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M E M O R A N D U M

From: William Doering and Leo Szilard

To: Cass Canfield

A proposal to create two interdependent research institutes operating in the general area of public health, designated as:

Research Institute for Fundamental Biology and Public Health

and

Institute for Problem Studies

There appear to be a number of important problems in the general area of public health which could be solved today and yet for some reason or other progress toward their solution is conspicuously slow. In some cases the state of scientific knowledge is far enough advanced to make it possible to set up projects aimed at finding a practical solution to the problem; in other cases more fundamental research in the biological area involved is needed.

Throughout the United States at present there are scattered many spirited men among scientists who pursue fundamental research in biology with manifest success. These men engage in fundamental research primarily because it gives them pleasure to do so. Their interest is not limited in any permanent and irrevocable sense to a single specialty, and they are quite prepared to switch from one technique to another when the time comes to shift the emphasis from one set of questions to another. Many of these men are keenly interested also in the acute problems of our times, but they have rarely the opportunity to do something about them. Occasionally one or the other strikes out on his own from the realm of pure science into work on one of these problems. Jonas Salk, for instance, responded to the challenge of producing a polio vaccine by taking off several years from pure research (and he did this in the face of the prevailing notion that no dead virus can be successfully used for immunization). Usually such diversions from pure research involve a great personal sacrifice, and those who engage in them must struggle against heavy odds.

We propose that a setting be created which would offer men of this sort an opportunity for two kinds of activities:

a) to pursue biological problems of great intrinsic interest that lie in the general areas which may ultimately have a bearing on problems of public health (with the same kind of freedom that scientists enjoy in their research at universities) and

b) to shift their attention from time to time to problems of public

importance in the general area of public health and to work on projects aimed at finding practical solutions to such problems.

We believe that within such a setting the abilities of creative men could be brought to bear on problems of public importance - both recognized and unrecognized - where progress is conspicuously lacking.

Recognized Problems

Clearly it would be highly desirable to develop some biological method of birth control, adequate for the needs of the underdeveloped areas of the world. About three years ago the Conservation Foundation conducted a study in order to determine whether the problem was ripe for an attack on a programed research basis. The results are reported in The Physiological Approach to Fertility Control, the Conservation Foundation, 30 East 40th Street, New York City, April 1, 1933.

We participated in this study and concluded that there were a number of promising leads around which further research could be centered. Certain recommendations were made concerning the magnitude of the funds that were needed and the way in which they ought to be spent.

Subsequently the Population Council became interested in this problem and took some steps similar to those which had been recommended in the Conservation Foundation report. Currently, the Population Council is making available about $200,000 a year in the form of grants-in-aid for fundamental research in the field of mammalian reproduction. This money, added to the huge amount available at the National Institute of Health to support pure research in this field, has led to a situation where there is probably more money available now than there are worthy takers. In spite of this, progress is slow and it is by no means certain that any of the present developments, aimed at finding a really satisfactory method for birth control, are moving in the right direction. Too few of the men active in this field have the kind of imagination and productivity that one finds among those attracted by fundamental biological

problems of intrinsic interest. Too many are inclined to look upon the solution of the problem as a lifetime job.

The lag in progress in the field of birth control is not unique. It is just one example - though probably the most conspicuous one - of a general phenomenon.

Another example - taken again from the field of public health - is provided by cigarette smoking. For almost thirty years there has been reason to suspect (Doering & Lombard, 1928) that cigarette smoking is harmful to health, and by now there is a strong suspicion that smoking one pack per day may shorten a man's life by at least five years. It would not take large funds to settle this question once and for all within a period of three years. There is a great public interest attached to knowing the answer and yet somehow it is not forthcoming with the desirable speed.

There is much public discussion of the topic but no concerted effort to establish the relevant facts. If smoking one pack a day shortens a man's life by five years or more, then cigarette smoking is the single most important public health issue in the United States, for even if we found a cure for cancer we could do no more than to add two and a half years to a man's life expectancy.

More than one third of the deaths of middle-aged men in America are due to coronary disease. In Italy the contribution of this disease to the total death rate is believed to be one twelfth and in Japan one thirtieth. If the rate in the United States could be reduced to that of Italy, one might be able to add three years to men's life expectancy. For a long time now it has been suspected that the high coronary disease rate in America is associated with the diet. There are plenty of clues but no organized effort to find out what acceptable changes in the diet might remedy the situation. There is no reason why this question could not be settled within a period of five years, if a responsible group of men were to put their minds to it. The path from finding an answer to the relevant questions to the actual

suppression of coronary disease in America may be quite long (it may tke a generation's time before this can be accomplished), but the immediate, necessary steps seem clear.

The examples chosen above were taken from among the problems which are publicly recognized. It might well be that some of the unrecognized problems are of even greater importance. What are these unrecognized problems is, of course, not possible to say but an attempt is made in the Appendix to discuss what some might be.

It appears likely to us that progress will remain slow unless we create a setting that will provide for the scientists, whose help is needed, incentives -- intellectual, moral, and material -- sufficient to induce them to do something actively about these problems.

Most of these problems have in common that they require work on two levels:

1) The knowledge, which is lacking and without which no effective action can be contemplated, must be produced. In some cases this knowledge can be obtained by a more or less direct attack on the problem -- by setting up a "project." In other cases a direct study of the problem would be premature and progress must await advances in fundamental biological research in the general area.

2) Once adequate knowledge is available, its application to the problem must be promoted. Frequently this may involve merely bringing to the attention of the agencies which are responsible for practical action the knowledge that has become available.

Work at both of these levels might begin to move very fast if the kind of scientist whom we have in mind can be induced to enter upon the stage. We say this with some degree of confidence because we have seen what can happen when an old stagnant field is invaded by "outsiders."

The Achievements of Outsiders

In the last fifteen years a revolution has taken place in the field of microbiology, which had been stagnant in the care of the classical bacteriologists for over thirty years. When suddenly biochemists, geneticists and physical chemists - most of them young - invaded the field, things began to happen.

During the war, soon after the radiation laboratory was set up at M.I.T., nuclear physicists moved in and began to develop radar while the classical electrical engineers watched from the sidelines.

In the development of atomic energy theoretical physicists invaded the field of chemical engineering and presented a process design for the Hanford plutonium plant which was accepted, while the design produced by the engineers proved to be useless.

It is conceivable that "classical" nutritionists will solve the problem of "coronary disease and fat metabolism," or that gynecologists will come up with a really satisfactory method of contraception, but it is more likely that an invasion of "outsiders" may provide the right answers.

What kind of organization would it take to provoke such invasion of outsiders?

No organization was needed to provoke the invasion of microbiology. Here were problems of great intrinsic interest which could be pursued even though the new men working in this field were scattered all over the country. There was no need to induce these men to leave their universities and gather under one roof; there were no problems of public importance that required the setting up of projects aimed at their solution.

The situation was different in the case of radar and atomic energy. In these cases it was necessary to establish closer collaboration in order to have a coherent group capable of a concerted attack. And it was possible to organize the invasion because the universities were willing to grant their men leave of absence "for the duration" and because the emergency of war provided the men with a compelling motive to respond to the call.

Our present situation is quite different. There may be at present an emergency also - but the emergency is not recognized. If we are to say what kind of a setting it would take to provoke the needed invasion, we cannot derive our answer from any precedent and have to rely solely on our imagination. In the following we shall attempt to describe on this basis an organization that we believe might be adequate to accomplish our purpose.

Organization

There shall be created two interdependent institutes having independent administrations and budgets but being otherwise closely related.

One of these -- the Research Institute for Fundamental Biology and Public Health -- will engage in pure laboratory research. Its regular Staff Members will have tenure and will be free to work on any biological questions of their choosing. Thus the selection of these Staff Members will automatically determine the areas in which the Research Institute will be active. In selecting the Staff Members we would, therefore, have to keep in mind that we want to see the Institute active in areas which are both of intrinsic interest from the point of view of fundamental knowledge and at the same time of relevance for unsolved public health problems. An attempt has been made to indicate in the Appendix what some of these areas might be.

The Research Institute will have six to eight regular Staff Members and perhaps nine to twelve Affiliate Members. In addition the Research Institute will have twelve to sixteen Research Associates on its staff, appointed for a maximum of ten years. The Affiliate Members will be distinguished scientists who serve in an advisory capacity. They will have a major role in determining the direction of the development of the Institute.

The second institute - the Institute for Problem Studies - will have no permanent scientific staff. It will have only a small staff of administrators who need not necessarily all be scientists. The choice of problems on which this Institute may work will be determined by the members of the Research Institute, both regular and affiliate.

It is assumed that the Institute for Problem Studies will take up only problems where progress is lagging and where there is a gap that it can fill. It is further assumed that in the next five years perhaps two thirds of the attention of the Institute may be devoted to the problem of birth control and that most of the other problems tackled will also lie in the field of public health in the broad sense of the term. We may envisage two possibilities in regard to the scope of problems to be considered: The Institute for Problem Studies might:

a) be limited by charter to the field of public health in the broad sense of the term, or

b) be left free, by the charter, occasionally to take up problems that go outside the field of public health. Thus the Institute could pursue, for instance, some of the major problems of under-developed areas which lie in the area of "political thought" rather than "biological sciences." (This would involve bringing in for limited periods of time scholars whose interests are outside the field of science. See Appendix.) But in this connection the charter shall provide that the Institute may go outside the field of public health only with the approval of two thirds of the Affiliate Members, as well as the approval of two thirds of the Board of Trustees.

The Institute for Problem Studies will operate by bringing in from time to time, for a limited period, groups of men who may wish to collaborate with each other on a given project. If the Institute sets up a project that appeals to the imagination of an individual on the staff of the Research Institute, such an individual may, for as long as he wishes, go off the payroll of the Research Institute and transfer to that of the Institute for Problem Studies, where he may work jointly with others on a project. It is assumed that in the Institute for Problem Studies, of those who are employed on a temporary basis, about one third to one half will be on loan from the

Research Institute, and the rest will be drawn elsewhere. The regular Staff Members of the Research Institute might spend on the average perhaps one third of their time with the Institute for Problem Studies.

With respect to the problems assigned to it, the Institute for Problem Studies will assume the responsibility of creating or otherwise procuring and assembling the knowledge that is required in order to make effective action possible. The Institute will assume responsibility also for bringing this knowledge to the attention of those agencies which are in a position to take effective action. In this sense the Institute will promote activities that become possible through the newly derived knowledge. The Institute may have no clinical facilities of its own but it may have to assume responsibility for clinical tests in co-operation with medical schools and it may have to assume responsibility for field tests in co-operation with such agencies as the Population Council, Planned Parenthood, U.S. Public Health Service, the World Health Organization or individual national governments.

Dissemination of information to the public, general education, propaganda or the influencing of legislation will remain outside the scope of the Institute's activities.

The combination of these two Institutes will, we believe, attract the type of scientist whose help we need to enlist. Neither industrial laboratories nor research institutes of the classical type, nor universities, offer scientists comparable opportunities.

In the industrial laboratory, where the emphasis is heavily on commercial applications, the scientist rarely has the opportunity of satisfying his curiosity about fundamental aspects of nature, and he is almost invariably isolated, having few or no stimulating colleagues. He rarely survives.

In a pure-research institute a staff member is free to follow his inclination and move in his work anywhere his scientific curiosity may lead him, but this great freedom - which he possesses in theory - is to some extent thwarted - in practice - by his being under moral pressure to produce. He is not burdened by any teaching

obligation, and he is free to spend all his time laying golden eggs - except that it is difficult to lay golden eggs if you are expected to do so. He may be permitted to follow up his basic discoveries to the point where they can be applied to the solution of a problem of public importance, but he is not encouraged to do so, for setting up projects within a pure-research institute would exert a disruptive influence.

In a university a scientist earns his "right to exist" through teaching; therefore the moral pressure to produce is much less strong. Thus it is easier there for a scientist to leave an area of research which is safe (where he can produce results by just turning a crank) and to venture into uncharted seas, where he runs the risk that he may obtain no publishable results for many years to come, but where he also has a chance of making a really great discovery. His situation is quite satisfactory if he likes to engage in formal teaching. However his teaching load, even if moderate, leaves him insufficient time to devote attention and energy to the solution of the great acute problems and to develop his basic discoveries to the point where he can see their fruits.

In contrast, the Research Institute for Fundamental Biology and Public Health will offer a man the advantage of being able to combine his interest in fundamental knowledge with his desire to see knowledge that has become available applied to the solution of problems which are of public importance. In his research he will be as free as in a university. But he will not be required to teach, and he may, if he so desires, earn his "right to exist" by joining a "project" which appeals to his imagination by going off the payroll of the Research Institute and on to the payroll of the Institute for Problem Studies.

The attraction of the Institutes for scientists - of the kind needed - would, in our opinion, be further enhanced should some of the projects of the Institute for Problem Studies extend into the area of "political thought." If this were the case, the Institute would presumably bring in, from time to time, for short periods, men whose main field of intellectual activities lies outside the realm of science. Our

reason for believing that this would enhance the attraction of the Institute is based on the impression that, even in an institution which is as strong in science as the California Institute of Technology, spirited men among the permanent staff suffer from the one-sidedness of their contacts. They are deprived of the company of historians, economists and other scholars, and they are aware of this deprivation.

Affiliate Members

The Affiliate Members will not be employees of the Research Institute and need not spend very much time at the Institute even though they shall play a major role in guiding its work. They will, together with the regular Staff Members whom they shall outnumber, control the appointment of new members. They will also, together with regular Staff Members, determine the projects which the Institute for Problem Studies may undertake. In order to enable them to fulfill these roles, the Affiliate Members may be expected to spend at least one week each year at the Research Institute, and it is hoped that many of them will spend more time than this. The Research Institute shall make secretarial facilities available to them during their stay, and they may, if they wish, make use of their visit to prepare manuscripts for publication away from the disrupting intrusions of their daily duties at their home base. It is proposed that Affiliate Members be paid their expenses and a fee of $3,000 a year.

Regular Staff Members

The regular Staff Members of the Research Institute will enjoy tenure like a professor at a university. Each will have a budget from $35,000 to $50,000, from which his own salary and those of one or two research associates may be paid. It is assumed that each regular Staff Member will, in addition, have outside grants-in-aid averaging perhaps $40,000. It is proposed that each regular Staff Member have at his disposal laboratory space between 2,500 and 5,000 square feet.

Research Associates

Research Associates will be chosen by the individual regular Staff Members and may serve in this capacity no longer than ten years. A change of status from Research Associate to regular Staff Member shall not be impossible but shall require the concurring vote of three fourths of the Affiliate Members. This precaution is proposed in order to avoid the danger of inbreeding.

Staffing of the Research Institute

Following the selection of the first seven Affiliate Members and their acceptance, we may begin to discuss the selection of regular Staff Members. In order to do this intelligently, it will be necessary first to reach a consensus among the Affiliate Members concerning the areas in which they think the Research Institute ought to be active. Upon reaching such a consensus we may then begin to think of individual candidates for regular Staff Membership.

Our aim should be to recruit individuals with a strong overlap of interest, men who are likely to work harmoniously with each other under one roof. If appointments were offered to such men one by one, the most desirable candidates might be less likely to accept than if an offer were made to them as a group. What we must seek is a group of men who look upon fundamental research primarily as a source of pleasure and upon the application of knowledge to the acute problems of our times primarily as an opportunity for adventure; those others who are spurred to activity mainly by their sense of "duty" are not likely to be the most imaginative and productive ones.

The decision to offer initially an appointment to some such group will rest with the Affiliate Members of the Research Institute.

Procedure Concerning the Appointment of Members

The procedure that may be adopted concerning the election of new regular Staff Members and Affiliate Members (beyond the appointment of the two initial groups) may well determine whether in the long run the Research Institute may remain productive,

or whether it will decay. It is proposed to discuss this point with the Affiliate Members prior to the drafting of the charter of the Research Institute.

Financial Need of the Institutes

The Research Institute will need an endowment of $10,000,000. An endowment of $5,000,000, plus perhaps a fund of $6,000,000 to be spent in ten years, would also be satisfactory. In this latter case the income from the endowment would not be spent for the first ten years but rather be added to the capital in order to build up the endowment. An endowment is necessary if the Research Institute is to grant tenure, which it must.

The Institute for Problem Studies will require $5,000,000, spendable in ten years.

It is assumed that the cost of building a laboratory may amount to $3,000,000, half of which may come from the federal government out of a Congressional appropriation of $90,000,000 (to be spent over the next three years). Under the provisions of this appropriation, half the costs of facilities devoted to medical research or public health may come from the federal government.

Housing

The character of the housing problem will depend on the location of the two Institutes which in turn shall be determined by the preference of the regular Staff Members of the Research Institute.

We believe that it is essential for the success of the Institutes that the scientific staff live within walking distance of the laboratory. If they do, many of them will return to the laboratory after dinner, perhaps two or three times a week, as the need arises, and they will have many more informal contacts with each other (proved so valuable to creative individuals).

The Boards of Trustees

It is proposed that one half of the Trustees of each of the Institutes be drawn from the Affiliate Members of the Research Institute, and that the Affiliate Members take turns in serving on the two Boards of Trustees. Who the other members of the two boards might be is not for us to say, but we do wish to submit the following point of view:

For the Institute to be successful it is desirable that the non-scientist members of the Boards of Trustees and the Affiliate Members be congenial. In looking over the boards of trustees of other foundations it would appear as if their members had been selected primarily on the basis of "respectability." For a member of a board of trustees to be respected is necessary but in our particular case he also needs to be imaginative and courageous. This holds particularly for the Trustees of the Institute for Problem Studies; the activities of the Research Institute will not be controversial in any way, but those of the Institute for Problem Studies probably will be.

Perhaps in thinking of prospective non-scientist Trustees it might be a good guiding principle to aim at bringing together a group of men who will take real pleasure in exchanging ideas with each other and with the Affiliate Members.

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CONFIDENTIAL

APPENDIX to MEMORANDUM of Doering and Szilard

by L. Szilard

Introduction

The areas in which the Research Institute will work will be determined by the predilection of its regular Staff Members. Affiliate Members of the Institute can exercise an influence in this regard only by their role in the selection of the regular Staff Members. Therefore, prior to the appointment of any regular Staff Members, the Affiliate Members ought to arrive at a projection and decide in their own minds in what areas of intrinsic scientific interest they would like to see the Research Institute active. In order to make it easier to arrive at a consensus in this regard, I have prepared this document which I hope may serve as a basis of discussion.

The Institute for Problem Studies will have no permanent scientific staff. It will be left to the Members of the Research Institute, both regular and Affiliate, to determine what problems this Institute shall take up. This Appendix is written in part with the purpose of serving as a basis of discussion in this regard also.

I. Mammalian Reproduction: The attraction of the problem of mammalian reproduction to younger scientists is mainly due to the recognition of its overwhelming importance for population control in the underdeveloped areas of the world. A good solution would be a drug that might be administered once a month to women in the form of a pill. Even better, perhaps, would be a drug that could be mixed in with certain staple foods, such as for instance rice, and made accessible to large families who live in poverty. Such an "infertility brand" of staple food might perhaps be sold - with a government subsidy - at a price below that of the "commercial brand" of the staple. This type of drug administration would demand the use of a drug that is without any detrimental physiological effect for both women and men.

It is conceivable that such a drug might be found. It might for instance be possible to find some chemical analogue of progesterone that is physiologically inactive everywhere in the body, with the single exception of the endometrium of the uterus, where it might compete with progesterone and thus prevent progesterone from preparing the endometrium to "receive" the ova.

At present clinical experiments are being conducted with certain progesterone analogues which suppress ovulation, presumably through their effect on the pituitary. Whether drugs of this kind might have some long-range effects which rule out their general administration, we cannot say at present.

I believe there would be little point in my presenting here my own evaluation of the relative merits of the different biological approaches to the birth control problem, because as soon as a really imaginative group of people enter this field they may produce a host of new ideas, many of them wholly unpredictable today.

The Institute for Problem Studies if it takes up this problem - as I assume it will - need not remain idle in this field while waiting for fundamental research to open up new avenues of attack. There are a number of "non-revolutionary" methods that need to be explored in the meantime. It is even conceivable that some minor inventions and improvements applied to such a "conventional" method of birth control as foam tablets might make this method practicable in some of the areas where there is an urgent need of birth control.

Developing methods for birth control to the point where other agencies can take over will involve subjecting such methods to clinical tests and field tests. The Institute for Problem Studies will not have clinical facilities of its own, but it will work in this field in close collaboration with medical schools both in America and abroad.

The testing of fundamentally new biological methods of birth control is difficult in America where a married couple, if it does not want to have a child, wants to use a method of birth control that is close to 100% effective. Such effectiveness cannot

be guaranteed in the case of a brand new biological method. Here the best we may do is first to establish through toxicity tests in animals that the drug is harmless and then arrange for the clinical testing in countries where couples may be satisfied with slowing the rate at which the children come. We therefore assume that the Institute for Problem Studies will have to maintain close collaboration in this field with medical schools abroad.

This holds in particular for clinical experiments which are aimed at finding a satisfactory drug that will produce an early abortion. There should be no difficulty in arranging for clinical testing of such drugs in Sweden, or in Japan, where surgical abortion is at present the method of choice for population control. The drugs available at present are of limited usefulness, however, because if the therapeutic dose fails to cause abortion, surgical abortion becomes mandatory inasmuch as these drugs cause malformations in the surviving embryo.

Among those who have been working in the field of mammalian reproduction in the past, there may not be very many who would be suitable for the staff of the Research Institute. Dr. Chang of the Worcester Foundation has impressed Dr. Doering exceedingly well, and the possibility that he might be both suitable and interested should be explored.

At some point it will have to be decided by the Members of the Research Institute whether the Institute for Problem Studies shall concern itself with those problems of birth control that are peculiar to developed countries where there is no real emergency. In a sense these problems are peculiarly tempting because in thinking about them we think about our own future. For this reason these problems are even more controversial than those which relate to underdeveloped countries. What might these problems be?

Looking into the future, one is tempted to predict in developed countries that the method chosen for population control may one day be the cutting of the vas deferens. This method was not satisfactory in the past because it is irreversible,

and one would not ever want to preclude any man, permanently, from the possibility of begetting children. Today, when sperm can be preserved indefinitely at liquid-air temperature, we may predict that sperm banks will be established at some time in the future, and that such banks will carry on deposit the sperm of men who have had, say, 3 children and who subsequently chose to have the vas deferens cut. If they should decide later on, that they wanted to have more children, they could always draw on their deposit.

From such a practice there is only one step to a new social custom which, if it does develop, might mark the beginning of a new chapter in human evolution.

Artificial insemination, which is frequently practiced today because often a couple cannot have children on account of the sterility of the husband, is practiced in the most primitive fashion - as a "blind date." The choice of the sperm which is used is that of the doctor, and the woman has no control over what type of man the father of her child shall be.

When sperm banks come to be established, sperm may be sold on the basis of a detailed catalogue and women who wish to conceive through artificial insemination may pick the type of man whose child they wish to bear. Clearly this could be the beginning of a rapid eugenic development of mankind. The direction of the development would not be controlled by any preconceived notion of the authorities (who may think they know what kind of men they want to breed), but rather by the preferences of the women who would follow their "instincts."

As far as we know, there might be no inherent reason - apart from deeply ingrained custom - why a woman should look for the same qualities in a man whom she may want for a husband, as in a man whom she may want for the father of her child.

The study of the behavior of sperm, which may open up vistas toward practical applications of great importance, might be regarded as a branch of microbiology. (Some of the methods which might be used in such a study, as well as the kind of men who might use them, will be described in Section II under the label "Protein Synthesis.") What are these vistas?

The sperm is haploid (i.e., it carries one set of chromosomes), and it might be possible to separate in a sperm population the sperm carrying a Y chromosome from the sperm carrying no Y chromosome. This would mean that we should be able to change the sex ratio in the offspring, a possibility that could provide us with a novel means of achieving a really satisfactory solution to the population control problem in the United States.

It is likely that in the United States, with increasing economic security and prosperity, we shall have a steady and rapid increase in the population - even when all families achieve control over the family's size. People who are wealthy and secure want to have more children - so it would seem - than is optimal from the point of view of the country as a whole. To discourage them, by punitive taxation, is hardly reconcilable with one of the as yet unformulated basic human freedoms - the freedom to breed. The community could try to correct this tendency to overbreed by making life so attractive for bachelors that the marriage rate shall fall. This, however, would be somewhat unfair to the women! For, as Lichtenberger has said, "All women should get married, but no man."

One "natural" solution to this problem is to change the sex ratio. Many families may desire to have two sons and one daughter, and presumably an over-all ratio of 1.5 to 1 would solve the problem of an excessive proliferation of the population in the United States. The excess men would remain bachelors. This excess would raise the value of girls, and the law of supply and demand would lead to a stable, "optimal," ratio without any interference with individual freedom. Quite on the contrary, we would have created a new basic human freedom hitherto undreamed of -- the freedom of choosing the sex of one's children.

Clearly these observations about the law of supply and demand must be taken with a grain of salt. The ratio of boys and girls might be stabilized at a high level where so few girls would be born that the population would decline fast. In that case presumably a law would have to be passed limiting the supply of sperm that is enriched

in Y chromosomes. Frankly, it is difficult to know what one would do about the bootlegging of such sperm, and one is somewhat reminded of the story of Daedalus and Icarus. Still, we have no choice, I believe, but to brave "the brave new world."

I am told that experiments on rabbits carried out at the University of California in Berkeley have demonstrated the possibility of shifting the sex ratio, but I have not as yet seen the relevant paper. The economic importance of changing the sex ratio in cattle would be very great, for one could increase the ratio of cows to bulls.

II. Protein Synthesis: An area of fundamental biological research which is of great intrinsic interest, and has therefore strong attraction for the kind of scientists whom we would want to see active in the Institute, might be somewhat sloppily labeled "Protein Synthesis." The men active in this field, whom we have in mind, are those who participated in the revolution that occurred in the field of microbiology in the last fifteen years.

In the early phases of this development the interest was mainly centered on sexual processes in bacteria and viruses. Among the most productive men in this field are Joshua Lederberg, Professor of Genetics at the University of Wisconsin (about 30 years of age), and François Jacob, M.D. (perhaps 35), at the Institut Pasteur. Both are very much concerned with the problems of our times in addition to being passionately interested in fundamental problems in biology. The Research Institute would greatly benefit, in my opinion, if one of these two would join the staff.

Some of the participants in the above revolution have recently shifted their interest to animal cell cultures. They have also started a revolution in this field - which has been stagnant (under the care of the classical tissue-culture specialists) ever since Carrel. One of them, notably Renato Dulbecco, M.D., made use of animal cell cultures to develop new methods for studying the growth of animal viruses, such as for instance the poliomyelitis virus, and his work has opened up new possibilities

in this field. Two others who moved into the animal cell culture field are T. T. Puck, Department of Biophysics, Medical School, University of Colorado, Denver, and L. Siminovitch, Connaught Medical Research Laboratory, University of Toronto. It might be advisable to have one representative of this group join the Institute.

A few others who started out in pure microbiology are now shifting their interests to various aspects of the problem of protein synthesis. In particular they want to find out in what manner antibodies are formed and how "delayed sensitivity" is produced. Usually the field of antibody formation is labeled "immunology" and the study of delayed sensitivity is labeled "allergy." Of these two related areas the layman is more familiar with immunology, i.e., the formation of circulating antibodies in response to infection, rather than with the appearance of delayed sensitivity which is responsible for the fact that a skin transplanted from one individual to another will be rejected - after an initial period of healing - unless the transplant is made from one identical twin to another.

New methods which have become available should make it possible to make a concerted attack on the problem of antibody formation and the production of delayed sensitivity. In either case a specific chemical substance is presumably produced in response to the injection of an "antigen." The question how the animal accomplishes this feat is of great intrinsic interest and might furnish a clue to the basic problem of protein synthesis. In the following are listed the names of some of those whose interests are now shifting in this direction:

a) Mel Cohen, microbiologist. Assistant Professor in Kornberg's department in St. Louis. He has been working on adaptive enzymes in bacteria and is now writing a book with Jacques Monod on this subject. Lately he has begun to work on the formation of antibodies.

b) Ed Lennox (35 years old), a physicist turned into a very successful biologist. He worked on transduction in coli, decided last year that he must learn more biochemistry and spent a year with Gunsalus in the Department of Biochemistry at the

University of Illinois, Urbana. He now has decided to work on the problem of the formation of antibodies. Lennox has been offered a position in the Department of Biochemistry at Urbana and might stay there for the next few years unless he is enticed away.

Mel Cohen and Ed Lennox are in close touch with each other and want to arrange a meeting of a number of younger "rebels" who wish to take a new look at the problem of antibody formation.

c) Howard Green, M.D., worked with Herb Anker in the Department of Biochemistry in Chicago on antibody formation. He was for one term Assistant Professor in the Department of Pharmacology, at the Medical School of New York University, where he worked on adaptive enzyme formation in coli. He then joined the Army Medical Corps (under the doctors' draft) and worked on the Medawar phenomenon. He is now an Assistant Professor in the Department of Pathology of New York University Medical School and works on delayed sensitivity.

d) Donald Steiner, M.D., just finished medical school. He is now serving an internship and, therefore, will not be available for a year. Developed (with Herb Anker) an ingenious method for obtaining antibodies in vitro and is very highly regarded.

A few words may be said on the possible practical applications of the kind of basic research which attributes the type of men here named:

1) Advances in the field of immunology or allergy might open up new avenues for looking for a cure for cancer. The reason for saying this is as follows:

Malignant tumors are very frequently found at autopsies in persons who died of some other cause and in whom the growth of the malignant tumor was clearly arrested. This natural resistance to cancer might well be due to a natural immunological response, and the overt disease "cancer" might well be due to the breakdown of this immunological defense.

Since the problem of cancer is a difficult one, one man's guess may be as good as another's concerning the most promising approach to it. Still, if I had to bet on where the solution is going to come from, I should bet on the immunological approach rather than on the approach (heavily emphasized at present) which looks towards a chemotherapy of cancer.

Because of the great attention that the search for a cure for cancer is already receiving, I am inclined to think that the Institute for Problem Studies should concentrate on other fields. However, if some unexpected advance, made in the field of "immunology and allergy" in the Research Institute should open up a new avenue, one would not want to discourage a Staff Member of the Research Institute from pursuing a lead opened up by his discoveries.

2) The field of "immunology and allergy" is presently developing fast. It has been recently shown, for instance, that 10 mg. of bovine serum albumin injected into a newborn rabbit will impair the ability of that rabbit to form antibodies against bovine serum albumin. It is thus possible to make the rabbit "tolerant" against this antigen.

Whether a newborn baby is young enough to be made tolerant in this manner is now being investigated. In the somewhat unlikely case that newborn babies are "young enough" there would arise a number of interesting possibilities. I shall mention one of these, as an example. One type of mental defect is due to a disease of the newborn - erythroblastosis foetalis. This disease occurs because Rh-positive red cells of the infant evoke the production of antibodies in the mother, who is Rh-negative. If it should turn out that in man, as in rabbit, it is possible to impair the ability of the individual to form antibodies against an antigen by injecting that antibody within a few days after that individual is born, then it might be possible to get rid of erythroblastosis foetalis altogether. One would merely have to inject the newborn girls -- if they are Rh-negative -- with Rh-positive blood and thereby establish tolerance.

There is even a remote possibility that this field may conceivably have some bearing on the problem of birth control. The foetus may be regarded as a homo-transplant. It does not sensitize the mother and the transplant is not rejected, perhaps because the sensitizing agent of the foetus can not get through the placenta. If the mother is however sensitized against the foetus - by receiving a skin transplant from the "father" -- and if the substances thus evoked in the mother are able to pass the placenta, then it is conceivable that an early abortion may occur. This, admittedly, is a remote possibility, but arrangements are now being made with Dr. Howard Green for testing this possibility in rabbits. We mention this here mainly in order to emphasize the diverse connections that might unexpectedly appear between advances in "immunology" and some of the major unsolved problems in public health.

3) The new techniques of studying virus growth in animal cultures have opened up the possibility of developing new powerful methods in the search for a chemo-therapy for certain virus diseases. Some work along these lines might be carried out at the Research Institute but it is not likely that the Institute for Problem Studies needs to be concerned with this problem. Because of the obvious commercial interest of drugs capable of curing virus diseases, the pharmaceutical industry is likely to take over as soon as the practical significance of the advances becomes apparent.

* * * * * * * * * * *

From the point of view of staffing the Research Institute it might be well to keep an eye on the development of modern microbiology. Because this field is rapidly progressing, talent can be recognized at an early age. The names listed below represent a pool of younger men on which we might draw when the need arises. All these names are taken from the field of modern microbiology.

a) Seymour Benzer, a physicist turned into a very successful biologist. At present at Purdue University, studying the nature of mutations in bacteriophage with a view to learning something about the relationship between DNA and protein synthesis.

b) Al Garen, originally a physical chemist, at present working with Benzer but along his own lines of research. Previously he was at Cold Spring Harbor and, while there, he collaborated with Zinder in the Rockefeller Institute. Their joint work on lysogenic viruses is a very nice piece of work, along much the same lines as some of the work of Jacob.

c) Norton Zinder, microbiologist, is at the Rockefeller Institute. Discovered transduction jointly with Lederberg. Was the first recently to prepare protoplasts in coli.

d) Maurie Fox, physical chemist. At present at the Rockefeller Institute. His present experiments concern the transformation of pneumococci. Mainly interested at present in learning something about the role of RNA and DNA in protein synthesis.

e) Milton Weiner, M.D. Started out in microbiology, working on adaptive enzymes with Aaron Novick. His interest is now veering toward animal cell cultures. Will join next year the Department of Pharmacology at the Medical School of New York University.

By going beyond my own immediate experience and beyond the field of microbiology I could probably expand the list five-fold. This would only need an inquiry conducted for a few weeks with this purpose in mind. We might thus assemble perhaps fifteen names of younger men who have a broad spectrum of interest in fundamental biological problems and who are likely to be attracted by projects which relate to biological problems of public importance.

III. Fat Metabolism and Coronary Disease: Our knowledge of fat metabolism in mammals is very limited. Fat metabolism is not without intrinsic interest and therefore a few men on the staff of the Research Institute might well work in this field. The Institute for Problem Studies might also concern itself with this problem - because of its great practical importance to coronary disease in the United States. If the Institute takes up this problem, the staff of the Research Institute would almost certainly wish to guide the explorations of the Institute for Problem Studies in this field.

There has been much public discussion of this topic for a numver of years but no concerted effort devoted to a really promising approach. Rather there was a strong emphasis on trying to establish the predictive value of a high blood cholesterol level, for individual middle-aged men. This is a rather unproductive approach - at least from the point of view of the major public health problem involved. Concerning this major problem hopes have been raised through the following observations:

1) The coronary death rate in Norway fell by perhaps 30% within 18 months after the Germans occupied the country, during the last war, and consumption of animal fats dropped to about half.

2) The blood cholesterol level and the level of beta-lipoproteins appear to be low in population where fat consumption is low, and so is the coronary attack rate.

3) Bronte-Stewart and his co-workers report that the blood cholesterol level can be lowered - temporarily perhaps, but conceivably permanently - by adding unsaturated vegetable oils to the diet.

On the bais of these observations - which needless to say do not permit the drawing of any conclusion - some people hope that by cutting down the fat consumption to perhaps 10% of the caloric intake (or to about 20 gm. of fat a day), a middle-aged man can appreciably reduce his chances of suffering a coronary attack. Others hope that he can accomplish this even though he maintains his total fat intake at perhaps 40% of the caloric intake (or 80 gm. of fat per day), provided only that this additional fat intake is in the form of unsaturated vegetable oils.

If the Institute for Problem Studies were to concern itself with this problem, and if it succeeded in bringing about a concerted effort to settle it, we could have the answer to all the relevant questions probably within five years. This would involve::

a) Animal experiments to determine the effect of various diets on both blood levels and athero-sclerosis;

b) Clinical experiments on groups of a few hundred patients with a coronary history who would volunteer to go on a prescribed, tightly controlled diet and whose blood levels would be closely followed, as well as their survival rate;

c) Observations on large groups of volunteers (of the order of 20,000 men or more) who agree to modify their diet, if so requested, or to remain on their old diet for 18 months, if asked to do so. Blood tests on samples of these volunteers would indicate how much "cheating" goes on, and the survival rate would be followed. Significant results could be available at the end of a five-year period.

IV. The Effect of Cigarette Smoking on Longevity: I have reason to believe that some of the large life insurance companies have some difficulty in investigating this topic themselves and that they would be glad to co-operate with some such organization as the Institute for Problem Studies. With their co-operation this particular issue could be settled within three years.

It is conceivable that we could, with the co-operation of a large insurance company, settle within a five-year period some more refined questions of great practical importance, such as:

a) Can a middle-aged man who stops smoking cigarettes thereby decrease his age-specific death rate, and if so, how fast would such an effect take hold?

b) Is there any relevant difference between the effect of smoking cigarettes with and without filter tips?

The Institute for Problem Studies need not enter this field of vital statistics, if other suitable organizations are willing to carry the ball. This Institute could, nevertheless, takes an interest perhaps in the relevant problems of experimental psychology. Should it turn out that cigarette smoking is as dangerous as it now would appear, the Institute might possibly take a hand in finding methods for making adolescents psychologically immune to the pressures inducing them to take up cigarette smoking.

Assuming that the parents want their children to be immune, and the children

themselves are willing to be made immune, are there any psychological tools that will accomplish this? Hypnosis, for instance, does not seem to be very effective when used to break the habit of smoking - but would it be effective if used to condition children against taking up smoking? These are questions which to some extent can be decided by experiment, and such experiments might interest some of the staff of the Research Institute itself.

V. Advances in Neurology - Pharmacology of the Nervous System - Mental Health and Sleep: Some recent advances in neurology seem to attract a number of imaginative younger men and therefore it might well be that some work in the Research Institute might be carried out in this field. Advances in the field are likely to find practical applications also.

One of the advantages which the Institute offers to its staff is an opportunity to pursue really imaginative and unconventional goals. Such a pursuit is rarely encouraged in the existing type of research institutes. Among several possibilities in this regard we wish to mention one which might soon come within the reach of available methods: the elimination of sleep.

Because during evolution the best use for the hours of darkness consisted in spending the time asleep, we have developed biological mechanisms forcing us to sleep about eight hours a day. There is no evidence that sleep fulfills an inherent biological function other than doing obeisance to a built-in mechanism that compels us to sleep. Perhaps no greater enrichment of human life could be brought about, at a single stroke, than getting rid of the tyranny of sleep (at least for extended periods of time, when other forms of activity could be substituted to great advantage).

The only one among the younger men of real ability who, to my knowledge, has shown an interest in the problem of sleep, is Maurie Goldstein, M. D. During the past two years he was attached to the Army Medical Corps (under the doctors' draft) and while serving there he worked with a group of neurologists on sleep. He might be a valuable addition to the staff of the Research Institute - whether or not he wants to

continue to work on sleep - because he is an excellent mammalian physiologist. Most of his past research was in carbohydrate metabolism and he worked in this field at the Michael Reese Hospital in Chicago before he entered the Army Medical Corps. He is Assistant Professor in the Department of Physiology at the University of Chicago.

If it is desired that the Research Institute shall be active in the field of neurology we probably ought to consider, among several other young men, James Olds, at present at the Medical School of U.C.L.A., who has made a remarkable discovery related to the electrical stimulation of certain regions of the brain in rats.

VI. The Problem of Aging: The general phenomenon of aging is of great intrinsic interest and it is therefore possible that some of the men in the Research Institute might want to work on the aging of mammals. I do not think it likely, however, that the Institute for Problem Studies will set up a "project" on aging, at least not until there are some really good leads. No such leads have so far been detected - to my knowledge.

In the last few years there has been an enormous amount of talk on the subject, and there is pressure on the U. S. Public Health Service to go into this field in a big way. But at the same time there is a conspicuous dearth of ideas.

Problems Outside the Field of Public Health -- in the Institute for Problem Studies

The advances of science occasionally create problems which may require for their solution advances in the realm of political thought. Advances in the field of public health have led to a rapid fall in infant mortality and thus to overpopulation in Southeast Asia, and this is probably the most important single cause blocking the path of these areas toward progress. It is conceivable that if the overpopulation problem were solved by the development of an adequate method of birth control, these areas would be on their way toward a rapid, orderly industrial development.

Infant mortality is now also beginning to fall in a number of British colonies and former British colonies in Africa, but clearly in these areas overpopulation is only one of several major obstacles that must be overcome. How to achieve political stability in African colonies which are about to receive self-government is another of these problems. And the dearth of men who possess the qualifications needed for the administration of such areas poses a related problem calling for a solution.

The development of underdeveloped areas is likely to be of concern to the Members of the Research Institute, and they may want the Institute for Problem Studies to deal not only with the issue of birth control, but to give attention to all major aspects of the problem. This may cause the Institute for Problem Studies to venture beyond the field of public health and into the area of "political thought." With this possibility in mind it is suggested in the Memorandum that, if the Institute is not limited by charter to the area of public health, then it may, with the approval of two-thirds of the Affiliate Members and two-thirds of the Board of Trustees, attempt to take up certain problems outside of it.

In the following I shall discuss in some detail - as an example - a problem in the area of "political thought" that appears to be of major importance for certain underdeveloped areas. I shall try to examine why no real progress has been made

toward the solution of this problem and to describe what procedures the Institute for Problem Studies could adopt if it were to take up this problem.

The underdeveloped areas which have recently achieved self-government, and those which may achieve self-government in the near future, can develop successfully only under a governmental system that will assure them a certain measure of political stability. Clearly it is desirable that these areas be administered with the assent of those governed and be - in this sense at least - under a democratic government. There is grave doubt, however, whether the parliamentary form of democracy is a suitable form of democracy for many of these areas. Yet, in spite of this doubt no other forms of democracy that might be more suitable have ever been devised and adequately examined, let alone tested.

If such forms of democracy were devised, there might be an opportunity to try some of them out in the next two generations in Africa, where one colony after another may be expected to be given self-government by England.

There would be no need for the Institute for Problem Studies to concern itself with this problem were it not for a certain lack of leadership on the part of our universities in the general field of "political thought." Why social scientists in our universities have not tackled this problem, and why none of the foundations has set up any project adequate to fill this gap, is not clear. Perhaps the explanation lies in the fact that in the social sciences too much emphasis is being placed today upon "research." Problems that do not require "research" but require thought and reflection are therefore frequently neglected.

Unfortunately, the areas where insight can be gained through research in the field of social studies are, by and large, the unimportant ones, and thus their current predilection for "research" leads many social scientists to work on unimportant problems. Many of them are more interested in methods than in results, and clearly we cannot turn to this type of social scientist if we wish to gain insight into certain important problems. In the circumstances we may have to make a new start and to begin

pretty much where Plato has left off. Who could do this work?

In America, the study of the humanities has tended to wither away, and it might therefore be impossible to find enough men who are led by inclination to think about the kind of problem here described. Accordingly it may be necessary, in order to assemble perhaps 10 to 15 scholars who may wish to work on the problem, to go beyond the confines of the United States and look for additional men abroad, particularly in England where there exists more of a tradition of "political thought."

If the men who are needed can in fact be found, the Institute for Problem Studies might bring them in on a full-time basis for a limited period of time, perhaps three months, in the hope that they might come up with convincing answers. The same group of men, perhaps with slight variation in membership, might be gathered repeatedly, for a period of three months each, over a period of perhaps two years. It is not likely that there will be any universal answer; the form of democracy which appears best suited for governing a given underdeveloped area, where the problem has arisen or is about to arise, might not be suitable for another such area. For this reason it seems probable that in the more advanced phases of this study it will be essential to obtain the participation of men who know from personal experience the political and administrative difficulties that have arisen in areas emerging from the colonial status.

If the Institute for Problem Studies is in a position to offer "solutions" to this problem, it would presumably want to promote the "field test" by acquainting the British Colonial Office with its work. Perhaps the British Colonial Office - having been forced in the meantime to recognize that there is a need - might be willing to try out new political systems in the colonial areas which are about be be given self-government.

* * * * * * * * * *

The following is another example of an inquiry that the Institute for Problem Studies might effectively conduct. It relates to the problem described above and is, in fact, part of it.

One of the main problems in many underdeveloped areas is the scarcity of qualified men on whom the elected officials may lean for the administration of governmental operations. To build up a civil service utilizing native talent will take a long time. Accordingly, it would greatly help if, in the meantime, the governments of underdeveloped countries could obtain on loan for limited periods qualified men to fill the gap. A beginning has been been made in this regard by the Technical Assistance Administration of the UN. Could one go further and create an adequate international civil service, say under the auspices of the United Nations, that could loan its members to governments of countries which ask for such help?

Clearly it is impossible to answer this question without first determining by an inquiry -

a) is it possible to persuade men who have the required qualifications to enter such civil service as a lifetime career, and

b) what would it take to make such civil service attractive to the kind of men in the United States and other politically developed countries who have the desired qualities?

The United States has a large number of men who are attracted by public service. There have been, for example, many able young lawyers who have entered government service in the past 25 years and who after a number of years of distinguished service found that serving the government is not a satisfying lifetime career in the United States. They then reluctantly left the government to go into private practice. But those who are of a certain bent of mind find private practice devoid of the kind of satisfaction to be derived from public service. Thus it would seem that there is a wealth of human material upon which an international civil service could draw in this

country if it offered a satisfactory lifetime career. The same might hold for other politically developed countries.

There are serious difficulties, however. In such an international civil service a man would be abroad most of the time and could not count on staying longer than perhaps five years in any one country. Wives do not like to be shifted around in this manner, and the schooling of the children presents a major problem. Would the idea of an international civil service founder on such difficulties? Or could such a service draw, to some extent, on a dedicated minority?

A discussion of these topics which I recently had with Sir Robert Jackson (former Associate Director of UNRRA and the man in charge of the huge Volta dam project on the Gold Coast) leads me to think that there is an increasing general awareness of the problem here discussed. It is therefore conceivable that if the Institute for Problem Studies were able to make practical proposals to the governmental agencies which are in a position to take appropriate action, such proposals would not fall on deaf ears.

The End

MEMORANDUM Jan 15/57

Apart from Hahn's discovery of the fission of uranium, the possibility of a chain reaction rests on two discoveries - a) that in the fission process uranium emits neutrons, and b) that it is possible to find a system in which the neutrons can be slowed down without losing too many neutrons through absorption.

The neutron absorption of uranium was discovered independently and at about the same time by Joliot and his co-workers; Fermi and his co-workers, and by Szilard and Zinn. (See Szilard and Zinn Physical Review 1939). The possibility of maintaining a chain reaction in a system composed of uranium and graphite was to my knowledge first stated and discussed in detail in a paper sent by Szilard to the Physical Review in February 1940. This paper remained unpublished because of the necessary secrecy but the corresponding government report, Report A 55 of the Uranium Committee, has been de-classified. This chain reacting system is also described in the U.S. Patent No 2,708,656 which has been issued in the name of Fermi and Szilard to the Atomic Energy Commission according to the attached clipping from the New York Times.

Fermi received an award of $25,000 from the Atomic Energy Commission shortly before his death; Szilard received no financial compensation for the invention which he assigned to the Government, beyond a compensation for his actual expenses which amounted to less than $16,000.

May 24, 1957

Memorandum on an experiment concerning antibody Formation

By Leo Szilard

The Enrico Fermi Institute for Nuclear Studies
The University of Chicago, Chicago, Illinois

In the following is described an experiment which is easy to perform and which, I believe, is crucial from the point of view of enabling us to decide between various alternative theories that are related to antibody formation. There are two variants of basically the same experiment which are designed to give information on two different questions.

(1) A rabbit is fed with radioactive glycine, and while kept on this diet is injected with bovine serum albumen in order to ellicit a primary response. An appreciable amount of antibody would be formed on about the 8th day after injection. In the experiment proposed, a group of, say, twenty rabbits are used, all of whom are injected with the antigen on the same day. Three of these rabbits are injected one day after the primary injection with a sufficient quantity of anti-bovine serum albumen rabbit serum obtain from a separate group of rabbits. Another group of three is injected with such anti-serum on the second day after the primary injection. A third group of three rabbits is injected with such anti-serum three days after the injection, and so forth.

In this experiment the purpose of injecting anti-bovine serum albumen rabbit serum is to remove the circulating antigen, and the object of the experiment is to determine in what manner this premature removal of the antigen affects the primary response.

(2) A rabbit is immunized against bovine serum albumen or bovine serum globulin -- perhaps by repeated injections -- and to the point where the rabbit shows a consistent level of combining the antibody against the antigen. After that level has been established, rabbit anti-serum against the antigen (obtained from a different rabbit) is injected in an adequate amount. The purpose of this experiment is to see whether the injection of anti-rabbit serum again antigen will affect the level of the (radioactive) antibody that the rabbit had sustained prior to having received the injection of rabbit anti-serum.

May 27, 1957

Memorandum on Control of Enzyme Level and Antibody Formation

by Leo Szilard

The Enrico Fermi Inst. for Nuclear Studies
The University of Chgo., Chgo., Ill.

1) The need for assuming a trigger

It is difficult to see, unless one assumes a trigger, where a vector, R, can carry argine, citroline or ornithin, how raising the arginine concentration could repress enzyme production. The value of K for the combination of arginine with the enzyme must be high. How high can be estimated from the consideration that we have 100 to 1000 enzyme molecules per bacteria, these enzyme molecules have an equilibrium constant, K_E, with the arginine molecules carried by trinucleotides (K_E is about thirty times higher than K), and we may demand that the enzyme molecules do not interfere appreciably with protein synthesis by combining with the trinucleotides that carry arginine.

$E = 100$/cell

$\rho_E = \frac{1}{6} 10^{-6}$ (mol/l)

Postulate

$$\frac{\rho_E}{K_E} < \frac{1}{10}$$

$K_E > 10\,\rho_E$

$K > \frac{1}{3}\rho_E$

$K > \frac{1}{2} 10^{-7}$

$K = \frac{1}{30} K_E$

1000/cell

$\rho_E = \frac{1}{6} 10^{-5}$

$K > \frac{1}{2} 10^{-6}$

Another consideration that permits setting a lower limit for K, the equilibrium constant between "arginine" and the enzyme, E, which makes arginine, is as follows:

We assuming 100 molecules per bacterium, and assuming that all of the enzyme molecules is saturated with arginine, we must produce in ~~30 minutes per cc~~ 3×10^{16} arginine molecules per cc per second on the following assumptions: $\frac{1}{10}$ of the met weight is protein and $\frac{1}{20}$ of the protein is arginine". — i.e 1 cc of bacterium contains 1/100ths gram of "arginine". ~~From this it follows that one arginine-enzyme complex must evaporate 600 arginine moles per second, and from this it follows that K must be~~

$K \geq \frac{3}{2} 10^{-8}$

(and therefore per minute the amount of arginine made per cc is $\frac{1}{100}\frac{1}{30}$ gm. —

per sec per cc $\frac{1}{100}\frac{1}{30}\frac{1}{60}$ gm

$\frac{1}{100}\frac{1}{30}\frac{1}{60}\frac{1}{100}$ gm mol $\cong \frac{1}{2}10^{-4}\,10^{-3}\,10^{-7} = \frac{1}{2}10^{-14}$ gm mol

$\frac{1}{4}$ $6\times10^{23}\,\frac{1}{2}\,10^{-7}$ ~~or $3\,10^{16}$ (molecules)~~

per cc per sec. —

or per enzyme (compolexed) $\left[\frac{10^{-9}}{6}\right]$ 10^{14} enzyme molecules / cc

300 per sec per E-A complex

$2AK = [10^{B}\cdot e^{-\frac{Q}{RT}}]_{\text{enzyme rate}} \geq 300$

XX $2AK \geq 300$

$K \geq \frac{300}{} = 3\,10^{-7}$ $\quad \sigma\rho = 10^{-16} \quad A = 10^{9}$

If we now tentatively assume that citrolin enhances the formation of the enzyme, E, by combining with the enzyme which is in statu nascendi, then for arginine to repress the enzyme formation it would be necessary to assume that arginine can successfully compete with citrolin for the enzyme.

$$\frac{1}{1 + \frac{S_{cit}}{K_{cit}} + \frac{S_{arg}}{K_{arg}}} \quad \Big| \quad \frac{S_{cit}}{K_{cit}} \quad \Big| \quad \frac{S_{arg}}{K_{arg}}$$

If conc. of Arg = 1 mgm/l = $\rho_{Arg} = 10^{-5}$ mol/l

I assume that $K_{cit} < K_{arg}$ is possible.

Still such competition is possible.

Alternative theory that trypsin acts on template would explain otherwise that antigen keeps on producing antibody; yes it destroys template so that deformed enzyme (the antibody!) is then released.—

Enzyme Induction and Repression
(Scheme No. 2b)

We obtain a modification of the Scheme No. 2 if we assume that free templates produce the enzyme at some rate, $\frac{1}{\tau(0)}$, and templates which are combined with $I^*(1)$ produce the enzyme at a lower rate, $\frac{1}{\tau(1)}$. In this modified theory $I^*(1)$ is not an inducer but a repressor and what may appear as an inducer is a weak repressor. In addition to reactions a), b), c), and d), we have here

e) $T + n_i AA_i \longrightarrow (T\text{-}E)$; rate of this reaction: $\frac{1}{\tau(0)}$

and

f) $(T\text{-}E) \longrightarrow T + E$

In this modified Scheme No. 2, the rate of enzyme production, s, is given by

$$s = \frac{1}{\tau(AA) + \tau(0)} \frac{1}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \frac{1}{\tau(AA) + \tau(1)} \frac{\frac{C_1}{K_1}}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} +$$

$$\frac{1}{AA + \tau(2)} \frac{\frac{C_2}{K_2}}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \ldots$$

Enzyme Induction and Repression.
(Scheme No. 2b)

We obtain a modification of the Scheme No. 2 if we assume that free templates produce the enzyme at some rate, α_0, and templates which are combined with $I^*(1)$ produce the enzyme at a lower rate, α_1. In this modified theory $I^*(1)$ is not an inducer but a repressor and what may appear as an inducer is a weak repressor. In addition to reactions a), b), c), and d), we have here

e) $\quad T + \sum_i n_i AA_i \longrightarrow (T\text{-}E)$; rate of this reaction: α_0

and

f) $\quad (T\text{-}E) \longrightarrow T + E$

In this modified Scheme No. 2, the rate of enzyme production, δ, is given by

$$\delta = \frac{\alpha_0}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \frac{\alpha_1 \frac{C_1}{K_1}}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \frac{\alpha_2 \frac{C_2}{K_2}}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \ldots$$

Enzyme Induction and Repression

(Scheme No. 2; repressors are weak inducers)

a) $I + R \longrightarrow (I\text{-}R) = I^*$, which we call the <u>real</u> inducer.

b) $T + I^* \longrightarrow (T\text{-}I^*)$; equilibrium constant of this reaction: K

c) $n_i AA_i + (T\text{-}I^*) \longrightarrow (E\text{-}T\text{-}I^*)$; for a given inducer concentration the rate of this reaction, $s = \frac{1}{\quad}$, depends on the concentrations of the amino acids AA_i, on K and on (I).

where $(E\text{-}T\text{-}I^*) = \begin{matrix} E & Y \\ T & R \end{matrix}$

d) $(E\text{-}T\text{-}I^*) \longrightarrow E + (T\text{-}I^*)$;

1.) $\frac{1}{s} = T = \frac{(AA) + (I)}{q}$; $q = \frac{(E\text{-}T)}{(T) + (E\text{-}T)} = \frac{\frac{C}{K}}{1 + \frac{C}{K}}$

where C is concentration of I^*

2.) $\frac{a}{b} = \frac{(AA) + (Ia)}{(AA) + (Ib)} \frac{qb}{qa}$

If there are a number of real inducers I^*_1, I^*_2, ... present in concentrations C_1, C_2, ... , for which the equilibrium constants for reaction b) are K_1, K_2, ... , then for a fixed conc ntration of the amino acids, AA, and all other things being equal, the rate of enzyme production, s, is given by:

$$s = \frac{1}{(AA) + (1)} \frac{\frac{C(1)}{K(1)}}{1 + \frac{C(1)}{K(1)} + \frac{C(2)}{K(2)} + \ldots} + \frac{1}{(AA) + (1)} \frac{C(2)}{1 + \frac{C(1)}{K(1)} + \frac{C(2)}{K(2)} + .}$$

Enzyme Induction and Repression

(Scheme No. 2; repressors are weak inducers)

a) $I + R \rightleftharpoons (I\text{-}R) = I^*$, which we call the real inducer.

b) $T + I^* \rightleftharpoons (T\text{-}I^*)$; equilibrium constant of this reaction: K

c) $\sum_i n_i AA_i + (T\text{-}I^*) \longrightarrow (E\text{-}T\text{-}I^*)$; the rate of this reaction depends on the concentrations of the amino acids AA_i, and on K and on $\tau(I)$.

where $(E\text{-}T\text{-}I^*) \equiv$ E ~ y, T ~ R

d) $(E\text{-}T\text{-}I^*) \longrightarrow E + (T\text{-}I^*)$;

The relative rates of enzyme production are independent of the concentrations of the amino acids AA_i.

If there are a number of real inducers I^*_1, I^*_2, ... present in concentrations C_1, C_2, ... , for which the equilibrium constants for reaction b) are K_1, K_2, ... , then for a fixed concentration of the amino acids, AA, and all other things being equal, the rate of enzyme production, S, is given by:

$$S = \frac{\alpha_1 \frac{C_1}{K_1}}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \frac{\alpha_2 \frac{C_2}{K_2}}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \ldots$$

$$S = \frac{1}{\tau(AA) + \tau_1} \frac{\frac{C_1}{K_1}}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \frac{1}{\tau(AA) + \tau_1} \frac{\frac{C_2}{K_2}}{1 + \frac{C_1}{K_1} + \frac{C_2}{K_2} + \ldots} + \ldots$$

1) $\frac{1}{S} = \tau = \frac{\tau(AA) + \tau(I)}{q}$; $q = \frac{|E\text{-}T|}{|T| + |E\text{-}T|}$

2) $\frac{\tau_a}{\tau_b} = \frac{\tau(AA) + \tau(I_a)}{\tau(AA) + \tau(I_b)} \frac{q_b}{q_a}$

where c is conc. of I^*

Remark to memorandum of May 27th

If we now ~~assume~~ take alternative 1), A or B, and assume that the concentration of the amino acid is 10^{-5} molar when the wild type grows in minimal medium (this corresponds to 1 milligram per liter amino acid if the molecular weight of the amino acid is 100). and if we further demand that by reducing the level of the amino acid the rate of production of an enzyme should rise one hundredfold ~~so that we have~~ then we have $\frac{\rho}{K} \approx 100$

~~And~~ Then we have ~~$\rho = 10^{-5}$~~ for $\rho = 10^{-5}$ m/l

$K = 10^{-7}$ m/l

assume $\rho = 10^{-4}$ Molar !

for tryptophane !

$\rho_{tr} \gg 500\,\gamma$/liter $= \frac{500}{100} 10^{-6}$/l $= 5\,10^{-6}$

Tryptophane is 1% of Protein!

$\rho_{Pr} \gg 2.5\,10^{-5}$

1% NaCl is 10 gm/liter

Molecular ~~25~~ $\frac{35}{23}$ $\frac{}{58}$

$\frac{20\text{ gm}}{30.}$

$3\,10^{-1}$ Molar

$\rho = 10^{-4}$ would permit easily 1000 compounds

Introduction to memorandum of May 28th, 1957.

We shall consider two main alternatives in which the rate of the production of an enzyme may be regulated in the cell.

Alternative 1

Here we assume that a metabolite, say, the fundamental amino acid is coupled to a carrier, a multinucleotide, which can combine with the template. This combination we shall call a trigger, and precursors of the amino acid as well as postcursors of the amino acid when attached to the same multinucleotide carrier form competing triggers. The competition is determined merely by the amounts of the different triggers present since the affinity of each kind of trigger for the template we shall assume to be the same. The rate at which the enzyme is synthetized -- assuming that the template is always saturated with these triggers -- may then be written as

Alternative 2

A) Here we shall assume that there is no trigger sitting on the template but that the amino acid or its precursors or postcursors are coupled to a carrier, and that the metabolite carrier complex has an affinity for the enzyme in statu nascendi while it is still attached to the template, and alternative B) which is the same as alternative A, except that we assume that the amino acid or its precursor or postcursor itself; ie. not attached to a carrier, will reversibly combine with the enzyme in statu nascendi while still attached to the template.

The difference between alternatives 1A and 1B becomes marked if we assume that along a single metabolic pathway leading to the amino acid and beyond there is only one coupled enzyme, E_o, which couples the fundamental amino acid to the carrier, and that from this the enzymes of

the cell, by acting on the metabolite moiety and leaving the carrier moiety untouched, can produce precursors and postcursors of the fundamental amino acid which remain attached to the carrier.

Mutations which require an amino acid for their growth

In the case of all three of these alternatives, an amino acid requiring strain can arise through mutations of three different kinds. A mutation may occur in the template which produces the enzyme which renders the template incapable of synthetizing a polypeptide chain. In this case, no functional enzyme is produced, no immunological analogue of the enzyme (CRM or P_Z) is produced, and no suppressor mutations can be found. We shall refer to mutations of this sort as type 1. Mutations of type 2 arise through alterations of the template that makes the enzyme which alter the polypeptide chain in such a way that one of the postcursors of the amino acid, which was a good enhancer of enzyme formation for the wild type, is not a good enhancer for the mutant of type 2. Such a mutant may be expected to produce an immunological analogue (CRM or P_Z) of the enzyme, and we shall expect to find suppressor mutations in which the production of this competing postcursor of the amino acid is low or absent. In the case of alternative 2, a mutant of type 2 might arise in still another way; namely, if the enzyme is so altered that the binding energy of the enzyme in statu nascendi is increased or the equilibrium constant is decreased for a postcursor of the amino acid which is a comparatively bad trigger.

A third type of mutants, which require amino acid for their growth, may be regarded as a reverse mutation occurring in a suppressed mutant oftype 2. Here the production of the enzyme is suppressed because there is an increased production in a postcursor which competes for the enzyme or for the template with triggers that are better triggers than this particular postcursor. We shall designate mutants of this type as type 3.

May 28, 1957

Memorandum on the Regulation of Enzyme Production, Suppressible Mutants, and the Behavior of Heterocaryons

By Leo Szilard

Introduction:

We shall consider three different ways in which the rate of enzyme production might be regulated.

Alternative 1

We may assume that an amino acid or a precursor of this amino acid, or post-cursors of the amino acid can combine with the enzyme which is on the template in statu nascendi, and that the enzyme metabolite complex ~~depending on the metabolite it contains~~ will evaporate from the template at a rate which is different for the different metabolites.

A suppressible mutant, type 2 mutant à la Yanofsky, might then be a mutant of either of two kinds:

(a) It might be a mutant which has an altered enzyme in statu nascendi so that some of the post-metabolites compete effectively with the precursor of the amino acid that ~~in the wild type has functions as a main~~ trigger. A suppressed ~~mutation~~ would then ~~consist in~~ the absence of this competing post-metabolite.

If this were the case, we should expect the following:

(1) Suppose we make a heterocaryon out of the Yanofsky type 2 mutant and the Yanofsky type 1 mutant which lacks CRM, and have in the nucleus of the type 1 mutant present the suppressor gene. We should then not expect such a heterocaryon to be able to grow in the absence of minimal medium,

Moreover, if the mechanism here assumed operates, we should expect ~~two~~ 3 kinds of mutants requiring an amino acid; ~~one where~~ of the mutation occurs within the gene which makes that amino acid, ~~and these mutants can be either of~~ we may have a mutant of type 1 when no CRM is formed and when no suppressors can be found, or of type 2 where a post-metabolite which is a bad trigger has an increased affinity, ~~k~~ lower k, with respect to the enzyme sitting on the template in statu nascendi (or where the post metabolite which was a good trigger is now a bad trigger).

In addition to the above mentioned types there ought to be, however, a third type of mutant requiring for growth the presence of the amino acid. This arises through what we might call negative suppressor mutations (which could be interpreted as a reversal of a suppressor mutation). In these mutants there is an increased production of a metabolite which is a bad trigger and which competes effectively with a metabolite that is a good trigger. Let us now contemplate a methionine-less strain which is a mutant of type 3 and, say, a tryptophane-less strain of any type. These two will now not be able to form a heterocaryon that can live on minimal medium that is not supplemented by methionine, for the post-metabolite produced by the methionine-less (type 3) will suppress the formation of an enzyme required in methionine synthesis in both ~~types~~ of the nuclei which make up the heterocaryon.

May 29, 1957

Memorandum on purine content of bacteria

Arthur L. Koch, Frank W. Putnam, E. A. Evans, Jr.
Page 105, Vol. 197 (1952)
The Journal of Biological Chemistry

DNA: ~~Micromol~~. per 10^{12} bacteria; guanine, 16 micromol., adenine 11 micromol.; ratio: 1.4.

RNA: Guanine 50, adenin 30; ratio 1.7.

Acid soluble, micromol. per 10^{12} bacteria. See page 110

$3\ \mu mol/cc = 3\,10^{-3}\ mol/l$

Arthur L. Koch, page 227, volume 203, The Journal of Biological Chemistry (1953).

16
11
27

$2 \times 27 = 54 \times 10^{-6}$ mol or $54 \times 325\ 10^{-6}$ gm/cc NA

$\sim 100\ 10^{-6}$ mol/cc $= 1.8\ 10^{-2}$ gm/cc

$= 10^{-4}$ mol/cc or 5×1.8 % of dry wt

15
15
15
180

June 24, 1957

Memorandum by Leo Szilard re manuscript dated June 7, 1957

I have in the meantime looked at the known amino acid sequences found in insulin A, insulin B, oxytocin, vasopressin, corticotrophin, glucagon, melanophore stimulating hormone, hypertensin, cytochrome, trypsinogen, and ribonuclease. On the assumption that trinucleotides carrying three amino acids each and tetranucleotides carrying four amino acids each are the "intermediates" in protein synthesis, we should expect to find about ten times in the above mentioned sample that a sequence of three amino acids occurs twice. In fact, we find only two "repeats" which are as follows:

A sequence of four amino acids occurs both in oxytocin and vasopressin, and a sequence of seven amino acids occurs both in corticotropin and the melanophore stimulating hormone.

As one may thus see, the known sequences of amino acids in polypeptides (all of them excretory products of mammalian tissues) do not support the assumptions made in the manuscript of June 7, 1957.

Lh.

July 22, 1957

Memorandum based on a meeting held
on the initiative of Bertrand Russell
at Pugwash, Nova Scotia in July 1957

by Leo Szilard

The Pugwash meeting was largely occupied with preparing a public statement. Had it not been for this preoccupation, it might have been more useful in other respects. This meeting was very important as a "preliminary experiment," because it may enable us to devise future, somewhat similar, meetings that might serve different, perhaps more important, objectives.

I am proposing in this memorandum the holding of a sequence of meetings of a specific kind and serving a specific purpose. Such meetings could follow each other at six-month intervals, beginning perhaps with the end of this year.

The subject of the meetings

The subject of the proposed meetings would be the following general problem: The large-scale liberation of atomic energy accomplished in America during the war and the ensuing development of atomic and hydrogen bombs, has created a situation which has brought unprecedented danger to the world and also unprecedented opportunities for organizing a really stable peace. It is clear that the unprecedented problems posed by these developments can be solved only if the governments are willing to revise their past attitudes, adopt an adequate code of behavior, and to take unprecedented measures. Discussions among scientists, who by tradition try to free their thinking from the shackles of precddent, could, I believe, contribute much to clarification of thinking in this particular area.

Attached to this memorandum is a discourse on the topics that might be discussed at the first post-Pugwash meeting. Out of this discussion could then come a more detailed agenda for subsequent meetings.

The current public discussion of these and other related topics is most unsatisfactory. The voices heard in the public discussion are mostly the voices of statesmen, who of necessity must also be politicians, since it is their job not only to devise policies but also to persuade others to accept these policies. Statesmen frequently believe that they know what needs to be done, and that the only remaining problem is how to persuade others to do what needs to be done. When a statesman says something, what we primarily ask ourselves is not: is it true what he says, but rather for what purpose does he say it? This is probably the main reason why the public discussion of a political problem which is conducted among statesmen contributes so little to the clarification of our thinking.

In contrast to this, a discussion among scientists aimed at discovering the truth is a much simpler affair. If a scientist says something in such a discussion, we need not ask ourselves for what purpose he says it; all we must ask is: is it true what he says.

This is the main reason, I believe, why a discussion among scientists might go a long way towards clarifying an intricate problem. There are among scientists in all countries men who are deeply interested in the problems with which we are here concerned, and who are capable of thinking dispassionately about what may be regarded as a controversial subject. If we can prevail upon them to cooperate, we ought to consider holding a series of meetings, perhaps at about six-month intervals.

There would be present at these meetings perhaps twenty scientists and an undefined number of observers who are not necessarily scientists. We would want to have

present among the participants and observers a broad spectrum of persons. At one extreme end of this spectrum will be those scientists who have no governmental responsibility and no special knowledge of relevant technical information which governments regard as highly secret. These men may examine all aspects of the problem with the same freedom and in the same spirit of experimentation as they are accustomed to examine scientific problems. At the other extreme end of the spectrum will be those of the observers who, because of their governmental connections, do not consider themselves free to say what they think. The main function of those participants, who are free to experiment with ideas and inclined to engage in a freewheeling exchange of views, is to catalyze fresh thinking on the complex topic in which we are interested. The main function of the observers is to transmit, after the meeting is over, their own clarified thoughts to others. Some of the observers may, by writing articles or giving speeches addressed to an informed public, contribute to the formation of an informed public opinion and thereby indirectly facilitate the formation of an adequate political and military strategy on the governmental level. Other observers may have a more direct influence on the formation of governmental policy.

The inclusion in the meeting of observers whose opinions carry weight is, I believe, essential, and without this the scientists whom we want to have attend such a meeting might be reluctant to take time off from their own work. Even though the problems to be discussed at such a meeting are not without intrinsic interest to scientists, their intrinsic interest is not as great as that of certain scientific problems. Therefore, one cannot very well ask scientists to devote considerable time and attention to these problems unless they have some assurance that the community will benefit from the result of their thinking, at least if they are able to come up with acceptable remedies as well as convincing diagnoses.

It would be my hope that each successful meeting would serve more and more effectively the purposes which I have outlined. Apart from its intrinsic usefulness, each meeting might also be regarded as an experiment that should enable us to make the next meeting more effective. The first meeting ought to be attended by only a few observers. At subsequent meetings, as our discussions become less and less confused and as the real issues emerge more clearly, the circle of observers could be enlarged. I see no reason why men like Walter Lippman, Stewart Alsop, George Kennan, Raymond Aaron, etc. should not be asked to attend one of the early meetings

And if the meetings prove to be very successful, we might in the end consider inviting as observers, perhaps to the fifth such meeting, men like Krushchev and Nixon, together with anyone whom they might choose to bring along.

Clearly I have gone now as far as thought can reach in trying to project the character which such meeting might take on in the future. As far as I can see the only limitation is our own ability to make meetings of this sort really productive.

Concerning the first meeting to be held, my thoughts are as follows:

1) The first meeting might take place between December and February and might last from ten days to two weeks;

2) The meeting will not devote any attention to the issuance of any public statement, and the nature of the communique to be issued at the end -- since a communique obviously must be issued -- would be agreed upon in advance of the convening of the meeting. The communique could well list the topics that the conference has discussed (though it need not list all of these topics), and thereby disclose what aspects of the situation were considered by the participants to be most important. The communique could further mention points of view that were expressed and thoughts that were put forward. No attempt, however, must be made to issue a public statement representing the consensus of the participants.

July 26, 0957 GENERAL

Memorandum on the possibility of
detecting charged photons

by Leo Szilard

It seems to me rather likely that there are still basic physical phenomena (the existence of which ~~could not be deduced~~ is not derivable from our present knowledge) which might be discovered by means of simple experiments. I shall talk in the following of one phenomenon which might conceivably exist. I do not know of any valid consideration that excludes the possibility that photons with a positive or negative elementary charge may not exist. If they do exist, they ought to be detectable in experiments which are rather simple to perform ~~even though~~, if such photons do exist - in fact even though - it is quite understandable why they have escaped detection in the past.

Because a positive and negative photon must arise simultaneously, the probability of the emission of such charged photons by ordinary light sources ~~is~~ may be exceedingly small; it may be comparable to the probability of the emission of two quanta, in place of one quantum, by an ~~irradiated~~ radiating dipole which has been estimated by Maria Göppert-Mayer (Annalen der Physik, 5. Folge, Bd. 9, 1931, Nr. 3, S. 273). The probability of emission of charged photons should, however, be quite appreciable in X-rays generated from an anti-cathode composed of a heavy element, if the voltage is high enough to ionize the K-shell.-

Many of the properties of charged photons -- assuming that charged photons do exist -- can be estimated with reasonable assurance. If a charge photon is restricted in ~~to a small~~ space, the electrostatic energy is always very small compared to the radiation energy, the ratio being ~~determined~~ set by the fine-structure constant.

Appendix

to memorandum of July 29, 1957.

(Discourse on the relevant topics)

by Leo Szilard

On July 22, 1957, the Secretary of State gave a speech in which he defined America's aspirations concerning international control of atomic bombs. These aspirations appear to be quite limited:

America, it seems, would be satisfied with an arrangement which would leave America, Russia and England in possession of large stockpiles of bombs, presumably large enough for America and Russia to be able to destroy each other to any desired degree. America would like to see all manufacture of bombs stopped after a certain fixed date to be agreed upon, because she hopes thereby to prevent most of the other nations from acquiring large stockpiles of bombs. If this can, in fact, be prevented, the atomic stalemate between Russia and America, towards which we are moving, might be more stable than it would otherwise be. For example, if many nations possessed large quantities of bombs and if one of America's cities or one of Russia's cities were destroyed by bombs in a sudden attack, it might not be possible to identify the nation that caused this destruction, and this would introduce a new kind of instability.

There is some indication that America would like to see the stalemate between Russia and America be based on the atomic striking power of their respective air forces rather than on intercontinental ballistic missiles, and that she would welcome an arrangement that would stop the arms race prior to the full development of the intercontinental ballistic missiles system.

America also desires to institute mutual aerial inspection and some additional ground inspection. The reason given for this desire is that such inspection -- as long as it is maintained -- would decrease the danger of a surprise attack and keep down the expenditures of the strategic air forces.

Scientists have learned not to take public statements issued by statesmen at their face value. In this particular case, I am, however, inclined to believe that the objectives stated above are, in fact, objec-

tives in which America is at present seriously interested, even though I do not assert that the particular reasons given are valid reasons in each instance.

The discussions which may take place in our proposed meeting could start out with an examination of the American objectives listed above.

Our discussions must of necessity differ from similar discussions that might be conducted by government officials -- in preparation of inter-governmental negotiations -- either in Washington or in Moscow. Negotiations between two governments in the general area in which we are interested usually serve a double purpose. On the one hand the negotiating governments want to make progress towards a distant goal which they both consider desirable; on the other hand, each one wants to approach this distant goal by steps which give it a temporary advantage. Very often for the sake of such temporary advantage real progress towards the distant goal is sacrificed.

In the discussions at the proposed meeting the emphasis will be different. We will try to discover what are the <u>right goals</u> that the governments ought to pursue, and how can these goals be approached through steps which give <u>neither government</u> any appreciable temporary advantage. We must also try to understand what the real reasons are for the objectives which the governments pursue, and examine whether the reasons they put forward for pursuing these objectives are valid. If they are not valid, we must try to discover whether there might not be other reasons that may be the <u>real</u> reasons that are valid and that lead to the <u>same</u> conclusion.

I may as well illustrate this point by starting out with Mr. Dulles' speech. Mr. Dulles tells those who would like to see the world rid itself of atomic bombs that it is too late for this because by now there are large stockpiles of bombs, and even if America and Russia made an agreement to get rid of these stockpiles, there is no way to make sure that no hidden stockpiles would remain. Thus those who are still pressing for getting rid of the bombs are now told that it is too late; several years ago they were told that it was too early.

We may examine whether the reason given by Mr. Dulles for wishing to retain the stockpiles of bombs is a valid reason. I personally believe that it is not a valid reason, but I am inclined to think that there may be other reasons which are valid and which lead to the same conclusion.

This is a point which ought to be carefully examined at our meeting. Because, if it is indeed true that there are valid reasons for America and Russia to wish to retain their stockpiles of bombs, then the stalemate between the strategic atomic striking forces of Russia and America toward which we are at present moving is likely to be maintained indefinitely or, to be more precise, for the foreseeable future. If this is indeed correct, then our immediate problem is not how to rid the world of the bomb but rather how to live with the bomb.

Should we adopt this thesis as the premise upon which we may base several days of discussions?

While I personally favor our adopting this as a valid premise for some of our discussions, I believe that, before we do so, we must spend one or two days in carefully examining the validity of this crucial premise.

Getting rid of the bomb

In the course of examining the validity of this premise, we ought to discuss a number of points mentioned below:

What might be gained if atomic bombs were outlawed, in the sense that each nation involved would agree not to use atomic bombs if there is a resort to force, except if atomic bombs are used against her or one of her allies? Clearly a number of unilateral declarations would have in this respect exactly the same force as an agreement which, by its very nature, must remain unenforceable. In this context we might have to consider past experience with the convention outlawing gas warfare, and we must try to understand in what respect the situation with respect to atomic bombs is similar and in what respect it is different.

Next, we might consider whether a program aimed at getting rid of the stockpiles of bombs as well as means which are adequate for delivering bombs (assuming that both Russia and America desire to accomplish these objectives) could be carried out without the risk that dangerous secret violations of the agreement might remain undetected.

If we come to the conclusion that such a program would be practicable and the previous attempts to devise inspection schemes were too narrowly conceived, we must then next examine if there are any valid reasons why Russia or America or both may regard such an objective as practicable but undesirable. We might come to the conclusion that there may be valid

reasons for thinking that such an objective may indeed be regarded as undesirable by both America and Russia. In this case we may then want to shift our full attention to the question of "how to live with the bomb" rather than continue to discuss "how to get rid of the bomb."

Stabilizing the stalemate.

At present we are moving towards a stalemate between the strategic atomic striking forces of Russia and America. When this stalemate becomes an accomplished fact, America may be able to destroy Russia to any desired extent and Russia may be able to destroy America to any desired extent. Under what conditions can such a stalemate remain in existence for an extended period of time and be stable enough to permit Russia and America to live through this period without getting entangled in an all-out atomic war?

I believe we ought to discuss the stability of the stalemate under the optimistic assumption that no nation except Russia, America and England have at their disposal substantial quantities of bombs and means suitable for their delivery.

At some point in our analysis, we will have to distinguish between the stalemate based on Russia's and America's strategic air forces and the stalemate that might later on develop on the basis of intercontinental ballistic missiles. At that point we must then discuss the merits and disadvantages of current proposals aimed at aborting the development of intercontinental ballistic missiles, for instance by prohibiting the testing of such missiles.

The stalemate between the strategic atomic striking forces of America and Russia would be inherently unstable if either side could knock out in one single sudden blow or several repeated blows the power of the other to retaliate. For the purpose of our discussion, we may assume that efforts will be made both by America and Russia to safeguard themselves against this possibility. But a stalemate that is not inherently unstable may become so if a technological break-through occurs, either in America or in Russia, and this might lead to a dangerous transition period.

There are three factors of very different character which have a bearing on the stability of the stalemate, and we shall discuss these three factors separately. They are as follows:

1) The magnitude and kind of disturbances which will occur while the stalemate is maintained;

2) The restraints which America and Russia may impose upon themselves in order to keep from being entangled, if there is a resort to force, in an all-out atomic war, and

3) Technological break-throughs which may introduce an inherent instability during the period of transition.

These three factors might be discussed at the proposed meeting from the following points of view:

1) Disturbances

Today the greatest danger appears to be a conflict between two smaller nations which may lead to a resort to force and military intervention on the part of America and Russia on opposite sides. What measures might be taken to eliminate the danger of disturbances of this sort?

Clearly this danger can be eliminated only if there is a political settlement between the Great Powers which makes it reasonably certain that in case of any of the foreseeable conflicts between two smaller nations the Great Powers will not intervene militarily on opposite sides. Once such a settlement is reached, it might then become possible to take measures aimed at preventing the smaller powers from resorting to force in settling their conflicts.

At the end of the last war, it was generally believed that -- as long as the Great Powers act in concert with each other -- the United Nations Organization may be able to guarantee the security of the smaller nations and may make it impossible, for them to go to war with each other and unnecessary to waste their resources on defense. Attempts to use the United Nations in the past ten years for purposes other than for which it was designed have weakened this organization. Have they damaged it beyond repair? Or should it be possible to restore the United Nations to its original function, once there is a political settlement between the Great Powers that will eliminate the danger that these powers will militarily intervene on opposite sides in a conflict that may arise between two smaller nations.

Assuming, for the sake of argument, that this might be possible, what measures might the United Nations then take to forestall the outbreak

of local conflicts? Should one think in terms of maintaining in the various troubled areas of the world small armed forces equipped with conventional weapons of high-fire power which would be strong enough to enforce maintenance of the territorial status quo? Should such armed forces be under the central control of the United Nations or should they be placed under the control of those few nations, presumably chosen from the smaller neutral nations, who would man these forces, and the role of the United Nations be restricted to financing and equipping these troops?

2) Restraints

Another factor relevant for stability in the atomic stalemate depends on the restraints which America and Russia may impose upon themselves concerning the use of atomic bombs in case they do intervene militarily in a conflict on opposite sides. It is generally recognized that, in the absence of such restraints, which must be clearly formulated in advance and understood by all nations involved, what might start out as a local disturbance might end up in an all-out atomic war.

This does not necessarily mean that America and Russia must reach with each other an agreement that lays down a code of behavior for both parties to obey in case of war. Such a code of behavior, which would clearly define the restraints to be exercized, could also be proclaimed by unilateral declarations either by America or by Russia or by both.

We might examine to what extent the code of behavior advocated at present by informed groups both in America and in England is or is not adequate. This particular code of behavior might be phrased as follows: "If war breaks out, either America or Russia may use atomic bombs in combat, within the tactical area and perhaps also in the immediate vicinity of the tactical area. But they must limit the use of atomic weapons to the area of the local conflict and, depending on the circumstances, either America or Russia must be willing to concede defeat when the war has reached a certain point, rather than extend the war and thereby get entangled in an all-out atomic war."

Is it likely that it would be in the interests of both Russia and America to impose just this kind of restraints on themselves? And even assuming that they should both proclaim, in peace time, a rule of conduct based on this kind of restraint, what are the chances that this rule of conduct would in fact be obeyed, if put to the test when there is a resort to force?

I believe we ought to devote one or more days to a very careful examination of what might be in fact the crucial question of the atomic stalemate: What are the proper restraints which America and Russia might impose upon themselves, in case of a resort to force, which would satisfy the following conditions:

a) The restraints upon which this rule of conduct is based must not be such as to encourage a resort to force. One of the favorable aspects of the atomic stalemate is that it discourages a resort to force and the proposed rules of conduct must not nullify this effect of the stalemate.

b) The rule of conduct, if it is to survive, when put to a test, must be such that there shall be no appreciable incentive for either side to throw it overboard if a resort to force does in fact occur.

c) The rule of conduct incorporating the proposed restraints should be capable of commanding widespread public support, and in order to deserve public support should be satisfactory from the moral point of view.

d) The rule of conduct proposed need not depend on an agreement between Russia and America, which in any case would be unenforceable, and it should be possible for either of these two nations to put such a rule of conduct into effect by each making known the restraints whichshe proposes to impose uponherself, in case there is a resort to force, and by declaring that she will abide by these restraints,as long as the adversary shall abide by the same restraints.

3) Technological break-through

If there is a stalemate between the strategic air forces of Russia and America which is inherently stable, such a stalemate might be temporarily upset either by a technical break-through (in one of these two countries) or by a race in defensive arms (which is won by one of these two countries).

If, for instance, one of these two countries develops a defense which enables it to shoot down 99% of the jet bombers, there will result an imbalance. For instance, one of these two nations might make a determined effort to defend her cities against jet bombers by an elaborate system of anti-aircraft rockets carrying an atomic warhead. This, incidentally, might start a race in "atomic defense" which might make it impossible ever to fix a date for stopping the manufacture of atomic bombs.

In this respect the stalemate based upon the strategic air forces might be less stable than would be a stalemate based on intercontinental ballistic missiles. ~~To develop a defense for intercontinental ballistic missiles.~~ To develop a defense for intercontinental ballistic missiles is far more difficult, and when a stalemate which is based on such missiles is reached, one might adopt a somewhat Utopian solution for safeguarding it against being upset by a further technical breakthrough. A large-scale research research operation on rocket research, jointly carried out by America, Russia and several other nations might be such a solution.

Before we can reconcile ourselves to accepting as inevitable a stalemate based on intercontinental ballistic missiles, we must carefully examine the arguments of those who believe that the development of such missiles ought to be aborted. Their arguments fall into three categories:

a) In the transition from the strategic air force to the intercontinental ballistic missiles, there might be a dangerous period in which either Russia or America is ahead of the other nation.

b) At the time when defense is largely based on intercontinental ballistic missiles, there is likely to be a decentralization of the authority to fire a given missile. It is not clear whether sufficient safeguards can be had in such a situation against a war being started by individuals or groups taking action on their own initiative.

c) We must not give up the hope that sooner or later the world may be ready to rid itself of the bomb. This will be very difficult to accomplish once intercontinental ballistic missiles have been manufactured in quantity and installed in subterranean command centers. Assuming that Russia and America would want at that point to conclude an agreement that would eliminate these weapons, how could they convince each other that no such weapons have been retained in hidden positions, ready to be fired at a moment's notice?

Miscellaneous

We may hope that, by discussing all problems with which we are confronted as broadly as outlined above, we can establish a framework, and that it will then be possible to discuss intelligently within this framework a number of questions which are currently discussed in an inadequate manner. One of these questions is as follows:

It has been proposed to safeguard America and Russia against a surprise attack from each other by establishing aerial as well as ground inspection. As long as such inspection is maintained, each of these two nations could count on 1-3 days warning before a large-scale attack could occur. This safety margin would enable each of them to reduce considerably the costs of the strategic airforces.

If one takes the point of view that a wanton attack by Russia against America or by America against Russia is far less likely, at least under present-day conditions, than the military intervention of America and Russia in a conflict between two smaller nations, then one is led to the raising of the following question:

Assuming such an intervention, just what are the chances that America and Russia would be able to keep in force throughout such a period the inspection system that has been mutually agreed upon? Would the "safeguard" against a surprise attack not be likely to break down just at the time when the probability for a surprise attack begins to be appreciable?

Assuming that we conclude that such a safeguard against a surprise attack would indeed be very valuable, we would then want to discuss the following question:

Could an adequate aerial and ground inspection be organized without giving the strategic air forces of the potential enemy information concerning the exact location of important targets which he does not now possess? And if this is not possible, is the advantage of the proposed aerial inspection sufficient to overcome the reluctance of Russia to let a potential enemy get possession of such information?

There is one favorable aspect to the proposed aerial inspection which I believe we must not underestimate. The strategic stalemate confronts the world with an unprecedented situation, and it will take unprecedented measures to cope with the problems which it raises. The reciprocal aerial inspection has all the earmarks of a highly unprecedented measure. Those who take the position that it does not make much sense may still favor it for this reason alone. They may say that once we start to cooperate in such an unprecedented manner the ice will be broken, and it might then be easy to establish other unprecedented forms of cooperation that may make more sense from the point of view of all the nations that are involved.

THE UNIVERSITY OF CHICAGO
CHICAGO 37 • ILLINOIS
THE ENRICO FERMI INSTITUTE
FOR NUCLEAR STUDIES

August 20, 1957

From:

To:

Early in July of this year a meeting was held at the invitation of Bertrand Russell in Pugwash, Nova Scotia. The participants were guests of Mr. Cyrus Eaton. There were twenty-two scientists participating, and also Brock Chisholm (now retired from the World Health Organization), and D. F. Cavers (Harvard Law School). The statement issued by the meeting is not very exciting. (I did not sign it beczuse it advocated the stopping of bomb tests in a somewhat misleading, even though very meek, fashion). Yet, this meeting was, I believe, a very important experiment.

I have now discussed with Professor Morton Grodzins, Chairman of the Department of Political Science at this University, the possibility that his Department and the Institute might jointly arrange a meeting, somewhat similar to the Pugwash meeting but different in many respects. The enclosed memorandum and appendix will show you just what kind of meeting I have in mind. A list of those to whom this inquiry is addressed is attached to the memorandum.

If the comments received from you and others to whom this material is being sent are favorable, Mr. Grodzins will explore whether the University of Chicago might want to assume responsibility for arranging for <u>the first</u> of a series of meetings of the kind described. I assume that if the University of Chicago assumes responsibility for such a meeting it would want the first such meeting to be held somewhere in the Western Hemisphere, possibly in Canada or Jamaica, B.W.I.

Only after one meeting of this kind has been held can we really know whether we ought to hold further such meetings, perhaps at intervals of six months.

Could you jot down a few lines and give me, for my own guidance, your personal views on holding one such meeting? And would you also say (provided you are in principle in favor of such a meeting) whether you regard the University of Chicago as an institution that may be suitable for arranging such a meeting?

* * *

m

August 25, 1957

Memo on Milt's work.

In weak constitutives the enzyme level is proportional to the generation time; in strong constitutives, it is not -- it is then independent of the generation time. This may be interpreted by saying that the constitutive makes a direct inducer at the rate which is independent of the generation time and that the rate at which the enzyme is made is proportional to the concentration of the direct inducer. In Experiment 642-644, the inked curve is obtained by switching the generation time from three hours to nine hours. The enzyme rises four-fold instead of rising three fold, which is a discrepancy.

Milt has obtained a super-Monod rise in a strong constitutive which was depressed by lactose when he added TMG which, he says, did not take the enzyme up to the ceiling. Assuming that the TMG drives out the depressing lactose from the inside of the cell, and that the rise of the enzyme is due to the real inducer, it is difficult to see why super-Monod curves could be explained on the assumption that the real inducer sitting in the trigger position has great affinity for the enzyme so that the enzyme regulates its own level. One cannot explain such a super-Monod curve on the ground that the enzyme makes an inhibitor out of the real inducer, for in that case the enzyme level in the weak constitutive should not proportional with time.

September 26, 1957

Memorandum on proposed experiments concerning the nature of the anamnestic response in the rabbit

by Leo Szilard

The Enrico Fermi Institute for Nuclear Studies
The University of Chicago, Chicago, Illinois

Some basic experiments that might shed light on the nature of the anamnestic response have apparently so far not been performed, even though they appear to be rather simple and straightforward. These experiments can be performed in a manner in which the essential results are not blurred by the variability of the rabbit population with respect to the anamnestic response of the individual rabbit. This insensitivity of the results to the variability of the individual rabbit may be accomplished by using each rabbit as its own minitor. What this means will be made clear in a moment.

In each set of experiments one may use as antigen either bovine serum albumin or bovine gamma globulin. We may designate as the "standard" dose of antigen that dose which makes it just about possible to evoke, four weeks later, the maximal anamnestic response.

In experiments 1), 2), and 3), discussed below, the second injection and the third injection (the latter given four weeks after the second) may consist in the standard dose of the antigen and the response to the third injection may serve as minitor. In these three experiments the circumstances surrounding the first injection may be subjected to diverse variations as follows:

1) In this set of experiments one may vary the amount of antigen given in the first injection, and give the second injection (standard dose) four weeks after the first injection.

2) In this set of experiments, following the first injection of the antigen, the antigen is eliminated from the circulation in the different rabbits after different periods of time by injecting rabbit anti-serum against the antigen into the circulation. In the first injection one may use the standard dose, 1/5th of the standard dose, and 1/25th of the standard dose.

3) In this particular set of experiments -- mentioned to me by David W. Talmage in a discussion which we recently had on the subject -- one may vary the time period between the first and second injection. This time period might be 10, 15, 20, 25, and 30 days, for different doses of antigen given in the first injection.

In experiments 4, 5, and 6, the first injection of the third injection may consist in the standard dose of the antigen and the third injection may be given eight weeks after the first injection. The response to the third injection may serve as monitor. In these experiments the circumstances of the second injection may be subjected to diverse variations as follows:

4) In this set of experiments the second injection may be given four weeks after the first, and the amount of the antigen given in the second injection may be varied.

5) In this set of experiments the second injection may be given four weeks after the first injection and one may inject then the standard dose of the antigen. The antigen circulating in the rabbit following the second injection may be removed at different time intervals by injecting into the circulation rabbit anti-serum against the antigen.

6) In this set of experiments the time interval between the first and the second injection may be varied for each of several different doses of antigen given in the second injection.

September 25, 1957

Memorandum on proposed experiments concerning the nature of the anamnestic response in the rabbit

Some basic experiments that might shed light on the nature of the anamnestic response have apparently so far not been performed, even though they appear to be rather simple and straightforward. These experiments can be performed in a manner in which the essential results are not blurred by the variability of the rabbit population with respect to the anamnestic response of the individual rabbit. This insensitivity of the results to the variability of the individual rabbit may be accomplished by using each rabbit as its own monitor. What this means will be made clear in a moment.

In each set of experiments one may use as antigen either bovine serum albumin or bovine gamma globulin. We may designate as a "standard" dose a dose of antigen that makes it just about possible to evoke, four weeks later, the maximal anamnestic response. In experiments 1), 2), and 3) discussed below, the second injection and the third injection (the latter given four weeks after the second) consisted in the standard dose of the antigen and the response to the third injection serves as monitor.

continued same paragraph next page

In these three experiments the circumstances surrounding the first injection may be subjected to diverse variations as follows:

1) In this set of experiments one may vary the amount of antigen given in the first injection, and give the second injection of the standard dose four weeks after the first injection.

2) In this set of experiments, following the first injection of the antigen, the antigen is eliminated from the circulation after a different period of time in the different rabbits used by injecting rabbit antiserum against the antigen into the rabbit. This can be done with the first injection amounting to, say, the standard dose, 1/5th of the standard dose, and 1/25th of the standard dose.

3) In this particular set of experiments -- mentioned to me by David W. Talmage in a discussion which we recently had on the subject -- one may vary the time period between the first and second injection. This time period might be 10, 15, 20, 25, and 30 days, for different doses of antigen given in the first injection.

In experiments 4, 5, and 6, the first injection of the third injection consists in the standard dose of the antigen and the third injection is given eight weeks after the first injection, and the responses to the third injection serves as monitor. In these experiments the circumstances of the second injection may be subjected to diverse variations as follows:

4) In this set of experiments the second injection may be given four weeks after the first, and the amount of the antigen given in the second injection may be varied.

5) In this set of experiments the second injection may be given four weeks after the first injection and one may inject then the standard dose of the antigen. The antigen circulating in the rabbit following the second injection may be removed at different time intervals by injecting

into the ~~rabbit~~ circulation rabbit anti-serum against the antigen.

6) In this set of experiments the time interval between the first and the second injection may be varied for each of several different doses of antigen given in the second injection.

October 2, 1957

MEMORANDUM

From: Leo Szilard
TO: Mr. Cass Canfield
Dr. William Doering
Dr. Harrison Brown
Dr. Fritz Lippmann
Dr. H. J. Muller
Dr. Linus Pauling

I am leaving for Europe on October 3rd, and expect to be back in about four to six weeks. At that time I hope to get together with Dr. Doering and Mr. Canfield, and review our chances of raising funds within the confines of the United States for the Research Institute which we have been discussing. It is conceivable that we might have to decide to abandon further efforts to raise these funds in the United States.

Since this might be our conclusion, I wish to raise an issue with you at this time, in order to give you time to think about it so that I may have the benefit of your thinking upon my return from Europe. This issue is as follows:

In general, it is customary to think in connection with the problems of underdeveloped countries in terms of attempting to solve such problems with the help of American funds and "native" manpower. Oddly enough, in connection with the problem of birth control, the appropriate solution might be exactly the opposite. America has the scientific manpower but for various reasons American funds appear to be unavailable for an adequate research effort devoted to this problem. In these circumstances I feel tempted to put to you the following proposal:

Let us set up an endowment fund in some neutral country, perhaps in Switzerland, perhaps elsewhere, of about 20-25 million dollars, put together out of contributions solicited from the Chinese, The Russian, and Indian governments. The Associate Members of the Institute may serve as the Trustees of this fund.

The income should be used to operate a Research Institute located in England -- either in London or in Cambridge -- which would draw its permanent scientific staff from England and America. The Research Institute would serve three purposes: 1) It would engage in basic biological work with particular emphasis on molecular biology. 2) It would pursue practical application in the general domain of public health, with particular emphasis on the problem of birth control. 3) It would train scientists drawn from China, Russia and India, as well as from other scientifically underdeveloped countries in research in modern biology.

In submitting this proposal to India, one would have to present the plan to Nehru. Prior to doing so, it might be advisable to discuss the matter with Krishna Menon on the occasion of one of his visits to New York. In the case of Russia, one would probably have to present the plan to Krushchev, but prior to this it might be advisable to take up the matter with the Russian Academy of Sciences. In the case of China one would want to present the plan to Chou-En-Lai, and I do not know as yet what intermediate step would be most appropriate prior to such presentation.

One could not expect from India more than a token payment and the main financing would have to come from Russia and China. Russia has greater resources than China but, on the other hand, the problem is more important for China and the importance of this problem is now clearly recognized by the Chinese government.

I think it would be necessary for us to say why it is not possible to raise the funds in the United States in spite of the fact that the problem is clearly recognized and in spite of our professed interest in the problems of underdeveloped countries. My own answer to this is as follows: (1) Our professed interest in underdeveloped countries is based on a short-range political interest or on our desire to alleviate suffering on an emergency basis. In either case our interest does not go very deep. (2) Those who control the funds of the large private foundations are almost as conservative in their disbursement -- sometimes they are more conservative -- than the agencies of the U. S. Government. (3) There is an almost imperceptible, yet appreciable, Catholic influence that seems to play in this case the role of the straw that breaks the camel's back.

m

Heidelberg, November 24, 1957

Der Europäische Hof
Hotel Europa
Heidelberg
Telefon: 27101
Fernschreiber: 046 1840

From : Leo Szilard

To: Whom it may concern.

I received a telephon message to-day from Berlin, saying that I shall receive a letter in the course of the coming week from the Senator fuer Volksbildung of Land Berlin offering me the directorship of the Institut for Kernphysik which is to be built near Wannsee in Berlin. Projected are twin Institutes, one for Kernphysik and one for Kernchemie, each to be built at an expense of about 10 million DM, i.e. a total of about 5 million dollars, and each having a budget of about 1 million DM, i.e. a total of fivehundredthousand dollars. The Institute for Kernchemie is under construction and an atomic reactor is being delivered these days. Its director is Prof. Ziemen who used to work with Otto Hahn and moved fromSweden to Berlin to accept this position, about a year ago.

The directors of these two Institutes hold automatically professorships at the Free University of Berlin and the Technische Universität of Berlin respectively, but this does not necessarily mean that they must engage in formal teaching.

To an early inquiry which I received in the Spring from Prof. von Laue I had replied in detail pointing out that my interest had shifted from Physics to Biology after the War. I understand that my reply was circulated by Prof. von Laue among those concerned and that the position which is now being offered to me is offered in the full knowledge of the doubts which I myself entertain concerning my own suitability for this position.