Q  Somehow the notion that you only worked with one virus is something that I want to dispel or have dispelled. Because I am not a virologist, could you tell me just what hemagglutination is.

A  Hem refers to blood. And the glutination is the glutination. The original work was done, started with influenza. And I think it was George Hurst who in harvesting allantoic fluid from eggs that had been infected with influenza virus, noticed that when there was, by accident a puncture of a blood vessel in some of the red cells got into the allantoic fluid instead of being clear, that they clumped together. And it was in this way that he discovered that viruses, influenza virus, had receptors, had groups on it. Which could combine with receptors and chicken red blood cells. This became the basis of measuring influenza virus activity. You worked it out and it turned out to be one measure of influenza virus activity that became very important because you could also measure antibodies that way. By inhibiting the glutination of the red cells you could determine whether or not you had an antibody that would inhibit the combining groups of the virus to combine with the red cells. But then there were many other things that were found. It was found for example, that there were non-specific inhibitors. And it was a whole problem, but it was very useful. But basically the way you do a hemagglutination test is that you must have the proper red cell. And you add the virus to it. If there is no virus activity and you have it in a plate, you see, a well, or a tube the way it was done originally. If there is no virus activity, the red cells settle out in a solid little button. But if there is a
glutination of the red cells it isn't necessarily great big clumps the red cells settle out in a shield at the bottom of the tube or at the bottom of the excavated plate that has little things like that. And in that way you study. There are very fundamental problems associated with that too.

For example in our work with after we discovered how to do things with the arthropod borne viruses it turned out that the non specific inhibitors of a glutination, not antibody but non specific inhibitors were quite different from those that were involved in the respiratory tract virus. And the discovery that was made was that certain lypo-proteins or lipids in the serum were able non specifically to combine with the virus and thereby prevent the glutination. And you couldn't measure antibody. So we developed methods for extracting very simply by a quick thing that we settled on aston of taking out the lipid proteins from the serum and then the non specific inhibition of the glutination disappeared, and then you could measure antibody. If there was antibody present you would get an inhibition of the glutination and you would again just get a button instead of a shield, the red cells settling in the button. And if there was antibody you could measure how much antibody because you diluted out the serum literally and find out whether it had a little bit of antibody or whether it had very high titers of antibody. It became a very, very important tool for studying a number of things but in the process of making it work, you have to discovery many new things. It isn't all that simple. There were many things that have to be learned. There
are obstacles that say oh, well, it doesn't work. So you either, as some people do, drop it and they go on with something else. Or you find out why didn't it work. And when you do that, then not always, it looks like something that becomes more generally useful.

Q I have always heard that when you have a virus laboratory it is not good to work with too many viruses at the same time. And yet here in your own laboratory in the post-war world you are working with a wide variety.

A There is always a reason. It is not a question. I mean, if one person--there are one virus virologists who really are a little bit like horses with blinkers on them. They look at the whole field of virology through what they have learned with that one virus. But I have never been a one virus virologist. From the very beginning. We have concentrated at any one time on certain problems and on methodology that was absolutely necessary to make progress. But I have not been a one virus virologist for the simple reason that as problems arose, and usually in the field, because my choice of problems--I don't want to make a comparison but like Pasteur, almost everything that Pasteur did, whether it was absolutely fundamental in biochemistry or in microbiology, was related to a problem in the field. That is how it started. And which I will digress again--goes to show that fundamental observations can be made in the pursuit of solutions to practical problems if you stop to acquire the new knowledge that is necessary to be able to pursue that problem because it isn't really out of--you don't wait twenty years of a hundred
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years until somebody is totally disinterested will find the basic laws that are needed to make progress. Alright. So. Why did I work for example when I got to the Rockefeller Institute with the vesicular stomatitis virus with Eastern equine encephalitis, Western, all of those. I was using those viruses merely as tools to investigate basic problems of the way viruses spread in the nervous system. And if I would study just one virus-I did—I concentrated on polio. I wouldn't learn of the variety of mechanisms that were involved. So I used many different viruses in order to elucidate a larger phenomenon of how viruses behave in the nervous system. How they spread in the nervous system. It was essential to have a broader understanding.

So let me move on now to some other viruses. I come to Cincinnati. Alright. Now, let's say, how did I come to work with toxoplasma in the middle. You speak of concentrates. My God while I was chasing viruses through the nervous system something happened which was totally unexpected. I happened to have inoculated fresh bits of guinea pig tissue from different parts of the nervous system into mice, and mice died in a way that was not characteristic of the virus, and so I became intrigued and I found that guinea pigs that we were using happened to have toxoplasma. And so I became intrigued in toxoplasma. Why did I become intrigued with toxoplasma? I became intrigued in toxoplasma because here was a big parasite. It was almost the size, half the size of a human red blood cell. But it behaved like a virus in many respects. You couldn't culture it in vitro the way you could tripanosomes or a certain lichmania
or other things. You couldn't culture it in the absence of living cells. And it behaved like an obligate intra cellular parasite. One property, aside from size, which it had in common with viruses. Mind you we are talking now about 40 years ago. We are not talking about the newer knowledge that we developed. So to me it became a challenge in studying obligate intracellular parasitists — you see, and I studied toxoplasma not because of the disease problems, which something came along later, but I studied it because of the phenomena of obligate intracellular parasitism that I believed could be elucidated by seeing something.

Alright. So let me take some other things. Why did I become involved in so called pleura pneumonia like organisms now called microplasms. They again complicated my work with viruses. And because of very extraordinary findings, and I was always an experimental pathologist, because I studied everything histologically in sections. I became very much intrigued by these organisms which were in size sort of in between viruses and bacteria, certainly the basic reproductive unit comparable to the size of larger viruses. And in working it out in the process that they didn't come labeled as pleura pneumonia like organisms or microplasma. It was only after trying to identify what was mucking my tests for the viruses I was chasing them through the central nervous system, I discovered very interesting phenomenon. The production of progressive migratory poly arthritis in mice that looked like rheumatoid arthritis. So one thing leads to another. Now, when I came to Cincinnati, because of the experience that I had acquired in working with various neura tropic virus diseases
while at the Rockefeller Institute I had become involved now in the neuratropic virus commission. Some of the problems are encephalitis, western equine encephalitis, St. Louis encephalitis, Japanese encephalitis. I take on this obligation for different people. I had a team in my laboratory. I wasn't doing all these things by myself so I was like a little headquarters in which different problems would be worked out at different times by different people and sometimes concurrently by myself and various associates on this. Now let's go a step further. So you can see that becoming involved in dengue and sand fly fever was merely an outgrowth of the fact that I had been involved in arthropod borne viruses. So when I go to the Middle East with an assignment to learn about sand fly fever that was the problem that was facing the armed forces. So I become involved in viruses, sand fly fever. And when I come back with sand fly fever there are these problems in the Pacific, so immediately I became involved in the Pacific and as I isolated the agent, I identified it as dengue virus. There was no dengue virus on a shelf. There was no test at that time. Nobody had a dengue virus in hand or in a refrigerator or any other place. I isolated something from the blood of sick soldiers which epidemiologically looked like dengue and then it had the characteristics of dengue, and new methods were evolved. So you become involved in that. Well, if you say many viruses and then as you continue to study dengue and yellow fever and then the serendipitous thing of which leads to the discovery by a very extraordinary accident of the hereditary factors which determines susceptibility and resistance to virus affecting the nervous system.
In other words, if serendipity turns up something and I find it very exciting, I don't just leave it. In other words it is a balance. There is a balance between sticking to the end point of decision on something to start and concentrating in one field and also exploring things that turn up as a result of the work you are doing or of the necessity.

Q So you would have Busher and Channock working on hemaglutination and other people in the lab working on other--

A Yes we were still working on problems, oh yes.

Q And so on.

A Well because you see Busher worked for a year and then he went off to Japan because he became a member of the regular army. Channock comes over and I acquaint him with this work and get him started and then he made this a full time job, and then he had to serve in the army so he goes back and by arrangements again through the Armed Forces Epidemiological Board he gets assigned to the same laboratory in Japan where Busher is working and now they are a team and now they are working together on problems in Japan on the basis of these are my scientific sons, you see. I, now through Busher and through Channock have both, scientific grandsons and great grandsons.

Q Well this is an important point but the army epidemiological board is not the only government activity you are involved in and almost immediately after the war you become involved with the tropical medical section of the U.S. Public Health Service, and I wonder if you would tell me something about your work with--

A Well the National Institutes of Health began their extraordinary rise and development immediately after World War II
As a result of that there were established a number of so called study sections. In different fields of activity, to evaluate the applications for research that were coming in to the national institutes of health more and more as the appropriations grew and then to recommend whether they were scientifically valid or not.

One of the study sections that was established chiefly through the efforts of General Simmons who I think by that time already maybe he was still in the army or had become dean of the school of tropical medicine and public health at Harvard. And because I was very closely associated with Simmons in work on I mean he knew the work he was chief of preventive medicine in the army, he asked me to serve on this study section, tropical disease study section because of the familiarity that I acquired in the field of such, of particularly the arthropod borne viruses in the tropics. So in 1947 I joined this group and then continued on in this study section for many years in which I came to learn about the problems of tropical health in general, tropical health research in general because I was only representing let's say arthropod borne virus diseases of the tropics but there were people concerned with amniobiosis, with parasitic diseases, with malaria and so on and so on. So that I became knowledgeable in that field. It is an education. It is not only a service and then I served on other study sections, the virus and rechettzal study section which was not tropical public health and then after service on that I was elected to the central, the board and the advisory board to the national institute of allergy and infectious diseases. This board had the responsibility by law of going over the whole program of
this categorical institute. And going over the recommendations of maybe ten, fourteen, fifteen different study sections because research grant applications go into to study different study sections then they come back to the institute that presumably has the responsibility in this field in research and it has an advisory board. I served for many years on the advisory board and it was there that we came up against problems of policy and decisions of how do you divide up a pie. How do you establish priorities. Is an elephant and a mice, both of which are very interesting animals, and you have just so much to feed them, how do you decide how much to feed to the mouse and how much to feed to the elephant. And what is an elephant and what's a mouse. I am making this very symbolic here. But this is a very important function and I was never one to just follow along the routine because I, right now I am not discussing the problems that arose in those areas. I am only discussing my involvement in them. And I continued to serve although I started in 1947 I continued to serve until I left for Israel at the end of '69. So that was a very important period and then also as a result of the involvement in the tropical studies section and as a member of the national academy of sciences I then was asked to head up a special group and organize a special group to make a study of the problems in tropical health in general. And there is a publication that came out of that. I was the chairman of the group that got together and I was always for collaborative effort and that also taught me a problem. Taught me some lessons. Taught me problems as well. Lessons of trying to solve problems and a thick book came out
with a very extensive analysis of the present situation regarding tropical health, the lack of knowledge, the kind of research that was needed, where it was done, how it might be done and I learned then that reports like that in which a lot of people do a lot of work, if they are not directed to a specific agency for implementation and execution it is again just a prayer and it ends up on the shelves of libraries and perhaps in the offices of some professor or sometimes even a person responsible for policy but it doesn't do much good. So, I mean, this was the school of experience of policy connected with biomedical research in general, research in the tropics, the implementation of needs that I started to be involved in away from the laboratory bench from 1947 I would say up till the present.

Q Where do you find time to do that?

A You just stretch it. And actually if I think back now what comes off the top of my head, the top of my mind is that we always somehow or other work with a feeling as if the sort of Damocles was hanging over your head. That you are always working against deadlines. You are always under the pressure of more things to do than you have time to do because when you serve on let's say on a study section or then on a council or it isn't just going there, taking a few days out although many people served like that. And you listen to something and then you do something, not very well, very often, and then go back home to what you were doing before you left. You get a tremendous amount of material. You know, you get a hundred, two hundred. It kept on increasing as the years go by, of applications to go over. And to study them, evaluate them, in
the later years in the '50s, late '50s very often before going to a study section meeting I would have about 20 pounds of papers to go through beforehand and then you would go there and sit for two days and sometimes then three days. And discuss all of these things, and it means a lot of work. But I also learned at that time that ultimately having advisory groups like that, study sections and others, you don't get the benefit out of them if it isn't backed up by a professional, full time staff who then carries on, because the people who serve on study sections and councils, take time out for a few days and then they go back to their regular work. Whereas the problems that are presented are very important problems, ongoing problems and if they are then carried on by people of relatively low competence, you lose much of the input of the expert people and I think that as I became involved later as a full time expert consultant of the national cancer institute under the rules and regulations of the new cancer act I had to think of other ways of, based on my experience, in which the national expertise could best be utilized to deal with problems of decisions, involving biomedical research policy so that we could make better use of whatever good brain power there was at the time.

Q Now, sometimes this committee work involves you really interesting problem. One of the problems was the use of gamma globulin. Now how--

A Yes, go ahead.

Q Hammond in 1950 and '51 of course had had a huge gamma globulin test, but subsequently CDC under Alex Langmuir ran another gamma globulin test with family contacts. And I
wondered whether I can get you to speak something about the gama globulin program.

A I think the gama globulin program is totally unimportant itself in the perspective of history but from the point of view of acting on committees I would make the point that during the years of my association up to the early '60s when there was a clean cut separation between the national foundation for infantile paralysis and myself when we became adversaries as a matter of fact in public health policy, that one of the good things of the national foundation and particularly during the late '40s and early '50s when there really wasn't a good national institute of health yet is that there were committees to deal with various problems that involved public policy and prior to the availability of any kind of polio vaccine, there was a need to determine what you can do with the tools you have at the time and gama globulin was one of them so in order to reach certain decisions, a committee was established by the national foundation and I served on a number of different committees, that other grantees of the national foundation. The way the national foundation operated, some of the very good things of it were that it wasn't just a that it gave grants to people. There was also involvement in decision making and so this is an example of that. But otherwise I think that the place of the gama globulin tests. It was an interim thing that had to be done. We could go into the details of that I don't think would serve a useful function, purpose.

Q I don't want only to speak of institutional relationship I would like to speak of some substance but every time I bring up a question of substance you, you know--
A Because I regard the substance you've brought up as a speck of dust on the ocean of history of these activities, I choose not to take up five minutes because I think in the total things that are necessary to discuss, the gamma globulin except for the, as the way certain decisions are reached, it would not be worth it.

Q Alright. Now let me put another question to you.

A Basically, if I may interrupt you. Under the outline we had made it is not so much the specific problems with which the armed forces epidemiological board dealt because obviously I am not giving you a history of the armed forces epidemiological board because it is a lot of things in which I was not involved. And when I have listed here W.H.O. the World Health Organization, a lot of things in which I was not involved. But they are listed there because I was involved in some of them and I can make certain comments on the modus operandi, what made them work, what did not make them work because of the impact that this historic development of certain institutions in reaching decisions of importance either in pursuit of biomedical research or in reaching decisions of importance to public health policy, have a bearing and when I have listed the N.I.H. study sections and councils, it is not so much to deal with gamma globulin or feces or hispiratory secretions or fever or this or that. It is to deal with the mechanism of operation with the mechanisms that are being used in which I participated and which have an impact on the very broad subject of biomedical research and public health policy decisions rather than any one little item unless it can serve as an example.
Q Well one item had cancer as an example and as I mentioned earlier today it was an item that was attacked with some passion and that was the enteral virus committee of which you were a member for some time.

A Let me say that this also falls under the scope of committees established by the National Foundation for Infantile Paralysis. We discussed previously the problem of the tremendous number of viruses that were discovered in the enteric tract. It was necessary to find some way of dealing with it on an international basis and I would say the passion is not really passion. It is now, in retrospect it is terribly unimportant and when people discuss certain issues of how to call something so you would have a language of communication, scientists are human and they are sometimes passionate in the expression of their judgements, but I wouldn't regard that as a terribly important thing. Again, it is one of those activities done as part of committee activity under the National Foundation for Infantile Paralysis.

Q Well you have put me at. You've really pushed me.

A I intended to push you. I intended to push you in another direction because these things that you raise I regard as very, very, very very small potatoes. Now how much smaller can I make it than that?

Q You can't make it much smaller. Then, why don't you tell me what you regard as large potatoes as you look at things.

A Alright, I will tell you. Let's take them one by one. Let's take the armed forces epidemiological board., which we have listed. Here is an organization that is set up first of
all by the U.S. army which I regard as a very important mechanism. It was a very important mechanism for getting the best people in the United States to leave the regular work they were doing and to become involved in research on problems of importance to the army. We have discussed the specific things in which I was involved. But, what happened after a while. After a while it turned out that the people who were members of the board itself and there was a sort of central board under which there were many commissions. And the people who were serving on the different commissions were using—not were using. I will have to back track, a little, had become a sort of club in which the research activity that they wanted to do in their department that by the longest stretch of the imagination could hardly be related to dimition of the army, or the armed forces, were being carried out and they asked for money to support activity. The reason I look upon this as a very important problem is that it still exists now. The problem of division of labor and how certain kinds of research have to be supported and by whom, because ultimately the armed forces epidemiological board was dissolved and I was in favor of that because I already spoke up at meetings to ask what is the relationship of what is being proposed here or requested as research to be supported by the army or navy what is the relationship to the specific, armed forces problem, armed forces medicine if you will. In contra-distinction to it being a very general problem of importance in medicine regardless of let's say specific army requirements. And the reason why there was a certain transition is because there
was a time in 1941, 42, 43, when we didn't have a big research establishments such as we have now, such as developed later after World War II. It was a situation you will recall when the yellow fever problem was being attacked by the Rockefeller Foundation in a way in which the fundamental research on viruses which did not exist had to be carried out under the Rockefeller Foundation because the knowledge was not there to make the necessary progress in yellow fever—not because it was necessary to just do general virus research under that heading. But in order to make progress in that it was necessary to do certain things and the same way with the army epidemiological board. In order to do research on certain problems of importance to the armed forces, it was necessary to do certain research which was methodological, was discipline oriented. In order to obtain the tools with which to be able to deal with those armies. Because there was nobody else doing it. But what happened after World War II.

After World War II there was the extraordinary growth of the national institutes of health with the growth and development of a biomedical research establishment in this country that was unequaled to that anywhere else in the world. And it was quite evident that some of the work that had to be done under the auspices of the army epidemiological board could not now be related. There was no use trying to do things that had to be done and were being done by the national institutes of health to have them done through the army epidemiological board simply because the man who was in that department was either on a commission or was on the board and get the money from the army instead of from the national institutes of health. Now you say
what difference does it make how it is being done. Well it makes an awful lot of difference because if the army has a certain amount of money for research on special problems related to army medicine, for protecting the health of armed forces when they have to operate anywhere in the world in a way that civilians in the United States could not, that money has to be spent on those problems. You cannot stretch a dollar beyond 100 cents and if you are going to spend on one thing, you are not going to be able to do the other. Now this is much more, basic principle of organizing expenditures for scientific research at a more sophisticated stage of its development than merely whether or not it is done under the army epidemiological board or the national institute of health. So that became a general problem. The general problem because the navy continued to support research which was really by the remotest stretch of the imagination you just couldn't relate it to directly to army problems, armed forces problems, couldn't. But what really happened, what was wrong, what was wrong was that in doing what was easy, what the people in the department wanted to do, that the specific problems of military medicine were being neglected. Now I will come back to the N.I.H. because it comes up again. Well, under pressure then and I think justified pressure from the congress that was meeting the, had to meet the budgets. You know you can't do research without money you are not an artist who sits in his attic drawing something on a piece of paper, on a piece of canvas. To do research you've got to have money. And when you've got to have money you've got to get it from somebody and when you've got to get it from somebody you've got to make out a case to compete with all sorts of other national needs, some of my colleagues, scientific colleagues, think
that they belong in an outer planet where that thing shouldn't even be questioned. But I think it should. And scientists have a responsibility of justifying it. As a result of that, people were making appropriations for research by the armed forces in congress, the representatives, the people of the United States, began to ask more and more for avoiding unnecessary duplication of effort by the research activity under the armed forces and the research growing expanding research activities under the national institutes of health. There were always considerable battles in the armed forces epidemiological board. I wouldn't say they were entire self-serving although many of the members of the board or had commissions had this, were getting money for operations of their apartments that way. And I always held out against it. I was like the most mission oriented general, a military person because I always, in my mind, carried the conviction of the necessity for proper division of labor in order to achieve certain broader objectives so that ultimately the armed forces epidemiological board was dissolved. It was dissolved because it was realized that the army in order to do research on things that are important for it had to operate differently. That's why subsequently there was a panel set up under the U.S. Army Medical Research and Development command, and the old so called army epidemiological board became, came to serve another function. And that is provide consultation service for preventive medicine decisions. In other words, what do we do, what kind of influenza vaccine do we use now? Or, what should be the regulations for the use of gamma globulin against infectious hepatitis or what kind of a drug schedule should be used for malaria in Vietnam or things like that. In
other words, a professional consulting service. And not a research arm. So much for the broad principles that grew out of the necessity of making decisions on expenditures of limited knowledge because I found what happened too, that we would sit for days you know and talk about this application, that application, because it came through from the commissions up to the central board. In latter years I served on the central board. And then what happens after all that talk was over some third level or fourth level young major or captain who had to make an ultimate decision because the buck stopped there. There was so much money to spend, and he had to make a decision between this and that and the other things and you know, because there wasn't money to cover everything, and what would he do. The board didn't serve its function. It didn't make decisions on priority. It didn't say if there is so much money we spend it on this. If there is so much money, this comes next and this comes next and so on. No. This low echelon person who ultimately had to deal with dividing up the pie he would call up some friend again, and the lowest echelon of somebody who might be on the central board and decisions were made in a way that the whole armed forces epidemiological board, a useless club from the point of view of serving the needs of research for the armed forces. And that's why it was abolished. And what I learned then was that it was not enough of making policy about one or another type of activity in biomedical research to merely say this is good, this is bad, this is medium. You had to have some guidelines for a decision about priorities that already during the period when I was serving on the board. I mean I was always conscious of it although I found that most of my colleagues were
not. That we are working in a society with finite resources. We cannot merely say this is important and therefore ask the public to give us what we want. Never mind why because you are too stupid to understand how this has a bearing. So I became very much a person on the side of those who believed it necessary to plan and have guidelines for planning. And to have a guideline for deciding why is this the first priority. If we only have one million dollars. Why should we do this. And therefore that we must have an input from the armed forces who themselves weren't doing their homework. What is the magnitude of the problem for the army. Now, potentially, and in the future, of this, that and the other. We didn't--I didn't want the army just to come and I sit there and say you tell us. You tell us what the problems are. I would say to them, I don't know what the problems are in the army now. You are an authority, you in the surgeon's general's office. Of either the army or the navy or the air force, should be if you are not in touch with the planning people.

Q What was--
A Wait a minute. Let me finish this sentence.
Q Alright.
A Should be in touch and should bring to us your advisory group, what you regard to be the really high priorities from the point of view of the magnitude of the problem that this represents not something that may involve a miniscule problem so you have the obligation to come prepared to us and present in a problematic an evaluation of the magnitude of the problem and very specific definitions of what problems need to be solved for lack of new knowledge and what the priorities are.
Q Well, wasn't something like namruth's three
a mission oriented--

A My dear friend to label everything in the army and
biomedical research is mission oriented. The mission is to obtain
understanding, to obtain knowledge relative to understanding,
prevention, treatment of a disease but how you pursue that mission
is quite another problem because if in amru three you are
talking now about the unit in Egypt.

Q Yes, that's right.

A That's right. Some people are doing things rightly that
can be done only in Egypt. But other people who do things there
who could just as well be done in Podunk you see. Anywhere
in the world are not fulfilling their mission and this, this has
down even now. I have just come back from a meeting last week.
We spent two days of this panel of the U.S. Army and medical
research and development command and were back on that again.
A proper definition of what is actually the mission of what
work belong and what work does not belong. Just because you
call it a mission oriented unit doesn't mean that either the
army, navy or air force in their research unit haven't been
doing a thousand and one things that are not relevant and the
congress was right. The congress was right in saying that there
is a need for distinguishing your mission from the mission of
the National Institutes of Health, collaborate where collaboration
is necessary, concentrate on your problems where nobody else will
do it because they are not civilian problem. They are special
problems. They may be special problems for the navy, you concentrate
on those for the navy. Special problems for the army, you concentrate
on those. Special problems of the air force has, you concentrate
on those. So merely establishing a so called unit doesn't mean that it is fulfilling its function.

Q Good.

A Just like, as I'll come later to the national institutes of health. Merely establishing categorical institutes does not mean that they have been fulfilling their unit, their duty. They have not. We will come to that when I discuss national institute's development. Now we find, as the record shows that my voice is raised, that I speak with emotion on the problem and I speak with emotion on the problem because I cannot regard it with equanimity. Or philosophically as if which way it goes doesn't make much difference to me. In my judgement it makes a lot of difference. It makes a lot of difference whether biomedical research shall be carried out to a very large extent in the--

END OF TAPE