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Some examples of the kinds of errors to be found in the transcripts are provided below.

Filename	PDF Version Page	Error
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Portraits mailed + CV?

Dr. Pettinger: Interview

I'm a professor of pharmacology and internal medicine and director of the division of clinical pharmacology, so let me start off by telling you a little bit about what clinical pharmacology is. Clinical pharmacology is a discipline in which we attempt to develop, as precise on a scientific basis for decison-making processes concerning drugs, as occurs in diagnosis, evaluation of the state of the disease proeess, and the molecular mechanism of disease processes. Now internal medicine, particularly here at Southwestern Medical School, is a very, very strong and effective teaching and investigational discipline in disease processes in man. But there tends to be relatively little emphasis on the decision-making process concerning drug utilization, particularly in the educational realm. And the clinical pharmacology division is attempting to build a sufficient base to effectively carry out this role. That's from the viewpoint of the institution. The second role of the clinical pharmacology divi on is to carry new breakthrough-type medications from animal investigations into humans, oftentimes for the first time. And we do this, in fact we're starting a completely new drug entity within the next six to eight weeks in patients. It combines the most effective and least side effects of any of the anti-hypertensive drugs at this point in time. It combines several different drug entities into one, and we'll be evaluating this in man within another six to eight weeks. Another role ~~from the pharmacologic viewpoint~~ of the clinich pharmacologist is ~~oftentimes~~ to evaluate ~~in much~~ more detail what some of the medications that have been around for a while, ~~exactly what they~~ do. In other words, how do they most effectively produce their beneficial effects, or, alternatively, why do some of the medications produce less toxic effects than others. And this is the type of study we have going on now in the clinical research center. In fact we just admitted a patient, the first patient for a particular type of study, and I'm going to give ;you a little bit of a background and expand on that.

Hypertension, of course, is high blood pressure. And it's a disease of regulatory mechanisms.In other words, mechanisms that regulate blood pressure. Now, blood pressure, of course, is simply the result of a pumping action of the heart into the aorta, and then the flow of the blood out of the aorta controlled by resistors, or resistance portions of the circuit, the arterioles, small blood vessels. They, by a minor change in their tone, or their cross-sectional diameter they can cause tremendous changes in blood pressure. And both the pumping action of the heart, and peripheral resistance is controlled by a number of neuro-endocrine regulatory mechanisms. And during the last eight years our laboratory has been shooting for the capacity to simultaneiously assess each of the neural-endocrine regualatory mechanisms, and simultaneously the hemanonemic effects of these regulatory mechanisms in hypertensive patients. And we just achieved that goal, that's kind of an historic landmark, heh, heh, and now we're going into patient studies in which we're looking simul= taneously at the disease process and the interventions of old and new types of anti-hypertensive drugs.

? What's the history of this program you've just described? ?

It's about eight years. I went back to a basic laboratory ago to develop the chemistry of proteins and peptides it was required to do, in turn develop radio-immuno-assays, radio-label peptides, and develop these very spphisticated radio-immuno-assay-type techniques, and enzymatic-chemical assays, so that we can measure the tiniest quantities of materials circulating in the blood, which ultimately regulate the cardiovascular system. So it's an eight year commitment, but I'm very pleased, we're there, after a few million dollars, and, heh, heh,heh.....

?So after eight years, what was the arrival like, did you just walk into the lab one day, and.....

No, it's not like that, you're continuously evolving. The important thing

is to have a very definitive ~~xxxxxxxxxx~~, long-range goal ~~of sufficient~~ importante and sufficiently challenging that you don't reach it to early. It's terribly important, I think, for career investigators to have that ~~terribly important~~ long-range goal, ~~xx~~ and that it is of sufficient importante and sufficiently challenging, so that even if you get a fraction of the distance in your lifetime, you've achieved an incredible amount. I mean, you may actually achieve an incredible amount, so it isn't the sort of thing that one day you arrive there. But this is kind of a fascinating day, in that we've admitted our first ~~x~~patient, which will be comprehensively studied for the first time. It's the only place in the world where ~~xxxx~~ all these can be assessed in one place.

?Were there similar landmarks before you reached this point? Or did you anticipate this day eight years ago?

Well, kind of looking forward to it, not holding your breath till you get ~~xxxxx~~ there, or anything like that. So this just happens to be a day that we've admitted our first patient, in which we can do all of the things effectively, and without discomfort to the patient.

?Can you paraphrase in fairly simple terms your goal eight years ago?

Oh the goal is not dissimilar to the goal of a number of investigators in the hypertension area, and that is that they would really like to be able to either establish the mechanism of the disease process, or try to make a definitive and major breakthrough in terms of control and regulation of the blood pressure, so that people don't develop strokes or heart attacks or renal disease, or aortic disease, but it's primarily renal disease, heart disease and stroke. If you recall, these are the big killers and they're three or four times as common as cancer, and they're siphoning off. You know the complications of these problems--and these are all complications of hypertension--these problems are siphoning off a major part of our health care dollar in the United States. If you look over in

the dialysis center, each of those patients on chronic hemodialysis is costing you and me at least $25 G a year, through our tax dollar, and there are tens of thousands of these patients, and so there's virtually billions of dollars, and there's an unlimited capacity for just renal disease to siphon off billions of dollars. There's no limit to that. And, just from the renal disasex alone, if we can prevent just fifty percent of those renal problems you can imagine, not only the dollars andcents, but the tremendous, you know, human tragedy that's involved in chronic hemodialysis. By and large, there's a small percentage of those patients who have fulfilling ways of life--they're married to that machine, but then you go up to the coronary care unit, and you see all the heart attacks, and that tremendously expensive ball game up there, it's just terrible. And then of course you have the strokes, and the nursing homes, and all this sort of thing. There are strokes, and there are heart attacks, and there are renal diseases which are not due to hypertension, but alternatively, many of them are. And even though we've been able to normalize blood pressure, in a lot of our hypertensive patients, they've, that has been achieved at the cost of side effects, and the nuisance of taking of pills, etc. But the side effects of taking of the medication have been pretty unpleasant and oftentimes severe, from the drugs and the patients readily recognize that these side effects are from the medications. And they will often just stop taking their drugs, because they produce side effects. And without the drugs, you see, when they feel well, you know they feel very comfortable. So place yourself in that fashion, suppose you are taking medication, and you can't effectively carry out your work and (here interrupted by interrogator) but not be able to think, you know, and at least half of our anti-hypertensive drugs interfere with the thinking processes of people. Others of them interfere with their work capacity, you know, their physical work capacity. But about three years ago, we became tremendously impressed by a combination of hypertensive drugs sulfiazodylators (???) in other words those that open up the blood vessels out here, the resistance

vessels, and the ~~beg~~ Beta-blocking drugs. It's a whole new ball game in treating hypertensive subjects. It's a new ball game in that we can control their blood pressure, more within the normal range. You know, previously we were happy if we brought a patients diastolic blood pressure down to 90 mm of mercury, or 95 with some of 'em, or even 100, but with the new combination of drugs we can reduce them down into the 80 range, in other words right into the normatensive range. And, according to Framingham's statistics, this has an additional benefit or gain to the patient in terms of preventing these things. Okay, not only in terms of the viewpoint of efficacy is this drug combination so fantastic,but patients by and large have no side effects--they feel well! They can live normal lives, it doesn't interfere with sexual function, even some of the surgeons, I have them on these medications and have had relatively severe hypertension and were able to go into the operating ~~g~~ room for as much as 30 to 60 minutes and then they'd get lightheaded and weak from the medications, and with these medications that they're now taking, these fazodialatorbetablockers (?), they can function ten or twelve hours if they need be. And their personal life is normal, it's just a whole different world for them.

?Let's go on to the clinical investigation...

Where does the clinical research center fit into all this...

?What fascinates me is the scale, the relationship between the laboratory work and the patient...

You want me to take the laboratory work first? No, let's go on to the CRC first and I'll tell you why--it blends into the patient thing we were talking about more. Because in the last three years we have this tremendous advance with the combination of the phaso-dialators and beta-blockers, we feel that if we understood more precisely which of the hemanonemic I mean which of the neuro-endocrine regulatory mechanisms and hemanonemic mechanisms were being affected, by the individual drug--say,the

phaso-dialating drug on the one hand the beta-blocker on the other hand, and then the two in combination, we feel that if we understood rather preciselyjust exactly how much effect it's having on which of the regulatory mechanisms that just bey being a hell of a lot smarter about mechanisms that we could assess totally new compounds in a much more intelligent light, in terms of where to go--where do we go from here.

?Can you characterize how that's been done, how the effect of regulators like that has been judged?

It's been terrible. In the past we've only measured the blood pressure--in other words we'd get a new entity that in a rat or a dog had lowered blood pressure, and then we'd put it into mand and see if it lowered blood pressure, and then we would--after studying a ten or a hundred or a thousand or a ten thousand patients we'd find that fifteen percent of them might have this side effect, ~~ex~~ ten per cent have this side effect, etc, etc.

?The whole time your only guage was the...

The blood pressure--right. There are several different potential outcomes of tnese regualtors that we're talking about. One is that in ten patients, maybe twelve or fourteen hypertensive patients studied with very precise quantification of each of the regulators that we've talked about, we can predict what's going to happen in the first ten thousand patients in terms of side effects, tolerance, acceptability, etc., for these drugs--we don't have to do ten thousand patients to make a rational decision of what should happen with this drug. That's one of my goals over the next two to three years, and I think that we're going to achieve that. We're going to be able to tell--with ten patients--just what the FDA, what decision they should be making about a given drug. Okay? So one is a decrease in the incredible cost to the federal government in their NIH funding programs to federal investigators, to the pharmaceutical industry, and also to the academic community, of the tremendous cost now to study ten thousand patients to compare one drug with another. So you must differentiate this--

we don't have the evidence to claim that we can do that, but that's one of our goals. Okay? That's a goal. Another goal associated with this--it's a fascimating one--you know, between forty-five and fifty per cent of airline pilots are grounded now by the time they're fifty-four years old for medical reasons. And the most frequent cause is high blood pressure. And because we can regualate blood pressure in normal levels, and obviously prevent the complications of hypertension, and because our patients are asymptomatic and highly functional, we have a suspicion that airline pilots may be able to continue to fly. But before we can come to that conclusion, we have to be able to demonstrate the reserve capacity of these regualatory mechanisms, in the patients treated with the combination and under circumstances in which we simulate the stresses that a pilot is likly to undergo under emergency conditions. So we reproduce those circumstances in our patients in the control period, during the administration of one of these entities alone, and with the other entity alone, and in combination. You know, we induce a lower body negative pressure, which is like putting a G-force, like people taking off, in fact NASA---oh, I'd better stay out of that here. Anyway, the way the CRC fits into all this here is in numerous contexts. One is that they have a very nice section of the hospital there, so that it's as comfortable and pleasant for our patients to be there. You know, it's not very pleasant for patients to come into the hospital, to be excluded from their society for a two or three week period. And the CRC provides this environment. The second thing is, a significant part of the blood pressure regulation has to do with regulation of blood volume, or cardiovascular volume, and that's a function of the salt and water balance of the patient. And so we can provide a precise salt intake. We also regulate the temperature. See, salt and water balance is affected by warm environmental temperature, perspiration, etc. Okay? So we can't have our patients, during the control

and treatment phases of these studies undergoing sizable changes in salt and water balance. Okay? And another thing, even though peculiar, is it is extremely difficult to get 24-hour urine collections in any circumstances but a research center or unit. It's amazing how natural it is to run over to the batheroom and urinate. & But God dern, and we need to monitor every day to make sure we have a x constanty in the salt balance. And if there's changes in water balance we'll be able to detect that in the volume. And by collecting the urine and the blood at different occasions, we can precisely monitor the changes in kidney function, you know, by calculating clearance values for different constituents in the blood. Another thing is Charlie Pack is doing a marvelous job of training and staffing that CRC. I just can't give him too much credit--he really has done a superb job. And he's very supportive of sound clinical investigations on the CRC, so it makes it actually a pleasure to do studies up there. It's a very, very important aspect of it.

Well, the other thing is cost. See, if we had to pick up the cost for the patient hospitalization at Parkland--a number that you should find out, I dunno, it's a $118, $124, $134 a day--if we had to fit that into our grants mechanisms, the grant programs would be so extremely costly, and of course you'd have the inadequacies of an open, regular ward in a hospital. So that bottom line item is extremely important, and by having a center or a facility in which multiple groups interplay, the cost is considerably lower. And that's where Charlie Pack comes in, so he's really doing us a good job of administering it.

?Is there competition for the space there?

Well, it's a healthy competition--I think there's a good, healthy competition for space on the wards there. But one of the unique things about SW Med school is that the competence of so many good clinical investigators results in a capacity for us to make decisions, value judgments among ourselves through the --I want to say board of directors, but that's not

the right term, anyway there's a board of directors of the CRC, which establishes the priorities in the investigational programs, and I think that it's worked out extremely equitably among the investigators. In other medical schools where you don't have such competent people, you have all sorts of political defense mechanisms, but those are at a minimum, at least I haven't felt there being any problem here at all. It's a very unique medical school in that regard.

?It seems to me that thaat group or board would be one of the chief intersections of all the...

Investigators? Yes, I've been on the board since the first of the year, and I think it's been a very, very worthwhile experience.

?Several people have spoken to me about developments in one line of research which have not been applicable to their interests but which is useful to someone else...

Well, Charlie Pack has been a genius in that. He has interrelated with a number of different disciplines, in fact I had lunch today with an orthodpedia surgeon who's working with Charlie on problems of calcium balance in osteo products who fracture their hips, and I think that Charlie's really kindled a tremendous interest in that. So much so in fact that it's started working against itself. He'd much prefer to maintain a balance between areas of investigational work that he's involved in and others to make it function instead of a monolithic structure with Charlie Pack and calcium. He's really aggressively supported other people like our own group and they're working in there. We have two new faculty members who are coming in in March who will double or triple our capacity to contribute to the CRC, and we'll be doing an awfully lot of work up there.

?Now have you had patients up there before?

Yes, we've just finished a study of five patients. We're oriented more to

mechanisms, we're not just drug testers. You know, we'll go in there with a very specific hypothesis, and we use drugs as tools and we really get at the heart of the matter, ~~xxxxxxxxxx~~ in terms of the dynamic mechanisms that are going on, and also the effects of the drugs.

?How do you recruit your patients?

Well that's very interesting. The patient who just came in today, I first met him after I'd given two talks down at the AMA meeting here in Dallas last May or June,and he was in the audience, he works with one of the ~~xxxxxx~~ pharmaceutical industries, and he came up to me after my talk and asked if he could participate in our investigationalprograms, because he had high blood pressure. But the airline pilots association, which is a union, is very, very interested in this problem, and so they're going to be sending some of their pilots in for an initial evaluation to see if they're applicable for the investigational program. Some private physicians who are aware of our investigational programs select out patients from their own private practices, which I tend to encourage. I think that's a very meaningful interface between the academic community and the medical community here and in fact, about a third of our patients who are on investigational programs come from private physicians. And they're oftentimes the problem cases that they have, the patients that they just can't handle, and they call up up and we help them when we can. It's a service cost to us, but again, I think it's one of the functions of the medical school here in the community, and I must admit I get some personal gratification out of taking care of those things that are terribly difficult but relatively easy for us to do. I might mention that the interface between the basic science and the basic pharmacologist and clinical pharmacologist has been an extremely healthy one for us. Already four years ago we had worked up this interaction--the phasio-dialator/beta-blocker interaction in animals--before we went into man. Before we took the hypotheses into

man. And then we did the initial phase--you know, you do these, you say Gee, doesn't it feel great to be at the point of completeion of the thing on any one day--well, that just isn't the way it is. We had completed the animal studies about three years ago, and then we went into human studies, and it was a very initial component of the hypothesis, just one single component that we'd tested in seven patients. And we published that in the New England Journal of June of 1975, that was a very important step. And it's interesting, out of those studies we made an observation that we just didn't anticipate at all, and it was a very key one in terms of the regulatory mechanism in the release of the hypertensive enzyme in the kidney. One of my people was just moving to get his Ph.D. degree, and this was just an exciting finding that came out of the patient studies, and we went back then and we could much more thoroughly investigate it in animals, so he did that for his Ph. D. thesis. So it goes both ways, it isn't just the profit from the animal studies into man. Human studies often tell us things that we've got to go back in and really look at in great detail in animals. It was a very exciting thing to us.

?Tell me something about publishing and the role of publishing in your work.

That's a very interesting and challenging area. There aretwo things that require the greatest intellectual discipline. One is the experimental design for the patient studies. Many think that you draw up a protocol to carry out a complex clinical investigation by just sitting down and writing up a series of steps. It isn't that way at all. We just completed one protocol for this one patient, and I bet I spent forty hours on that protocol of my own time, and one of my colleagues spent additional time, the cardiology division has put in time--now that's the mechanics of it, obviously there's a theoretical background behind that, etc., that's a very complicated business. You know when you've got half a dozen

different things going on simultaneously, you have to know the chronology

you know, the dissipation of that particular intervention, and each of the neuro-endocrine regulatory mechanisms, their half-lives, etc., before you can establish a base-line, from which to induce the next intervention. And it's just incredibly complex. And we're not even going to be able to get the final protocol completed until we do a couple of more patients under the circumstances, then we'll draw up the final protocol. Now that is one of the great difficulties that we have at the moment, we're on the interface between legality and illegality, because we can submit a protocol to the human investigation committee, and here we're using an investigational drug as a tool. So I have to file an investigational new drug application with the FDA, and I have to send the protocol up there/ And you're supposed to wait thirty days before you start studies in case they want to question this and make a delay. Well, suppose that they establish a six-month delay? And yet I've got a program going here that's probably going to cost me a $150,000 to run, and we'd like to be halfway through it within six months. Well, I've got faculty personnel who's budgeted into this, and technical--and some guy up there at the FDA could pull the carpet out from the whole thing and say it would be illegal for you to continue with your studies. Now with such a sophisticated and complicated protocol we have here, we have to go back here--let's suppose we do two studies as we have it set up there, and we find that the time interval between two of the interventions is off a bit; I should legally re-write the protocol, change that time schedule, submit it through the human investigation committee, get it approved, back again and submit it to the FDA, and wait thrity days again before we go on to the next patient. So progress in clinical investigation is extremely difficult. Now there's another type of protocol--and we're faced with this in the pharmaceutical industry from time to time--they'll bring a protocol down, say

well, the ph. industry will often bring protocols down, and it's all cut and dried, and you just kind of plug the patients in xxd for the numbers to come out, and they'll pay you so much to do it. I suppose someday we'll do some of those, but we haven't yet, because the investigational part of a new drug has already been established by that time, and from an academic and scientific viewpoint, it's a pretty dry run. You're not gonna make any new discoveries by that type of activity. Occasionally, through, you can piggyback a terribly important hypothesis onto that type of investigation, and unless we can do something like that, we just don'tx utilize out precious resources to run through a pharmaceutical industry protocol of that type. No, the pharmaceutical industry dowsn't like us, because we call ourselves clinical pharmacologists. I should put it this way, some people in the pharmaceutical industry don't like that, you know, those people whose salaries are dependent on whether or not they can get their protocols churning. Now they're usually not the important decision-making processes in the pharmaceutical industry, you know, so certain people are alienated because we don't spend our resources in xx "me too" stuff.

?That's also part of that ten thousand sort of evaluation.

That's right, that's right. We don't think that we're going to contribute to progress by just fitting into a lock and key that gives somebody the numbers from three thousand to three thousand fifty.

? I suppose in designing your protocols there's always the difficulty of realizing in advance what the protocol will give you the information you're seeking...

Oh yes, once you can completely design the protocol, that means that you've already got the answers. You betcha, and that's a terribly important concept. The fun is now during the next three to four months--you know, once we develop the protocol, once we get our impressions, and we're fairly sure where we're going, then we can xxxx develop a protocol. There's this

sort of basic question until you get to that point.

?Once you know where to look, then you already know the answer.

That's right, it's kind of like drilling for oil, once you get that geyser from one of those wells, you can predict the cost of the next well, etc. But it's the exploration process, the decision-making process, the trade-off between cost and the potential for bringing something in, the hardness of rock you have to go through, the softness of the soil, this sort of thing. The challenge is up to that point in time when the oil starts running, and I think the same thing here. I have over the past twenty years developed the equivalency in biochemistry and pharmacology and in physiology--and ;I had my boards in internal medicine. And I can bring the different disciplines to bear on this tremendously complex problem.

(T A P E C H A N G E)

I think we're on the threshold now of where we're gonna be in five years. You want to talk a little bit about publications now and where they fit in? Well, the second real intellectual challenge--it just takes every neurone that I have--to devlop new scientific publications, you know, new discoveries and how you most effectively describe them, write them up. I think that most of us will say the same thing, that is the most challenging part of our work. We all like to go and discover the things in the laboratory or in our patient studies, you know, it's fun and you get the data together, but the tough part is then to put this together in its most meaningful fashion and interpret correctly the data but don't oversell it. It's a creative endeavor, like putting together a painting. I'm sure outstanding artists really sweat blood over doing an outstanding piece of work, and the same is true of the development of a new discovery, in describing it, etc. We're very fortunate here, this year with just my small group, we have about a dozen publications, last year we had ten, and it looks like we're going to continue at this high productivity.

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Not only do we have the dozen publications, but during this last year we've published some entirely new discoveries, a discovery of a receptor mechanism that we have suggested may be a root development of the future new generations of anti-hypertensive drugs. It's a receptor in which drugs with a high degree of specificity for can ~~xxxixxxx~~ activate this receptor mechanism within the kidney and possibly control high blood pressure.

?It seems that it would be relatively easy, once you had carried out a course of research in pursuit of an hypothesis and had completed it, ~~x~~to then simply almost retrospectively document what you had done.

Well, I think in certain circumstances it becomes easy if you're using identical methods and just filling in a series of, or pieces of information in series, so that you can use very similar bibliographies, similar method--ologies, etc. And in some areas of investigation, that actually occurs, particularly descriptive clinical programs. But we don't work in that simplistic context. We are each time testing new hypotheses which require a whole new process of creation of most of our manuscripts.

?Can you really look back over the experiement and reconstruct it step by step, or is that a misleading way of putting it?

In other words, to what extent was it predictable from the time you initiated it to the completion? It depends on what areas you're looking at.

When we discovered that new receptor mechanism, let's just go back and consider individual publications. Now this, here's one here in which we've confirmed ~~that~~ this receptor mechanism by a very sophisticated technology in dogs. We had chronic catheters into the renal artery, one-kidney artery, and the other kidney we took out, so whenever we ran something in there it profused the whole kidney mass, and we had other catheters in the carotid artery and one in the jugular vein, and that was a very clear=cut one and it didn't take me an awful long time to write it, either. Here's one in patients that went pretty well too, because it was simply descriptive. Here's one that was tough, you'll laugh at this. This is a study that I did fourteen years ago at Yale. It's a study of how a new drug at that time

(inscrutable name), how it worked. And we had the receptors that we thought it worked on in the frog skin, you know, it's analagous to the receptors in man whereby it lowers blood pressure. Well, we got the opposite result ~~kkak~~ than we predicted, and I couldn't interpret it, so I didn't publish it. But our initial hypothesis was correct--that receptor was relevant to how ___ lowered blood pressure, but at that time we were interpreting an effect out in the periphery, vessels out in the periphery. But in fact, the doggone drug works in the central nervous system, and the frog skin was a perfect receptor. In fact, it's in press now in one of the sophisticated pharmacology journals, Journal of Pharmacology and Therapeutics. It's a beautiful demonstration of these receptors in the central nervous ssystemx; thrirteen years ago it didn't make any sense, and so I didn't publish it, but over the last couple of years it's become increasingly apparent that we're thinking in the wrong context. They're in the central nervous system, and anyway...it's very rewarding. Here's a study here (reads obscure title), this is a study in which we did cardiac catherization studies on some of our patients. This is a drug that we first introduced into very, very, severely hypertensive subjects back in 1971 here at SW Med School and it was fantastic. We were able to control the malignant hypertension in these patients and prevent their progression onto, in fact the title of our publication was Menoxydil: an alternative to Nephrectomy,for refractory hypertension--You didn't have to take the kidneys out anymore!That was a terribly important publication. And there were, I think, seven or thrteen centers in the USA that were taking the kidneys out of patients to prevent their strokes and heart attacks, then they put them on chronic hemodialysis. So this was a very expedient paper, it really had a tremendous impact.en-- It came at the right time.

?What's the obligation to publish?

Did you ever see any farmers who raised their wheat, and let it blow over and die? Did you ever see farmers who didn't go out and harvest it?

They go out there and they harvest it, and they take it to market, and they get their money out of it. That's the reason why you publish.

?You were talking about the importance of not overselling.....

Overinterpreting it. It's a sales job, don't kid anybody, you've got to I don't know of any walk in life in which you don't have to be a salesman, I don't care whether you're in communist Russia, or whether you're in the USA, you have to be a salesman.

?But the context you put it in, it could determine the future course of...

Oh, yes, it depends on how well-known you are, and how much respected you are. See, if you've oversold early on in your career development, your peer group recognizes it, and they disregard what you publish, or you have difficulty getting it into peer-reviewed publisations, because your peers don't respect you.

?How tight-knit is the peer group? How ~~in~~ sensitive, how in touch are they in terms of developments, what's the ripple effect?

Oh, we know pretty darn quickly what's going on. We each attend three or four meetings a year at least, and important new discoveries are communicated pretty effectively. We probably have the best system that we could possibly have. It's a free enterprise system, it's a very good one, very efficient. I suppose I would have to be somewhat critical, though, ~~in~~ of our peer review in ~~terms~~ terms of monies. I don't think ~~it's~~ it's working very well in terms of NIH grants. I just don't think it's working.

?How does one have any influence on the other interms of money, I don't understand.

You know whether or not you can get money to support your research programs is a function of your publications, it's one of the determinants of publications. You know it's nice to be well-known ~~in~~ and respected by your peer-group, it's intellectually a very satisfying thing, but I've been here overy five years now and we've spent well over a million dollars. That

money came by virtue of some things, I mean it isn't state money. You know it's money that I've generated for the research programs, and it's come from a number of different directions, some of it from NIH, probably a thrid of it from NIH. I still think that peer review system up there just isn't working like it should, I just don't think it exists.

?Something we should touch on is the financing of research. How much of your time does it take to generate research funds, and how much of your work is dependent on funds you generate outside?

Almost all of our work is dependent on funds we generate outside. I probably spend twenty per cent of my time generating funds for the division of clinical pharmacology. It's a lot of time. I'm hoping it will decrease within the next year. What we're trying to do is to get a program project grant which ~~xxxxxx~~ would be more encompassing of our research programs.

?Is it a problem that you can only raise money for a short period of time, or does that have some beneficial side effects?

What you try to do is to have a base of support. We have a special project grant for developing clinical pharmacology which is what $70,000 A year, and that goes for five years, and the Veteran's Administration has provided us with 50 or 55 thousand a year for seven years. And then I got the Merrill/Swarkam scholar award, which is thirty thousand a year for five years. Then we pick up other monies--like NASA was aggressively interested in this blood pressure regulatory mechanism, so they will~~x~~probably support a sizeable portion of our needs for the next couple of years.

E N D O F T A P E