KURT HIRSCHHORN INTERVIEW

August 7, 2002

1. The Early Years in Vienna

AM: Good afternoon. It's August 7th, 2002, and my name is Andrea Maestrejuan and I'm with Dr. Kurt Hirschhorn in his office at Mount Sinai Medical School to do his oral history interview for the Oral History Project in Medical Genetics. We'll start where we like to start and I'll ask you when and where you were born.

KH: I was born in 1926, May 18th, in Vienna, Austria.

AM: I know a little bit from your C.V. that you were educated, at least in the early elementary years, in Austria.

KH: The elementary years which, in school in Vienna in those days, if you were heading at all towards an academic career, you had to decide by the time you were ten, lasted four years. Then high school began at age ten and was an eight-year school. I left Austria when I was twelve, so I went through elementary school and started in what's called a Gymnasium for the first year and a half, at which point Hitler came in, my father was arrested and thrown in jail, and I was transferred to a Jewish Gymnasium, where kids were sort of prisoners of the place. We were, in a sense, protected but not really. Then we left a couple of months later.

AM: To go back a little bit, when you made the decision -- and I'm sure your parents may have had something to do with it -- when did you make this decision to go to the Gymnasium and -- or even have the idea of an academic career?

KH: It was expected. (laughs)

AM: What did your parents -- what occupation --

KH: My father [Emanuel Hirschhorn] was a lawyer, who was actually one of the first people, I guess, around anywhere who had a business degree and a law degree, sort of like an M.B.A. and a Doctor of Law. His brother [Elias Hirschhorn] was a physician who also was a dentist, because dentists in those days were physicians, and then specialized in dentistry. And he was a very important influence on me in terms of being interested in science. Quite a guy.

His other brother [Julius Hirschhorn] was a mathematician, and as his hobby he translated all of Shakespeare into German, so he came and we played mathematical games when I was a kid. So there were a lot of people around. Another sister [Tinka Leah] of my father's was a physician in Poland, what was then Austria, then became Poland, then became Russia, is now the Ukraine. (chuckles) It was that funny part of Eastern Europe. She was a physician there, and she and I had a very good relationship. We'd visit periodically.

So there were doctors, thinkers, and so on, around. My mother's sister [Munia

Ginsberg] was married to a physician, also in Poland, whom I met many times. These were all nice people whom I interacted with.

AM: How did your uncle, the dentist -- you said he was very influential in your life. In what ways can a dentist influence --

KH: Well, the thing is that he was a dentist by practice, but he also taught at the medical school. He taught histology at the medical school, and he used to show me all kinds of things under the microscope. Got me excited about stuff.

AM: And your mother's [Helen Majberger Hirschhorn] family?

KH: My mother's family, her father [Mendel Majberger]was the mayor of a small town in this area of shifting countries. He was quite a guy. We used to go out there. They had this huge farm that I loved. He had a pony out there, climbed -- picking cherries from the trees. They were nice days. Of course, all of those people are dead. Many of them died during World War II and were killed -- interesting story. My grandfather -- it doesn't truly relate to this, but it's part of my history -- he was in this little town where there were maybe a hundred, hundred and fifty Jews in that town. And when the Germans came in, because of his position as the mayor, he was put at the head of the Jewish Committee, the only purpose of which was to provide them with names to be shipped off to the extermination camps. When that happened -- and we have this on very good authority from people who were there -- he put himself, his family, his son, his daughter, everybody on the top of the list, and they went. So he was a family hero.

AM: Did your father's family come from Vienna, or also from this --

KH: No. Also from this area some fifty miles away. My father, actually, was hired by my mother's father to tutor my mother because they didn't think the schools were adequate there when she was a young girl. So he came, he was about six years older than her and he was a student at the time, so he tutored her. Then he went off to Vienna, went to law school and business school. When he finished, he went back and collected her and married her. (chuckles)

AM: And the rest is history, as they say.

KH: Yes. And I'm the only child.

AM: And [were] there any expectations that you needed to go into law or business?

KH: No. The expectation was to go to one or another form of Gymnasium. There are two kinds of gymnasium. There was the really academic Gymnasium called Realgymnasium. Then there was a humanistic Gymnasium where you went if you wanted to do law or social sciences, or whatever. The only question was, do I go where they're going to teach you Latin for eight years and a lot of science and math, or do you go where they're going to teach you Greek and a lot of philosophy, and so on? My choice -- and this was, I think, in great part influenced by my uncle, above that of my father, who really didn't push one way or the other. Because I think if it were up to him, I probably would have gone the other way, but I opted for the scientific direction.

AM: Because this is so different from the American system of education, where at ten you don't even think about -- maybe you want to grow up to be a fireman because they're our public heroes. At ten years old, what were you envisioning yourself becoming?

KH: Unclear, because the options were quite big coming out of one of those Gymnasiums. You could go into science, you could go into medicine, you could go -- and you could even revert to humanistic stuff. So it gave you the biggest options, as opposed to the humanistic one where science was out of the question. So I really -- I guess I must have thought about medicine, but it wasn't a major part of my decision.

AM: Just because this has come up in many interviews that I've done, in comparison to other kids around you, how well did you do in math?

KH: I did very well, and the guy who really turned me on to math was my other uncle, the mathematician, who I used to play math games with. So, yeah, I did nicely in math. And I was also doing quite well in music, which I sustained even to this day. And the combination of medicine, math, and music is a very common combination, especially in Europeans.

AM: So these games and things you did with your uncle, these were kind of rather than going out and playing soccer with other kids?

KH: Yeah. I would play soccer, but that was part of school activity. There wasn't this business of go out with your friends and don't do anything except do your sports or play games. It wasn't done that much. We used to visit each other. I had a very, very close friend who was actually -- this is an interesting history -- named Fritz Starer, who is in England and is a radiologist. The two of us went through school as far as it went, those first six years, together and were the best of friends. We lived near each other, always in each other's house. He was very similar in his ambitions, although not in family, not in family. His father had a stocking factory, which was a fascinating place where they were, you know, spinning the silk.

AM: Before your father's arrest, how much was your family's Jewishness part of your identity?

KH: Traditionalistic, not really seriously religious. We used to go Saturday morning to the synagogue, high holidays. Eventually I had a bar mitzvah when we were in England, but we'll get to that part later. So it was identity rather than orthodoxy.

AM: How did you experience discrimination? I mean, clearly, in 1938 the atmosphere had changed quite a bit. But do you have any recollections before --

KH: Well, anti-Semitism was almost born in Vienna and existed all the time. But with the exception of some special times in history, which '38 represents in its most violent form, it was sort of part of the culture rather than a malignant thing. Although, between you and me, the worst of all were the Austrians. They were worse than the Germans, they were opportunistic people who wanted to make their lives easier. So when the Nazis came in, they were the best Nazis, and after the war, when I was stationed there for a while, the communists came in, and they were the best communists. Whatever makes

life easy. (chuckles) Totally amoral as a people.

There were certainly individuals there who were very important in bringing this into the open. One of them, if you've ever heard of or read this man's work, named Robert Musil, wrote a thing called The Man Without Quality. It's a big three-volume -- really exposes the Austrians for what they are. There was a man named Karl Kraus, who from the earlier part of the twentieth century wrote a weekly newspaper magazine called Die Fackel, which is The Torch, who constantly was telling what bad people they were. But this was all taken as part of the culture and fun. Nothing was taken very seriously except by these few people. It's not a very serious place.

AM: How long was your father in jail for? What was the excuse that they gave for arresting him?

KH: Well, this happened a week after Hitler moved into Austria. The story -- just to make it a quick one because it's a little complicated. He and another guy owned a lumber import-export business, and he handled the business end and also was the lawyer for the whole lumber industry. That's how he used his education. He was a full partner in this lumber business. One of the things that happened very quickly, within the first week, was that significant Jewish businesses were taken over. The first thing they did was assign a Kommissar for that business, who, by the way, later when I was stationed in Vienna, I found and had put away for a while. (chuckles) This guy was really a creep, really didn't want my father and his partner looking over his shoulder, because the first thing he did was just rob the place. So he complained. The excuse for my father that was given was he was always very active in the Social Democratic Party.

A little step back -- this was in March of 1938. In January of 1938, I had an appendectomy. I had appendicitis. And the thing that middle-class families did in those days is, you spent your week in the hospital, then you went for a couple weeks up into the mountains to recuperate. So my mother and I went and my father would come up the couple of weekends that we were up there. A very close friend of his was the guy who was, at the time, the mayor of Vienna, a man named Seitz, who was also the head of the Social Democratic Party. He came up that same weekend to this place called Semmering, which is south of Vienna, a resort. And he joined us for lunch, because they were good buddies. He said to my father -- I can remember the conversation as we are sitting here. I was eleven and half years old, almost twelve. He said, "If I were you, I would pick up and leave." This was now February. This was a few weeks before the Germans walked through Vienna. And my father turned around to him and said, "Are you crazy? I have a business here, I have a home." So he said, "At least get together whatever money you can and send it out of the country." My father looks at him and says, "That's illegal." Three weeks later he was sitting in prison.

Then -- and this is perhaps an important part of our family unit -- my mother, who was a classic Viennese coffee house lady -- she met with her friends in the afternoon at Demels or some other place and had their cake and coffee and chatted. Never lifted a finger in her life to do work. And my father wouldn't dream of letting her. Not a stupid woman, well read. When my father was arrested, she went to work to see what she could do to save the family.

The first thing she did was -- how she found all these things out, I don't even know -- she bought steamship tickets from Greece to Shanghai. It was one of the routes by

which people could get out. With those tickets in hand, she stood in line for days on end at the Greek Consulate and eventually got Greek visas. With the Greek visas in hand, she stood for days on line in front of the Swiss Consulate, and couldn't get anywhere until one day -- and she was a rather good-looking woman, I'll show you a picture of her -- she's standing out there, and a well-dressed gentleman comes walking by. She's looking distraught. And he says, "Can I help you with something?" And she says, "I've been trying to see the consul for days now and I can't seem to get in." He was the consul. So she got in and he gave her a two-week transit visa to Switzerland. By this time, we're around the end of April. [She] bought plane tickets to Zurich. My father's sitting in jail all this time. Plane tickets to Zurich. Mind you, who flew in those days?

Then came the business of how do you get my father out of jail? Well, by that time, she had figured out that one of the guys who my father had enormously helped in the lumber industry was, in fact, a Gestapo agent. So she went and she stood in line at Gestapo headquarters until finally she got in to see him. And he said, "Okay. I'm going to let him out and his partner out. All four of you with your kids have to be out of this country in two weeks after he comes out; otherwise, I'm in deep trouble. So a few days later, he comes home, my dad.

We're sitting there with a Swiss visa. We have no intention of going to Greece or Shanghai. Because by then, we had also applied for an affidavit for the United States. He had a cousin, she had an uncle who were here, had been here forever, and they arranged an affidavit. I could have left immediately because I was on the Austrian quota. I was born in Vienna. They were on the Polish quota. Enormous waiting list to wait until a visa would come. So we had to get out of Austria but couldn't go to America.

A week after he gets out, on a Sunday -- I remember this very well -- he picks up the phone and calls his partner, which is the same thing that happened the day he was arrested. The Gestapo answered, as it had that time, and they were back re-arresting him. My father hung up the phone. He said to my mother, "Each of us will take one suitcase. Take what you may absolutely need, and we're going to take a train this afternoon to Zurich."

So that's what we did. We got on the train and got to the border. And we were in no-man's land. We had both the German and the Swiss people on the train at that particular time. At that moment, a telegram came to the border to get my father off the train. Now, by this time, the Swiss were there, too. Not that I have great love for the Swiss -- we'll get to them in a minute. But they were there, too, and they're being very correct, as it were, couldn't take him off without a reason. And what was the only reason they could potentially come up with? The rules said that each individual could only take ten marks out and nothing else of value. So they stripped us all, went through our clothes, looked for seams, pulled the heels off shoes to look for jewels or whatever we might have been taking out. My father, being a very careful guy, as you could imagine from the conversation with the mayor, we had ten marks each.

Then they started going through all the suitcases, and they got to my suitcase. Here I was, a twelve-year-old kid, right, what had I thrown in my suitcase? My stamp collection. Some clothes and my stamps. So the German guy opens it up, and he says, "Aha! A valuable stamp collection." The Swiss customs guy says, "Let me look at it." He looks at it and says, "It's a valueless child's collection." And that's how we got out.

It's an interesting part of my life that really, in many ways, shaped a lot of sort of what went on personally with my life, that whole period of three months or so.

AM: You mentioned that you were good friends with a boy named Starer, which sounded very Austrian. When your father was arrested, how did your identity then --

KH: Well, he was Jewish. He was Jewish, yeah. In fact, his first cousin, whom I also became quite friendly with, just recently died. He was a professor of composition at [The]Juilliard [School]. He was a famous composer.

AM: Your friend or his cousin?

KH: His cousin. No. My friend became a doctor eventually in England. He was sent out. You see, he did what I didn't do, or his parents did what my parents didn't do. They put him on a transport, on a Kindertransport, and he went to England. He waited there for them. They eventually got out not too long after and joined him in England. Somehow it was arranged that they got English visas. I don't know the details. But they went there. Then during our one-year stay in England, which we can get to, we again met up and saw him.

AM: Because of your father's arrest, were you still going to school after he was arrested?

KH: Yeah, to this Jewish Gymnasium, where half the days we'd come out and get beaten up and get threatened with knives, and all sorts of things, but managed to make it home each time.

AM: How did this affect your outlook on human nature and society? For somebody like me who actually has gone to the concentration camps in Germany and Austria, it seems very foreign that this would be a way of life. But when you read the histories, it is a way of life. You shrug, but it seems also that --

KH: Well, twelve-year-old kids look at things differently, and to me, it was very sad that my dad was not home and in jail, it was sad to see my mother floundering about trying to get stuff done, but -- and I just concentrated more on school and played the piano. (chuckles) It wasn't until we became actual refugees that the impact became great.

AM: Were any members of your parents' families able to leave?

KH: Yes, some of them left. My uncle left. He went to what was then Palestine. He ended up on one of these illegal ships going there, as did his older sister’s daughter from Poland. His older sister ended up in a concentration camp in Theresienstadt [in present day Czech Republic] and I found her after the war, because I was stationed in Germany at the time. I found her in a rehab[ilitation] hospital and got her to her daughter in Israel.

But the worst, immediate tragedy and the one that hit me the most personally, that sort of made it different than just going on, was my mathematician uncle, who was the youngest brother. Within the first week or two of the Anschluss [annexation of Austria by the Nazis], he was caught in the street by a bunch of Nazi toughs. And one of the things they used to do, and I'm sure you've seen -- I don't know if you've been to the Holocaust Museum, but if you have, there are pictures of Jewish people having to clean stuff off the

street, where they would put in tar, “Jew”, and you had to clean it with a toothbrush, and spit on while you were doing it, and being kicked, and so on, real humiliation. This was a very sensitive guy, unmarried, lived with his mother. He was in his early thirties, I guess. Went home and sliced his wrists and died. His name was Julius and my third child, our one son -- we have two daughters [Melanie Hirschhorn Vetter and Lisa Hirschhorn Goldberg] and a son -- is named Joel [Hirschhorn], which was his Hebrew name.

But some of them did get out.

AM: I think you left us at the -- this, I think, is a fascinating story and I'd like to just continue with it. You left us at the Swiss border that you barely made it out.

KH: Then we went into Switzerland, went to Zurich. At this point, we became taken care of by a combination of HIAS [Hebrew Immigrant Aid Society] and the Joint Distribution Committee, the two outfits that used to help refugees. My father went to work for them in Zurich, helping them with some fiscal stuff, and so on. I was sent to a day school that went all day, including food. In theory, we had a two-week visa. Every two weeks my parents used to be called before the Fremdenpolizei, foreign police – awful people --who sent many people back. There were suicides of people who were moved to the borders. My mother would throw a hysterical fit at the foreign police, and they would give her a two-week extension. This went on for almost a year. (chuckles) Until finally we got a transit visa to England, with which we got a transit visa through France. Stayed a month in Paris and then went on to London.

We arrived in London about February, March '39. Again under the auspices of these organizations, again my father was given stuff to do. And I went to school. I had my bar mitzvah in London. Somehow my father got to know the guy, who was the chief rabbi of London, and he arranged the whole thing. It was an interesting experience.

Then we were resettled. We went to a town that you may know of called Stoke on Trent, which is where the Wedgewood factories are. There was a little sort of a suburb called Basford. For some reason, that particular region, that small region, had an MP [Member of Parliament] who was Jewish. His name was Strauss. And he persuaded the old Josiah Wedgewood to buy a house for four refugee families, and we were one of those families by pure luck. We went up there. The local people were just unbelievably nice to us, invited us. We lived in this house, I went to school up there, and every two weeks, old Josiah Wedgewood, who was in his seventies at the time, would come to the house. And he would give money to the adults for food and cleaning materials and things. There were five kids in the house, and we each would go and shake his hand and he would give us a half crown for candy for the next two weeks. This went on until we left in February of '40 to come to the States.

It was very interesting. Just as an aside, when I was Chairman of Pediatrics here, we needed another neonatologist, so we put out an [advertisement], needing a neonatologist. A bunch of people came through. One walks in, and he says, "My name is Josiah Wedgewood." He was a young guy, M.D., Ph.D. I said, "He must be." In fact, it turns out I knew his father very well. His name is Ralph Wedgewood, who was Chairman of Pediatrics in Seattle. And he said, "Yes, it was my great-grandfather." So I had to hire the guy. (laughs) You know, the world goes in small circles.

2. Arriving in the United States; Early Education in Pittsburgh; Military Service and Returning to Europe

AM: Was there any thought that you could stay in England?

KH: No. England was purely a transit visa for us. It wasn't for the Starers. For the Starers, they stayed there. The only time he left England was to come train in radiology at Mass[achusetts] General [Hospital]. Then he went back. No. For us, this was not an option. The expectation was we would get an American visa and come here.
So that sort of takes us to February of 1940 when I arrived in New York with my parents, on the last French ship to cross the Atlantic. We had tickets on the Normandie, which had burned in New York Harbor and sunk. So French Line honored the tickets and put us on the De Grasse, which had about four times as many people as officially they could take. I mean, the place was just totally jammed. It was the last trip. We were in a convoy and several boats were sunk. U-boats were after the convoy. But we made it through.

We arrived in New York and again HIAS took over and put us for a few weeks into the stopping place, which no longer exists. It was called the Hotel Broadway, which was down in the [Greenwich] Village on Broadway. In fact, it's on Mercer Street and part of it is now a dormitory for NYU [New York University]. That's where we stayed for a while. It was quite phenomenal. Then they found us a room in one of these single-occupancy things up in the Upper Westside in the seventies while we were waiting for what was going to happen to us.

Meanwhile, we met these cousins and went visiting and met relatives we hadn't seen, and so on. Then it was decided that our fate originally was to go to Denver. No, sorry. The first one was to go to Binghamton [New York]. Well, my mother heard Binghamton and she became deathly ill, so we missed that one. (chuckles) Then Denver. And that was okay. I truly became -- a hundred and five fever. I got some terrible viral thing and missed that one. The next one was Pittsburgh. So we went to Pittsburgh.

AM: And why Pittsburgh?

KH: That was what was on the list next. So we went to Pittsburgh. The idea was we weren't going to stay in Pittsburgh. The outfit in Pittsburgh wanted to move us to a place called Jeanette, Pennsylvania, which is a suburb of Pittsburgh in the steel area. They wanted my father to run a drugstore in Jeanette. That was the -- they sort of ran your lives.

At that point, my mother put her foot down and said, "Enough. We will try to survive in Pittsburgh." No Jeanette. So my father went to work for about a year selling greeting cards door to door. She went to work as a saleslady in Kaufman's Department Store. She had always done pettipoint and very good stuff with sewing and knitting. So she went into that department and was selling wool and teaching people how to do these things. I held every job a high school kid could hold. We went there in the summer and I started high school that September. So I delivered newspapers, I was a soda jerk, I delivered groceries, I was an usher in a movie, I did everything. I probably brought in more money than either of them at that point.

And we survived. We lived in a single room in somebody's house and had kitchen

privileges. We moved to another house that was a little bit better when we got a little bit of money together. Then my father started looking around, and he was hired by a scrap company in McKeesport, which is another suburb of Pittsburgh, to be their bookkeeper, eventually their office manager. So a little money started coming in.

I went to Taylor Alderdice High School. This was an important part of my development in science. Two teachers in Taylor Alderdice - Taylor Alderdice was kind of the Stuyversant High School [in New York City] in Pittsburgh. They got -- whatever Westinghouses were won were won by Taylor Alderdice. A wonderful school. Two teachers who had enormous influence on me -- particularly one, but both of them. One was a biology teacher named Mae Weber Smith, who had a lab in back of her classroom and used to take us on -- she had a club called the Microscope Club, so a bunch of us did this, primarily so that we wouldn't have to stay in homeroom. The excuse was we were going to club. (chuckles) We had fun. She used to take us up to Ligonier in the Alleghenies. We used to catch rattlesnakes and squeeze out the venom and sold it for five bucks an ounce. (chuckles) We had one in the back room that we used to feed mice. Occasionally, one of us used to take it out of its cage and throw it into the classroom and watch everybody scream. (laughs) And learned a lot about biology from her and about -- just thinking.

But the main one was a guy named Lon Colborn. Lon Colborn was probably, in his time, the best chemistry teacher in the country, high school level chemistry teacher. He eventually was picked to write the national chemistry curriculum. He was one tough cookie who had no patience with stupidity. And he used to teach to the top third of his class, and the rest just passed. If they came, they passed. He had, for example, a chemical mathematics test that he gave around the middle of the year. Seven questions. It was well known to everybody, seven questions. If you got one right, you got an A. And very few people got more than one right. His former students used to come back from college to take that exam.

Every year he picked sixteen people from his junior chemistry class to take a semester of qualitative analysis in their senior year, and I was one of them. It was unbelievable. This man was an unbelievable teacher. By the time you got through with his course, and then especially with the qual [qualitative analysis course], college chemistry was a joke. You were way ahead. Nowadays it would be advanced placement. There was no such thing in those days.

He had enormous influence on many, many kids at Taylor Alderdice. A number of us -- I have it at home -- a number of us got together and put together a publication in which we followed the qualitative analysis kids and what they were doing. The vast majority are professionals in this or that. Many physicians, a number of scientists, well-known people. We fought two or three years ago with Carnegie [Institute of] Tech[nology] where he graduated to give him an honorary -- posthumous, because he had died by then -- posthumous honorary doctorate, which his family would have appreciated. They only acceded to give him an honorary master's degree. They said they can't give an honorary doctorate to somebody who doesn't even have a master's. It's stupid, but -- (chuckles)

So he and Mrs. Smith, both of them pushed me towards [science] -- nevertheless, my other major activity in high school was music. I started playing the clarinet and I started thinking about a career in music. I became interested in conducting and took some classes and learned theory and harmony, all that stuff. That went on. I went to

high school for three and a half years. I graduated a semester early -- they allowed you to do that in those days -- and started Pitt [University of Pittsburgh]. Went through one semester at Pitt and turned eighteen. And much to my parents' disgust, especially since I was a chem[istry] special student, which you were automatically deferred from the army, I volunteered for the army.

I went into basic training in the artillery and became what's called an instrument and [survey] guy. So when I then went over in January of 1945 to Europe at the tail end of the [Battle of the] Bulge, which is where we were all thrown into, and because forward observers had the highest death rate in the army of any type, all the instrument and [survey] guys became forward observers. So I became a forward observer, which for a month or so was scary, because you went behind the enemy lines and called for artillery shells in that area. In fact, many of them died because of their own shells. But then it became very easy because then we were just chasing the Germans through Germany and forward observer meant standing on a ridge and saying, "Okay. Hit that." (chuckles) So that's what I did until May when, at the end of the war, we met the Russians at the Elbe. I was in the first outfit that came through there. My first action at that point was to go to the personnel tent that they had up, looked around, and I saw -- they were little desks, field desks, where these guys would assign people to this, that, and the other thing. I found the T5, Ralph Goldberg, walked over to him and introduced myself, and I said, "I'm in the artillery but I speak German. I think it's time I did something else. Because I knew all the artillery guys were going to do was stand guard duty. And that was not what I wanted. So I got assigned to military government as a court interpreter.

Soon thereafter, we left Magdeburg because we turned it over initially to the British and then the Russians came in there. We went to Weimar, where we turned it over to the Russians. Then we went to Stuttgart, where we took over from the French. And there I became a court interpreter for the local military government summary court, and I began doing all the work for the prosecutor, who was a drunk and who eventually went home on points a few months later. So they made me the prosecutor for the court. I did that for a while.

We had two things that we had to do there. One was to catch Germans in lies. They wanted a job with the military government, so they had to fill out a questionnaire, the famous Fragebogen. It said, "Are you a member of the Nazi Party?" They'd say, "No." Of course, the Germans, we had all their records. We had everything. (laughs) So we'd look up their name, and if they said, "No," they came to court and they got their few months, or whatever, of jail, and they didn't get the job.

That was fine, no problem. But the difficult part of the job was that we were the only ones who could try the displaced persons, foreign nationals from Eastern Europe, because we couldn't let the German courts, in those days, run it. The German courts could run German civilians for civil crimes, but we had to do all the stuff for these Yugoslavs and Poles. And each time we tried one of them -- you know, they were starving people, on the whole, went and stole a loaf of bread, got arrested by the Germans and given to our court to try. The moment they came to our court, the military government law said that there had to be a liaison officer from their country. Of course, if they were found guilty, which most of them were, because it was obvious what they were doing, they were turned over to the liaison officer. They didn't throw them into a German jail, and they weren't going to be in an American military jail, right? And they sent them back to their countries and a number of them were killed.

And that got to me. So I got myself transferred to Vienna into military intelligence, and that's how I spent the last year or year and a half of my army career, where I became a targets-and-documents man, which meant that, first of all, you learned how to crack any lock, and so on. Then you went and you stole things before the Russians got to them. Also, we interviewed a lot of the Russian displaced persons to try to find out about the Russian military and what was going on. It was all that sort of stuff. So I did that until I got out of the army in '47.

AM: Before we get to this fascinating episode of your career in the U.S. Army, I wanted to go back and ask just a couple of questions of your high school years. This tech high school that you went to in Pittsburgh, was that a conscious decision to send you there, or was it just --

KH: No. We lived in Squirrel Hill, which was sort of the place where many of the Jewish people in Pittsburgh lived and almost all the refugees that came there lived -- so it was almost by chance. And Taylor Alderdice was the high school for Squirrel Hill. So I went there purely on that basis.

AM: It sounds like you were an amazingly resilient teenager to incorporate all this dramatic change in your life between the age of twelve and fourteen, fifteen.

KH: Yes.

AM: How did you adapt with things like language and cultural differences, as well as just making new friends in a completely different world?

KH: Well, the language is an interesting thing. Of course, I spoke essentially nothing when I came to England and learned English by going to school. You learned English very quickly. So that by the time I came to the States, I was fluent. I could speak English as well as German. I worked very hard in Pittsburgh on trying to lose my accent. I was a musician, so it was not as difficult for me as for some other people. I can mimic their sounds very easily. So I worked very hard on that because I needed to fit in.

In England it was elementary school, and friends were very temporary. I'd get into fistfights with boys and would flirt with girls, you know, the usual. But in Pittsburgh, it became different. Because of the music and because of the club, the Biology Club which I became part of in my second year, my sophomore year, and in the orchestra I was in my first year, I made friends through those. Friends, some of whom I'm still in touch with occasionally. [They were] an amazing group of people that I became friends with. Some of them then went through that qualitative analysis with me.

One of them is a doctor in Pittsburgh, named Lee Hershenson. Another is a doctor in Miami, named Jerry Kramer. Another is a doctor in Sharon, Pennsylvania, named Matt Brown. Another guy was, I think, the number two guy in the U.S. meteorological thing, [Stanley] Ruttenberg. Phenomenal people.

Many of them were musicians. In fact, Hershenson played the bass clarinet and Kramer played the oboe and Matt Brown played the trombone. We were all in the band and the orchestra together. That was my circle of friends [with] the girls who were

associated with us. It was still in the days where your initial and main friends were boys if you were a boy. Then the girls were companions. I had some rather interesting girlfriends there, one or two of whom also then became professionals. But it didn't happen so much in those days, interestingly. Smart. Couldn't have gone through Taylor Alderdice without being smart to some extent. But ambitions? Very few. Housewife ambitions to a great extent.

AM: During this time, to get back to your identity as a Jew in the United States now, how were you practicing or not practicing being a Jew?

KH: I never had much interest in it personally, in religion. It was always interesting, the traditional aspects, Passover, Chanukah, the celebrations were great. My father, for a while in Pittsburgh while he was doing this other stuff which didn't take his full time, selling greeting cards and stuff, became an assistant cantor in the synagogue. They needed somebody and he knew this stuff cold. His father was rabbinically trained, although he eventually became a businessman. But he was trained as a rabbi. So he was brought up in a much more religious atmosphere. Not that he was particularly religious, but he knew all this stuff. And I picked up a lot from him and taught some of it to my kids. Interestingly, two of whom now regularly attend synagogue with their families, which is beyond me. (laughs) I mean, the last time I was in one was when my son, who is now thirty-five, was bar mitzvahed. I don't think I've ever been in -- oh, no. I was there for my son's wedding, which also happened in a synagogue.

AM: In high school, was your dad becoming more active?

KH: We belonged to that synagogue, and I got dragged there on high holidays, but that's about it.

AM: You had spoken a little bit about even thinking about pursuing a music career. So when you were going off to college, what were you thinking about?

KH: I was undecided. I was undecided. Music, I think, was ahead of medicine at that time because medicine was always the other thing that I was aiming for, for many years. But music attracted me. And I didn't change my mind until I was in the army. Somehow I got this strange idea that one occasionally hits one unexpectedly and said, "Hey, I can do music any time. I don't have to be a professional. I want to do something that really helps people." It was craziness, but that's what happened. So that's when I changed my mind and decided when I came back that I was going to be a premed.

AM: Why the University of Pittsburgh, and since it sounds like your family had a tough time making ends meet, how were you going to afford college to begin with?

KH: When I entered that university, I won a thing called an Allegheny Scholarship, which paid my full tuition. So that became possible. Then, of course, which we'll get to later, when I went to college then at NYU when I came out of the army, I had the G.I. Bill. And in medical school, I still had the G.I. Bill for much of it, and I won a New York State professional scholarship between those -- we'll get to our scraping through financially until we made it, because neither of our parents had anything.

AM: To get to your decision of why join the army, you just barely managed to escape this nightmare that was Europe in the thirties and you now volunteer to risk your life and --

KH: Because of that. Well, it was -- one was sort of a vague sense of revenge, but the main thing, I think, I had this, again, strange concept of gratitude to this country and felt that it sort of was the right thing to do to go fight for the American army.

AM: When did you make this decision that you were going to do this?

KH: I think in my mind it was there probably for a couple of months before I turned eighteen, because I had to decide a month after I turned eighteen whether I was going to continue as a chem special at Pitt. And I said no.

AM: You talked about it was a conscious decision to become attached, to get out of the artillery and become more involved in the war effort than just guarding.

KH: In the postwar, the occupation part.

AM: Why change that level of involvement?

KH: Desire to do something that I considered useful, as opposed to -- being an artillery instruments guy and observer, and this and that, was useful within that time when I was doing it. It wasn't going to be useful after that. Whereas, helping with sort of managing one aspect or another of the occupation and then eventually getting involved in the whole intelligence effort was, I think, a matter of that it would keep me interested.

AM: Then why, of all places, go back to Vienna?

KH: One of the things that drew me back when I actually visited before I got transferred in order to try to see whether there was a job for me down there, it was at that time when I went after this guy who had my father thrown in jail and had him thrown in jail. So that was one small piece.

The other one was, why have I gone back to Vienna another four times? It's sentimentality, it’s where I was brought up. It's where you have some of the best music in the world. Its good cakes. (laughs) And also, I wanted out from this court business. They wouldn't have let me out. The only people who could get me out was Intelligence.

AM: So then you entered the world of cloak and dagger. How well adapted were you to do this spy work?

KH: Oh, I loved it. It was fun. It was kind of -- a lot of it was a combination of a physical and intellectual exercise. There were interesting people who were in the same unit whom you could have good conversations with, so it was fun. There were episodes that I still remember. One of them, actually, when we were in Vienna last year at the International Human Genetics Congress, and I told my wife [Rochelle Hirschhorn] of this story when we stole all these aerial photo maps of all of Eastern Europe that the Germans had made from under the Russians' noses, because they didn't want us to have them, obviously. So we pulled a real fast one on them, me and another guy. We got them all

They were in the old War Archive building. This was in the center of Vienna, which was -- Vienna was under Quadripartite control like Berlin, and the center of Vienna rotated every month between the four occupying forces. When we found out that these maps existed, it was the Russians' turn to be in the center. We knew the building, and we went and looked at the building. It had two doors, and they only had one guard and he would march back and forth between the two doors. One evening, we pulled up with a pickup truck with a tarp over it, and when he was around the corner, I zoomed out, cracked the door, and went in. By then, we knew where the maps were. They were on the second floor. And every time he went around the corner, I opened the window and threw out a bundle of maps and the other guy would shove them under the tarp and go sit back in the truck. We did this for about two hours and cleaned out the whole place.

And when we were in Vienna, we were walking around and looking at some of the old houses from the time of the Secessionism, the art movement from the 1910s, '20s. I turned around and I said, "Hey! There it is." It was no longer the War Archives building but I recognized the building right away.

AM: What is it now?

KH: It's a big office building.

AM: Well, it sounds like you were very good at this cloak and dagger stuff.

KH: It was fun.

AM: That was a big business. It became a huge business and still is a big business.

KH: The guys we worked with when I first got to Vienna in this little detachment, around the corner from us was a house where the OSS [Office of Strategic Services] lived. We became very good buddies, and we did some stuff together between army G-2, which is intelligence, and the OSS. And a couple of months in, they disappeared. We go over to the house and we see things are being ripped apart in the house and put back together. We said, "What's going on?" And nobody would talk to us. The next thing we see is a bunch of guys who occupy this house, with suits and ties and looking very Ivy League-ish. It was the first CIA [Central Intelligence Agency] group. (chuckles)

AM: Did you ever consider a career with the --

KH: God, no. (laughs)

AM: Just did your time and got out. Okay. Well, to pick up where we left off, you finish up your duty with the army and how do you end up in New York? Why not go back to Pittsburgh?

KH: My parents moved to New York while I was in the army. Remember, this was the days of Pittsburgh when you went out with a white shirt and five minutes later it was black. This was the dirtiest city in the country. And she just got tired of it. So when my father was offered a job of being the office manager -- it was his first New York job -- for Barton's Chocolates, which was owned by a Viennese Jew named Klein, they picked up,

while I was in the army, and moved. So I came back to New York. I was twenty-one when I left the army. They had an apartment in Washington Heights where they had an extra room. They purposely rented with an extra room so that when I came home I could live there. So that's how I came to New York.

Then in the next couple of months, I had to get accepted to a college. Remember that this was a time when spaces were at a premium because a lot of veterans were coming out at that time and all of them with their G.I. Bill. They all wanted places. So a friend of my father's knew a guy who was a professor at NYU, a history professor. He taught history. I went to see him, and we got along, and I was accepted. I started in January of '48 at Washington Square College, and I took an average of between twenty-three and twenty-six credits a term and got out in two and a half years. All I had from Pittsburgh -- they gave me like eight credits for what I did at Pittsburgh. I went through the summers and I was out by June of 1950. By then I'd been accepted to NYU Medical School.

3. Decision to Pursue Medical Studies; New York University and Developing Interest in Endocrinology and Medical Genetics; Training in Sweden

AM: At what point did you know you were going to pursue a career in medicine?

KH: By then I was -- I became a premed. When I went into NYU, I became a premed. That's the decision I had made in the army was that was what I was going to try for. So I became a premed. I had a major and two minors in that two and a half years. My major was German literature, and that's how I got involved with [Robert] Musil. I needed something that was going to be relatively easy for me because I had all these premed requirements to do in this planned two and a half year race for time. I'd lost three years. So I was an honors major in German lit, and I was a chemistry and a biology double minor. I didn't make summa, I made magna [cum laude], which was fine. (chuckles)

AM: You under-achiever.

KH: Which was fine. Getting into medical school was not easy in those days. They accepted about one out of eight applicants. It was very competitive, again, because a lot of veterans were out. I applied to only New York schools because there was no way that I could have afforded to go to school out of town. So I applied, actually, to three New York schools. I applied to [SUNY] Downstate as a so-called safety, which was at the time called King's County something-or-other, Columbia, and NYU. Columbia put me on the waiting list and told me in no uncertain terms that they think they have their three Jews whom they were willing to accept.

AM: How did you respond to that?

KH: What can you do? I mean, that was reality in 1949, '50. The whole quota system didn't get destroyed until the sixties, really, until the early sixties or late fifties.

AM: Although you'd just gone and risked your life.

KH: It didn't mean a thing. There's a wonderful book by a guy I know very well, this pathologist at the NIH who used to be a professor of mine at NYU in pathology, about discrimination in medical school admissions, chapter and verse, the whole thing.

Anyway, they put me on an alternate list in case somebody else wasn't going to come.

Downstate, I had a very interesting experience. I was very skinny. Until six years ago I was very skinny. Why am I no longer so skinny? Because when I went to the hospital to have my prostate taken out because it got too big and obstructed me, they wouldn't let me smoke my little cigars. So I quit for the five days I was in the hospital and I figured, "I didn't really miss it, I'm not going to smoke." Even though my wife had continued to smoke. She quit about three years ago. She was a cigarette smoker. And I did what everybody does. I gained twenty, twenty-five pounds within six months. And she did the same thing when she quit.

But I was so skinny when I was applying for medical school that at Downstate they were convinced that I must have active TB [tuberculosis], or something. They called me back for more medical exams and this and that. Meanwhile, I got an interview at NYU. I was interviewed by a famous man named Alwin [M.] Pappenheimer [Jr.], a leading microbiologist of his day, [who] then went to Harvard afterwards. And we got into a rip-roaring fight during the interview about the inadequacy of college premed counselors.

AM: And which side were you on?

KH: I said they were inadequate. (chuckles) I got no help at all. So we got into this big discussion. But I got an acceptance very quickly thereafter and got this professional scholarship, which helped. And that's how I got into NYU.

AM: Given that many people who were studying chemistry during World War II were granted deferrals, if they wanted to, and you did not do that and went into the service, how well did you integrate back into the college life after not only doing all this --

KH: There were lots of other veterans. And also, I didn't have time to think of other things. I went to school literally from eight in the morning till ten at night and tried to do whatever you have to do at home in between, and also held down a couple summer jobs while I was doing it because we still didn't have very much money. I needed clothes and needed this and that, needed to take out a girl now and then. So I did that. And held jobs also a couple of the summers during medical school. But during college in the summer, I spent half the summer being first a busboy and then a waiter up in the Catskills when I was not taking a course in Hunter, New York. Then in medical school, I wrote the paper and became a host for an outfit called Wentworth Village in Jackson, New Hampshire, which was a big resort. And fortunately, I was a good dancer, so I could dance with all the ladies who were up there. That was the days of the mambo and things like that. One of the guys in the band with whom I became very friendly eventually was a Viennese musician named Max Hamlisch, the father of Marvin Hamlisch, who played the accordion. He had played the accordion in many movies in Austria, which I had seen, which starred a man named Joseph Schmidt, who was a famous tenor in those days in musicals. Max and I became very good buddies when we were up there in New Hampshire. Eventually, he came with a couple of friends of his and played at our wedding and had this six-year-old kid with him named Marvin.

AM: Were you able to continue with your music in college?

KH: Yeah. In college I played in the orchestra and played in a couple of -- occasionally played in some chamber stuff. But mainly in the orchestra. I played a couple of concerts and rehearsals. In medical school, I played some chamber music with some friends occasionally. We made a glee club in medical school, which was a lot of fun. A bunch of us, did some singing.

I continued playing for a long time. While I was on the faculty here, in fact, for a number of years we had a Mount Sinai orchestra, and I played. Two of my three kids were old enough by then, and we came. We were all wind players. I played the clarinet and they played flute and oboe, my two daughters. I had a lot of fun with that. Somewhere -- I think it's at home -- there's a marvelous picture of the three of us playing.

So I kept up with it. My son eventually played. They all started on the piano because I had a strong belief that they should start on the piano. Then they switched to winds when they were about twelve. My son kept it up the most. He's still a superb pianist. Then he went to the bassoon. So we played quartets and trios and stuff. We had a lot of fun together doing music with the kids. I tried to persuade my wife to take up the French horn because then we'd have a real wind quartet, but she wouldn't have any of it. (laughs

AM: Okay. On this argument with premedical counseling at the undergraduate level, who won the argument?

KH: I don't think either of us did. I think we both probably gave a little at the end, and he said, "Yeah, I can see that some people come without a clue," and I said, "Yeah, but I guess some of them are all right." And ended up --

AM: How has your attitude changed since those early days in terms of the kind of counseling premeds get?

KH: Well, I think it was pretty bad for a long time. I think it's gotten a lot better. And that better is because of special programs that the medical schools have started more than what the colleges have done. For example, we have some interesting programs here that I've helped out with a great deal. One of them is called Humanism in Medicine, where we take college kids from five colleges -- Williams, Wesleyan, Brandeis, Princeton -- and we interview them in their second year if they apply, and if they pass muster, we accept them for after their fourth year at the end of their second year. They can go on doing their humanities. Then we do a summer for them, a couple of months for two summers, in which they come here and learn about science. By the time they're half way through medical school, you can't tell them apart from anybody else. They're fine.

In the days when it wasn't so popular to go to medical school for a while, people went for law and business and this and that, we really wanted to attract the best that we could, so we did some of these programs. At the same time, of course, we also had remedial programs and have consistently gotten at least ten and often more of a percent of minorities. I think two years ago was the first year that we had more women than men. This is as opposed to my days when we had, in my class, five women out of a hundred and twenty-some. Then in my wife's class, which was two years later, they had, I think, ten. Now its average is 50 percent.

AM: We're probably going to get back to this in a later session when we have both of you sit down in front of the camera, but to go back to when you started medical school, at that time, when you started, at the very beginning, what did you think you'd be doing with an M.D. degree?

KH: That was a long and changing story. My goal when I went into medical school was to practice medicine. And gradually as we went through the various experiences, particularly in the third year when you do your clinical clerkships, I was interested in internal medicine. Then gradually I figured out that just plain internal medicine was going to be boring and I needed a subspecialty. And a field that was growing at that particular time was endocrinology. So my goal was to become an endocrinologist in practice.

AM: What was it about endocrinology and its growth that --

KH: There was an excitement about the discovery of new hormones, of the interaction of the pituitary and the adrenal and the thyroid. It became an exciting field with enormous clinical importance.

Then when I became an intern at Bellevue, my boss was Chuck [Charles] Wilkinson, who I'll get back to, because he was -- I would say that post-high school, there have really only been three major mentors, people whom I respected. And he was the first. He was the Chairman of Medicine in one of the four divisions of Bellevue. It was the NYU Postgraduate Division. And I liked him when we interviewed and I did my internship there. Then I did a residency for only one year. I did two years of house staff training, which in those days was very common. Nowadays you need special permission. In the third year, if you're going to be a specialist, it's a waste of time. But that's a separate question.

During that second year, I had to decide what I was going to really do. So Wilkinson offered me a fellowship in metabolism. I applied to the NIH and I got a fellowship grant and I did a fellowship in metabolism. I started on that in 1956. The work that was going on in his lab -- which he became famous for and had been already famous as how he became a chairman, came from Michigan, originally came from Georgia but went to Michigan as a professor, then he was recruited to NYU to be the chairman, a young guy -- was hypercholesterolemia. So that's what I did for a year. And not just hypercholesterolemia but all the hyperlipidemias and wrote some of the early papers on the importance of cholesterol and triglycerides and all that stuff. What I figured out right away was that all these patients that I was seeing with these lipid abnormalities had family histories. And I knew zilch about genetics. I figured that one should learn something about this.

So within a month of my starting the fellowship, I registered at Washington Square in the graduate school for a master's degree, with an absolutely magnificent guy [Morris H. Harnley], to do a master's in genetics. He was a Drosophila (fruit flies) geneticist. I did this, and it was fascinating. This was 1956 to '57. Meanwhile, we had a visit from the head of human genetics at the University of Uppsala in Sweden, who came and gave some talks and talked about the potential use of tissue culture to study genetic diseases. This appealed to me and it appealed to Wilkinson. Wilkinson helped me get two grants. One, actually, I got by myself from the American Scandinavian Foundation, which I got four thousand dollars on the excuse of studying chemistry in Sweden. They had these

John [G.] Bergquist fellowships. So I got that and spent a good bit of it [time] before I knew that I was -- when I realized that I was going, we went one evening a week to the American-Scandinavian Foundation and learned Swedish.

The other grant was interesting, which he got for me. He knew a guy who was the head of the Population Council at that time. They had fellowships available for foreign study, so he got me that. So between the two, I ended up with seven thousand dollars for the year, out of which we still have our dishes, a lot of the furniture, we bought a car. Money went a long ways. (chuckles)

At that time, I was doing my master's in genetics, and then the next year I did my second year of fellowship in genetics in Uppsala.

AM: During your first couple of years in med school when you were taking classes, how many times was genetics referred to as part of the medical training of a physician?

KH: Bacterial genetics was about as far as it went. This was the days of the discovery of DNA, all of that stuff was happening. My Chairman of Pharmacology, who later became Chairman of Biochemistry, was Severo Ochoa who won the Nobel Prize for RNA polymerase. I mean, all these guys were sitting there doing their stuff using E.coli. The basis of genetics was going on but not the basis of inheritance. It was the basis of the genetic material and the action of the genetic material, all of which was fascinating. It was all brand new. But regular genetics was considered Drosophila. The science of human genetics, which was closely interwoven with eugenics in this country, had a bad name. See those gray books? They started off over there, if you look at the beginning, with the Annals of Eugenics and ending with what became the Annals of Human Genetics. People weren't too anxious to do human genetics in those days, so it was very little. Yeah, we knew that hemophilia was an X-linked disease but didn't go much beyond that.

AM: But did they teach courses in basic kind of genetic history, Mendel or --

KH: You got that in college biology in a couple of lectures.

AM: That was it. What about pedigree analysis?

KH: Wasn't even mentioned. Wasn't even mentioned. We were kind of told something that you can find, by the way, in the old Talmud where they say that if a woman's boy bleeds to death at circumcision and it happens a second time, or if it's also happened to her sister, the next boy doesn't have to be circumcised. So they figured out how X-linked inheritance works, and that's as far as -- (chuckles)

AM: Did you know this at the time or is it something you learned about the Talmud afterward?

KH: I learned that later. (laughs)

AM: Okay. Also, at what point could you understand that there was this other option, besides just being a pure clinician, that some M.D.'s became bench scientists with no clinical responsibilities, or else there's this opportunity --

KH: That's where we have to go through our year in Sweden, because that's when it happened.

AM: Okay.

KH: Arrive in Sweden -- institute run by this guy Jan[A.]Böök, who came and talked to us, a psychiatric geneticist interested in inheritance of schizophrenia, and ran this institute. One of the people working in this institute, which is where he came with the tissue culture stuff that I became interested in, was a guy named Marco Fraccaro.

Marco Fraccaro was an Italian biologist-physician who had initially gone to Holland to study with a man named [Alexis] Carrel, who was one of the founders of tissue culture, and then was hired by Böök to establish a tissue culture genetics lab in this genetics institute, which, by the way, was not called a genetics institute at the time. It was called the [State] Institute [of] Race Biology [and Human Genetics].

I started working with Marco and we became very good friends, he and his Swedish wife and the two of us, because Swedes themselves are not easy to crack into socially. You went to these formal dinners, and you had to learn -- that's one of the things I learned at the American-Scandinavian Foundation, that if you sit to the left of the hostess, you're the guest of honor, and a woman is never supposed to drink unless you first skål her. Then she can pick up her drink. So you have to be careful. Then at the end of the dinner, just as she puts down her last spoon of dessert from the dessert, you're supposed to tap your glass and hold a speech thanking her for the dinner and making, you know, seductive notions. It's a whole rigmarole. (laughs) My wife knew nothing from this and didn't want to know, so when I did this at the end of Böök's dinner for us shortly after we came, I tapped the glass, and she went merrily along chatting with the guy next to her. And everybody -- (laughs). So Marco [was] the other foreigner in the place, and we became good friends.

Marco, after we worked together for a bit on some fun stuff, started to talk to me about, "What? Are you crazy? You're going to go out into practice and not have this fun and do these things?" We had these violent arguments about it. I said, "But it's what I wanted to do." After maybe six or eight months of this, I became convinced, and I applied for a fellowship, a certain advanced fellowship, because I already was a fellow. When I came back, I moved into that and started doing what I've done all my life, which is to combine clinical medicine and science. I would never want to drop clinical medicine. That's been a principle of mine. I must continue seeing patients; otherwise, what's the point?

AM: When you decided to get a master's degree in genetics, what did you think you'd be learning about? What did it required to get a master's degree in genetics?

KH: Well, you learned the principles of genetics, of inheritance, and using what was the experimental animal at the time, which was the fruit fly. The reason I thought that this was going to be important is because I really didn't understand what was going on in these complex families with their lipid abnormalities, and how were you going to go about studying the genetics of this, beyond just drawing a pedigree?

AM: How many of your colleagues, your fellow medical students, were exploring options that there were more opportunities than just a pure clinical --

KH: We had an unusual class. Remember, we were a little older, a lot of veterans. And difficult to get into school, so it was a bright class. It was the highest ever anywhere. Twenty-five percent of our class ended up in full-time academic medicine. A number of them became chairmen here and there, a number of them became highly recognized scientists or clinical leaders, and so on. So it was quite a phenomenal class. We get together, some of us, periodically still, and they're still an amazing group. Quite an amazing group.

AM: What was the atmosphere like just being at NYU at the time?

KH: We made our own atmosphere. When we were in the early years, the basic science years, Friday afternoons we started a tradition.

We went out and bought a barrel of beer, and we dragged our faculty down there Friday afternoon to come have beer with us and chat and talk and become colleagues. So we managed to loosen up the atmosphere a great deal.

Then when we were in the clinical thing, none of us took any crap from anybody. I'll never forget the day we started our clerkship in internal medicine. Our group sort of went through all the clerkships together. We were all good buddies and all veterans and stuff. We walk onto this floor the first time, and the guy who happened to be in front was a guy named Ammiel [D.] Schwartz, who is now an obstetrician up in Brewster [New York]. We walked in and this resident meets us at the door with a long sheet of paper with big lists on it, and hands it to Ammiel. Ammiel takes the piece of paper and looks at it and hands it back to him. "What's this?," Ammiel says. He says, "That's your scut list for today." Ammiel looks around at us all standing there shrugging our shoulders, and Ammiel says, "All right. We'll do every one of these things, but we won't do any of them until you explain to us why we're doing them." We became great friends with this resident. (chuckles)

So we kind of made our own atmosphere. We arranged for important research, electives that we got people to take us for. I worked one whole semester up at Goldwater Hospital in vascular physiology. Art [Arthur] Karmen worked in biochemistry. The major enzymes you measure for heart attacks and for liver disease called transaminases, they're Karmen units. It was while he was a medical student. Bob [Robert S.] Schwartz, who is up at Tufts [University] and is now the associate editor of the New England Journal [of Medicine], a couple of years later -- and that's when he had started in medical school -- discovered 6-mercaptopurine, which was the forerunner of all the chemotherapeutic agents. Gerry [Gerald] Weismann, who was at NYU, did a lot with the lysosome, one of the top experimental rheumatologists around, and started all this when he was in medical school. Lots and lots of them. Gerry [Gerald L.] Klerman, who became the head of the National Institute of Mental Health, started doing psychiatric research while he was a medical student. So it was a great class to be with. It had an enormous impact on all of us.

AM: How aware were you of the strides being taken in genetic research and genetics up the street at Rockefeller?

KH: Very little at the beginning. I became aware of it, actually, during one of the summers when I went with the same Ammiel Schwartz to Cold Spring Harbor for a few weeks. And we got involved there with -- I'm blocking on her name, the corn geneticist that got the Nobel Prize, who died a few years ago. I'll think of it.

AM: McClintock?

KH: Barbara McClintock. We ended up at her shop. And it was just phenomenal. Sure, it was corn genetics, which --what do we know? (chuckles) I mean, just to be with this lady and to go to the seminars out there on mostly microbial genetics still at that time, what was going on. That's when I first got a clue that something's happening. Of course, it was while we were in medical school that [James] Watson and [Francis] Crick [1962 Nobel Prize Winners for discovery of DNA structure] wrote their paper, which didn't mean too much to us at the time.

AM: And how did you end up at Cold Spring Harbor in McClintock's lab?

KH: It was an elective situation. In the summer, they gave us an opportunity to spend a couple of weeks just seeing what science was about in odd places. So Ammiel and I decided to go out there.

AM: I'm going to pause the tape for just a second.

[tape off, then resumes]

4. Medical Genetics in Europe; Eugenics of the Past and Medical Genetics of the Present; 1958 Meeting of Medical Geneticists in Colorado Medical and Developing a Critical Mass in Medical Genetics

AM: To continue then, how was it different in Sweden, what you were learning in genetics, compared to, say, what was going in at NYU and --

KH: Totally different. The Swedes for many decades at that particular point had been doing population and family studies of human disease. They had a library, which they used to spend a fair amount of time in, with an enormous number of books of these studies, including a whole series of large volumes full of photographs of people with various congenital malformation diseases and showing all the members of the families and the beginnings of some of the biochemical genetic diseases that were happening there and in England to some extent, early studies on enzyme abnormalities causing genetic diseases.

So they had been doing real human and medical genetics for a long time. Now, they started off with this, as I indicated before, not from a genetics point of view but from trying to define the ideal Aryan Swedish race. That's where they started, so it became the Institute for Race Biology. I guess the second or third head of that was a man named [Gunnar] Dahlberg, who was gone by the time I got there, who became very interested in mathematics of human genetics and developed a number of equations that were important in population genetics and in calculating inheritance and gene frequencies, and stuff like that. So that's when it really moved into human genetics, so around the thirties, forties.

Then it became relatively famous for this kind of thing, but it didn't happen in too many places. There was a small institute in Copenhagen [Danish Institute for Genetics and Eugenics]. There was a fairly decent institute at Ann Arbor [University of Michigan] run by Jim [James V.] Neel. Not much else. There were dribs and drabs of it in various places. So it was an eye opener that, yes, you could study human families. What we'd always been sort of told was that you can't do human genetics because the generation time is too long and you can't see what happens, and what's more you can't take two people with specific characteristics and tell them to breed, which you can do with Drosophila (fruit flies) and, eventually, the mouse, and so on. So it was a big eye opener that, yes, you can do human genetics without waiting for other generations. And tissue culture was one of the ways of doing it.

AM: Given your own personal experience in a society that made racial hygiene a political platform and a political agenda, how did you incorporate this kind of tradition of genetics being used for all the wrong purposes -- and which you were willing to die for, I guess, if you want to extrapolate that far -- with your own personal interests and professional career interests?

KH: It became relatively clear in the fifties that there was a difference between the sort of eugenic aspects of race biology and medical genetics. The real study of heredity of disease, and even of normal human characteristics, inheritance of normal human characteristics. Blood groups had been really discovered. Started in 1900 with [Karl] Landsteiner with the ABO blood group, although he didn't have a clue as to the genetics of it, but it gradually became clear. So these things were beginning to happen.

One of the guys who really made the beginnings of biochemical genetics happen is a guy named Harry Harris, who is another one of my big heroes. He had begun to work with a man named [Charles E.] Dent in London on paper electrophoresis. That's how they got started, showing that proteins differed from individual to individual in their movement on paper. And out of that the field of biochemical, genetics really was born.

Also at that time, in the mid-fifties, the normal human chromosome number was discovered by virtue of a technical fluke. And that's one of the things that Marco and I were playing with when I was in Sweden, looking at humans, to begin to look at human chromosomes for abnormalities. It's a field that I have never left. That's been sort of a continuum. I've also done biochemical and molecular and immuno-[genetics] and this and that and the other thing, but cytogenetics has been the real continuum, and the use of tissue culture.

So I looked at it as an opportunity to learn something that was a true medical subspecialty, rather than just the population end of it that was being misused by a number of people.

AM: How easy or difficult was it to convince your advisors as you're needing to finish up your medical training to say, okay, this is a medical specialty, human genetics, even though, obviously -- so how did you achieve this?

KH: The first thing that happened was this meeting that I was alluding to that Chuck Wilkinson took me to in 1958. We came back in June of 1958. Actually, I'd gone to my

first human genetics meeting when I was a fellow with him, but then we were invited to this meeting that Ted [Theodore T.] Puck ran in Colorado. Several of the people whom he invited were, in fact, M.D.'s who had developed an interest in human genetics, Wilkinson out of the hypercholesterolemia stuff, [Victor A.] McKusick out of the connective tissue diseases, Marfan [syndrome], Ehlers-Danlos [syndrome], those kinds of things, and a couple of other people like them came together. And I very well remember that Curt Stern was there, who was one of THE Drosophila geneticists, to sort of keep us on the right track. He was a wonderful man.

And this conversation started over a couple of days between us as to, where is all this going? And I remember Wilkinson saying, "Look, we're here because we're doctors, and we're here because we recognize that many diseases have either a complete or a partial genetic component, because they run in families. Therefore, there is a future to doing clinical genetics and to developing ourselves as providers in that kind of medical care and of responding" -- it was the first time I'd heard the word used and I hate it -- "to a number of consumers who have these problems." (laughs)

Everybody kind of shook their head and went back and started thinking about education. Courses started in the medical schools on the basis of this. I remember at that time I taught a twenty-six hour course at NYU single-handedly in what was then known about human genetics every year. I taught in the graduate school at Washington Square to biology students. We were kind of going to proselytize. (chuckles)

And it happened. And it happened to the extent that we persuaded the American Board of Medical Specialties to allow us to develop a board -- I was one of the founders of that board -- so that people could become certified in various aspects of medical genetics. We then formed a college, which is like an academy, a pediatric college of medical genetics, which allowed us to have impact on organized medicine, because when you have a college, it sort of hooks into the AMA [American Medical Association] in terms of rule making. That brought further recognition of genetics as a medical specialty. So in the long run, it worked out.

KH: -- the last couple months of the fellowship, I was to visit all the, by then, established European human genetics units, of which there were maybe ten or fifteen in the various countries. We had a great time. One of the places -- there were a couple of them in Germany, and one of them was in Münster, which was run by a man named [Otmar Freiherr] von Verschuer, which was one of [Eugen] Fischer's people and was a part of this whole thing, who then later, it turned out, was one of the doctors who sent Jews, mentally defectives, and so on, into concentration camps for experiments and for extermination. There he was sitting across the desk from me as the head of this genetics unit. I didn't know the details of what he'd done, but I had strong suspicions.

He asked me what I was doing and what I had done before, and I told him, "The last time I was in Germany, I was here with the American army." (laughs) The time before was when I became a Jewish refugee. So he was getting more and more uncomfortable. (laughs) Well, shortly before he died, they finally published what he was responsible for. It was far too late to do anything about it. But it was difficult with those guys.

Another guy who ran a unit in Hamburg named Widukind Lenz, who was the son of the Lenz in this book, was all his life an anti-Nazi. There's good evidence. Despite his

father. He's the guy who discovered the whole thalidomide connection to losing limbs. So he was a totally different kind of guy, very disturbed by what had happened.

AM: I think before we started talking about this, you were talking about the meeting and then kind of moved forward very quickly. I want to go back and ask a question about the meeting. What would you say was the critical moment that started the whole idea of even having a meeting and getting the human geneticists together?

KH: The moment, I think, derived from a conversation between [Theodore T.] Puck and McKusick. Puck was one of the important figures also in tissue culture genetics, or somatic cell genetics as the field is called. And McKusick became interested in how could this technique, which was my interest, too, how could this technique be applied to studying the basic mechanisms of some of these genetic diseases? In fact, when I was in Sweden with Marco, we used Puck's techniques for cloning cells to figure out different functions of cells derived from people who were normal or who had some genetic illness. So we got involved in that.

And I think McKusick, who is very good at sensing what's important for the field, or for the field in relation to the public. His Mendelian Inheritance in Man just completely transformed human genetics, that collection which is now mainly online. He understands these things. He has this knack for -- and I think he figured out that maybe it was time to try to do this in an organized fashion. He then gave Puck a list of whom he thought should be invited to this meeting: [Arno] Motulsky [pharmacogeneticist], [Barton] Childs, I think, was there, Malcolm Ferguson-Smith [cytogeneticist], who had worked with McKusick at the time and is now in Cambridge, a few other people. There were maybe a dozen people.

I felt honored by being allowed to be there. Wilkinson was the one that was invited, and he said, "Come on." And it's interesting -- and we may get back to this later. When we came back in 1958, Wilkinson had gotten the first NIH training grant in human genetics, on the basis of which he stepped down from the chair, which he had written to his whole faculty. He said, "If I get this grant, I'm stepping down because that's what I'm going to be doing." He got the grant.

And in the summer of 1958, he lived up in Westport [Connecticut] and his kids were out on a boat in the bay. They got pulled by a tide. They were relatively small, and they got very scared. And he swam out and he pulled the boat and had a heart attack. He survived. Every time that he tried to work with any kind of vigor, which was, of course, what he was looking forward to -- he got this grant to go train people in human genetics -- he would get chest pain. It was before the days when you could do very much about these things. There were no stents and tubes to stick up and take out plaques and stuff.

He was fifty-two years old at the time. He became more and more depressed. He'd always been a heavy drinker and became a very heavy drinker. He was one of these rugged individualists and described himself as the only ordained Druid priest on the East Coast. And he was a friend and great fan of Ernest Hemingway, a very educated, wonderful man. And he became so depressed that he blew his brains out.

This was in '59. I'd been back by then for a little over a year. Our first daughter was born in July of 1959. He came to visit Rochelle in the hospital and brought her a book, The King Must Die [by Mary Renault], inscribed very nicely to her. And he was dead

within a month. I happened to be in the right place at the right time for a very unfortunate reason, and I took over his grant, took over his lab, and that's where my career really started.

AM: By standing in the right place at the right time, was this even something you had considered doing? At that point, you were thinking about your own choices that you needed to make. What were they?

KH: Yeah, and I was having a great time, and I was setting up a tissue culture lab and beginning to do chromosome work, and all that sort of stuff, and figuring a few years of writing a number of papers, going out and getting my own grant, and meanwhile running a genetics clinic. That was what my future looked like to me at that time.

AM: You mentioned that Wilkinson had just invited you along. He was the person who received the invitation to this meeting, and he invited you along because you were working with him. How did you feel as a member of this group?

KH: I was very well received. I was very well received. They were all very kind, nice people, and they did not make me feel like this young intruder, that I sort of felt I was, and made me very welcome. I didn't say very much at the meeting; I did a lot of listening. And I've known every one of them ever since, and we're all good buddies. I'm getting the Excellence in [Human Genetics] Education Award this year from the American Society of Human Genetics. My predecessors in getting that award were Barton Childs, Victor McKusick, Arno Motulsky, and [F.] Clarke Fraser from Canada. Barton is going to introduce me for the award. So we have really, literally closely known each other since that meeting. We've also all gotten the [William] Allan Award from the Society, and I think all of us were at one time president of the Society.

AM: Is this a tight-knit group, or a little genetics Mafia?

KH: No, it's not really. It's interesting. Very little -- some of them, I won't say there's none, because Arno and Victor are a little Mafia. They do like to control things, which some people pay attention to. Many don't. But many of us don't think that way. Barton certainly doesn't, and I don't, and many of our friends who did rise to leadership in that and have remained friends, we don't do politics. We do science. In fact, many of us, including me, are unhappy with some of the stuff that has happened, obviously, in the Society, because 1956 when I went, there were under a hundred members in the Society, and at that meeting, which was in Storrs, Connecticut, there were twenty-eight members of the Society. We all gave papers. (chuckles) And everybody was supportive of everybody else.

And that remained for many years, and then gradually, as it became bigger and bigger and more money was involved in genetics, more grant money, more industry money, more this and that, a good bit of the Society has become like a number of the other societies and not anymore universally supportive, friendly to each other.

AM: How do you account for that?

KH: Too big. But it had to be. It was very important, for example, for us to allow the counselors to become members of the Society, very important people to the field now. It

became very important, and I was in part involved in that, to persuade the molecular geneticists to become part of the Society rather than starting their own society. And if you read my Allan Award thing, that's the theme: Don't let this discipline get fragmented.

AM: I think I will come back to this, probably tomorrow, because there are some really big questions here I would like to ask. But because your own development as a geneticist kind of reflects the development of the field, I want to ask a couple more questions before we wrap up about after you've come back from Uppsala [Sweden] and you have these new tools to work with. What happened then in combining your specialty interests in endocrinology with these new things that wasn't a field, really, but were new tools you could apply to genetics?

KH: Well, I dropped endocrinology completely. I never took a fellowship in that. I took a fellowship in metabolism, but metabolism became then, as it is today to some extent, really biochemical genetics. Our metabolic clinic handles the phenylketonurics and the galactosemics. All these inborn errors of metabolism are what metabolism has become. So that remained. Endocrinology is a question of being dubious about the existence of all these hormones anyway. (chuckles) So that stopped me, except where it became part of genetics, the adrenogenital syndrome, all these important genetic endocrine diseases. My son is now a pediatric endocrinologist. He's an M.D., Ph.D. up at Harvard at Boston Children’s [Hospital Boston], but what he does four days out of five is genomics. The fifth day, he does his clinical pediatric endocrinology. So endocrinology as it relates to genetics, fine, but not as a field. I have no desire to take care of a bunch of diabetics. (chuckles)

AM: So with genetics not being a medical specialty, how did you decide --

KH: It was internal medicine. I taught internal medicine. I was an attending on the floors three months of the year and gave lectures to the medical students and taught the residents internal medicine. I frequently managed to inject some genetic lore into this. In the medical school, I taught genetics, in the basic science years. But I was an internist.

AM: Right. So you had two different identities.

KH: Yeah.

AM: Were you like a covert -- was this like covert operations, your genetic interests?

KH: Yeah. It was in a sense. We managed to do a clinic under the auspices of the hyperlipemia clinic. That became the genetics clinic, and we saw all kinds of genetic things there. But Bellevue wouldn't have bought in on establishing a genetics clinic in the late fifties. So you played around the edges of it, and you managed to get it done.

And of course, again jumping ahead a little bit, when I moved here to establish a genetics division here -- this was now '66 -- thanks to Horace [L.] Hodes, who's the other of the three mentors -- the logical place for it became pediatrics. So suddenly I was in a Department of Pediatrics. Ten years later, they thought I was a pediatrician and they made me chairman. (chuckles) So you always have this other identity, because I'm part of pediatrics, I still teach pediatrics, I still go to morning report once or twice a week and discuss cases and go on rounds.

5. Building a Genetics Research Program at NYU; Tissue Culture Techniques, Cytogenetics and Early Molecular Work

AM: This is interesting. And what opportunities did you have then to create your own agenda when you inherited -- if that's the correct word -- the training grant?

KH: Well, I didn't inherit the training grant, I inherited his research grant. The training grant was inherited by Colin [M.] MacLeod of [Avery-]McCarthy-MacLeod DNA. He was at NYU, he was the head of microbiology, and he was a bacterial geneticist, and he inherited the training grant. I did all the training but he inherited the training grant. He then hired another guy, named Rody [P.] Cox, who was an internist also trained in genetics by the early sixties, and the two of us really did the training. But he officially was the program director. And managed to get good basic science training into it in -- what's DNA and you know -- very important. What I inherited from Chuck was his research grant. Now, that research grant I held until about the thirteenth year, or so, of my chairmanship [Oral Author Annotation: I held for about thirty years, or so, until about the 10th year of my chairmanship] when I decided I couldn't do it anymore because being a clinical chairman at that point just became too difficult, and I gave it up.

The first thing I did when I came here is I applied for my own training grant in human genetics, and I got one of the very first ones from [National] Institute of Child Health and [Human] Development, which had both pre-doc and post-doc, which I got when I came here. It started in '67 and allowed me to start a Ph.D. program here [Mount Sinai School of Medicine] in human genetics, also. And that still exists. I turned it over to Bob [Robert J.] Desnick, whom I hired when I became chairman because I wasn't going to do both and turned over the training grant to him. And that is close to forty years the grant has existed. The other one existed for thirty-some years. So that was how I sustained myself. I had a program project grant, or a center grant, for a while in human genetics here for a few years when they were popular.

AM: A couple more questions and I think we can wrap for the day. One thing in the history of genetics, there was this critical moment in the late fifties and sixties where all these separate -- and we'll get back to this idea of fragmentation because genetics, even towards the beginning of the twentieth century, was very fragmented in terms of the statistical part of genetics, the more biological aspects in biochemistry and embryology and cytogenetics. By the late fifties, you're publishing, and you do return back to the research you did before you went to Uppsala where you just made these observations that people with hypercholesterolemia had --

KH: Those are some of my first papers.

AM: And you used pedigree analysis.

KH: Right.

AM: A very traditional approach to --

KH: That was helped by the master's course.

AM: It seems to me, from Uppsala you come back aware of all these other kinds -- and with the ability to use all these other tools of genetics. Why then choose cytogenetics as a tool you're going to use?

KH: Well, it was interesting. First, Marco and I tried to do chromosomes, and we semi-succeeded, not really very well. Then during my tour of all these genetic centers in Europe, one of them was [Jerome] Lejeune in Paris. I walked into this place, this sixteenth century hospital that he was working in, in this huge, huge hall, a ballroom practically, with very little stuff in it. There was this one little cubby with a monocular microscope sitting there, like from the thirties. And he's jumping up and down. This is in 1958. And he says, "I'm so glad you came! I've got to show you this!" And he showed me the first 47 chromosome Down Syndrome preparation that he had. And it was enormously exciting to look down this microscope and see what has produced this complex congenital syndrome. And it really was very interesting.

Then what happened, when I came back and I set up the tissue culture lab -- we had started working on using peripheral blood when I was still with Marco and tried it. And then [David] Hungerford in Philadelphia came up with the whole phytohemagglutinin business, so I immediately started using it. We were one of the first three or four labs in the States getting clinical chromosome studies done.

Of course, it also led me to a sidetrack, which was the whole lymphocyte biology business, which we can get into some other time, because that was a very exciting five or six years, I'll tell ya'. Many stories about that.

So it kept me interested. Then the techniques kept changing and improving. Banding came along and then molecular cytogenetics, FISH [fluorescence in situ hybridization] , and now CGH [comparative genomic hybridization], which is what I've been playing with the last few years, and all those kinds of things. So it remained a vibrant field.

But at the same time, I was working on a number of inborn errors. I was working on lysosomal diseases, I was working on this lymphocyte stuff. It was never enough. And I didn't believe that cytogenetics was a sufficient discipline, that really I was a human geneticist and I wanted it all. Whatever was interesting, let's do it.

AM: How did you learn all these techniques and incorporate it?

KH: The molecular stuff, for example, I went on sabbatical to Boston, Sam [Samuel A.] Latt's lab, who, unfortunately, was already very sick at the time, so I ended up more or less running his lab for the six months that I was up there. But I hooked up with a marvelous lady named Uma[Umadevi] Tantravahi, who is now in Providence [Brown University], who taught me how to work with DNA and how to do Southerns [blotting] and how to do all of those kinds of things. It didn't take very long.

KH: I was very nervous at the beginning. I'd never worked with DNA. And it turned out -- pipetting was pipetting and gels were gels. In fact, it was easier than working with proteins. So it was a lot of fun, and that's how I learned that end of it. The enzymology and the protein stuff, I really had begun to learn with Wilkinson already when we were playing with some of the lipids. You can't do anything if the technology ain't ready for you. And sometimes you help it along and apply it to what you want to do with it. You

can have all the ideas in the world, but if the techniques aren't there, you can't do them. And cytogenetics was there at the moment.

AM: In my experience in interviewing younger scientists just getting started on their careers, it seems to me that it would be frowned upon these days to go in all these different directions. Not only would your chair be wondering if you're going to get tenure or not but the NIH would probably be hesitant to -

KH: Absolutely, which is why the title of my long-range grant was "Mechanisms of Genetic Disease." And I could switch it every five years as to whatever I happened to be doing. Because remember, you don't really write what you're going to be doing, you write what you happen to be doing and then play on it. But I've never been able to stay totally focused on one thing without constant participation in the other.

AM: How do you think that's hindered or helped your career?

KH: Well, I think it's hindered to some extent. Some people, for many years, considered me a bit loose and not sufficiently dedicated to the advancement of one particular thing. I think I didn't care. In fact, I know I didn't care. I had fun. I always say that since I started with genetics in '56, there hasn't been a dull day. I was eating and had a roof over my head and a family, gradually. And I didn't really care about those opinions. If you did a few things well enough, you could get funding. And if you published some papers in decent journals, stuff like that. So I wasn't really worried about that end of it.

Belonging to the right organizations? Well, eventually you do-- I mean, I didn't make it into the IOM [Institute of Medicine] until I was a senior member. So what? I made it into all the medical things, Young Turks, Old Turks, and all this nonsense. And into the American Pediatrics Society. For example, a couple of people who thought I was perhaps worth it put me up for the Academy [National Academy of Sciences]. I told them, "Don't do it because I won't make it." I'm not a cut of that cloth.

AM: And why is that?

KH: Because the people who vote are really very, very sort of rigid, "this is what I do" kind of people. And they do it very well, obviously, which is fine. You need people like that. It's great. I've always felt, if I make a discovery, which I've been fortunate enough to make a few critical ones, the details often don't interest me. Lots of other people then take them up and will make a career. Fritz [H.] Bach has made a career out of the mixed lymphocyte culture and what came out of it. He started that in my lab when he was a fellow, and that's fine. I gave up on the whole lymphocyte stuff after about five or six years when I sort of milked it dry of new things. (laughs) Went back to genetics.

AM: And how successful were you in recruiting converts? You talked about proselytizing converts to your own lab to --

KH: I fortunately had this training grant, and I ended up with well over forty people coming out of the lab, of whom about three-quarters have one or another level of positions that deal with genetics, anything from chairmen to professors to scientists to whatever. So obviously, it was good.

One of the things in which I perhaps also differed from the regular people is, I had no objection to hiring ambitious young foreign graduates. A number of these are, and they all hold very good positions now. Some of them went back to their countries. One became a chairman in Japan, one became a chairman in Greece, one became -- and so on. Others are division chiefs, or whatever, here. Boris [G.] Kousseff in Florida, Eva Sujansky in Denver. These were foreigners who just struck me as being hungry and interested, so we helped develop them and it paid off. Then there are a number of Americans. Many of them I found very good. I just don't worry about these things. I think I'm a decent teacher, and I like teaching, so when these people come we spend time together and we talk about things, and we talk about their experiments. That's what mentoring is about, I guess.

AM: What is the difference between M.D.'s and Ph.D.'s who come into your lab now, or from the beginning and now?

KH: Not that much when it comes to the science. There's the big difference that the M.D.'s will actually -- they ask different questions. They ask questions that derive from their exposure to patients, and the problems they want to solve are based on some clinical reality, more so than the Ph.D.'s. The Ph.D.'s are interested in the problem per se. The M.D.'s want to solve the problem because it solves a question that they had about one of their patients or about a patient they read about. So that's the main difference.

Of course, the smartest ones these days are the M.D./Ph.D.'s. They're wonderful. They're absolutely wonderful. Not just because my son happens to be one. (laughs)

AM: Well, my last question today, because we just mentioned him briefly, but I know he's an important person in your life, is Harry Harris, because I'm not clear how you became in contact with him.

KH: When we did our tour, one of the places was London. Two people I had to visit in London were Lionel [S.]Penrose and Harry Harris. Penrose, of course, is the person who attracted some of the early Americans to come in the Galton Laboratory [at University College London], including Barton [Childs]. He was the first one who went of the group. He went to Penrose, he went to the Galton Lab. So I met Penrose, and we got along fine, but he wasn't really my style.

Then I went to the London [Hospital] Medical [College], which is south of the river in the poorest section of London. And there was this marvelous Laboratory of Biochemical Genetics [Medical Research Council Human Biochemical Genetics Unit] run by Harry Harris. And we immediately hit it off. I spent about a week in London and we spent much of that time with him and his marvelous wife Muriel. So that when three years later, in 1961, I took a sabbatical and went to him. He by then had moved to King’s College [London], so I spent a year at King’s College. No. I spent a half a year at King’s College. It was a six-month sabbatical.

Then in '71 when I decided to do another sabbatical -- and by the way, that's where I learned electrophoresis and I learned a lot of the enzymology, and I learned that from him, because he was the master biochemical geneticist. And in '71 when Rochelle had gone back to work already and we took the three kids and spent a full year in London on

a sabbatical. Again both of us now working in [Harris's] unit at the Galton, because by then he had taken over the Galton. Then he came to this country, to Penn [University of Pennsylvania], when he had to retire in England, and we saw each other many times. Eventually, unfortunately, I had to give the eulogy at his funeral. A lot of people didn't like him because he was ruthless in his sarcasm and his criticism, teasing. Rochelle sometimes would go crazy when he started teasing her.

AM: Were you spared this?

KH: Yeah, mostly, because I could give it as well as take it, and we reached an understanding very quickly. (laughs)

AM: Okay. Well, I think we've done quite a bit today, and I know I need to regroup. So I think we're at a good place to stop and we can pick up tomorrow.

KH: Okay.

AM: Thank you very, very much.

AUGUST 8, 2002

6. Minorities in Medicine and Genetics; Translational Research in Clinical Genetics; Balancing Research and Clinical Practice; Developing a Program in Medical Genetics at Mount Sinai School of Medicine

AM: It's August 8th, 2002, and I'm Andrea Maestrejuan with Kurt Hirschhorn in his office at Mount Sinai to continue his oral history interview in the Medical Genetics Oral History Project. I guess I'd like to start today with a couple of follow-up questions from yesterday. One is, what did your parents have in mind in terms of, when they were forced to flee, where they were going to flee, since you did have some relatives who headed to Palestine? Why were they set on coming to the United States?

KH: There were two schools of thought among those who made it out. They were headed really in two directions. The minority was headed for Palestine. The majority was headed for the United States, and they were among that majority. They had relatives here. They were not anxious for additional adventures.

AM: Were you a part of these larger discussions?

KH: No. That's not the way it was done. (chuckles)

AM: Then to move a little bit more forward, you had talked about, when you were going to medical school, that there were very few -- less than 10 percent of your class were women, and now it's more like 50 percent. I would like to ask you, what do you think accounts for the difference now, that more women are coming into the medical profession, as well as, what does this mean for minorities as well? Have you seen a change there?

KH: Yes, both. What it means in terms of what happened with women was that it was an early component of the attempt to integrate women into professions. It worked faster and better on the medical school level than it did, for example, in some of the other professions. Better than law admissions. Although law has now also caught up with it, about half and half almost in some of the law schools. But in medicine, it really took hold.

There's an old tradition of women in medicine. Not much in this country, but in the rest of the world, there is. So I think it was easier, in a sense, this understanding that, yes, women have practiced medicine for a long time. In Russia, the majority of physicians are women. So it wasn't all that unexpected that it would work. But at the beginning, there was great resistance, and in some of the specialties, to this day, there is resistance. You don't see many female urologists, orthopedists. Ophthalmology has begun to bend a little, but that was difficult for a while. Surgery took awhile.

AM: What about genetics?

KH: Genetics has had women in it almost from the beginning, almost from the beginning. There were some women who really were of my generation who were in genetics for a long, long time: Irene Uchida from Canada, who was the president of the [American]Society [of Human Genetics] the year before I was, and -- I'm blocking on her name. There was a wonderful woman who worked in retinoblastomas, who really was one of the first practicing medical geneticists around. She preceded me. But they were unique in that not many people were doing genetics, so they were sort of into this. Then later on, many, many women entered the field. Marjorie Shaw was one of my favorite ones, who also has been in the field for many, many years. So there have been a great number. I don't know why, but there was never a question in genetics of any real discrimination against women.

Minorities are a different business. Minorities are very difficult. We have, with great effort, in [Mount Sinai] and in some others achieved about a 10 percent minority student membership. And that with great difficulty. I don't think that there is the pressure on the kids to enter the professions; whereas, for women, this began to happen around the fifties and sixties. So it became much easier and it was not difficult to find them; whereas, minorities, you really have to go search. Many of them are superb people, and the best ones, of course, there's enormous competition for. Every school wants them. So it's not easy to find them.

AM: How has this worked within your own lab over the years, the composition between gender and minorities in your lab?

KH: If you look at, first of all, the list of my fellows, which you can find at the end of the Allan Award, you'll see that the majority are women. Not a great majority but more than half. I've always had women in my lab. I enjoy having women in the lab and as co-workers. It's a much more collegial thing, interestingly, to have them. More men look upon you, even when they're young and just coming in, as their competitor or potential competitor; whereas, women really are more team players in that sense. It makes it a greater pleasure, I think, to have them around.

Minorities? Yes, I've had a moderate but not great number. One of my first fellows, who got his Ph.D. with me is a guy named William [I.] Waithe, who now is in Canada,

who is black, relatively light black. There's an interesting story related to him. He joined me, actually, still at NYU and then came with me to Mount Sinai. And in the late sixties some time, when the test for Tay-Sachs carrier state came about because of [John S.] O'Brien's work in {University of California,] San Diego, we immediately set it up. I mean, it was a perfect situation. The largest collection of Jews in the world besides Tel Aviv, or something (chuckles), so we might as well do this.

So we set it up. The first thing we did was we tested the whole lab. Among the lab, there were a fair number of Jewish people, so we expected something. And one person of these sixteen or so people whom we tested came out as a carrier. But it was William Waithe. So I said, "William, we've got to do your sample over again." So we got another sample from him and I split it. I sent half of it to O'Brien and I kept half. And he was a carrier. I said, "William, I got to tell you something. All of us Jews were not carriers, but you're a carrier for Tay-Sachs." He said, "Oh, that's interesting." He came back a few days later, and he said, "I've spoken to my mother, and it turns out that my maternal great-grandfather was a Jamaican Jewish slave trader." And that's where he got his Tay-Sachs gene. And he says, "And now I understand why I'm so happy at Mount Sinai." (laughs)

AM: I'll ask you a real broad question. I was going to ask something similar later, but since it's come up -- because Victor McKusick also had a student who, just because he was in the lab and they were doing gene studies, he decided to do his own and came up with this very interesting mutation and, basically, made a career of it. So it seems like there are these instances where it's just kind of personal, anecdotal perhaps, observations [that] create these opportunities. In terms of what drives genetics, perhaps when you were starting out and maybe now, is it -- because for you, in the clinic, you noticed these family histories of people with cholesterol problems and it prompted you further. But now we also have new techniques that your basic scientist, who has no clinical experience, can come up with discoveries that have major implications for clinical work. So what do you think drives genetics forward?

KH: Well, one of the things -- and I say this, actually, in my Allan Award address -- I say that clinical genetics is an opportunistic specialty, and the discoveries are made on the basis of serendipitous observations, in the clinic or at the bedside, that you pursue. That's how most genetic diseases have been studied, because some astute guy asked the right questions about the family, and there it was. Then you can pursue it.

It's the beginning, really, of what I consider genetics as a perfect model for, which is -- nowadays they give it a fancy name of “translational research” -- but of taking a clinical observation, bringing it to the lab, and then trying to bring it back to the patient in the form of counseling, therapy, whatever. And genetics lends itself to that very well.

AM: Where does basic science fit into your work?

KH: You read a lot and you learn what's happening, and you apply it as best you can. You interact with basic scientists. I've had plenty of Ph.D.'s in my lab that have come up with great ideas when you start discussing stuff. And a number of them, interestingly, then went on after getting their Ph.D. in the lab or doing a post-doc, go on and go to medical school because they suddenly are bitten by this bug and realize that they are limited in what they can do.

AM: Okay. You brought up translational work, and that was one of my last follow-up questions. Translational research is something more of a current term that we use, but it seems like your generation -- what was it about your generation of colleagues within your medical school class, or within the lab, or within this group of people who met in '58 in Colorado to establish this college--

KH: No, the college wasn't established by them. It was the field that was established. The college didn't come for a while later, many years later.

AM: So what was it about your generation that you were able to move to this middle ground between pure clinic and pure bench science?

KH: I think that it was a trend that was happening in medicine anyway. It was happening in several subspecialties. And it was thanks to the close interaction of scientists and clinicians. In the fifties was sort of the beginnings of that, when NIH really began to hand out money for doing research, and Ph.D.'s and M.D.'s started to interact in a lot of this research.

An example in another field, when I was a medical student at NYU, the head of physiology was a man named Homer Smith. Homer [W.] Smith was a famous physiologist, an excellent writer. He wrote all the books about the lungfish and all those kinds of things, of how land animals developed from water animals. He was an expert on renal function, and he established, really, until today I would say, the majority of principles of how the kidney works. We had some excellent clinical nephrologists who started working in his lab and began to apply this to the study of renal disease. So there was this opportunity offered at that time, because of the availability of research money, of merging lab science and clinical work.

And I think it was a general thing. It's just that genetics, once again, lent itself so well to that. And the techniques in genetics, which had sort of already been established to some extent -- chromatography, electrophoresis, enzymology, and eventually chromosome work -- the techniques lent themselves to this merging of clinical and laboratory work. That's what kept it exciting.

AM: In your address, you did make the plea to M.D.'s and M.D.-Ph.D.'s to always keep hold of the clinical aspects of their work. But it's also increasingly more difficult. I've interviewed several M.D.-Ph.D.'s who ultimately have to make a choice of whether they're going to have a bench science career or they're going to have a mediocre bench science career and keep a clinical --

KH: Okay. I disagree with that totally.

AM: How do you see them overcoming these pressures?

KH: The thing is that they are pressures -- and some of my colleagues are responsible for them, who make this conclusion that it's not possible to do both well. And it's not true. I see lots of them. I think people should be permitted to choose of which they want to do and talk to a lot of people and come to a conclusion, but they shouldn't be pressured into one or the other. And I've seen them go both ways. I've seen M.D.- Ph.D.'s give up their lab, and I've seen M.D.- Ph.D.'s give up their clinical work.

But there are plenty of them around who do both. I hate to use personal examples, but my son is an example. One day a week he's a clinician, a clinician independent of his genetics work, except he may pick up stuff from a patient or something, especially now that he's gotten into diabetes and obesity. But he's a clinical endocrinologist that one day a week, and he sees lots of patients, and he gets involved, and he teaches fellows how to deal with patients and residents. And four days out of the week, he's in his lab.

What my advice to people when they come to me and say, "Hey, I've been told that you can't do --" "You know that in the first few years after your fellowship, you're going to have to spend the majority of your time in the lab, but don't make it 100 percent. None of the grants for career development of scientists say 100 percent. They all say 75 to 80 percent. Keep that 20 to 25 percent and continue teaching and seeing patients. But spend most of your time in the lab those first few years. If you're successful, you'll get some grants, and when you get some grants, you'll be able to hire people with the money from those grants to do a lot of the routine work that has to be done as part of research in the lab and which takes up a lot of your time. So if you hire these people and train them properly and they do your work, suddenly you find out you can in fact do a third of your time, or even a half of your time in clinical and teaching and still be successful in your research."

I am always disturbed when I hear these necessary choices and that you can't do top-notch work in both. Or that you diminish your science work by going and seeing a few patients.

AM: And why is there this pressure? Why do some of your colleagues put pressure to make this decision? And what is it about the funding situation that many physician-scientists work under that puts this pressure on them?

KH: I think a lot of M.D.- Ph.D.'s have gotten all their research training from Ph.D.'s. Some of those training experiences are very negative insofar as the clinical aspect is concerned. Their preceptors in those departments resent it when they go think about patients, or they go and see an interesting patient, or get called by an old patient of theirs who needs something, or something like that. It's one of the reasons that, for a number of years, I ran the clinical advisory committee for the M.D.-Ph.D. program in this school, where I hooked up every M.D.- Ph.D. student during their Ph.D. time to a clinician who also does research and made sure that at least a couple of times a month, they sat down together or made rounds together and kept them aware of the fact that they also are getting an M.D.. Then I also ran a catch-up physical diagnosis course before they went back to the wards, because they were always very nervous and shaky about that. But that's how we have succeeded with many of them, in getting them into sort of a mixed career.

AM: For genetics in particular, if they choose this as a specialty, how is this more or less essential to keep the clinicians --

KH: Let me give you an example. Bruce [D.] Gelb, who is one of our recently made professors, who came here, actually, straight out of his fellowship at Baylor [University] with Ed [Edward R. B.] McCabe when he was still at Baylor, did a prolonged fellowship down there of three years of cardiology and a last year of cardiology and an extra year of

genetics. So he's a union member of pediatric cardiology, but he's also trained in genetics.

He came here and we gave him a double job in cardiology and in genetics. Now, this guy has succeeded beyond anybody's dreams. He just found the gene for Noonan Syndrome. He's found a number of other genes. He's done really phenomenal basic work in genetics. Meanwhile, he's in charge of the pediatric cardiac transplantation program, and he has a very committed participation in cardiology, and at the same time, he runs a successful lab with a couple NIH grants and does beautiful work. He's an example of why it's so important. A number of the things that he has discovered -- not the initial ones because he was just trying to get in and do something -- but the last few things have all been genetic aspects of cardiac disease in kids.

AM: Okay. Well, M.D.-Ph.D. programs are a relatively new thing, and there aren't that many programs in the U.S. They have to decide, as an undergraduate, that this is what they're going to commit to, and it's highly competitive. What are the mechanisms in place once a medical student gets into med school to encourage them to do bench work. Or Ph.D.'s. What is the chance that a Ph.D. might be convinced to pursue an M.D. degree?

KH: The last one is, again, a matter of right place, right time. The Ph.D. who goes to medical school, happened to be doing his Ph.D. in biomedical sciences, gets turned on. That's a separate question. The medical student is interesting. Many schools, particularly the better ones, have programs that offer often an extra year in the middle of medical school to do a research project. The [Howard] Hughes [Medical Institute] has funded a whole program where in the middle of medical school you can go down to NIH for a year and do a research project and then carry it on when you come back, when you have time in your last two years. And remember, the last year of medical school is a waste of time. I mean, you've got lots of time to do things.

So those that get turned on, get turned on. Then they'll go on and do their fellowships and do their research during their fellowships and look for a position. And there's lots of positions for these people available. They're not that common, the people who really have learned the equivalent of a Ph.D. level lab experience and learned how to properly do research. There aren't that many. So when somebody has succeeded and gotten a couple of papers out of their medical school time and then in their fellowship time, they'll get a job and they'll get grants.

AM: Within your own experience of training med students -- and perhaps you can talk about how many Ph.D. students have come through your lab -- have you been able to identify certain people who you think might be --

KH: Absolutely. They come often in their first year, and they say, "I'm interested in this stuff." We all have what we've done on the internal Web. And the students, the ones who are interested, go through and they see what turns them on. They'll come and see you and say, "Hey, can you tell me more about what you're doing? Can I do an elective to see what's happening?" Those are the guys you latch onto and encourage and make things possible for them and take them to meetings and expose them to what's happening and continue to turn them on. You don't always succeed, but when you do, it's terrific.

AM: Okay. Well, to go back, I guess, to where we left off yesterday and return a little bit to the chronology of your career, you left NYU in '66 to come here to Mount Sinai.

KH: Right.

AM: Why did you make the switch?

KH: Okay. There are many factors involved. At NYU, I had a total of eight hundred square feet of space, had a big NIH grant, and had fourteen people. Doesn't work too well. We were beginning to work shifts in the lab. (chuckles) Space was at a premium. We didn't have the new buildings yet, so I couldn't persuade them to give me more space. Until that moment, I had never gotten one red cent towards my salary from NYU. I raised it all myself from grants, from career awards, from this and that. So while I was loyal to the place, I certainly didn't feel appreciated (chuckles). So I was getting fed up.

The interesting thing that happened earlier that year at some point, it was the year that we bought a piece of land on the Cape. We had been going up there and renting for a while, and we became very friendly with the guy who found the piece of land with me, who was the chief selectman for Wellfleet [Massachusetts], Henry Atwood from one of the Pilgrim families, Atwood. Marvelous man, who began to work on me to give up all this stuff and come and be -- they needed a doctor in Wellfleet. Rochelle and I talked about it. It seemed unlikely, but it sounded enticing. Suddenly, I figured, if that entices me, I really want to get away from where I am.

So I sort of made it quietly known that I may be looking, and several jobs arose, some rather good ones, all out of town. We didn't really want to leave New York. At that moment, a new school was being founded. Mount Sinai got their charter in 1966 to become a medical school. I had been doing the genetics work for Horace Hodes, who was the chairman of pediatrics. When they had a puzzling case, I used to come up here, and I did chromosomes for them, diagnostic stuff, counseling, whatever. So he knew me very well. And in their planning, he was one of the two major faculty planners for this new medical school, he and Hans Popper, who was the chairman of pathology.

One of the things they realized was that there's this new field and they've got to have it. It was genetics. So he called me, and he said, "I'd like you to come up here and talk about possibly coming up here to set up a genetics program with this new school." So I came up, and we chatted. I met a few of the other people here and that's how I ended up in the Department of Pediatrics, because he was the most welcoming. He offered space, he arranged for [Henry M.] Stratton, who was a publisher and who gave a fair amount of money to this institution, for him to give a hundred grand to outfit a lab, to convert what was really unused patient space into a lab in an old building.

Then I met with the other leadership of the place, the hospital director and the first dean. The first dean was George James, who until then had been the Commissioner of Hospitals, maybe Health, maybe both, for the City of New York. A highly respected community medicine type. So he became the dean. I had a discussion with him, and it all sounded terrific, so I pretty well decided this is what I'm going to do.

I came up just before to finalize things and met with James, and we shook hands on the whole thing. He said, "By the way, we've never discussed salary." Now, you have to

understand that at that point, I was making nineteen thousand dollars as a career scientist of the New York City Health Research Council, which he was one of the founders of. That was where my salary was coming from. It was nineteen, and I knew that if I stayed at NYU, it would go up a thousand dollars a year. That was the agreement from this career scientist. So he says to me, "What do you think your salary should be?" I figured to myself, Well, if I stay at NYU, I'd make twenty, so I'll give myself a big raise. So I said, "How about twenty-five thousand dollars?" He looks at me and he says, "I wouldn't pay a full professor less than thirty." I said, "Fine, give me thirty." That's how I came to Mount Sinai. (chuckles)

AM: I can see where it probably wasn't a difficult choice.

KH: (laughs)

AM: What was the level of commitment to genetics at NYU in general?

KH: Well, the commitment was entirely dependent on the availability of outside money. So the training grant was the training grant, and that's how we taught people and had fellows, almost all of whom worked with me. My research grant was my research grant. The school didn't contribute anything. We taught a course, and set up counseling work and the clinic, but they didn't pay for any of it.

AM: What about lab space here?

KH: Well, I got this rather nice -- two labs, actually, in two different buildings. I got the lab for tissue culture and cytogenetics, which was from pediatric space, this unused patient space, which amounted to about two thousand square feet. Then for the biochemical work, I got some space in another building, which was empty, of another maybe thousand, so I ended up with about three thousand square feet, which was quadrupling what I had before.

AM: Were these new labs starting from scratch?

KH: No. They were -- well, the pediatrics lab was totally redone with that hundred grand from Stratton, which then became the Stratton Laboratory. I think the plaque is in fact now out here somewhere, although it's no longer -- that wasn't the lab.

AM: What were the other institutions you were possibly considering going to?

KH: UCSF [University of California at San Francisco] had a chair in genetics, which was meant for human genetics. I had a very good friend who was working out there at the time, [H.] Hugh Fudenberg, who ran immunology. Holly [Lloyd Hollingsworth] Smith, who was the Chairman of Medicine, ran a search committee and asked me to come out. I went out. The atmosphere was terrific. Great school even then.

It's much better now, but even then it was obviously good. But it turned out that this whole thing consisted of an office and a secretary and a salary. And there was nothing else with it. So that wasn't for me.

[University of California,] San Diego, I went out twice, actually. It was formed then.

AM: I was going to say, it must have been brand spanking new.

KH: New school with a totally new idea that all the basic sciences were going to be one department. The vice-dean who was arranging all this stuff was a guy named [Robert N.] Hamburger, whom I had known for a long time. So he asked me to come down and look at genetics down there. And it was all very vague. To this day, genetics in San Diego is the most fragmented thing in existence. It has never jelled. Some good people, but it has never jelled. Mike[Michael M.] Kaback tried to pull it together when he was chairman of pediatrics.

He's a geneticist, as you probably know. And he never succeeded. So that was San Diego.

Then I went to Chicago. They were also starting a new school, or reinventing a school, Rush [Medical College], by taking two of the big hospitals in Chicago and making them into a medical school with an old name. They offered me a double Department of Genetics and Immunology with enormous brand new space. But I couldn't see myself in Chicago. (chuckles) It was a good job, it was a very good job. Rochelle didn't even come with me to Chicago. She went with me to San Francisco and to San Diego to look at what was available for her, but she didn't even come to Chicago.

Those were the major ones, but there were probes from other places.

AM: Was that a sign that half of the partnership was going to be reluctant to move to Chicago no matter what?

KH: Right. We have a long-lasting -- we can get back to that when we're both there -- commitment to, if one of us retires, the other one retires, and we've got to both be sort of okay with being in a place. And Chicago wasn't going to do it.

AM: What has kept you here at Mount Sinai?

KH: First, it was primarily Horace Hodes, whom I have enormous respect for, who also understood me better than a lot of other people. For example, I was here a week and he said, "Six months from now you're going on service in pediatrics." Even though I was not trained in pediatrics. So I spent the next six months following around some of the senior pediatricians and reading textbooks, and it worked out. And as I said, ten years later, they thought I was a pediatrician and they made me chairman.

Horace was enormously supportive and a pleasure to be with and allowed me to expand as much as I could. By the time I took over the department as chairman -- it was a small department, actually. We had maybe fifteen or sixteen full-time faculty in the department, of whom nine were on my grant. So I spent the next five years bringing it up to fifty full-time people in all the subspecialties and built the department. But it was Horace.

And then, of course, the commitment to building a first-class Department of Pediatrics, which was a different effort. But the first ten years of it were really a lot of fun. Tough, but a lot of fun. After that, it became pissing on brushfires and I tried to get out of it. (chuckles) And it took another almost ten years before I could work my way out of it.

The deans kept giving me stuff to keep me in the chair. "What will it take for you to stay in the chair?" So I'd write these letters that I want this and this much more money on the budget and this space, and so on. They said, "Okay." So I stayed.

Then eventually I just had enough of it, so I quit in '95.

AM: Now you're just a professor of genetics.

KH: Well, I'm a professor in three departments, actually. I'm a professor of pediatrics, human genetics, and medicine.

7. Overview of Research Program; Opportunities and Explorations in Immunogenetics; Impact of New Technologies in Medical Genetics; Pre-Implantation Diagnosis

AM: Okay. I want to talk a little bit about -- to go back to your science over these years, and it's going to be brief and very general questions. With this [1958] meeting and your own work with cytogenetics, you were a committed geneticist. But then you start working with lymphocyte activation and publish quite a bit in the field of immunology.

KH: That's an aspect of opportunism. What happened was that we kind of became interested in what these cells were that we were watching replicate. You throw in the phytohemagglutinin to make them replicate and then look at the chromosomes. But if you looked at the cells while they were doing this and looked at the cells when you had them fixed under the microscope, the cells were these large round mononuclear cells. I had, not long before that, read a very interesting paper by a guy named [Sir James L.] Gowans, who eventually became the head of the Medical Research Council in England, who worked on a thing called "graft versus host disease," which is what happens if you give somebody an organ graft that is not compatible with them. Not only do you reject it, but if you don't reject it, the graft, or the immunological cells within that graft, attack you. That's graft versus host disease, which can kill you. Often you get over it, and almost everybody who gets a graft gets some of it. The cells that cause this attack are called GVH cells, graft-versus-host cells. They looked identical to the cells that we were looking at when we stimulated cells with phytohemagglutinin.

So first we did a couple of experiments in which we proved that the cells that were growing were lymphocytes. That was just a fun thing that I had learned in my fellowship in Sweden, that you can separate out lymphocytes from polys [polymorphonuclear neutrophils] by feeding the polys iron filings and using a magnet and fooling around, which was kind of neat. (chuckles) So the lymphocytes were left, and you put the phytohemagglutinin into them, and they grew.

So we knew they were lymphocytes, and they looked like these immunologically very active cells. But the dogma at that point was that the peripheral blood lymphocyte, which is what we were using, which is a small cell -- it's a small round mononuclear cell -- was an end cell, that it didn't do anything. It was finished. It's life was done. It was just circulating around but it wasn't doing anything. Well, clearly, it was capable of doing something because it grew and it looked like an immunologically active cell.

So I figured that maybe these cells do react to antigens and maybe they have a

memory in them for these antigens. We started doing some experiments in which we threw tuberculin in from people who were or were not PPD [purified protein derivative test] positive, tuberculin positive when you get your skin tested. And in fact, those that were positive, the cells grew, and those that were negative, the cells didn't grow. So clearly, they were memory cells.

Then I had a fellow who was named Nemat Hashem. She was an Egyptian pediatrician geneticist, who became a friend of the chairman of pediatrics at NYU when I was there and asked him whether he could arrange for her to come and do some work at NYU. He approached me and said, "Would you take her? She wants to learn some tissue culture genetics." One of her interests had been eczema. By this time, we knew that the cells were capable of responding to this, that, and the other thing, so we said, "Why don't we take some skin cells from eczema patients and non-eczema patients, culture them up, and put their own lymphocytes on and see if the lymphocytes respond. It's suspected that it's an immunologic disease." This was a long time ago, before it became clear. "And let's see what happens."

And yes, lo and behold, the lymphocytes responded. But the interesting thing was that, if we -- as controls, we mixed the lymphocytes from the non-responders into the eczema skin cells, and the lymphocytes simply responded to skin cells when they were crossed over to somebody else's skin cells.

KH: That's when we started thinking of the thing called the mixed lymphocyte response as a possible test for graft compatibility, which was kind of a genetic thing, taking the lymphocyte thing to genetics. So we did it, and in fact it worked. And played another few years with a couple of games with lymphocytes, and that was enough. Immunology, it can be a fun field, but it's exquisitely Talmudic. (laughs) No matter what happens, there can be seven different explanations, and it's if, but, and, and so on. And I got a little tired of it and went back to just the genetics.

We were doing genetics all along through this but eventually dropped the lymphocyte stuff. Did a number of papers actually with Rochelle in lymphocyte biology, immunology, because she was, at the time, working with the Division of Rheumatology, which is closely related to immunology.

AM: Did you consider this foray into immunology as a tangent to what you were doing, as an integral part of what you were doing? Were you trying to force the genetics sub-theme to your work?

KH: I don't think I ever thought of it that way. As I said, there was this observation, decided to follow it up. I almost got totally destroyed by it at one point because when the first word got out about lymphocyte responses in tissue culture and mixed lymphocyte, I was invited to NIH to the big hall to give a talk. I was a young assistant professor at the time. This was 1963. I give this talk and I end up by saying, "As opposed to what we were all taught in medical school, it looks like the peripheral blood lymphocyte is a memory cell." That's how I ended up.

And there were questions. Then some old guy in the back of the hall gets up, and he says, "We who have been in immunology for many years know that the small lymphocyte is an end cell" and sits down. There I am in front of these hundreds of

people (laughs), what was I going to do? I said, "Thank you." (laughs) I was shook. There's this guy, an old immunologist, and he doesn't believe me.

AM: What was your reaction when you went back to your work? Did that influence --

KH: No. I forgot about it rather quickly because, meanwhile, other people had picked up on it and papers were beginning to come out. Within a month of our publishing this whole thing, two other groups came out, one with the antigen responses and another one with the mixed lymphocyte culture. So clearly, it was quickly replicated.

AM: Since the old immunologists were clearly seeing you as a dilettante, how was this core of geneticists, who you had just been invited into the inner sanctum a few years before to attend this meeting, reacting to your work?

KH: They didn't pay any attention to it. They were interested in what I was doing with chromosomes and what I was doing with some lysosomal diseases, and that's what I presented at the genetics meetings. I presented a lot of the lymphocyte stuff at immunology meetings. I submitted papers, I was invited to give papers, and so on. But it was really a totally separate group. Some of them became very close friends and I did some work later with them. This is how more Rochelle than me got involved in inherited immunodeficiency diseases. She did all the work on ADA [adenosine deaminase], and she and I have now written, I guess it's the fourth version in this book, the [David L.] Rimoin thing on immunodeficiency diseases [Emery and Rimoin’s Principles and Practices of Medical Genetics]. So it was still a little bit connected.

AM: Yeah, okay. And I want to get to this issue -- it of sounds like you're forcing these issues together -- what was the state of immunology, the relationship between immunology and genetics at that point?

KH: Immunology, at that point, didn't believe much in genetics. The only guys who began to believe in it were really the guys who were involved in histocompatibility. They recognized that this is clearly a genetic phenomenon. But ordinary immunology, remember that in those days, it was thought that the whole determination of the immune response was antigen dependent, that the cells were just responding willy-nilly depending on what the antigen was that came around. It wasn't until people like [Baruj] Benacerraf who worked down the hall from me at NYU, came up with that there were strains of mice who couldn't recognize a particular antigen and that, therefore, there had to be some kind of mutational event going on. So they were beginning to think genetically.

But the field that really began at that time, and that I think our stuff had a significant influence on, was the field of cellular immunology, which almost didn't exist then. It was all antibodies and stuff like that.

AM: You mentioned yesterday that one of your students -- and I'm going to assume it was the same student who was working with you on the lymphocyte --

KH: Made a career out of it.

AM: Made a career out of it. But you kind of dropped it.

KH: Yeah.

AM: In particular, what was it about this particular research program that you didn't find interesting anymore, and what, in general, kind of drives you?

KH: It became involved in what I said before was sort of the Talmudic aspects of immunology. It became extremely complex, and to get hard facts that one could work with was an enormous amount of work. The field of immunology was populated by many, many people. They were doing this stuff and some of them were doing it very well. But the things that were exciting, that were moving fast, were the advances in genetics. So why bother with -- (chuckles)

AM: Right. Okay. I would like to ask a couple of very broad and general questions.

KH: Sure.

AM: One is that I notice -- and it could be just an artifact of the selection I made in looking at your repertoire of publications -- is that you have many publications that evaluate technologies, particularly in cytogenetics. I was wondering, what do you consider your strengths and your weaknesses as a scientist? Is it moving existing technologies forward? Do you see yourself more as a thinker, a theorist, rather than a technologist? Or do you see yourself as a technician?

KH: No, none of those. I think my strength is in recognizing a new technology in terms of its potential for solving problems I'm interested in and applying it that way. Sure, making sure it works, which is evaluation of technology, but applying it to a problem. Let me give you as an example the most recent paper that we currently have in press. I think it's an ideal example as an answer to your question.

For a long time I have been convinced, and there are data that have developed over time from other places, that the vast majority of fertilized eggs dies, that no more than 25 percent of fertilized eggs make it, and that a majority of those that don't make it are chromosomally abnormal. Very difficult to prove all this.

Well, a few years ago, Brynn Levy, who is now a young faculty member, did his Ph.D. with me, stayed as a post-doc, is now here. I had gone, in 1996, on a sabbatical. Rochelle and I both went. We spent three months in San Francisco and three months in Boston. The reason for that, obviously, was because we have kids in San Francisco and in Boston. (chuckles) In San Francisco I worked with a crew that was led by Joe [W.] Gray and Dan [Daniel] Pinkel, who were sort of the molecular cytogeneticists of the world. They got a big prize last year at the [American Society of] Human Genetics meeting. This new [Curt] Stern [Award], which I partly nominated them for. They worked out a lot of -- FISH -- without them, there would be no FISH, okay?

Then, shortly before I got there, they described this new method called CGH, comparative genomic hybridization. So I went out there, and one of their young people in the lab, I sort of latched onto her, and she taught me how to do it. We did a couple of bits. It was only three months, but I learned how to do it, CGH.

So I came back, and at that point, Brynn started his graduate student work with me in

cytogenetics. The first thing I did was I sent him out to San Francisco to also learn CGH, and we started a bunch of experiments. His thesis was on the CGH of uterine cancer cells and a variety of things like that.

We are now probably sort of the reference lab for people who can't figure out something with some kid's chromosomes or something that might be helped by CGH. They send us the stuff and ask us.

But then, I wrote a March of Dimes grant application in which I said, "Really, this thing could be very helpful for in vitro fertilization (IVF)." The best they could do at that point was to take an eight-cell embryo after IVF, take off a cell, and do FISH on that cell for maybe five chromosomes so that the most common abnormalities that lasted through pregnancy and were compatible with the birth -- Down Syndrome, sex chromosome abnormalities, and so on -- could potentially be detected in that embryo and you don't use that embryo for implantation, you look for ones that are normal, using FISH.

Well, that was not good enough because lots of other things were going to happen. Of course, what we realized was that if my assumption was correct, the fact that there's only some 20 percent success in IVF, which is the reason they put in four or five embryos and you end up with quadruplets and triplets, is that the reason for the failures could well be the chromosomal abnormalities that they weren't detecting, because they were only looking at five chromosomes. So since CGH allows you, on a molecular basis, to do a complete karyotype without looking at the chromosomes, the possibility was there to look at these cells from the embryo and see whether other chromosomes were abnormal, and if they were, you don't put those in. And the success rate should immediately rise and the need for putting in multiple embryos, more than two perhaps, should diminish. So that's why we started on that.

Of course, it required the rather difficult business of amplifying the DNA from one of those cells so that you had enough DNA to do CGH, for which you need -- not a test tube full, but you need a decent amount of DNA to label with a color so that you can then do this comparative hybridization.

We were working on this, and there was a young guy also in England working on it at the Galton Lab, [Dagan] Wells. We both came out more or less at the same time with some reasonable successes. Then, Wells came over and started working at Saint Barnabas [Medical Center] with a guy who probably runs the most successful IVF service around, Santiago Munné, and they were beginning to try to use this in a clinical way in his service. So I said, "Why don't we look at polar bodies?" I don't know how much biology -- you know of egg formation, right? To make an egg, you've got the oocyte and it splits in half, and half of it becomes the egg and half of it's the polar bodies. And if there's a chromosome too much in the egg, it will be missing in the polar bodies, and if it's too little in the egg, it will be too much in the polar bodies. "Why don't we look at polar bodies before they do anything and see if we can predict that the egg will be abnormal and, therefore, the embryo will be abnormal? And by the way, we may be able to find out what the real frequency is of chromosomal abnormalities early on." So we did ten polar bodies and nine were abnormal. Then we tried to fertilize the eggs that were the partners of these polar bodies, and several were so abnormal that they didn't even take. And of those that took, where we could check, the prediction from the polar body was, in fact, right in the egg. So it confirmed the high incidence of chromosomal abnormalities in the early embryo because of these abnormalities in the egg. I'm sure

there's some in the sperm too, but it's mostly egg.

And it potentially provides a method of pre-implantation diagnosis where abortion doesn't even come into the situation, because you don't even have to make the embryo, if this turns out to be right and is verified with a larger number. Of course, you can only do it with IVF. You can't do it in a regular -- but if this thing works and if enough fetal cells can be found in the maternal blood stream, which -- they're there but still not a very reliable thing to find them, but if we could find them reliably, with this method, finding them in one cell, we can then make a noninvasive prenatal diagnosis probably in the seventh or eighth week of pregnancy.

It's a matter of taking a new technology and applying it to real clinical problems. So that's a long-winded answer to your question, how do I look upon myself as a scientist? (chuckles)

AM: To use an example that I found interesting was, in the early seventies, you published a paper discussing the uses of computer technology for genetics, and in the last couple of years, you've published a couple of things on association studies using computer technology. It seems to me that in the early seventies that was probably not a technology being used widely in genetics. But certainly has pushed the genome project forward.

KH: The first interesting computer technology I had was because I was asked to be on a committee by NIH to look at -- several companies had started to work on computer karyotyping. So they asked me to get on this committee to evaluate whether this was worthwhile. So I reviewed some of it. That's actually what that paper in the seventies was about. And it was not very good. In fact, there's a very amusing story. Around that time, some of the population epidemiologists up at Columbia wrote a paper in the Lancet in which they said, "Why are we hesitant to do amniocentesis on everybody? Because that way we could really eliminate all Down Syndrome, because most of them are born to younger women because they have so many more children. Let's do prenatal diagnosis on everybody. People say it's too difficult, but now that computer techniques for karyotyping are available, probably this could be automated."

A couple of issues later, a friend of mine named John [H.] Edwards, who is now the head of genetics at Oxford, wrote a paper -- he's a very amusing guy -- he wrote a paper back. First he critiqued the whole amniocentesis stuff for everybody, with the risks. Then he said, "As to computer chromosome diagnosis, hope in the face of years of failure is no guarantee of success." (chuckles) Because people had been trying that, at that point, for about five, six years already, and nobody really had succeeded. Now it's routine. That's how we do our karyotyping.

AM: So in the early seventies, this wasn't you grasping onto this great -- foreseeing great things?

KH: No, no. And the use of computers for straightforward genetic studies now -- which is now routine and this big paper I published with my son earlier this year is an example of it -- is once again, I think, the same kind of thing. Here's this very powerful technology. Now, what practical use can one make of it? And some of it is also a little bit of destroying false concepts to some extent.

Just because you can show associations using a computer program doesn't mean that they're true. That's what this paper was about, showing that, yes, there were 5 that were very strong, another 20 that were probable, and 180 of the ones we looked at that had zero evidence.

AM: Do you see your role then as kind of the damper effect?

KH: Partly. Partly. I occasionally have to catch myself when I get too enthusiastic, so it's easy for me to see when people are being over-enthusiastic about something too soon.

8. The Legacy of Eugenics; Ethical, Legal and Social Implications of the New Genetics; Formalizing the Field of Medical Genetics; Fragmentation in the Medical Specialties

AM: You mentioned abortion. You've written, across the years, many articles on discussing the role of geneticists and their ethical responsibilities. You've certainly entered the fray on the issues of abortion. You've discussed a lot about the risks and benefits of amniocentesis, not only in terms of the technology but in terms of the more social implications about it, the physician's responsibility in terms of genetic information given to patients. How far removed are we from this notion that genetics is really some alternative form -- that the new genetics is some form of the old eugenics? And have we really moved into a new paradigm where we don't have to worry about the broader social implications of what human genetics means or can do for the future? From the sixties through today, you have several representative publications discussing in a larger audience form of publication these more public policy issues. You even mentioned health care and universal access to health care and what it means for the geneticists.

KH: Let me go to the core of it first and say that, no, we never can stop our watchfulness of what use people make of genetic technology. The current example, which isn't so current, is cloning of human beings. I mean, there are people running around testifying before Congress that they've cloned human beings. They're lying, but nevertheless, look what this does to the image of the field. There are these mad scientists doing eugenics all over again and making Frankensteins, and all this sort of stuff. So one has to watch it all the time.

Let me maybe broaden it a little bit. My interest in this kind of stuff derives from many years ago when I was invited to give a talk at Marymount College in a symposium that was put together by Dan [Daniel] Callahan, who eventually became the president of the Hastings [Center], and we'll get to that in a minute, who at the time was the editor of Commonweal magazine, which was the sort of more liberal Catholic lay publication. He had organized this symposium, the theme of which was remaking mankind. It was quite a phenomenal thing. Ralph Ellison talked about the impact of minorities and trying to remake people. [Abraham] Maslow talked from a psychological point of view trying to make everybody a Type A personality. I forget the man's name who was then the Chancellor of Schools, a black guy, very wise guy, who talked about education.

And I was assigned genetics. I wrote a thing that now has been published in three

different places, in which I get involved and talk about cloning, I talk about eugenics, I talk about all those kinds of things and end up with a statement that we should worry about these things and we should discuss them before they happen, because what can be done, in the long run, will be done.

Dan [Callahan] and I sort of remained in some contact. Then when he and Will [Willard] Gaylin, who is a psychiatrist, decided to explore the question of structuring an institute on bioethics -- they called it originally the Institute for Society, Ethics and Biology -- and invited me, along with three or four other people, to meet in Will Gaylin's living room once a week in the evening to discuss this. We spent a year at this. I used to come home all excited, and Rochelle used to say to me, "You guys are crazy. It'll never work." (laughs) "Nobody will give you the money. People don't care about it."

But we persisted, and more and more people were invited into this thing as it developed. Then we decided to go apply for money. The institute became real and here it is. It's still there. So that's how I began to be interested in these kinds of issues. And then was involved in a number of projects with the institute.

Because of this, I sort of began to read in ethics. I really knew nothing, I never got a degree in philosophy. Then about twenty-eight years ago, or thirty maybe, I was asked to run the Ethics Committee for the hospital here, for the medical board of the hospital. So I've been doing that ever since, and I'm the chairman of this now twenty-five member committee. It used to be just me and a couple of ad hoc people whom I'd drag together when questions arose. Now it's very formal.

It's required by the JCAH [Joint Commission on Accreditation of Hospitals]. So I've been doing all that and teaching the ethics course here.

So I've gotten myself involved in those things and, of course, obviously thought about them in relation to genetics because that's, after all, what my field is. So that's where all this stuff comes from.

Yes, I am concerned that people do things too rashly and that they don't think them through. I'm concerned about patient rights, not just from a genetics point of view, but it certainly becomes very obvious in the genetics point of view. Just because you've got a BRCA1 gene [breast cancer 1 gene] doesn't mean that you willy-nilly test every woman without her understanding what is going on and what the outcome of that test might be. Ethical principles of prenatal diagnosis that we did out of the Hastings back in the early seventies in the New England Journal[of Medicine], and a variety of other things like that. It's been a hobby of mine, more or less.

AM: What was the motivation and/or intentions when you jump into an entire other area of behavioral genetics with the chromosome aberrations and its relationship to criminality or aggression?

KH: Oh, well, that was some interesting stuff, yeah.

AM: That must have been very provocative.

KH: That was an interesting story. What happened was that there was an increasing to-do about XYY, which was clearly a chromosomal genetic problem. Guys who were walking around with an extra Y chromosome that were very big. Pat [Patricia A.] Jacobs found the first patients like that in Edinburgh [Scotland] in a school for the criminally insane. She wasn't looking for them, she was looking for Klinefelter Syndrome patients, who are XXY, was screening for them and did it with a very simple technique at that time called a buccal smear, where she looked for how many X chromosomes -- she was looking for males that had two X chromosomes and then verified them with chromosome studies, with ordinary studies. And among the guys who had two X's, she found some that not only had two X's but they also had two Y's. So then she decided to screen for Y chromosomes, and she found a bunch of them that were XYY.

And she found them in an institution for the criminally insane. Now, you know, there's an old thing that you try to teach fellows, particularly who are going to do clinical studies, that if you look for a biochemical abnormality that you think might be associated with mental retardation in an institution where they are mentally retarded, they're all going to be mentally retarded, and it doesn't tell you anything. So that's what happened.

The word went out that these guys are murderers, and this and that, and gradually became a very tricky business because, for example, [Richard] Speck, the guy who killed all the nurses in Chicago, his criminal defense was that he was XYY. He wasn't. He was not an XYY, it later was found out. But that's what the lawyer brought up and tried to get him off on the basis that this is biological, it’s a disease.

I was approached at that point by a man named Hy [Herman A.] Witkin, who was the head of psychology at Downstate, marvelous man. He and another buddy of his named [Donald R.] Goodenough, who was also a psychologist in [New] Jersey after whom a whole test was named, very respected types. They approached me saying, would I be interested in doing the chromosomes on a thing that they are planning to apply for, which is to study a number of people and see whether this connection holds true of criminality and XYY?

Because a lot of fuss was being done. They were finding them in newborns. There was newborn screening for a while. Then [Richard C.] Lewontin started screaming bloody murder that criminality is an environmental phenomenon and to forget about this stuff. So it had to be resolved. The idea that we came up with was, if we could get cooperation to do two populations in New York, policemen who were big and big tall criminals, and see what we could find. We were getting close to getting permission, but it became clear this wasn't going to work. We weren't going to get unbiased samples, and we weren't --

So, Witkin had worked with a guy named [Sarnoff A.] Mednick, who is a psychiatrist who had done studies in Denmark, where he showed that in identical twins who were adopted by other parents, as compared to ones that grew up with their parents -- or when they were separated, for example, identical twins -- that certain things were clearly inherited because the characteristics were there in the twin who never even met his parents. Among those were criminal behavior, alcoholism, schizophrenia. So there were hereditary components to these. And he did all this with a psychiatrist in Denmark. We approached that psychiatrist in Denmark, and he felt this was a great idea.

Hy Witkin and I went over, and we incorporated another guy who was an old friend,

John Philip, who was the head of obstetrics in Copenhagen, who was a cytogeneticist, in fact. He had worked at Rockefeller [University] for a number of years and we became friends at that time. We approached him, and he was prepared to do the chromosomal screening over there, and the psychiatrist was going to do the psychiatric screening, and we could get the famous Danish registry [Folkeregister] so we knew how they did in school, how many arrests they had, what crimes they had committed, what their IQ was, everything, whatever you wanted to know about anybody. We took four birth years so that by the time we did the study they were in their late twenties. It's well known that if you're in your late twenties, if you've been in trouble, by then you will have been in trouble. So we took these four consecutive birth years of all males born in Copenhagen and went into the Registry and found, because they all -- there's a military part to the Registry and people in hospitals -- so we took the top 15 percent in height, because we knew that error had already been definitively shown, that these people on the whole were in the top 15 percent in height, usually in the top 10, so we'd be safe with 15 percent. We took all of these people -- and it's amazing how compliant they are -- we explained to them what we wanted to do and they said, "Fine."

So the process went on. What we showed, basically, was, yes, they were in trouble with the law more than others, but if you categorized them by intelligence, it was only the ones with low intelligence that were in trouble with the law. We also found, of course, while we were doing this, all the Klinefelter patients, and among them you have a number that are moderately retarded, and the frequencies were essentially the same. The stupid ones get caught. And they were not crimes against persons. We had one minor arson. All the others were property crimes, stealing and this and that. So the whole concept of these criminally insane went out the window. That's how I got involved in that.

AM: You had mentioned that one reason why you may have served in the military was this vague sense of revenge and that when you did go to Austria, you threw the Kommissar who took over your father's business in jail. Would you also say that would be a similar motivation in this project, where clearly there has been misuse of genetics? And why do you feel compelled to?

KH: I think a sense of justice. One is justice, but perhaps the stronger one is the misuse of science. Going back to Nazi times, since you're connecting them, up to and including [Josef] Mengele, there were so many misuses of medicine and science that were being done. The whole [Eugen] Fisher-[Erwin] Baur-[Fritz] Lenz thing [co-authored Human Heredity, Teaching and Racial Hygiene]. Whatever one can do to make sure that things are done right and ethically, and these discriminatory concepts destroyed, and so on, I'll participate.

AM: I'll go back to more specific questions about what happened after your meeting in '58. You were just becoming an assistant professor. What did it mean to go out and create this new specialty of medical genetics? You had this great invigorating meeting in Colorado, and then you dispersed to your institutions. How does one make an idea an institution?

KH: Well, again, so much of what happens to one's career is dependent on place, time, and more [importantly], the right person involved. I think that the fact that Wilkinson became so committed to this concept, to the extent, as I said, that he gave up his

chairmanship just to get into the field, and that I went there with him, came back, and that we immediately began to look at what else could be done to further this field. He's the guy who encouraged me. Unfortunately, he was dead in a year, but that's how it started. And once I got started in it and it became clear that this was going to be fun and it was going to be important, and the techniques were coming around, so that it -- I just then had to stick with it.

AM: How did you balance the desire to pursue all these very intellectually stimulating things at the bench versus the more administrative side of getting the field going with an administrative structure that you could actually train students, get money and grants to do nothing but genetics? How did you balance the intellectual side plus the dirty day-to-day administrative things that had to be done to get --

KH: It was a fortunate time. Again, the opportunity of time and place. NIH was rapidly expanding. Money was available if you had any decent ideas. Training grants became thought of, which is why Wilkinson got that first one from the Heart Institute and then allowed me when I came here to right away apply for one here and being funded for a training grant here.

That concept of what one needs to do really brought me to a couple of other things. And it's really the same idea all the way along. When I was chairman of pediatrics -- there's an organization, which is probably the most boring organization in the world, called the Association of Academic Pediatric Medical School [Chairs], AMSPDC.

AM: That's actually an organization?

KH: Yes. Every specialty has a chairman's organization, where once a year, all the chairmen get together. Terribly boring meeting. All I can tell you is they were always around fifteen people that one could talk to. The rest of them were interested in DRGs [diagnosis related groupings] and how to create a residency program, and how to do this and how to do that. Science was not on the agenda. But a few of us decided that pediatrics was far behind internal medicine in training young clinician scientists. So we worked on a proposal, and the six of us got up and held impassioned speeches to the rest of the chairmen and were able to persuade them -- I think half of them must have been asleep -- but were able to persuade them to apply to NIH for a thing called a Pediatric Scientist Training Program, now called the Pediatric Scientist Development Program.

We even asked for contributions to allow us the administrative help to get this thing started. We were met, although with some doubt, but also a reasonable amount of enthusiasm by a number of them. And it happened. And I was one of the founders of this and a few others. One guy whom you may know, Larry [J.] Shapiro, was one of them. Geneticists, I would say, represented half of the group. We figured genetics has to be done within clinical departments, and it has to be done scientifically, well trained, and so on. So we led this thing along with a neonatologist and an endocrinologist, and so on, and we got it through. And this still exists and is quite successful.

It's the same kind of thing. It's seeing a need. What was clear to me was I wasn't going to sit there by myself in this lab, even though I had a couple of other people working with me, and do much to further this field. I could further one little piece of it, but

the field wasn't going to grow because I was sitting there in the lab. So there became the need to propagandize it a little bit and make the funding agencies more aware. And it grew very rapidly.

I don't know if I mentioned yesterday, the first meeting of the American Society of Human Genetics I went to was in Storrs [Connecticut].There were less than a hundred members of the society, twenty-eight of them showed up at the meeting. All of them gave papers. And in 1963, I was the program chairman for the annual meeting. It was in New York, so I was the local guy. A few hundred people at that point. It was much increased in terms of general interest. And then it was exponential for a while. But it had to get started, and I still think that it was the Motulskys and the McKusicks and Wilkinson and me and Barton Childs that really did this. Barton was very instrumental in bringing it to the educational end. He was the one who really pushed medical schools to start courses in medical genetics.

AM: We know a little bit from your Allan address what you think has been the downsides of this massive growth. But what were the immediate advantages of creating a more institutionalized structure to this specialty?

KH: We were able to attract people with quite varied interests into this. We always sort of say, tongue in cheek, everybody thinks they're a human geneticist because they've studied one family. But you took some of those people who have studied a family and studied them well and became interested in the concept and attracted them by this into the field so that they brought their clinical expertise, or in the Ph.D.'s, their scientific expertise, into the field, and that's how it grew. And that's how it became multidisciplinary. My favorite statement is that all medical specialties and all basic sciences are nothing but subspecialties of genetics, which causes great to-do sometimes.

AM: Why do you think that is?

KH: Well, people don't like to be told that what they're really doing is just looking at one end of a biological spectrum. (chuckles) But that's really what it is. All these people with their different talents, you could turn them on by showing them that there's something exciting happening, and then they join in, and they get trained. Or they send one of their young guys to be trained. And then suddenly you have this real critical mass of people all working towards the development of this field. It happened very fast.

AM: Right. Because at the same time that the core is moving and shaking the medical schools and, later, creating the board and creating the college, there's also on the other end this complete revolution in techniques that is, at its core, dealing with the gene. How much of an impact was it that just techniques that made it easier to do genetics had on this development versus what you and the Motulskys and the McKusicks were doing and creating it as a specialty?

KH: I think what you're asking is really a much broader question, because I think nothing advances in medicine, or for that matter in science, without the presence of the appropriate technology. It can't happen. Sometimes you've got to stop and try to create the technology, but you're not going to get anywhere until you have the technology.

Really, if you want to know what allowed this whole thing, there are several things, but one of the major ones was really [Herbert] Boyer and [Stanley] Cohen with recombinant DNA. The moment you could play games with the gene and its expression and its structure and what it does, lots became possible. And it led to the genome project. Without any of those things, you have no genome project. And they all fed into that. Without cytogenetics, you have no genome project. Without recombinant DNA, you have no genome project. Without the more clinical or medical aspects of inborn errors of metabolism and understanding them and trying to find the right patients to find these genes. So it all sort of came together, and it all derived from these rather major advances in technology. Of course, the computer helped speed it.

AM: In your address, you have a more pessimistic view of the future and that the growth of the society helped congeal all these different groups and interests together, but now, as it keeps growing, it's starting to fragment the field of genetics.

KH: What causes me to have this pessimism is what has happened to the important major clinical research societies. The major example is the American Society for Clinical Investigation, the so-called "Young Turks," which meetings were undoubtedly, from the fifties on, perhaps even in the forties when I didn't know anything about them, the most exciting meetings around. Why were they so exciting? Because every clinical scientist from every medical specialty came together and gave their work, and it was in a great place. It was in Atlantic City [New Jersey]. It was on the Boardwalk. You walked around and you could talk -- whatever was interesting, you could find six other guys who were from a different point of view, perhaps interested in it. The interactions were just fantastic, the papers were phenomenal, the critiques of the papers were fantastic, and the fights -- everything.

Today, it's a paper society. Why? Because every specialty broke off and formed their own society. So there came to be an American Society of Hematology and Gastroenterology [American Gastroenterological Association] and the American Heart Association, the cardiologists. And they were encouraging their fellows and their young faculty to give their best papers to their own subspecialty society because that's where they would be appreciated and that's who would be judging them for grants.

Then the main meeting, the ASCI meeting, became lectures by invitation, review what's happened during the year in the field, this, that, and the other thing. It became monotonous, and I was beginning to see some of that happening. We avoided it with some because we managed to keep in the population geneticists to a great extent, and we got many of the counselors involved. Although they did form their own society in addition, but they meet just before, so it's okay. The main thing is we did manage to keep the molecular guys, who were particularly interested in human disease molecular genetics, and they do come to the Society. So that is a good sign. But there are too many other sort of more private meetings going on, which is the beginning of a sign that they consider it more important to talk to each other than to talk to the field.

9. The Future of Medical Genetics; Creating the Social Issues Committee of the American Society of Human Genetics; Teaching to Think Genetically; Identifying Wolf-Hirschhorn Syndrome; Serendipity and Mentorship

AM: Where do you see -- to use a worn out phrase -- at the turn of the millennium we have seen incredible things: the completion of the genome project and cloning, which, as we speak, some Italian doctor is saying, "We can do humans." Where do you see genetics moving?

KH: In two quite disparate directions, I think. One of them is that it will become, over the next I think twenty years or so, mainstream medicine. And the thing that's going to drive it there is the beginning of understanding of the genetics of common disease and susceptibility. The whole concept of creating a chip for a person with polymorphisms that can be shown to vastly increase their risk for a disease or vastly increase their bad reaction to a drug. In other words, pharmacogenomics, common disease genetics, and so on. It's going to be unavoidable for people to ignore this.

Many departments of medicine still don't have a clue as to what's happening. Departments of pediatrics are much more clued into it because traditionally, even though the original people, like me and McKusick, we're all internists. But pediatrics took it over, because most of the obvious genetic diseases were pediatric diseases. But now it's becoming obvious that the vast majority of genetic disease is, in fact, not these rare inborn errors or the chromosomal abnormalities, but they're cancer and heart disease and hypertension and psychiatric diseases.

So it's going to become mainstream. The techniques have begun to be developed with Affymetrix [Inc.], of trying to look at a thousand genes at once. But it's hard to know what people will do with it. And that's where some of the ethics part of it is going to become absolutely critical, of not going haywire with this stuff and scaring people to death and starting to get people to tell you about their six-year-old's susceptibility to disease when they turn sixty, or going even further and doing a prenatal diagnosis for susceptibility to this, that, or the other thing. People can go crazy with this stuff.

And it's the old story which we used to say if people want to destroy detrimental genes and do prenatal diagnosis for carrier state for these, then the solution is very easy because there will be no people, because we all carry genes, and we all have susceptibilities. And fine, if you can use them appropriately so that if you do identify something, which you should only do when you've got an established preventive technique available, then it becomes powerful. And I think that's the positive direction in which all this is going to go.

The negative direction is really part and parcel of the same thing. It's this concept of you've got to have ideal children, imperfections are no good, and so on. That's going to have to be guarded against because the techniques are going to allow you to figure this out. You've got to guard against that very strongly.

I think those are the future major directions, positive and negative, of clinical genetics.

AM: The historian in me is compelled to go over some ground we've covered before, but perhaps to rephrase it. Historians tend to period-ize everything, so there's this kind of the first wave of genetics -- and I think I'm using what McKusick has done in his history of medical genetics -- this first wave that started with the rediscovery of Mendel and also with [Thomas H.] Morgan and Drosophila --

KH: And Garrod with inborn errors.

AM: -- which kind of was broken by World War II and the Third Reich and then was reestablished with this new -- and then there was the new genetics. The new period is the new genetics, and '56 was getting the chromosome number of human chromosomes, and pushed forward by all the revolutions in techniques. And here we come with all these increased ethical concerns and questions about where we can go and people who don't seem to be heeding any of this. How do you see this? Are there big breaks in terms of what you have experienced in your own development as a geneticist? Have we moved forward? Or are we destined to repeat some common history?

KH: Maybe some of each. I think we've moved forward enormously. I think the recognition of the ethical problems -- when I was president of the American Society of Human Genetics, I established the Social Issues Committee, which was really meant to be a committee on the ethical applications of genetics to the human race. So there's been recognition of this, and some of it has, in fact, gone overboard. There are some people around, without mentioning names, who have become so sensitized to these issues that they become paralyzed, and they try to paralyze the field. That's just as bad. Some of them, in fact, are very powerful in the ELSI [Ethical, Legal, and Social Issues] part of the genome project. And that's bad too.

But I think we've gone an enormous way in understanding, obviously, of the biology and in the understanding of the clinical part and the understanding of population parts of it. Even human evolution, of understanding the different backgrounds of different peoples. It's the old Catch 22, you can't talk about race but you believe in diversity. (chuckles) That's terrific. And it's exciting, and it's going to go on. And the next years when we really get to analyze the genome, it's going to bring many surprises and many exciting things.

I think there has been a parallel development in the ethical applications of this and people's concerns, but not nearly to the same extent -- and as I said, in two different directions. Some that sort of say, yeah, we need to pay attention but kind of slough it off. And the others who get so involved in it that nothing will work. And that needs to be cleaned up. I think we need to have rational aspects of the ethical and societal issues that are going to become more difficult, not less difficult, as time goes on.

AM: As I start to wrap up, I'm going to be jumping around a little bit. To follow this up a little bit, you have been one that hasn't been shy about bringing up all the taboos of American society: abortion and its uses and policy issues relating to that, embryonic research, behavioral genetics, many of these topics that are --

KH: Uncomfortable.

AM: Uncomfortable, thank you. Have you had any repercussions from being comfortable with talking about these issues?

KH: Yeah, from both sides. I remember in the early days of prenatal diagnosis, I gave a paper at the Young Turks [American Society for Clinical Investigation] about some of the early stuff in prenatal diagnosis of inborn errors, it was at the time. Within a day, I got

this call initially from a colleague of mine, who said that one of the people who supports his work a great deal had heard about this and was very upset. That person was Eunice Schriver. And I got a rather nasty letter about all I'm doing is promulgating abortion with this. How can I do that to the sanctity of human life, no matter how bad it may be? I didn't get upset by this. I said, "We're all entitled to our opinions, and you come from a different religion than I do. And you practice what you want. You don't have to have an abortion."

So that was one example of the negative from one side. In 1960 or so -- it was just before Roe v. Wade, which was '63, so it may have been '61 or '62 -- I was invited to participate in a panel and to give a talk at the Society for the Study of Abortion, a rather large society, surprisingly, which dealt with many different issues. It was in Warm Springs, Georgia, or Hot Springs, whatever it is, the thing that sits on top of a mountain where Roosevelt used to go. The talk I was supposed to give was about prenatal diagnosis, because it was clearly an abortion-related issue. Then I'm sitting there with many interesting panelists. One was a bunch of religious people. There was a rabbi and there was a protestant minister and there was a standard Catholic priest and there was a Jesuit. And the most liberal of them all was the Jesuit. He saw no problem with this. (laughs) It was a fascinating meeting.

This was the real drive at that point towards Roe v. Wade of leading towards abortion on demand. That was their thinking, that's what we've got to get through. It's the mother's right. Then they started mixing into it that one of the strong arguments towards this is the discovery of genetically abnormal children and, therefore, allowing an abortion. Well, I wouldn't have any of that. I said, "You guys want to fight for abortion on demand, that's fine, you do what you want. Maybe in another persona I even applaud you, but don't even dare to use the genetic piece as a propaganda piece to get you in that direction because all you're going to do is ruin us. All you're going to do is say, hey, prenatal diagnosis is abortion." When, in fact, we were able to show already by that time that the vast majority of prenatal diagnosis led to more normal births than without it because people knew that they could find out whether they were going to -- and, therefore, were willing to take the chance of getting pregnant.

AM: How do you think your life as a geneticist has been shaped by practicing genetics in American society? It may be a little hard to discuss, but as compared to some other cultural traditions where some issues --

KH: Well, some of my friends have certainly had a harder time doing it. The classic example is France. I have several very good friends -- not all still alive -- who are French geneticists, and the most daring of them was a couple, Andre and Joelle [G.] Boué, who were the ones who really were the major reference prenatal diagnostic lab in France. They had a huge lab in the Bois de Boulogne and samples came from everywhere in France.

And their arch enemy, Jerome Lejeune, who discovered Down syndrome, a brilliant man, but was an ultra-orthodox Catholic and fought his entire life against prenatal diagnosis and made life very difficult for the Boués. He had a lot of influence in politics and he got the whole church organization behind him, and it's a Catholic country, after all. People had to fight and be exposed to terrible insults and attacks in order to carry this forward. So here it was a snap. I mean so I got a letter from Eunice Schriver; it doesn't matter. (chuckles)

AM: You mentioned in your address that the Society needs to keep its eye on its common theme, and I just wanted to ask you, what do you see as the common theme in genetics?

KH: Before I do that, let me just go back one step. When I was president of the Society, the guy who was chosen for the Allan Award my year was Jerome Lejeune. I spent months in correspondence and on the phone -- this was before email and faxes, it was 1969 -- to try to persuade him to talk about science, which is why he got the Allan Award, not because of his beliefs but because of science. I tried and tried, and when he came, he gave his talk which was entitled The National Institutes of Death. I had to introduce him, I had to say all these good things about him, then he gave this talk. It was sad.

What's the theme? The theme to me is to teach people in all fields to think genetically, to look at a problem in medicine or in science -- and while it's perfectly legitimate to look at a blocked coronary artery from the cardiologists point of view of how do I open this and let the blood go through, that's fine and that's important and it's practical, but think about this individual who closed off his artery from a genetic point of view. Why did this happen to him? What genetic predisposition, with what environmental factors caused him to close this artery off?

If we can get everybody to pay attention to this common theme of having medicine and science consider things from a genetic point of view, it will keep everybody more or less together, because the ones who are doing the genetics are the ones who have to teach the others to think that way. But the only way that they're going to do that is by being aware of everything that's going on in human genetics. That's why the American Journal of Human Genetics is a good journal, because they do cover the waterfront.

That's, to me, the common theme. It's the genetics that's the common theme. Remember that what genetics is traditionally is the study of variation. Now that it's proven beyond any shadow of a doubt that we're all different, the differences are, in the majority, caused by genetic factors. Sure, it's environmental stuff, and the reason identical twins are often different is because early influences, perhaps beginning in utero but certainly after they're born, causes different connections in their brain. But the flexibility, the malleability of the brain is a genetic characteristic.

AM: There was a time when a biochemist discovered a protein and their career was made, or a molecular biologist discovered a new gene and their career was made. What did it mean to have a syndrome with your name attached to it to a clinical geneticist?

KH: I think again we need to start at the beginning of that one. It started with finding -- when we established sort of this genetics clinic, clinic for kids with abnormalities at Bellevue. This kid was brought in. The kid had these defects described originally as defects of midline closure. By this time we were doing pretty decent chromosome studies, so we decided it was the chromosomes, and yes, a piece was missing from a chromosome, a deletion.

We first saw the kid in early '61 or late '60, or something like that. And at a meeting of the American Society of Human Genetics, the people who were doing chromosomes got together and we sort of tried to make a few rules for ourselves, because there were a lot

of papers being published with some weird thing in one case, and then it didn't pan out. So we said there is a publication that T. C. [Tao-Chiuh] Hsu runs at MD Anderson [Cancer Center] called the "Mammalian Chromosome Newsletter." And T. C. Hsu, who is a superb cytogeneticist, offered the pages of this newsletter, which was just a paperback thing, for case reports, a picture and a description, and used that as the place to store these things. And the cytogeneticists were going to read them, and then they were going to see is there a kid whom they've seen and then take a look, and if it's the same thing, fine. It becomes a syndrome. Then one can publish it in the regular literature.

So we found this kid, and we found this deletion, and it was before you could really tell chromosome-4 from chromosome-5, so we called it "deletion of the short arm of chromosome-4-5 with midline closures" and we published it in his "Mammalian Chromosome Newsletter" in '61.

In 1965 I get a call from Motulsky, who is the American editor of a German genetics journal called Humangenetik now called Human Genetics. He says, "I've just been sent a paper from [Ulrich] Wolf in Germany describing something that I think you described in the 'Mammalian Chromosome Newsletter.'" If you can put it together into a paper rather quickly, we'll publish them back-to-back. So it became the Wolf-Hirschhorn Syndrome. (chuckles) Which I did not expect. People started attaching names to stuff, and we don't all believe in that. But suddenly it appeared in the literature as the Wolf-Hirschhorn Syndrome.

And yes, it was pleasant. I have a picture here that Marco Fraccaro sent me from some celebration or something. They made a postcard.

AM: This is the person you worked with --

KH: -- in Sweden, yeah.

AM: So was your career made then as a clinical geneticist because you had a syndrome named after you?

KH: No. But what it did do is it gave me name recognition among people who didn't really know me from that point of view. The syndromologists began to recognize me as a clinical geneticist. As far as I was concerned -- there was this whole story of human genetics versus medical genetics versus clinical genetics. I considered myself more of a medical geneticist than either a human geneticist, where the tradition is more population and mathematics, or a clinical geneticist, which is descriptive science, but being a medical geneticist trying to work out mechanisms of genetic disease.

AM: I guess one last very broad question, and that is, you've talked many times about being at the right place at the right moment, and certainly your entire life has been amazing stories of that. But how do you see the role of serendipity or fate, or whatever you want to call it, playing in your success as a physician-scientist?

KH: If I could make it even broader, I think the two things that led to whatever success I've had are the presence of three major and a couple of minor mentors. The ability that I guess I must have always had of open eyes and ears, of looking at something and

seeing it or hearing it and not noticing it. And then saying, "Hey, this could be important, could be interesting." That's what really serendipity is. Serendipity doesn't come from nowhere. It comes from good observational abilities and then following them up. And that's what I have liked doing all my life. You start with something, you recognize a technique and think, what can I apply to it? Or you come with a problem and then you see something that might relate to it and you apply it.

What I am not, in this field, is a detail man. I will go after the big thing, I will finish it, I will prove it, but the cleaning up bores me. (chuckles) Which is why some people have not considered me as a serious basic scientist, because I don't take -- the answer, of course, is that nothing is ever finished. And I know that you can get hung up on something -- and many, many people in science have -- and continue with it and continue with it and continue with it. Yeah, they write another paper on some other new discovery, but it's boring. When something exciting happens, you grab it, as long as it's somewhere related to what you're doing, and you do it. That's why, as I said yesterday, I think I'll never be a member of the Academy, because I don't take things that seriously. I always must retain an amount of light spirits about things.

AM: Well, I think that does it for my questions, so I'd like to turn it over to you. What would you like to add that we haven't talked about?

KH: I don't know. I think we've covered a lot of ground. I don't think back that much, but the question that I think of these days, having turned seventy-six this year, is, what I really want to do with myself for whatever time I've got left. I think that's better, perhaps, discussed with Rochelle and me together.

I've lived a good life in the field and managed to survive other things. And I feel I've been well rewarded with a decent life and good family, despite early difficulties of money, and this and that, and now pride in one's children and seeing grandchildren grow up. Really, to me, in the long run, that's what it's all about. That's what success in life, to me, and I think to Rochelle as well, really meant. And as long as one can have fun while succeeding and allowing one to develop a life together and a family, that to me is the most important thing of all, far more important than any recognitions that I may or may not have done in genetics. The real genetics is the generations. (chuckles)

AM: Okay. I thank you very much for this opportunity to interview you, and it was certainly my pleasure.

KH: Happy to have done it.

END OF INTERVIEW