INTERVIEW WITH DR. MICHAEL B. SHIMKIN

This is a transcript of a telphone interview by Victoria A. Harden and Ramunas Kondratas, March 17, 1982. Dr. Shimkin is at the University of California, San Diego in La Jolla, California.

SHIMKIN: "As Memory Serves" was published in the Journal of the National Cancer Institute (hereafter JNCI) in August 1977, vol. 59. There were three other essays in the JNCI: 60:479 ff (Feb. 1978); 62: 1295 ff (May 1979); and 63: 223 ff (July 1979). In addition, two other essays in that series were published in Cancer Research 38: 241 ff (1978) and in Perspectives in Biology and Medicine in two parts: 22: 565 ff and 23: 118 ff (1979). That completes that series. I've also published an historical piece on George McCoy in JNCI 58: 457 ff (1977) about his role in the epizoology of cancer as an offshoot of his anti-plague work. I also have a long essay on the history of cancer research in the last century in the Josiah Macy Foundation Bicentineal two volume work that appeared in 1976, called Advances in American Medicine. There is also an essay that would be particularly useful to you by Dr. G. Burrows Mider, who was associate director of NIH when I was there, and he has the federal involvement in biomedical research, which is, I think, a key kind of paper. As far as profiles of the Public Health Service people, you undoubtedly know the R.C. Williams history of the Public Health Service --

KONDRATAS: The "Bible" you mean!

SHIMKIN: Yes, but the more unofficial Bible that has more penetrating kinds of analyses -- unfortunately Marty Cummings cleaned it up too much -- is by Bess Furman. That has quite a number of vignettes in it. These are some of the references that might help you.

Now about your specific questions. Number one: I only knew a few of these people because I came into the Public Health Service in 1927. But I knew Dr. Cumming. I did not know Dr. McCoy. I knew Tom Parran very well. I was one of his small boys. I knew Jimmy Thompson very well. I also met Senator Magnuson, who took Homer T. Bone's place. Well, what would you like to know about them?

HARDEN: Tell me about Surgeon General Cumming.

SHIMKIN: He was very patrician -- tall, thin. When I knew him he was quite old and had already retired; he was head of the Pan American Sanitary Bureau. He was very Southern, very straight-laced, and formal in all regards, and this was during the time that the Public Health Service met those criteria. He was a very pleasant individual, but you couldn't get close to him -- at least not a young man like myself. I have that impression of him only. He is of what I would call the formal phase of the Public Health Service, which had relaxed by the time I came into it.

HARDEN: I have a feeling of a split between an "old school" and a "new school" in the Public Health Service. Dr. Cumming and Dr. McCoy were in the "old school," while Dr. Parran and Dr. Thompson were in the new. Is my intuition correct?

SHIMKIN: There is no question about it. We are dealing with two different historical phases of which the Public Health Service was a part but which were national in nature. You come to question three eventually about Coolidge, Hoover, and Roosevelt. You know that the whole federal government through Hoover was meant to do as little as possible and couldn't do anything aobut anything except defense and a few other things that were allocated to it. And then in the Roosevelt era, a completely different concept of the federal role, not only in the government but in the life of the country, was enunciated and then followed through on. There is no question about it that Hugh Cumming was of the "old school." The main top figures of the Public Health Service at that time were graduates of the University of Virginia and William and Mary, old southern gentlemen to whom the private practice of medicine in their part of the country was not very remunerative. They went heavily into the government fields for that reason, just like they did in the army, where at that time the top ranks were also overrepresented by people from the southern part of our country, where the economic opportunities -- the professional ones -- were not equivalent to those that you could find, say, in New England. So this is part and parcel of the whole national life, and I hope you do not divorce the movement at the NIH or the Public Health Service from the great national or international movements that were occurring.

HARDEN: Oh, no. That was not my intent. You commented that the leaders of the Public Health Service came heavily from the University of Virginia. Do you know how scientific research was taught at the University of Virginia, in comparison with methods at, for example, Johns Hopkins?

SHIMKIN: I have no idea about specifically the University of Virginia. I do know that biomedical research as we know it now simply did not exist at most universities, including the bigger universities, but it was carried in a few places like Johns Hopkins. We'll come back to that when we get to later years. The fellow that transcribed the German model of biomedical research to this country was William Henry Welch. He established Johns Hopkins school of medicine, which has been a model for medical education in thiscountry ever since. At the same time he ws also the main consultant to -- and was offered the job of being head of -- the Rockefeller Institute for Medical Research. He, in effect, set a model, again from Germany, because the Rockefeller Institute was modelled after the Kaiser Wilhelm Institutes in Germany. So he is really the linchpin of biomedical developments in this country. After him, the next big step in developing biomedical research in this country was under Tom Parran and Roosevelt, when research was done under government auspices. The philosophy was enunciated by the Roosevelt administration and translated into biomedical research and public health practices by Tom Parran, who gets very little credit for all this, but who is a very important linchpin. This is probably coming to the end now, and industry has to take its role more forcibly because many of the biomedical research fields -- recombinant DNA, etc. -- are becoming economically profitable. The way I look upon biomedical research in this country is exactly this: there was very little being done before the twentieth century. There were a few places here and there which you can name, but they were small peanuts. As usual, the first great development was under the barons. The whiskey baron of Baltimore, Johns Hopkins (he is not labeled like that in our encyclopedias, but he made his fortune essentially by selling whiskey during the Civil War) gave the money for Johns Hopkins University. The oil robber baron, John Rockefeller, and his son established the Rockefeller Institute, the University of Chicago, etc.

KONDRATAS: Carnegie, as well -- Carnegie Institute, Carnegie laboratories.

SHIMKIN: Well, Carnegie didn't lean heavily on biomedical research. His great role was libraries. At any rate, we certainly can't limit it to just these two, but these were commanding figures in that field. The private money of that time was insufficient and limited. Then the federal government came in around 1925, 1937, thereabouts, and developed research to the present role that we have in which the United States became completely preeminent. All you have to do is count up the Nobel prizes to find that out. and now, I think that with Reagan trying to shove us back to Coolidge, the next step will be that the torch of biomdical research will probably go to the Japanese. This is my prediction anyway. We will be important, but the Japanese will probably be preeminent because they have greater involvement of their industry in their government and they have prosperity which we seem to be no more developing as we were a few years ago.

Anyway, there is Hugh Cumming. He was a man of his time. I do not associate him with anything to do with research particularly. He was interested in fulfilling the orders of the Congress and the President in terms of public health and his obligations.

George McCoy was also a man of the same type. He was primarily the man who did the plague control work in California, and then he was head of the Hygienic Laboratory and the NIH for over thirty years, I believe. He had a falling out with Tom Parran -- Miss Furman records this in her profile. He, incidentally, was a graduate of the University of Pennsylvania, not Virginia. Cumming had a man that he was raising as his successor, William Draper, whom I knew very well. I served under him in SHAEF in Europe during World War II. William Draper, again, was of the old school, though he was a New Englander. When Roosevelt came in, he picked up the Public Health Service officer who was the health officer for New York state, who made his name in venereal disease control, Tom Parran. He came down to Washington, and because he had the keys to the White House, as I said in my article, he could do an awful lot of things. He had a whole group of people around him who felt the same way, of which Jimmy Thompson was one. But the man that I think had more to do with the philosophical arrangement of the new phase of our development was Joe Mountin, who died, unfortunately. Joseph Mountin was a very able officer who did a lot of planning both in public health and in research for the Public Health Service. Tom Parran was a fairly small man with a blonde face and red nose, who had the tragedy of losing his first wife to cancer -- this is one of the reasons for his interest in cancer. He then married a science writer who helped him in writing his speeches and was very much of a confere of his. Tom Parran picked me up as a youngster because I know something about Russia, and he was very interested in Russia like Roosevelt was, to develop associations with it. I had the fortune of being pretty close to him, including setting up the Office of International Health Relations after World War II. Tom Parran was a very dynamic individual. He worked hard and his vistas were much broader than the Public Health Service ever had before. He believed in being a leader rather than just an instrument through which certain dictates were carried out. Therefore, he had a lot of falling outs with the old crowd, because it couldn't be otherwise. It wasn't his wish, but, for example, Hugh Cumming wouldn't have the World Health Organization, which Parran practically created after World War II, because the Pan American Sanitary Bureau would become a branch of the World Health Organization, and Hugh Cumming saw all kinds of communists under the bed. He said that this would give an opportunity for the communists to infiltrate the Pan American Sanitary Bureau or its descendants. This was so incompatible a viewpoint that Tom Parran had to use his influence to get rod of Cumming, which he regretted very much, because he certainly didn't want to do any harm to the old man. By the same token, George McCoy, although he started a lot of cancer work himself by studying cancer among rodents on the Pacific Coast, didn't tucker to Tom's ideas of an expanded NIH which inclued mental health and all kinds of diseases beyond the classical microbe hunting that McCoy was beholden to. So Tom Parran with regret had to retire McCoy, and McCoy went down and spent some years as a professor of tropical medicine in New Orleans before he died.

Now Jimmy Thompson, who was a very pleasant character, very diplomatic --he had an old tuberculous lesion so he conserved his strength -- he was a thin man, very pleasant, and I loved Jimmy. He didn't know any science particularly, but that wasn't his role. He role was first to get that land in Bethesda where the NIH was resettled and to head it administratively. He did a beautiful, diplomatic job, and he depended on people like Rolla Dyer, who was his successor, to advise him on the scientific aspects of the intramural program. He was a very successful administrator for that enterprise.

These are about all the people I really know on your first list.

HARDEN: Is there anyone I have left off? In your own institute I know I left off Dr. Schereschevsky and Dr. Voegtlin.

SHIMKIN: I knew Voegtlin; he was a Swiss. I never met Schereschevsky, who had retired before I came to Boston as one of the first National Cancer Institute research fellows. Schereschevsky: everyone who knew him was in full adminration. He was apparently a Renaissance man who could do almost anything. He was the son of an ex-Jewish, Episcopalian bishop in China, who translated the Bible into several Chinese dialects and who was a tremendous scholar.

KONDRATAS: Was he of Russian origin, do you know?

SHIMKIN: He must have been of Russian, Polish, or some similar origin, but I think you'll find his father well represented in encyclopedias related to religious enterprises in the United States. He was quite a man, and Joe Schereschevsky, his son, rebelled, and he was sent to Dartmouth and apparently got into some scrapes, and then he, I think, volunteered for the Spanish-American War and had some more adventures. He joined the Public Health Service after finishing mdical school, I think at Dartmouth, and everybody I worked with at Harvard was full of tremendous respect for him. "Sherry" wanted to be the first head of the NCI, but at that time Parran had introduced a mandatory retirement age, at age 62 or 64 or something, and "Sherry" fell under that. He went down to some state and set up their cancer control activities an died very quickly afterwards. I think the whole thing kind of broke his heart, but this is just my interpretation.

Voegtlin was a taciturn, big Swiss who had mellowed an awful lot by the time I got to know him. He selected me as one of his first research fellows, and I always felt very kindly toward the old man, but he was a dictator for a long time. For example, as I indicated in that article, in contrast to the publications of the Harvard unit, which very seldom had Schereschevsky's name on them, all or a great proportion of all the papers which came out of the division of pharmacology where the other cancer research institute was established, had Voegtlin's name on them. This just shows the different relationships with his staff. Voegtlin mellowed in the later years, but he still was very adamant about the fact that the intramural National Cancer Institute was his and nobody better kibbutz him on that one, whereas the grant program, which was first established under the Cancer Institute, and then was duplicated and dessiminated throughout the other institutes as they were established after World War II -- these, of course, were under the National Advisory Research Council -- he wouldn't let anybody from the intramural staff get into the business of the National Advisory Cancer Council or vice versa. This was forbidden territory under his immediate command. This, incidentally, had some very good features to it. It wasn't a unilateral business. It was sometimes hard on some of these more ambitious people in the intramural group and some of the more ambitious ones on the advisory council. It wasn't a bad idea to have split them up like that. One of the problems of having government support research, you know, is you can't draw the lines of how far to go. For example, if you announce a program of cancer centers, then every state and every representative bids for it and lobbies for it for obvious reasons. There is no good way of stopping it. Now how many cancer centers to you need in the United States -- fifty-two? Can you hold them down to ten? These kind of logistic questions are very hard to meet when the pool of money is a national one and no such limitations are politically feasible. Incidentally, just the other side of the coin -- you get someone supporting your research projects like Magnuson and Bone from Washington state, and Washington state, an unlikely area, suddenly blossoms out with all kinds of cancer centers and grants, because those powerful senators were key in the budgets for the National Cancer Institute, and they automatically have to have their cut. Their cut was to be sure that Washington state was not neglected. This wasn't said; it was never even referred to, but this is the way our government operates: tit for tat as you well know.

Well, OK now. What biomedical research was most exciting in the 1920s? Well, of course, I was just a youngster. I went into college in 1928, so it is difficult for me to say, but in retrospect, I would say the biochemical. This is where biochemistry was coming into biomedical research and practice. Peters and Van Slyke were developing procedures by which biochemical things could be measured in organic fluids and organisms. These are the years which mark the great advances in treatment of pernicious anemia (liver factor), diabetes (insulin, from Canada, of course), gout (the involvement of uric acid metabolism). You could measure ________________ and other things in tissue fluids. I think this is the most exciting area of the twenties. At the same time physiological measurements of heart function and gastro-intestinal function were coming in -- EKGs were being applied, various radiological ________________ , appearance of the gastro-intestinal tract was related to function, etc.

All right. Three. What was the climate of opinion within the Coolidge, Hoover, and Roosevelt administrations? I've already told you that under Coolidge and Hoover there wasn't any such climate. It was probably thought that this was something the government had no business in, and there was a great strong feeling about that. One beautiful example of that was Clarence C. Little. Little was head of the American Cancer Society for years and years and years. He was a brilliant student of ____________ from Harvard who introduced the new science of genetics into the curriculum of Harvard University and then nationally. C.C. Little became president of Michigan University at age thirty, I believe, and then established the Jackson Laboratory up in Maine. It was called Jackson because Jackson was the president of the Hudson Automobile Company which went bankrupt later on and became a part of General Motors. Well, Hudson was going to endow the Jackson laboratory but he died, and only a little money was left to Jackson. C.C. Little was a tremendous antagonist to the federal government in research. He thought it should be done by rich barons. I think that may be why C.C. Little went with the tobacco industry rather than accepting the obvious, that tobacco smoking caused lung cancer. He became the first scientific director because he thought he would get a lot of money from the tobacco industry for his enterprises in research. It was a philosophical difference that greatly influenced that relationship. There were opponents to getting the "nasty" federal government involved in research, and that was the feeling of the Coolidge and Hoover administrations so far as I know them. The Roosevelt administration turned 180 degrees around and said that the federal government has a definite place in the life -- intellectual, economic, and educational -- of the country. Its limitations are not to be building battleships and the usual classical ones. This difference of opinion immediately implicated the Public Health Service, particularly since its leader at that time, Parran, was a friend of both President Roosevelt and Mrs. Roosevelt. This feeling was continued, particularly under Democratic administrations up to now.

KONDRATAS: Do you think that Cumming and McCoy reflected the feelings of the Coolidge and Hoover administrations or that they just went along with them?

SHIMKIN: I don't know about McCoy. McCoy sounded to me like a pretty wide ranging individual. I don't know what his philosophical trends were. I think that Cumming reflected and agreed with this limited role. Among other things, this feeling of <u>state</u> superiority or priority in these matters was particularly noted in the South, and he reflected that kind of opinion which, to some degree was resolved by the Civil War but to some degree is coming back again.

Now your next question. I don't know anything about the 1926 bill -- $15,000,000. It is another example like giving a million dollar award for the cure of cancer, a typical American measure which is, I think, more public relations than anything else -- that you are going to solve a problem with one big shot.

HARDEN: The real question was <u>could</u> the Public Health Service have used that much money had they gotten it? Could they have taken the money, built a great institution, hired the right people, and used the money wisely?

SHIMKIN: You have some adjectives there, like "wisely," that are hard to interpret. As William Henry Welch showed in 1901, you could do tremendous things _if_ you had enough time to build up your actual workers. Now, for example, at Rockefeller, the main people who made the advances were imported from Europe, like Alexis Carrel, or they were graduates of Johns Hopkins, like Peyton Rous was. Now _if_ you spent that as a long term investment and not something that has to be finished in a year and then re-examined -- it's a little bit like having a championship football team. You don't do that in six months. You start recruiting, you start practicing, and you start building up. Peyton Rous was just a student at Johns Hopkins, and then he came to the Rockefeller Institute, an in 1911 he made the great discovery of the Rous sarcoma which was the first filterable virus tumor in the literature. Some of the earliest development of tissue culture came from Carrel and a student, Burrows, which was carefully developed at Rockefeller. Now if $15,000,000 were given to the Hygienic Laboratory, which was already a going concern, I have no doubt that it would have been turned down if it had to be used in one year, because it couldn't be. If it were phased in so that it was used to develop and educate promising young research people and facilities through which they could carry out their research, men like George McCoy had enough imagination, brains, and foresight to have evolved the National Institute of Health long before it became so effective twenty years later. But it needs a long viewpoint. It cannot be done over night. But the ideas and possibilities in 1926, even in cancer research were just as wide as they are now. Looking backwards on it, there were so many things that could have been done and developed and perhaps the pace may have been accelerated, but I do not know how much.

HARDEN: I was reading the transcript of a 1928 meeting of physicians about cancer research, and I was impressed by how well they defined what needed to be done.

SHIMKIN: There is no question in my mind. We're no wiser than the guys were in those days. With the knowledge they had available to them, they had just as much imagination and drive as any of us, and they could have done well with the resources if they became available. Incidentally, in the twentieth anniversary issue of the JNCI (we also had an anniversary volume at that time -- I was editor at that time so I know it well: I put it together) it had some historical aspects including the history of the National Cancer Institute Act. I at this point copied some of the research proposals of cancer, the first of them being in 1801 from Edinburgh and from the London group that talked about cancer at that time. I called the essay "Thirteen questions" because they asked thirteen questions about it. And then there was the outline that Dashford (?) gave that established the Imperial Cancer Research Fund in 1901. There is a copy of this advisory committee on cancer research, which C.C. Little was the chairman of in 1937 or thereabouts. You can see that the approach to the problem was commensurate with the knowledge of that time and not because the group in 1937 was much more clever than the one in 1801.

Question five. That I know very well. This refers to this dichotomy of the functions and the role of the Public Health

Service before, say 1937, and thereafter. The Commissioned Officers Corps of the Public Health Service were the top dogs, certainly until World War II. You couldn't be the head of a division -- for example, the Natinal Cancer Institute -- without being a commissioned officer. Carl Voegtlin, who was a Civil Service worker for years and years there, finally got a four stripe commission, and his portraits are all with the four stripe uniform. Our role was very non-egalitarian. I remember when I was a research fellow and took out a commission in the Public Health Service, when I was assigned at Harvard in I think 1938, I suddenly became second man in the whole unit because the man who headed the laboratory -- he replaced Schereschevsky (I think his name was Floyd Turner) -- and I was his second in command by the fact that I was the only other commissioned officer in the whole unit. Much older members of the institution who were Civil Service people all had to line up after me. This disappeared during World War II. The tremendously important Jim Shannon -- who was an Irish drunk among other things -- who really led the National Institutes of Health into preeminence in the 1950s (he was very dynamic), went into the Public Health Service Commissioned Corps. Then when he found out that the Civil Service was getting a little more money, he would jump to the other place. But this was the last one -- the preeminence of the Commissioned Corps was no longer the issue.

HARDEN: This brings up another question. Was there tension over who should make decisions about biomedical research directions, especially between physicians and basic scientists?

SHIMKIN: I think that has to be on an individual basis. Obviously the majority of the people were not physicians, but they were trained as M.D.s. Don't mix those up. I never practiced medicine in my life. Neither did Jim Shannon. He was a pharmacologist. Rolla Dyer certainly never practiced medicine; neither did George McCoy, Hugh Cumming, or Tom Parran as far as I know. But they had M.D.s an these were the top dogs because Commissioned Corps assignments could ony be given to M.D.s until, I think, during the Roosevelt administration they added dentists, sanitary engineers, and eventually even nurses to the Commissioned Corps hierarchy. But this is artificial, and I think you ought to distinguish not so much between M.D.s vs. Ph.D.s as between clinicians vs. non-clinicians. For example, my experience in the early days at the uiversities was that some of the greatest opponents of the scientific method were well traind clinicians. The scientific method came into medical practice late. Certainly not until after I was a medical student. Then the <u>art</u> of medicine was preeminent and how to hold hands and make a diagnosis, and the scientific methodology, with exceptions of some people at Johns Hopkins and perhaps Harvard and the Rockefeller Institute, was practiced by either Ph.D.s or by M.D.s who retrained themselves in the laboratory. You could get even the professor of medicine at Harvard. He was an astute clinician. They weren't scientists as we would describe them now. They were practicioners.

KONDRATAS: The large question here was how medical research policy was formulated.

SHIMKIN: What the hell is policy?

KONDRATAS: If you are running an institution, you have to determine which projects will get funding and which will not, etc.

SHIMKIN: I think I would expunge the word "policy" in this.

TAPE ENDED -- SOME MATERIAL LOST IN RESTARTING

SHIMKIN: (talking about Surgeon General Parran): . . . art of getting venereal disease out of the coat closet in the back to public recognition. He also realized that it was an important public health problem. About one third of all the patients in mental institutions then were here because of syphilis and cardiovascular disease. It was an important problem until penicillin came in. So he dragged it out of the closet and allowed it to be mentioned on the radio. He won a lot of mileage and publicity that way. He became front man not only in the New York administration of Roosevelt but also in the national administration here. He also saw that this was only one part of a broad public health attack on other problems. This was just a spearhead for that. Incidentally, one of the things that it allowed was a training program for Public Health Service officers that began at Johns Hopkins. The main training field there was in venereal disease, which was a model for how to approach those problems both scientifically and in the field of public health. Almost all the whole leadership field of the Public Health Service went through this training program, which was limited at that time, to verereal disease at Johns Hopkins. One of the people who served longest as a Cancer Institute head was John Heller, who was essentially a venereal disease man -- the same techniques are applicable to any field, although some of us, as I put in that article, wanted to rename the National Cancer Institute the "National Cancer and Clap Institute."

KONDRATAS: In the light of what you are saying about venereal disease at that time, how should we analyze the Tuskegee study?

SHIMKIN: Tuskegee is a beautiful example of a reinterpretation of something that was completely different in the national and scientific feelings in the early thirties. They were reinterpreted with bitter conclusions in the 1970s when the total outlook was completely different. During the time that Tuskegee was set up as a so-called "experiment" (which wasn't very well done for a variety of reasons), we din't know very much about the natural history of syphilis. There was one study in Sweden which indicated that of those who were infected by syphilis, 25% or so had complete cures naturally. We didn't know that, at this point, and this was a very limited experience from Sweden. It was of great interest to determine what the natural remission of syphilis might have been, because that would give you hints for looking for natural methodology to reverse the process. We are seeking the same things with interferon and other things against cancer at this present date. At that time what we now call "blacks" and before were called "Negroes" and before that were called "colored folk" -- the attitudes of society were completely different. We know that at Tuskegee that we -- I'm speaking of the Public Health Service -- were faced with two sociological problems. These fellows didn't know from beans and would not get treatment, particularly treatment that was difficult, long term, and painful, which, of course, salvarsan injections were. If we started that kind of program in that area, they would disappear and we would never see them after the first injection. So the idea was broached: "Look, let us watch what happens naturally in this thing." Also, we did not know at this point what the effects were of treating syphilis that was already in the tertiary phase. There was a great feeling among clinicians that you could convert a rather benign tertiary syphilis into some active florid stage if you treated it too actively in the tertiary stage. So a population that was already there, that had no real public health aspects to it and had no future about it was set up as an observational research procedure. It was probably let go too long, so that by the 1970s some of our social leaders that arose and started talking about the rights of blacks, and poor Southerners as well, found this thing, and it looked terrible and horrible to them. It wasn't terrible and horrible at all, although I think if I had been the Surgeon General around 1965, I'd have said, "Look, we will take these individuals that still have syphilis and divide them at least in two groups -- treat some of them with penicillin and use half of them as controls." That would make a therapeutic experiment the basis of the observational one. I personally think there was nothing wicked about it, except perhaps that it was neglected too long. By that time they were confronted with a relatively small population that was left in an advanced age group, and I don't see anything that was "illegal, immoral, or fattening" that was done there. This is my opinion.

Question six. Well, my early years start in 1938. You'll find this article in <u>Perspectives in Biology and Medicine</u> on my adventures with the Russians, because that was my specific area of expertise. Tom Parran always mentioned international asspects. He, in effect, founded the World Health Organization on the skeleton and ashes of the League of Nations Health Organization. We looked upon it with great favor. There is no question about it -- before about 1930 not only the Public Health Service but the whole United States looked upon Europe as the center of research and not America. We took up the torch at that time because German research was destroyed in World War I pretty effectively, and, of course, what was left of it was effectively destroyed by Hitler, and we got some of the benefits from that. But we were second string stuff, bush league, surely before 1930. Now of course, we are top dog, but I don't think we will last out the century before the Japanese are top dogs in this. So this is the way it goes.

KONDRATAS: Could I ask abut your role with Russia? There was a great fascination with the "Russia Experiment" as it was called, and if you read Sigerist you can see the infatuation with the Soviet model. This was in the twenties. Had opinions changed and moderated by the late thirties?

SHIMKIN: It was completely different. The United States views on the Soviet Union had a tremendous change in the Roosevelt era. The first reaction of the United States to the Bolshevik takeover was one of horror, particularly when they murdered that beautiful czarist family they became monsters. Hoover, of course, was one of the great proponents of the fact that communism could only be equated with the devil because of the way they used their food during the starvation, and Hoover was head of the commission to try to help them along. This feeling of anti-communism as a knee jerk reaction maintained itself forcibly through Foster Dulles, who also considered communists at least first order devils instead of Satan himself and mugged up our foreign policy on that basis. That is still obviously the primary viewpoint of General Haig, who is going to get us into a war if we don't look out. But this is one trend. When Roosevelt came in he opened up negotiations to recognize the Soviet Union, which had not been recognized by the United States for all these years, just like we didn't recognize China. We sort of wrote them off the planet because we didn't like them. We dealt very nicely with the stupid czars and the stupid Manchus in China; they were OK. But these were unclean. Roosevelt reestablished relations with the Soviet Union. I knew Sigerest very well, and Parran appointed me as a liaison with him on the American-Soviet Society that was founded during World War II. You will find this in detail in volumes 22 and 23 of Perspectives in Biology and Medicine, particularly my role in it, because I was writing from a personal perspective. Parran also rubbed off on this same thing -- look, the world was occupied by the Soviet Union, the single biggest country in the world, and we better start talking with them. We don't have to love them, but at least we have to know about them. One of the main criteria for the foundation of the World Health Organization was how to get the Soviet Union involved. I was key in that process because I happened to speak Russian. Again, the national feelings set by the Roosevelt administration rubbed off in the Public Health Service. We became very much involved in these international exchanges, although the actual exchanges were a post-World War II development.

Question seven. I think this has been well written up by Miles, among others. His manuscript in the National Library of Medicine has never been published. The National Cancer Institute was founded because there were a lot of people that were interested in it. There was a lobby group, the Association for the Control of Cancer, which was the predecessor for the American Cancer Society. Also, there were representatives of professional groups -- like the head of the Memorial Hospital in New York, Ewing, and some people from Harvard and Buffalo always were talking to some of their favorite Congressmen. It's very, very easy to be against cancer. The National Cancer Institute in 1937 was a natural development, although it had many predecessors, even in the government, going way back to 1910 as I recall.

HARDEN: Did the National Cancer Institute get through Congress more quickly because Roosevelt was President, because people understood cancer but not basic research, or a combination of these factors?

SHIMKIN: A combination, definitely a combination. There are more -- what is the old statement?: "Success has more fathers than you can wave a stick at, but failure is an orphan." The fact remains that the time was right. The National Institute of Health was moving to Bethesda, and a natural framework about which there could be very little controversy was to be against cancer. This didn't have the patina of venereal disease even then. It didn't have the limitations of an exotic fever or something -- it was almost in a leadership position because of public interest, and societally, also, because by then cancer had been taken out of the closet. Twenty years before that, one of the limitations of the statistics of cancer was that families thought that it shouldn't appear on death certificates because it was a "dirty" disease. It was not a bad as venereal disease, but it was something not to be mentioned among polite people. Thus the societal attitude toward cancer, through public education, etc. became different, and cancer could be more openly discussed in 1937 than it could be in, say, 1927. There were some politics involved. Because there was a strong lobby for it and people who could speak for it, this was a natural thing to which Parran and his cohorts -- particularly Joe Mountin and Jimmy Thompson -- could use as an example for other determined goals. Now the National Institute of Health became a great proponent of so-called "basic research." I don't see what could be more basic than cancer -- not micro-organisms, leprosy, or Q fever. But Q fever and leprosy were "clean" but cancer activities were foreign to them. What was even more foreign to them was mental health. Mental health labors under the same delusions that it was somehow different from the other diseases of mankind. It had its proponents -- Mary Lasker and others that you know. It was secunded (?) from the National Institutes of Health, especially when the question of budgets came up. This was much later. The National Cancer Institute was a definitely designated disease institute. It was so successful, especially during World War II, that after the war was concluded, Congress passed a whole lot of bills that were "Me, too" bills, using the National Cancer Institute law as a boiler plate. They had all kinds of institutes for various diseases planned. I forget -- they actually founded about five other institutes at the National Institutes of Health at that point. The only one there was an argument about -- there is a story about this. The people who were the classical microbe hunters wanted an institute of microbiology. I think it was Mr. Fogarty or someone else in Congress, told them, "Look, I never heard of anyone dying of microbiology." He clearly showed where there were off beat. Although it was scientific, it would not reflect well in Congress. That institute was named the Institute for Infectious Diseases and Allergy. People knew waht allergy was -- you sniffed and had trouble with your sinuses. And, of course, infectious diseases made sense. But microbiology -- which was the new term for bacteriology -- was foreign and not acceptable to Congress for allocating budgets.

So the idea that a man put down a constitution for biomedical research is nonsense. It is a constellation of happy or unhappy occurrences, of rubbing the right Senators the right way, having a dear lady married to a head advertising man who is in charge of millions of dollars and able to lobby well, etc., etc. -- which makes the kitty go.

KONDRATAS: In that same light, you mentioned mental health. Before that there was a division on narcoticss and they were concerned with alcoholism. When the Mental Health bill got passed, they got shoved in with mental health. How do you explain that? Is it a part of these connections you mentioned?

SHIMKIN: I could spend a long time talking about that. The societal feeling about the so-called role of narcotics and heavy important drugs of that time has changed 180 degrees. When I was a medical student you couldn't use heroin, not even physicians could use heroin. Opium -- you had one shot of opium and you were an addict for life. All crimes were committed only by addicts. Now it is a part of the trash culture -- Belushi. . . .

KONDRATAS: Leisure drugs -- it is a pastime now.

SHIMKIN: Yes, pleasure, leisure -- mostly it is associated with the ability to have the proper amount of money. It is all very expensive to feed criminal types who import the stuff because it is illegal. The main drug of this type in our environment is not opium or cocaine, but alcohol. The Public Health Service is involved with that, but the official in the Department of Justice concerned with this was as bitter about narcotics as J. Edgar Hoover was about crime and Comstock in a previous era was about dirty books. He had no way of reconciling those things, and he was influential enough to get some very restrictive laws written about these sorts of things. Now the Public Health Service operated at that time some opium hospitals, one in Texas, I believe.

KONDRATAS: Yes, there were two hospitals, one in Texas an one in Kentucky.

SHIMKIN: These were revolving door institutions. They would cure them right and left, and then the same fellows would be back in thirty days. They were all ineffectual methods because narcotic addiction isn't that simple. It is a deep psychological problem which we still haven't approached very intelligently. For example, you take narcotics addicts in New York City. You soon learn that a number of them want to be narcotics addicts because they had rather be identified as such than as members of the black community. Being black is so reprehensible to them that they had rather be something else. It is an interesting kind of approach, but nevertheless. . . . Also, the proportion of the population that is involved in this habit makes it an aberrant habit or a habit that is general. We use alcohol as a natural one, and all of us, I presume, have a cocktail before dinner. This is all considered quite normal because the majority of the people do it. You go over to Iran, as I did during World War II, and 70% of all the males, after they had completed work, had a nice, pacifying small pipe of opium. How can you consider that an aberrant habit if 70% of your population does it? In our population only one per cent or so indulges in that habit, and that means that they are an aberrant portion of our population. Now, of course, narcotics is a part of the Belushi type of thinking -- self indulgent and non-responsible.

KONDRATAS: Several other qustions deal with lines of research in the thirties and instruments that were developed to aid that research. Keep in mind that we are interested in collecting public health artifacts.

SHIMKIN: You mean artifacts in terms of old microscopes and things?

KONDRATAS: Microscopes we have, but other types of equipment, especially that was associated with a particular person or work. For instance, recently I have gotten some of Landsteiner's blood serum tubes and materials he used with the laboratory equipment labelled in his hand from Merrill Chase, who was his student and colleague at the Rockefeller.

SHIMKIN: I personally am not a gatherer of those kinds of artifacts. My gathering has been of the printed page. So I don't have many of those old relics.

KONDRATAS: I hoped in your knowledge of people and collections that you might know of old attics or basements that needed to be examined.

SHIMKIN: Marty Cummings at the National Library of Medicine does a considerable amount of that, and, of course, Rockefeller is another one and Harvard. I don't know if the old Bassy (?) Institute is still standing, but that's another place.

Anyway, to go on to question eight: The most promising research in the 1930s was the same as in the 1920s although more developed. The great change in mdical research comes in the 1950s when molecular biology is introduced. This is a complete revolution. The start of molecular biology goes way back, but Oswald Avery at Rockefeller with his student first associated DNA with hereditary transmission. The next big moment was the clarification of the DNA model by Watson and Crick in the 1950s. We are now in the era of DNA recombination, monoclonal antibodies, etc. Certainly, during the 1930s there was an elaboration of biochemistry and biophysics. I can't think of any new techniques, with the exception of radioactive isotopes and heavy isotopes that allowed us exquisite methodologies by which to follow metabolic processes and biochemical reactions. These were a result of the physics developed during the 1930s.

KONDRATAS: I have to leave now. I want to thank you for talking with us. I have one more odd qustion -- have you read about some early nuclear explosions in Siberia?

SHIMKIN: There was no question about a major disaster in

Siberia, but my information is from the newspapers, from the CIA reports.

Let's cover points nine and ten. Could the private sector have supported research from 1930 on? Absolutely not, absolutely not. Particularly after we got into the Depression. It's a natural thing -- and this is obvious from Napoleonic days in France when research developed to centralize in Paris at the turn of the nineteenth century, to the Germans, who gave leadership in science through most of the nineteenth century but diversified it because they had a lot of principalities that had to be placated. The German model, which we inherited, is what we are still following, both in medical education and in research. There the partnership with government is essential because it is the only place where adequate funds may be obtained an diversified nationally and not held as private property of a small group. These are natural evolutionary asspects, and I expect our next one will be a greater involvement of self-support by medical research, because you can sell monoclonal antibodies, for example, and greater allocation from industry. There are some very important research institutes now, under Merck and du Pont, etc. Of course, Ma Bell has a great research program in physics. This is the pattern, but it is not one or the other. It is an addition of one to the other.

HARDEN: I have found, looking at private sector funding for research, that new funds in the late twenties and early thirties were smaller on the average than earlier in the century. Were people aware that the private sector simply couldn't keep up?

SHIMKIN: I don't think there was a rational way of saying, "Aha!

We don't have enough of this." It was a great movement -- the belief, for example, that the federal government should be involved in the life of its citizens an not simply build battleships. It was a national feeling and, as historians tell us, Roosevelt probably kept at bay a national social revolution with his New Deal. The people had had enough of being monopolized by a few people or a few major industries, and something had to give. Unfortunately, things that he tried were solved by munitions manufacturers in the war. This is the way mankind operates. It's never simple; it's always complicated, and I don't think 90% of the public of the United States knew from beans whether there was biomedical research or where it should be and how it should be supported. It was always the leadership people that gave you the tone. I'm not an egalitarian. I believe in justice for all and opportunity for all, but history shows that the great jump in man's intellect and science are done by a very few people. Now they arise from the great mob, of course, and that is why the great mob has to be educated and given opportunity. Some of the greatest figures in biomedical research did not come from noble families but from very poor families -- Pasteur and Meuller (?) to mention two examples. It's a complicated complex, and what I don't like in history is some very pat theory, whether it is psychoanalytical or whatever, and everything flows from that interpretation. For example, take the statement, "All wars are economic." That is nonsense, because some wars are religious in nature. It is a very complex picture and each one is different.

HARDEN: That is what I am trying to get at -- the complexity.

SHIMKIN: Good! That beautiful book, very fun to read, Susan Sontag's Illness as a Metaphor, is interesting, but it is so pat, using one kind of a framework, interpreting man's complex activities in simplistic ways. Let's go on.

There is no question that the federal government had to come into it at that time, and this was a time of tremendous flowering of biomedical honors and contributions that American contributors made.

Now last -- instruments. Of course, they were coming all the time -- methodologies on a small scale like the colorimetric things like Foley used for the determination of biochemical reactions to electrocardiagrams to the great one I have already mentioned, radioactive and heavy isotopes which gave us an entrance into processes which were impossible before these were availble. Such simple things -- such as paper chromotography which isolated and separated things that were laborious. Now we have even more complicated and better instruments which can separate things over the weekend. For example, the Curies took a ton of pitchblende and finally isolated radium from it in 1899 or thereabouts. A similar process was done in isolating 3,4 benzpyrene -- it's called benzoapyrene now -- the active carcinogen from tar -- by the English group in 1929-1930. They also had to start with a ton of the stuff and laboriously trace it down to something they they isolated chemically. Now that can be done in a weekend by the methodology of paper chromotography and electrophoresis -- methods that separate molecules almost automatically and put them into different test tubes for analysis. As an example of that: in the 1950s there was a question of carcinogens in peanuts. That came out to be aphlotoxin. It was identified as a specific lactone which fluoresced in practically days or at least weeks in contrast to the laborious thing with radium or benzpyrene. Another great breakthrough was the technology of tissue culture, which allowed you to study individual mammalian cells rather than the whole complex organism. This began at Yale when Harrison put some nerve cells on a microscope slide with some serum around it. This interested a fellow at the Rockefeller Institute, and he sent a student up there. When Burrows came back, they developed a tissue culture and published their work in 1913 and 1915. The great era of tissue culture, as it was called -- it was actually cellular culture -- evolved slowly and the media improved, etc. But the idea of getting clones -- descendents of the same cell -- was introduced in 1948 at the National Cancer Institute in the laboratory of Wilton Earle and Kathryn Sanford. This was simplified, and then clones became the natural thing to work on, and obviously monoclonal antibodies came right from there as an obvious development. The methodology was simplified and with cells grown in culture, including clones and DNA recombinations, here we are. These are all new techniques. They don't have to have expensive armamentarium like radioactive stuff under the cyclotron, but they were just as powerful.

HARDEN: Would you comment on Derek J. de Solla Price's theory that certain instruments <u>must</u> be developed before certain discoveries can be made?

SHIMKIN: Price is very well known in the history of science. He is rather ponderous, in my opinion, and I only know him by reputatin. I have read several of his things, and they are well thought of, but he is rather pedagological in my opinion.

Science is indivisible from instrumentation. Galileo did drop some weights off the leaning tower of Pisa, but he also developed some slides and other simple instruments including the telescope, of course. Only through that instrument could he see the moons of Jupiter. It doesn't have to be a complicated instrument -- or it may have to be complicated. For example, a high powered microscope can't be a simple child's toy. Nor can the cyclotron. Incidentally, one of my teachers at Berkeley was the inventor of the cyclotron -- E.O. Lawrence. The microscope -- people get the wrong idea of that. Van Leeuenhook, who first used magnification that allowed him to see the little animals, didn't have a microscope; he had magnifying lenses. The real achromatic microscope came into use early in the nineteenth century. That was when the microscope became a powerful tool in the hands of the histologists and anatomists which then led to the idea of cellular pathology. It would have been impossible without some clever people devising methods of fixing tissues and staining them. One of the people who was very helpful in bacteriology and microbiology was a Mrs. Hesse. She was the wife of a bacteriologist, and she introduced the use of agar for growing bugs.

TAPE ENDED -- SOME MATERIAL LOST IN RESTARTING

SHIMKIN: (talking about Paul Ehrlich): . . . the idea of chemotherapy. It was the specificity of these attachments that caught his eye. And now we have Jennsen and others who have determined the attachment sites in the cells and the tissues which allow biochemical reactions and pharmacological reactions to occur. We know now that women with breast cancer which still attaches estrogens to it are more likely to respond to estrogenic an hormonal treatments than those who have cancers which don't have estrogens attached. There is a different follow up from staining tissues and their affinity for some specific tissues to finding the affinity sites to designating chemicals that will do what we want them to do. It goes back to 1805. Instrumentation is absolutely indivisible from science. What we tend to forget, however, is that the simple slide rule and adding machine is as useful as the most complex computer, which is necessary for handling a tremendous amount of data. It gave us a completely different idea, incidentally, about how to survey populations and demographic measurements, which would have been impossible or at least tremendously burdensome to do on a hand basis. When I came into the NIH there was only the adding machine. Then we had the Marschant calculator which was a tremendous step forward, and now you just have terminals on you desk. Now, of course, we are having to deal with illegal elements that can break into these systems!

HARDEN: I suppose this demonstrates the old adge, "Where ever there is a system, people will find a way to beat it."

SHIMKIN: No question about it. This is what makes me fearful of the main threat to mankind that we face today. As long as we have atomic energy and the building of atomic weapons, we have a Damocles sword hanging over our heads. Somebody, either by intent or by an accident -- and it might just as well be an American as a Russian or an Israeli or an Arab -- will push that button, and then the whole biological process on this planet may well have to go back to the cockroach. Our main scientific drive in physics and other areas should be to find some way to disarm nuclear materials -- not simply to bury it, because that produces its own problems -- but in some way chemically to change it back into something innocuous. And that can be done. If I had enough money from the government to invest, it would be in this. There can be no regulations that can be established nationally or internationally that can keep the material from falling into the wrong hands. And wrong or right hands, if you have the instruments, somebody is going to use them. I think it was Checkov that said that in a play, if you have a gun over the mantle, if you know how to write a play, that gun will be used sometime in the play. As long as we have atomic weapons, it doesn't take virtue or vice -- sooner or later someone will pull the trigger, accidentally or on purpose. I'm a mystical kind of a guy. It's a very peculiar thing that at the time that mankind has learned to breed without limitation on this accelerated exponential rate, so that mankind has become a cancer on the globe, unto our hands has been given, by the Good Lord, the means for destroying ourselves completely, which is the first time this could be done in history. Even Ghengis Khan couldn't accomplish that. But we can now, with atomic weapons.

HARDEN: It is very interesting, isn't it.

SHIMKIN: It's almost prophetic. Unless we have the wisdom to control that, and I'm afraid this is not contained in trying to get ahead of the Soviet Union and having Mr. Haig huffing and puffing up and down the country. This is not the way to solve the problem. There must be other approaches.

HARDEN: We have covered all ten questions. Is there anything I have omitted that we should discuss?

SHIMKIN: No, I think we have covered everything very well.

HARDEN: I will prepare a transcript to send to you for you to read and edit as you wish.

SHIMKIN: I would have been a lot less wordy had I known this would happen!

HARDEN: Well, I don't want to misquote you.

SHIMKIN: I am hard to misquote. I find that most people who say they are misquoted want to eat their words.

HARDEN: Many, many thanks, Dr. Shimkin, for taking the time to talk with Dr. Kondratas and me.