

Dr. James A. Shannon, NIH, Bethesda, Md. July 27th, 1963

I think we need some footing, some piling in personal terms. I suppose one way is what were the circumstances, human and otherwise, that took you into science and, more particularly, into medicine?

Chance really. Well, it's a fairly complex story. I graduated from high school at age eleven--I mean grammar school at age eleven, high school age fifteen, and my parents felt I was too young to go to college. Apart from that, they selected Holy Cross as the place they wanted me to go, and I didn't have the classic languages to get in, so I went to Brooklyn Prep for a year and got enough Latin to satisfy their requirements. Then I went on to Holy Cross.

Now, my intention in going up there was a rather vague idea--staying for two years and then going on to M.I.T. for either electrical, or chemical engineering; probably electrical engineering, but I became interested in athletics up there. I'd been a reasonably good athlete in high school, but I started running track at Holy Cross, and my track coach convinced me that if I'd give up basketball, I'd stand a good chance of making the Olympics. He said, "This means that you ought to give up M.I.T. Besides, why don't you become a physician instead of an engineer?"

I had no fixed idea. At that time I was ^{not} particularly in-

terested in hard work, and I knew that if I went to M.I.T., it would be hard, so I decided to go into medicine with no particular emotional drive at all. I stayed in athletics, both track and basketball, and the injuries that I accumulated along the way removed me from any importance in track.

Well, I knew so little about medicine I thought that all you had to do was to apply to medical school and be accepted. I had lousy marks, and my only distinction was that the only thing I busted in four years at college was Greek Literature, but basically I didn't crack a book for four years, so I finished as a bachelor of arts with low marks and with a minimum in the way of pre-medical courses and low marks in these.

At that time you applied to medical school at Easter Vacation, and I was turned down in rapid succession by Cornell, P & S, Yale, Harvard, and even Long Island College for Medicine. The only reason I got in medicine was that the man who was interviewing me at New York University at that time, a man I came to know very well later--eventually he became Dean and Professor of Medicine, John Wycoff--had a rather checkered background too. His father was a medical missionary, and he came back to this country, went to Rutgers, and again, he was a track star rather than a student, and I think basically that's how I got in.

The thing you probably don't realize is how competitive New York University was at that time. It drew most of its students from metropolitan New York, and there were a lot of second generation students from Europe, Italians, Slavs, and a very heavy component

of really bright young boys of Hebrew origin who really had burned things up at City College. I found myself in a wholly new world. It was the most striking awakening I ever had. By then I knew that medical school was tougher than I thought it would be, and at that time--you have to realize now; this was back in the fall of 1925--it was much more a course in memory than it is at the present time. We started off with Anatomy. They gave you a box of bones, and in two weeks you had to learn every bone in the body and every ridge on every bone. I went home the first night and after two hours of study I was exhausted. I thought I had studied pretty hard, but by the end of the two weeks period I found that one had to spend about four, or five hours a night, and do it consistently.

Then I got interested in the subjects, caught fire, and before I finished, had spent a good deal of my third and fourth year and the summer between my third and fourth year doing investigative work in the department of medicine. At that time I had no idea of going into science; I took physiology for a two year period presumably as part of a recognition, or a beginning recognition at that time that as medical research developed in the future, it required a broader base than one obtained as a medical student. As it happened though, I became very productively engaged in investigative work there. Things just turned out right. I happened to hit it right most of the time, and I stayed there ten years. I returned to medicine in 1940, not particularly because I wanted to, but because positions in physiology were so few and if you

looked over those who were going to retire in the next ten years, very few places that I would want to go would have a post open.

There was a growing awareness in New York of the fact that chronic illness as such had not been viewed with the dignity that it should, that the individual with chronic disease in New York was viewed as no problem. He was put in the corner of the ward and forgotten. The biggest problem of the acute hospital such as Bellevue was and most of the others were in the Thirties, had as its primary job clearing the ward out. Well, a number of people in New York when Goldwater was Commissioner decided that although this was not an infective area, it was an important one. In the late Thirties with the conquest of infectious disease with the sulfilamides, these people realized that chronic illness was something that would have to have considerably more attention in the future. They designed the Chronic Disease Hospital, the first of its kind in the country, the Goldwater Memorial Hospital, and as part of the design of the hospital right from the beginning, it was visualized that there would be three research units and there would be three university services--P & S, Cornell, and New York University.

They started with the Columbia Unit long before the hospital was built. Dave Segal went down there in charge of it. I was asked to set up the New York University Unit that would have its beginning when the hospital was completed. A chap by the name of Abe Miller was asked to set up the Cornell Research Unit, so that when the hospital opened about 1940, I moved in as director of the

New York University Research Unit.

The rather tenuous position this hospital held in the community was perhaps exemplified by the fact that Cornell pulled out because they were quite unwilling to make a dime available. If the City wouldn't pay for it, they weren't going to put their faculty there. Columbia was committed, but they said that they would lend their support to the development of grants-in-aid as a wiser means of carrying the operation. New York University--by that time Wycoff had died; he was one of the ones responsible for the concept--gave me a shooting license on the foundations. New York University was quite unwilling to put any of their money into the operation, so with the help of a scientific advisory committee for the two research services Segal and I got going in the latter part of 1940. I pieced together grants of about thirty-five thousand or forty thousand dollars from such places as the Carnegie Corporation, the National Research Council, and a number of others I don't recall now. I got together a staff that was small in number, but very high in quality, and this is the origins of the Goldwater Memorial Hospital Research Services.

All this happened in 1940. Of course, Pearl Harbor was in 1941. We had just started our research service that was addressing itself to the problems of water electrolyte metabolism and its various relations to cardiovascular disease. That was one of the problems into which you would go. We were not required to work on arthritis. We were given a complete free choice. Columbia's service was primarily concerned with problems relating

The lab became
Nobel laureate

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rheumatic fever and problems of chronic pulmonary disability. That was rather an extraordinary operation because out of that--well, that's where ^{Richards} Al Richardson and ^{Courmand} Courmand did their basic work. During the war time period ^{The Columbia Division} they ~~also~~ did some of the better work that was done on blood substitutes. On the other hand, our unit completely dropped what it had been doing and undertook a systematic study of malaria.

This is important because this was the first time that all the modern tools of science were brought to bear on an important disease that had largely been studied only in a tropical setting. That's not entirely true because there's a man by the name of [at the] in England who had been some work in induced malaria, but we had become involved in it in a very peculiar way. First, let me say that I finished medical school--as a matter of fact ^{close to the} top of my class. I had no difficulty at all in getting a hospital appointment, had been very productively engaged in physiology so that when it came to set up the service I could get really good people, quite young people. They had to be very young because I was very young too, but we talked over the problem presented by the war. It was perfectly obvious that we could do one of two things--we could join the service, or we could take the facilities and resources and try to really hit a really important problem that needed to be done. It was perfectly obvious that there were going to be a number of these in the medical field.

In a very naive sort of way I went down to see A.N. Richards who was head of the Committee on ^Medical Research at the time.

I'd known him quite well personally because of an amusing incident that I'll tell you about. I said, "We'd like to be helpful."

I told Dr. Richards that we had a wholly new resource. We had a limited number of very interesting scientists with broad training, and we could undertake just about anything--we thought probably we were best suited to move into the area of blood, blood substitutes and the like. He said to me, "Jem, for God's sakes--everybody wants to go into that. There are plenty of people working on it already. We have more people than we have good ideas. Everybody is willing to give me a resource, but nobody is willing to give me ideas. Why don't you look the field over and decide what you'd like to do and then come back, and we'll talk it over."

Well, because of summer work up in Maine I had become quite closely associated with a chap by the name of Ken^M Marshall who is P^rofessor of Pharmacology at Hopkins, and he had become involved in malaria the year before, and I was aware that the conventional textbook picture of malaria was quite different from that which actually obtained in the field as problems, so I went down to Baltimore and asked him to tell me what he was doing, why he was doing it, and what the problems were. We had become involved in some of the work that Marshall was doing because we were using sulfilimides~~d~~--these were actually studied in Marshall's laboratory--as a convenient series of drugs with progressive modification in the chemical structure, to study some of the characteristics of the distribution of organic substances in the body.

This we had taken because they are very easy to analyze. ^{and} As I say, there ^{was} is a whole array ^{of related compounds}. You could select your series from about four or five sulfilamides which we could synthesize for our purpose, so we were quite close to what he was doing, and I really learned in depth about our ignorance of malaria as related to drug therapy and the organic substances and their distribution in the body. It was quite apparent from the sulfilamide story that the problem of the effectiveness of the drug was related as much to how the body handled it as it did to the nature of the drug itself, so we decided that maybe it might be worthwhile to go to suppressive and curative treatment of malaria.

The problem here was that in the sulfilamides you had a simple method. You had very high concentrations--these ran from five to twenty milligrams per hundred ccs, but with the anti-malarials we were dealing with things in the order of magnitude of micrograms per liter, so this was going to be a much tougher job. Nobody had any idea what concentrations ^{we} were dealing with, but we used one tenth of a gram per week instead of five grams a day, or two grams a day, so obviously you were dealing with much lower levels.

I sent one of my people, a chap by the name of _____ to study the natural history of malaria in Florida, and he ^{was} quite discouraged. To him this was much too complex a program, but he decided that he would have a try anyway. We applied for support because the City funds only covered about a third to a half of our total operation, and for these additional studies we would

have to find support elsewhere, so I asked people who were with me at that time to stick with the unit for a period of three or four months to find out whether we couldn't find a solid place for the investigative aspects of medicine because it was perfectly clear that we were a hell of a lot better off there than in a tropical climate. None of us had the experience for that. We ^a applied for a contract. The National Research Council advisory committee in malaria just turned us down cold and again on the assumption that none of us had ever worked in malaria, and "if you want to work in New York rather than the tropics, just forget this." Fortunately A. N. Rigards intervened. His attitude was that the group was good, and if they said that they could do something, then give them the money. He said that if we said that we could do it, the chances were that we could.

The reason for that attitude is largely that his group was working on physiology back in the mid-Thirties as was I, and we happened to do almost identical experiments on a very important area that was a key to ^{a)} the whole host of ^S subsequent developments in physiology, an ability to measure attrition rate in an indirect manner. Doing the same experiments we came out with a high degree of precision. His came out with an extraordinary wide variability, and my conclusion was that the measure was valid, his that it was not valid. Heⁱ's a very interesting individual, and his attitude was that you can't do the same thing and get two such strikingly different results, that one of them was bound to be wrong. He said that he'd send his people up to my laboratory--I was working

on this stuff at the time--or I could go down to his laboratory and study together. Hell! I was young and cocky--I'd take the challenge. I knew I was right, and I'd go down to Philadelphia. So I packed my chemicals and stuff and went down to his laboratory and ran the experiment with his people. They came out right on the nose with what I had done previously in New York. So he told his people to withhold any publication of their results and redo their methods and then restudy the question. This held them up fifteen, or eighteen months, and when they came up they were precisely the identical results that I had had previously. That contact gave me enough of a feel for Richards, and Richards enough of a feel for me so that when the chips were down in 1941, he said, "Give the guys money!"

It's funny how these things turn out.

Well, before we were well under way, it was perfectly apparent that atabrine was not holding malaria. This was now the spring of 1942, and casualty reports in the early days of the Southwest Pacific were most disturbing. Most of the casualties were due to malaria, and the use of atabrine was accompanied by such toxic manifestations that if you put a battalion on atabrine, you'd have nausea and diarrhea in as much as thirty percent of the men. It would inactivate the group, and those that did take it got malaria anyway, so there was a crisis.

The basic problem was that the United States had never completely synthesized atabrine. They had imported it through intermediaries from Germany, and this was the final reaction. The

question was was there some trade secret that related to the chemical structure of atabrine that the Americans weren't aware of, and in fact, they were putting out a highly toxic substance. There was substantial pressure because quinine was in the process of being exhausted, and the Army did two things--they stopped the purchase of all atabrine, and they put a stop on all the use of quinine in the country except for medicinal purposes, malaria. They appropriated all the stores of quinine held by the commercial enterprises. Then they asked the National Research Council to take a look at it.

Our group then became involved in what was a really urgent problem and together with a few others, including Ken Marshall in Baltimore, we set up the concept that this could be studied both chemically and for its medical effect in experimental animals. Well, the chemical study was handed to Harvard, and they came up with a very high concentration of what they called a toxic substance and said, "Well, this is what is causing the trouble."

We worked with dogs then, and we found that the toxic contaminant did not cause ~~causes~~ ^{URESIS} in the dog in any greater extent than the atabrine itself, so we decided on direct human experimentation. We got supplies of atabrine from South American pharmacies. We got current supplies of atabrine that was being used in the Armed Forces. We got some English atabrine made by ICI. We had some samples of that, and then Jacobs of the Rockefeller Institute made highly purified atabrine--probably the most pure atabrine that was ever produced. I talked to the student body at

Ohio State University, the Commissioners of Correction in New Jersey and New York State. We had the whole student body of Ohio State and about three hundred and fifty inmates in the Rahway Reformatory and about four hundred and fifty people in Sing Sing. We put them on dosage regimens of these four different types of atabrine, and they all showed precisely the same toxicity, but what did turn up, and this was a very important clue, the medical students at Ohio State had the same toxic reaction as the Armed Forces, about thirty percent. The reformatory people in Rahway had five to ten percent, and the Sing Sing people had essentially none. We tried to figure why this was, and we suddenly realized, or we came to realize that this experiment was done in May when the Ohio students were looking forward to their final examinations, and the others were protected groups, particularly the Sing Sing one, the long term prisoners.

By this time Brody who is now in charge of Chemical Pharmacology here, was a young chemist with me at that time. I'd asked him to develop methods for the estimation of atabrine so that we could face the problem of therapy ⁱⁿ a little more rational way--not with any idea of what we would find, but just that our contribution to the field, if it was to be anything, would be in quantitative biology. Well, by that time he had developed methods. We were beginning to work with students at New York University on different dosage regimens, and as soon as we had methods, then some very interesting things began to turn up.

Well, I might say that out of this study on the human volunteers, we said to the Armed Forces that all atabrine is the same

and "you might just as well go ahead and start purchasing again. We'll try to find out how to use it so as to minimize toxicity."

The conventional dosage was two tablets a day--I mean two tablets twice a week, and our initial thought was that we were getting with this type of therapy--and interestingly enough, the World Health Organization had called this "the shock type of suppressive therapy." Everybody had difficulty with this dosage regimen; a fact that was not generally appreciated until the war. We thought that this was being rapidly absorbed in the treatment concentrations possibly precipitating toxicity, so long before we had any idea of what we were doing, we took the same amount and gave it in varied amounts compared to two tablets twice a week. The striking thing we found out was that it didn't make any difference how you gave it really. The blood levels you got depended largely upon how much was given in a week and how long you had been giving it rather than what the discharge rate was, but this gave us a clue immediately then as to how it might be taken without toxic effect, and we immediately moved over to higher dosage given daily--that is, a high weekly dosage given daily as compared to the standard therapy.

By this time we were getting information on what happened to atabrine, and we found extensive localization in tissues. There was rapid absorption and there was localization, and then there was feed back into the system. We found then that the blood levels were not reliable because most of the atabrine was in the white cells just as it was in the liver cells, used it as a storage

depot, but one could make plasma levels, but these in the suppressive area were down in the order of magnitude of ten micrograms per liter. By this time we had very sensitive measurement. We compared dosage regimens, and it became clearly apparent that we could give much larger weekly dosages of atabrine if we gave it a different way.

By that time we also had model experiments going in induced malaria and knew the general levels that were required to terminate the disease, or to suppress the disease, and while heretofore people had always said that malaria that was induced was amenable to very simple treatment as opposed to naturally occurring malaria, we didn't believe it and subsequently showed that this wasn't true, but that's unimportant. The point was that we had a model that showed that the shock treatment, so-called, two-tenths of a gram twice a week, gave levels that by our prediction should terminate most malaria, so we used this as the floor of the dosage regimens that would produce no less than that distributed broadly in a fashion that would not produce toxic effect. Really in a period of two months the total answer was apparent. Before you put millions of men on a completely radical dosage regimen, as a result of the work done in New York we had to have more evidence than that. We had four hundred and fifty medical students, but our data was precise. It was consistent. It was reasonable. We had the total answer, and still we felt that it should be extended. We got two companies down at Fort Knox and put them on a variety of regimens, and the thing came out as predicted, and it was then

ready for general use in the Army.

This is a long story but the importance is that this experience very early in the war made it abundantly clear that in the search for new antimalarials, that if one used highly quantitative techniques and used highly stylized infection, one could get very rapid answers on very few cases and could expect the results of these answers to obtain when they were explored later in the field, so that that experience quite early with atabrine jelled the experimental approach to new antimalarials for the remainder of World War II. The application of that approach to the human volunteer with very broad and very good animal support led to the development of the _____ and the _____ as the drugs of choice; one to suppress malaria and the other to provide what was called a radical cure for recurrent relapses. The differentiation between these two types of action was clarified again--it was not proven at that time, but the hypothesis was set up and assumed and was pretty well established experimentally--that the natural infection differed from the induced infection, and this was produced by blood. The characteristic of vivax infection was its relapse. It was not the difficulty in terminating the infection, but rather in curing the disease, and there was established an initial tissue form that progressively, or periodically invaded the blood and caused the relapses whereas if you just used blood to infect an individual, you'd just have the single episode.

It was also possible to show with malaria, whether by

by mosquito induced, or blood induced, each disease had the same sensitivity to drug and was a common strain, so that our primary contribution was to ~~set~~^{set} up models to approach this from the standpoint of highly quantitative biology, demonstrate that the physiological disposition and a series of drugs could be more important in antumalarial activity and that the qualitative assessment of any therapeutic agent required knowledge of this general sort.

Basically this has conditioned a good deal of the development of new therapeutic agents for the last fifteen years.

It was a very productive effort. Now what it did for me--I was invited to return to the pre-clinical sciences in 1943, as Professor of Pharmacology which I accepted, but Richards asked that I not assume responsibility at that time because our work was much too critical. By that time we were not only running the Goldwater Unit. We were using the current therapeutic concept, and we had access to a large group of wholly non-immunes for the induction of malaria. We had another unit up at Manhattan State in association with the New York State Mental Health Authority and at Bellevue in association with the City. We had a field unit first at Costa Rica and the~~N~~^N at Panama, and at that time, or as a result of this striking beneficial effect from a relatively small unit in New York, the Army agreed to start assigning medical officers and broadened the activity, and we were able to fortify by that time the Public Health Service unit in ~~A~~^Atlanta, set up a new unit in Boston Psychopathic, a new unit in Chicago, first in State and later in the Statesville Penitentiary,

and this was largely staffed by Army officers who were selected from the service for as long as three years so that one had a very great operation, but one, as Richards pointed out, which required a fair amount of direct supervision, so I didn't go to Pharmacology in 1943, but we did set up a laboratory there and detailed one of the people who came with me in 1940, as a young assistant resident, John Taggart, who is now at P & S as Professor of ^Medicine, to set up some of the studies on the systematic observations and pharmacological disposition of malaria.

I came out of the war with a keen ^eappreciation of the absolute need, if I was to do what I wanted to do, of ^awell controlled clinical service with ^avery broad support program in basic science, and I had no idea of continuing in the field of malaria; as a matter of fact, our whole group dropped it as soon as we could pull out, but we had made our major contribution, and the thought was, "What the hell! Let somebody else do it."

There was a change of attitude at New York University. By that time they decided to go for a new building program, and while I had acquired the funds for a complete rehabilitation of the ^Pharmacology Department--I had about a hundred thousand dollars for that purpose--they were unwilling to let me do a complete job because they ^said they ^were going to build new buildings and this would be a waste of money. Then while they were quite willing that I use clinical material, the Professor of ^Medicine decided that he could not give me a service. ^Now, I had been running a service for five or six years during the war, and in addition to

that had run the entire primary medical service ever there. It wasn't a question of competence. It was a question of academic rivalry, things of that sort. So I said, "Nuts!"

I left and went to industry. I was at the Squibb Institute for three years. It was extraordinarily interesting. The Squibb Institute was started in 1938 as a basic science extension of the pharmaceutical industry unrelated to product development. When the competition really got bad with the antibiotics in the late 1940s, and I went out there, I found the whole Squibb Institute being misdirected in the development of work for which they were not well suited, so that it became necessary to reorganize the operation, and we ended up three years later with three very strong developmental groups with the return of the basic institute personnel to the longer range type of investigative study that they were trained for. By that time I had gone on the board of directors of E. R. Squibb & Sons on their committee on executive management, director of the Squibb Institute, and I was looked to for determining advice on the whole developmental aspects of science even though we had split off the development division. I was spending about half of my time in New York, and I decided that I hadn't developed for the better part of a couple of decades in science to become an executive, so I left there and came here.

I had previously been invited to take charge of medicine out at Brookhaven. This was in 1948, but I decided that was too restricted a setting, and when Tepping, Dyer and Scheele asked me to come down here, this was during the first year of the operation

of the National Heart Act which had set up a wholly new research operation addressing itself to the broad aspects of cardiovascular disease. I left industry and came down here to acquire, or re-acquire immediate contact with science. I left industry because I wasn't doing precisely what I wanted to do.

Well, then the rest of the history--I developed that operation over a two year period.

Was this the internal....

This was the direct operation. Norm Topping left for the University of Pennsylvania, went up there as vice president for medical affairs. It's interesting how these things happened. When Dyer retired, the logical successor was Topping. He was the so-called "crown prince." I don't know what happened. He was not appointed director. This was given to Henry Sebrell. I think Norm must have felt he had to get out. It was ridiculous, but nonetheless he did, so he went up there--I guess in 1952. I came over here as associate director, again in charge of the direct operation--that is, the local laboratories here, and when I came over here, Sebrell said that I wouldn't have to worry about any aspect of the public. All I'd have to do is run the operation. Nothing could be farther from the way it turned out, but that's all right. Then after two years Sebrell retired, and I became director here.

Now, the interesting thing, I think, so far as I'm concerned, is that I've had a series of pressure jobs since I've been here.

One was to develop a wholly new direct operation for the Heart Institute which has turned out extraordinarily good. I went over into Topping's position, and my problem there was to open and integrate clinical investigation with the laboratories, all the problems of opening a new hospital. The next year when I had this job--that is, the associate director's job, the polio fiasco broke, the live virus and the Cutter Vaccine, and I was asked because of my scientific background to head an advisory committee, and I had to work through that. Then I came over here in 1955, and my first responsibility here was to convince an extraordinary Secretary, Mr. Folsom, that medical sciences were getting grossly inadequate support, that the concept of the job was being done piecemeal and was out of balance. He bought the whole thing, and that was the beginning of our really spectacular rise in budget because with the Department and the Congress looking forward to the 1956 budget, he accepted those generalizations and our development extramurally has gone up from that time, so that the primary job was to adapt our ways of doing business to the circumstances which were changing very rapidly, from the use of very small funds--you see, when I came here our grant budget was thirty-eight million. It was truly a grant-in-aid--small amounts of money to make things possible by adding on to university resources as opposed to the present where we have provided resources and total support for the medical sciences. Finally, I think--well, by law I have to retire within a five year period, should leave here probably in two or three years and let somebody else take over

from there on, and if by that time we have stable, well-established relationships that relate the independence of the university on the one hand and the federal government on the other with realistic programs, I feel^e that I've done my job there, and I'll let somebody else worry about the future from there on because I think by then we will well established the concept of providing broad resources to the university as a whole through general research and training grants in specialized areas such as animal resources, computers, things of that sort, as well as to have research supportⁱⁿ both project and career areas. That should take place in the course of the coming three or four years. This is not to say that there won't be any problems after that, but as far as I'm concerned, these are the things that must be accomplished. This will have to be done not only by the things that we do, but also by things that of necessity will be done by the university, but that's another whole story, but you wanted personal background.

I wonder--in terms of developing a heart research program where one had theretofore not existed--what that process was. Did you pick areas, or men? What was your thinking and its implementation?

I think you have to take a look at the setting. Scheele, or more particularly, Dyer and Topping first talked to me in the fall of 1948, before they even started the facility. They just had authorization, and they were in the active stage of planning, and in the aggregate this was about a sixty to seventy million dollar

construction program. The University ~~World~~ in general rejected this as a reasonable program. The general feeling was that it was bound to be mediocre, that we couldn't buy results with dollars, and that this would drain off all the trained personnel from the universities and would result in positive harm rather than good. Now, it was in this setting that I was approached and quite frankly, it was very important that they get somebody with both a national and international reputation in order to start on this development program. It was good fortune for me, and quite frankly also good fortune for them that I came because my reputation was made as a scientist. I had done very productive work in physiology and water electrolyte balance, had been extraordinarily fortunate, or my group had been extraordinarily fortunate during the war. I had a productive three years in industry, so that I came to them with a scientific reputation.

Bill Palmer who² was then Professor of Medicine at P & S, a very close friend of mine--I valued his advice a great deal, told me previously that I ought to be very careful about whether I went into industry or not because my going in at that time with such an eminent position in New York science would have a profound effect on other people entering industrial science, and he didn't know whether that was good, but, as I said, then I felt I had to leave, and I wasn't going to fuss about it. This was a reasonable job, and I moved, but then later coming down here, his reaction was a curious one--that is, he was generally opposed to the

development, but it was going to go forward. The money was there. The law had been passed, and he just hoped that if they were going to do it, as he knew they would, that they would try to go outside the government and get good people, and I'd be a good beginning in that direction.

When I came down, this place had no reputation as a thing in itself, although--well, put it this way: it had no current reputation at that time. It had no reputation in terms of really large science, although in the 1920s when you had people like William Mansfield Clark in the Hygienic Laboratory and Goldberger in Nutrition, and actually Pete Cannon was one of the early fellows here, Brad Hastings who subsequently went to Chicago, and then to Harvard, was the first Public Health Service fellow back in the 1920s. The Hygienic Laboratory in the 1920s was an extraordinarily productive scientific environment characterized by very high excellence, very high standards of accomplishment, but during the Thirties and during the war particularly when they moved out here in 1939, as viewed from the university, was fairly characterless. They had set up their Cancer Institute that had done, I think, very fine work, but they hadn't solved the problem of cancer. It was just the idea that the needs of the medical schools were so great and here the federal government was setting up its own establishment with access to unlimited funds, and they could only do harm to the university world by draining off personnel.

In that environment it was perfectly obvious that I was going

to have a tough time recruiting top scientists. Salaries weren't good even then--well, I myself came down here at one third the industrial salary I was getting, and further I came down to recruit for a direct operation of a categorical nature in a laboratory environment that had never had access to human material before. Now, in a situation like that, you can't pick the men and depend upon them to develop the program because if you're going to give them a clean shot at science, they have to have this clean shot in a pretty unrestricted fashion, if they're good. So what you have to do is decide what are the elements of a broad program in cardiovascular disease, what is the character of the scientific opportunity that would be offered and then having decided what that is, then try to pick the people who fit into such a pattern and give categorical emphasis to the selection of people and their relationships to a pattern rather than just get a bunch of hot scientists and say, "Now, go to work!"

The thing I carried into this environment was the interdependence of clinical and laboratory work, the broader relationships. The organization of our setup was certain fundamentally oriented operations such as physiology, organic chemistry, technical development and things of that sort that had broad relevance to the cardiovascular field, but were not really part of it. Then a layer of laboratories that would provide an interplay between the clinic, the basic ones--electrolyte physiology with its broad relationship to cardiovascular problems as such, metabolism because of its general relationship and so on. We had

one or two others, experimental therapeutics, surgery at the clinical level together with special provision for those intermediate laboratories to have their own patient material and to be responsible for it. Now, what I found as soon as I started ^Urecruiting that--this was 1949. I wasn't going to have much space until 1952, and 1953, so there was a very small amount of space in Building 3 over here, just two floors, and yet in 1953, I was going to have roughly the equivalent of eight units each of which would have nineteen units of space. It was a very broad program--this together with the whole of Building 3. So how do you do that?

I didn't offer a single position to a full professor. People ~~I~~ was convinced could make a contribution in the future were in the age group, 32 to 34, broadly trained in the fundamentals of science, and I looked upon the clinic as the proving ground, but not as the developer of knowledge. There I came up against--how do you employ these people? I found that I couldn't get them by the normal Civil Service procedures. I had these long lists of people who ~~were~~ certified, and then I had these people in the age group of 32 to 34 who couldn't qualify for a top commission, so I arranged with the Public Health Service to sit with top management of the Civil Service Commission. These were not the Commissioners themselves. These were heads of division--Classification Division, this kind of a thing, and we had about a three or four hour conference. By this time I could tell who were the three or four best people in the country ^Yfor the jobs I had, what their experience was, why they were the best and why they would ^{NOT} fit in the

present Civil Service system. I convinced them in this period of time that if I did not have access with reasonable salaries for these people, they wouldn't have an operation to work for them.

Now, this is important because this set a pattern for the total employment of the newer people who came on here because at the end of that they said, "Well, your problem is very simple. You can hire all of your key people on your schedule there which is non-competitive. When you finish the staffing of your key people, let us know, and we'll blanket them to the regular career system of the Civil Service."

I was given free shooting rights on this young group of top scientists in the country. Then the problem was--what do you do with them? Well some of them I stacked in Building 3 and told them to recruit their group, and others I left in the universities a year or two while they brought their group together. That's how you get _____ who was with me at Goldwater, then had moved over to P & S, to come down. I was fortunate to be able to tag some of the really brilliant people I'd had past experience with. Broady came down, another person who was with me at Goldwater. Bollen whom I knew first when he came to our physiology laboratory and even then was primarily concerned with the development of new technology, came down as head of research and development. These were the first three appointments made. Then we got people like Antorcine who was associate professor of biochemistry at Harvard, and we got him primarily because we could offer him broad resources and broader opportunity, and other people of that

vein. Fortunately the selection has been very good.

When it came to developing the clinical staff we took Terry who was a ~~good~~ clinician, but who had not had broad research background. He wasn't selected for that. He was selected because of very high excellence and standards in relation to patient care. We could find no surgeon who would come for the money we had, so we deferred that decision until a later time and eventually ended up on recommendation from Blalock to take one of our young surgical Public Health Service officers who was being given advanced training first with Blalock and then at the University of Manchester and brought him in as Chief of Surgery. He came not because of his accomplishments, but because of his potential, and he's paid off and again good fortune in the selection. As a matter of fact, all of them were brought in because of their great potential rather than because of their scientific reputation.

During the war when I said we had army officers assigned by the Army--I'll tell you how we got them because I got the clinical staff of the Heart Institute, the resident staff in precisely the same way. Immediately after the war the Public Health Service officer can satisfy his military obligation when he becomes a commissioned officer. I went to my close friends in medicine-- Walter the head then of the Massachusetts General Hospital, Bob Loeb, Professor of Medicine at P & S, David Barr, Professor of Medicine at Cornell, Barry Wood who was then Professor of Medicine at Washington University--well, people of that general sort, and asked them of their then current assistant residents to

~~to~~ give me the top two or three men in the entire group and give me an opportunity to talk to them, so I talked to about thirty-five or forty people who were selected by the best medical minds in the country to be the best in their groups. I was looking for twelve people. I invited fourteen to come, and twelve came. This is because we offered them research opportunities in a situation where they knew that they had the better part of two years to satisfy the military obligation. For my money, I felt that the first group of residents we had would set the standards of excellence from thereon in--I'm getting ahead of myself.

We did that during the war. We asked our friends to give us a list of their best people and then we assigned them to Goldwater, or to Chicago, to Memphis. We did the same thing here, except we invited them to come with us, and even as I think eight out of ten of the people who joined the Goldwater Unit--we had about twenty, or twenty-five people there--at the present time now rank as heads of departments. So will this group that came in the mid-Fifties rank as being ^{any} (extraordinarily able and outstanding group, so that we depended upon youth and potentials of individuals who would find satisfaction in areas that obviously had relevance to cardiovascular disease. This was for our clinical and laboratory leaders, and we depended for our young people on the recommendations of our friends. This is not a democratic way to set up an organization, but I don't know of any other way.

Has there been continuity with these people? Do they tend to re-

main, or is there turnover?

There is a lot of turnover at that level, although I would say half of our original group that I selected to be assistant residents are still with us and doing extraordinarily well. The important thing, you see--a pattern was set there. This was followed when the Arthritis Institute came along--as a matter of fact, the list of people I originally interviewed I turned over to Arthritis, and I think ninety percent of those selected were selected from the same list.

When you went from the Heart Institute to the Office of Director as associate director, it was still with reference to the development of the direct operation?

Yes, the direct operation.

This, as I understand it, had been complicated by the emergence of the Clinical Center and the increase in the number of institutes. Was it a recognition that what had been found fruitful in the development of the Heart Institute, the direct operation developments, was usable throughout NIH? Other impulses may have been in the air, like the grants program, but the basic concern was refurbishing the direct operation.

Yes, but the other things really took place at the same time. There was more of a changing of names really than anything else, but--well, the Institute of Neurology was wholly new, but the beginnings of the neurology program had previously been contained

in Mental Health. Arthritis had previously been National Institute of Experimental Medicine, National Institute of Biology and Infectious Disease was more or less the Biological Institute, so there was not a burgeoning of institutes at that time. It was a reshuffling, a renaming and redesignating their missions.

Rather than designing new intramural programs for new institutes, it was an emphasis toward expanding institute concern to include programs offered by the existence of the Clinical Center--again a concern with local development here at Bethesda.

The primary problem that I had over here was getting a very complex installation into being. You see, if you look at the conventional good medical environment for a good clinical investigation program, you're looking at an environment that has been developed over thirty, or forty, or fifty years. There are no wholly new clinical environments, or there were none at that time. A good example of one that's been done just as fast and just as good as this is the Albert Einstein Medical School. Very few--up to that time. I might say that they used the same devices that we used here, but be that as it may, this involved a very strong arbitrary setting where the laboratory chiefs really resented the intrusion of the clinicians. They saw that this was going to change totally the environment of the National Institutes of Health. There was going to be a bunch of clinicians around that were going to dominate the scene. Their idea of clinical research was a very bad professor with a stethoscope hanging out of his

pocket. This is what they viewed was going to happen. They couldn't conceive of a clinical setting that would be to their advantage. The second thing is the old timers who were here were comfortable. They didn't want to see the operation blown up. They felt that the sheer size would ^Sdestroy the spirit, and in fact it did destroy the old spirit, but it created a new one, and this they ~~respected~~, but, more importantly, when you develop a modern hospital along a concept that heretofore has never been established purely for purposes of investigation, where ^oyou have broad service responsibility, where the nursing department, for instance, must be decentralized in program terms, you ruin the hierarchy that heretofore had characterized nursing departments. When you set up an organizational structure that heretofore has not been in being, this is a rough job, and you have fights.

One day I was over there I had a chief of nurses, the chief clinician of an institute all wanting to resign at the same time because they all found for various reasons this was an impossible situation. You realize how bad it was--in the first five years we had three chiefs of the Clinical Center. Two of them were brought from conventional settings, Public Health Service Hospitals. They were the best the service had, but they couldn't perform. Finally, I went to the Surgeon General and asked to have Maseur back--Maseur by then was Chief of the Bureau of Medical Services, a position comparable to mine, so we got Maseur back, and he was the one who developed the plan of the physical plant. So this was a very rough couple of years because you start any new

had at the same time a broader training mission than they had had before. They felt that if we took personnel, how were they going to do their training? They had a complete lack of vision. Their attitude was dominated by the short term, the fast buck rather than what could evolve over a period of years, and I think you'll find nobody in the university world today that thinks of this other than as a superb place to do research and for training young people, particularly at the post-doctoral level. Most of our service is now--the appointments are made to assistant resident two and even three years before a man comes on duty. They are eagerly sought for. We get ten applications for every one we take, a lot different from 1948 through 1951, so I think it's extraordinary, the tradition that has been built up here in such a short period of time.

Fortunately--you see, in retrospect, a lot of things we had going for us at that time. One--we had resources at the time when medical schools didn't have resources, and two--at a time when the medical schools dug themselves out from the immediate post war period, training doctors and getting residency training programs underway. Then our program started to expand, and they could take off with us, so if you tried to plan this, you couldn't have set it up better. There is no doubt in no small measure that the people who planned the NIH did not plan the program we have at the present time. On the other hand, the people who implemented the NIH program--they had the intelligence, and this goes back to the traditions of excellence that established the Hygienic Laboratory

were able to sell ourselves, but our ability to utilize the effect of dollars would depend largely on the competency we had here. The dollars came because of what we talked about earlier. The inadequacy of the university support of science, the lack of support led to the establishment of these extramural programs, subsequently the NSF programs. The general education, the expectations of the people in better health research, and the influence of the voluntary agencies helped. This whole complex of things are the things that made available to us a response of Congress, set the sights of the Congress in a straight forward political thing very high, but had we not the internal competence here to handle vast sums in an intelligent manner, it would have been quite a different program.

This leads us to your discussions with Secretary Folsom, and that context from the standpoint of expenditures certainly is an interesting one. I haven't seen the record. Mr. Murtaugh said that he couldn't find those for me when I talked with him.

I don't know. He said....

That he couldn't find them, that they were in the office somewhere.

Well, I think you'd better get them because that will give you a view on this development. ^{to} Let me see what I can find here. The hearings you want are in the spring of 1956. Well, this is my opening statement. "Here are a series of assumptions...." This is the 1957 proposed brief on budget assumptions. This of course

is an official statement. This is the proposal. "The current aid to manpower training facilities are interrelated....The plan in progress toward full capabilities implies research needs exceed current research capabilities....Increase of broad basic laboratory research is needed and plant exploitation....Laboratory research manpower pools are to expand....More adequate research facilities are needed....Research and application of basic findings....Full use of NIH facilities are desirable....The sustained growth of medical research is in the national interest"--these are the points we hammered on, and this was the beginning of that development.

Now, what--document. I haven't looked at these things, so I don't know where to find them. Now this is the reaction, their reaction. Let me see if I can find the document. Here is Folsom--this is his testimony before the Senate. Read this down to here.

Now, this you have to realize is the Eisenhower Administration when he was trying to cut back on expenditures, and this is the Secretary who is now supporting a thirty percent increase in budget during this period when they were trying to cut back.

These are some of the documents you ought to get. This is the critical period.

Yes. If I understand you, the development of what might be called an extramural medical research program waited upon the firm establishment here of the institutes and the clinical Center, in

being with the intramural programs here.

That's not the way to put it because these were carried--well, I would say that up until this period of time in 1956, and even up to the present time, these two programs have largely been separated one from the other. Before the Congress they were never intermixed at all. The development here in the direct operation was predicted, foreordained by the legislative happenings of 1947 and 1948. This was when the plant was built that set the general order of magnitude of the operation which persists today, somewhat larger than we anticipated then, but the ~~same~~ order of magnitude.

During the 1940s the Public Health Service program initially just took up the termination of the OSRD contracts to wind them up in a logical fashion, but then with the readily apparent fact that funds were not available to utilize resources, or well trained people that were in being, the decision was to continue and expand the Public Health Service programs. This is 1944, 1945, 1946. Then there was a push for a National Science Foundation, the beginnings of that, with all the frustrations that went with it, but with the establishment of voluntary agencies and the push for health as a thing in itself--forces grouped together that resulted first in the setting up of the Heart Institute as a counterpart to the Cancer Institute which had been established in the Thirties, the conversion of the Division of Mental Hygiene into a National Institute of Mental Health. These occurred in 1948. These had extramural programs and in both Heart and Cancer there were programs

for training and construction as well as for the support of research, but of a completely different order of magnitude than we see today. These were of the purely grant-in-aid type of things such as the Rockefeller Foundation had done traditionally over the years. The pressures in terms of personalities, the Adams, the Laskers, and some of the others, felt that the sights of the universities were much too low, and in fact, the sights of the voluntary agencies were much too low. Now, this was in a period of time when on the floor of Congress the NIH were offered amounts up to a hundred and five hundred million dollars to solve cancer, and Dyer on several occasions had to say, "We can't use that type of money." One could not solve cancer in any crash program, but there was this general unrest. Now, the budget did in fact increase, and when these happenings took place in the spring of 1956--I guess it was the spring of 1956, wasn't it? Well, whenever it was--the plant budget was thirty-nine million, the training budget was--you can look it up--twelve to fourteen million, and the first significant increase proposed by the administration was then proposed, and this was a thirty percent increase.

Now, the important thing is that it was realized--Folsom fully realized it--that while sums that had been made available up to the present time had been effectively utilized in establishing a base, they were more important in indicating the opportunity that existed rather than in satisfying that opportunity, and it was on the basis of that ~~that~~ that he proposed a thirty percent increase. The budget was then about ninety-seven million, and he

proposed a hundred and twenty-six million. The Senate came along and added to that, in conjunction with the House, but primarily the Senate, an additional fifty million increase. This was the beginning of the big push when both the Congress and the Executive branch said that medical science today is grossly underwritten in terms of both the needs and the opportunity. We have a base, but from here on we must develop it to satisfy the needs of the scientists in being both in terms of facilities and in terms of support of research, and we must expand the training of scientific manpower. I saw this was followed through because Folsom proposed a construction program for research facilities. Actually he proposed forty million, and he got thirty. This is the basis of our current research facilities construction program which now is at a level of fifty million, and I'm hopeful it will go higher. This was the first broad expansion of training. This was the first time that the smaller institutes did not have the large amounts of pressure from outside. Mental Health received an impetus from within through Folsom--Arthritis and Allergy--for the provision of research grants which has subsequently become the Division of General Medical Science. It was at that time that one went from the grant-in-aid type of support to the beginnings of full support of medical science in proportion to the national need and in proportion to the opportunity offered by the scientists.

These proposals were based upon staff analysis of need and potential in terms of decade projections of what conceivably might be needed.

Well, yes.

Good staff work was also a creation of this period. I think that
perhaps this had been one of the needs of the Public Health
Forties, study
given information, facts, upon h
could projected judgment development.
gather continuing impulse.

Yes, but you have to realize that the dollars have become available primarily because of external pressure rather than an inherent appreciation of our net worth as operators. Now, it's been--the Congress up to the present time have not been concerned about giving us more money than we can use effectively because we've turned it back systematically. This is now being used against us by some of our critics. They're visualizing this as our being stuffed with dollars and various derogatory terms like this. Oh, I'm sure that there have been instances in a program as large as this where certain grants were made because there were balances, but in general as a matter of policy we've attempted, as within human powers to do so, to adhere to standards of excellence regardless of the balances that might accrue, or the lack of expenditures. We've held whole programs back for one or two years until we were certain we had the basis for it. For example, in this career award program--during the initial year we had this, we had the money, we had the nominations, we had the preliminary selections, but we were convinced that we didn't have

a valid basis for the program, and we turned all the nominations back on the basis of our experience, outlined more effective guide lines for the utilization of the funds and picked it up the following year simply because we felt that we did not have an adequate understanding either in the schools, or within our own staff, of the elements of the program that would assure a long term, high quality program, and rather than start it with inadequate information we withheld it for a year.

We've done that in a number of programs. We're doing that right now. We have in the budget, and we're turning back the funds a program to develop truly graduate education in the medical sciences leading to MDs that are equivalent to Ph Ds, or combining degrees--I don't know which. We have four or five schools that want to undertake such a program. We could have started it last year, but we felt it was not a sufficient understanding of what was desirable. These programs won't be activated until some time--I would guess maybe at the end of this current fiscal year because we felt to start a program as important as this with inadequate understanding is to place it in very serious jeopardy. We turned back the money, and we'll begin it this year. As I say, this is not an unusual action. As long as I'm here, we'll start no program unless we're sure that it satisfies a real need, the elements of selection of schools in competition are well spelled out, so that our decisions can be objective.

Of course, it's this attitude that has revealed us of a great deal of political pressure, and I think that our ability to

do it--I might say that this has been done equally well in other areas like ONR. I think that NSF benefitted greatly by our having been in the field eight years before they came in, but I think in general the grant program of the federal government in science, at least as far as the university groups are concerned on the basis of the decisions that are made with a high degree of objectivity, they've been very good, quite apart from our own program. Of course, I think ours are a little bit better, but I'm prejudiced.

When you arrive at a judgment that new facilities are needed,
you your
required, appropriations purpose,
do you wait upon the initiation of demand for new facilities from
?

No. Let me give you--well, how are you going to use this information? Is this purely between us?

Yes, I want to understand it.

Let me tell you what we're doing now. You can't wait for outside. We've been under pressure for three years to extend our program to encompass the need^s of libraries. I^s said that our programs can never satisfy the needs of libraries in that it creates a further artificial separation between research and education, and if there's one thing in the whole educational system that is multi-purposed in nature, it's the library. I fully

realize that they're in desperate straits. I've taken the attitude that I won't bet our programs will relieve one bit of the pressure because of the necessity to resolve this problem as a thing in and for itself. Otherwise, it's on a very unsound basis. In trying to get our Public Health Service Department to support a broad program of construction and support of operation and research in problems of storage and retrieval, I've gotten nothing from them. DeBakey last year wrote a very good article in Medical News. It happened just before our appropriation hearings. I brought it to Hill, told him that I thought that unless he created pressure on the Public Health Service he would never get from them a proposed solution. I said furthermore the Board of Regents of the Library does not have the political sophistication to bring pressure from outside, and I gave him a series of questions that he could ask me and move over to the Public Health Service studying from DeBakey's article as a key. This is the thing that theoretically triggered his interest, and ending up by a request for a report on what they proposed to do about this critical situation. They sent in a ~~Mealy~~ mouthed report containing no real solution to the problem whatsoever.

Now, what do you do? I know Hill will support broad legislation. I've talked to DeBakey, and ~~we~~ are preparing for DeBakey to present to Hill a National Medical Library Assistance Act which will provide construction funds. It will provide training. It will provide a frank subsidy for libraries. It will provide for research on library methodology, storage and retrieval. DeBakey

who is a former regent of the National Library of Medicine will take this package that contains proposed legislation together with all the supporting information as his proposal to Hill. Hill will buy that legislation. DeBakey with our help will develop support for it outside. He will have to check with the department to see whether they will object to it. They can't say no, because these are obvious needs and hopefully this will be enacted into law in the next Congress.

Now, I haven't felt it's been wise to do it this way, but I've tried every way within my normal role as director of the NIH to see that this is done. I think it's so important that if it's not, then I'll use whatever political device I can use externally.

Let me give you another example of precisely the same thing. I objected to a program for the development of primate resources-- this started about five years ago. The Heart Council proposed the establishment of a single national primate center at the cost of about twelve or fifteen million dollars as being something that would satisfy our need for the use of primates in experiments. I convinced the Heart Council that this was unrealistic and convinced Hill it was unrealistic because the outside group who were testifying had sold him on the center. I tried to get this converted into a general animal resource program. I failed miserably, but at the very least what we have now instead of a single center-- well, we will have good primate resources, but established in seven primate centers around the country. This is reasonable,

and this will do the job. I've been trying to get resource money into our budget but with no success. Our outside supporters--I can't put it internally because the Department won't but it. It will cost more money, and our outside supporters won't support it, and yet it's desperately needed. Well, we will try to take the present impetus for antivivisection language as the means of accomplishing our results. I've talked to Hill, and I've had our Division of Facilities and Resources prepare a program for animal resources that relate to the establishment of programs for construction and support of animal resources within research environments. We'll bring the veterinary schools in from the standpoint of the study of the diseases of laboratory animals and serve as a training program for laboratory attendants. We'll set up a series of centers for genetically pure laboratory animals of a fair variety and will provide research funds for the development of the animal resource as such.

Now, this report asked for about six months ago is now complete. I saw it last week. It's been modified. It's in the process of redoing. I'll give this report to Hill next Tuesday and point out to him that the only control measure that would be logical for NIH to exercise is the control over the quality of animal care in these installations that it subsidizes and more particularly that the bill subsidizes, that this is primarily a local responsibility and since animals are used in clinics and hospitals and whatnot across the land, it would be impossible to ride herd on them, but that we've already published standards of

animal care. We can insist through the use of punitive procedure, if necessary, on high quality of animal care in these facilities which we'd build. These, in turn, would be considered as models for communities who wish to have broader legislation encompass them. I'll tell him that this is an approximate program, but one that I've wanted for other purposes for a number of years which he knows and that the only answer to the antivivisectionist pressure is to provide adequate animal care, or provide for the investigator's access to adequate animal resources, and that I feel that we've come to the point where we can no longer continue our defensive posture in relation to the antivivisectionists. They have a real reason, an important point--then, let's satisfy the fundamental reason and remove that at the very least, not that this would totally satisfy them, but at least it would put us in a position of greater invulnerability from the standpoint of attack. This bill now will draw support from the Congress that feel that they are under compulsion to do something. It will draw support from those people who support the medical scientists. The people who feel medical science is getting too much money already can't object to this bill because of its relation to the problems of the antivivisectionist people. I think it's going through.

Now, if I tried to put that through normal mechanisms--it's going to cost money--it would never see the light of day, but I'll see Hill on Tuesday or Wednesday. He will write me a letter saying that he knows from our hearings that we have studied the

problem of animal care. He feels the time has come for more positive action, and has our study come to the point where we're in a position to make recommendations? I then can send him this report formally which he then can propose legislation on, so that we can't wait for outside pressure to create these situations. The running of an operation like this is a mixture of an understanding of the politics of public policy as well as the needs of the medical sciences. Anytime you use a public dollar, it's as a result of a mixture of these two things. However pure or however good the scientific opportunity may be, the judgment as to whether a dollar will be made available here as opposed to here-- this is the mixture of the scientific and political judgment, but we have to exercise that our programs are sound, and we'll take help from wherever we get it, but we cannot wait for others to tell us what needs to be done. This is the value of having a very soundly based scientific group at Bethesda. We're in a better position to interpret the needs of the nation than are most of the people to whom we must turn for support in the acquisition of funds.

As far as construction funds for new facilities is concerned, is the need for new facilities arrived at on the basis of studies here, or does the idea for new facilities with construction funds germinate in the university world?

Oh, no--not at all. The construction funds--this is handled in a straight forward way. We're in a better position to assess

the need than is any university, and I think we're intelligent about it. This is our business. The proposals for revisions of construction are wholly internal as a result of our interpretation of need and possibility and the interplay of the political versus the fiscal decision, and when we move from thirty to fifty million in our research facilities construction, it was not that we thought that was adequate. We recommended a hundred million and this was a sound assessment. We couldn't get it, but now what we will do--and I'm perfectly sure that if we come up with a hundred million again we won't get it. We will try to use the fifty million for general construction purposes. We will try to get the library needs satisfied by a special National Library Assistance Act. We will try to get the animal need for construction satisfied by a research animal assistance act, or some fancy name because the fifty million has to be supplemented, but it's our job, not the university's job, to determine both what the need is and the strategy by which that need can be satisfied. Now, it's equally our job to see to it that the private groups who can support these concepts are sufficiently well informed to do this in an intelligent way. I think that the day of the private citizen, the voluntary agency can in itself define the need and provide the political pressure to satisfy the need is long since gone. The budget is much too high now. This now is a highly professionalized job and requires the type of information that the private individual no longer has. I think where these programs go now will depend in no small measure upon the intelligence of

how my office operates and the extent to which they can inform the outside groups of our appraisal of the need , the opportunity, the mechanics, and see if you have a well informed series of people who can see the reasonableness of a proposition and who will support. On the other hand, I think the generalities of the profession of the American people for better health, that education in such better health can only come from a soundly constructed research program, and this still remains the problem of the voluntary agencies, but how you accomplish it from here on is a highly technical one. I would hate like hell to be in a position of having to convince outside people to convince Congress what we ought to do. I wouldn't be here.

The development over the years then has made this not only a research center, but a center for pooled information collected from whatever source so that you know the area of medical science and its needs throughout the country.

Yes.

So that rather than being specific as between one university and another you're in a better position to add and subtract.

These are the generalities of the situation. There is no getting away from it.

We're almost at the end of this tape. How do you feel? There is another area--well, let me turn this over.

The intramural and extramural programs, the direct operation here and its support programs through the institutes and the general support programs outside--what impact has this new state of the art of support had on the areas of science? Take heart as opposed to cancer, or mental health.

The things that I've talked about are very broad generalities, and a pretty highly crystalized view as to ~~hwa~~ ^{what} has happened here in terms of generalities. I trust that you're going to get some place else, or from me at some other time, some of the general background against which these happenings have taken place over the past fifteen years. It is equally important to give some attention to the generalities of an institution which contains its direct operations and its support programs through a series of categories as opposed to a general support program and the impact this has had on the development of quite different characters for different areas of science, heart versus cancer, these two versus mental health, these three versus arthritis and metabolic disease that reflect, in part, from the leadership of the discrete programs and, in part, from the stage of development of the science that are relevant to that category at any given particular time because the subsequent ^e programs themselves have evolved in relation to these considerations rather than in relation to anything we've talked about today, but I would point out again, that these have only been reasonable and in most cases quite logical, and this is the broad generalization I want to

make.

It is important because quite apart from a broad understanding of the needs of the scientific world as represented by the university, the medical school and the research institute, our ability to interpret the needs of science more generally and our ability to devise techniques of satisfying those needs in large measure stems from the fact that Leadership here in general, scientific leadership, is of a very high order of magnitude in terms of its excellence. I think we have a group of senior scientists on this reservation that I can seek advice from that in the aggregate and in their general excellence are superior to any university group you can point to. This is important because in the absence of this type of setting in which these decisions must be made, I am absolutely certain that tragic mistakes would have been made. Now, we've made mistakes, but I don't think we've made any tragic ones, so this total development of our philosophy-- when I say "our", this is not an editorial we, but the NIH in the aggregate, stems in no small measure from the scientific excellence of the total operation. This is why I think we make more intelligent judgments than ONR, than NSF, than AEC, or than the other federal agencies because this environment is characterized by scientific excellence in the doing as well as in the support, and that is a very important generalization.

You mentioned the last time I was here and we talked briefly that there is another critical moment in the development with

Secretary Fleming.

Yes. Well, that really started--again it goes back to Folsom. Folsom's decision to support us broadly, and I do hope you can get a chance to talk to him sometime because he was so critical a person at this point, but he did not talk with us and decide, "Well, they are nice people. They are good scientists," but he was very frank in his skepticism of our operation when he first became secretary, not that he felt that they were bad, but because he didn't know they were good. Now, he came from Eastman Kodak where he was--I believe he was treasurer of the organization and where in a very general way he had the responsibility for funding research in a modern industrial empire, and the first time I had the pleasure of sitting down and talking science with him, he told me that he thought from his industrial experience that the easiest place to waste money in any industrial enterprise, and he assumed in any government enterprise, was the support of bad science, or the over support of poor science.

You see, the thing that has been important to me was that two years at Squibb. I think I knew industry, and I think I've seen science under all the pressures that come from the need to maintain a productive enterprise. The deficiency that results from science are inadequate; nonetheless, I was fully able to appreciate Folsom's attitude that the appraisal of science in industry is a sharp one, sharper than it ever could be from the type of a support program we have here, so I understood his attitude. He said that he would like to send for a conference with

us a series of people that he placed very ^obr~~i~~ad dependence on within industry, and he'd like us to disc~~u~~ss our problems with them. We had three industrial groups over a period of three or four months. They came in and sat down and for a solid day discussed the mechanics of the operation, the basis of our judgment, the generalities of what we were doing and what ~~w~~^we had accomplished and what we hoped to accomplish. The advice that they gave him was that this was a sound operation, that this was something he could depend upon, something he could support. He didn't attempt to make the interpretive judgment, but these people who came here were ~~h~~ard-headed heads of research and development operations drawn from industry, and he had enough savvy to know that a group of industrialists weren't going to come in and look at a federal operation and say it was good if it was lousy, but he realized that if he was going to take the attitude of fostering a development of medical science to the extent that he was going to push for more resources and satisfy the needs of good science right across the board, and this year when he submitted this thirty percent increase in budget, he said, "This is the first step."

That's the important thing. He did not say, "Give me this, and I'll solve all the ills of the nation."

He realized that he had to have a study in depth of the needs, the capabilities and the potentials of medical science, and about that time the American Heart Association was headed by General Mark Clark. I think he was president, or some such thing

as that, and he sent to President Eisenhower a recommendation that was comparable to the one I was talking to you about earlier, that President Eisenhower set up--this was after President Eisenhower had his coronary--a study to assess the needs of research in heart disease in the nation as a guide to budget. This went from Eisenhower to Folsom and came out here, and I answered for Folsom. This commission was supposed to be a presidential commission, but I said that this is not what is needed. Rather what is needed now is a group of carefully selected external advisers to you, not to the president, who will look upon generalities of the medical sciences and chart some series of goals that can be adhered to by the administration in the development of science during the next ten years and look at it broadly in such a fashion that this will encompass the type of thing that Clark wants, but will go far beyond. We prepared an answer to Eisenhower for Folsom where Folsom proposed this, and Eisenhower told him to go ahead.

Well, this is the genesis of the Bane-Jones Committee which you may have run into, and we did not select, although we advised on some of the members of that group. If you look back, it was the president of American Cyanamide, the man in charge of research and development at DuPont, people of this general sort. These people studied our programs for about nine months and made the report of record. This is the first report that looked forward by 1970, to a billion dollar enterprise. You'll have to remember that our budget at that time was ninety-seven million, so this

was shocking, but then Folsom developed a stream of acts in minor form. He was frustrated with the Eisenhower Administration, and in no small measure because of our programs, because the thirty percent increase he got for it that first year was the only increase he could ever get. He told me repeatedly how he had fought with Ike for an increase in subsequent years, but was turned back every time. He retired within a month or two after the Bane-Jones Report was completed. He was delighted at getting it because this generally substantiated the action he had taken, but he said, "This is for my successor, not for me. I will call this to his attention as the first order of his business."

When Fleming came in, the pressing thing was to develop a position that was based on the Bane-Jones Report. He wasn't technically oriented, although he was academically oriented, and he was a great man for polls in the Eisenhower Administration. They never did anything with the polls, but they always wanted them anyway, and so he took the Bane-Jones Report, and this was very politically hit because Congress kept giving us increases, even though Ike didn't ask for them. He wanted to put reserves in and not let us use all the money, but he was afraid to. It was not politically expedient. There was no fear about it, but the Secretary was faced with pressure from the Eisenhower Administration to hold back and here he had a report that said this is a flourishing empire, and it should go, so he said, "I must find out about this personally," and he arranged with me to sit down and discuss our problem and our program seriously.

This is one of the first things he did after he took over, so we arranged for that initial fall to give him the full treatment, a full explanation on 1) what was our reaction to the Banes-Jones generalities, and 2) what did we propose in terms of a program. We prepared for him a series of written documents. He took it very seriously, went through it program by program, and at that time having evolved a philosophy--well, I might say that the Bane-Jones Report saw a lot of outside witnesses. They spent a great deal of time with us too where we argued through with them the reasonableness of our current activity and its projection into the future. The report reflected generally our view because by the time the report was put to bed, there were no differences of opinion between ourselves and the committee. Having played such an important role in conditioning what was in the report, we obviously were in favor of it, but the report dealt in generalities rather than in mechanisms, and our next step was to reduce that to a program. Viewing the deficiencies of the program then, it was perfectly obvious that research facilities and construction should be greatly expanded, that there should be a more purposeful training program with the end in sight, the development of careers, that we were coming to the end of our sitting wherein we could support such a complex establishment of research through the limited use of projects, and felt we had to expand into the broad multi-purpose type program rather than project, although legally it's still a project, and we had to face up to the need for stabilizing funds for institutions as institutions. These are the

things we argued through with Fleming. This really marked an approach to a need to satisfy the basic resources of institutions as institutions, and then expand the project ^N grants as the need occurred. But in relation to the institution resources in terms of general funds, resources in terms of facilities, resources in terms of the expansion of permanent faculty. You ought to get those documents, if they're still around. I've probably--we prepared so dam much stuff that I lose track of it. I'm not a very good archivist.

Those Mr. Murtaugh was able to find--the survey of twenty medical schools and others.

That came toward the end of the study. Those are the basis for that. Our present attitude now, an extension of it is now to introduce a broader sense of administrative responsibility in the institutions for the funds that are expended therein, but our attention to institutions as institutions really stems from the Bane-Jones projections. As I say, we participated in that--as a matter of fact we sold it to the committee. The consequence of that are a very broad base for science and the need in that very broad base to find devices other than simple project to satisfy the need, and that--let's see, that would have been 1959, or 1960. I can't recall just when. Do you remember?

Wasn't it the summer of 1959?

I guess that was it.

It's certainly an expanded view over the project system--to see an institution whole.

But again I would emphasize that that program that is coming into being now and is reaching full flower now--will with the animal resources; will with the library--has been a continuing theme that we've hammered at since 1959, and that again is a thing to emphasize--that unless the official agency is willing to go all out, this government moves very slowly, and you rarely accomplish a broad objective within a single year, or you rarely accomplish it with a single piece of legislation. It requires, and I would guess that it is going to require another two, or three years before we're where we should be, and, as I say, that's par for the course. We propose a program in the summer of 1959. It's now the summer of 1963, and the final two or three elements hopefully will be in operation maybe in another two years.

Now, if you want to get into the politics of this. Again they're internal as well as external. The decision of the Surgeon General to assign medical education and medical school construction to the Bureau of Community Services--it appeared that we had too much power and too much impact. He will not admit that, but basically the Public Health Service is restless and unhappy about the position that NIH has in the general community as compared to elsewhere and to put medical education on top of medical research as our responsibility for long term development would be to further depress the remainder of the service so they're trying to pick us apart. This is good bureaucratic maneuvering.

Success in an endeavor has bred those who wish to now sit in on further refinements.

I don't really care who handled^S it. I suppose medical education has to be by formula basis. I think it's ridiculous that the type of people we have^E in the present Bureau of State Services will do it intelligently, but that's their decision. I have too much to worry about.

I hadn't supposed that what had been happening here all along hasn't had its effect on medical education.

Oh, it's had a profound effect, but yousee, there should be a frank appraisal of the need and this need should be satisfied in a very direct manner. A good deal of our present difficulty comes from the fact that within the complex mechanisms of the medical school, you cannot wholly separate construction from research. The same people^P do it, and where research leaves off and education takes up is always difficult. Now, you can differentiate from that the extremes, a lecturer, or a series of undergraduate laboratories, or a straight research project. There's a broad area of overlap, but the abilities of the schools to expand their facilities has been wholly as a result of our ability to support research on whatever scale seems desirable, supply the resources within which research is performed and to provide a stability for the environment that otherwise would be quite impossible. So modern medical education in this country is

what it is because of our programs. There's just no doubt about it, but it needs more than that.

What of the area of outside administration of research? A
percentage has brought on the need for some form of busy work,
bookkeeping, whatever, may really piece 1
gained past insuring 2

There doesn't necessarily have to be any involvement there because--and there is not in a well run university. How the university keeps its books, keeps track of its funds in no way interferes with the individual who spends those funds. We have had to impose some restrictions on the expenditure of funds during the past year. Although it's not commonly appreciated, the restrictions we have imposed now are precisely those that obtained in 1959, except that now in addition one must report the proportion of effort. That's the only new thing. I never heard such anguished cries, but having been faced with a series of situations wherein in the general accounting survey of sixteen schools, there was shown to be very little relationship between the salary paid from a grant and the proportion of a man's time spent in purposes of the grant. It's basic. This was a diversion of funds for purposes other than which they were given to the schools and in substantial amounts. The Fountain Committee was very proper in pointing out that the controls that we required were inadequate to serve as a guide to the schools for the expenditure of that

fund, so what we had to do is to excellerate what we were already doing; namely, the development of a set of regulations, the development of a comprehensive series of guide lines to make that more restrictive than we otherwise would have. Now, we know the things that have to be accounted for. We know the things that can be determined by the investigators, and we know the things that must be determined by us.

We are now developing information through two quite different studies to find ways and means of decentralizing decision making in those areas of the school. There are two general types of decisions that the school will have to make, that some schools can make now but they can make if they set up the proper apparatus. One is a straight forward decision whether something is legal, or is not legal, whether a cost is a direct cost, or an indirect cost, things of that sort, and to help them make that we have one study group in Boston trying to find out the worthwhileness of setting up a peripheral unit in a large metropolitan area as a point of consultation for the business end of it. The secind general study relates not to decisions that determine whether an expenditure is legal or illegal, but decisions that have relevance to the substance of science--that is, whether a thing is scientifically advisable, or scientifically unadvisable. Now, this relates to the purchase of large items of equipment; to change the funds in a grant from one category, say, personal services to equipment, or viceversa, things which now above a certain level

we must determine. This is looking forward to the establishment of a scientific advisory group in the administration of an institution that will make these judgments for us, but who will make them in a visible, well documented way so that if the question arises, there will be a record that will show that the decision to divert funds for this purpose as opposed to a grant purpose was on the basis of this information which indicated that this was the desirable scientific thing to do. When these things have been done, they will have been decentralized back to the university, but under controls that are regulated and are highly visible, but again, these will not interfere with the freedom of the scientist, but the decision making will be by his institution rather than by him as in individual contained within an institution, and we feel that what we're trying to establish now is roughly the equivalent of a public ethic of expenditure of public funds for scientific purposes in a fashion where the characteristics of this ethic are defensible.

You see, there has never been a time when such large amounts of public funds have been expended under circumstances where accounting is so difficult. Most expenditures of public funds are guided by rather rigid guide lines where you expend funds, you obtain something, and you can relate the items. When you expend funds for these purposes you obtain something which is not priceable, if you will, so that you require quite a different system--not a different system of accounting, but a different system of evaluation. What we're attempting to do in our work with

universities now is to make quite clear the characteristics of the ethic of giving on our part, the ethic of receiving and performing on the part ^o of the university, so that there can be greater confidence in the expenditure of these very large sums. Right now the Congress is very uneasy. They spent last year some twelve and a half billion on research and development. They are not technical people. They're taking the word of both internal and external scientific advisers. They have no real ability to know--do they get twelve and a half billion dollars worth of result, and this is an important area when expenditures are very small, but it becomes more important now.

Decentralization seems like borrowing the study section, council, advisory council devices and planting them in the university world.

Well, the granting decision probably will still be central in a highly competitive way. I don't see any other way, but after a grant is made, the programs under that grant, you see, involve broad variations in strategy. It involves variation in expenditure within a given dollar ceiling--these are the things which should not be the concern of the study section, or the council, but by other devices.

The university, in turn, could establish its own independent group comparable in size to handle the detail of performance so far as finances are concerned.

That's right.

Or the shift within meaning or some limits from one line in a

They should establish a group that will stand for them as the objective group of scientific accountability and responsibility-- these are the scientific leaders of this institution that in general characterize the scientific integrity of the institution, and unfortunately, I think, this has to be a visible group. It's deliberations don't have to be public, but they have to be visible on inquiry. This is not something that can be done in camera. You see, in some institutions our program constitutes more than fifty percent of the total income^H of the institution. Now, for the other funds, you have boards of trustees--you really have accountability there.

You're so right.

So that there's no reason when funds are such a large part of the total funds of institutions why they shouldn't have equal accountability for one half as for the other. The funds intermix, you see, so I don't think that--well, at least I don't think we'll have any difficulty. I think the administration in schools is going to have to settle some questions they'd rather not. They'd rather have us settle them for them, but this is not in their long term, best interests.

And besides I don't see how sitting here you could devise a scheme of control that would be applicable in every case. The grants are

rather unique.

The facts of the matter are--well, I was talking to scientists at Atlantic City this spring. I was ⁱinvited to discuss these things with them. A discussion followed a brief presentation, and one of the young scientists said, "We would like you to retain that decision making because your decisions are more sensible than our own faculty would make."

This is the general comment we hear. My rejoinder was that this was not entirely true, that we are more liberal in our decisions because we are less certain of the elements that go into the decision and consequently an investigator is also given the broad benefit of the doubt. Decisions locally give the appearance of being much tougher because the people locally have all the facts on which to base a decision and this in practice is the way it works. When we decentralize the decision making to the institution and when these groups that will assess the needs to move funds around, or the needs to take a trip, or an international trip to visit other laboratories, when these decisions are made locally, they'll be made much more realistically and in general they'll be much tougher than we'd be able to make them. The individual investigators know that. It's very difficult for us to say, "No", because we don't have the fact^s to say it. It's much easier for an institution to say it, because they have the facts on which to base such a decision.

It's comparable in some ways to what I learned several days ago

obtains in the international field--that is, a better basis for making a determination as to whether something should wash, or shouldn't wash is related to the accumulation of facts on the ground by people peculiarly equipped in the area to make available to a decision making body a more realistic assessment of what the situation in fact is.

Yes.

So that conclusions reached would be more valid than they would be otherwise.

Or at least they're more apt to be valid.

Fixing the locus of responsibility once a determination has been made to lodge something somewhere on the local organization has its difficulties--clash of temperament, a not inconsiderable part of the history of any collectivity.

Oh sure, but the point is that they can do a better job than we can.

Yes.

Then too, you see, institutions are fairly comparable. Take the University of Chicago and their expenditures--they are traveling a large number of people who are international leaders. Harvard with a comparable set up is traveling practically none. This raised questions in our mind whether we should not discuss with the institution more of the guide lines that result in this

circumstance. This is a series of controls that will evolve with time, and I think it's really true, that we here are scientists first and federal administrators second, and I think that on my top staff I have enough quite superior scientists too--well, we're not prone to make deficiency decisions, but again coming back to our area--this is the advantage of running these really high class programs out of a scientific environment rather than an office type operation.

Why don't we knock off--I'm running down and so are you.