

Dr. Edward Beeman

Office of NIH History  
*Oral History Program*

Interviewee: Dr. Edward Beeman

Interview Date: May 4, 2004  
Transcript Date: May 12, 2004

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\*\*\*Beginning of transcript\*\*\*

Buhm Soon Park: Today is May 4th, 2004. This is an interview with Dr. Edward Beeman. BSP is Dr. Buhm Soon Park of Office of NIH History. Today's subject is the research and careers of Dr. Charles Armstrong and Robert Huebner.

[break in audio]

BSP: Thank you very much Dr. Beeman for agreeing to have an interview with me. I'm just glad to hear about Drs. Charles Armstrong and Robert Huebner. Tell me – start talking about your careers, your educational and family background and when you came to NIH.

Edward Beeman: Okay. Yes, my full name is Edward Arthur Beeman. I was born May 1, 1923 in the Roxbury section of Boston, Massachusetts. I went through grade school primarily in the Boston area. I attended Boston Public Latin School for my high school years. When I graduated from Latin school I entered college at Washington Square College of New York University. I stayed there for one year, and, then, I transferred to Harvard College. I graduated with a degree of Bachelors of Arts in 1943.

BSP: What was your major?

EB: My major was biochemical sciences. There was a lapse of about nine months between graduation from college and the start of medical school. It was during the period of World War II, and I was then accepted at Boston University School of Medicine. I graduated from medical school in May 1947. I started my internship at the Massachusetts Memorial Hospital, which is now known as University Hospital. This is the university hospital of Boston University. I had a straight internship in internal medicine ending June 30, 1948.

It was during the internship period that I met an assistant resident – or actually, he was a fellow in medicine who knew of my interest in infectious diseases. This was Dr. William Hewitt who was detached temporarily from active duty at LID/NIH to further his training. He suggested that I might be interested in spending some time at NIH to get some laboratory experience in infectious diseases. He arranged an interview for me at NIH in January of 1948 with Dr. Charles Armstrong who was then the Chief of the Laboratory of Infectious Diseases.

I met Dr. Armstrong at that time; it was one of the outstanding experiences of my life because Dr. Armstrong, in addition to being a world famous virologist and scientist, greeted me in a warm, friendly and engaging manner. He introduced me to various members of the laboratory. During the course of the afternoon a young officer dressed in his official Public Health Service uniform came into the room. Dr. Armstrong introduced me to the young officer who happened to be none other than Bob Huebner. I was somewhat familiar with Bob Huebner's early career since he had already published some findings that I had found very fascinating.

BSP: Before getting more into the details of NIH years I am wondering you said that you had an interest in the research in infectious diseases and was it your intention to spend a couple of years at NIH and then coming back to academia or the general practice?

EB: Well, when I came to NIH I had planned to spend only several years and then I planned to go ahead and finish my clinical training in order to prepare for the specialty board in internal medicine. I had originally thought about going into an academic career combining research with care of patients. I stayed longer than I had anticipated at NIH. I stayed a little over four years rather than two because I was 'frozen' during the Korean War. After I finished my time at NIH I went to the Mayo Clinic in Rochester, Minnesota and had a fellowship in internal medicine – actually it was a residency program for a little over three years in preparation for practice.

I won't go into some of the things that happened during the course of my trying to become involved in academia –actually I had thought about coming back to NIH and working in the new Clinical Center, but because of personal reasons I decided against it. Were there any other things that you'd be interested in as far as background?

BSP: I just want to know more about the reputation of NIH as a research institution among the medical students in the late 40's. You mentioned Dr. Charles Armstrong was a well known virologist and – but other than Charles Armstrong do you have – did you have any reservations about going to the federal agency or what about your advisors response to your decision?

EB: Well, actually I had no reservations about coming into a federal research institution. One of the reasons that I actually felt very fortunate in being able to come to NIH is when I was finishing my internship the physicians who had served as medical officers during World War II were returning to finish their training and most of them – or many of them were taking up the available positions for post graduate training in residencies and fellowships. So the opportunity to come to NIH was really a unique one for me because this afforded me an opportunity to fulfill part of what I considered to be preparation for a future career.

BSP: I see, so during – when you were in medical school you were in the Army Specialized Training Program or...in the Navy program–

EB: Well, actually I was inducted into the Army in September 1943. I went to Camp Grant, Illinois for basic training and then [laugh] after spending a rather anxious month in December of 1943 the orders finally came through for me to be transferred to Boston University School of Medicine. So, I was very happy to be on the train from Camp Grant, Illinois to Boston.

I was enrolled in the ASTP, or the Army Specialized Training Program. Now World War II ended with the surrender of Japan in August of 1945, my class was kept in ASTP

until about March of 1946, as I recall. Then, when we were discharged, we were told that we were entitled to the GI Bill, and, also, that we had no further responsibilities to the Armed Forces of the United States. This did not turn out to be true as events of the Cold War developed in the next few years.

BSP: So your coming to NIH was not motivated by fulfilling your obligations for –

EB: No it wasn't; actually what happened, when I had my interview with Dr. Armstrong, he told me that my position, or the position for which I should apply, was that of a Post Doctoral Public Health Service Fellow. That's what my status was when I came here. However, seeing what was happening in world events and having an intuition that I was not going to be entirely without near future military responsibility, I decided that since I was at NIH and I liked what I was doing, I would apply for a commission with the Public Health Service. Some time in 1949 I did apply, was accepted and I spent the rest of my career at NIH as a commissioned officer.

[break in audio]

EB: Are we on now?

BSP: Yeah we are on.

EB: So, as I say I spent the remainder of my time at NIH which I left in September 1952, as a commissioned officer. I was in the Commissioned Corps reserve for several years after that, but then just resigned my reserve commission as well. So...

BSP: So, tell me a bit more about your later careers. So, you left NIH in 1950 –

EB: I left NIH in 1952 and I left the Mayo Clinic January 1, 1956 having fulfilled the requirements for training to qualify for the boards in internal medicine. Also, while I was at the Mayo Clinic, I did what all the other residents there did – I became a “graduate student” at the University of Minnesota. I had a little research project that involved looking at a bunch of slides of non-Hodgkin's lymphoma, classifying them according to the current classification system then in use, wrote a thesis, took an examination for the master's degree and received a Master of Science Degree in Medicine [laugh] from the University of Minnesota.

After I left the Mayo Clinic in January 1956, I moved to Detroit for a year. I was in a multi-specialty clinic, but it was not a very wise move. I decided to return to the Washington area in March 1957. During the interim period I had been in touch with people at NIH – actually the person I'd been touch with was the Chief of the Clinical Laboratory (actually at that time it was the), National Microbiological Institute in the Clinical Center. We were discussing and negotiating about whether I should return to NIH. Political upheavals were happening, mostly to him at that time. I felt somewhat uneasy of how these events would affect me, and I decided I would take my chances with the practice of internal medicine.

After I was in practice for about a year I was able pass my boards in internal medicine, and I continued on with the practice of internal medicine. In addition, I also started practicing the subspecialty of infectious diseases before the American Board of Infectious Diseases was actually established. So, I was actually the first infectious disease specialist in Montgomery County, Maryland.

And then in 1972 when the examination was offered, the first examination for certification in infectious diseases, I took the examination, and I became certified in infectious diseases. I then just continued with my practice of internal medicine and consultative work in infectious diseases until my retirement January 1, 1993.

BSP: So, after you returned to the Washington area did you keep in touch with Drs. Armstrong and Huebner?

EB: Well, I saw Dr. Armstrong and Dr. Huebner occasionally. As a matter of fact, when we first came back to Bethesda in 1957, I would go out to Dr. Huebner's farm in Fredrick County occasionally with my family. I was married in 1949 (Jean Saperstein) shortly after I came to NIH. By 1957 I also had three young daughters. I used to see Huebner periodically. We kept in touch over the years, but we gradually lost contact as I became more involved with my practice.

BSP: I'm wondering what made you interested in writing about Bob Huebner and –

EB: Well the thing is I've always been interested in medical history. As a matter of fact I'm sort of a history buff, general history, but medical history in particular. What happened all to often toward the end of my career in the early 90's were disturbing conversations that I had with contemporary professional colleagues. They would ask, "What did you do before you started practicing?" I told them about my experience at NIH working with Dr. Huebner and Dr. Armstrong, and when I mentioned the name of either one, I usually would draw blank stares of non-recognition even among infectious disease consultants as well as prominent internists.

Dr. Armstrong had passed away at that time. Dr. Huebner, of course, was ill with disability caused by Alzheimer's disease, but, nevertheless, during the careers of both men, they were the subjects of a great deal of publicity in the lay press, they had extensive bibliographies and were well known in the scientific medical community. However, just a relatively a few years after they dropped out of public view, people had a tendency to forget about them. So I decided – I mean, not at that time, it wasn't until later, that I really shouldn't let the memory of the accomplishments of these men be completely forgotten.

This was just a germ of an idea even before I retired, but I really didn't do anything about it until I happened to meet Dr. Vicky Harden at a Washington Society of History of Medicine meeting. When I mentioned I had worked with Dr. Huebner during the latter part of his studies with Q fever in California, she said to me, "You know, I don't have

any information at all about the Laboratory of Infectious Diseases at that particular period”. She said, “Would you mind writing up your experiences?” I don’t know whether you’ve had a chance to look at my own personal file, but I wrote of my experiences during that period. Anyway I turned in a manuscript, and she seemed to like what she read. She said, “What are you going to do for an encore?” And at that time I really hadn’t seriously thought about doing anything, but then as I kept talking to people and mentioned the name of Dr. Huebner especially, and I kept getting all this lack of recognition of the name, I thought, “Well, this situation really should not continue”. I happened to see Dr. Harden again. I said, “You know, I’ve been thinking about possibly writing a history of Dr. Huebner.” She replied, “That sounds like a fine idea, why don’t you go ahead and do it.” So this was – I guess maybe about 1998. This was even before Dr. Huebner passed away. He passed away, I think it was August 26, 1998, and I had started collecting relevant material even prior to his death. I knew his widow, Harriet; she had worked at NIH. I had met her on many occasions. As a matter of fact she brought her son to me as a patient, and, also, she brought Dr. Huebner to me at one time, before he was hospitalized for his Alzheimer’s disease. So I started putting some material together on Dr. Huebner. I started working at the National Library of Medicine getting together reprints of some of his prominent publications. Harriet Huebner, his widow, gave me a copy of his extensive bibliography, and I used that as the basis to start gathering information about his life.

BSP: Did you have access to his personal letters, correspondence –

EB: Well, that actually happened later. When I talked to Harriet initially, I asked, “Do you have any personal correspondence, or anything that you retained from the time that you were at NIH?” Harriet was Bob’s administrative assistant for many years. Well, unfortunately, she and Bob did not realize the historical importance of retaining this material, and they had eliminated a lot of office files. However, later on, after Bob died, she did refer me to one of the Huebner children; this was Suzie, or Roberta Sue Huebner–Creamer. I went out to the farm, and she gave me three great big notebooks filled with newspaper clippings, and also a whole set of testimonials that were written by many of Huebner’s colleagues, students and friends, that were really very helpful in putting together some of the information that I was able to glean about his interaction with colleagues and friends. I saw Suzie Huebner after he passed away and shortly after the memorial service that they had for him at the farm. I continued gathering all this source information, and, then, one day I encountered Dr. Harden. I think it was over in Building 10, the Clinical Center; I was going to a meeting over there. She asked, “How are you coming along with Huebner’s biography?” So, I told her what I was doing, and she remarked, “You’ve done so much, you must become official.” So she made me a contractor. [laughter] Then, I started using the facilities of the Office of NIH History, and I’ve been associated with the office ever since. I continued the writing, and everybody’s been very helpful and very supportive in my ability to at least get a Huebner manuscript put together.

BSP: So and then you expanded your research to Charles Armstrong

EB: I finished the manuscript on Huebner first. Actually, in the back of my mind I had always thought about doing one on Armstrong, and I thought it was going to be easier to do the Armstrong biography first, because he had a much shorter bibliography, but then when Huebner passed away, I said, "Well, this is a little more immediate." So I decided to try to finish up with Dr. Huebner, and after I had completed that I started working on the Armstrong biography. That's still in the early stages, but again I was very fortunate in having access to several great big notebooks that Dr. Armstrong's daughter, Mary Emma, had kept, and they contain a lot of anecdotal information, a lot of newspaper clippings and articles descriptive of the old Hygienic Laboratory, the predecessor of NIH and, more specifically, the Laboratory of Infectious Diseases. So I have that material, and I'm using that to, you know, try to put together the Armstrong biography. Right now, I'm still on his early career. The aspect I'm working on now is one of his research endeavors that he considered one of his major accomplishments, namely, how to prevent tetanus from occurring in youngsters and people who were getting smallpox vaccination. He considered this a very important contribution, and I'm working on that at the moment.

BSP: Is there anybody who wrote about Armstrong and Wagner, ?[spelled phonetically] like biographical memoirs of the National Academy of Sciences? Both of them –

EB: Well, actually – Dr. Armstrong was one the first scientists at NIH who was elected to the National Academy of Sciences, and then Dr. Huebner, of course, much later on. As far as I know, no one has ever written a full biography of Huebner. As I said, there were a lot of newspaper articles, including articles in the New York Times Magazine about Huebner. Armstrong had someone who was very interested in him – this was the medical science writer Paul DeKruif who wrote a number of very interesting articles that appeared in some of the lay literature and periodicals, describing just isolated segments of his work. I think there was one about his investigation of psittacosis, and there was one on his attempt to protect the children in Alabama from polio by putting picric acid into their noses. Over the course of his career Armstrong received a lot of newspaper publicity.

One of the events that received a lot of prominent newspaper coverage, was the donation of Armstrong's blood serum that was flown by air to Mrs. William Borah, wife of the Senator from Idaho, because she was very sick from psittacosis and Dr. Armstrong had recovered from psittacosis. Well, the custom and practice in the pre-antibiotic and immune globulin era was to obtain blood for antibodies from persons who had recovered from serious infections and to administer the serum, after suitable preparation, to patients seriously ill with the same infection. Physicians ignored the possibility of potential or unknown hazards about this practice because the currently recognized blood-borne pathogens were unknown or unimagined in earlier days. The physicians were primarily interested in providing antibodies as a way to combat life-threatening infections. Fortunately, Mrs. Borah recovered. She made a special trip to Washington to visit the Hygienic Laboratory, and she especially wanted to meet Dr. Armstrong in order to express her gratitude to him for her recovery. There were a many illustrated newspaper articles showing her and Dr. Armstrong together with her thanking him for saving her

life. However, Dr. Armstrong, a very critical scientist, said, he wasn't really sure that his blood is what saved Mrs. Borah's life.

EB: So, when you came to NIH, you specifically had in mind working with Dr. Armstrong, or somebody else?

BSP: Well, actually when I came to NIH, Dr. Armstrong introduced me to most of the members who were in the Laboratory of Infectious diseases at the time. I met Dr. Karl Habel, Dr. Dorland Davis, Dr. Carl Larson, Dr. Chester Emmons, and, as I mentioned, the only person whose name I really knew was Huebner because I had read his articles on rickettsialpox. I knew he had also written something about Q fever. There had been a second laboratory Q fever outbreak at NIH. I thought originally that I'd like to perhaps begin studying rickettsiae first. Anyway, as I said, I had an opportunity, it was a very fleeting moment. Huebner was in an out of the building – out of the office, in about 30 seconds. Huebner and I shook hands and Dr. Armstrong said, "Dr. Beeman is thinking about possibly coming down here." Huebner said, "That's great." And he was off.

Anyway, at the end of the interview after I had met all the men, Dr. Armstrong said, "With whom do you think you'd like to work?" I replied, "I think I'd like to work with Dr. Huebner." And he said, "What do you think you want to do? Do you have any research project in mind?" I said, "No. I'll just go into the laboratory, and I'll get started on something and just see what develops." He said, "That's fine." As a matter of fact, I didn't realize that this is the approach that he took with Dr. Huebner. I think Huebner mentioned this (in the biography). Then Dr. Armstrong shook hands with me and said, "You'll be hearing from me sometime in the middle of June," [laughter] and then he said, "And apply for the postdoctoral fellowship because that will be your status."

I was really quite impressed and elated after the interview, and then I returned to reality in Boston. I had taken a couple of days off to come to Bethesda - one day to get down from Boston, one day for the interview, and then I took the train back to Boston the same night. I went to work the day after I got returned, and for the few days away for the interview, I had to work three extra weekends and a few extra days. This was back in January 1948. Then around April and May, people started saying, "Gee, you know, you don't have anything in writing from Dr. Armstrong. Don't you think you better make sure you've got something set up, because come June 30<sup>th</sup> if you don't hear from him you're not going to have any position." So, to protect my "flanks", I applied for an assistant residency at the Boston VA hospital, which was then in Framingham outside of Boston. The Chief of the Department of Internal Medicine was Maurice B. Strauss, who wrote the classical textbook on renal diseases. Around the middle of June I started biting my fingernails because I still hadn't heard from Dr. Armstrong. Then around the 15<sup>th</sup> of June I received a telegram from Dr. Armstrong that said, "Come to NIH, report August 1<sup>st</sup>, 1948." The very next day, I had a telephone call from Dr. Strauss offering me the assistant residency [laughter]. I thanked him, and I told him that I had been appointed to a position more in line with my current primary interests. So that's how I got to NIH.

BSP: Were there many medical students or interns or residents wanting to come to NIH to have a research experience like you?

EB: Well, I wasn't aware of too many in my school. One of my classmates, Dr. Roger Cole, joined me the following year at the Laboratory, but not too many of my schoolmates planned to go into research. When I arrived at the Laboratory I found that there were a several other physicians, Post Doctoral Fellows, one of who (Dr. Carl Mattern) actually stayed on at the Laboratory. I don't know what ever happened to the others. So there were a couple of us at the lab who had the same status, but back when I was graduating, the ambition of most of the medical graduates at that time was just to get their clinical training completed or, if they were going to go into a specialty, get their specialty training completed. But then many of the 1947 and subsequent graduating classes had to change their plans. The Korean War intervened while many were in the middle of their training, They had to interrupt training programs and go into the Army or Navy or whatever service they'd been affiliated with. As a matter of fact, my office associate had started a private practice. He had finished his training. He was trained in pulmonary diseases, and he had already – I think he had already served in the Navy for something like 20 months, and he was four months shy of completing his obligation to the Navy. He had just started his practice; it had been going for about six months when he was called back into the Navy for another term of service. He served the Navy for two more years, and he had to start his practice all over again...

BSP: Could you portray NIH campus at that time and in what building did you work in?

EB: Well, I worked in Building 7 that was, at that time, the newest building on the campus. The campus was beautiful. It was like a small Ivy League school with lots of green space. Building 7 at that time was known as the Memorial Building, and it had been dedicated to people associated with NIH who had lost their lives during the course of working in infectious diseases. The worker who had passed away most recently was Dr. Richard G. Henderson of the rickettsia unit who died from scrub typhus. So, anyway, this was supposed to be the state of the art bio-containment building. It was supposed to be a bio-safe facility, but it turned out that it was not. I mean it was designed to be that way. I don't know if you went through Building 7?

BSP: No.

EB: Briefly, it contained three floors of laboratory working space and central administrative areas with offices arranged in south and north wings. It also included an attic, basement levels and storage space. Before a worker could enter the working space proper, he was required to go through a series of outer chambers where he removed his street clothes, used the sanitary facilities, take a shower and then put on protective clothing before entering the working space. However, none of the laboratory personnel followed these procedures except for taking off their street clothes and putting on working coveralls.

BSP: Take a shower?

EB: Yes. You were supposed to change clothes. As a matter of fact we all wore these coveralls. They were either a light brown or blue herringbone. As a matter of fact, I saved one of each during all the years I was in practice and then, before I became associated with the NIH history office and museum, I donated these to the National Museum of Health and Medicine. I told Vicky Harden about these coveralls, and she said, "Oh, I'd love one of them for our museum." So, I said, "Well, you know, it might be a good idea to get the blue coverall, because that's the one we wore most of the time." Anyway she negotiated with Alan Hawk, Head of Collections at the Health and Medicine Museum, and after a little red tape he sent her one of the coveralls, but it was not the blue one. In any event, the DeStetten Museum has a laboratory coverall from Building 7.

I don't know if this is a true story or not but Dr. Armstrong was very skeptical about whether Building 7 was truly germ proof. He did an experiment as follows: he used a bacterium called, *Serratia marcescens* which, back in those days, was thought to be just a harmless commensal. It since has been found to be a very potent pathogen especially in sick people who have had a lot of instrumentation and immunocompromised people. He took a culture of *Serratia marcescens* and put it into one of the exhaust ducts of the building. Theoretically this stuff was supposed to be taken through a series of ducts and out through an incinerator grill that would destroy all the germs. Then Dr. Armstrong left a series of open Petri dishes in the attic of Building 7. Now, this particular organism leaves a distinctly pink colony on a plate in agar so it was expected to serve as a very efficient marker. After several days Dr. Armstrong went up to the attic to check his suspicions – I don't know how many Petri dishes he left - but every single one of them was just loaded with these germs.

In this way he showed that the building was really not all that efficient in preventing the escape of infectious agents; actually it never did prevent the third outbreak of Q fever but, on the other hand, the outbreak did not involve people working in the laboratory. Most of the people involved in this epidemic were un-immunized visiting scientists or other NIH personnel who entered the working space during a period of intensive Q fever antigen preparation. The only exception was that the landlady of one of the laboratory personnel came down with Q fever, and it was felt that this worker probably brought Q fever home from the laboratory because the landlady used to wash the linens, the bedclothes, the sheets and apparently she must have inhaled some of the organism. Then when she became ill her husband took over the household chores and he became ill [laughter]. So, anyway –

BSP: Were there animals and insects as well as bacteria and other...?

EB: Well, actually Q fever is one of the potential organisms that –

[audio break]

EB: – Q fever was actually isolated from ticks at the Rocky Mountain Laboratory. Davis and Cox isolated Q fever from the same ticks that harbor Rocky Mountain spotted fever.

BSP: So in Building 7 there were only researchers in infectious disease or other labs also?

EB: Right. Building 7 housed the Laboratory of Infectious Diseases and all the men there were associated with the Laboratory. Now, infectious disease research also was being carried on in Building 5. All LID personnel were in Building 5 before Building 7 was built, and, then, when Building 7 was built, some of the men moved over to Building 7. But Building 5 also housed the Laboratory of Tropical Diseases and the Division of Biologics. If my memory serves me correctly, those were the major units. Actually, the Rocky Mountain Laboratory was a part of the Laboratory of Infectious Diseases at that time until it became an independent laboratory. I think that occurred when the National Microbiological Institute was formed around 1948.

BSP: Was there any project going on for biological warfare or...?

EB: No there wasn't any as far as I know – I'm trying to remember. I think Fort Detrick may have been set up as a focus for the research on biological warfare.

BSP: But as far as you know Building 7 was not –

EB: No. There were no research efforts being expended on biological warfare agents as such.

BSP: So, when you finished your research you want to publish it in the journal and do you have to send it to someone to read it or screen it?

EB: Oh yes. Usually what happened – well, working in Huebner's laboratory he reviewed all the manuscripts – actually when we wrote manuscripts we all reviewed them, because I wrote a number of manuscripts in collaboration with Huebner. And then, of course, I wrote a number as senior author, but after we were satisfied that initial review by the authors was finished, the manuscript was turned in to the chief of the laboratory. Actually, Dr. Armstrong retired as the chief. I came in August but he was – I think he actually retired in November of 1948, but he continued working in the lab. Dr. Karl Habel became the chief. So, all the manuscripts went to Habel and then he would distribute them to various members of the Laboratory for initial review. Then, once it had gone through the general review in the laboratory, the authors would send it off to the journal where, of course, the journal editors would review it.

BSP: So there is no classified research or –

EB: No, nothing was classified. I mean everything was in open journals, at least at that time. I don't know about...

BSP: What are the main journals you wanted to publish in –

EB: Well, actually the main journals that we were writing in at that time were: *The American Journal of Hygiene*, *The American Journal of Public Health*, *Proceedings for the Society of Experimental Biology and Medicine*. We wrote a couple of review articles for *The New England Journal of Medicine* and *Journal of the American Medical Association*, *The Journal of Immunology*.

BSP: What about *Bulletin of the Public Health Service*?

EB: Oh, as a matter of fact, my very first article [laugh] I submitted to the *Public Health Reports*.

BSP: And *Public Health Reports* has a good reputation as a scientific journal or just that you know a channel for –

EB: I think that it sort of functioned the way *MMWR* functions nowadays.

BSP: What is *MMWR*?

EB: *MMWR* is the acronym for “Morbidity and Mortality Weekly Reports”. It is a publication of CDC that contains descriptions of current infectious disease outbreaks as well as discussions of other non-infectious public health problems. It also lists statistics and current incidence of reportable infectious diseases. *Public Health Reports* served in this way as a sort of an informational journal, but a lot of good research appeared in that publication because this was the primary organ available by which the men associated with the *Public Health Service* could publish their findings. So, the majority of Dr. Armstrong’s articles appeared in the *Public Health Reports*, and also Dr. Huebner’s articles, many of them, the early ones appeared in the *Public Health Reports*. I don’t know when the *Public Health Reports* stopped publishing, but I know it was after I left.

BSP: And, of course, you had frequent interactions with the people in Building 7, but what about the researchers in other buildings like NIAND had, at that time, Arthur Kornberg, Leon Heppel and also NCI had Dr. Green...

EB: Jessie Greenberg.

BSP: Greenstein.

EB: Greenstein.

BSP: And other people and there were a lot of biochemist and also –

EB: I don’t think there was that much interaction. I used to go to meetings of what was called the Junior Officers Association, and I would meet some of the young researchers at that time; but I don’t think there was that much interaction between the

people – you know the Laboratory of Infectious Diseases and other people. They all knew each other because it was a small campus; but, again, they were working in different fields and they were pretty much confined to their own particular research projects.

A lot of the research that was done at that time in LID was sort of strictly biological, and I don't think anybody was really doing anything in the chemical or physical sciences related to infectious diseases, at least while I was here. Later on there were some people out at the Rocky Mountain Laboratory who started becoming interested in applying other disciplines to the study of infectious disease problems, but this was well before – well, it wasn't that far before, you know, the development of recombinant DNA technology and, you know, the working out of the structure of DNA by Crick and Watson reported in 1953. That was 1953, so when I was here there was very little interaction or application of related scientific disciplines to microbiological research problems.

BSP: I don't know whether you sensed at the time, but after World War II, about a decade after World War II, there was a change in emphasis from infectious diseases to chronic diseases like cancer, heart and other –

EB: Oh yeah.

BSP: – things that while you were working in Building 7 did you feel, well, NIH was really changing its emphasis? Did you feel that somehow –

EB: Well, I didn't. I didn't feel it personally, although I knew that this was going on. I'll tell you what happened. See, I grew up in the era of the introduction of antibiotics and everybody said, "Oh antibiotics – infectious disease is a dead science."

BSP: [laugh] Did they [unintelligible] opening?

EB: Oh yeah, yeah. It was the end of history, you know?

[laughter]

EB: And I remembered – let's see when was it? I know I came up for some examination, I think it may have been for one of the license examinations, and I met one of my college classmates. He asked, "What are you doing?" I answered, "Well, I'm working at NIH in the Infectious Disease Lab." He said, "You know, that's an obsolete science now." He remarked, "With antibiotics we're curing infectious diseases." So, I rebutted, "We'll see."

EB: [laughter] So because that's what [unintelligible] said then.

BSP: What about Charles Armstrong? Charles Armstrong you said had resigned from his position as a lab chief in 1948. Is there anything to do with it?

EB: When I came down here he was still a pretty vigorous man, and there were some political machinations going on and –

BSP: What kind of political –

EB: Well, I – this is something that I've heard rumors about and information I got through the grapevine. I don't think there's any documentation for any of this so, I don't want to go into this in any detail, but I think that Dr. Armstrong was a victim of political maneuvering. I know that there were several people who felt that he may have been sort of outmoded or past his time. He was still a pretty sharp –

BSP: This is a general mood about –

EB: I'll tell you. If you turn this off for a second, I'll tell you.

[break in audio]

BSP: Okay, can you tell me more about Charles Armstrong and his accomplishments and his leadership in the laboratory, any other things you could observe at the time?

EB: Well, my actual observation of Charles Armstrong was somewhat limited because he was not all that active, but I had an immediate favorable impression when I met him for my interview. Then, when I came to NIH, when he saw me, he said, "When you get ready to start working you can order anything that you want." As a matter of fact, Dr. Armstrong had the reputation of running a very well organized and ordered laboratory that was economical. As a matter of fact, he was somewhat – I don't know what to say – envied or admired, because at the end of the fiscal year, he always had money left over and the NIH administrators didn't know what to do with the extra cash. [laughter] But he ran a very efficient laboratory; there was never any problem getting the necessary equipment to do the work, you know, as long as it was an approved project.

BSP: Is he an MD or a Ph.D.?

EB: No, he was an MD. As a matter of fact, Dr. Armstrong graduated from Johns Hopkins Medical School back in 1915, and one of his very famous classmates was Dr. Thomas Rivers, a well known, actually, he was the dean of virologists in the 20<sup>th</sup> Century. Dr. Armstrong actually wanted to go into private practice, but then he started thinking about all of the financial obligations that he would incur, including – he said, he would need a wife. [laughter] So he decided he'd better do something else.

It was during his internship that he saw a notice for examination for the Public Health Service, and he decided that maybe he ought to apply to take the examination. This was back in 1916. So he applied for Public Health Service. In the early days the examination was really very difficult, and admission into Commission Corps was very selective. I mean, they just took the best, and he passed. Then he went through a series of assignments, like any junior officer. He was stationed at Ellis Island for a while

examining immigrants, and then when World War I broke out, he was assigned to the Coast Guard. He actually saw wartime combat service, sea duty during World War I. He was also involved in treating seamen, Coast Guard seamen, during the influenza pandemic of 1918-1919. He spent his early post-war years studying influenza. One of the things that kind of thrilled me a little bit, when I started doing his biography, relates back to one of my medical school experiences.

During my bacteriology class, our professor, a very wonderful lady, was giving us a lecture on botulism, and she wanted to describe the extreme lethal potential of botulinum toxin. She cited an epidemic of botulism caused by spoiled ripe olives, and she was trying hard to describe the toxicity of the toxin. Just a small amount of one of these spoiled ingested olives, she said, would result either in severe illness or even death. When I started doing Armstrong's biography, I became excited that his very first publication was a description of this epidemic of botulism in Ohio. He reported this when he was acting as an epidemiological aide to the State Health Officer of Ohio. Subsequently, he investigated an influenza epidemic in an isolated, closed community on an island in the middle of Lake Erie during which he made important observations about the way that influenza spread. It was after reporting these two episodes that he was invited to join the Hygienic Laboratory where he continued his subsequent career making major research discoveries.

Of course, the thing that he considered his first major contribution was the elimination of tetanus as a complication of smallpox vaccination. He reviewed and postulated current theory of the etiology of post – vaccinia encephalitis. He was involved with the psittacosis epidemic, I guess around 1930, and it was while he was investigating psittacosis that he became ill, but also he discovered that psittacosis was a filterable agent. He and his associates at the Hygienic Laboratory never visualized it, they never grew it, but apparently they did not, at least in the laboratory at that time, have the tools for isolating that particular organism.

His next major accomplishment was the isolation of the virus of St. Louis encephalitis. While he was investigating that organism, he discovered an unrelated virus from a patient who died during that epidemic. It was from this patient that he isolated the virus of lymphocytic choriomeningitis. This was really an amazing accomplishment considering that he noted the difference on the basis of the pathologic changes in the brain between the laboratory animals that had St. Louis encephalitis and the new virus. Of course, the people who worked in the Hygienic Laboratory were really very highly skilled specialists in almost all medical basic and clinical sciences, and Armstrong also happened to be a very excellent pathologist, as well as an epidemiologist. Armstrong also discovered the reservoir for this new virus in urban mice, and he was the first to describe a flu-like infection in humans caused by this virus. The French honored Armstrong by naming this illness "Le Maladie d'Armstrong".

This brings him up to about the period of the middle to late 30's when he started becoming interested in poliomyelitis. Working in the laboratory, he found that he could block the spread of certain neurotropic viruses in mice by instilling astringent material

into the nasal passages because apparently, by blocking the receptors of the olfactory nerves, he could prevent the virus from penetrating to the central nervous system,

He thought that this was also the way that polio might be transmitted; apparently, this was really not the main mechanism. Anyway he speculated that if he could block the nasal passages with an astringent material, he might be able to influence an epidemic of polio. He went down to Alabama, started putting picric acid into [laughs] the noses of people, but the epidemic got out of hand, the way the insurrection in Iraq is getting out of hand. I mean, people just started spraying each other, and there was no way that he could run any kind of controlled epidemiological experiment.

BSP: Do you know what he did during World War II?

EB: Well, actually right before World War II, I think it was 1939, he was able to adapt type 2 polio virus to rodents. This was a major advance because before that people working with polio had to use monkeys; it was the only known experimental animal, but then he adapted polio first to the cotton rat, the eastern cotton rat, and then to mice. For ten years, this was the only experimental animal other than monkeys that could be used to check – do research on polio. As a matter of fact, it was one of the mouse adapted polio – one of the Lansing type strains, type 2, that Enders used to cultivate the polio in non-neural tissue – Enders and, his associates, Weller and Robbins.

But during World War II, I think Armstrong was primarily – actually, back in 1940, he was involved in the first epidemic – or the first laboratory outbreak of Q fever at NIH. He became ill himself. He described some of the pathology of Q fever and, then, I think during World War II, he mostly just administered the laboratory. He also, went out to Rocky Mountain Laboratory to help with the production of yellow fever vaccine. It was while he was out there – somehow or other, he was exposed to tularemia, and he almost died from tularemic pneumonia. As a matter of fact, his daughter and wife were on constant alert to be ready to go up to Montana at any time. Fortunately he recovered from that illness and so – then – let's see, that was back around 1942, and the war was still going on. In 1944, he recruited Huebner into the laboratory, and he helped Huebner with the rickettsialpox study in 1946. And – I don't know whether you – did you read the chapter on –

BSP: Rickettsial, yes, yeah.

EB: And the way that Armstrong immunized mice against lymphocytic choriomeningitis. You see, the colony in Kew Gardens, the mouse colony in Kew Gardens had endemic lymphocytic choriomeningitis as well as hosting the agent of rickettsialpox. When Huebner tried to transmit tissue from the Kew Gardens mice into laboratory mice, these mice came down with an illness; but, it wasn't rickettsialpox, it was lymphocytic choriomeningitis. So, Armstrong immunized a group of laboratory mice against lymphocytic choriomeningitis. After these mice were immune, Huebner injected them with tissue from the Kew Gardens mice. In this way, Huebner and Armstrong were able to isolate rickettsialpox from the Kew Gardens mice. This is the way by which Armstrong collaborated in the rickettsialpox investigation. After that, he really didn't do

an awful lot in the laboratory. He collaborated with some of the medical practitioners in the area. I think he isolated toxoplasmosis from a lymph node. He became somewhat interested in cat scratch fever. Then, actually in retirement, he started doing some atmospheric studies to see if he could correlate changes in temperature and humidity with the prevalence of polio. I don't think this work was every really of any major significance. Most of his really significant research studies occurred, I guess before World War II.

BSP: Could you comment on the size of his laboratory, and how many principal investigators are working with him, and how many technicians, and –

EB: Well, actually, he –

BSP: Or by himself –

EB: Well, in the Hygienic Laboratory, he worked with several other people. He collaborated quite a bit with Dr. James P. Leake, who was head of the epidemiological unit. He worked with him during the St. Louis encephalitis period. He worked with occasional other members of the Hygienic Laboratory. He usually had, I think, one laboratory technician to help him. He worked primarily by himself. When he became Chief of the Laboratory of Infectious Diseases, I think it was 1942, he continued doing his own research, but mainly administered the activities of the other members of the Laboratory. These included the Rickettsial Unit, which consisted of Topping, Shepherd, Henderson (who died of scrub typhus), and then Huebner; some of the other units were those headed by Dr. Carl Larson, Dr. Dorland Davis, Dr. Chester Emmons (the fungus unit including Dr. Samuel Salvin), Dr. Karl Habel, Dr. Birdsall Carle (who was head of the Brucellosis Unit) and, of course, Huebner when he became head of the Rickettsial Unit. So, Dr. Armstrong had maybe about a dozen investigators who were part of laboratory that he administered.

Every day he would go in and sort of putter around the laboratory, but he made major contributions when Bob Huebner and I started the work on the Coxsackie viruses. Bob Huebner wanted to make sure that we weren't dealing with any poliovirus, so Dr. Armstrong took some of the test material from our epidemic – specimens that we knew harbored Coxsackie viruses, injected them into monkeys, and showed that they contained no poliovirus. He helped exclude polio while we were studying our first Coxsackie virus outbreak. He then made a significant observation noting the difference in appearance between mice infected with Coxsackie group A type 1, and the other Coxsackie herpangina viruses. I don't know whether you have a copy of the paper that I wrote on the laboratory aspect of the group A Coxsackie viruses. The paper contains pictures of the differences in the appearance of the mice, the ones –

BSP: Yeah –

EB: Dr. Armstrong demonstrated this point, and also, it was shown by microscope that there were definite differences in the histologic appearance of the infected mice. The

payoff for this observation was that, at least from my perspective, when I was asked by Dr. Huebner to stop working on my own little project and take over the pleurodynia project, was recognition that the first isolates we had from the outbreak were of this Coxsackie group A type 1. We surmised that this was probably a contaminant because during the course of the herpangina studies we knew that people could be infected with more than one enterovirus type. So, sure enough, we neutralized the tissue of mice that had demonstrated the Coxsackie group A type 1 appearance, and passed their tissues into other mice. In this way we isolated the Coxsackie group B type 3, which was a cause of the pleurodynia epidemic. But it was the observation contributed by Dr. Armstrong that was a tremendous help in, you know, helping to elucidate this particular problem.

BSP: Right. In your book on Huebner you mentioned a little bit about the relationship between Armstrong and Huebner. Huebner – why Huebner came to NIH and he had an interview with Armstrong and there are several other versions. Could you start talking about Huebner and when he came to NIH?

EB: Well, Huebner is very remarkable from the standpoint that he really had no scientific training. He came – he had only medical school training, but the thing is that Huebner started off with a great mind. He was elected to the honorary society in medical school, and he had his sea duty with the Coast Guard up in Alaska during World War II, but nothing outstanding. He was just a good officer, a good medical officer. And then, when he was transferred from Alaska, he was put into the ear, nose and throat clinic downtown at the Public Health Service headquarters. I remember talking about this with Huebner. I asked, “How come you came here?” He said, “I was interested. I wanted to do something different. I thought I’d like to do a little research”. He said he went to a commissioned officer’s gathering and he met Dr. Armstrong. He just talked to Dr. Armstrong and wanted to know if there were any opportunities out at NIH. Dr. Armstrong replied, “Well, come on out and I’ll show you around.” [laughter]

EB: I mean this may not be the exact conversation, but basically he became acquainted with Armstrong. He came out here. Armstrong interviewed him and Armstrong took him on. As a matter of fact, I was talking to Mary Emma Armstrong, and what Huebner wrote in his condolence letter after Dr. Armstrong’s death is at some variance with what she remembers her father telling her about Huebner’s arrival at NIH. Apparently Armstrong came home and he would share some of the information with Mary Emma, his daughter, and his wife. He reportedly said, “A new young fellow came out,” and he continued, “He’s a bit of a smart-alec. We’ll have to teach him a thing or two.”

EB: [laughter] I may put that in the Armstrong biography because it is a little bit of – so you see there is some variation in oral history about what’s spoken and what people hear, but in any event I think what Huebner wrote in his letter, relating about the way he started here, was probably pretty true. The fact that he was just put into a room like this, maybe a little bit larger, and told, “Well, here’s your lab and office; get started.” And he went scrounging around, found some furniture and picked up, I guess, some test tubes and beakers and all that stuff, and, then, apparently, he must have been taken on by the Rickettsial Unit to replace Dr. Henderson who had died of scrub typhus.

Something that wasn't in the Huebner biography is that there were two people who came down with scrub typhus at that time, Henderson and also his laboratory technician Leroy Snellbaker. Apparently Henderson was a ruddy, healthy, rather large person and Snellbaker was not a very tall person, a kind of skinny, scrawny guy. Snellbaker survived, and Henderson, of course, passed away. During the last couple of years that I was at NIH Snellbaker, fortunately, was my lab tech. He was great, really was.

BSP: Let me stop our tape one and I will change the tape.

EB: Okay.

BSP: Thanks.

[end of tape 1 side B]

BSP: This is tape 2 of the oral history interview with Dr. Edward Beeman.

[audio break]

BSP: So, you mentioned that Dr. Huebner had relatively little research experience before coming to NIH.

EB: Absolutely none, yeah.

BSP: And by the time you came to NIH in 1947 / '48 did you see Huebner establish himself as a researcher?

EB: Well, let's see, he came in 1944 and I came in 1948. He already had one major research accomplishment. That was the rickettsialpox study. He had participated as a member of the Rickettsial Unit in another study; it was a comparison of the immunologic properties of six Q fever strains. It was during the course of this study that the second outbreak of Q fever occurred in laboratory. This happened over in Building 5 and Bob Huebner studied the epidemiology of that outbreak. He correlated the incidence of the outbreak – of the incidence of cases in the outbreak - with the activity during the preparation of Q fever antigens, which produced tremendous contamination in the environment. He also participated in a clinical study of the cases that were hospitalized in the Marine Hospital in Baltimore.

In fact, it was the rickettsialpox study, and also the Q fever outbreak, with which I became acquainted before I came down to NIH; I remember reading about the clinical aspects of Q fever in one of the medical journals. When I came down here in August 1948, Bob Huebner was in California working on the Q fever in the dairy industry in Southern California, and this was also his second major accomplishment. As a matter of fact, this was probably some of the best work done in Q fever since people started studying it. As a matter of fact, I arrived in August and he didn't show up until either

October or November so for three months I never saw him after I arrived here. He said that the laboratory had three new strains that he wanted to have checked against the six original strains that had been studied – the Q fever strains that the lab had studied back in 1944. This was the project on which I “cut my research teeth” and that’s when I became involved in learning how to deal with rickettsial laboratory techniques, growing the organisms in eggs, immunizing guinea pigs and making antigens and all that and –

BSP: So, by that time Huebner was quite experienced –

EB: He was –

BSP: – on top of everything?

EB: He was a very experienced investigator by that time. As a matter of fact, it was very interesting when he started working on California Q fever. He went out to the Los Angeles area originally with Dr. Charles Shepard, who was a very brilliant guy, but mostly a lab man; he really didn’t like to do epidemiology, and they uncovered the fact that Q fever cases were occurring in relationship to the dairy industry in Southern California. So, anyway they determined that this really had to be investigated because they felt it was a disease of major public health significance; but Shepard didn’t want to be involved any longer. So, Bob Huebner took over the entire project, and it was at this time – you know, this is when Dr. Armstrong really gave him tremendous support in terms of personnel, funding for the project and also, apparently, he got him out of a lot of administrative difficulty. Bob had the habit of – if he needed something while he was out in California, he’d just go ahead and buy it and then send the bills back without consulting with anybody. He got into all kinds of [laugh] bureaucratic, administrative hassles, and, apparently Dr. Armstrong, rescued him from all these administrative quandaries. Also, Dr. Armstrong gave him tremendous moral support in the California Q fever activity. It was also at this time that Bob Huebner began collaborating very actively with one of his other major collaborators, namely Dr. Joseph Bell who was Chief of the Epidemiology Unit, Laboratory of Infectious Diseases.

BSP: That’s what I want to discuss a little bit in detail. How Huebner’s work / research got started. There is an outbreak – epidemic outbreak in some area in the United States and then he was asked to go there and examine things and come back to the lab and he’d do the lab work, and so it seems like there was a combination of field work and laboratory work and epidemiology work and etiology work and other chemical experiments. Could you explain the flow of the research work and how it got started?

EB: Well yeah, this is actually a continuation of the tradition of the old Hygienic Laboratory. The men combined field work with bench work and –

BSP: And sometimes clinical.

EB: And occasionally clinical work if they had the experience. Now Huebner had clinical experience so he did clinical work early on. The Q fever epidemic started when

one of the practitioners in Southern California, in Los Angeles county, I think it was Dr. Frank Young, saw a lot of patients with atypical pneumonia, and he suspected Q fever. He sent blood to NIH, and more than one sample of these bloods came back positive for Q fever antibodies. Then, I guess, the local health department became concerned because actually one of their health officers came down with Q fever. So, what happened? Now this is in the days before CDC. Any request from the states for federal help would come to NIH, and usually to the Laboratory of Infectious Diseases, or its previous entity, the Division, or before that the Hygienic Laboratory. And most of this assistance was to help with an infectious disease.

So, anyway, the word got to LID/NIH that sent out a team, the initial team of Shepard and Huebner. With help from the local health officers and practicing physicians, they started looking for old and new patients, getting blood and other clinical specimens from them, which they sent back to NIH. They tried then to see what epidemiological factors might be operative. They looked closely at the dairy industry in Southern California that was rather unique, I think, as I discussed in chapter on Q fever. In this manner they came to the conclusion that this was a disease of major proportions and somehow it was related to the dairy industry. Bob Huebner felt that this was a situation that really had to be looked into. Shepard decided he just wanted to work in the laboratory. Bob Huebner then assumed primary responsibility for the investigation. He organized this program, enlisting the help of some of the community physicians, the public health people at the county and state level, and personnel at the Rocky Mountain Laboratory. Bob recognized the need for extensive case finding and he realized he had to have experienced epidemiological help. This was when he called upon Dr. Joe Bell, and Joe Bell, in turn, got some of the state and local epidemiologists involved. So this turned out to be a rather large-scale study of an outbreak involving a lot of people, and Huebner sort of coordinated the entire effort, I mean he –

BSP: Could you comment more on the collaboration between epidemiologists and virologists, in other words Bell and Huebner, and what kind of information epidemiologists provide for –

EB: Well, the epidemiologists would go out into the population and –

BSP: Do the interviews?

EB: They would do interviews, and physicians would examine patients, collect clinical specimens including blood specimens for antibody studies. In the meantime, Huebner was collecting material from the cattle – he was the first one that tested the milk and showed that –

BSP: Oh, I see.

EB: So, in other words, it was a collaborative effort – everybody worked together, and they pulled the information and correlated the results say between blood, isolation of organisms, history of illness and with various epidemiological factors – occupation,

proximity to the sources of infection, such as whether a person lived near a dairy or far from a dairy, and what the study would do is try to have enough of a population to act as a control on the persons with illness and those with Q fever antibodies. They used a large group of normal persons as a control to the patients who were infected. This was the same principle we used when the laboratory started doing the studies on the Coxsackie viruses; basically, the same thing but on a smaller scale.. So the Q fever study was done on a tremendous scale compared with the smaller scale that we used, when we went into the herpangina studies. Pleurodynia studies in Texas were also done on a large community basis and again, you know, we used more people, but the principles were the same. In patients with a possible infectious illness during an apparent epidemic, attempts are made to get material to isolate the organism, or the causative agent, and then, if it's something that's deemed to be of public health importance, then it is important to employ epidemiological principles in to try determine what the factors are that bring about the establishment of an epidemic of this particular organism.

BSP: What about the clinical, such as it seems like the next project, or the following project, was done in the junior college – Junior Village, and it seems like –

EB: Well that came, actually that started in 1955, so this was a few years afterwards.

BSP: But this case –

EB: But there are some other things that happened in between Q fever in California and Junior Village. In any event, Huebner was able to definitely establish that Q fever in dairy cattle was spread by means of the milk, and then later the veterinarian, Laurie Luoto, showed that the placentas and birth membranes of parturient cows were also heavily laden with Q fever organisms. This was another factor; that accounted for infection among people that worked in tanneries, slaughter-houses, creameries and related industries. So all of these factors together built up a picture of Q fever in humans related to the cattle and their raw products. Milk, hides and things like that, so this is the way that the study established the connection. Interestingly enough, when CDC became established and started utilizing its Epidemiologic Intelligence Service, NIH really just stopped doing these sorts of investigation. The only time NIH really resumed these kind of population studies was later during vaccine development. In between California Q fever and Junior Village, there was – well, actually what happened after Huebner finished with his studies in California, he was sort of “kicked out of the state”, because the men who ran the certified dairies were very upset. [laughter]

Anyway, when returned to the lab from California, this little project I had – we never wrote it up because it showed basically the same results that the original study showed, and we figured that it just wasn't worth publishing. Beside which, we never really tried to get into the reason to explain the results. It was actually somebody out in Rocky Mountain Laboratory, Dr. Richard Ormsbee, who found that the difference in the immunologic behavior of the different strains was due to whether or not the organism was in phase 1 or a phase 2. But that's another story. In any event, information of this sort was something that Huebner was not interested in initially as a major focus of his Q

fever investigations. He was interested in the big picture, and Ormsbee on the other hand started employing bio-chemical methods to tackle this particular problem. Huebner was not equipped by training or intellectually, at this time, for basic biochemical investigations.

But the next thing that happened when Huebner came back from California, having been kicked out, was that apparently he started thinking he wanted to find out what were all of these quote unquote unknown “virus” infections that were producing respiratory symptoms. He wanted to work on those agents, but he really didn’t have the background to do this, and the technology was still not fully developed. But instead, Coxsackie viruses were just becoming recognized, so Joe Bell took us up to a meeting in Pittsburgh, and we heard about Coxsackie viruses. We returned to Bethesda. This was around late summer, and the following was typical of Huebner’s thinking. He said, “You know, these Coxsackie viruses tend to follow the temporal occurrence of polio”. He continued, “We’re entering polio season now. What we should do is to maybe try to handle some small epidemics that occur locally that we can study.” So, he said, “Let me go around and talk to a few people in the laboratory, most of them live in the area, and see if they know of any epidemics of fever”.

So he started asking around. We used to have a room in Building 7, a little larger than this one, where the doctors used to eat “brown bag” lunches together. Huebner would come into the lunchroom and ask the men, “Have you heard of any epidemics in the area lately?” [laughter] – of cases of fever that are spreading. So one day, one of the men said, “Gee, you know, there are a couple of kids ill over in Parkwood,” this is a little area right across Wisconsin Avenue, going up Cedar Lane. So Bob said, “Well, why don’t we go and see what’s happening?” So the first thing we did is we got hold of a nurse and some material to collect stool specimens. We started collecting stools from these people and Bob said to me, “Ed, you’re going to start isolating viruses from stools.” So I said, “Okay, fine.” I had never worked – I had just been working with eggs and guinea pigs, and hadn’t worked with suckling mice, so I had to start from scratch to learn how to work with these animals, and learn how to harvest their tissues in order to get the proper reagents needed to study the problem.

So, lo and behold, I think there was an epidemic of something like eight cases within a week in the first year of the study. Every time we’d put sample of the stool from a case into the suckling mice, they came down with paralysis, so we put them in the freezer, and we kept collecting stools. Then Huebner and Bell organized the epidemiological study and the community survey. It was at this time that Roger M. Cole, my classmate from medical school, came to NIH and he joined me at LID; he had spent a year up in Boston working with Louie Weinstein. So Roger went to work with Joe Bell, the epidemiologist, and Roger really did the epidemiological leg-work on the epidemic. As the study progressed Roger, Huebner and the nurses went into the community taking histories, examining patients, collecting stools, and collecting blood specimens. All this material was arriving, being logged into the laboratory, and stored in the deep freeze until I could get to it. We started putting these specimens into suckling mice and before you knew it we had numerous isolations. After a while, we recognized that there were different

serological strains of Coxsackie viruses among the isolations from the total community – from the initial outbreak we isolated just a single serologic type. But then the subsequent isolations we found were similar viruses of different strains, apparently just in the community, but not associated with illness.

So, anyway, you might say, I mined gold out of all this fecal material. We wrote up our experience for the first year, and, then, I was sent out to San Francisco in June 1950 to deliver our first paper on the Coxsackie viruses at the annual AMA Convention. We didn't recognize the illness as such because we didn't see the cases really early when they had the typical symptoms that we recognized with the second outbreak in September 1950. So I gave the paper out in California. Then, also, I monitored the Q fever exhibit out there at the convention. This was in June of 1950, and all – I was in San Francisco, the Korean War broke out, but fortunately [laughter] I was in the Public Health Service. I was actually taking a six-week break away from the lab– it was a combination of vacation leave, travel time, and meeting time. It was a six-week period, and I was about halfway through the six-weeks. I had another three weeks to go, so I called up the office at the Laboratory, and I said, "We're at war. I'm here in San Francisco, and I have three weeks left on my leave, shall I come home immediately?" The reply was, "No, take your time."

As a matter of fact, on the way back, I had arranged an interview with the Mayo Clinic. [laughter] So, after we left San Francisco, we (my wife and I) took a slight detour to Yosemite, [laughter] then, we went up the coast of Oregon by way of the Redwood Highway, and then we went up the Columbia River Valley. We stopped off at Glacier National Park, and then traveled south to Yosemite National Park. From there we traveled homeward. I stopped off at Rochester, Minnesota, had my interview at the Mayo Clinic, and then we came home. No sooner had I come home, when Huebner and I heard about another outbreak of illness in Parkwood. This time, however, Dr. Carle's, (who was head of the Brucellosis Unit), daughter was the first patient, the index case. Dr. Carle, being a compulsive physician, looked down his daughter's throat because she was complaining of a little sore throat. He noticed the spots that were very typical of the condition that we call herpangina. He called up Bob Huebner, and he said there were some other children in neighboring houses with similar illnesses. Dr. Carle said, "You ought to take a look at them." So Bob went out, he saw these other cases of herpangina, and then there were some other scattered cases, so that's how we happened to –

BSP: By the time, you know, the CDC was created –

EB: Well, CDC was created, but they weren't really into looking into these epidemics. NIH – the Laboratory of Infectious Disease was still doing, I would say, most of the federal assistance in the local communities, if they wanted help with investigation of febrile outbreaks. CDC started, I guess it was maybe the middle of the 1950's decade. Actually, I think one of the last community outbreaks that the laboratory investigated was the outbreak of pharyngoconjunctival fever caused by adenovirus type 3 in Northern Virginia. Bob Huebner, Joe Bell and associates conducted this investigation. This was back, I think, around 1954.

BSP: So, about – before that time, when there was a – outbreak, NIH scientists were asked to investigate, and then if it happens to be Huebner, Huebner goes, and if it happens to be others...

EB: Yeah, they would be called to investigate, say, tropical diseases, the men from that lab would go. But often the states had their own laboratories, their own epidemiological expertise, so they could do it without calling on the federal government for help.

BSP: I think it's very interesting that the research, original research, was initiated by some epidemic outbreak, or call from [unintelligible] service, and then serious lab work and field work going on, and then after it's finished, scientists came back to their labs, and was there any ongoing project while the people like Huebner were away?

EB: Yes. While Huebner was in California, he and his co-workers were sending all these specimens back for testing by the lab technicians in Bethesda. Now, while we were working on Q fever, Bob had a project going with his chief bacteriologist, Betty Ransom. He was interested in the resistance, of *Coxiella burnetii* (Q fever) to various chemical and physical agents. They found it was very resistant. As a matter of fact, one of the things they found was that the Q fever organism resisted temperatures that were used in the normal process of pasteurization – commercial pasteurization.

The other thing that he started to do – well it wasn't with Q fever, it was when we got into the Cocksackie viruses he started becoming interested in the physical properties of the Cocksackie viruses, or at least the group A viruses. We had a guest worker from Germany, Angela Briefs, who had a PhD in maybe biochemistry or physics. I supplied the material, and she, Huebner, and several researchers at Walter Reed Army Institute of Research performed electron microscopy studies on the organism. They used just one strain of group A Cocksackie virus grown in mice and the same strain that had been adapted to grow in eggs. They compared the sizes of two by electron microscopy and by determination of the sedimentation constants and found them to be similar.

They didn't do any special chemical studies, just these physical properties that they were really interested in, but this was really the first time that Huebner started doing anything of that sort. Before, he was interested mostly in the biological aspects of the organisms. Then, of course, later on as time went by, as he had the people who had the interest and also the training, that he was able to get into the biotechnology age. It was with the appearance of Wally Rowe that he really started, became interested and was able to expand the study the organisms in greater detail.

As a matter of fact, right after we finished the studies with the group A Cocksackie viruses, I became interested in the question of the age susceptibility of mice to infection with these viruses. I started doing some preliminary experiments. In retrospect now, I realize that I probably was taking the wrong approach. I don't think it's ever really been shown definitively why there's a difference in age susceptibility. There have been some

papers written on whether the development of interferon in tissues helps protect mice of a certain age or whether the loss of cellular receptors at a certain age also prevents infection with the virus. Those were some of the approaches that have been taken, but I don't think I've seen anything really definitive about the age susceptibility of suckling mice to infection with the group A Coxsackie viruses and the apparent tropism for skeletal muscle susceptibility.

BSP: So in early 1950s he was still working, field work and the laboratory work and then –

EB: Yes

BSP: – and here is a case of I really want to go to the '60s and his virus cancer program, but before that there was another community-based research Junior Village –

EB: Well, actually what happened is that when I left Huebner decided that the only way he could study respiratory viruses was to have tissue culture capability.

BSP: Okay.

EB: And fortunately that's when Wally Rowe came in, but it was again Huebner's intuition that prompted him to use explants of what appeared to be normal adenoids and tonsil tissue to put into tissue culture. It was from these "normal" explants that Huebner and Rowe isolated the first adenoviruses. Then, of course, once they had patients who were acutely ill with adenovirus infections there was no problem isolating the viruses from throat swabs. Wally Rowe really set up the tissue culture system in Huebner's laboratory. Dr. Alex Shelokov, who was working with Dr. Karl Habel, actually set up the first roller tube tissue culture system at LID. Alex was sent up to Harvard to work in Dr. John Enders's Children's Hospital laboratory to learn the setup and to learn the technique. Alex came back; then, he instructed Wally Rowe about how to do it. As a matter of fact, I think I have this all outlined in the Huebner biography section on the adenoviruses.

Then Dr. Bob Parrott, working with Huebner and Rowe, recognized the first distinct clinical entity caused by an adenovirus, namely, pharyngoconjunctival fever; that was one of the first clinical infections that was studied in the Clinical Center back in 1954. Also, the epidemic of pharyngoconjunctival fever in Northern Virginia was the last community outbreak that Huebner and Bell studied. It was after this study that they conceived of doing a longitudinal and cross-sectional study of the prevalence of infections during good health as well as illness in a closed orphanage nursery population group. That was the Junior Village study initiated in 1955 during the course of which the group isolated all kinds of viruses and previously unrecognized, newly discovered respiratory viruses and –

BSP: So it's going to the community and it is examining what kind of viruses are there?

EB: Well, actually it wasn't a community. It was a closed institutional population. Before that Huebner was in the general community, out in the population, but here he was taking a group of nursery kids who were confined to a hospital ward or a nursery ward, and they were checked on a regular periodic basis. The group collected throat and stool specimens from them on a regular schedule and obtained blood from them at scheduled intervals. The investigators isolated all these different viruses. As a matter of fact, they isolated so many of them that sometimes they couldn't correlate which virus [laugh] went with what disease.

BSP: Virologist's dilemma?

EB: Yes, that's what Huebner philosophized about - how to tell when a virus is causing a clinical entity. As a matter of fact Vicky Harden paraphrased his postulates about this dilemma in one of her publications. It was after this time – about this time, towards the end Huebner's major involvement with the Junior Village Study – the first three years were the most active and around 1958 he became interested in working on the cancer viruses.

BSP: So, in the Junior Village he mainly collected viruses –

EB: Well he –

BSP: – rather than doing any clinical trials or other...?

EB: Well, they didn't do any clinical trials primarily – actually they did some small clinical trials. Joe Bell was interested in the effects of penicillin on some streptococcal infections; he was also interested in studying different vaccines. The study had a full time pediatrician who examined the kids on a daily basis. So, Huebner actually didn't do detailed clinical examinations. The study collected so much test material and specimens that deep freezes kept crowding out the available laboratory space. That's when the major physical changes occurred in Building 7. The renovation crews started getting rid of all of the anterooms where people were supposed to change their clothing, and they started cutting up the space into little cubicles to make additional offices, because that's also when Huebner started increasing the number of personnel in the Laboratory of Infectious –

BSP: Could you give me number of the viruses that they – roughly? Hundreds?

EB: I recorded the numbers in the Junior Village chapters in the biography. It was in the thousands, but I think the group isolated 20 new individual serological types of viruses including several new genres. There were thousands of isolations and there were some viruses that they never even – for instance if an isolation appeared to be a group A Coxsackie virus the lab didn't even bother typing it.

BSP: Then what motivated him to study the cancer virus in '58?

EB: I think the motivation was related to the experience he was having with the multiplicity and the ubiquity of the viruses. He had a very fertile imagination, great intuition, and he began speculating. He said, "People have these viruses" and he speculated that some of the frequent exposure to viruses could possibly lead to chronic illnesses later on in life. His speculation led him to state further, "Maybe even something like cancer" and then he – you know, back in the early '50s –

BSP: There were some reports.

EB: The animal cancer and leukemia viruses were becoming established as subjects for study in the 1950s. Polyoma virus (DNA virus) was discovered during this period by Dr. Ludwik Gross, co-existing with the leukemia (RNA) mouse virus he had isolated. Dr. Sarah Stuart and Bernice Eddy, of NIH (and NCI), working with polyoma virus made many important discoveries about its properties. Huebner, along with his associates Wally Rowe and Janet Hartley, began collaborating with Stuart and Eddy on several polyoma studies. Huebner theorized, "These look like good viruses to study in the animal population," because he felt that in a way the cancer experience in the animal population might mirror what was happening in the human population. He, Rowe and Hartley then started their studies of polyoma virus among various mice laboratory colonies, later extending their investigation among mice in human urban and rural ecologies. In the late 1960s when he was involved in the NCI Virus Cancer Program and was interested then in the RNA viruses (retroviruses), he was able to recruit Dr. Murray B. Gardner at the University of Southern California. Dr. Gardner was able to continue the population study in animals of the various retroviruses of mice, made many significant discoveries and became an outstanding investigator of retroviruses.

BSP: I was reading your manuscript; I was quite fascinated to see at NIAID, the Allergy and Infectious Diseases Institute, the cancer research, Huebner's cancer research, was cut and cut and then generally at NIAID had some difficulties and, at the same time, NCI was getting bigger and bigger and NCI also studied virus cancer problem. And could you say a little bit about the institutional changes? I mean his transfer from NIAID to NCI and the situation of these two institutes.

EB: Actually, Huebner started his cancer work while he was still Chief at LID. This was acceptable initially since he was still working with infectious agents. He was fascinated with polyoma as an animal model that he thought might mirror the human experience. He had willing and enthusiastic associates in Wally Rowe and Janet Hartley when they started doing their studies on the animal cancer viruses. The National Cancer Institute was also becoming interested in virus cancer research at this time and the NCI administrators began to take note and interest in the investigations of Huebner, Rowe and Hartley. The embryonic development of the Virus Cancer Program really started toward the end of the 1950s, and, then, because of the work that Huebner initiated, the administrators at NCI started inviting him to some of the early meetings of the organizations that eventually became the Virus Cancer Program. It was at this point that Bob became more and more interested and, of course, they were very –

[audio break]

EB: – people and he had all kinds of projects that he had planned about ways to study viruses and cancer. He was still involved with the epidemiologic approach, but then early on, I guess it was 1962, when it was discovered that adenovirus type 12 caused cancer in suckling hamsters that he really became deeply committed to cancer research. Bob's subsequent work discovering the tumor (T) antigens and his concept that a cancer transforming factor or factors were being transmitted genetically, I think stimulated a lot of his work and the interest in the cancer program. He was instrumental in helping to set up and organize the Virus Cancer Program, and he was the one who was really given primary responsibility for establishing the widespread network of collaborators all over the country. He was one of the prime originators of the Virus Cancer Program, and he really worked very efficiently in setting up the whole network and the whole collaborative effort of numerous cancer investigators.

The demonstration that the adenovirus, which was widespread in the human population, was a potential pathogen influenced his attempt to study whether or not the adenoviruses had anything at all to do with human cancer causation. Also, around that time, because of the development of recombinant DNA technology and molecular virology, he became very interested in work that his alma mater was doing in the person on Dr. Maurice Green who headed the Institute of Molecular Virology at St. Louis University. He collaborated very actively with Maurice Green on studying the molecular virology of DNA viruses. Of course nothing much came of that because they never established that adenoviruses were ever a cause of human cancer, but in any event Huebner gradually got into this.

Apparently there were political ramifications of Huebner's increasing involvement with the cancer activity. There were some turf battles about whether the cancer viruses should stay with the National Cancer Institute or whether they should stay with LID. Apparently, there were some marked differences of opinion and some tempers flared at times. As a matter of fact at that time, I think, Dorland Davis was director of NIAID. He was very uneasy that so much cancer work was being done in NIAID, and also the fact that NIAID didn't have control of all the virus work. So, anyway –

[break in audio]

BSP: So, we talked about Bob Huebner moving to NCI and starting his own program within the larger virus cancer program of the NCI and how did it go? Did it go very well? It started in 1965, right?

EB: Well, actually, I think the program started in 1964.

BSP: '64, okay.

EB: And he was very actively involved in the program until he finally transferred over to NCI. I think it was in 1968. So for three years he was at – it was either '68 or '69, he was very actively involved with the program, but he was also still Chief of the Laboratory

of Infectious Diseases. He was supervising his own laboratory work, he was administering the LID, and he was also administering the network of his collaborators who were working on the Virus Cancer Program.

So, actually he would have moved over earlier but there was not enough room to accommodate him and the people that he wanted to bring with him. The National Cancer Institute Cancer wanted Huebner; and they also wanted Drs. Rowe and Hartley. However, Rowe and Hartley decided they just preferred to stay in LID. They were still working with cancer viruses, but they were working on them at LID, and they were perfectly happy. At least LID was happy with that arrangement because, after all, they were still investigating infectious agents using sophisticated techniques including molecular virology.

BSP: I see, so at NIAID the cancer virus program, research program, has been going on even after Huebner left?

EB: Yes, they were working on it, but LID was also working predominantly on other things as well. After Bob Huebner transferred over, Dr. Robert Chanock became Chief of the laboratory, and another laboratory within LID for Wally Rowe called the Laboratory of Viral Diseases. Actually, I think, Huebner may have been Chief of that unit for about a year before he moved over to NCI, and, then, Wally Rowe took over after that. I have it all documented in the biography.

BSP: Was it an amicable arrangement getting out of NIAID?

EB: Yes, it was amicable. That is to say that there had been some tension and also some difference of philosophy between Bob and the Director of NIAID, but I think they –

BSP: What kind of difference?

EB: Well, it was – I don't think that I –

[break in audio]

BSP: You know the late 1960s after all the genetic codes were deciphered and people got interested in molecular biology, and certainly a virus as a carrier of RNA or DNA became a focus of interest for many people and how Bob Huebner's group started working with the genetic manipulation of the virus in cells and how that led to the hypothesis, oncogenic hypothesis. Could you make any connections with that?

EB: Well, actually, Bob Huebner personally did not do any work with molecular virology or DNA technology. The ones who were doing this were Wally Rowe and Janet Hartley while they worked on cancer studies with Bob and after he moved over to NCI. They became interested in the molecular approach to virus cancer research. However, Bob realized that this was going to be the future of virological research, and he started recruiting people who had expertise in molecular virology and molecular biology and he

started this recruitment probably in the early '70s. The other thing is that even though he had formulated the oncogene theory for the transmission genetically of the transforming factor that he called – incidentally, he was the one that coined the term “oncogene”, a mechanism had to be postulated to account for incorporation of an RNA viral genome into a DNA animal cell nucleus chromosome. The only thing is that if this was a group of genes that was transmitted genetically the model that he was using, namely the RNA viruses and the retroviruses, posed a bit of a problem because, according to the dogma of inheritance, let's see, DNA led to the formation of RNA and message RNA and not vice versa –

BSP: Protein, right.

EB: But RNA did not necessarily lead to DNA so some mechanism had to account for the genetic transmission of RNA into the chromosome of DNA, and that was the thinking invoked independently by Howard Temin and David Baltimore, the people who discovered reverse transcriptase in 1969, for which they won the Nobel Prize. So, anyway, as soon as that discovery appeared it opened up a whole new era, a whole new field, of molecular virology. Also around 1969 / 1970 Bob realized that the future advances were going to be made in terms of the molecular mechanisms involved in virological and biological research, so he started recruiting people into the Virus Cancer Program who could provide that kind of expertise. He recruited people like Renato Dulbecco, Sam Spiegelman up in New York, and, then also, he apparently became acquainted with J. Michael Bishop who was at the University of California San Francisco, and he recruited him into the Virus Cancer Program.

BSP: To? To NIH NCI?

EB: Actually, Bishop remained in San Francisco and that's where he and his group (including Harold Varmus, later Director of NIH) did their pioneering work. Huebner felt that people, with expertise, working on the molecular basis of virology were really needed in order to get the program moving, and, also, he was interested in learning more precisely – finding out about the nature of the oncogene. I mean he was only able to go so far personally. I mean he could postulate. He could present the hypothesis, but he himself didn't have the capacity to discover the nature of the oncogene scientifically. He had to get – he needed people who had the expertise so that this might become possible and that's the reason that he enlisted the aid of the people who had this kind of expertise.

As a matter of fact I think it was in the 1972 annual report of the National Cancer Institute in the section that Bob was writing as Chairman of the Virus Carcinogenesis Branch. In the very first sentence he stated that “we have to find out more about the basic structure of the oncogene” and then he went on to further discussion; but also, in the same report, was the first appearance of Bishop as one of the people who had received a contract from the Virus Cancer Program. As a matter of fact, Bob was the one who really provided major financial support for the project, and, also, he put one of his associates as the project officer to observe the progress of the research. This was Dr. Edward Skolnick who also was one of young people who was becoming very expert in molecular virology.

As a matter of fact Skolnick was one of the people who later discovered one of the oncogenes – I think the RAS oncogene.

BSP: So, Harold Varmus was one the young –

EB: I beg your pardon?

BSP: Harold Varmus – Varmus the former NIH Director?

EB: Oh, Varmus, yes. Varmus was an associate of Bishop (they both shared the Nobel Prize for their discovery of the nature of the oncogene); but, I'll tell you if you want to read something interesting, read the interview that Carl Baker conducted with Harold Varmus. Varmus said that when he was in California working with Bishop he had absolutely no interest in any of the administrative aspects of the way their lab was run. He had absolutely no idea where the money was coming from. All he knew was that as long as the money was there, he was happy. Bishop was the one that supervised all of the administrative details. Bishop was the one with whom Huebner had most contact, and he was appreciative of Huebner's support. In the paper describing the identification of the oncogene as a normal component of animal cells the authors listed the contract number that Huebner had arranged for Bishop and his laboratory. One of the things that also was very interesting was the note that Bishop wrote at the time of Huebner's testimonial retirement dinner, saying how much he owed Bob for giving him financial support at a very critical time in Bishop's research activity. So, in any event Huebner recognized that molecular techniques were very important for virological research.

In the later part of Bob's career he was working on the immunology of cancer, and, really, I don't think it was very sophisticated research. As a matter of fact, the Zinder Committee found that this was the one aspect of the Virus Cancer Program that they thought was not going to be very helpful in trying to elucidate whether or not viruses –

BSP: When does the Zinder Committee setup and give the final report?

EB: I think the final report came out in March of 1974 and basically they criticized the way the Virus Cancer Program was being administered. I think that probably the best thing is to look in the chapter where I talked about the Zinder report. I outlined all of their objections and also their recommendations that were pretty much followed. It was shortly after the report that the Virus Cancer Program began to diminish gradually. There had been the ongoing conflict about the way to administer and dispense research money – whether to do it through the grant or the contract process. Contracts to the various investigators had been the primary method of financing the Virus Cancer Program. After the Zinder report, gradually, from about 1975 on, the ratio of the monies awarded between contracts and grants reversed, and more grant money was being awarded for cancer research. The Virus Cancer Program finally disintegrated back in the early 1980s. The new Director, Vincent DeVita, reorganized the NCI, and, actually, a lot of the people who had been involved in the Virus Cancer Program began to feel that viruses, that at least RNA viruses – the retro viruses, were not a very important cause of human cancer.

BSP: Human cancer?

EB: Human cancer. So, they abandoned the program, and they went on to other things. Many of the people who had worked on the retroviruses had had sufficient training in that discipline so they became very prominent as AIDS researchers.

BSP: That's right. That's right. Yeah. Yeah. Do you know why the Zenda Committee was setup originally? In other words that people outside, the extramural community, began to fear that the contract system is not really fair.

EB: Well, there was a lot of pressure from the academic community, and all of this pressure was communicated to the administrators of the National Cancer Institute. Now this was shortly after the National Cancer Act was formulated in December 1971, and new administrative bodies were set up. The new National Cancer Advisory Board, the NCAB, responded to the pressure and appointed the Zinder Committee to evaluate the criticism of the way the Virus Cancer Program was functioning. The primary criticism was directed against Huebner, and the way Huebner was administering the program, especially the manner in which he was awarding contracts. The Zinder Committee put out a preliminary report with their recommendations. That came out sometime around December of 1973. They put out a final report in March 1974 that was basically unchanged from their preliminary report in which they had made their recommendations. Again, I think that I had most of the recommendations in the chapter in the manuscript.

BSP: With the contract system Huebner was in control of giving contracts, was that the –

EB: He was the –

BSP: Or is there a committee –

EB: Huebner was Chairman of the Review Committee that was responsible for reviewing and giving out contracts. One of the criticisms was that his review committee consisted mostly of his contractors, and they were the ones who were approving the contracts. The academic community complained that most of the contracts were really not very valid scientifically, stating that they were second-rate research. Huebner defended vigorously the scientific merits of the contracts that he and the committee awarded.

BSP: Where did the contracts go, I mean, to the industry?

EB: Yes. In the biography, I provided a partial list of the people in the network. The other place to find listings of the contracts are in the Annual Reports of the National Cancer Institute. To find them you have to go down into the belly of the NIH library in Building 10 where there's a whole cellar of large shelves devoted to those Reports. Usually, as part of the reports of individual NCI branches, the reports list the contracts

that were given out for that particular year. That's where I obtained the information about the amount of money and number of the contracts. As I recall, Bishop was the project manager for the contract and Edward Scolnick was the project officer. Very frequently Huebner was the project officer for many of the contracts in which he had a personal interest. The Zinder Committee found fault that Huebner was often project officer for his own contracts.

BSP: I understand that in the '60's – late '60s that cancer virus had a high hope for curing human cancer and you said in the 1980s that hope was almost –

EB: Well, actually the –

BSP: – what – '70s – can you?

EB: I think the main reason is that the investigators looked rather extensively for viruses, especially retroviruses, in patients with cancer and never could find any except for the relatively few cancers related to some DNA viruses such as the various herpes, papilloma, and hepatitis B viruses. As a matter of fact, one of the indirect results of the search for retroviruses as a cause of human cancer was the discovery of HTLV 1 and 2 by Robert Gallo. Robert Gallo, apparently, was very much influenced by some of Huebner's ideas about the role of the retroviruses in disease. Gallo and associates started looking for evidence of reverse transcriptase in different tissues to see whether or not they could detect any viruses. Finally there was a patient who showed up in the National Cancer Institute in the Clinical Center with the HTLV 1 virus. As a matter of fact Dr. Tom Waldmann - I don't know if you are familiar with –

BSP: Yeah.

EB: He was the one who was taking care of the patient, and he brought blood from the patient over to Gallo. Gallo had found that he was able to maintain a continuous line of lymphocyte T4 cells, and, using the cytokine interleukin 2 as a sort of a facilitator or stimulator, he was able to keep the cell line going. It was from a patient who had the HTLV 1 or T-cell lymphoma that he was able to isolate the virus. And then, later, HTLV 2 that causes hairy cell leukemia with Sezary syndrome, so those were the only ones. Of course, during the 1960s it was recognized there were some viruses that were responsible for human cancers – some DNA viruses. There was a whole group of herpes viruses that cause cancer. Even though they were probably discovered initially they really have not been a prominent – well I shouldn't say – I'll take that back, because they do cause a certain amount of human cancer like hepatocellular cancer, which is caused by hepatitis B and C (an RNA virus), then Burkitt's Lymphoma from the Epstein-Barr virus, the herpes viruses, the papilloma viruses that cause female genital tract disease and then the virus that causes the cancer that's in AIDS.

[break in audio]

EB: It's human herpes virus 8. I'm blocking on the name (Kaposi's sarcoma). However, in the totality of the incidence of cancer these viruses constitute just a small proportion. So, I think the current theory holds that most cancers are probably just due to genetic mutation caused by various influences.

BSP: Could you comment on the development of techniques and evolution of ideas [?] the relationship. You mentioned a little bit in you manuscript – what's leading?

EB: Well the point is that the research, at least the way virus microbiological research has been done, requires having a system of living cells to act as a host, since viruses are obligate intracellular parasites. Early research started off using some of the usual laboratory animals, initially, mice, rats, rabbits, guinea pigs and then, of course, monkeys. These were the major laboratory animals with which the early investigators worked. Back in 1933, investigators found that ferrets could be used to grow influenza virus. The next major technique or laboratory host was the embryonated egg. With the egg you could grow influenza and rickettsias. Various tissues of the egg provided the substrate for the manufacture of vaccines for influenza and rickettsias..

BSP: Outside the living organism?

EB: Well, no. The embryonated egg is living and develops growth in an incubator. When I arrived at NIH in 1948, the lab had the usual laboratory animals, the rabbits, the guinea pigs, the mice, the embryonated eggs and access to the others mentioned previously. The next major laboratory host that appeared in the lab in 1949 was the suckling mouse – yeah the suckling mice.

BSP: Suckling mice?

EB: Yeah.

BSP: What is it?

EB: For growing Coxsackie viruses, and, then also, of course, they were used to grow the mouse leukemia and cancer viruses.

BSP: Is tissue culture techniques is the –

EB: Tissue culture technique was the latest development, appearing in the Lab in 1950-1951. As a matter of fact, tissue culture techniques started in the National Cancer Institute going back many years around the – I think Alexis Carrell with the Rockefeller Institute was a pioneer in this field in the early 1900s, but Wilfred Earle, at the National Cancer Institute, had been experimenting with tissue culture techniques for many years. He was using these large, cumbersome glass containers and using large pieces of tissue. It was only during the late 1930s / early 1940s that innovators developed the other techniques where they would use specific cell lines growing in nutrient fluids, and using

monolayers of cells, to grow viruses that enabled modern virology to advance and develop.

Dr. Alexis Shelokov set up the first tissue culture system at the Laboratory of Infectious Diseases around 1951 after he joined Dr. Karl Habel's Unit in 1950. Dr. Shelokov and I were fellow interns at Boston (along with my medical school classmate Dr. Roger Cole). He followed me to NIH after he had spent several additional years as an infectious disease resident with Dr. Louis Weinstein in Boston. Dr. Habel, at that time Chief of LID, sent Alex to Dr. John Enders's laboratory at Harvard – actually it was Children's Hospital – to learn the technique of tissue culture in roller tubes. In this technique, test tubes containing a monolayer of living cells bathed in a nutrient solution were placed in a rotating drum containing many test tubes after having been inoculated with specimens suspected of harboring viruses. The roller drums were incubated at various temperatures to encourage viral growth. At appropriate intervals the tubes were examined under the microscope to detect evidence of virus presence. Several self-sustaining lines of cells from various sources had been developed, and were adapted suitably for use in this technique. The roller tube tissue culture technique lent itself admirably to the rapid and efficient examination of numerous specimens for the presence of viruses.

One of the other major developments was the successful employment of the nutrient solutions that were used to bathe these cells to keep them healthy for a week or ten days until the fluids had to be changed to allow for continued growth. Dr. Harry Eagle – I don't know if you are acquainted with that name -, formerly with NIH, devised what was known as the Eagle Special Medium, a balanced combination of amino acids, minerals, vitamins and small amounts of protein in the form of calf serum protein. Eagle's medium has been used extensively, as well as other nutrient solutions, in tissue culture maintenance. These, then, represent the techniques that were developed and used to propagate viruses and, of course, this represents the innovation that led to the successful development of the polio and other vaccines.

BSP: I see. In one other chapter you mentioned that it is the public health concerns, not the techniques, that are leading the research direction.

EB: Well –

BSP: Is it?

EB: Well, at least in virology it was the techniques that determined what one could accomplish. As a matter of fact, with the availability of tissue culture brand new viruses were discovered. In the Huebner manuscript I mentioned the so-called ECHO (Enteric Cytopathogenic Human Orphan) viruses. These were viruses that were only isolated in tissue culture and grew in no other animal hosts. For that matter, the Coxsackie group A viruses, for instance, grow almost exclusively in suckling mice, and most of them don't grow in tissue culture. Some of the group B viruses will grow in tissue culture, but the ECHOviruses and agents such as the parainfluenza, respiratory syncytial, REO, and the cytomegaloviruses, were all discovered in tissue culture.

As a matter of fact, this was what happened during the Junior Village study because the investigators used tissue culture almost exclusively and they discovered all of these other viruses. Among many new ECHOvirus serological types, they isolated what was then described as a relatively new group of viruses, actually discovered by Dr. Albert Sabin, called the REO (Respiratory-Enteric-Orphan) viruses. Also, Wally Rowe was one of the three people that almost simultaneously discovered cytomegalovirus. The above viruses were isolated almost exclusively in tissue culture.

BSP: Going to the '70s recombinant DNA technology was developed and then molecular biology was well-used [?] by that time and I met many biochemists, molecular biologist, just technique, what is the view from the biologist? Is it a molecular biologist's technique or very integrated –

EB: Well, it's integrated. I mean you use whatever technique is appropriate for what you're trying to accomplish. If you're going to grow or isolate a virus you have to use tissue culture or another living animal host.. If you want to study it genetically, you use DNA technology. It all depends what you're trying to do. If you don't have the technology, you're limited in what you can do. So, part of the research is finding new tools depending on what you're looking for and what you're trying to accomplish.

BSP: Right. Could you finally comment on the general NIH context for Bob Huebner's work and Charles Armstrong's work and your work and generally it's growing importance, or are there other things that you'd like to say?

EB: I think Bob – well, Dr. Armstrong, I think is a – they were pioneers. They provided shoulders for other people to stand upon. They made very important fundamental observations. I think Dr. Armstrong remained sort of – had a biological approach throughout most of his career because of the limitation of the tools he was working with. I mean he really never – I mean his active research career stopped probably in the mid-'40s, and this is before some of these techniques became available.

Bob Huebner started off the same way, but I think that Bob Huebner grew in terms of the sophistication of his techniques and what he was able to do in the field of virology besides isolating many viruses. I think he also made some very important contributions to the understanding of virology and also I think the – his contribution to the pathogenesis of cancer was very important because despite the fact that he didn't discover the fundamental nature of the oncogene, he was the one that conceived of a group of genes that directed the development of cancer, and he stimulated enough interest in this so that other people did go on and develop some of the other very fundamental knowledge in understanding carcinogenesis. But he was the one that I think really initiated the concept – as a number of authors have said that they spent many years just chasing Huebner's ideas.

My work was limited to my association with Bob Huebner during my time at NIH from August 1948 to September 1952 when I made modest contributions to the Q fever,

herpangina and pleurodynia investigations. Because of my interest in Huebner, Armstrong and NIH history, I just consider myself a dinosaur with memory.

BSP: That's great. Thank you very much.

EB: Okay. Is –

\*\*\*End of transcript\*\*\*