NCI ORAL HISTORY PROJECT

INTERVIEWS WITH

JAMES HOLLAND

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National Cancer Institute
Interview with James Holland
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PD: I would like to discuss with you your involvement with the National Cancer Institute over the course of your career, as well as your broader contributions to cancer policy, research, and treatment. The first question that I'd like to ask you is about your upbringing, your education, and the time before you came to the National Cancer Institute.

JH: I was brought up in a family of four boys. My father was a judge, my mother was a housewife. Three of the sons became doctors and one was an engineer. I went to high school in Morristown, New Jersey, and then attended Princeton University on the accelerated basis, starting in September 1941. The War came in December 1941, so we were accelerated: no vacations, went all year round. I came to Medical School at Columbia on January 1, 1944, in the Navy program, having been enlisted as a midshipman in the Navy, in the V-12 program.

I went through Columbia, which was then also on the accelerated schedule, and started there in 1944. When the War ended, we were demobilized from the Navy and the school decelerated. I interned at the Presbyterian Hospital in New York and took a residency. Then, because of my Navy service, was importuned relentlessly by the Secretary of Defense, that they were short of doctors in the Army and Navy. I get terribly seasick, so I joined the Army in 1949 and went to Europe for two years, having been extended because

of the Korean War. Ordinarily I should have gotten out on June 30 but was extended until sometime in September 1951.

Before I came back, I had letters from Dr. Robert F. Loeb, one of my great idols, the Chairman of Medicine at Columbia. He indicated he couldn't save a place on July 1, 1951, for me because I was extended but that when I came back I could go to the Francis Delafield Hospital, which was a new hospital opened on the Columbia-Presbyterian Medical Center campus by the city of New York for cancer. One of the house staff would certainly drop out from tuberculosis or psychiatric disease—they always did—and I could be called back to come to Presbyterian Hospital. About December, indeed, a man did develop tuberculosis. But by that time, when Dr. Loeb said, "All right, Jim. Now you can come back," I said, "Thank you, Dr. Loeb. I think I'll stay."

Under my mentor Dr. Alfred Gellhorn I had been able to treat a child with acute leukemia and the child had gone into remission. This was new and exciting and really enormously important to me. Alfred Gellhorn, who's still alive at about age eighty-five or eighty-six, and a very important man in cancer research, recognized that I wanted to do cancer activities. The salary I was getting at the Delafield Hospital was $4,000 a year. I had just been divorced and needed more money. He arranged that I meet Dr. G. Burroughs Mider, who was then the scientific director of the National Cancer Institute, and it was arranged that I would come to the Cancer Institute, where the salary was a fantastic $7,200.

I did come and opened the Clinical Center, as part of the original senior contingent, on July 2, 1953. Some of the junior colleagues who were residents at Columbia Presbyterian who came with me were John Fahey and Donald Tschudy. There were about a dozen of us who opened the clinical service. I was in charge of the particular segment of chemotherapy under Dr. Leonard Fenninger, who was the chief of general medicine for a while. I was assigned by Dr. Mider to help Dr. Lloyd Law. Lloyd had been asked to write a critique of leukemia chemotherapy for the scientific directors of the several institutes, and since he was a Ph.D. and I had been interested in leukemia as a physician, I was to go and help him.

I knew of Lloyd's work. It had been discussed in New York, in Dr. Loeb's morning professor's rounds when Law's original research came out on combination chemotherapy. Lloyd was obviously a senior scientist and I was a raw recruit who had really done little but clinical medicine until that time. He gave me an appreciation of science. Together we decided that it would be a good idea to try combination chemotherapy in children, and in patients with leukemia in general.

Having charge of the clinical associates—having had about four years of clinical medicine myself, and the clinical associates, Fahey and Tschudy and a few others, had only a couple of years—I set up a program treating children and adults in the first combination chemotherapy program of the National Cancer Institute. I used 6-mercaptopurine and

methotrexate. Both drugs were given daily by mouth and, indeed, we did have remissions. It seemed like a tolerable treatment and was going well.

I got an offer in 1954 to go to Roswell Park Memorial Institute, which has subsequently changed its name to the Roswell Park Cancer Institute, in Buffalo, New York. It's not a location. Roswell Park was a very famous surgeon there. And again for a significant increase in salary to $11,000. I accepted, but before going, attended an International Cancer Congress in Sao Paulo, Brazil, in the summer of 1954. Lloyd Law and I, and I remember, Bill Hueper from the Cancer Institute and a couple of others went with others on a chartered propeller plane from Miami. This was my first taste of an international congress for medicine and science, although I had been in the United States Army in Europe and had seen a little European medicine at the time.

Then, coming back to NCI from the congress, I met Gordon Zubrod. He and Philip Tumulty had left Hopkins to go to St. Louis University. When they got there, I've heard that some of the original promises made to them were not fulfilled and within a very few weeks they left. Tumulty went back to Hopkins, but Gordon Zubrod, who had trained with E. K. Marshall as a pharmacologist, came to the Cancer Institute as clinical director. He came around to meet all the senior people and we immediately were mutually attracted, I think, in a very friendly relationship. He said to me, "I don't have a program in acute leukemia. Would you mind if I continued your program when you go to Roswell Park?" I thought that was a wonderful opportunity. Indeed, he had his staff here at the

Cancer Institute and I had my activities at Roswell Park, and was soon able to recruit the Children's Hospital of Buffalo to do the same program of 6-mercaptopurine (6mp) and methotrexate (MT_x) treatment—at that time still called amethopterin.

In about 1955 he was able to recruit Dr. Emil Frei III, whom he had known in St. Louis, and then he summoned me to Bethesda and introduced us. Frei and I have been the closest of colleagues for the forty-five years since that time. Tom took the position that I had had at the Cancer Institute, at which point Gordon, who was certainly a mentor to both of us, indicated that indeed we should conduct a prospective randomized clinical trial—a phrase which was probably unknown to me at the time.

We did set up a program of using chemotherapy for leukemia with a defined protocol, and with a biostatistician, Marvin Schneiderman, set up and effectively to carry out a rigorous clinical study. At the time Gordon thought that we should compare the combination of 6mp and MT_x against the single drugs, but I was so sure that the combination was working and was valuable that I thought it was unethical not to use the combination. He very graciously and nobly said, "Nobody should have to do something they consider unethical." So we designed the protocol that took advantage of Lloyd Law's observations of continuous administration of methotrexate and 6-MP and also took advantage of Dr. Abraham Goldin's observations that if you gave methotrexate twice a week you could give it in higher dose than daily. We did, in fact, use a random allocation to methotrexate twice a week or daily, which was the clinical standard, together with daily 6-

mercaptopurine in each regimen. We set up an operations office with Tom Frei as its head here at the Cancer Institute, because he had a staff bigger than I did.

We completed this study at the NCI, Roswell, and Children's of Buffalo and demonstrated that there wasn't a great deal of difference between the two regimens. We published it in *Blood* in about 1958. That's the first publication of a controlled clinical trial in cancer in the United States: Frei, Holland, Schneiderman, and a few others of our relatively then junior but subsequently very senior colleagues: Freireich, Pinkel, Regelson, Selkirk, and others.

I want to divert for a moment to two other topics. First, as I left the Cancer Institute to go to Roswell Park—the world was smaller then—I made an appointment to speak to Dr. James Shannon, the director of the NIH, to say good-bye and to thank him for having worked here. He suggested to me that I should try different doses of the drugs because sometimes dosing schedules made a difference. I indicated to him that we were at maximum tolerated dose (MTD) as it was, and he said, "Well, okay." But I was wrong. We were at the MTD for the schedule we used. In fact, Goldin's observations in mice were that you could get in more than three times as much drug if you gave it intermittently. Subsequently this was carried to an extreme by Dr. Isaac Djerassi, who showed you could get in thousands more if you gave MTX intermittently with leucovorin to children. This became of some significance; dosing schedules did make a difference, as I will tell you later on, for methotrexate.

Secondly, at that time, about 1956, or 1955, Mary Lasker, who was by far the most important non-scientist in health matters in the world, had persuaded Dr. Sidney Farber and perhaps Senator Magnuson—I didn't know the politics at that time—that there should be a concerted effort to improve on cancer chemotherapy. There had already been confirmation of Dr. Farber's initial observations in 1947 that chemotherapy in children's leukemia could make for remissions. There was burgeoning and interest in this, and Mrs. Lasker knew it would take government participation and resources. Although I do not know how it came about, subsequent familiarity with Mrs. Lasker's strategies and tactics persuaded me she made it happen.

So the Cancer Chemotherapy National Service Center was set up with Dr. Kenneth Endicott as its director. Through Gordon Zubrod's recommendation, I presume, Ken invited me to serve in the CCNSC on two panels, the clinical panel and the pharmacology panel. Gordon Zubrod was by far the most important person on the clinical panel. We met in Dr. I. S. Ravdin's office in the hospital at the University of Pennsylvania. We'd assemble there at nine o'clock in the morning. Dr. Ravdin often would come in in his surgical greens and say, "Well, you guys are just arriving. I've done four operations already." He was a relatively short man with a wonderfully dominating personality as if lightning sprang from his fingers. He introduced himself to this clinical panel by saying, "I don't know anything about chemotherapy, but I do know how to knock men's heads together." He was a towering figure in surgery who had been a general in the Army Medical Corps, and President Eisenhower's surgeon for his ileitis.

We set out to find something that could accelerate clinical progress in cancer. There was a good deal of discussion about how to measure tumors—with plaster casts, with calipers, with other concepts. CT scanning and ultrasonographic imaging hadn't been invented, and radiology was known to be relatively limited in its impact in looking at tumors, particularly leukemia. After we had met three or four times, group process had taken place, but we didn't really produce any sizzling ideas. Gordon Zubrod then reported that the British had demonstrated conclusively that combination chemotherapy of tuberculosis was better than single-agent therapy by conducting a prospective clinical trial. He introduced the precepts of Gaddum on how to perform a clinical trial. Gaddum was a Scottish clinical pharmacologist who pointed out that there had to be a protocol comparing two defined therapies, patients had to be randomized, and that patients had to have the same disease. And Gaddum's last tenet was that generalization of the results to the general population needed to be cautious.

There was widespread support for Zubrod's idea, that we ought to set up groups of individuals who would, in fact, do studies of chemotherapy. This devolved into a series of groups largely defined by geography: eastern, southeastern, central, western, southwestern, and a few veterans administration groups. Acute leukemia was the seminal success story, so it underlay a disciplinary rather than a geographic basis for a group. Then it turned out that there were several people working in acute leukemia, so there was created an Acute Leukemia Group A, of which Dr. Joseph Burchenal was the chairman—and he was senior to both Dr. Frei and me—and an Acute Leukemia Group B,

of which Dr. Frei became the chairman for about five years. I then served as chairman for eighteen years, and then Dr. Frei came in for another ten years. The Acute Leukemia Group B (ALGB)—which has changed its name to the Cancer and Leukemia Group B (CALGB)—but we always have liked to keep the"group B," because it was anointed second at the outset but may have wound up first—has really had a major influence from Frei and Holland over most of its lifespan. The CALGB is still thriving 45 years later. Its subsequent chairmen have been O. Ross McIntyre and Richard Schilsky. Gordon Zubrod was really the father of the cooperative groups.

Now, going back to the original discourse, after we showed that there wasn't a great deal of difference between combination chemotherapy with the methotrexate given on a daily basis or the methotrexate given on an intermittent basis, the second study in about 1958 was 6-mercaptopurine alone followed by methotrexate, or methotrexate alone followed by 6-mercaptopurine, or the two drugs in combination in childhood leukemia. And there we did begin to see a difference, with combination chemotherapy being slightly superior.

Shortly thereafter it became recognized. It was already known that corticosteroids—and ACTH—were active against acute leukemia, and in addition to methotrexate and 6-mercaptopurine, a fourth drug became available, vincristine (VCR). VCR was discovered by Irving Johnson, using P-388 leukemia. It was not very active in L-1210 leukemia, which was one of the tumors used in the Cancer Chemotherapy National Service Center (CCNSC). The CCNSC used sarcoma 180 and carcinoma 755 and leukemia L-1210 as

their screening tumors. But Johnson, who worked for Eli Lilly, deliberately used a different tumor and found a different batch of compounds. The vinca alkaloids were originally sought as anti-diabetic agents. Dr. Noble in western Canoa and another individual—it might have been Johnson, but I'm not certain of that—recognized that the extract of the vinca plant caused leukocyte depression. Since many of the drugs that were available, methotrexate, 6-mercaptopurine, nitrogen mustard, sulfur mustard, and by that time busulfan all caused depression of white blood cells, this was taken as a surrogate for something that could depress actively growing tissues and thus actively growing leukemia and cancers. Therefore, the vinca alkaloids were isolated.

The first one was vinblastine, which does have activity in Hodgkin's disease and a few other diseases. But vincristine came along next and this had activity in leukemia. Vincristine was used in children by Karon, Freireich, and Frei at NCI, and virtually at the same time by Costa and myself in Buffalo in adults. We found that it had broad-scale activity on cancers. Freireich, Frei, and Karon put 6-MP, methotrexate, prednisone, and vincristine together and came up with a four-drug combination with the acronym VAMP: vincristine, amethopterin, mercaptopurine, and prednisone. That was a very interesting and highly regarded treatment at the time.

Dr. Frei resigned from the Acute Leukemia Group B chairmanship to devote himself to activities in the Cancer Institute and I was elected chairman in 1963. We made use of the vincristine/prednisone observation. Vincristine and prednisone gave opportunity to follow

an important observation made by Freireich in one of the very earliest of ALGB studies in 1962 or 63, which was to give children prednisone to the point of clinical remission, and then to give them 6-mercaptopurine or not to determine whether, despite the clinical absence of leukemia, one could have an impact on it. The 6-MP treatment was significantly superior. That was the first human evidence of the ability to treat a tumor when it was no longer obviously present, and was the initial demonstration of successful adjuvant chemotherapy.

That was a very important publication, which established the concept of induction versus maintenance. Shortly after the Freireich, Frei, and Karon paper on the four drugs, as chairman of the Cancer and Leukemia Group B, I initiated a series of studies with vincristine and prednisone alone as an induction treatment.

Now, retracing a little bit, we had already studied Goldin's high-dose intermittency of methotrexate. We had taken children with florid acute leukemia at diagnosis and treated them either with high-dose methotrexate or daily methotrexate. About 20 percent went into remission on both arms. The children we got into remission were re-randomized to the high-dose intermittent or the daily dose regimen. Although there weren't enough patients to make a statistically significant difference, it was clear that the high-dose group did substantially better than the daily dose group when started at a low-body burden of residual leukemic cells, but not at the high body burden before remission was induced.

Immediately thereafter, on recognizing that vincristine and prednisone were active, Oleg Selawry—unfortunately recently killed in an accident—became the principal investigator of a similar study of methotrexate schedule and dose after induction of remission. We published a study in *The Journal of the American Medical Association* in which vincristine and prednisone was used as the induction treatment, followed by either twice weekly methotrexate, a la Goldin, or daily methotrexate. With a small number of patients we demonstrated a highly significant difference in favor of the intermittency of methotrexate. That was the first randomized controlled trial that led to five-year survivors. There had been five-year survivors before that, but only sporadically and not in a prospective trial. So the ALGB dealt in great part not only with combination chemotherapy but with dosing schedules.

At about that time, in about 1957, [Min Chiu] Li, [Roy] Hertz, and [D. B.] Spencer from the National Cancer Institute reported in the *Proceedings of the Society of Experimental Biology and Medicine* on three patients, one with choriocarcinoma and two with what was then called chorioadenoma destruens by methotrexate treatment—which is probably metastatic mole. They described the regression and elimination of these tumors. I learned of this work through Delbert Bergenstal, also dead, unfortunately, as is Roy Hertz. Bergenstal had joined Hertz at NCI and knew of this work. He and I had been interns together before their paper was published. I treated the second patient with choriocarcinoma. Roy Hertz graciously did the hormonal titers on a woman with metostatic choriocarcinoma following a full-term delivery. She was cured by the

treatment in 1956 and I published the report in the *American Journal of Obstetrics and Gynecology*. This was a confirmation of Li, Hertz, and Spencer's first cure of a cancer by chemotherapy. Paul Conditt, working with Abe Goldin, was doing pharmacologic studies on methotrexate given in high single doses. Li recognized that the human gonadotrophic hormone, five-day course of high-dose methotrexate, 25 milligrams a day for five days in a row, with time-off for recovery.

As the new chairman of the Acute Leukemia Group B, I devised study 6301 to test this regime which was curative for another cancer. Children were treated at 15 milligrams per square meter per day or methotrexate for five days, after vincristine and prednisone administration. Vincristine and prednisone put about 80 percent of children into remission. We were then dealing with a low-body burden of residual leukemic cells. This intensive treatment was tested in a single-arm study with the deliberate intent that after three courses we would stop the treatment and see how long it took to relapse. There were many ethical dilemmas raised about stopping treatment. But we thought that putting 80 percent of children into remission was as good as anybody else could do, and we would learn something from it.

And we learned an enormous amount from it. We estimated the total number of leukemic cells in each child's body by the percentage of leukemic cells measured or approximated in the blood count, the marrow cellularity, the size of the liver, the size of the lymph nodes and spleen. We came up with a value very close to two to the thirty-eighth power, which

is nearly one trillion cells. We then estimated the killing of leukemic cells based upon similar extrapolations from regressing organ size, blood count, and marrow cellularity, until leukemic cells got below the measurable level in blood and marrow. We performed systematic exams during remission and marrow in the relapsing period to see the repopulation of leukemic cells. We graphed the slopes of leukemic cell regression and repopulation and extrapolated the lines to see where these two lines might intersect, to give us some idea of how much killing we had done.

This was based in part on fundamental studies that had been published by that time in 1963 or 64 by [Howard] Skipper, [Frank] Schabel, and [W. S.] Wilcox, which was a profound analysis of the quantitative kinetics of anti-leukemia therapy in mice. And, in fact, it looked from the analysis of our data, which are published, that two-thirds of the leukemic population had been killed. As a matter of fact, we got down from two to the thirty-eighth to about two to the tenth cells, which is a thousand cells. We never thought it was appropriate to call it a thousand cells left but maybe two-thirds of the way toward cure.

So then came the next study, which was an important study—a classic study—called, "66-01." In 66-01, we extrapolated the line of killing and it indicated that if we had kept using methotrexate for four months of courses instead of just three, we would have eradicated the population. And so, since I'm often wrong and often 100 percent wrong, we devised the study to go for eight months of intensive five-day courses of methotrexate. This time we used 12 or 15 or 18 milligrams per square meter for eight months after vincristine and

prednisone induction and compared them with the initial three courses, and with eight months of courses interspersed with reinforcement doses of vincristine and prednisone. All these children had been put into remission by vincristine and prednisone, and we thus used what amounted to eight months of courses of combination chemotherapy of intensive methotrexate and vincristine and prednisone.

The outcome of that study is that we cured a lot of children. That's the first prospective study of anti-leukemia of childhood where we very clearly demonstrated cure. My recollection is that it's about 25 percent cured on the eight months of methotrexate courses with vincristine and prednisone treatment. We have survivals out to about fourteen years on an absolutely flat plateau when the followup was terminated, with no relapses.

PD: So when you say cured, you mean past five years? Or for good?

JH: Fourteen years. Out to fourteen years, that is cure for good. Some of them at the time of followup had reached adulthood and had children of their own who were healthy.

We continued to study intensive chemotherapy, using combinations. In perhaps the most complex study of all, the first study in 1968, which was known as 6801, there were two induction regimens, selected at random, vincristine and prednisone, or vincristine, prednisone, and daunorubicin—another drug that had been identified as active in leukemia.

Patients were then randomized to receive methotrexate or 6-mercaptopurine and methotrexate. They were also randomized to receive intrathecal methotrexate or not, because we thought the central nervous system might be a privileged sanctuary unaffected by the systematic treatment. We had already shown that giving methotrexate into the spinal fluid was significantly superior to no treatment, a study brought by the initial observations on meningeal leukemia by Burchenal and Whiteside. During the course of maintenance treatment patients received either vincristine and prednisone reinforcement or vincristine, prednisone and daunorubicin reinforcement. So there were really five randomizations or two to the fifth of thirty-two separate treatment arms. We identified the most successful arm, which was vincristine, prednisone, and daunorubicin induction with intrathecal methotrexate with 6-mercaptopurine and methotrexate with vincristine and prednisone reinforcement. Daunorubicin during maintenance was too myelotoxic and produced too much immunosuppression.

The cure rates became higher and higher. The survival through the entire program of the Cancer and Leukemia Group B while I was chairman went from no child surviving two years to about 51 percent surviving ten years.

PD: Over how long a period?

JH: Over a period of 2,500 children studied from 1956 to 1975. The evolving graph of this progression was frequently used by Zubrod and by myself for testimony to the Congress

to show that we were making progress. The point was emphasized that this disease, which was metastatic from its incipiency, the absolute prototype of disseminated cancer, was curable. Many people have failed to recognize that metastatic cancers are potentially curable, just like acute leukemia is curable. What keeps us from curing metastatic cancers is ignorance on our part of what drugs to use and how to go about it. But subsequently, we have made some inroads on other cancers, using the principles established in acute leukemia back in Law's laboratory, Goldin's laboratory, and Skipper and Schabel's laboratory. These three groups—Lloyd Law working alone; Abe Goldin with a small staff; and Howard Skipper and Frank Schabel and their colleagues—have enormously influenced clinical cancer.

PD: And were these the first combination chemotherapy experiments done by anybody?

JH: No. The first combination chemotherapy in cancer models report that I could find was by Shapiro and Gellhorn. Shapiro's name was Daniel Martin Shapiro. He changed his name to Daniel S. Martin, so in the literature you will see him under two names. He's alive, working in New York, a very vigorous investigator still, and a very good man. In 1951 they studied carcinoma 755 with combinations of drugs. Not combinations of chemotherapeutic agents at first, but one chemotherapeutic agent and other agents to try to enhance its value. Subsequently Martin—I think his name was still Shapiro at the time—did do combination chemotherapies in metastatic carcinoma. He was the first man in 1962—and I make a reference to this in an editorial I wrote for the *New England*

Journal of Medicine—to take spontaneous breast cancers of mice, reset them and treat the mice with adjuvant chemotherapy. He showed that he could significantly increase the cure rate of surgery by using adjuvant chemotherapy. Breast cancer adjuvant chemotherapy in patients has become part of our daily lives, and Martin was the first man to do that experimentedly.

PD: I have two other questions about the early years. Were those controlled clinical trials the first of their kind?

JH: They were the first of their kind in this country. There were no other trials like that in cancer. Gordon Zubrod was the guiding genius and Tom Frei and I put together that first trial in leukemia. We were the first to publish in 1958. It is, I think, considered a classic, even though the study didn't demonstrate any significant improvement, but the methodology was there.

At the same time that the leukemia groups were formed by the Clinical Panel, many other groups were established. There was an Eastern Solid Tumor Group, of which Zubrod himself was the chairman, and I was a member, as were Emil Frei, Thomas Chalmers, Louis Lasagna, Bruce Shnider, and Ralph Jones. We published the first prospective trial of solid tumor chemotherapy in 1960, comparing nitrogen mustard and thiotepa in lung cancer, breast cancer, Hodgkin's disease, and melanoma. Some of the principles of clinical trials are found in those first two papers—the one on leukemia and the one on solid

tumors. There had been many anecdotal reports of cancer trials. Somebody would report a series of something or other, but the report never had in it the [ ] of randomization, and mainly the criteria for how the patients were selected through a specific method of analysis. Those first trials were funded by the National Cancer Institute.

PD: The other ground-breaking aspect I wanted to ask you about had to do with the cooperative group that you and Gordon Zubrod formed. Wasn't that the first of its kind, among medical organizations?

JH: I don't know that. Certainly not between medical organizations, because it was copied after the British Medical Research Council for the Treatment of Pulmonary Tuberculosis. They had already published their result in 1948, showing that para aminosalicylic acid plus streptomycin was better than either drug alone. Zubrod was familiar with that paper, because he was a pharmacologist. I wasn't.

Just a little personal note: I sat on the Pharmacology Panel also and there met Charles Heidelberger—also, unfortunately, gone—the man who discovered fluorouracil. He was a brilliant cancer researcher. I was always distressed that all they talked about was the pharmacology of animal tumors and the treatment of animal tumors. I said, "You know, these are all model systems but patients are what this all about." So I wrote an editorial that Heidelberger prompted me to do. Then he added some things and we joined in authorship in an editorial in *Cancer Research* in the early 1960s called, "Human Cancer:

The Primary Target." It's one of the better things I've written. Subsequently Heidelberger and I wrote an article for an encyclopedia about cancer therapy. There was less work in human tissues at that time, and that has evolved so that now, of course, we're using human cancers as the test objects many times, because there are lots of artificialities about animal tumors.

[End Tape 1, Side A]

[Begin Tape 1, Side B]

JH: I'll tell you about the Yarborough Commission, because I know parts of it that are not widely known.

PD: I'm very interested in how you came to be appointed to that.

JH: I'll be glad to tell you. The members of the Yarborough Commission were picked. The concept was Mrs. Mary Lasker's Senator [Ralph] Yarborough was involved in health matters in the Senate, but was beaten in the Texas Democratic primary by Lloyd Bentsen.

JH: He was a conservative Democrat, not a liberal Democrat like Yarborough, so Mrs. Lasker picked Teddy Kennedy to carry the proposal forward. Senator Yarborough had introduced the proposal and it was the unanimous vote of both houses of Congress, that

there should, in fact, be a war against cancer. President Nixon was the president at the time and he was dead-set against increasing the budget of the National Institutes of Health and the National Cancer Institute. I have the actual figures in a slide, but I don't have it with me.

Hearings were conducted about this in the Senate. The members of the committee to formulate and support the proposal were people picked by Mrs. Lasker. She first picked Thomas J. Watson to be the chairman, but he sustained a cardiac infarct and declined to serve. Then she picked Benno Schmidt.

Benno Schmidt may have participated in the choices. Among the laymen were Laurence Rockefeller, formerly chairman of the board of Memorial Sloan-Kettering Cancer Center and at least one of Benno's Texas friends, a man named Jubal Parten, an elderly Texan, a lovely, distinguished man. The other scientists were directors of cancer institutes. Dr. Joseph Burchenal represented Sloan-Kettering as did Dr. Mathilde Krim; Dr. Sidney Farber, pathologist of [] at Children's Hospital of Boston; Dr. Lee Clark, the director of the M. D. Anderson; Dr. Harold Rusch, director of the McArdle Laboratory; and Dr. James Grace, the director of Roswell Park, was to be a member. But he had a terrible automobile accident that killed his wife. He died a year later, having been unconscious the whole time. I believe Dr. Burchenal told Benno Schmidt that I should be the representative of Roswell Park. So I got on the committee through the death of the director of the Institute.

We used to meet in Benno Schmidt's office in New York, which was the brokerage house, Jock Whitney and Company, of which Benno Schmidt was the managing partner. A staff was appointed from the National Cancer Institute—a couple of engineers who had previously worked on nuclear submarines. Benno Schmidt had very little interest or tolerance for those men. Benno thought that the Cancer Act should be in the department and that the director should report to the Secretary of Health, Education, and Welfare, Secretary Elliot Richardson, who was a friend of his. Benno said, "If I were Elliot Richardson, I sure would want this coming to me." Mrs. Lasker must have thought differently on more than one occasion. Mrs. Lasker's Washington lobbyist, Luke Quinn, came to the meeting advocating a direct presidential report. Benno expressed disdain for Colonel Quinn's opinion privately noting that Quinn had only been a Medical Service Corps officer, whereas he, Schmidt, had drawn up the important documents of the peace of World War II. Suddenly, at one meeting, after what I surmise was his [ ] astute and artful persuasion, Benno said, "Well, it really ought to go to the president."

At the Senate hearings, Senator Humphrey, who had a sister who had died of cancer, came and testified tearily. Several other prominent people came. Senator Dole was Nixon's operative. Dole championed an alternative bill which was a budget cut for the Cancer Institute. Nixon and Dole were dead-set against the Cancer Act with its expected funding. When it became clear that Senator Kennedy's bill was going to win in the committee, Kennedy and Nixon must have had a meeting—which only Senator Kennedy could tell you about, or Dole—and the next day the Government Printing Office came out

with Dole's bill but Kennedy's text. I'd give a tidy sum if I had kept a copy of that, which I haven't. The entire substance was the Kennedy-Lasker bill, which Nixon had opposed, and then when he saw he was going to lose, politics being politics, he supported it.

I did go to the White House for the signing ceremony. All of us who were on the committee knew this was one of the great charades of all time when Nixon signed it and said, "This may be the most important Act of my presidency" which, of course, it was, but it wasn't his idea.

In the course of the Committee's efforts to present the Senate the plan we had drafted, a speaker was invited to present the concept at the Marine Biological Laboratory at Woods Hole. Benno said he was too busy to go and Lee Clark declined. Benno asked me to go. I guess he thought that I had spoken well at a luncheon for Senators—where Anna Rosenberg Hoffman said the Cancer Act was as important as the Distant Early Warning (DEW) line of [ ] that she had successfully advocated before the Senate as Secretary of Defense. I was strongly in favor of the program and moderately articulate, so Benno picked me. It was the most hostile audience I have ever stood before in my whole life. They were absolutely against the concept, thinking it would sink the NIH and drain all the money into the Cancer Institute. These were fundamental biological scientists. In the course of the evening, only one person present supported my viewpoint, the eminent scientist, Seymour Cohen, who had found out that thymine was essential in DNA metabolism, and its absence led to thymineless deaths.

Just before the intermission of the lecture-colloquy, I had said, "You know, the NIH isn't perfect. They didn't even fund James Watson when he asked for a fellowship to go study the structure of DNA," a fact I learned from a footnote in the *Double Helix*, Watson's recounting of the discovery of the structure of DNA. During intermission, somebody went out and actually called Watson who said, "Well, that was true." But he was against the bill, even though subsequently he became a large supporter when the NIH did not founder as predicted and the Cold Spring Harbor Laboratory got lots of money out of the National Cancer Act.

Albert Szent-Gyorgyi, a Nobel Laureate who had discovered vitamin C, got up after the intermission and, in effect, said, "You know, all of this is poppy-cock, because you tell them what you're going to do but you don't do it anyhow. You get the money and you do research because the research is what you should be doing, not what you tell them you're going to do." As the senior man present, he calmed a lot of angry and excited people. It was a very interesting night in my life. Benno didn't give me any gift when he sent me to Woods Hole.

The night the bill was signed, Mrs. Deeda Blair, Mrs. Lasker's longtime favorite and important lieutenant, had a dinner party. Mr. Blair had been ambassador to the Philippines and to Denmark. It was an impressive dinner party, three or four tables, and I was privileged to sit next to Mrs. Lasker on her left, and Benno Schmidt on her right, which I take to be the places of honor. Ahead of the dinner, during cocktail hour, Mrs. Lasker

said to me, "Now, Jim, we must start on the heart and on the brain. We must do the NIMH and the Heart Institute. We must get those going." She was not stopping a moment in triumph, but was constantly working for her goal, health for the people. Impressive!

In the course of the dinner, Mary Lasker turned to Benno Schmidt and said, "Benno, do you and Jock take other people's money or do you just invest your own?" He said, "No, Mary. We just invest our own." She said, "Well, that's so much nicer that way." That, of course, was a private remark, but since both people are gone, I do them no harm by repeating it. I wouldn't have had that access if I hadn't been on the Commission.

PD: What role did you play as a member of the Commission?

JH: Benno Schmidt was enormously important. He organized us. He wrote the statement of purpose and promise. There's an excellent little book that came out which is a very important document. I have a copy of it but they're hard to find. The book details the state of cancer research and what could be done. That was written primarily by Mathilde Krim, Joe Burchenal, and me. Mathilde Krim wrote a letter to every important cancer investigator in the world, which I thought was going to be a blank. But I as wrong; many, many people wrote back. From those answers the three of us put together that little book, which is an assessment of cancer research at the time.

Of the other people on the Commission, Laurence Rockefeller was a very important person. Others were distinguished laymen, politicians, doctors remote from the practice of cancer medicine. I think Joe Burchenal and I, and Lee Clark perhaps, out of fifteen were the only three that I can recall who had any actual first-hand experience in taking care of cancer patients. So I think that I gave the commission some medical credibility.

PD: How did you feel about the claim that major forms of cancer could be cured by 1976?

JH: I don't think anybody on the panel ever made that claim. I don't think President Nixon made it. I think that's a strawman. I think you'll see in the book that it was considered to be a long-range problem. We were, indeed, curing children with acute leukemia and I considered that a harbinger of things to come. But I've never thought that anybody who was responsible picked a date certain for cure.

PD: How did you feel about the idea of moving NCI outside of the National Institutes of Health?

JH: I don't think it's outside the Institutes of Health. I think that it has turned out as Mary Lasker thought and Benno Schmidt later voiced, that a rising tide lifts all the boats. If you look at the budgets for the National Cancer Institute in recent years, there has been a successive increase at a higher rate for the other institutes. Nixon would have had the

budget going down. The budget has increased since then, when it was something like 172 million to two plus billion. It's gone up by a factor of more than ten-fold in thirty years.

PD: But wasn't there a proposal to remove the Cancer Institute from the NIH that did not come about?

JH: Mary Lasker's view was that the NCI Director should report directly to the president, and indeed that aspect remains in the bypass budget. The rest of us, I think, believe that science is a continuum. Cancer science is not uniquely different from other kinds of science. It just happens to be more fascinating to me, but we certainly learn from fundamental science that comes from other places, not just from cancer investigators. Look at the fantastic progress that's been made by people who know something about fruit flies or bacteria or fish and the genome project. It isn't just cancer, but science. Human science is critical, but very difficult and expensive. Model systems are easier to work on.

PD: Were you pleased with the National Cancer Act? With the final form that was signed off on?

JH: Oh, sure. I think we all felt a level of triumph that we had done it. Everybody except Mrs. Lasker, who was ready to start out on heart disease and mental disease. Not a moment's rest for her. She was really targeted on health for the people. Before that Commission, because I had done a fair amount of work on leukemia, I remember once

being invited to her house in New York for lunch. I flew down from Buffalo, New York. Just the two of us, and a maid. She said, "Well, what do you think ought to be done?" I said, "Well, I think, Mrs. Lasker, there ought to be more research done." She had her black handbook with her. She laid it out brusquely and unfolded an accordion-pleated sheet from the [ ]. She had all the budgets for the National Cancer Institute for the last ten or fifteen years and she knew exactly how much was being spent on everything. She said, "Don't tell me about basic research. Look at all that money they've had! We need more research for patients, Jim." A wonderful woman! People don't appreciate what a fantastic impact she had.

I think you should talk to Dr. Burchenal and Dr. Krim. They would know. They were there and they knew of Mrs. Lasker's importance. Both are still alive.

PD: I made a note of that. I just want to ask you a few other questions. I've jumped around a bit here. What would you say you are proudest of in your entire career in terms of major event or . . .

JH: My wife and my children.

PD: Tell me a little bit about your wife. She deals with the psychological aspects of cancer.

JH: She's the chief of psychiatry at Memorial Sloan-Kettering Cancer Center. She has written two major texts on psycho-oncology, founded the field, really; founded the international society of Psycho-Oncology; founded the American Society of Psycho-Oncology; and has just written a book for laymen called *The Human Side of Cancer*.

PD: Have you two collaborated?

JH: We collaborated on five kids. And a good life together.

PD: And professionally have you worked together?

JH: Yes, we're coauthors on a few papers. I think she's probably in psycho-oncology because I was in cancer and that seemed like an important topic for her. Our first activity together was through the activities of the Cancer Institute. I got a contract to study patients in germ-free rooms, a premier technique of isolation. She had originally studied people who were in iron lungs during the polio epidemic, in Boston, when she trained at the Massachusetts General Hospital, and found out that many had delirium when they were isolated like that. It's a kind of sensory deprivation. So she became very interested in studying people who were in the isolation compartments of germ-free rooms. She studied some of the cancer drugs that influence brain function, such as asparaginase. We live separate professional lives in separate institutions, but we share virtually every day.

In terms of other activities, one of the things I didn't get a chance to tell you about is that we have translated some of the concepts of acute leukemia to breast cancer. We have looked at combination chemotherapy in breast cancer and the concept of induction chemotherapy followed by intensive therapy, the same paradigm as in leukemia. We have a line of progressive increase in survival in the adjuvant treatment of breast cancer that is looking like the early stages of the progressive increases in survival in acute leukemia. I'm very proud of that. I'm proud of the evolution of the Cancer and Leukemia Group B, which I ran for eighteen years. And then Dr. Frei and I, having been brought together by Dr. Zubrod, have done now five editions of Holland and Frei *Cancer Medicine*.

PD: You coedited it?

JH: Yes.

PD: Who would you say have been your major influences or mentors over the years?

JH: Robert F. Loeb; Alfred Gellhorn; Lloyd Law; Gordon Zubrod; Robert Guthrie, of the Guthrie test—I guess those are the senior people who have really influenced me most. The rest have been colleagues. Of course, I learn from colleagues, I learn from students.

PD: Are there other individuals that you suggest we interview for this project that you haven't already mentioned?

JH: Every name that I have given you, Alfred Gellhorn, Lloyd Law, Joe Burchenal, and Daniel Martin, are still active. I think you really should talk to Ezra Greenspan, who worked with Goldin and Schoenbach. Before the Cancer Institute came to Bethesda, there were certain areas of the Cancer Institute activities. You ought to talk to Howard Bierman and to Nick Petrakas and to Laurence White. Bierman, Petrakas, and White were at the Cancer Institute subdivision in Laguna Honda, California. Greenspan was in Baltimore with Schoenbach when it was a portion of the Cancer Institute activities. All these people are still alive. Catch us before we die!

PD: One of the other questions I wanted to know is: have you donated your papers to a particular institution, or are you planning to?

JH: That's an interesting thought. No, I haven't. About the first twenty-five years of my reprints are beautifully bound in a fantastic set of leather volumes that one of my best secretaries over the years arranged for. I have thought to give that to my son, who works at the National Institutes of Health, but he's not an oncologist. I have a son who works here.

PD: Which office?

JH: In the National Institute of Allergy and Infectious Diseases. Of course, that's a source of great pride to my wife and me that he's here. He's a star.

I would like to make a couple of comments, one about the peer review system and another about the integrity of the National Cancer Institute. It has certainly served as the embryonic incubator for most of what's happened that's really good in clinical cancer in the country. And if you look at the leaders in clinical cancer activities of the country, most of them have spent time at the Cancer Institute. Many of them were trainees of Dr. Frei. It's always been of high quality. There's never been a scandal since 1953, the day we opened it. There's never been a scandal of ineptitude or falsification. It's been an outstanding clinical operation and it's been an outstanding interaction of feeding concepts to the periphery. It's fulfilled its mission and I think since 1970 it's been even more important.

The staff of the Cancer Institute has always been extremely cordial. I think Dr. Klausner is probably the ideal director, in terms of understanding fundamental science *and* having an appreciation for the integrity of other viewpoints and other people on the outside that hasn't always been true of the directors of the Cancer Institute, but maybe after a few starts they're learning how to pick a really good director. When Klausner was picked, I had never heard of him and I was opposed because he didn't have a background in cancer, but I certainly have changed my view.

[End of Interview]

National Cancer Institute
Oral History Interview Project
Interview with James Holland
Conducted on January 25, 2001, by Peggy Dillon
In New York City

PD: This is a second interview with James Holland. Today is January 25, 2001. We are at his office at 1450 Madison Avenue, in New York City.

JH: Which is the Mount Sinai Medical Center.

PD: You're picking up fine on that.

JH: Yeah, I'm sure of that.

PD: This afternoon, I'd like to continue the conversation we started in September, regarding your career in cancer research and involvement in the National Cancer Institute. One question I wanted to ask you goes back to how you decided to pursue research in the first place. You originally wanted to be a cardiologist, and then you changed your mind after anticancer drugs came out?

JH: I came back from the Army, not on the thirtieth of June as was planned. I had gone in on the first of July two years previously, but the Korean war was in process, and by fiat, the president extended all Army officers. So that instead of getting out on the thirtieth of June, I was extended for an indefinite period. I subsequently got out in about September.

I had received a letter from Dr. Robert Loeb who was the chairman of medicine at Columbia Presbyterian Medical Center, and who was one of my idols, really. Dr. Loeb said, "I can't save a place for you, because we need the house staff, but I will find something for you to do, and someone will drop out from tuberculosis or psychiatric illness. They always do. And then I will put you back in the residency program, and we have just opened this new cancer hospital, called Francis Delafield Hospital, and you can go there with Alfred Gellhorn."

It turned out that Alfred Gellhorn had been my physiology instructor as a first-year student, and I had written my thesis on the prostate gland, and he corrected it, and I still have it someplace. And since . . . he said, "A+ . . . since I have no corrections, what do you think about . . ." and then there were several . . . treating me like a colleague. In my second year of medical school, Alfred Gellhorn had moved from the department of physiology to the department of pharmacology, which was a second-year course. So we interacted again. In my third year of medical school, he had moved to the department of medicine, and had begun studying anticancer drugs, about which I knew nothing at the time, and I had sort of lost contact with him. But knowing of his favorable response to my thesis in the first year of physiology, when I found out that he had become the head of Francis Delafield Hospital, in the medical service, it seemed like a wonderful opportunity, and it was fine.

I planned to go back to Presbyterian, but, in fact, a child came who had acute leukemia and in 1948, Farber . . . and this was 1951 . . . Farber had reported temporary remissions in children with leukemia with a drug called aminopterin, and that became amethopterin, which was a slight modification in the molecule. That drug today is called methotrexate. But amethopterin is what it was then, and aminopterin had dropped out in that two-year period, or three-year period, and I treated this youngster with amethopterin and her leukemia went away. It was a dramatic difference. And so when I did get a call from Dr. Loeb, saying, "Okay Jim, I've got a place for you . . . so and so dropped out with tuberculosis," I said, "Thank you Dr. Loeb, I think I'll stay."

And some people thought that was almost suicidal because I would have been the chief resident. I was a pretty good internist, and that guaranteed a wonderful job at Presbyterian. But I stayed and the salary was $4,000 a year. And I was in the middle of a divorce and had a daughter and I told Alfred Gellhorn, who was really an extraordinarily good friend of mine, and still is an extraordinarily good friend of mine, and you must interview him . . . I told Alfred that, you know, I needed more money. So he negotiated for me a position at the National Cancer Institute, where I got $7,200 a year.

PD: Through Dr. Mider, right?

JH: Through Dr. Mider, who was a friend of Alfred Gellhorn's, or at least they were on speaking terms, in some way, because Mider . . . Alfred Gellhorn used to arrange for senior people to come and deliver rounds and lectures at Delafield, and Mider had come once.

PD: Okay.

JH: And then I went to the Cancer Institute and was interviewed by Murray Shearer who was a senior pharmacologist there. And I walked into his laboratory and he was in the process of dissecting a mouse. And he said, "Here, do this autopsy on this mouse." And I said, "I've never done an autopsy on a mouse." And he said, "Well, all the better." And so I got what was really a baptism by fire of having done that. Interestingly, and as an aside, as a medical officer in the Army, in Orly, France, a soldier had skidded on his motorcycle and smashed his head open and died and they took him to the American hospital in Paris, and, as was true of soldiers, somebody had to autopsy him.

So they called me to go to Paris and autopsy this fellow, and, of course, I had seen autopsies, but I'd never done an autopsy. But I did my first autopsy with an Irish diener, the worker in an autopsy room, and he was very impatient with me because I did a full autopsy, as I had seen, stripping out the small intestine and other kinds of things, and he couldn't get over the fact that I was really taking a hell of a lot of time. He expected me

just to make a cut and say, "Okay, he's dead," and finish up. So it was quite different [laughter]. So, I went to the Cancer Institute really out of money, and because I had become interested in chemotherapy at Delafield, where, in addition to that one child, then we did Alexander Haddow, the director of the Chester Beatty Research Institute, now dead, in London, came through. He was, perhaps, the world's preeminent oncologist at that time, and he gave Alfred Gellhorn GT-41, which stood for George Timmis, the chemist who had made it, 41, and subsequently became the drug Myleran, which is still available as busulfan.

And this was a new drug that had had activity in rat bone marrow, and so we tested it in a whole spectrum of patients with a whole spectrum of tumors in what then would have been considered . . . what today would be considered a rather sloppy way of looking for drug activity. But we had an opportunity to do that.

PD: You had mentioned that that child who was treated for leukemia went into remission. Tell me a little bit about what children . . . how they acted when they had leukemia with no treatment, versus what happened when you treated this child.

JH: I can recall distinctly, as an intern, having a girl of about nineteen or twenty on my floor . . . lovely girl . . . who had constant nose bleeding and gum bleeding and there was no platelet transfusion and no chemotherapy for leukemia. And cortisone had not yet been

discovered, and certainly wasn't available as a drug. And in those days, it was known as compound-E of Kendall. And a hematologist, then chairman of the hematology group at Presbyterian, came to me and said, "Look, this girl is very sick," and he had found in his mice, or someone had found, that their tumors were parasitized with a virus which was a very close relative to the vaccinia virus.

And that is a disease of mice . . . I've forgotten what the disease is called in mice, and it may come to me . . . and he wanted me to give this girl intravenous vaccinia virus, which is what you got vaccinated with to prevent smallpox, because we might be able to parasitize her leukemic cells, and thus help her. So I thought that was a very good idea, because we were looking at an otherwise irretrievable situation. And we did. We gave her intravenous vaccinia virus. I honestly don't remember what happened. She didn't die from it, and she lasted another week or two, but I don't know what happened to her blood counts, or whether there was any evidence or whether he was able to recover the virus from her cells.

But that was, perhaps, a very early interest in that kind of thing. My preceptor, as a third-year student, was a man named Randolph West, a wonderful hematologist who had spent much of his life on the study of pernicious anemia. And Merck had just purified liver extract and made B-12. And he was one of the first people to get B-12 as a vitamin. And this was to be the treatment for pernicious anemia. So he brought a young woman into

the hospital who was anemic, and gave her injections of B-12, and every day himself and a technician would count her reticulocytes, which are one of the first blood cells that increases after appropriate treatment of pernicious anemia. And he could see them begin to rise, but the technician couldn't. And she didn't really have pernicious anemia, I think, and she didn't really have a rise and didn't get better with B-12.

And that was a profound disappointment to him, but for that first week, his enthusiasm in having this, he was sure she was going to feel better. And so that was another investigation that I saw. But I really had done nothing experimentally until I went to Delafield, and in Delafield, as part of learning about cancer, one of the problems with cancer, and still is, that people get a high serum calcium level when tumors invade their skeleton. And that high serum calcium can kill . . . many other complications along the way, but eventually, can be a lethal complication. So, some way to decrease the serum calcium was of importance. And just at that time, Alfred Gellhorn had heard that EDTA . . . ethylenediaminetetraacetate, EDTA, had become available as a chelating agent. So I got this drug to study. And I studied it in patients, and that was one of the first papers I had written myself . . . I will tell you about earlier ones in the Army . . . that was one of the first patients I treated myself, including one patient where we gave EDTA and then every few minutes we took blood, and she had a cardiac standstill . . . and quickly recovered. And we saw her serum calcium go down to levels that are really extraordinarily low, and then bounce back up. And that was an interesting phenomenon.

But I also used this because the question came up, does the calcium level control your parathyroid, and what is the mechanism of the parathyroid, which is a gland not controlled by the pituitary. And so nobody really understood the control mechanisms for the parathyroid and I got dogs and would give them a hypocalcemic stimulus and see, from measuring their urine phosphorous and their urine creatinine and their urine calcium and the serum levels, whether or not they did, in fact, have an increase in their parathyroid secretion. And then I parathyroidectomized the dogs and took out their parathyroids to see whether or not, indeed, we could abolish that response. And I had . . . and you have to use female dogs to catheterize them so that you can get the urine . . . too hard to catheterize a male dog. And I couldn't really see where the urethra was. So Alfred Gillman, of Goodman and Gillman . . . a world famous pharmacologist . . . he was thrilled. He said, "By all means, he'd come over and he'd show me how to catheterize a dog." And he did.

And that was the kind of mentoring that was very good. And I must have done fifteen dogs. Alfred Gellhorn gave me a technician, and it was a systematic approach. We would give them EDTA and show the thing . . . then return them back to the cage . . . then a week later parathyroidectomize them and do it again to see . . . about seven of the dogs came out yes, this was a hypocalcemic stimulus of their parathyroid. You could see that they changed their phosphorous excretion. And the other seven dogs didn't. So, I wrote this paper up for the *Journal of General Physiology* and sent it was rejected. And then I

went to Dr. Loeb and to Dr. Gillman, and Loeb said, "Jim, this paper isn't going to do you any good because it doesn't really arrive at a conclusion, and therefore, I don't think you ought to publish it." And Gillman said, "Well, man alive, of course you should publish this to keep somebody else from wasting their time trying to reproduce it." A good example of two great men having diametrically opposite opinions. I submitted it someplace else, I believe. I can't recall. It never got published and I gave up because I went to the National Cancer Institute.

PD: You were going to tell about the patient who had leukemia who you treated, and the dramatic response you had?

JH: This was a child, yeah.

PD: Okay.

JH: This was a child at Delafield Hospital. I mean, a child who has leukemia does have a dramatic response. There is a rapid decrease of the leukemic cells in the blood. In those days, we didn't do marrow aspirations as we do now, making sure that the cells are gone from the bone marrow, which we do now with abandon, really. That was 1951 that we didn't do it with abandon then. And it was a big deal to do a bone marrow then. In fact, nobody did iliac crest marrows in those days, which is where all bone marrows are done

now. You like on your belly and there's a bone in your back, and you can stick there, and if you don't stick correctly, you stick into the buttock. But in those days, all the bone marrows were done on the sternum. And if you stick too far, you stick right into the heart, which I have seen happen. I . . . her normal cells came back. Her platelets came back.

She stopped being sick, and I don't recall how long it lasted, but it was the first instance I had seen of a dramatic turnaround, and I think it was the first instance . . . because I presented that child at grand rounds for medicine . . . the Delafield Hospital being part of Presbyterian, got to present once every few weeks at grand rounds. And grand rounds, in those days, were much more important than they are today, where you have the Internet and a zillion journals. The teaching experience was very centered on this kind of verbal communication and grand rounds were important. And I was good at it, and one of the high points that I have always remembered is David Siegal, who is a professor of medicine and a notorious wit and a wonderfully energetic man who could really spellbind you with delivery, said to me once in the elevator, after I had presented at rounds, "Jim you mesmerize me."

PD: What high praise.

JH: Yeah.

PD: And then you were also going to tell me about the early days at the [NCI] Clinical Center. You said . . .

JH: Well, the Clinical Center, I . . . that's a different topic and I'll be glad to . . . yes, I . . . having gotten an appointment at the Cancer Institute after having been interviewed by Murray Shearer and by Bill Meyer, I went and, on day one, Ovida Kolpabi was the administrator of the federal agency of some sort which was the forerunner of the Department of Health, Education and Welfare. And I've forgotten . . . Federal Security Agency, it was called, I think.

PD: It wasn't HEW at the time?

JH: No, no. It was before HEW had been formed. And I'm not certain that it was a cabinet level position, but she was the wife of the publisher of the Houston paper, and so, obviously, had a lot of political clout and got this position . . . and was a very able administrator. And a ceremony was held in front of the clinical center and it was opened that day. And there were a few patients in it who had been transferred from the Navy Hospital across the street, which preceded the clinical center, and I don't recall . . . I think they were Navy personnel that were brought to the clinical center to show us extraordinary things.

These were people who had been given LSD. LSD was a new drug that was active and could change the brain in doses of micrograms, which was absolutely phenomenal in those days, and this was thought to be an opening to studying mental disease, because these people became temporarily psychotic and could draw wonderful pictures of heaven and sunshine and other things. And it was very phenomenal and this was shown off . . . their pictures were shown off, and a discussion of this new drug that could affect the brain . . . don't forget this is before all the brain drugs and things that affected the brain were alcohol and maybe phenobarbital and the rest of it wasn't known.

So, this was a real breakthrough and wasn't looked on as a street drug or a recreational activity. This was research to see what happened in the brain and what were the problems that led to schizophrenia and other things. And that was . . . because it was active in such a small dose, this was considered a major event.

PD: And they were among the first patients at the clinical center?

JH: They were brought over because it would . . . gave something to show. I think it was a dog and pony show and this gave something for people to see rather than just looking at the building.

PD: Had you been hired and started woking the day that it oened?

JH: I had been hired. I don't think that first day we worked. There weren't patients there. I also . . . I must say . . . I had gone down to be interviewed ahead of time, I guess, or maybe shortly after . . . I don't know . . . and was interviewed by Roy Hertz. Roy Hertz was a major factor there. He was very interested in nutrition and vitamins, and had shown, in a very important paper, I think, that the chick oviduct, which was under hormonal control, the chick oviduct growth could be stunted by giving the same drug that was given for leukemia . . . which was one of the first interactions between an antimetabolite and a hormone. And that interested me. I didn't know why and they complexity of tissue metabolism hadn't matured, but that was an important thing.

And Hertz used to go to George Washington University as an endocrinologist. And he was forever measuring vitamins and things of that sort. And he had women with different kinds of hormonally related tumors on the floor, including women with choriocarcinoma. And he was giving huge doses of estrogens to these women . . . huge doses . . . so much, so huge, that, in fact, it wouldn't dissolve in the infusion bottle, and Leonard Fenninger was one who suggested that, in fact, he should suspend them in albumin . . . that albumin made things stay in solution. And Fenninger was quite critical of Hertz doodling with vitamins and giving massive doses of things.

So, once when Hertz was on vacation, or disappeared someplace, I remember Fenninger stating, you know, that he was going to see that it got done right. And subsequently, after

I left the Cancer Institute in November 1954, but having seen such women, many women with choriocarcinoma around, that Hertz was doing hormonal studies on . . . they often just lay around the clinical center in the Cancer Institute . . . a man named Paul Condit, who was an acolyte of Abe Goldin, was looking for subjects that he could give high doses of methotrexate, the same drug that was used in leukemia too. And he gave a high dose of methotrexate to a woman with choriocarcinoma, or hydatidiform mole, hydatidiform mole being a relative more benign form, but not completely benign, of choriocarcinoma.

And Min Chui Li, who was a Chinese fellow, or junior attending in Hertz's stable, recognized that the human chorionic gonadotropin, HCG, decreased in that woman after the methotrexate was given. And so, he refused to let Condit continue and he gave the woman twenty-five milligrams of methotrexate by injection for five days, and that led to the cure of choriocarcinoma . . . the first cure of cancer. And the paper is Li, Hertz and Spencer, who was the technician who did the HCG levels. And there is a footnote in the paper . . . which I doubtless have a copy of here somewhere . . . there's a footnote thanking Dr. Condit. But Condit and Abe Goldin never got any credit and Hertz fired Min Chui Li.

PD: I knew there was a controversy surrounding Min Chui Li.

JH: Right. Yeah. And Hertz then garnered huge amounts of credit and fame for it. And I'll continue with that, because I had gone, in November 1954, from the National Cancer Institute to Roswell Park . . . at that time, Memorial Institute, in Buffalo, New York . . . Roswell Park having been the chief surgeon in Buffalo who was to have operated on McKinley when McKinley got shot, but arrived too late to operate on him. Somebody else had done it. He had been out at Niagara Falls and came back by train. And I tried to hire M.C. Li. I had him come to Buffalo and give a talk, which was excellent, and I spoke to Gordon Zubrod about him, and Gordon said, "Well, I thought he was a good fellow, but Roy Hertz really recommended that I not take him."

So, Min Chui Li wound up in Nassau County here, in what was, at the time, called Nassau Hospital, I think, and I subsequently saw him twenty years later after I had come to Mt. Sinai. And he was still a very good man. And Joe Burchenal became the head of a committee for the World Health Organization and decided that this particular committee should have a meeting on Burkitt's tumor. And we went to Africa and then he said to me, "Do you have anything we should have a meeting on?" And I said, "Lord, we ought to have a meeting on choriocarcinoma, because that's a curable tumor. And we ought to have it in Asia." And he thought that was a great idea.

So, I organized the conference with Myroslav Hreshchyshyn, which I will spell for you . . . M-Y-R-O-S-L-A-V H-R-E-S-H-C-H-Y-S-H-Y-N . . . Myroslav Hreshchyshyn. When he

came to the United States, an immigration officer said, "Your name is Richardson from now on." He said, "No. It's Hreshchyshyn." And I was one of the few people who could pronounce it. He was a gynecologist that had applied at the Cancer Institute. Zubrod said, "I can't take foreigners," and he sent him to me. So, Hreshchyshyn worked with me for many years, and eventually became chairman of gynecology and obstetrics at the University of Buffalo. But we . . . I said to Burchenal, "Let's have a conference on choriocarcinoma, and in the Philippines."

And there was a fine man named Manuel Borja, who had worked at Roswell Park in the Philippines. He was delighted to be the local chairman and set up the arrangements. And we convened . . . Burchenal, [Dave] Karnofsky, Hreshchyshyn, myself, and we wanted Hertz and a group of Asians. And Hertz made it very clear that he would not come unless there was some encomium involved. So, I had to beat on some of my friends in the pharmaceutical industry to put up enough money to give him a fat honorarium for those days, which . . . and I can't remember when it was . . . but it was 1960 something or other, and I guess it was $1000, I think.

PD: Wow, that was a lot of money.

JH: Yeah. And here is the book that came out of Burchenal's conference . . . the treatment of Burkitt's tumor. And . . .

PD: May I?

JH: Yeah. And I have a similar one, and my copy of it may be home . . . also red, like that, which is choriocarcinoma. And I have a very good paper in there, I think. And, so, Hertz had been in the government long enough to know how to present things to his best advantage . . . let's put it that way. Go ahead.

PD: I wanted to ask you what a typical day was like in the early days of the clinical center. I mean, you were there right at the beginning.

JH: I was there right at the beginning. Let me tell you the two men went with me from Presbyterian Hospital as clinical associates. One was John Fahey, who subsequently became chairman of immunology at UCLA and the other was Donald Tschudy . . . a good Swiss name . . . who remained at the Cancer Institute for his entire career. And I was quite friendly with these three . . . these two fellows . . . the three of us were. I was only a couple of years older than they and a couple years ahead of them. They had been residents at Presbyterian, hadn't gone through Delafield or the cancer activities, and then came to the Cancer Institute. And in the beginning, Bo Mider served as the clinical director and he made rounds every morning at eight o'clock. And at eight o'clock, when the hand hit the eight he began.

He was the most punctilious man I ever encountered, and was very good. And they were, in essence, walking rounds with discussion of not so much the medical problems of that particular patient, but of the conceptual activities . . . I can remember distinctly once on rounds where Hertz was there and Mider and myself . . . and undoubtedly many others . . . in which there was a vigorous discussion of what is a virus. And maybe acid phosphatase, which is an enzymatic elevation that occurs in the course of prostatic carcinoma, maybe acid phosphatase is a virus that is elevating because the virus is growing . . . and don't forget, things were more primitive in those days, which was certainly very, very vigorous. I also can remember Harry Eagle had been the director of the Cancer Institute for a short period of time, but couldn't stand the administrative work and wanted to figure out exactly what it was that a cell required to grow in vitro. What were the essential nutrients for a cell? And he was figuring out Eagle's medium. And he was . . . he had made . . . I had known Harry Eagle since I was in medical school, when he came and gave wonderful talks about penicillin and syphilis. [pause -- telephone call]

PD: Okay, we were talking about a day in the life of the early clinical center. You were talking about rounds with Dr. Mider.

JH: Rounds with Mider . . . and then there were electoral discussions of what was going on, in different fields of science, and the translation of laboratory experiments that were being done by Law and Goldin particularly, because they did the exploratory combination

chemotherapy . . . Law did . . . and pharmacology of how to best give drugs, which Goldin did, and whether these were relevant to the kinds of diseases we saw, and how to proceed. And because I had done some work with leukemia at Delafield, I ran the leukemia service and I had children and adults with leukemia and treated them all the same, because we didn't have any other treatments and didn't know there was a difference in the way children and adults would respond.

And there are several kinds of leukemia and even several kinds of acute leukemia that had become more obvious now that we've got better studies. But in those days they were all lumped together and they were all treated the same. The clinical fellows of Fahey, Tschudy, would have responsibility for a very few patients and would see them and take care of them . . . excellent nursing service, excellent care of patients . . . it was really terrific . . . a wonderful occupational therapist who used to come and play with the children, and her fiancee . . . I have forgotten her name, but she was a lovely girl and she was very helpful to me. Her fiance used to come and say, "And she gets paid for that. Look at that. She's sitting on the floor having a great time with these kids, and she's getting paid for it."

It was a very ivory tower atmosphere because there was so much expectation of us. At the time, I took care of the daughter of the chaplain of the Senate . . . a wonderful man named Russell Straup, and his wife, and their only child. And this girl was very dear to me

and very dear . . . and I was very dear to them. Because of that, Nixon, as the vice president, came once to visit this child and brought two dolls . . . big dolls . . . that had been given to his daughter. He had two daughters . . . he had given to his two daughters . . . and he gave one to Susan and one to Susan's roommate and said that his daughters got too many presents and he was glad to give them away. We, of course, were, in essence, on dress parade for Nixon to come. But he was a young man at the time, with a heavy beard. Russel Straup subsequently married my wife and me when I got remarried. And he came to Buffalo and married us. And he was a wonderful man. He died and his wife died.

PD: So, those early days, there were endless resources?

JH: I don't know that there were endless resources. I had a laboratory and was studying the metabolic products of leukemic cells that came out in the urine. And if you destroyed DNA and RNA, it winds up as uric acid. Uric acid comes out in the urine and you get a huge peak, and I studied that . . . to do it with precision, James Wyngaarden was there, who subsequently became director of the NIH, but he was, maybe, a year or two ahead of me, and a far better chemist than I, and he showed me how to isolate the enzyme from a pig's liver to make a precise estimate of uric acid by destroying it and then seeing a difference in the starting solution and the solution after the enzyme had acted on it.

I had never purified an enzyme before, but it was old hat for him, so he showed me how to do it, which was very good. And he was in a different institute, but there was this kind of collaboration and interest and the expectation that was this fantastic new glorious hospital, and patients didn't have to pay . . . that we could really make a dent in disease. And there were some outstanding . . . I can remember the United Mine Workers took advantage of the situation because they had a string of hospitals in the Appalachian area but they didn't really have people who could do anything about leukemia. And they made an arrangement with someone . . . I don't recall with whom . . . that they would bring the patient to the door of the clinical center, in an ambulance, and take him away when we were finished, in an ambulance, and we had no worries. All we had to do was say, "Yes, we'd accept so-and-so."

And I had many leukemic patients who came that way. Miners and miner's children, through the UMW, who took advantage of this free hospital with superb people. At that time, it was right after the Korean War. I went there on July 1, 1953 and the draft must have been in activity at the time because many people came there and were pushed by their professors of medicine to go, because, in fact, this way they could continue in an academic life and not go off and inspect beetles in San Francisco Harbor or something like that.

PD: [inaudible] . . . NIH drew a lot of great scientists in that way.

JH: Eventually, when the Vietnam war came, I guess they were known as the yellow berets. But it wasn't an act of cowardice. It was taking . . . because the criteria for selection were very high, and they were taking people who were really talented enough to be academic leaders and NIH became the embryo breeding ground . . . it became the incubator for academic medicine all over the country.

PD: Let me just turn this tape over.

JH: Sure.

[End Tape 1, Side A]

[Begin Tape 1, Side B]

PD: Okay. Let's talk a little bit more about what the early days were like back at the clinical center, doing grand rounds with Dr. Mider.

JH: They weren't grand rounds, they were walking rounds . . . every day, every day. And there weren't any grand rounds that I can recall, which were an assembly of everybody from the NIH sitting down with a lecture and a presentation. I don't recall . . . they may have happened, but it doesn't stick in my mind. These were work rounds, but the work

rounds were really aimed at conceptual concepts of cancer and not specifically at a particular patient's problems for the day, which are what ordinary work rounds were. And Mider, for example, had done a great deal of work on protein metabolism in animals with cancer. Why do animals lose weight? Why do patients lose weight? That was a very important part of why you die from cancer . . . shriveling up . . . and we discussed that at great length. Viral oncogenesis, chemical oncogenesis . . . there was a man at the Cancer Institute named Hueper . . . Bill Hueper . . . H-U-E-P-E-R . . . who was deeply involved in chemical carcinogenesis.

And most of us didn't know anything about it except for the recognition by then that the cigarette was a fairly dangerous thing. And Evarts Graham and Arenst Windor had reported that cigarette smoking caused lung cancer, and Mark Levin, who was an assistant commissioner of health in New York State had reported this also. So, these were topics that were fairly widely discussed. And Hertz's group had breast cancer and GYN cancers. I had leukemias. Bob Smith was the head surgeon and he did a lot of work on head and neck surgery, so there head and neck surgical patients there. And it wasn't a general cancer hospital. People were admitted for specific diseases and, as I mentioned to you, the United Mine Workers took advantage of that and transported people with leukemia to the door and picked them up at the door in order to get them out of the mine worker's hospitals.

I had a very interesting patient . . . I don't know how she got there . . . but a very interesting patient who had been a radium dial painter in New Jersey. In New Jersey, there was a factory where girls who painted the dials used to tip their brushes by sucking on them . . . putting them in their mouth, and then they'd have a fine point. And Harrison Markland, who was the medical examiner of Essex County at the time, was the man who figured out why these girls got bone sarcomas from the radium . . . it's really mesothorium, but it's called radium . . . but from radium dial painters. And that is a classic epidemiological study that was done in the thirties, and the medical center in New Jersey is named after him now. And this woman had . . . and the play on Broadway, Hazel Flagg, is about this. And this particular woman had all the radiation damage to her bones from the radium. And I was very interested in that. And, at the time, a radiation biologist/physician named Bill Looney was across the street at the Naval Hospital and he had a total body counter, which was an extraordinarily rare instrument. I haven't seen one since, to be honest.

But this was a total body counter because of all the great interest in atomic energy and atom bomb fallout. And this particular woman, then, had tremendous amounts of radioactivity in her body, from which we could see the effects, and Looney was able to put her in the counter and show that he could measure the isotopic activity in her body. At the time, there also had been no iodine dyes to pacify blood vessels, and so one of the techniques of pacifying the liver or blood vessels for brain surgery, was to use a

compound call Thorotrast, which was made of thorium, and thorium had radioactivity, and so many of these people got radioactive problems. And this particular woman, and the thorium problems led me to try to chelate thorium out of the body, as a potential salvage mechanism for people who might have been involved. And I did some work with EDTA and looked for other chelating agents to chelate thorium, in the course of which I got to meet Egan Lorenz, who was a fundamental scientist at the Cancer Institute at the time.

He was the forerunner of bone marrow transplantation because he showed that if you radiate a spleen of mice, the . . . if you radiate the whole mouse, they die from radiation sickness. But if you excluded the spleen from the radiation field, they'd survive and it worked out that this was because there were cells in the spleen that repopulated the marrow. There had been a theory that it was a chemical substance from the spleen, but it turned out to be cellular, and Egan Lorenz was a big fellow there at the time. Other clinical memories of activities at the Cancer Institute . . . I don't recall specifics. This is before Freireich came and showed that platelets were useful. And he did that . . . I take it back . . . he did that in part with a man who gets too little credit, named George Brecher. George Brecher . . . B-R-E-C-H-E-R . . . was a Czechoslovakian refugee from Prague who was a laboratory hematologist.

And he and I were very good friends, and when I would do a bone marrow aspiration on somebody with leukemia, he would come to the bedside and make the slides. That would

be unthinkable today. But he was a meticulous man and bone marrow morphology was new and very important. And Brecher and another man across the street at the Bethesda Naval Hospital . . . Cronkite . . . Eugene Cronkite . . . showed that if you radiated dogs, their platelet count would drop to zero, and you could give platelets to dogs and make them survive longer. And it was just becoming known at the time that platelets contained serotonin. And so I got some serotonin and had given it to patients to see whether that would stop the bleeding from thrombocytopenia . . . whether thrombocytopenia really was serotonin deficiency. Not a very good experiment, not well done, but it was part of . . . that we knew that you had to do something about bleeding.

Freireich came along and, in part, based upon the Cronkite/Brecher experience in dogs, showed that if you take blood bank blood compared to fresh blood that had the platelets in it, that the platelet rich blood stopped bleeding much better than the bank blood. And that led him to stimulate the IBM executive whose son had leukemia to design the centrifuge, for which he deserves all the credit . . . no question about that.

PD: They had a falling out at some point, and then the centrifuge design was finished off by some other people involved?

JH: I don't know. I . . . he . . . Freireich's story on that would not be off the mark because he deserves all the credit for having pushed that. It was not a very popular thing at the time.

But Zubrod supported that. I don't recall anything more, specifically, about the clinical activities there. There was a lot of camaraderie among the fellows. The group that worked for Hertz were pretty close with each other. The group that worked with me and Fenninger were pretty close with each other.

I left about a month after Zubrod came. Zubrod said he didn't have a program in acute leukemia, and would I mind if he continued my program at the Cancer Institute, and that blew me away. That was a level of collaboration I had not known, and so I . . . I think I . . . in the first interview . . . and Zubrod was really extraordinarily important in bringing Frei and me together. He recruited Frei to take my job about a year later. He had known him in St. Louis where he had gone and where there were unsuccessful negotiations at the St. Louis University. And he came back to the Cancer Institute. Subsequently, the collaboration between Frei and me . . . and I recruited the Children's Hospital in Buffalo . . . led to the formation of the Acute Leukemia Group B, which are some of the papers that I presented . . . that paper from the Burchenal book on Burkitt's tumor . . . that's work that we did in the Acute Leukemia Group B, which subsequently changed its name to the Cancer and Leukemia Group B, which still exists and still is a functional organization and still is making significant contributions.

PD: And which you chaired for eighteen years.

JH: Right.

PD: Can you talk a little bit about the ripple effect that those early years had on leukemia studies. I mean, your collaboration with Zubrod gave way to the cooperative groups which, in turn, studied and treated thousands of patients. Talk about the effect that those early years eventually had on you.

JH: Well, by ripple effect, I would have thought you meant what effect did the groups have on the practice of medicine in the country. That would be the ripple out to the rest of the pond. The group itself were academicians, and part of the value of the group is this kind of camaraderie that goes with meetings. We used to meet four times a year. Now we meet twice a year. But they were smaller. It was interactive, and the group was, maybe, a hundred people. Now it's five or six hundred people It was a wonderful training ground for young fellows, and it was sort of like mountain climbing. There's Mount Everest and we've got to get there and we're going to do it by hook or crook . . . and that kind of enthusiasm with a small focused group had tremendous impact on each of us who were in it.

And as we reported significant improvements, they had impact on the country by virtue of being published and by virtue of loads of lectures. I have a number of things in my bibliography, which I asked her to Xerox for you . . . speeches that are in books which

represented some conference somewhere, where there might have been 500 people . . . at a hematology congress or a cancer congress or something. And word of mouth is really very important among medical researchers . . . not just written stuff, but people go to meetings because there is something like . . . it is sort of like going to the theatre. It's a little different from reading a play and seeing a play acted. So, the original fellow who is involved in something, talking about it, has lots of appeal for people. And thus, I do believe I was a vigorous spokesman for the treatment of acute leukemia of children, and that graft represents the work when I was the chairman of the group. And the lowest curve there represents the first study we did in 1956, and no child survived two years.

And the last study . . . that line has subsequently . . . . the top line, has been projected out and lasts through about 55 percent at ten years. And, I take it back . . . I think it's 51 percent at ten years. But, it's now up to about 80 percent. And you can see the fairly big gap there in the middle, after the fifth study, which . . . a succession of improvements . . . there's a big difference in there, and that's the use of the concept of two treatments . . . induction treatment and an intensive treatment to eradicate the residual cells. And then it becomes harder and harder to make advances, as you can see, because all the easy ones have already been taken care of. And that's about 2500 children there, that were done. And that slide, in its various progressions, was used by me and by Zubrod and by others in front of congressional committees, that we are making progress and you can see what we are doing is in need of further prosecution, because it's successful.

PD: You then branched into other areas of cancer research after leukemia. Is this the base from which . . . I mean, how did you expand from leukemia to other areas?

JH: Well, the concept . . . the principle of using drugs . . . the principle of leukemia is, by definition, a metastatic cancer when it begins. And the problems with cancer aren't cancer surgery or local disease which can be killed with radiation or removed with surgery, but the problems are metastatic disease . . . disease in the body outside the scope of the surgery, and that's a perfect paradigm for it because that's true with every leukemic. So, how to translate the conceptual advances made in acute leukemia to other diseases . . . and both Dr. Frei and I are strong exponents of that, and have collaborated a lot during the last nearly 50 years. And so, this is . . . it was not hard to take this same concept that you use, chemotherapy, and when do you use it? You use it when the disease is at its lowest ebb, which may be right after surgery . . . adjuvant surgery, adjuvant chemotherapy . . . combinations of drugs . . . two different kinds of treatment, which is what happened there in the middle. And I could show you similar data in breast cancer that inscribe a set of curves not terribly dissimilar from that.

PD: Oh.

JH: In that sense, not everybody agrees with it. I wrote the editorial for the *New England Journal of Medicine* when Bonnadonna's first paper was reported. And I can tell you

about that because that's a relevant thing. A student of mine, Richard Cooper, in Buffalo, New York, had worked with me, became interested in hematology and oncology, took a years fellowship with . . . in Malmo, Sweden, with . . . and I'll think of that name, sorry . . . it's . . . and then took a year in Cleveland with Harris and then came back to Buffalo to practice, and had gotten his early interest with me in leukemia. We wrote a paper together about leukemics presenting with pericardial effusion, which never got published because people didn't accept it for publication. It disappointed me greatly and disappointed him. And his office was filled with women with breast cancer.

That's what medical oncologists do in large part. Because, one, they live a long time, and two, it's common. Lung cancer doesn't live a long time, so there aren't so many people in the office at any one time. And after taking care of women with many different breast cancers, he came upon the literature and said, "Well, here's a drug that works 20 percent of the time, and here's a drug that works 20 percent of the time," and five such drugs he could identify, and he put them together in a five-drug regimen, which is . . . was known at the time all over the world as the Cooper regimen . . . vincristine, prednisone, cyclofesamid, methotrexate and fluorouracil.

PD: And this was when?

JH: About 1969.

PD: Okay.

JH: And he reported this in the *American Association for Cancer Research Journal* as an abstract that he got 90 percent results in women with metastatic breast cancer. And nobody had anything other than 20 percent results. So many people tested his regimen, including ourselves, and we didn't get 90 percent, but we got 50-60 percent in the group, and that was a big advance. And then the leap of genius that he made . . . and it really was a leap of genius . . . was to say to himself, "Every woman I see who has four lymph nodes involved or more, winds up with metastatic breast cancer. So, why the hell do I wait for them to get metastatic cancer? Why not treat them at the time of surgery, when they've got four nodes or more."

And he did that in his office, and treated a hundred patients in his office, and finished in about 1971 or 1972. And he wrote it up and sent it to the *Journal of the American Medical Association, JAMA*, and they refused it. And he came to me crestfallen and it was written in Chinese. It was just un-understandable, the way he had written it. So I, as his mentor, said I would rewrite it with him, help him to rewrite it, and I got my statistician at the time, a long time wonderful colleague of mine, named Oliver Glidewell and we went over his hundred cases, and saw that everyone did have four nodes or more involved and everyone had a diagnosis and a date of operation and a date of recurrence and they did get the treatment, and found that, in fact . . . and I've got slides of this that I

could show you . . . that these women had a plateau at about 60 percent survival whereas the data . . . he didn't have a control group of his own . . . but the data that were available at the time showed that about 85 percent of these women would relapse so there would be a 15 percent plateau.

And, using data from others, we could draw a graph that was very persuasive. And also, split his group of a hundred women into seventy-three who just got chemotherapy, and twenty-seven who got radiotherapy and chemotherapy. And the radiotherapy group did much worse than the group that got just chemotherapy. And we couldn't get that published. So we split it into two papers and sent the radiotherapy paper saying, "This is a disadvantage to surgery, gynecology and obstetrics," a journal which we knew would have surgeons on it and the radiotherapists had been the ones who always refused to publish it, and publish the other seventy-three, which were pure chemotherapy, in cancer.

And it created quite a stir. And when I went to the Soviet Union . . . and I'll tell you about that later . . . on the back of the door, I was always delighted to see, and I wish I had taken a picture of it, written in Russian, Schema Coopera, and here was the drug doses of the things. The Russians adopted it right off. Well, it . . . the Cancer Institute said they heard about this, decided that it was, you know, too unusual to accept at face value and sent a group of people interested in breast cancer to look at Cooper's records. And they came back and said, "Yes, this is authentic." And about the same time, CMF was being

studied in the Cancer Institute. A breast cancer task force was set up in the Cancer Institute, I think under Paul Carbone, and about the same time, phenylalanine mustard was recognized as a drug that you could take by mouth that was active, and they said to Bernard Fisher who, by that time, had become the chairman of the National Surgical Adjuvant Breast Program, "Which of these drugs do you want to study?"

And he said, "Well, if surgeons can give the pills easy, let me take the phenylalanine mustard." And they didn't have enough resources in the United States because, by then, the acute leukemia group B was not studying breast cancer, so they contracted with the National Cancer Institute of Italy and Bonnadonna and Verinaze did a study of adjuvant chemotherapy with CMF versus a placebo in women with breast cancer. And I wrote the editorial when that was published in the *New England Journal of Medicine* a few months after Fisher had published the phenylalanine mustard. His phenylalanine mustard paper . . . the first published paper . . . showed an activity in premenopausal women, but no activity in postmenopausal women.

Bonnadonna published his paper, and I was asked to write the editorial, which is one of the better things I've written, and it was . . . I was very enthusiastic, and said that now American physicians could have something to admire in Milan besides the Lascala. And Verinaze always thought that was very good. And, in the *New England Journal of Medicine*, there was a blizzard of hostile responses from radiotherapists and from

conservatives, and Barbara . . . I can't remember her last name . . . who wrote for *Science* . . . wrote a paper in *Science* about this overenthusiastic assessment. And, so, I got a chance to retort to both of those and, again, my retort in *Science* is one of the better things I have written.

One of my colleagues here was particularly interested in it, to the extent that she said, "You know, this was bad for premenopausal women . . . I would ruin their childbearing capacity." And I pointed out that 90 percent of breast cancer occurs after the age of fifty and the dead women tell no tales, nursery or otherwise. And, so, that became a factor. And then, I was disturbed, as chairman of the Cancer and Leukemia Group B, that the chemotherapy that had been given to Bonnadonna to study CMF wasn't really Cooper's original regimen. So, in 1975, we sat up a study known as 75-81, "8" stood for breast cancer and "1" was the first study in the year 1975 in breast cancer . . . comparing CMF with CMF-VP.

And CMF-VP was significantly superior in the group of women who had four nodes or more, and it has continued to be significantly superior now, twenty odd years later, when the last analysis was done. Based on that, we had women who relapsed from either CMF or CMF-VP, so we needed to study drugs that would be useful for the relapsed women, because they already had failed on CMF or CMF-VP. And we established a new regimen VATH, which stands for vinblastine adriamycin thiotepa and Halotestin, each having some

activity in breast cancer. It was active in about 50 percent of these women, so we set up another study in which CMF-VP was given for eight months, I think, followed by VATH or CMF-VP followed by CMF-VP.

And we tested this concept of changing the regimen. And, of course, the CMF-VP followed by VATH was significantly superior, and continues to be significantly superior, about fifteen years later. This gave rise to a fellow here with me at the time, Roy Jones, who recognized, as we did, that VATH had adriamycin in it and that was, by far, the best drug, so he started studying adriamycin alone in metastatic breast cancer, and came to the dose that we could really give, which was much higher than we were giving. Then, we then set up a study . . . CMF-VP followed by high-dose adriamycin. And that gave excellent results, better than any we had had.

And Norton, who is now the head of solid tumors at Memorial Sloan-Kettering, had come from the Cancer Institute and was with me for ten years. He went to Memorial and started, again, sequences, because we both believed, for reasons that he put in mathematical terms, and I derived from the leukemia, with a vincristine prednisone induction, and then some intensive treatment, that it was important not to have all the treatment at once, but to have it staged. This is in contract to what Frei believes, who thinks that maybe you need eight drugs at once or fifteen drugs at once. And Norton began with three drugs in sequence. That is an excellent regimen that is in the literature

now, and we subsequently have just reported in meetings, and it hasn't been published yet, because the *New England Journal of Medicine* won't accept it yet, a combination of adriamycin and cyclophosphamide followed by Taxol, which is an excellent treatment regimen, and shows substantial integrity of this concept that you have to have at least two regimens of differing drugs, so that the drugs that are resistant to the first regimen may be sensitive to the second regimen. And so there is a sequence of regimens of treatment in breast cancer that lead to progressively better survivals. I want to go back and talk about the Soviet Union because that is interesting . . . what did I do in the Soviet Union.

PD: Could you tell me how you came to be invited to go there and what . . .

JH: Yeah, I . . . Nixon and Brezhnev had met and had looked for things where there could be some more open cooperation between the United States and the Soviet Union. They agreed on environmental science and cancer research, which is noncontroversial. The Secretary of Health, Education and Welfare at the time was a man from the University of Southern California, whose name I have forgotten, and I won't remember him, but he appointed Jesse Steinfeld, who had been one of his faculty Surgeon General of the United States. He had said we'd be glad to send somebody to Russia and the Russians would send somebody to the United States, so that the onus fell on Zubrod as the clinical director of the Cancer Institute to find somebody to send.

He called me . . . "Haven't you got somebody to send?" And I didn't have anybody to send. And I'm sure he called lots of others of his friends to see whether we couldn't send somebody, and that was, maybe, four or five months after this agreement had taken place, and then a major political change at Roswell Park made me decide that I wasn't going to stay there. I wouldn't work for the new director, and accordingly, I went home one night and said to [my wife] Jimmie, "Let's us go." And she said, "Okay." And so we went. And she went as a representative of the National Institute of Mental Health without salary, but still official, and the Russians hadn't counted on that, and were not very happy about it.

And I went as an official representative of the National Cancer Institute. We went by way of Israel, where I gave the Dammashek lecture and went by way of Sweden, where I visited George Cline and went through . . . bought a Volkswagen and went through Helsinki. In . . . then, from Helsinki, we went from Sweden to Finland on a ship, then drove to the border town of Hamina, and it was snowy. And these . . . it was a brand new microbus, red microbus . . . everybody in Europe liked it. It was a brand new style. So, when the Finnish boys . . . some of whom spoke English . . . asked what we were doing in Hamina and I said we were going into Russia, they spat. They hated the Russians. We drove to Russia after having finally gotten visas, and I had started by telling you that in Israel a Russian emigrate, Bracha Remaud said she knew why we didn't have visas to go, because they were all sitting around the table.

No one would take responsibility for saying, "Yes, he should come." They would wait until it became urgent for al of them to agree that "We must let him in." So, there was no responsibility attached to it if I screwed up. We got to Sweden. I asked for . . . got to Finland . . . no visas . . . "Hey, we're supposed to go to the Soviet Union." So I went to the American Consul's office in Finland saying you know, what's up. And, well, it was the fiftieth anniversary of the Soviet Union and the fifty-fifth anniversary of the Russian revolution coming up on November 7. This was about November 1 or November 2. And so I said, you know, "We're coming in." They said, "Impossible. You've got to wait," you know. And I said, "Why?" He said, "Because we can't get hotel reservations for you en route to Moscow." And I said . . . and this was all by teletype to Moscow and back . . . and the fellow in Leningrad, the consul in Leningrad said, "Hotel reservations in Leningrad have to be cleared through Moscow."

Unbelievable. I said, "Well, we could stay in the consulate office." And he would teletype back, "Unfit for man or beast." [laughter] And I still have that teletype. Finally, however, we did get in and we drove through Leningrad to see eight- or ten-story pictures of Stalin and eight- or ten-story pictures of Brezhnev and fantastic decorations . . . red flags over everything. We went from Leningrad to Moscow and arrived at the American embassy. And the American embassy in Moscow said, "Well, everything will be closed down. You can't do anything." Then we stayed in a hotel where they had told us to stay . . . the Hotel Ukrainia, and we went on, November 7, I guess it was, to the American

embassy and watched the parade. There were gigantic missiles and so forth, standing out on a balcony overlooking this parade route, and an Army officer standing next to me said, "They're taking your picture now." And here, across the street, was a gigantic lens. And he said, "It's standard. They'll take your picture. They know you're here."

And so they took my picture. The following day, or the day after the celebration was over, a car came to pick me up to take me to the Institute Blachein . . . this man that I had met, but he didn't remember, in Brazil at that International Cancer Congress, was the director of the Cancer Institute. He spoke perfect English. But he conducted the entire meeting in Russian so that all of his department heads would hear, and all the department heads were assembled, and a translator, and he said to me, "You will think this is like your wild west of fifty years ago," and when I wrote that back to Zubrod, who then gave it to the State Department, nobody had ever said anything like that before. They had never admitted how far behind they were. And they were.

Blood transfusions were given in a funnel with a piece of gauze over the top. They used rubber tubing where we long since had changed to plastic tubing, and they had transfusion reactions. Fluids were given intravenously with an open funnel. I mean, very, very primitive facilities . . . very primitive scanners, x-ray machines, no CT scanners. And what I did was to meet with about a half a dozen young people . . . thirty . . . who, in the Russian system, had gone from about the third year of medical school into the Cancer

Institute . . . never had any general medicine and had done all their work there in the Cancer Institute. These half a dozen had all studied English, and English was big at the time. There were English tutors everywhere trying to bring people up to speed in English. And the best of them was a Jewish fellow who was, then, never given any status because he was Jewish, and the . . . what I did was to teach them how to write a protocol. And we would discuss gastric cancer, melanoma, lung cancer, breast cancer, and we would talk about how you have to get everybody at the same stage to put them in the protocol, so you don't have people with metastases and people with primary tumors . . . this kind of thing. In an extraordinarily organized society, they had never organized their medicine.

So, they would take notes and discuss, go home and write it in Russian, translate it into English and we'd meet again the next day or the day after and go over. And I would read what they had written in English and change it back and forth, until finally we had written a protocol for each one of these. Some of the drugs they didn't have, so America would have to provide the drugs, which they were perfectly glad to do. There was a patient with a synovial sarcoma, which is a disease that I had treated with adriamycin at Roswell Park. And I said, "Well, this patient ought to be treated with adriamycin. It's a wonderful drug for this disease." "Well, we don't have adriamycin, and our drug committee hasn't purchased any yet." So I said, "Well, I'll get you some." So, I knew the fellow who was the head of Pharmatalia. Achimoni is the man who discovered adriamycin . . . I can't quite recall this fellow's name . . . and he wasn't there.

So I said, "Well, let me speak to Bonnadonna," who I had known from international meetings and I said, "Johnny, I need some adriamycin. I'm here in Moscow and, you know, I've got . . . " Well, about ten days later, two cartons came that were half again bigger than that . . . gigantic cartons of adriamycin shipped in by air to Moscow. And I had to go with two or three of these young people to get me through the customs. The customs were very, very tight and very tough there at the time. We brought the adriamycin, treated this fellow . . . excellent response.

The next day, there were three or four people with synovial sarcoma, because they had sent out the message, "Send our synovial sarcomas to Moscow." A general's daughter, who was one of the fellows, and a woman that I came to be very friendly with, said, "I wish I had a friend in Milan." Subsequently, when we finished these half dozen protocols, and I wrote back critiques of what was going on to Zubrod . . . I have a couple of those . . . I wish I had kept them, and I should have written a book about them . . . and decided not to because I'll tell you later . . . but, in any event, then the Jewish fellow who was really the ringleader and the brightest . . . and they all knew he was the brightest . . . and now he is the oncologist of Moscow and a very good friend of mine . . .

PD Who is this?

JH: Misha Lichinitser . . . L-I-C-H-I-N-I-T-S-E-R . . . Misha said, "Now it's time for you to travel. What cities would you like to visit?" So, I didn't know many Russian cities, but he said, "Well, you should go to Achidemigorsk," which is the Russian city behind the Urals, where they did all the nuclear research. They wouldn't let me go there. But I went to Leningrad, Riga, Urivan, Tablessee, Alma Ata, which are places that some of the . . . even the director of the institute had never been to. And I had six children with me, so I would take different children to different places.

PD: Can you hold that thought while I change the tape?

JH: Sure, I can talk . . .

[End Tape 1, Side B]

[Begin Tape 2, Side A]

PD: Okay, this is tape two, side one, of an interview between Peggy Dillon and Dr. James Holland, on January 25, 2001, and you were talking about your travels while you were in Russia.

JH: We went to . . . I went to all of those cities that I mentioned, with different children in each one, and lectured. In Alma Ata, which is right out over India, and the farthest west I went . .. the farthest east I went, it . . . I lectured at eight o'clock in the morning three mornings in a row, in a large circular room and there must have been 400 people seated, and standing room only. And I was the first westerner they'd ever seen.

PD: Who were they, local people?

JH: Doctors. Oh, doctors. This was all medical lectures . . . doctors and nurses. I suppose there were nurses there. You can't tell in the Soviet Union because the predominant physician is a woman, a female. And a man who was a superb translator . . . one of the best I encountered in the Soviet Union, who had learned his English off the radio . . . and I lectured and there was tremendous interest. And, in Alma Ata, I was entertained by the director of the Cancer Institute, who was a radiation oncologist. And their predominant disease there was cancer of the esophagus, which is not a major disease in the United States. And this was their commonest cancer. They had loads of this cancer of the esophagus.

The question is why. Is it because they drink boiling tea? They drink it when it's boiling, and that's what he thought. Others thought it was vitamin deficiency or something specific in the soil or in the water . . . but clear evidence was that this was environmental. He was

a yellow-skinned Asian man . . . I should have practiced so I'd know these names. I can't tell you his name. He was married to a Caucasian Jewish woman from Moscow, whom he had met when he was there in medical school. And this was right after the Israeli six-day war. So, he spoke good English and was playful with me and said, "Well, you now, the United States will get tired and you'll stop supporting Israel and then we'll win." And I said, "No, no. The United States isn't going to get tired. The United States is going to continue to support Israel and Russia may get tired of supporting the Arabs. Then what will happen?" "Ah, then it will be a six-hour war."

So they were completely . . . I remarked that that was a beautiful cassock pheasant. I said, "What kind of a pheasant is that?" It was the biggest pheasant I ever . . . "Oh, that's a cassock pheasant, from Kasakhstan." When I left, he had his son pack that pheasant in a suitcase, and I have it in my home now . . . a beautiful pheasant. He gave me two kilograms of caviar . . . gigantic things. My son, one of my sons loved it . . . would slather it on bread like peanut butter. And there are two more things I want to say about him. He said to me, with great glee, because of this bavardi, "I'm the only man in the Soviet Union who can shoot ducks in the springtime." "How come you're the only man in the Soviet Union?" "Because I told the people in Moscow that if the Chinese set off any bombs, it will get into the shells of the ducks and if I shoot ducks in the spring, I can tell whether or not there's any strontium," because he was a radiation . . . and he said, "There's no strontium in the eggs, but I shoot ducks every spring." [laughter]

So, beating the system is part of the Soviet Union. The night . . . I was there on International Women's Day. International Women's Day is the equivalent of Mother's Day here, but it's a national holiday and it's much more significant. I took my oldest son, the one who is at the NIH, with me at the time . . . and this was not an appropriate place for him, so he went out with the son of Valmahanoff. Valmahanoff was his last name . . . I have forgotten his first name for the moment . . . and I went with this general's daughter who accompanied me everywhere on the trip to handle all of the details. I didn't find out until later, when we got to Urivan, that she had forgotten to sign me out of Moscow, and was panic stricken that I didn't know somebody was signing me out of Moscow and signing me into Urivan, and the director of the institute, who was an Armenian, said he could fix it up and don't worry. But my travels were closely monitored by all the people. And I once offered to take her daughter with me, and she had to get permission from the daughter's teacher, who would not give her permission to take the daughter on a trip to Urivan.

PD: Did you know that you were being so closely watched . . .

JH: No. I didn't know that. I didn't know. I didn't know that until this general's daughter told me that she had forgotten to sign me out of Moscow and she had the panics. I didn't realize that. When we got to Moscow, in the apartment, I knew we were being monitored. Because we did, after spending six weeks in the Hotel Ukrainia, I said to the

director of the Institute, "You didn't keep your promise. You said you had good housing for us, and we're in a hotel and we have to cook on a two-burner hot plate and I've got five young kids with me and that's just unacceptable." "Oh boy." Then the wheels really began to grind and they decided they'd give us two apartments in the new apartment house that they were building for the staff right out by the hospital, and join them together, which was paradise from the Russian's point of view.

My wife said, "No. We'd have to take the children out of school to do that because they'd be in a different school and they'd miss the culture of Moscow out here in the country." So I said, "No thanks." Well, that created a stir that everybody knew that I had turned down two apartments. So, they finally . . . that same week, they got a . . . this fellow had clout. He was a member of the Supreme Soviet and he knew every president. I was taken by the administrative man . . . here was an apartment where four families lived. Each had a single room with a common bathroom and a common kitchen. Their time had come to get a separate place so we could have this apartment. I said, "Okay. This is fine." My wife saw it, "This is fine." They said, "Well, it will take about two weeks because we have to redecorate it." I said, "I don't need to redecorate it. I like the wallpaper just fine." "Doctor, we have to rewire it."

So they put listening devices, which you could see, in the chandeliers and we knew that we were being listened . . . we, the very second day we got there . . . the first day we got

there, all the young doctors helped move us. They got a truck from someplace, using my Volkswagen microbus, they moved out trunks and suitcases and so forth from the hotel, and took us there. My two young daughters . . . at the time they were thirteen and eleven, made cookies. I bought some German beer because all they had . . . there were no imports. All they had was Russian beer. And I had a bottle of scotch. One of the fellows who was wizened and had no fat on him . . . because he had been a boy in Leningrad during the siege, and had been starved as a boy . . . I can't tell you his name right off either . . . I poured him a glass of scotch and he . . . I should have warned him, I guess. He just went [drinking sound] and then he said, "Very strong wine." [laughter]

The second day, a policeman appeared and wanted to welcome me to the neighborhood. He knew my name, knew the name of every one of the children already, and they paid very close attention to us. I traveled back and forth to the United States several times, looking at the job here at Mt. Sinai, looking at a job in other places. My wife stayed there with the kids. One night the fuses blew. Russian fuses are very different from American fuses. The lights were out. They didn't know what to do, so they knocked on the next door. It turned out it was a woman doctor and her husband who was an engineer, which is an even more auspicious profession. The engineer fixed the fuses for them. My daughters, again, baked some cookies, and the next day took the cookies to these people. They refused them. They were very, very wary about having any contact with Americans because it was very dangerous in those days to be considered a spy.

There was a woman in the building who was known to my daughters as "the old lady." The "old lady" had been born in the United States and brought back to Russia by her family when she was about eight or ten. So she was tremendously interested in these young American girls, and wanted every book they could give her and wasn't afraid of the Russians at all. The children would play chess on the stairway with other children in the building, and learned how to play chess fairly well, and the boys learned how to play street hockey on the ice outside. But there was no social contact with the Russians in the building. The ambassador had said, "We'll stay as far away from you as we can, because nobody else gets to live this way in a Russian thing." We didn't have diplomatic passports, and so they wouldn't take us in the diplomatic corpus where they isolate all the embassy people and all the others that are related to a foreign government. And this was still a very tight Russian authoritarian militaristic regime.

PD: So, it was so sensitive an issue that [inaudible] from the Americans because it aroused suspicion?

JH: Absolutely. Absolutely. I went and visited . . . I want to . . . I want to get back to Valmahanoff and Alma Ata . . . but I visited a man that I'll tell you about in a moment, in his laboratory . . . Svet Boldovski, in his office . . . a very important scientist in the Soviet Union. As I told him, we were really very, very starved for news. I couldn't understand that much Russian to get it off the news and there were no English T.V. stations. The

Herald Tribune got mailed to me by way of Vienna, because then it would come in the diplomatic pouch, and I would get it ten days late.

I didn't know what was happening in the world. He said, "You can read the *New York Times* or the *Herald Tribune* in the Lenin library." And I said, "Really?" And he said, "Sure. A foreigner like you could read the *New York Times*." I said, "Oh." It's isolated and limited to the foreigners and to the people. Nobody like you could get to see it." He quickly scribbled on his paper, "I can't tell we're not being listened to." And we had to . . . and it was a very militaristic thing.

PD: You wanted to get back to . . .

JH: . . . Valmahanoff. We were in International Women's Day. My son was parked with his son and they took me to a banquet in . . . with Irina . . . it's good you're getting this this year. Maybe next year I won't even remember her first name . . . and in a rehabilitation hospital . . . a rehabilitation place where people, after a hospital stay, could go for a month or two for rehab. Part of the "free" system, even though doctors were paid 300 dollars a month, this was considered free. I'd just point to them, "No. You're paying for it in advance." But, two things about it . . . it was an extraordinary banquet. The communist secretary for Kazakhstan was there. I was big-time stuff because this was the first opening to the west. He had all stainless steel teeth.

And I sat at the head of the table, next to Irina, who sat next to . . . and the toasts began. And they'd pour me cognac, they'd pour her wine. And I said to Irina, "I have had enough. I need wine." But they . . . if I pushed the glass away and tried to get some wine, they'd pour cognac. And then a typical Russian stunt, "Let's drink to the amir drushbah, peace and friendship," and then pour it over your head to show that you had drunk it all.

And I have seen deliberately at banquets for visiting American scientists, because there were many teams that came over, and we were always invited to go on dinners . . . where there might have been four or five of them . . . with these visiting teams of people from the Cancer Institute, coming to see Moscow. I was sort of the resident and they were the visitors. And they'd target one person, and toast his wife, and toast his children, toast his . . . until they made, more than once, I've seen them deliberately make a man drunk. They deliberately made me drunk the first day I got there . . . drinking to Nixon, drinking to Brezhnev, drinking to peace. I was drunk and vomited the very first day. I had a lunch with the director of the institute and the assistant director, who is now the director Trapeznikov. They are used to drinking heavy and I wasn't, in the middle of the day, and I was so dizzy I vomited on the way back.

PD: So it wasn't . . .

JH: It wasn't by chance. It was deliberate.

PD: Is that a rite of passage for a visitor, do you think?

JH: Well, it's a rite of passage for them to show that they are men and you are not, kind of thing. In any event, this banquet started with a whole lamb, and I was given the head of the lamb, roast lamb. I was given the head because, as the guest of honor, I was supposed to take pieces from the head and make clever sayings for someone . . . you know, "here is the cheek for the beauty in the director's wife," and so on . . . around the table, toasting each time . . . vegetables, all sorts of appetizers first. They're very . . . the Russians, in a banquet, are really great at providing all sorts of pickles and cold meats and salads that are on the table that you're supposed to eat ahead of time. Then came this lamb.

Then we all got up from the table and, with the director, who had one arm . . . he had lost an arm in the war . . . and with his one arm, he could shoot pool with fantastic ability. And I had grown up with a pool table and I couldn't shoot as well as he could with one hand. Try using a pool cue with one hand. He was excellent. After about thirty minutes of pool, we went back, and here the table had been reset. Now came a half a chicken, with a whole different set of vegetables and more toasts, another pool game and then a trout caught in the streams of the mountains there in Kazakhstan. So, really, three meals in succession, with loads of fruit.

So, at the end I was really just blind drunk . . . blind drunk. At the end, they had a huge box of fruit . . . oranges, grapes and other things that they insisted I take home to my son. I was sitting in the car with this on my lap and I said, you know, "I'm going to be sick." And that was . . . they stopped and I got out on the side of the road and vomited, and that was considered par for the course, for an American. And I went home. My son had to handle me for the rest of the night. I was . . . unbelievable quick association with alcohol and social activities. Because it was such a restricted society, a good Russian meeting . . . a very famous Russian scientist whom I had known of, Larianov, died.

So the fellows said, "We're going to go to Larianov's funeral." I said, "Oh. I'd be glad to go." I saw a Russian funeral . . . very interesting . . . opened casket carried through the street with a picture . . . in a labor hall. No church or anything. Afterwards, we all went to have a banquet in a Georgian restaurant, where they had swastika chicken cooked in smoke and beef . . . singing . . . a bottle of cognac, a bottle of vodka, a bottle of cognac, a bottle of vodka . . . between each two people and they were 500 cc bottles instead of 750 cc bottles, and you're supposed to drink a half a bottle, 250 cc of cognac or vodka. That's a standard celebratory kind of activity . . . very interesting.

PD: In one sitting?

JH: Yeah. Sure. In one sitting. And this is part of the way they relieve this tension of a military life. So, well, I took the caviar home from Alma Ata. I want to tell you something about two women . . . Natalia Periavotchekeva, which, periavotchek is a translator. Periavotchekeva is her name, married to a man named Periavotchek, who was the head of the medical service there, and was the person who made international tours . . . a handsome woman, pure Communist party member, very so . . . in her office every morning would be a meeting. But, the day in the Russian hospital started with a meeting at nine o'clock for the whole faculty, in which they would discuss every patient in the hospital who had had anything happen during the night . . . "So-and-so was confused last night, so-and-so bled last night." Unbelievable . . . 200 doctors.

And they'd list the operative schedule for the day . . . "So-and-so is going to have a gastrectomy, so-and-so is going to have" . . . an hour . . . total waste of time. At ten o'clock, we'd go to another meeting in her office, in which there would be a discussion of a medical problem, or, one day a week, there would be a discussion of a political problem, in which, I can remember, Katchalov . . . this is the fellow from Leningrad who had no fat, who had been through the siege of Leningrad . . . Katchalov had to present a paper to ten of the doctors, which he read in English, for my benefit, of why Moscow was the proper capital of the Soviet Union, and not Leningrad. Unbelievable. The work day was from nine to four. At about five minutes to four, every woman put on her hat and her coat and was out of there at four o'clock sharp to go market because it was so hard to find food.

PD: And stand in line for a couple of hours.

JH: And maybe not get it then. It was very, very difficult. All men carried a string shopping sack so that if they saw something that they could buy, they could snap it up and have something to carry it in. Nurses worked twenty-four hour shifts, and sleep . . . be on for twenty-four hours and then give a report, then a whole different crew of nurses would come in. The work day was very short and the accomplishments were very short. We made rounds . . . I made rounds and taught on rounds. I had a good relationship with the younger people . . . and a good relationship with Periavotchekeva.

When her father got sick in Leningrad, with prostatism and urinary tract infection, and looked as if he were going to die, I said, "Jesus, you know, gentamycin is a new drug in the United States. It's really very good." "We don't have gentamycin." I said, "Well, I probably could get some from the American embassy." "Would you get some from your American embassy?" I went to the doctor at the American embassy. He was a friend of mine. I said, "Have you got some gentamycin?" I can't remember whether he said, "I've got polymixin," which was another good drug at the time, or kanamycin . . . I can't remember. I don't think it was gentamycin. But in any event, I got an antibiotic that was useful for urinary tract infection. Her husband got on the train that night and went from Moscow to Leningrad and her father got cured. She never acknowledged that at all.

PD: Why?

JH: Never . . . well, just because that would out of the Communist . . . thing. When I was there, a man came in with a mass in his chest. He was being worked up for lung cancer. It seemed like that's what he had. He had been there a long time. Things moved very slow in the Soviet Union. After about two weeks, as I recall, they decided he didn't have lung cancer. He had an aneurysm of his aorta. They were going to have to transfer him to the vascular hospital. This was the cancer hospital and they couldn't operate on him here. He, out of gratitude for their care of him, had brought a cake. Russians are very big on cake . . . bakeries . . . which was a chocolate cake with a ring in the center . . . a hole in the center, and in it was a chocolate champagne bottle . . . a champagne bottle made out of chocolate, which the doctors ate and enjoyed. That was fine.

I came back to the United States and I was thinking of writing a book, but I was organizing a whole new service at Mt. Sinai, but the fellow from *Medical World News*, a reporter from *Medical World News* . . . he was a very fine fellow . . . cagey fellow . . . took me to dinner at a restaurant called La Guliu, which is here in New York, in a different place from where it was . . . a good French restaurant . . . try it sometime . . . and ordered a bottle of wine. And after I had a couple of glasses of wine, of course, I talked more easily, and he recorded my immediate things . . . and that write up . . . I've got that at home, which is sort of interesting, because they took pictures of us in the family and we

written up in the Soviet magazine the equivalent of *Life*. And this was big-time stuff back . . . thirty odd years ago. So I said, well, you know, what an experience. Here was a guy in a hospital for two weeks, and then they found out he didn't even have cancer, and then they had to ship him to another hospital. That's not what would happen at Mt. Sinai. You know, at Mt. Sinai he would be shifted to a different surgeon and they'd operate on him on the third day, or something like that. Well, Periavotchekeva got a copy of this and she was mighty offended that I had criticized their medical expertise. I remember that very distinctly. One of the finest men I met there was a fellow name Lariae, whose grandfather had been one of the jewelers with the fellow who made the eggs for the Emperor . . .

PD: Faberge?

JH: . . . Faberge. He had been a Swiss who had came in with Faberge and stayed. And, of course, he cursed his grandfather that he was a Russian living there rather than a Swiss living in the outside world. And he knew what the outside world was like because he was a prominent hematologist and had been able to travel to international meetings on occasion and was a very cultured fellow . . . a wonderful guy. I want to tell you about Svet Boldovski, who was the best scientist I met in the Soviet Union, who was the man who said, "I can't tell if we're being listened to." Svet Boldovski was a microbiologist who had worked with viruses and mammalian cells, was Jewish, and therefore was always on a precarious level because Jews had a very tough time in the Soviet Union. Svet Boldovski,

while I was there, asked me for a chapter out of my, the first edition of my book, *Cancer Medicine*, which I edited with Frei. Svet Boldovski is a worthwhile story.

PD: Right. You were saying he was the most impressive . . .

JH: He was the most impressive scientist I saw there. And he asked me for the chapter on chronic leukemia in my book, which I gave him, and, not realizing until later that some of his questions were perceptive . . . in fact, it was he. He had gone, in the typical Soviet fashion, to get an annual check up and they found out he had chronic myelocytic leukemia. The treatment with myelocytic leukemia, at that time, was busulfan, the compound we had studied as GT-41, and that had no curative potential at all. But Clarkson at Memorial Sloan-Kettering . . . a good friend of mine . . . had shown that if you use two drugs in combination, antimetabolites, that, in fact, he might get down to the point where chromosomes in the marrow look normal . . . reducing the abnormal chromosomes. And this was fairly dangerous.

You had to have good protection from getting infected if you're going to do . . . so, Svet Boldovski, as a microbiologist, converted his lab into a hospital room. He put ultraviolet lights in it and stayed there. His wife was also a laboratory worker . . . ate there, and had Lechinitzer treat him according to this program that had been adapted from Clarkson, that I authenticated. His marrow did go down. The abnormal chromosomes went down, but

they didn't disappear, and it was impractical. Finally, he came out of the ultraviolet room. And, with Lechinitzer, he contrived a scheme. Lechinitzer had a woman with breast cancer, so he said to her son, who was the secretary of the Academy of Mathematics," how would you like to have a world-famous doctor come and give a consultation on your mother?" "Oh, very good, because she is dying of breast cancer." "Then why don't you ask the president of the Academy of the Sciences to ask him to come over and see the president of the Academy of Mathematical Sciences, who had cancer of his esophagus. "That's a great idea."

So, I got a letter of invitation from the president of the Academy of Sciences, which is a very powerful position in the Soviet Union, would I come and see Professor So-and-so. And so I said, "Fine." And my wife didn't want to go. It was Christmas season. So I decided I'd take my number two daughter . . . or number three daughter with me. She was about fifteen or eighteen at the time. Two men from the Soviet embassy came and said, "Here are your tickets." And I said, "These are one-way tickets to Moscow." And they said, "Well, you'll get your return ticket when you go to Moscow." I said, "No. I have been to Moscow and I'm not going to do that, and that's impossible." "Well, you know the Aeroflot is closed." I said, "Well, that's fine. I'll just send a telegram to Professor So-and-so, the President of the Academy of Sciences, and tell him why I'm not coming." "Oh my God." About an hour later they had contacted the ambassador in Washington and gotten authorization to buy two return trip tickets on FinnAir, because they couldn't get to

Aeroflot. It was closed, and they needed to get permission from the ambassador to spend money for FinnAir. So I went.

And the Secretary of Mathematics took us out to dinner the night we arrived . . . caviar . . . everything was spread fantastic. The next day, they took me to the Kremlin Hospital. I had never seen the Kremlin Hospital when I was there. This was for the members of the elite. It was an elegant hospital, in a pine forest nowhere near the Kremlin. It meant it was for Kremlin people to be in. Here was Blachein, the director of the Institute, Periavotchekeva, three or four other people, head and neck surgeons who were there and a radiotherapist named Rosenberg. I said to myself, "Rosenberg in the Kremlin hospital . . ." perfect English. He had an excellent British x-ray machine. This man was very seriously ill. So, after hearing the presentation in this concilium, it was time to go see the patient.

We started to walk down the hall and Rosenberg sidled up to me and said, "Don't forget to say the radiotherapy was good." I made the consultation, said he ought to be treated with chemotherapy, with methotrexate . . . a drug that was originally used in children . . . and Lechinitzer could do that. And Lechinitzer could even fly to his home community, and he could go home . . . he didn't have to be in the hospital. Lechinitzer could do it flying back and forth. So, the ruse to get me there had worked and Svet Boldovski had set up that he had applied to the Ministry of Health to go to the United States so I could

treat him for his chronic leukemia. So they had a concilium . . . two assistant commissioners of health for the entire Soviet Union came to the Cancer Institute and then I presented what I was going to do. They listened very attentively. Five minutes later, "nyet."

So we went to Svet Boldovski's house just before leaving. This was, I guess, New Year's Day or something. His wife had gotten strawberries from someplace. It was fantastic to be able to do that in Moscow. And, he then said, you know, "In the Soviet Union, on New Year's Day, every man likes to be wished long life and good health. When you go home, wish long life and good health to the president of the Academy of Sciences, and tell him I helped your friend, now you help mine." So, I came home, and I didn't think that was official enough to charge it to Mt. Sinai, and I wrote about a 250-word telegram. It cost me a bundle of dough, and sent him a long flowery telegram that "I really took care of your friend and he's going to be fine and he'll get a good remission out of this. Now, here's this other problem I'm facing."

Three days later, Svet Boldovski got a call from the visa office . . . "Who do you know? How do you do it?" And out he came. You're allowed to come out with your wife, but I had written in the letter that his daughter had to come as a platelet donor. He came out, had about four and half months, because he had a six-month visa. The director of the institute, Blachein, said, "Your visa's up. Come home." Svet Boldovski said, "I know

exactly how it's going to work." He said, "If I were to defect, and overstay my leave, he would have a black eye." So, at about five months and a half, his visa got extended. And he was able to pull that racket until he eventually died, knowing how to work the system, because the system was so important in the Soviet Union that Blachein couldn't afford to be seen as a fool who would let a man out. Isn't that something? [laughter]

And Svet Boldovski here did some very good work . . . some very good work, and is the man who discovered granulocyte colony stimulating factor . . . GCSF . . . which is, when I tried to get one chemist here to purify it, he said he couldn't divert his work to do that. So, Svet Boldovski gave it to Malcolm Moore at Memorial Sloan-Kettering Cancer Center and Malcolm Moore purified it enough, using my successor here, Janice Gabrilov as one of his fellows . . . that they then gave the sequence to AmGen and AmGen now markets it as Neupogen, and Malcolm Moore and Janice Gabrilov are now millionaires and Memorial Sloan-Kettering got fifty million dollars and an indefinite supply of GCSF. But it was Svet Boldosvki and me who discovered it. And the people at AmGen knew that. And it has always bothered me that Malcolm Moore never acknowledged that in his first paper.

But subsequently, poetic justice . . . the woman who worked, not as a technician, but as a junior colleague with Svet Boldovski, is still here . . . her name is Svetlana Zintzer and she was the primary person doing this work, showing that different cell lines produced

something that would make mouse marrow grow. And when she got her pin for twenty years of service, Dr. Gabrilov . . . who had to give her the pin in a big ceremony . . . had to say to her that she had worked on the material that she, Gabrilov, had purified. [laughter] I've seen a lot of water over the dam.

PD: You have. That was quite an experience. It was eight months . . . I mean, your . . .

JH: Eight months. We went in November and left at the end of June.

PD: So, even though it was a political overture that got you there, it sounds as if you made some scientific inroads . . .

JH: Oh, I helped them enormously. I was famous throughout the Soviet Union. Generals would come to me from out in Siberia because they had, themselves, a tumor, or their wife had something . . . I mean, the elite of Moscow got to see me, as well as all of these young doctors. Near the end . . . the newspaper in the Soviet Union that corresponds with the *New York Times* is called the *Literatournia Gazetta*. And I was to be interviewed by a reporter from the *Literatournia Gazetta* named Diatkin . . . a Russian man came to interview me with a Russian woman translator.

By that time, I could speak some Russian. We took tutoring lessons. And, so he said, "Well, what did you find here?" So I said, "Well, you're perilously far behind. This is, you know, terrible. You're so damned isolated and nobody goes to international meetings and nobody knows what's up and nobody is current. There's one copy of *Cancer Research* that comes to this institution and it gets passed around. There is one copy of *Nature* that comes. And these . . . you don't have your own equivalent journals. It's very, very bad. It's terrible." So, a week went by and he came back and here was this article in Russia . . . if you get interviewed, you have to read it and then you have to go and sign off with the editor of the paper that, in fact, that's exactly what you said, and then you get paid, because they pay you for an interview.

PD: Okay.

JH: So, he came and brought this and I read it. And I said, "Geez, here are all my comments," you know . . . "terribly far behind . . . " So, in the car, riding to the editor's signing, I said to him, "I'm surprised you put all this in." I could say that in Russian, and he spoke some English, and he said, "Sheauskins Scheidman." His name was Scheidman. He was a Jew who had an adopted Russian name as a pen name. And so this was his way of getting at the system.

PD: Everywhere you went, people were getting at the system.

JH: Yeah.

PD: It defined how they operated.

JH: Absolutely.

PD: Interesting. So you did . . . I mean, you had a considerable scientific impact in the eight months you were there.

JH: Right. And continued to. I get letters from Lechinitzer by fax once a month . . . with consultations about somebody who is important enough, or a problem that he does . . . and once a year I get somebody who flies over from Russia. And they flown over by the government because they are some big individual with one or another problems. I want to tell you about one other person too. I told you there were two women. The other woman is a woman whose name is Maria Nikalavna Preabrazhenskia . . .

PD: We can get the spelling later. [laughter]

JH: Okay. And she is a chemist . . . was the head of the chemistry department. And when I went there and said, "You know, I'm not going to send my children" . . . the Russian officialdom said you send your two older children to Vienna to high school, and you send

your three younger children to the embassy school. And I said, "No. I came to Moscow." Well, she had working for her a chemist who had gone to the English- language school, which was a school where they taught English as their prime factor, and I went there and spoke to the headmistress and she said, "Yes. She would be very glad to accept my children . . . five children in one thing . . . you need a sprauvka." A sprauvka is a permission slip signed from officialdom. I said, "Yes. I'll bring the sprauvka, but my children are sitting in a hotel room. Please, can they come . . " "Yes, come tomorrow." You couldn't do that in an American school. So, every so often I would see her and she'd say, "You owe me a sprauvka." And I would say, "Yes. I owe you a sprauvka. I'll pay you a sprauvka . . . I'll get the sprauvka." I never got a sprauvka. She knew I wasn't going to get a sprauvka. She accepted five children in her school and they were the hit of the school because they spoke native English, and I paid their teachers for after-hours tutoring in Russian.

PD: Which was gold to them.

JH: Absolutely, that was real money for them.

PD: Hold on one second while I turn over the tape.

[End Tape 2, Side A]

[Begin Tape 2, Side B]

PD: So, your children attended the school, and you paid the teachers . . .

JH: Yeah . . . after school to tutor them some. But the school . . . this was an English language school, and all in the same building from grade one through grade ten. There are only ten years of school in the Soviet Union. The school assigned tenth grade girls to sit with the two youngest boys, who were in first grade and third grade, and they put the third-grader back in first grade, which was terribly damaging to him psychologically because he couldn't speak any Russian, and he picked it up very fast. They put these two tenth-grade girls next to them, sitting on the bench, to translate for them and to help them with Russian. And they all learned, as kids can do, very quickly. But my daughter, who is now forty-one, was thirteen at the time, and she learned it like that . . . and looks Russian and speaks perfect Russian without an accent and was recruited several times by different agencies, including the CIA, "would she be a spy?", which she would not do.

PD: Hmm.

JH: But she subsequently majored in Russian, Slavic languages at Harvard . . . she's a very bright girl . . . at Harvard, and then took a master's degree in Russian activities of some sort, at the Harriman Center at Columbia, and then took a law degree, and then went and

lived in Russia for a couple of years as the . . . after she had been in a New York law firm . . . as the head of the Russian office, and ran a group of Russian lawyers. So, it had a major impact on her life. Preabrazhenskia, on New Year's Day, which was a big holiday, managed to get a turkey, and apricots and other things, and invited my family to come.

And that was six kids and my wife and me, so she had to borrow silverware and plates and other things . . . very, very impressive friendship in a westernized woman who understood the west, whose husband . . . fine man, whose name was . . . I can't recall . . . but he was Jewish . . . . so she kept her name and had her children's name, Preabrazhenskia, so that they could go to college. Because, at the time, Jews couldn't get into the good universities. She made this fabulous meal for us, and was always very friendly, and has maintained the friendship over the years. Both of her children now live in the United States, but she feels an obligation to her chemists, because life has been so hard in the Soviet, that she stays back and works as a chemist in Moscow and raises money from different drug companies for the synthetic work that they're doing because she is very good at the chemistry she does and gets, maybe, ten thousand or twenty thousand dollar grants, which goes a long way in the Soviet Union.

And she refuses to leave because of the obligation she owes to her fellow workers. Yet, she is an anti-Communist as they come, and she is a wonderful woman. And whenever she comes, she visits us. And we . . . I love her . . . I say, "Maria" . . . I always used to

call her Maria Nicholia [inaudible] . . . that's the formal Russian, to speak with the patron that Maria Nicholia [inaudible] . . . and she says, "Just call me Marie." And I treat her like my younger sister. She is a lovely, lovely woman.

PD: Well, we could talk a long time . . .

JH: And let me just tell you one more thing . . .

PD: Okay. And then I'll ask my last question.

JH: Okay. And she arranged for me to give a lecture in . . . she and Lechinitzer . . . to give a lecture to the Russian Academy of Sciences. And I have my picture taken standing underneath Mendeleev. And in my view, Mendeleev was one of the real geniuses of this world because he is the man who figured out the relationship of all of the elements and made the periodic table in chemistry that shows which things are related to one another. And she got me to write an article on chemotherapy from Mendeleev's *Journal of Chemistry*, which she then translated into Russian for me.

PD: Over your entire career, which professional accomplishment has brought you the greatest satisfaction or made the greatest impact? I mean, you have done so many things . . .

JH: Impact on me or impact on the world?

PD: On the cancer . . . on the world?

JH: Well, I think that graph . . . leading a group of individuals to organize the chemotherapy of childhood leukemia to make it into a curable disease, is probably what I have done the most for the world about . . . and was criticized along the way for being too enthusiastic. And once, when Zubrod testified in front of Congress and said that leukemia was a curable disease, there was an outcry from some of the conservatives who said, "That's poppycock."

And Zubrod asked me . . . and they wrote it in a pediatric journal . . . and Zubrod asked me whether I would write a refutation for that, which I did, which pointed out the improving survival and other things. And I think that, in reality, that was the best of it's time, and no other group could do it. Karnofsky, a man of great stature, said, "Well, if somebody could show . . . our survivals stay at thirteen months, and if somebody could show me how to do it better, I sure would like . . . " and I . . . that was at a meeting and I did . . . got up and showed the results, and they adopted those.

So, I think that that is probably up to now, however, on the fifteenth of February of this year, in cancer research, Dr. Pogo, who is one of the people I called, who is a virologist

that works with me, and who, when she came to work with me said, "I don't want to work on mice anymore. If I'm going to work with a clinician, I'd like to work on something human." And I said to her, it has always occurred to me that if human breast cancer were due to a virus, it would be a cousin of the virus that causes breast cancer in mice. So we set out eight years ago to look for the virus that causes human breast cancer, and 38 percent of American women's breast cancer has in it a sequence that is extraordinarily similar to the sequence of that same part of the virus in mouse disease.

And now we have, no the fifteenth of February, in *Cancer Research*, the entire structure of the provirus. And we don't have it in this paper, but we've got pictures of the virus and I think we will establish, with a level of certainty that people will accept, what has been postulated for many years . . . that human cancer may be due to a virus . . . human breast cancer may be due to a virus. Thirty-eight percent in the United States . . . 60 percent in Africa . . . different parts of different . . . in the world, different percentages. And my guess is, even though I am not the virologst who did it, my input is consequential and I . . . Dr. Pogo and I are a good team. And it may turn out that the most important thing I do will be to demonstrate that because I have always said acute leukemia in children is a viral disease. And we have demonstrated a technique, and unfortunately, Dr. Pogo says I can't go further . . . I've got to retire . . . and she's not as old as I am, but she's a senior lady . . . and I can't do it at my age. So somebody else, I am hoping, will take it up and do it, because, for sure, that's a viral disease.

PD: It could be the next breakthrough.

JH: Sure.

PD: Any other thoughts that I haven't brought up that you would like to add?

JH: Well, I have had a wonderful life with my wife, who, I may have mentioned . . . I don't remember, in the first interview, who, because she had studied people in Boston as a . . . when they . . . during the polio epidemic in 1954, she studied the psychological problems and the psychoses in people who are in iron lungs. And then, when I got to Roswell Park, Tom Frei had made some what were called in those days "life islands," which are an entire plastic enclosure to put people in to keep them from getting infected when they had leukemia and when we knocked their bone marrow out. And subsequently, I made some . . . designed and made some, with support from Gordon Zubrod, some laminar flow rooms where the air came down the ceiling and where people walk into the room in a suit, which was on a tunnel, so it was pseudopodia, so they never came in contact with the outside world. My wife became interested in these people, and subsequently shifted her entire focus, and began to do the psychological problems of cancer patients, and then became Chief of Psychiatry at Memorial-Sloan Cancer Center and has just written a book.

PD: I have actually seen it in the library.

JH: Have you? And has written . . . she has written two books for the profession . . . one called *Handbook of Psycho-oncology*, about ten years ago, and another one just about two years ago, called *Psycho-oncology*, which is here someplace. There it is. That's her most recent book. And, so, we have had wonderful opportunity to share an understanding of work. She works just as hard as I do. And so, as the kids grew up, we've got plenty to keep us occupied.

PD: Has her work influenced your manner in talking with patients? I mean, has her . . . have you learned from each other and applied what you've learned in your professional life?

JH: Yes and no. I think I was always empathic to patients. I have always had a good relationship with patients. I do . . . I take care of patients the way I think I saw doctors take care of them when I was a boy, and not specifically because of my wife's influence. But it has been a good ride, so we are . . .

PD: Yes. It sounds like a good collaboration.

JH: It is. It is.

PD: Well, thank you very much for your time.

JH: You are welcome indeed. And, you know, it would be hard to get somebody to be disinterested in himself, so this is sort of an ego trip.

PD: Well, thank you very much.

[End of Interview]