try to get an invitation to some of those dinners. Rowinsky first started out in Phase I studies and he talked last night about the importance of passion in working in cancer research and that he respected Frei and Freireich because he could see that they were passionate about being successful in that field. That was the one element that he had picked up. I guess that was reinforced today in that he talked about some of the Phase I studies that he had worked with where he was the principal investigator and shepherded this drug through the process and its toxicity and maybe some response. But you really have to know what you're all about. He went from there to saying the way things are these days. One of his slides showed the evolution of the support of cancer research, that it was primarily government up until maybe the early 1980's, then the government's support kind of went down and what was pharmaceutical company here has gone way up. This has led to more administrative decision-making and bureaucratization of the whole process. One of these slides set some example of a clinical trial being stopped for kind of administrative reasons. The investigator [said], "You can't stop that trial. We haven't finished our objectives and so on." "Yes, we can stop the trial. It's on page

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seventy-eight in the protocol.” He gave certain reasons in the protocol about undue toxicity, or about this or about that, the last reason being “at our discretion.” “We can stop it for any reason we want.” I guess it was the whole notion of the influence of pharmaceutical companies on the type of research that is being done. He talked about the global Phase I study, which is being done on several continents, and multiple investigators, where the Phase I PI may have treated one patient on the study. So how could he have the passion and interest in it? I think his talk was well received. Just getting a copy of all of the slides would give you the story. Some of what he said was, in fact, supported by Dr. Levy [Robert] that he has developed some new therapies. His work led to the establishment of an entirely new class of drugs, the first monoclonal antibody ever to be approved by the FDA [Food and Drug Administration], Rituxan, as well as the first agent approved for the treatment of lymphoma in over two decades. This was kind of a niche therapy, and I think it wasn’t, in his opinion, developed as well as it might have been by pharmaceutical companies because the market wasn’t big enough. They want a one size fits all [drug].

Tape ends.