NATIONAL HEART, LUNG, AND BLOOD INSTITUTE ORAL HISTORY PROJECT

INTERVIEW WITH

Maurice Burg

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HISTORY ASSOCIATES INCORPORATED
300 N. STONESTREET AVENUE
ROCKVILLE, MARYLAND 20850
Telephone: (301) 279-9697
Fax: (301) 279-9224
www.historyassociates.com

Dr. Maurice Burg

Biographical Statement

Dr. Maurice Burg was born in 1931 in Boston, Massachusetts, and grew up in Newton, Massachusetts. He graduated from Harvard College in 1952 with an A.B. and Harvard Medical School in 1955 with an M.D. After his medical residency at Boston VA Hospital and an internship at Beth Israel Hospital, Dr. Burg came to the Laboratory of Kidney and Electrolyte Metabolism [LKEM] at NHLBI in 1957 as a postdoctoral fellow. At that time, the LKEM was under the leadership of Robert Berliner (Lab Chief from 1950-62) and Jack Orloff (Lab Chief 1962-74). Burg then became an Investigator in the LKEM in 1960 and Chief of the LKEM in 1975. In 2002, he became a Senior Investigator and Chief of the Renal Cellular and Molecular Biology Laboratory. Dr. Burg is a renal physiologist who has made significant contributions to the field and greatly aided the understanding of how the kidney functions in health and disease. In addition, Dr. Burg's group has furthered our understanding of how organisms survive osmotic stress caused by dehydration and by high concentrations of salt and urea. Dr. Burg has won numerous awards for his work in physiology, most notably, election to the National Academy of Sciences in 1991. In 2001 he also became a Fellow of the American Academy of Arts and Sciences. Dr. Burg has authored or co-authored more than 240 scientific articles and is a member of the American Physiological Society, American Society for Cell Biology, and American Society of Nephrology, of which he was past president.

Interview Synopsis

Dr. Burg begins the interview with memories of his childhood in Newton, Massachusetts, working in his family's grocery store, the Newton Center Market, and briefly describing his college and medical school experiences. He mentions his internship at Beth Israel Hospital in Boston working under Hermann Blumgart and the Boston VA Hospital under Maurice Strauss. Dr. Burg recounts how he came to work at NIH through the Public Health Service, joining the Laboratory of Electrolyte and Kidney Metabolism. He discusses at some length the culture of the lab and leadership of the lab under Robert Berliner and Jack Orloff. Dr. Burg spends a large portion of the interview discussing and describing his work in renal physiology, including kidney tubules and their perfusion, eventually without collagenase. He recounts in detail the process of working with the NIH Instrument Shop and the Laboratory of Technical Development, and the important collaborations that impacted his scientific studies and the field. Dr. Burg is generous in recalling collaborations with other scientists, colleagues, labs, postdocs, and technicians. He also discusses his later interest and work with osmotic stress and high urea and salt on cells. Dr. Burg mentions many of the postdocs and technicians that worked in his lab, and the fact that when he was Lab Chief he tried to create an atmosphere that he calls a "Happy Lab." He mentions some of his international speaking engagements, including trips to Germany, China, and Africa. He speaks about being pleased with the intellectual challenge of his work—59 years at the NIH—and ends the interview with this advice to young scientists: "Work for the government."

NHLBI Oral History Project
Interview with Dr. Maurice Burg
Conducted on August 1, 2019, by Sheree Scarborough

SS: Today I'm at Dr. Maurice Burg's apartment in Washington, D.C., and I'm interviewing him for the NHLBI, it is August 1, 2019. This is an interview about his career and life. Dr. Burg, I don't really know where you were born and when you were born.

MB: The date was April 9, 1931, and the place was Boston, Massachusetts, at the Beth Israel Hospital.

SS: Tell me some things about your childhood, your background, and your parents?

MB: My father was Charles Burg. He was the proprietor of a market in Newton, Massachusetts, called the Newton Center Market. As a child the market had a big role in my childhood. When I was old enough I worked there as a cashier and carried bundles out, and things like that.

SS: How old were you?

MB: Not old enough to be legitimate probably. Old enough to run a cash register. It was a family business that had my father as the principal proprietor and his brother my Uncle Billy who was a favorite uncle, who had no children of his own, so he was sort of a

second father to me. The market did well thanks to my father's hard work and it supported our family through then end of the Depression and generated enough profit to send his three sons through college and graduate school with no debts, which I much appreciate. In those days also my mother was a professional violinist, a musician. She was playing the violin at Old Orchard Beach in Maine when she met my father and that led to their marriage eventually. We lived in Newton, Massachusetts for many years in a couple of different locations.

SS: So your mother was a professional violinist with the symphony?

MB: No, she was a soloist. She did play with a group at one point, which I have the name in my autobiography, [*Autobiography of Maurice (Moe) B. Burg*, self-published] which you're welcome to look at.

SS: Oh, thank you. That is a great resource. I wish I'd known about that!

MB: I was looking for an electronic copy, but I didn't find one, but I'll be glad to give a hard copy, which we located this morning.

SS: Thank you. Do you remember the Depression or were you too young?

MB: I was too young then. My memories are of World War II in which my brothers and I were too young to serve. My father was already too old to serve. The Newton Center Market

was a family business in that numerous members of the family worked there. I had an uncle whose name was Al Freeman and he ran the fish counter. He trained me to pick the meat out of lobsters and insisted that I whistle while I did it for obvious reasons.

SS: So you wouldn't hear them scream?

MB: No, so I wouldn't eat it. The lobsters were dead at that point. They were cooked. Ever pick the meat out of a lobster?

SS: Yes, when it's on the table in front of me, but not otherwise.

MB: My Uncle Billy who was trained as an engineer was unable to get a job in the Depression and so he ran the delivery service in the basement of the store. I had an uncle who ran the produce department and I was involved in setting the produce out at times. That was at the Newton Center Market, which was profitable and which my father worked very hard at.

SS: Did your mother work there, too?

MB: No, my mother took care of the house and the family.

SS: And you have two brothers?

MB: One is two years younger than I am, and the other, Gerry, is ten years younger. I'm the oldest. My brother Stanley, the next youngest, went as I did to Harvard College and he went to graduate school at Harvard. I went to Harvard Medical School.

SS: What were your high school years like?

MB: Very pleasant. I was a good student, which was beneficial to me in getting me into Harvard. Actually, I was not very savvy about places to go to college or to medical school, so I applied only to a couple of local ones, which were Dartmouth College, Harvard College and Harvard Medical School, and Boston University.

SS: You had some nice local colleges to choose from.

MB: Yes, Boston has a lot of colleges and higher institutions of learning.

SS: When were you first interested in science?

MB: I had no interest in being a scientist as a youth. My introduction to science came much later. After medical school there was a war going on at that point, the Korean War, and graduates of medical school were given the choice that they could volunteer for the Army and go in as an officer or be drafted as a private. I chose to volunteer.

SS: Wise man.

MB: I had received my orders by telegram to report to Fort Sam Houston for my basic training as a physician, but that was followed by a telegram saying they had oversubscribed for that year, so I could get a medical residency and I could do that instead for a one-year delay. So I looked around Boston for medical residency and the one that I found was at the Boston VA Hospital.

SS: Sounds like you made the right choice.

MB: During my internship at the Beth Israel Hospital, the chief physician was Hermann Blumgart, who was a cardiologist. I wanted to become a cardiologist, so I found a cardiology residency at the Boston VA. When I arrived there I discovered that there had been a miscommunication and I was in fact not a cardiac resident, but a resident in endocrinology and nephrology, so I began immediately seeing consults in those areas.

SS: What attracted you to cardiology?

MB: It is an attractive profession.

SS: Were there any professors that stand out for you in your undergraduate years at Harvard or your medical training?

MB: Yes. As an undergraduate I majored in social relations, which interested me because of the psychology aspects of it. My favorite professor was Henry Alexander Murray. He was director of the Harvard Psychological Clinic in the School of Arts and Sciences. Murray co-invented the Thematic Apperception Test.

SS: Are there any other experiences at Harvard that you'd like to talk about? That was the early 1950s, I believe.

MB: I graduated Harvard College in 1952 and Harvard Medical School in 1955. I chose to apply to medical school after three years of college and took summer courses after that to finish my degree.

SS: When did you meet Ruth [Cooper Breslauer Burg]?

MB: Ruth is my second wife.

SS: When did you meet your first wife?

MB: I met my first wife when we were both quite young. My first wife was Judith Braverman who was a student at Radcliffe. I knew her before she became a student at Radcliffe. That was the years before Radcliffe College and Harvard College were joined together. Judy's father was a psychiatrist at the Framingham VA Hospital, Harry Braverman. I used to drive out there. We were related at that point through my grandparents. My

grandmother was named Sarah and my Uncle Billy's first wife was also named Sarah, so Grandma changed her name to Sadie at that point to avoid confusion. Sadie Braverman, my grandmother, whose name was Burg, of course, later married after her first husband Maurice died, for whom I'm named. Actually, I'm named Moshe, which is Moses.

SS: Was it changed along the way?

MB: No, that was my Hebrew name. We had both a Hebrew and an English name, pronounced Mo-reese. I go by my nickname, which is “Moe.” So Sadie Braverman, my grandmother's second marriage was to Louis Braverman who fabricated men's clothing in Chelsea, Massachusetts. Louis had a son who was a psychiatrist and that was Judy's father at the Framingham VA Hospital. We had a close relationship.

SS: Was that when the Framingham Heart Study was being done at the NHI?

MB: National Heart Institute, yes.

SS: When did you marry Judy?

MB: It was while I was in medical school in the 1950s.

SS: You were married when you were doing your internship and residency?

MB: That's right and we had two children at that point. The oldest one is named Elizabeth or “Betsy,” the younger one is Robert or “Bobby.” I later inherited two other children when I married Ruth, Larry and Joan. Judy my first wife suffered from post-partum depression after Robert's birth, which was very hard on her and on me, and on the children. That led to her death eventually. After she died Ruth and I had mutual friends who got us together and so we married [in 1967].

SS: The earlier interview you did, didn't talk about your personal history, so I wanted to include what was going in that quadrant in your life while you were doing your work.

MB: We had gotten to the point where I had taken a residency at the Boston VA Hospital where the residency turned out not to be cardiology as I had intended, but nephrology and endocrinology. The head of medicine at the Boston VA Hospital was Dr. Maurice Strauss. He had an interest in kidney physiology, which led to my first papers in that field. His interest led him to do clearance studies on veterans. Clearance studies use the output of urine and the blood to determine the glomerular filtration rate and the addition or subtraction [of items] from the urine. The first papers were on water excretion by veterans. I had three collaborators, Sol Papper, Larry Saxon, and Jack Rosenbaum. Saxon and Rosenbaum died shortly after that. Saxon was a scuba diver and he suffered an accident while scuba diving. Rosenbaum as a young man had colon cancer, which was fatal.

SS: That's terrible.

MB: It was.

SS: The veterans you were working with, were they Korean or World War II?

MB: They would be World War II, mostly. I was in the Boston VA for my one-year deferment, which the Army chose, but I never went into the Army actually. Maurice Strauss had friends at the National Institutes of Health and he arranged for me to get enlisted in the Public Health Service and go to NIH instead of into the Army. The friends at the National Institutes were Robert Berliner and Jack Orloff.

SS: Is that the lab you went into?

MB: Yes, the Laboratory of Kidney and Electrolyte Metabolism, which was one of the early laboratories established at the National Institutes. LKEM, Laboratory of Kidney and Electrolyte Metabolism is in the Heart Institute, which seems strange, but that was because of the first director of the Heart Institute, who was [James] Shannon. Shannon knew that kidneys played a role in heart disease, so he had the Laboratory of Kidney and Electrolyte Metabolism at one of his first laboratories in the Heart Institute.

SS: You went into that lab in 1957?

MB: Right.

SS: And it was just started in 1948. That's pretty new.

MB: Yes. NIH was not that old at that point. NIH was sited on a land, which was a rather large campus that was owned by a family in Bethesda, Maryland, and the government in effect stole it from the family. Imminent domain. The family mansion is still there as far as I know. It was certainly still there when I was at the National Institutes.

The Laboratory of Kidney and Electrolyte Metabolism was headed by Robert Berliner and Jack Orloff, who were my first mentors. They were renowned scientists, and why they were renowned is interesting to me, which is that they were scathing critics and much feared in the field because of their scathing criticisms. I can recall at the meetings of the societies we belonged to in those days were in Atlantic City before it became a gambling destination. The societies that we went to Atlantic City for were the American Society of Physiology and the American Society for Clinical Investigation. Orloff and Berliner would attend the sessions and would often give their feared criticisms. I can recall standing out on the boardwalk with them and having people come to them for approval. Berliner was a renowned scientist based, I believe, mainly on his political skills and critical abilities.

He had come from the Goldwater Hospital in New York. And when he came to the National Institutes he brought a collaborator from his lab with him, Tom Kennedy. Years

later, Tom Kennedy came to the laboratory with a question, which was: What were Berliner's accomplishments in science, which made him so famous. Kennedy had an assignment from the National Academy of Sciences to help author a bibliography of Robert Berliner, who had been a member. And Kennedy was unable from the record to decide what it was that Berliner had discovered, and in fact, it wasn't very much.

When I first came to NIH I wanted to use micropuncture, which was then the state-of-the art in kidney physiology. Micropuncture consists of using micropipettes for tubules, which go to the surface of the kidney either in the cortex or the medulla. There was a great deal that was learned from that, particularly about proximal tubules and collecting ducts. However, I could not go into that area because Berliner was reserving it for himself and Tom Kennedy, whom he brought from Goldwater to the laboratory. So that was not available to me.

SS: That's a shame.

MB: No, not really.

SS: You found other subjects to research.

MB: Yes. I was impressed with the in vitro experiments, so I started doing in vitro experiments with the preparations then available, which were kidney slices, which are not terribly good for determining how the kidney works. The kidney has thousands of

microscopic tubules, which are fed from the glomeruli and each one contains something like twenty different segments, each of which is specialized for a special purpose, and micropuncture could get to only three of those segments.

The in vitro techniques I used with kidney slices, which are not very compelling because the fluid no longer flows through the tubules and access to the tubules requires an interstitial space between the tubules that complicates the analysis. I chose to do away with the interstitial space by using collagenase, which had been used for cultures of kidney tubules to separate the kidney tubules so that they were floating around and not connected through interstitial space. That was a preparation of separated tubules, which were used for studies—mainly isotope studies of sodium and potassium uptake—and released from the tubules. And the suspension of tubules was better for that than were the kidney slices because there was no interstitial space to confound the interpretation.

SS: That's fascinating. And I do want to hear more specifically about your experiments. But I'd like to hear more about what the lab was like when you arrived there with Berliner and Orloff, and the group of people working there and what it was like.

MB: When I arrived at the laboratory Orloff already had a fellow who was in his second year, Floyd Rector. My initial assignment by Orloff was to study chicken preparation where the chickens have a strange anatomy in their kidneys, which is a renal portal circulation, which can be accessed through the saphenous veins in their legs. You could study that by making plastic funnels and sewing them over the openings of the ureters in the

cloaca and then collecting the urine from the two sides separately. Since these two sides were fed from different legs of the animal you could use one side collection for experiment and the other side for a control.

SS: Were the chickens sedated?

MB: No. They never complained. There was a problem with that preparation, which led Floyd Rector to refuse to do the experiments, and that is that the cloaca in addition to producing urine from the ureters produces feces from the large intestine, so you could get unexpected spurts of feces when you were doing it. Orloff asked me to do it. I didn't know that you could refuse, so I did it. The experiment had to do with whether the recently discovered sodium potassium ATPase had a role in the sodium and potassium excretion by the kidneys. By putting an inhibitor of the sodium potassium ATPase into one side and using the other as a control you could poison the sodium potassium ATPase in one kidney and not in the other. The result of that experiment was changes in the sodium and potassium excretion on the side that got the glycoside called strophanthidin, which proved that sodium potassium ATPase was involved.

SS: That was a helpful study.

MB: I don't think it was particularly helpful since the answer was rather obvious to begin with. The laboratory, when I first got there, what I recall was the lunchtime sessions which

initially were in a smoked-filled room, which was unappetizing to me since I was a non-smoker from the very beginning.

SS: That's why you're still living.

MB: I don't know why I'm still living. There's an old joke about that, which comes from a jazz musician who said that if he had known how long he was going to live he would have taken better care of himself. I feel that now.

SS: You must have taken good care of yourself.

MB: Yes and no. I recall that my father was an assistant Scoutmaster in Troop 17 for the Norembega Council for the Boy Scouts of America. The Scoutmaster was a smoker, at that time the Surgeon General came out with his analysis of the harmful effects of smoking, and he asked me whether it was really bad for you, and I was able to tell him that it was.

Back to the Laboratory of Kidney and Electrolyte Metabolism and our noontime sessions, the fellows would present a paper, each noontime, and Orloff or Berliner would criticize it, and they were very good critics.

SS: Was your paper criticized by them?

MB: They could put you down very well.

SS: And they did?

MB: Sometimes. The one thing about the lunchtime sessions was that technicians were not included and there were no women there initially. The first woman at one of those sessions was a graduate student, a postdoctoral fellow, in my laboratory, Evelyn Grollman. When I became the laboratory chief eventually I made it a point to have the technicians and other women attending the sessions at noontime. I learned a lot from the way Orloff and Berliner ran the laboratory and used it when I became the laboratory chief. For example, sometimes the members of the laboratory would go out to a restaurant for lunch. Berliner was very good at mental arithmetic and would keep track of what everyone was eating and then made sure that the fellows paid for their share of the meal. When I became the laboratory chief I reasoned that I was being paid much more than the fellows and so when I would invite them out to lunch I would pay it.

SS: In your interview with Mark Knepper, you say that when you were lab chief you wanted a happy lab. Tell me about that.

MB: I wanted people to be appreciated and respected. Orloff and Berliner came from a tough school in which they put people down so that they would become tougher, so I chose not to do that. I never knowingly put down any of my people who worked in my laboratory and welcomed their happiness in the lab.

SS: Did people leave? Was the criticism too intense for some?

MB: It was done in such a way that you couldn't escape it and people didn't leave for that reason. So at the famous noontime sessions, eventually the NIH became a non-smoking area. One step along the way was the announcement that smoking was forbidden in public areas, and when that announcement came out Orloff went to the NIH lawyers and established that our conference room was not a public area, but he never smoked again in the noontime conferences.

SS: What building were you in?

MB: Building 10.

SS: You were always in Building 10?

MB: Yes, from the beginning.

SS: Okay. I wanted to ask, did you have contact with Martha Vaughan, Orloff's wife?

MB: Vaughan was a superb scientist and was the best scientist in her family. I knew her, of course. My wife Ruth and I eventually built a house in Bethesda, which was adjacent to the home that Orloff and Martha Vaughan lived in. I recall that our daughter Joan, who

eventually became a physician, would go from door to door soliciting for various things and Orloff always slammed the door in her face.

SS: Terrible.

MB: That's who he was.

SS: Do you remember there being a convivial atmosphere and socializing after work during those early years?

MB: No. After we worked we all went home. I don't recall many parties. I'm sure there were some.

SS: It seems that NIH hired a lot of Jewish people. Did you feel any discrimination though?

MB: No, I never felt any discrimination because I was Jewish. I'm a secular Jew. I spent considerable time in Israel, but I'm not religious. Ruth is more religious than I am and we are members of Temple Sinai in D.C., but I seldom attend services. Ruth is more religious and keeps up some of our family religious observances such as Seders and Passover and special meals and Hanukkah.

SS: Did you know James Shannon?

MB: I met him, but I had no personal contact with him.

SS: Is Building 10 now the Clinical Center?

MB: Yes. Well, there have been additions to the building. The part which is behind the original Building 10 is now a major part of it.

SS: Were there other labs there?

MB: Yes, it's a big building, a lot of laboratories.

SS: You told Dr. Knepper that in the early 1960s, renal transport physiology was in its infancy.

MB: Not a long history, from that point of view. I'd say the major ways of researching the kidney were clearance studies and micropuncture. Being excluded from micropuncture, I had to go my own way and that eventually led to my invention of the isolated perfused kidney tubule.

SS: Tell me about that process.

MB: I had gotten as far previously as discussing the suspension of kidney tubules, that lacks fluid flowing through the tubule lumen. I wanted to have a way of perfusing the kidney

tubules. It's difficult to insert a micro-bypass into the end of a kidney tubule. In fact the leading kidney physiologist in those days said he had tried it, and I tried it. You held the tubule with the forceps and tried to push the cannula into the end, and it was impossible. So I realized that I needed to hold the tubule from all the sides at once.

The laboratory next to mine was Joseph Hoffman who later left for a distinguished career at Yale Medical School. He and Walter Friegang had an apparatus that they used intended for studying the electrical voltage across red blood cell membranes. The apparatus consisted of concentric micro-bypass and I realized that they could be used to cannulate the end of the kidney tubules using the outer pipette to suck the tubule over the inner one. My initial experiments with perfusing kidney tubules used the Friegang [apparatus]. By the way, this is all in my autobiography in detail.

That was a way of perfusing the kidney tubules, which I got out of the tubule suspension. When I first tried to perfuse one, it ballooned and broke. I realized at that point that the collagenase for preparing the perforation was destroying the base of the membrane, which made it impossible to perfuse the tubule. I then had to go to tubules that were not separated by collagenase.

We had a visitor in the laboratory, Ivar Sperber, who was a Scandinavian investigator who specialized in dissecting tubules out of the kidney and he showed me how to do it. So I dissected a tubule out of a kidney without collagenase and then attached it to the perfusion apparatus and perfused it, and it worked beautifully.

SS: What animals were these from?

MB: Initially I was using rabbit kidney slices. I also tried rats and mice, but it was more difficult to dissect the tubules out of them without collagenase. I thought it was a species difference originally, but it turned out the rabbits I was using initially for kidney slices were from the NIH colony and they were germ-free. And the kidneys in the normal animals were not germ-free, so they had scarring and made it difficult to get the tubules out. It was also the case with rats and mice. Mark Knepper persisted in attempting to profuse tubules, to dissect tubules for perfusion from rats and mice, and he eventually succeeded, and that's the standard preparation rather than using the rabbit.

SS: Where were these rabbits being raised at NIH?

MB: There was a facility for raising them, probably Building 31.

SS: Did you bring them over to your building?

MB: Right. The tubule perfused well with the Hoffman-Friegang apparatus, but it was not convenient for that. The convenient apparatus came through the advice of Joe Hoffman who directed me to an investigator at Johns Hopkins, who had an apparatus for holding concentric micropipettes and advancing on axially within the other. His apparatus was fragile and required a lot of care to set it up. I went to the instrument shop at NIH and

Ken Bolin who ran a section of the shop that did fine machining. I challenged him to invent a way of holding the micropipettes, advancing them one on each other, which would work better and easier than the one I got from Johns Hopkins. He and his machinist, Jim White, worked out a way of doing it, which was used for many years after that by other kidney physiologists.

SS: There's a lot of collaboration going on at NIH.

MB: Yes, I benefited from collaboration. I recall the visit to Johns Hopkins to see the apparatus from which we derived and eventually used. I had my first two postdoctoral fellows with me, Maurice Abramow from Belgium and Jared Grantham from Kansas.

SS: It sounds like you brought in mathematicians and engineers.

MB: I had a lot of very good fellows after that who helped me to expand the use of the technology. The original perfusion was with the concentric pipettes from Bolin and from White. Jim White later left NIH and started a building business, building perfusion apparatus, which he built a lot of them and a lot of people were perfusing tubules. Initially I collected all of the reprints of all of the tubule perfusion articles, but I abandoned that when it reached a thousand. There have been many since then.

With Grantham and Abramow we had the ability to dissect tubules out of kidneys without collagenase. We perfused our first tubules, which were proximal tubules from

the surface of the kidney and collecting ducts. What we found was that the proximal tubules absorbed fluid and secreted para-aminohippurate, which proximal tubules were known to do and the collecting ducts could be perfused for up to six hours without deteriorating. So our initial preparations were proximal tubules and collecting tubules. The first paper showed the action of the anti-diuretic hormone to increase the water permeability of the collecting tubules of the proximal tubules absorbing fluid and secreting para-aminohippurate, and that was our first tubule perfusion paper.

SS: Was that a major discovery?

MB: Yes, that was my major discovery. The perfusion technology was expanded with the help of fellows who it helps to know the electrical resistance and the voltage cross kidney tubules for determining what their function is. They had a fellow, Sandy Hellman, who had majored in electrical engineering before he became a physiologist. He tuned me into cable theory, which you need for measuring the electrical resistance of a tubule. I had already invented a way of measuring the voltage across the tubules by putting an electrode into the perfusion pipette.

SS: How did you think of that?

MB: It was obvious. I first learned that it was important that I should use cable analysis for measuring electrical resistance. I was informed of that by a famous physiologist who I met in Atlantic City at our meetings. His name is Jared Diamond, who is an excellent

writer and published his famous book, *Guns, Germs, and Steel* [1997], which you may have seen. He was very smart and a very good writer. Unfortunately, he had a knack of reaching the wrong conclusions from his experiments with kidney tubules and he never became a great kidney physiologist.

SS: He went on to have a writing career. It is interesting—all the paths of the people you met along the way. It's fascinating.

MB: Jared was the son of one of my professors at Harvard Medical School, Louis Diamond.

SS: Jared Diamond went on to win the Pulitzer Prize.

MB: Yes. He was a very good writer, not a good kidney physiologist. We had a succession of very good fellows perfusing tubules and we eventually worked out the transport properties, the sensitivity to hormones, and the mode of action of diuretics with kidney tubules, and all the technology that we had invented for studying the transport.

One of the laboratories at NIH, which contributed importantly to this was the Laboratory of Technical Development. Robert Bowman was the Director of the Laboratory and Gerald Vurek was the postdoc. Vurek and Bowman invented many of the techniques that we used for analyzing the minute volumes of fluid that we could get from perfusing a tubule, which are nanoliter volumes, five to a hundred nanoliters. Bowman invented a photometer for measuring sodium and potassium and Vurek invented a picapnotherm

for measuring total CO2, which together with the pH allowed us to do studies of acid-based transport.

SS: Does the Lab of Technical Development still exist?

MB: I have no idea.

SS: It sounds like a good idea for people to make things.

MB: I think it met its demise while I was at NIH. I remember the laboratory well.

SS: It sounds like it was important to your work.

MB: Yes, and to many other people.

SS: Tell me about the Scandinavian researcher Ivar Sperber. He was giving a lecture on an important day in history at NIH. Do you remember that story? If you will, tell me that story again that you told Dr. Knepper.

MB: The Kennedy assassination. He had given his lecture and at the end of the lecture we were alerted that there had been an important development, which was the assassination of President Kennedy in Dallas.

SS: Your memories in your earlier interview were that a messenger kept coming in and telling Berliner something and he kept shoeing him away to let the lecturer finish. Okay, you became lab chief in 1975, while all of these studies and experiments were going on with your postdocs. As I understand it, then you decided what experiments would happen and would tell the fellows working with you. Is that how it works?

MB: I think it was more of a collaboration than that. I would talk with the fellows and we would decide what to do. A lot of it was my ideas, but it was also their ideas.

SS: Tell me about your speaking engagements out of the country.

MB: I visited essentially every continent and all of the major countries in Europe at one time or another to give invited lectures.

SS: What did you talk about?

MB: How the kidney functioned. One memorable experience was a lecture tour in China. I was invited to speak in Japan. Margie Schafer, who had been a neighbor of mine in Newton and who married Jim Schafer, one of the early people to perfuse tubules. I helped to set it up as he had been a fellow of mine. Margie decided that if we were going to go to Japan that we should go on to China, which Ruth objected to. [She wanted to know] why did I agree with Margie instead of with her? I wrote a letter to the president of the Chinese Academy of Medical Science telling him that Jim and I were

famous scientists and we wanted to visit China and lecture there. He mailed back to me that we were invited at our own expense. So we arranged to go to China. That trip was for just ten days, which was as much time as I cared to take off at that point. Ruth would have taken more time. So we went to China.

Each day Jim and I would lecture at a hospital or a medical school. We then spent the afternoon touring the tourist attractions in China. We went to three different cities, Beijing, Hangzhou, and Shanghai. When the bill came for our own expense—we were chauffeured around in two limousines, one for the Schafers and one for Ruth and myself. The limousines had a driver, a guide, and an English-speaking Chinese scientist. When the expended money reckoning came, it turned out to be $50, which at the time it was changed into Chinese money required a big basket. That was Ruth's and my first trip to China. We had another trip there later, much more recently.

SS: Was that with the NIH also?

MB: It was based on a Chinese scientist who had been at NIH, whom I had become friendly with in Hangzhou, and a second scientist who was in Beijing, invited us. Another memorable speaking engagement was in Batswana, Africa, and another city where I was invited to speak.

SS: What was memorable about the trip?

MB: One of the organizers was a frustrated tour guide and he recommended that we go to private safari camps in Batswana, which is where we started. In the city for the meetings you could take tours, but they were crowded tours. The tours in the private safari camps were better because they did not require that you stay on the road or that you yield to other drivers. That was our first trip for animal viewing in Africa. We later took two trips to Tanzania where we took our entire family, the two children I inherited with Ruth, plus my own two children. We took them all to Tanzania. The nicest trip we took with them was to the Galapagos, the whole gang, and also to Costa Rica, all of them memorable trips.

SS: Nice. Were those associated with your work?

MB: No, just tourist trips. Galapagos is a highly recommended trip. Ruth had arranged for us to go on a small cruise ship and it was very pleasant.

SS: Nice. Did you also take sabbaticals during your time at NIH?

MB: No. I had many trips overseas, a number of them to Germany. First you must understand, Ruth's first husband Max [Breslauer] was Jewish German. He and his family escaped to the United States. In all of our travels we never went to Germany because she wanted to avoid Germany. I asked her one day whether we could make a trip to Germany together, and she said only under very extenuating circumstances. I told her that the extenuating circumstance was a drug company that was paying for both of our trips to a fancy resort in Germany, so we went to that.

SS: Was that because of a discovery that you had made?

MB: That was a diuretic conference and the mechanism of action of diuretics that largely came from our studies of kidney tubules and poisoning them with different diuretics.

SS: You've mentioned the technicians that worked with you. One of the technicians that worked with you, Nordica Green, is she African American?

MB: I always thought she was, but it turned out she was Native American. She was just dark complexioned.

SS: Was it unusual to have women technicians during that period?

MB: No. That was a scientific job that women could get easily.

SS: Did you need a PhD or MD?

MB: No. Nordica worked with me in developing perfusion of kidney tubules, and through all of my earlier studies. There was second woman technician, Agnes Preston, who was Joe Handler's technician. I think I mentioned that Joe Handler was in the laboratory with me. We traveled together and became close friends. Unfortunately, he died several years ago from prostate cancer.

SS: Was there an important discovery that Nordica helped you make about Henley's loop?

MB: We worked together on all of them, much of the kidney perfusion work that I described to you was I hope important discoveries.

SS: So you shifted your focus in the 1980s? Tell me about that.

MB: I was aware, as Joe was aware also, of the developments in molecular biology. Joe and I went for several years to meetings of the American Society of Cell Biology.

Joe Handler and I started going to meetings at the American Society for Cell Biology, which had excellent symposia on molecular biology. That was our introduction to molecular biology. I also had a postdoctoral fellow at that point who had some experience in molecular biology, Arlyn Garcia-Perez. She was in my laboratory for many years and then unbeknownst to me, she got a new job at NIH as assistant to the director of all of NIH. Arlyn is still there.

SS: She left your lab?

MB: Yes. Joe Handler and I decided to study osmotic stress because there's a part of the kidney, which is the kidney medulla, in which the urine is concentrated and that concentration of the urine requires high concentrations of salt and urea around the cells.

High concentrations of salt and urea are injurious to cells. The urea enters the cells directly and affects the proteins that are there. High levels of salt in the extracellular fluid are accompanied by high levels of salt in the cells to balance them osmotically. This is a subject that I became aware of through an important review by a postdoctoral fellow named Paul Yancey and his mentor, [George] Somero. It is spelled like the Spanish word but he's not Spanish. He was careful to point out to me initially that he's not Spanish.

Among the animal cells that are exposed to high salt urea throughout the animal kingdom, there are two compensating effects. One is accumulation of organic osmolytes. The organic osmolytes serve to balance the osmotic pressure from high salt in a way that is not harmful to cells like the accumulation of salt in the cells would be. The urea in multiple organisms is counteracted. The action of urea to degrade proteins is counteracted by methylamines, such as betaine and glycerophosphocholine. By the way, Yancey later became a friend and spent a couple of sabbaticals in my laboratory.

SS: Was he a marine biologist?

MB: Yes. He is, as far as I know, still.

SS: Interesting that the different fields can interact and overlap, and work on similar things.

MB: When [C. Everett] Koop became Surgeon General of the National Institutes he decided to revitalize the Public Health Service by dismissing everyone who had been in thirty years or more, which included Handler and myself. So I was out looking for jobs at that time and one of the places I went was to Scripps in La Jolla Marine Laboratory because of this interest in marine biology.

SS: Did you leave the NIH?

MB: Handler left the NIH and he got the job as chief of nephrology at Johns Hopkins. I asked Orloff to convert me to civil service, which would mean I wouldn't have to leave. He did that for his wife, but he didn't do it for me. It turns out that at all the other institutes that's what the directors had done. That was Orloff's last mean trick to me. Not a nice man.

SS: What did you do?

MB: Fortunately for me, Orloff died shortly afterwards from prostate cancer and the new director immediately transferred me to civil service, so I stayed at NIH.

SS: Who was the new director?

MB: Ed Korn.

SS: I interviewed him in January. Nice man.

MB: Knowing from the Yancey and Somero review that all organisms accumulate organic osmolytes in their cells in response to high urea or high salt, the question was what are the organic osmolytes in the cells of the kidney medulla, where the salt or urea concentrations are very high. Fortunately, we had excellent collaborators in discovering that.

We had a former fellow who stayed on at NIH whose name is Robert Balaban. He used **nuclear** magnetic spectrometry to identify the organic osmolytes. It turned out that the principal organic osmolytes in kidney medullary cells were sorbitol, inositol, myo-inositol, glycerophosphocholine, and betaine. Then the question came in the next stage of the research was why are these increased. And it turned out that sorbitol increased because the enzyme known to produce it from glucose is aldose reductase. The aldose reductase level was known to be high in kidney medullas, so that accounted for the sorbitol.

I had fellows working with cell cultures who identified lines of cells that survived high osmolality, high salt, and high urea. And using those cell cultures were able to find out that for the sorbitol it was aldose reductase, for the myo-inositol, the medium, which meant that it was transported into the cells for glycerophosphocholine, it is a very complicated story, and the betaine like the myo-inositol is transported into the cells. These cell lines all accumulated the same organic osmolytes as the kidney medulla when exposed to high salt, high urea, or both. So the question then was more sorbitol

because the level of aldose reductase increased in cells and culture exposed to high salt so that the aldose reductase increased the transport measure of myo-inositol and betaine also increased when the cells were exposed to high salt, and the glycerophosphocholine increased with either high salt or high urea.

The reason the aldose reductase increased—what we found was that the messenger RNA for aldose reductase increased and suggested an increase in the transcriptional activity. The increase in transport of betaine and myo-inositol into these kidney cells was accompanied by characteristic changes in the transporters for them that indicated that there were more transporters. It turned out that the messenger RNAs for those transporters also increased. The glycerophosphocholine is an impossibly complicated subject.

SS: Okay.

MB: So we'll leave it at that.

SS: As I understand it, this is how the cells protect themselves from having too much salt and urea?

MB: Around them, yes. The urea is in the cells, too. Why was there more messenger RNA for the transporters than for aldose reductase and for the glycerophosphocholine? It turned out there was a decrease in the rate at which it was metabolized and an increase

in the rate at which it was produced, both, from a complicated series of events that were occurring at the same time. So the messenger RNAs were increased it suggested that the transcription of those proteins was increased. So we started looking for the transcription factor, which is what Arlyn Garcia-Perez was doing at the end of her career as an investigator. My laboratory did not find the transcription factor that was involved. Instead, it was Joe Handler's laboratory with a fellow named Moo Kwon in the laboratory.

The transcription factor, they called TonEBP, tonicity-responsive enhancer binding protein, which enhanced finding protein. There's also a laboratory in Asia, which found the same transcription factor and named it OREBP, osmotic response element binding protein. It turned out the transcription factor was related to transcription factors found in white blood cells, which were called NFATs. There were four previously identified NFATs, so this one was called NFAT-5, which has nothing to do with the transcription factors of the white blood cells, but has to do with the influence of the immunologists who studied them.

SS: Where is Joe Handler's lab?

MR: That's in John's Hopkins. He continued the research there. To revitalize NIH by dismissing someone who later becomes chief of nephrology at Johns Hopkins. It doesn't sound like much of a reinvention.

SS: So you've gone on to do important studies after you switched gears?

MB: Yes. Then the question was what increased the activity of this transcription factor. So we had a great many studies looking at the transcription factor and finding changes in phosphorylation and other changes in the transcription factor. Both of the enzymes that increased phosphorylation and decreased it. We also had a lot of studies showing that if the transcription factor is not active then the cells become susceptible to harm from high salt. The high urea is counteracted by betaine in the cells and also is counteracted by the glycerophosphocholine. That gets us toward the end of the osmotic stress studies.

We had studies after that showing how osmotic stress damaged the renal cells. For example, it causes changes in the mitochondria that are harmful to the cells and it increased proteins involved in apoptosis, which is suicide for cells. I started running out of steam at that point.

SS: I wanted to ask you briefly about—so Balaban was in your lab as a fellow?

MR: Yes.

SS: You worked with him for a number of years.

MR: Three or four years. Before coming to NIH, he had taken a fellowship in England working in a laboratory that did nuclear magnetic resonance spectroscopy. When he

came to NIH he expanded on those studies and our resident expert in those areas was Hank Fales. He and Balaban both collaborated with us in identifying the organic osmolytes.

SS: We're at the wrap-up phase of our interview. You said you had gotten to the point where you were running out of steam in your work. When did you actually retire?

MR: After fifty-nine years at NIH.

SS: That's amazing. You trained a lot of scientists.

MR: Yes, I had a lot of very good ones in my laboratory. I think I mentioned Eugene Kwon who worked on the mechanism of increase of glycerophosphocholine, which required biochemistry. And neither of us being biochemists, he was obviously very talented. He had come originally to the laboratory because of his concern as a urologic surgeon for treatment for disseminated prostate cancer and he chose my laboratory because he had a general education in research, rather than the laboratory, that was studying that at the time, at the [National] Cancer Institute.

After three years in which he worked out the mechanism of action of glycerophosphocholine I made him an offer I never had made to anyone before, which was that if he wanted to stay on in the laboratory for three years for whatever project he came up with. The project he came up with was related to prostate cancer. He enlisted

two collaborators, one at Baylor and the other one at Berkeley. The one at Baylor had lines of mice that got prostate cancer or failed to reject human prostate cancers that were inserted in them. The one in Berkeley later became famous for his discovery of Anti-CTLA-4, which prevented some cancer cells from dying from the cancers. Eugene found that the Anti-CTLA-4 cured the prostate cancer when transplanted into mice and prevented it in the line of mice all of which got prostate cancer. Unfortunately, like many cancer treatments in mice that one did not translate over to humans. Eugene went on to become professor of Immunology and Cancer Research at the Mayo Clinic. Very capable guy.

SS: Did he have a personal reason for his interest in prostate cancer?

MR: Yes. He was a urologic surgeon and he was frustrated by not being able to treat patients.

SS: Right. You had a lot of fellows and you trained a lot of scientists for the country. What's your secret for success of being such a good teacher?

MR: Letting them do their stuff. We collaborated, we worked together, and I was nice to them. It was different from what I was exposed to with Orloff and Berliner.

SS: You said you were shown how not to run a lab and that you wanted a happy lab. Are there other elements of a happy lab that you haven't mentioned?

MR: I tried to be considerate and helpful to everyone in the lab. You can ask Mark Knepper the question.

SS: Was there someone that you were trying to be that you had seen as a good role model, as a mentor?

MR: No, not particularly.

SS: You're just a nice person.

MR: I suppose if anyone, Maurice Strauss at the Boston VA and [Hermann] Blumgart at Beth Israel.

SS: At fifty-nine, almost sixty years at NIH, looking back, how do you feel about your career?

MR: I was fortunate to be at a place where I didn't have to write grant applications which would be approved by study sections. And I was able to assume my research based on my own ideas without getting anyone's permission. The positive from Orloff and Berliner came from allowing me the facilities to do that. It was interesting. At the time, the early years at NIH Orloff and Berliner were deaf on computers. They felt that they had no important role in research. Berliner could do the calculations in his head as well as the

computer or math machine. They were wrong about that. Many times when they had computer salesmen come into the lab, I had to hide them from Orloff and Berliner.

Our first computer in the laboratory came from my trip to Israel, when I visited the laboratory of Wilfred Stein at the Hebrew University. He sat down with me and with one of his prize students who was Yoloff Kabanchik who told me what he was doing. He was an organic chemist and he had synthesized an important inhibitor of iron transport. When he finished telling me about it I told him how terrific his research was. Stein looked at me and he said, "How come you didn't say that about my research?" The answer is his research was not as terrific as his writing.

I recruited Kabanchik to NIH, and when he arrived, he immediately, in Israeli fashion, seized the resources he needed, including going to Orloff and demanding that he get a computer for his studies of the kinetics of iron transport in red blood cells. Orloff was afraid to refuse him, but he did get his revenge by insisting that the computer be the cheapest possible by not having a hard drive, but having only a floppy disk drive. Kabanchik went back to Israel. Unfortunately, I would have liked to have him stay on in the lab. He was a very capable scientist. He was still there last time I checked.

SS: Did he leave because of the computer problem?

MB: No. He left because he missed Israel. My roommate in my later years at Harvard College, Charles Greenblatt, went to Israel. Interestingly, he was also in the Public

Health Service at NIH at a time when there was the wars going on in Israel. I don't know when there was a time when a war wasn't going on. The U.S. government had announced that we were not sending aid to Israel at that time. He was a Public Health officer going to Israel to fill in for a physician who went to the front treating physician's patients, and he stayed on in Israel. I saw him recently at my 65th reunion from Harvard College.

SS: That's amazing. How many of you were there?

MB: More than you would expect. Another friend who was at that reunion, David Rogers, who lived on the same block with me in Newton, Massachusetts, and had gone on to some fame in New York for a book he wrote on politics [*110 Livingston Street: Politics and Bureaucracy in the New York City School System*, 1968].

SS: That's interesting. Speaking of computers, you saw so many changes at NIH.

MB: When the first IBM PCs came in I got one and I realized that would do a lot of things and were better than the word processors our secretaries were using in the laboratory. So I got what was probably one of the first microcomputers at NIH.

SS: Were mainframes used?

MB: Yes, the original mainframe at NIH had vacuum tubes and occupied an entire room, which had less memory and slower speed than the iPhone I have in my pocket now. You needed to program it with a stack of cards. When I first used it I had to get a mathematician at NIH, Monas Berman, to do it for me.

SS: Where was it?

MB: I think it was Building 12.

SS: Orloff and Berliner were so wrong about computers. You can't do anything without computers now.

MB: I think they objected to the fact that to use a computer you had to use a keyboard, which was woman's work.

SS: That's also a big change, more women as scientists.

MB: Yes, a welcome change. Ruth was trained me to be a feminist.

SS: What would you say is your legacy?

MB: Everything I've already mentioned.

SS: Yes. Important experiments and discoveries, your papers, your fellows and scientists you trained. You're a member of the National Academy of Sciences, you're a member of a lot of academies and societies, and you published at least 240 papers. It's amazing.

MB: Thank you.

SS: Do you have regrets?

MB: Not really. I did as well as I could. I suppose I was a reasonably good physician. I could have been a good physician, except that I discovered that I found research to be more challenging.

SS: Is that why you stayed at NIH all those years?

MB: Yes.

SS: You could have taught at a university. Were there other options for you?

MB: I could have gone into practice, which has its own satisfactions but of a different sort, not intellectual.

SS: Are there exciting new developments in your field that you know about or wish you could work on?

MB: I've not kept up on it really.

SS: Lastly, do you have advice for young scientists starting out today?

MB: Work for the government.

SS: Is there anything else you'd like to add to this record?

MB: No.

SS: Well, thank you very much, Dr. Burg.

[End of interview]