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EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF CIVIL AND DEFENSE MOBILIZATION
BATTLE CREEK, MICHIGAN

FEB 25 1959

Health Physics Magazine
Pergamon Press
122 East 55th Street
New York 22, New York

Gentlemen:

I am very happy to transmit to you a copy of the Proceedings of the Conference on Research Activities in Radiobiology and Radiation Medicine for your information.

You may wish to note or review this in your magazine.

Sincerely yours,

Paul S. Parrino

Paul S. Parrino, M.D.
Director, Biophysical and
Medical Sciences Division,
Research

Enclosure

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Civil Defense
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PROCEEDINGS OF

CONFERENCE ON RESEARCH

IN RADIOBIOLOGY AND RADIATION MEDICINE

December 1 and 2, 1958 - Washington, D. C.

* * *

Under the Auspices of

OFFICE OF CIVIL AND DEFENSE MOBILIZATION

Governor Leo A. Hoegh
Director, OCDM

*

Mr. Gerald R. Gallagher
Director of Research, OCDM

Paul S. Parrino, M.D.
General Chairman, OCDM

Hymen Ezra Cohen, Ph.D.
Proceedings Editor
OCDM

*

February 28, 1959

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FOREWORD

In late October, 1958, Mr. Gerald R. Gallagher, Director of Research, Office of Civil and Defense Mobilization, issued a call for a conference on research in radiobiology and radiation medicine under the general chairmanship of Paul S. Parrino, M.D., Director, Biophysical and Medical Sciences Office. His office is directly interested in all research in this area which holds promise of preventing, minimizing, or treating the effects of nuclear radiation.

The objectives of the Conference were to coordinate current and long-range research and development activities of OCDM with those of other agencies in this field, to develop new and useful information for the Health Services, OCDM, and to provide a forum for the exchange of current thinking at the working level.

The call went to governmental and nongovernmental agencies engaged in research on radiobiology and radiation medicine. Along with it went a tentative agenda which requested from each agency participating, a report describing areas of research in which it had projects of interest to OCDM. Broad, tentative areas to be covered by the reports were suggested as follows: (1) dosimetry, (2) acute effects, (3) delayed effects, (4) genetic effects, (5) protective efforts, (6) therapy, (7) hazards from ingestion, (8) combined effects of ionizing radiation and other factors, (9) clinical radiology, (10) use of isotopes, and (11) all other areas of research in radiobiology.

Seven moderators were named. These were:

Dr. R. Keith Cannan, National Academy of Sciences;
Dr. Charles L. Dunham, Atomic Energy Commission;
Mr. Jack C. Greene, OCDM;
Dr. Crawford F. Sams, University of California;
Dr. Lauriston S. Taylor, National Bureau of Standards;
Dr. Edwin G. Williams, U. S. Public Health Service; and
Dr. Paul S. Parrino, OCDM, Chairman.

They and Dr. W. Palmer Dearing, Director of Health Services, OCDM, later became the members of the Panel on Evaluation for the Conference

The response to the call for the Conference was quite prompt and enthusiastic. The persons, agencies, and institutions actually participating are listed at the end of the Proceedings.

The participants discussed (1) the effects of radiation; (2) dosimetry; (3) protection; (4) therapy; (5) the nature of radiation fallout and isotopes; (6) training; (7) ecological and contaminating effects; and (8) informational and investigative services.

Under the effects of radiation, physiological effects were considered as: (a) acute, (b) chronic, (c) delayed, (d) genetic, (e) combined, (f) ingestion, and (g) clinical.

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They were considered as internal or external; and the approaches were of pathogenesis, pathological physiology, recovery rates, and so on.

In the study of dosimetry of effects, both standards of measurement and instrumentation were considered. Under protection, such aspects as shielding, drugs, diet, decontamination were included. Contamination studies covered water, milk, foods and drugs, crops and livestock.

The scheduling of more than forty speakers in the course of a two-day session resulted in limiting time allotted to individual speakers to fifteen minutes or less. This rule was rigidly adhered to, with but one necessary exception. The speakers came prepared to present a wealth of materials in a brief space of time. Many brought slides, exhibits, and film which they presented within their allotted time. Many brought supplementary materials, such as project lists and descriptions, reprints of articles, charts, and other data which were not presented to the general assembly, but which will go into the OCDM Research files for intra-agency use.

At the conclusion of the two-day conference, a transcription of every oral statement (except for one where the recording tape failed) was prepared and sent to its author for examination, correction, and approval. The transcripts were reviewed by the Panel on Evaluation. Each paper was first scrutinized very carefully by a subcommittee of the Panel, consisting of Doctor Edwin G. Williams, Dr. Crawford F. Sams, and Hymen Ezra Cohen, Ph.D., Proceedings Editor, Biophysical and Medical Sciences Office, OCDM. Their comments were then reviewed by the full Panel and the papers then given a second thorough review and evaluation. After this, the transcript of the whole Proceedings was prepared for publication in as close consultation with the original authors as was feasible under the circumstances.

It is our hope that this transcript, promptly published to preserve the timeliness of the report on research in progress, will be useful to those engaged in the field. The reader who sees reference to a project or an article which interests him may address himself directly to the agency of the speaker identified at the top of each statement, and request from it such materials as he may need for his research interests. The purpose of publishing this Proceedings is to aid participants and other interested readers in becoming aware of and reviewing or obtaining such materials as are available.

OCDM is publishing this transcript as an additional service to the community of researchers in the area of radiobiology and radiation medicine, to facilitate desirable awareness, exchange, and coordination of research efforts in this area. Beyond this objective, unless

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otherwise indicated, OCDM takes no responsibility for the accuracy or validity of any statement made by any speaker.

We are grateful to all participants for their cooperation in preparing and presenting their initial statements, for their assistance to our editor in publishing their remarks, and for the data, information, and good will which they brought to the Conference.

Proceedings Editor

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Governor Leo A. Hoegh, Director, Office of Civil and Defense Mobilization:

Dr. Parrino, ladies, and gentlemen. I am pleased to be here this morning and extend to you best greetings from the Office of Civil and Defense Mobilization.

In the promulgation of the National Plan for Civil Defense and Defense Mobilization, the President of the United States stated that civil defense and defense mobilization are vital parts of the total defense of this Nation. You therefore can readily see why we in this Office are keenly interested in a complete and a coordinated research program in the field of nonmilitary defense. This Conference, I know, will make a contribution toward that objective. We are anxiously wanting your recommendations, and your findings, and we want you to help in the best way that you can to make this a complete and a coordinated research program.

This is a good day to talk about golf. It is so much better to be playing golf than to be inside. Let me tell you this golf story. On the fourth fairway a man had a nice drive. His ball landed on an ant hill. He dug out his Four Iron and took a terrific swing. The ball did not move; but thousands of ants flew in the air. He took out his Five Iron. He really gave it all he had. This time again thousands of ants flew all around, but the ball did not move. There were two ants surviving. One ant turned to the other and said, "If we are to survive, we'd better get on the ball."

Well, in this Office of Civil and Defense Mobilization, with its responsibility of perfecting the overall leadership and direction for nonmilitary defense of the Nation, we recognize that we have to be on the ball.

I hope that your Conference will help us keep on the ball. I look forward to your recommendations, and I hope you have a most pleasant conference while you are here in Washington.

Dr. Paul S. Parrino, Chairman, Director, Biophysical and Medical Sciences Office, Research, OCDM:

Welcome to the Conference on Research Activities in Radiobiology and Radiation Medicine. Since we have a tight schedule, we would like to get going. This Conference is under the auspices of the Research Office of the OCDM. Mr. Gerald R. Gallagher, who is the Director of Research of OCDM, will officially open the meeting.

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Mr. Gerald R. Gallagher,
Director of Research, OCDM:

Good morning, ladies and gentlemen. As your program indicates, Governor Hoegh, Director of the Office of Civil and Defense Mobilization, will speak to you at 11:00. I think you can count that as the official welcome on the part of the Agency. However, I am happy to have this opportunity to express my own great personal pleasure in having such a fine turnout for this Conference on Research Activities in Radiobiology and Radiation Medicine. Dr. Parrino tells me that we will have more than thirty governmental and nongovernmental agencies represented here this morning.

The title, Office of Civil and Defense Mobilization, may well be unfamiliar to you because of its newness. This Agency was established on July 1 last to replace the Federal Civil Defense Administration and the Office of Defense Mobilization. Governor Hoegh, who had been Federal Civil Defense Administrator, is now Director of the Office of Civil and Defense Mobilization. The combined Office has been placed in the Executive Office of the President. By approving this reorganization plan, the Congress supported the basic concept of the plan that a single agency was required as a staff arm of the President to coordinate all activities of the Federal Government bearing on the problems of nonmilitary defense. Coordination of nonmilitary defense research activities is a highly important part of this approach. I trust that you are aware of the fact that the Office of Civil and Defense Mobilization has recently published a National Plan for Civil Defense and Defense Mobilization which was promulgated by the President last month. This plan states that "the Federal Government will fund, maintain, and support a complete and coordinated research and development program to determine optimum methods, materiel, and facilities for the civil defense and defense mobilization of the United States. The program will be coordinated by OCDM." In this first effort of bringing together the agencies which are active in radiobiology and radiation medicine research, we feel that we are beginning performance of another important function in our charter which is that of general dissemination of nonmilitary defense research information throughout the Federal Government, and throughout all interested agencies.

I venture to say that there are more separate research activities under way in the fields of radiobiology and radiation medicine than in any other areas of nonmilitary defense interest. It is imperative that we understand fully what has been done, what is being done, and what is projected, so that proper determinations can be made of what additional research may be needed. This research must

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be properly correlated and time-phased. It seems possible from my standpoint that there might be agreement that for the present time no additional projects need be immediately initiated, even though we agree that there is a great deal of research which must ultimately be undertaken in these areas.

OCDM must continue to make fullest use of existing research information. We are, for example, giving close attention to the important study conducted by Dr. Lauriston Taylor's Committee of the National Academy of Sciences during last Spring which, I think, Dr. Dearing will be talking about later; and, of course, agencies like the Bio-Sciences Information Exchange of the Smithsonian Institution are major resources.

We have been extremely gratified at the response to this meeting. It can be described as almost enthusiastic. We are particularly pleased in the representation of private agencies.

I believe that the approach we are undertaking here today is fully understood. Obviously time will not permit in the short presentations which have been scheduled any detailed analysis of the research activities to be described. We are seeking general information on the nature of these activities rather than on their precise content. If we get the full reading on present activity which we expect in this meeting, I hope that there can be effective follow-ups so that we can stay abreast of developments in the future. Whether this calls for future meetings of this type, or whether some other system will fill the need, I do not know. I would be very much interested in having discussion of this point in the general evaluation period tomorrow afternoon.

Let me repeat that we appreciate very much the fact that you are taking time out of your busy schedules to attend this conference. I sincerely believe that it will be most helpful to everyone concerned. Thank you.

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Dr. Paul S. Parrino, Chairman, Director, Biophysical and Medical Sciences Office, Research:

We next would like to have some word from Dr. W. Palmer Dearing, who is now the Director of Health Services of OCDM.

Dr. W. Palmer Dearing, Director of Health Services, OCDM:

Dr. Parrino and colleagues. I join Mr. Gallagher in welcoming you to this conference. Another word about our Agency which he just described to you. As Director of Health Services, my office carries the primary responsibility for directing and coordinating the development of peacetime health readiness measures and emergency health plans under various emergency conditions. My office serves also as a principal point of coordination for all the health matters within the Office of Civil and Defense Mobilization. We must arrange for or provide professional and technical guidance to other organizational elements in OCDM and to other Federal departments and agencies having responsibilities in the health field in times of mobilization or war. These are big, round, general phrases, and like all such, they take some doing, and we are in process, since we were established under the new organization pattern last October, of developing our ways of working and being of service both within the Agency and within the entire Federal Government.

Mr. Gallagher mentioned the report prepared six months ago by the Advisory Committee on Civil Defense of the National Academy of Sciences under the chairmanship of Dr. Lauriston Taylor of the National Bureau of Standards. The report was titled, "Adequacy of Government Research Programs in Nonmilitary Defense," and I am sure many of you here participated in its development.

It is a remarkably useful analysis. There is a tremendous amount of information brought together in a short time, and it is much more comprehensive than its title "Government Research" implies. The entire scientific community of the country contributed to it.

Dr. Taylor's Committee noted the importance of planning and leadership and the inability of research alone to prepare the nation for mobilization in civil defense. They noted areas where more research is needed. They pointed out that, "Much existing information and some resources are not now effectively utilized," and they suggested that "Frequent personal exchange of unpublished information at the working level and symposia having the objective of disclosing the nonmilitary defense applications of current research would greatly improve the present situation." (Page 2).

The report, with the accompanying subcommittee reports, makes a great contribution in the way of

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perspective. In addition to noting, for example, the need for development of a "simple, rugged and reliable dose-rate meter - - - - for on-the-spot measurements of the dose-rate by small groups and family units isolated by breakdowns in communication," and the need for projects related to survival in a contaminated area with expansion of research involving exposure to low-level or continuous radiation, (Page 18) the report calls attention to the limitations to be expected for civil defense purposes from biomedical research on radiation effects and their treatment, and the relation of this problem to the vast amount of work going on in radiobiology today.

The report states that -- and I am quoting, -- "Just as no traffic director should hope to solve his problems by improved methods of surgery, civil defense should not be expected to benefit much from improved methods in the handling of the injured. It would be exceedingly optimistic to hope for any treatment that would save the lives of those exposed to 1000 r, i.e., that would reduce the effective dose by a factor of two. In contrast, a fallout shelter of relatively simple design can reduce the dose by a factor of 100." (Page 19)

The biomedical subcommittee concludes: "The biomedical research program required for nonmilitary defense differs only in a few minor details from the biomedical research program needed to promote general knowledge and to achieve improving standards of public health. Hence, the radiation research programs of the country as a whole should quite adequately support the needs of civil defense. If there is a need for increased efforts in radiation research for the civil defense program, it is because there is need for an increased effort in this field generally. The material set forth in sections of the Subcommittee report on radiation effects makes it clear that radiation research in this country should proceed at a maximum level consistent with the available resources of manpower, facilities, and money." (Page 19).

I am particularly glad that the Committee stressed our lack of knowledge on radiation effects in the sub and minimal clinical levels, recovery rates, etc., such as we would be dealing with in a survival operation. This to my mind is one of the large gaps in the knowledge we need to conduct a survival operation.

Again, I welcome you here and appreciate your participation in this conference and look forward to its results. Thank you.

Dr. Parrino: Thank you, Dr. Dearing.

Dr. R. Keith Cannan, Chairman, Division of Medical Sciences, National Academy of Sciences and Executive Director, Atomic Bomb

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Casualty Commission:

The Academy has had a particular interest over the years in one phase of the problem that faces us today; namely, the problem of the attempt to seek out demonstrable, long-term effects of radiation in man. Whatever contribution I can make during the two days' session will be restricted to an attempt to moderate or evaluate the area of human studies on radiation effects.

Before turning to these, however, may I remind you, so as to get the story in perspective, that the Academy has made other contributions. You have already heard of the report on "The Adequacy of Government Research Programs in Non-military Defense" prepared by Dr. Lauriston Taylor's Advisory Committee on Civil Defense. I remind you only in a sentence of the so-called "BEAR" reports, the "Biological Effects of Atomic Radiation." The Committees established in 1955 by the Academy under the sponsorship of the Rockefeller Foundation, published summary reports in 1956. These, I think you will agree, along with the report on "The Hazards to Man of Nuclear and Allied Radiations" by the Medical Research Council of Great Britain and more recently the 1958 "Report of the United Nations Scientific Committee on the Effects of Atomic Radiation" form a valuable background for contemporary discussions of the status of the human hazard.

There is also one small study that I might tell you about since the report has not yet appeared in the literature. The Academy for a number of years maintained a Committee whose responsibility it was to undertake a follow-up study of the eleven physicists who had incurred cataracts as a result of the operation of cyclotrons. That study has now been terminated since it reached the point of diminishing returns. Doctor Alan Woods has completed a report which will shortly be published in the American Journal of Ophthalmology.

My main interest, however, is in the Atomic Bomb Casualty Commission. The ABCC, I am sure you all know, is the extended study in Hiroshima and Nagasaki of the exposed populations of those two cities. This was undertaken at the request of the President of the United States in 1947, and is supported through a contract with the Atomic Energy Commission. Since that time, and for an indefinite period in the future, it is proposed there will be a continuing surveillance of these populations. In the early days the study emphasized particularly the genetic problem, and from 1947 to 1953, it undertook what I think is undoubtedly the most ambitious study in human genetics that has ever been made. It surveyed some 75,000 newborn infants and followed them for a period up to nine months. The report on that study was published in 1956 by the National Academy, and I think is familiar to all of you. It was authored by Drs. J. V. Neel and W. J.

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Schull of the University of Michigan Medical School and is entitled "The Effect of Exposure to the Atomic Bombs on Pregnancy Termination in Hiroshima and Nagasaki."

As the project got under way, a continually better-refined medical surveillance was built up as census of the populations were completed. ABCC is now conducting a tightly designed epidemiological study that, in effect, attempts to document the natural history of a population over its whole life span.

The populations concerned total approximately 100,000 people, distinguished in three categories: those heavily exposed, within 2,500 meters of the bomb; those more remotely exposed; and the third group, a comparison group, of unexposed. This total population of 100,000 is under surveillance for mortality rate studies or life expectancies, as you may prefer to describe them, based essentially on death certificates and supported by such pathological information, from Tumor Registries, from autopsies, etc., as ABCC is able to assemble.

Behind this basic mortality rate study there is a much more intensive medical survey which is confined to a sub-sample of the exposed Master Sample. It includes about 14,000 people, again divided into three categories of heavily exposed, lightly exposed, and unexposed. The intent of this medical survey is to maintain close contact with this smaller population, bringing them into the ABCC clinics for periodic evaluation of their physical status, and associating with these examinations the collection of morbidity data and special studies of leukemia, malignancies, cardiovascular disease, ophthalmological effects and blood dyscrasias. The hope is that ABCC may gradually isolate from this total mass of information some indices of aging, which may contribute to the interpretation of mortality rate studies.

The other parameter of the study is the physical dose of radiation received. For this ABCC depends on reasonably good estimates of the air distance-dose of the two bombs, corrected for every single individual, for attenuation due to shielding. This requires a radiation history of every exposed person. This aspect is under the direction of the Oak Ridge National Laboratory.

I add, in conclusion, that this is not an American study carried out on foreign soil. This is a joint operation in which the Japanese national authorities are cooperating actively, and also the local medical groups, so that it is proper to describe this as a Japanese-American study of an international problem.

I would add only one more thought which may touch aspects of interest in civil defense. Within the overwhelming mass of data that ABCC has accumulated over these ten to twelve years in the personal histories of the exposed populations,

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there is undoubtedly buried information on matters remote from radiation effects. I refer to problems of the protection afforded by shielding and shelters, from burn and blast injury and the relation of traumatic injury to radiation.

Although we have not worked up much of these data, we have looked at them from time to time. There is certainly some information at ABCC that might possibly be exploited to our common advantage. Thank you.

Dr. Charles L. Dunham, Director, Division of Biology and Medicine, Atomic Energy Commission:

That part of the research program of the AEC Division of Biology and Medicine which I believe relates to the need of OCDM with respect to the effects of ionizing radiation on man and his environment and the development of methods to counteract or protect against these effects, has from the beginning been broadly conceived. It has attempted to develop in an orderly fashion over a number of years as much information as possible within the funds available to the AEC; but, I believe more importantly, within the availability of competent scientific manpower to work on these problems.

In 1947, the National Academy of Sciences Board of Review, which developed for the AEC an outline of appropriate activities, and the AEC's Advisory Committee on Biology and Medicine were both concerned with the need for a body of information on the effects of nuclear weapons which could be used by those who would eventually be responsible for non-military defense planning and administration in this country. They placed on the Division of Biology and Medicine, as one of its responsibilities, the development of such information and its transmission, first to the National Security Resources Board, later to the FCDA, and, of course, now to the combined agencies, the OCDM.

Because in 1950, there was no extensive program under way in any agency on the effects of thermal and blast injuries from atomic weapons, we developed sharply defined and programatic studies of these problems. As an example of how farsighted my predecessors were, when we came to gather information for the AFSWP-edited, new version of the handbook, "Effects of Nuclear Weapons," it turned out that the only information available on blast effects from atomic weapons, developed in this country, was the result of a rather modest AEC program conducted by the Lovelace Foundation under contract with us.

Similarly, in our program on

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burns. We started that in 1948 when there was little interest in this problem in other agencies. But as the Department of Defense program grew, we kept ours small and have tried to keep it coordinated with those activities of the DOD. As many of you know, the only work in thermal injury from atomic weapons that we support is Dr. Herman Pearce's work at the University of Rochester.

Now, our ventures in the shelter field as such have also been limited. They were undertaken originally to fulfill an AEC requirement for a cheap shelter which could be used at AEC installations, because it was determined that existing shelters built into structures needed supplementation in the field, but always on a fairly modest scale. We have tried to tie this into the much larger shelter programs of the FCDA at that time and the DOD.

Some of the studies on the shielding factors of buildings and the like we have conducted largely through cooperative efforts of such people as Karl Morgan's group at Oak Ridge. I am sure he will touch on that, so I will leave that alone at this point.

Now, to get to radiation biology programs themselves. I think our program includes a fairly wide spectrum of research, which is begun at the molecular level. It goes on up to mammals and even man, where there are materials for study, such as cases of radium poisoning, accidental exposures, either in the laboratories, or such as occurred with the Rongelap people on the Marshall Islands, and, as already mentioned by Dr. Cannan, the Atomic Bomb Casualty Commission activities in Japan.

Generally our program involves a number of areas, and I am not going to go into much detail. But, as we have them listed here in our project summaries, we start with the molecular level, which includes all sorts of enzyme and metabolic studies, vascular and molecular level, and then we have work going on, on the gastrointestinal tract, blood forming organs, life-shortening, and biological effects, etc., including a fairly extensive program in genetics.

Because of the demand for information to meet our own responsibilities -- direct line responsibilities in the health and safety field under the Atomic Energy Act -- we are presently attempting to define more precisely the effects of acute whole body exposure from neutrons, gamma and x-rays. Similarly, we are attempting to define the long-term hazards, including the genetic effects of the various ionizing radiations and of radionucleoids.

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Because the dose-rate relationship from exposure to fallout, whether from weapons or whether from accidents, is in neither category, we are attempting to fill the gap with studies which will help us determine the relative disability to be expected from a variety of dose rates. We hope soon -- and I hope NMRI will say a word on this -- to assist them in a joint effort on studying for comparison with a single acute exposure effect, the effect of an exposure curve approximating that which would be encountered in a rapidly decaying fallout field.

As to the long-term effects, it is going to take a long time and hundreds of thousands of animals to refine significantly our present estimates, which are accurate only to factors of plus or minus a few, and in some instances no better than an order of magnitude. Here we are not so much limited by funds as by scientific manpower to undertake and see through to the finish tedious chronic effects studies in longer-lived animals than the rodent. The matter of reparable versus irreparable injury must be worked over a great deal more extensively, using the information now available as a basis for more definitive studies.

In the field of specific prophylaxis and treatment for radiation injury, as you know, there are a number of means now, but no practical procedures for treating mass radiation casualties or for use as protection for civil defense workers who in the course of their duties must be deliberately exposed to radiation. AET has been found to work very well in mice and monkeys as a prophylactic agent. It has proved too toxic for dogs, rabbits, and man. Related chemicals are being explored. One or two are promising and will be undergoing trials. Now, whether dosages of such materials which might be inadequate to protect against lethality, reduce the effects of sublethal doses, needs considerably further exploration. I believe NRDL has some work going on in that field already.

For treatment after exposure, bone marrow transplantation works very nicely in rats, mice, and monkeys, but until we have a better understanding of the immune mechanisms involved and how to handle them, it has no value in humans. Work on typing marrow constituents seems to hold some promise here. Although the acute effects of ingestion and assimilation of fission products in the heavy fallout situation will be far outweighed by the external whole body exposure effects, we are endeavoring to develop chilating agents which will be useful in coping with Strontium^{90} and eventually others which will be useful against other fission products.

More definitive studies of the

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toxicity of fission products other than Strontium^{90}, Iodine^{131}, and Cesium^{137}, are already planned and some are under way.

Because of our current preoccupation with the possible hazards of low level fallout from weapons testing, we are sponsoring research with the Department of Agriculture at our own laboratories, notably Los Alamos, UCLA, Hanford, and the University of Tennessee farm at the University, and at the Island of Rongelap, to learn more about the movement of fission products into the food chain. A corollary to this is studies of methods to interfere with or to control, if possible, this movement, and also to identify plants in natural circumstances which limit the uptake of fission products by food crops. Liming of acid soils has been shown to be both costly and not sufficiently effective to be a useful measure in a post-disaster situation. Doctor Libby has recently done a pilot experiment which suggested Potassium would be cheaper.

We are arranging with the Department of Agriculture -- in fact, this study is already under way and partly completed now -- to support a pilot study of a variety of mechanical modes of removing fresh fallout material from soil surfaces. Such procedures would admittedly have limited applicability.

In addition, we are sponsoring jointly with the Department of Agriculture studies which will better define acute and chronic effects of fallout materials on farm animals. How hard this sort of study should be pushed will, I suspect, depend largely on discussions that grow out of this particular meeting. And I think the AEC wants to get, and asks for sincerely, any guidance that the OCDM and the assembled scientists here can give us as far as emphasis on research in our program which would help to more fully meet the needs of the OCDM. Thank you.

Dr. S. Allan Lough, Director, Health and Safety Laboratory, Atomic Energy Commission, New York:

Dr. Parrino: We would like to continue then with those agencies directly related to the AEC. Is Dr. Allan Lough present? Dr. Allan Lough, Director, Health and Safety Laboratory, Atomic Energy Commission in New York, will tell us about the program being undertaken by his group.

Dr. Lough: As most of you know, the Health and Safety Laboratory is attached to the New York Operations Office and is located in New York City. Our affiliation for direction of program is with the Division of Biology and Medicine here in

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Washington. We have a varied program, not all of which is directly applicable to the subjects of interest here today, but I thought perhaps two things that we have been doing might contribute at least to the picture.

We have been very active in the estimation of fallout, particularly with respect to the development of methods for collecting fallout and for the analysis of the fission products thus collected. We started the sticky paper or gummed film technique, which is shot at by a great many people on good and sufficient grounds, and the data from which are used more extensively in drawing conclusions regarding fallout than any other single set of data. It is shot through with shortcomings. We are just about ready to publish a study in which we compare the effectiveness or reliability of collecting fallout by gummed film versus the collection in stainless steel pots or tubs of rain and dry fallout.

We also have developed analytical methods extensively. We are not the only ones in this field by any means. The methods that we have developed, in our hands at least, seem to give reliable results, and are paralleled more or less by some of the other laboratories in the world who seem to be getting reliable results, notably the British and the Canadians.

We have examined other samples for fallout, of course. The food chain samples have been sampled somewhat by the Health and Safety Laboratory workers, although the bulk of this work has been done by other laboratories.

Another type of observation which bears upon the general problem of low dose rates of radiation to the human is the work we have done in an effort to estimate the natural background of penetrating radiation. This has been done with the use of an atmospheric-pressure, air-filled, 20-liter ionization chamber hooked to a vibrating reed electrometer acting continuously as a voltmeter, which is calibrated against radium. We have made several hundreds of measurements in various parts of the United States, outdoors, for the most part - indoors, in and around New York City - and compared these with readings just outside these dwelling places.

This apparatus was a part of the Health and Safety Laboratory exhibit at Geneva; and since the man who was exhibiting it was forced to stay in Geneva to help wrap up the safety problems and to help shut down the reactors, he took the device with him on a trip from Geneva to Sweden and made measurements along the way. Interestingly enough, the measurements showed about the same outdoor ambient background as we find in this Country at sea level. An exception is in Sweden, where the values went up to about twice what we find here, and parallel the values which Sievert has

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obtained. He measured the background in Sievert's water-lined cavern, where he has a whole body counter and other low level equipment. He attained the same results that Sievert had obtained, so this made us feel comfortable.

These data, we think, will form at least part of the background of information needed and will represent something of a springboard from which those who wish to study the effects of chronic doses of low levels of radiation on humans can take off.

The degree of precision with which these measurements can be made is relatively good, we think. The range of levels in the United States, as you know, is about eight to twelve micro-roentgens per hour, unless you get at higher elevations or over outcroppings of radioactive materials. We think the precision on an absolute scale is roughly plus or minus one micro-roentgen per hour.

I think perhaps these two projects bear more directly upon what you are discussing - and with that I should like to close. Thank you.

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Dr. Crawford F. Sams, Civil Defense Research Project, University of California:

Our particular program has been in effect several years. In the biomedical field it has consisted of a series of correlative studies of existing knowledge. A number of other studies by some of our people have been under way during this time with the ultimate goal of trying to relate certain physical factors to biologic response. I might break this relationship down in sequence.

The first variable being worked on by one of our groups is on the distribution of fallout. We have felt that over-simplification, perhaps, in the past, for lack of better information, has resulted in neglect of this very important variable. The group is trying to determine the factors responsible for and to determine the resulting non-uniformity of distribution in a fallout field within a given isodose area.

A second variable being worked on by members of our group is an attempt to evaluate this non-uniformity of the distribution of fallout in its relationship to shielding. The shielding being studied is not limited to panels but includes buildings as they exist in which people might be sheltered and the shielding of groups of buildings by each other. We have felt that we ought to know what we have in the way of existing shielding in communities where people live or to which they might be moved before we start to build shelters all over the country without any order of priority as to their need. We certainly agree with the National Research Council's Scientific Advisory Committee's latest report, and I think everyone in this group would agree; that shielding is a most important preventive as far as biomedical effects of radiation are concerned on masses of humans. However, we think this needs more study.

The only reason for studying these two major variables, that is, non-uniformity of distribution of fallout and the factors of shielding, is, of course, to try and find out what is the modification of the physical factors in radiation by these variables in relation to the biomedical effects on the people.

Therefore, our current biomedical study which has been under way for sometime, and is very complex, has to do with an attempt to solve the problem of partial exposures and fractionation which result from the modification of the physical factors of radiation by the two variables as compared to exposure to a single prompt radiation to whole body. What is the biomedical effect of partial exposures of different parts of the body to different intensities of radiation coming from different directions fractionated over time? Certainly the dose levels are not uniform in relation to time. Nor is the spectrum a constant over time. The variation of the proportion of soft to hard gamma is

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important.

I am sure that most of you are aware that I feel very strongly that we have to come up with a better method of evaluating dosage of radiation measured in air in terms of biological response than we have been able to do so far when we use whole body radiation.

In attempting to dig out and correlate the existing knowledge on the direct and indirect effect of radiation on various portions of the body under the circumstances I have outlined, we have developed some interesting facts.

Great emphasis has been given in radiobiology in recent years to the effect of radiation on tissue as it pertains to the inhibition of mitosis. Naturally, much emphasis has been given to the study of those particular tissues or organs or portions of the body in which cell mitosis is a major factor. These, of course, as we all know, are the hemopoietic and the gastrointestinal systems.

We have found that there is a great deal of evidence that functional response of certain critical tissues, in which mitosis is of minor or of no importance, may be more important in the over-all body response to radiation than the inhibition of mitosis in the hematopoietic tissue or in the lining of the alimentary tract.

However, we have found in our study so far that the more highly differentiated tissues which have always been considered to be radioresistant under one of the axioms of radiobiology, are really highly sensitive. The old standard criteria of histopathological changes indicating cell damage or destruction and the inhibition of mitosis have been the basis for evaluating the comparative sensitivity of tissues which led to the principle that the more highly differentiated a cell or a tissue, the less sensitive it was to radiation.

If we concentrate on a study of the existing knowledge of those highly differentiated tissues or organs, which consist largely of highly differentiated cells and which have highly specialized functions other than replacing themselves by mitosis, we find quite a different picture. The evidence indicates that these tissues, such as the central nervous system and the endocrine system, are highly sensitive functionally to comparatively low doses of radiation.

I have emphasized the word 'functionally' because the principal function in the case of the central nervous system is the conversion of chemical into electrical energy; and in the case of the endocrine glands the principal function is the chemical synthesis of hormones. This central nervous system-endocrine gland system is, of course, the controlling mechanism of the entire body. Therefore, I feel we have a sound basis for emphasizing

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the study of these systems and considering them as radiobiologically critical organs because comparatively small modifications in their functions have terrific impact on the body as a whole.

We have, therefore, come up with a concept of the sensitivity of tissues in terms of functional response to radiation which almost reverses the old standard concept which is based on the inhibition of mitosis or histopathological evidence of cell damage.

We feel that it is necessary to attempt to relate functional response to given levels of energy in terms of the direct and indirect effects which may be produced not only on the specific highly specialized central nervous system-endocrine system by partial exposures and fractionated doses, but the indirect response which may occur in other parts of the body.

We feel that it is particularly important to evaluate this functional response for several reasons:

It serves as a basis of an evaluation of recuperation as compared to non-recuperation of the whole body.

It may give us a better insight than we now have as to the mechanisms involved in whole body response to radiation injury.

It may illuminate the key points in the mechanisms which may be attacked through therapy to favorably alter the whole body response to radiation injury.

We believe that we have devised a method by which we can evaluate a very complex system of multiple parameters, which are dose dependent as a functional response to radiation, as a possible means of finding some answers which many investigators have considered it impossible to do. We have been working on this jointly with some very competent people at Rand Corporation. We may come up with an answer in time in which we can put these parameters into a system stressed by partial exposures of varying levels of radiation fractionated over time and read off the functional modifications which result, and thereby come up with some unit or some method of evaluating the effects of radiation in a fallout situation on masses of people better than we now have. At least the first attempts, which have been made on some very simple models, have given us encouragement.

Let me summarize. What we are trying to do is to take a new look at the biologic response of the human body to radiation; not by the old method of mass-dose relationships in which inhibition of mitosis has been considered one of the principal end products, but by focusing attention on the highly specialized tissues, the central nervous system and the endocrine system, and their functional response to varying levels of energy absorption. At least we

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are developing some very interesting facts. A preliminary report is in preparation and should be completed within a few months. We are not so presumptuous as to think that we can come up with the final answers to such a complex problem in this preliminary report.

Dr. Cyril L. Comar, Director, Laboratory of Radiation Biology, Cornell University:

Dr. Parrino: I think we will proceed. Dr. Comar -- Dr. Comar, Director of the Laboratory of Radiation Biology, Cornell University, is interested in a phase that is quite important to OCDM, and maybe he is going to tell us how to get Strontium^{90} out of milk or keep it from getting in the milk in the first place.

Dr. Comar: Thank you. I am very glad to be here, I think more in the capacity of learning what is going on than being able to contribute.

Our program at Cornell, about a year old, is just barely getting under way. Generally speaking, in setting up this program, we had the hope of bringing to the university community an awareness of the problems that exist and the hope that we could bring the first-rate manpower of our good universities to bear on these problems. We wanted to get first-rate students interested in these matters, so that they could develop the techniques, develop the interest, and, as they pursue their careers, perhaps contribute. We have three general objectives of coordinate importance. First is the research program. We are undertaking research programs of specific and direct interest to the various government agencies that support us. These are concerned primarily with the movement of fission products in the food chain, the evaluation of effects as they may occur, and then, of course the possibility of modifications at will if these can be made.

There is research of another category overlapping, but of perhaps a different or more academic interest. This involves all of the health sciences and agricultural aspects -- basic research involved in physiology, nutrition and pathology. You will recognize, of course, that this is the reservoir, the bank upon which we must eventually draw to answer some of the more specific and practical problems as they come up.

Finally, there are the training aspects. This is very important. We want to get our young people on the forefront of scientific techniques and get them to develop an interest, so that in time to come we will not have to say to them, "Now, drop this problem that you are working on and start thinking about this other problem for which we must have answers." The training is along the following lines, for undergraduates -- to get them aware of what is going on; for graduate students -- to give them very intensive courses

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in the subject matter; and finally, for people who are already in the professions -- to offer short courses to help them at least know where to go for the information that they need.

Our support comes primarily from three government agencies: The Atomic Energy Commission; the Department of Defense, Office of the Surgeon General, AFSWP; and the Department of Agriculture. We are also anticipating support from the Public Health Service. The arrangements are entirely between the University and each government agency as an individual arrangement. This is working out very nicely. Our research program and approach is really one research program with various phases, but each agency is supporting a particular part of the work.

Now, the program itself. First, in considering the movement of fission products in the food chain, we are crossing many disciplines, and we are getting into the business of soils, of nutrition, of calcium nutrition, etc. We are attempting to go into the literature, bring the material together, and bring it into focus on the problems that we have in mind.

We have recently completed an annotated bibliography which deals entirely with matters of strontium and calcium metabolism. One would think that we should know all about something like calcium metabolism, but when you come down to the answering of specific problems, you find there are big gaps. This annotated bibliography, which should be in press shortly, contains over 1000 references and will at least give people a chance to realize the status of the field.

As far as the experimental program itself is concerned, one of our major interests is the transfer of fission products through the food chain. Fission products of importance, of course, are strontium, iodine, cesium, and perhaps barium. We are carrying out experiments with farm animals, looking at the milk secretion process, because this is one of the important factors. We want to see how much of these things that are ingested under ordinary farm conditions will appear in the milk and how, by various methods, one can increase or decrease the amounts that get into the milk. We are looking into the fundamental physiology of absorption of these materials from the intestinal tract. We are looking at basic skeletal physiology. How do these things get into the bone and how may they be removed from the bone? How can one decrease the body burden?

Other aspects are concerned with the dosimetry problem. We need to know more about the actual radiation dose that will be delivered to the tissues by exposure of animals and of man, to these materials. We have been developing techniques of implantation of small glass dosimeters directly in the tissues, so that we get an accurate measurement of, for example, how much

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radiation is delivered to the intestinal tract from the absorption of unabsorbed material, or what is the actual radiation dose that will be delivered to the gonads from ingestion of cesium. This is one aspect that we are working on very intensively.

I think this gives an overall picture of what we are doing. We feel that a university type program has much to offer in the way of trying to uncover some of the basic aspects. And the university as a whole is very grateful, I must say, for the support that the various government agencies have given, and for the degree of freedom that this support has been given with. All of our people on the University staff feel an enthusiasm in undertaking the type of work that is not only of interest to them, but which will also in the long run be of interest to the Nation. Thank you.

Dr. Parrino: Thank you. Any questions of Dr. Comar?

Dr. Richard K. Blaisdell, Argonne Cancer Research Hospital, University of Chicago:

Mr. Chairman, ladies and gentlemen. Dr. Leon Jacobson, Director of the Argonne Cancer Research Hospital, as well as Drs. LeRoy and Hasterlik, have asked me to convey their greetings to you here.

The program at the Argonne Cancer Research Hospital, of course, is primarily concerned with the problem of human cancer. Some of the research activities are pertinent to the Office of Civil and Defense Mobilization. These can be divided into two groups: Those that deal with protection or treatment of radiation injury, and those that have to do with the study of the harmful effects of radiation.

The first, dealing with the protection or treatment of radiation injury, go back to the early studies of Dr. Jacobson, which concern spleen shielding; that is, the shielding of the spleen from the radiation, the radiation being given to the rest of the body, protects against death. The earlier studies suggested there was a humoral factor that was responsible for this protection. This led to the current studies which concern humoral factor or humoral factors that are concerned in red cell production. This factor or group of factors, as you know, has been, for convenience, erythropoietin. Methods have been developed for assay of this material, and a concept has been proposed, suggesting that this humoral factor operates constantly in governing the steady state of the red cell mass and in certain conditions, chiefly alterations in local metabolic state of the tissues, there is an increase or decrease of this humoral substance.

Other studies have indicated this substance probably arises from the kidneys. Chemical studies have been carried out in order to charac-

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terize this substance further and it appears from studies of the material in sheep plasma that it is non-antigenic to guinea pigs. This substance seems to be homogeneous electrophoretically by column chromatography and ultracentrifugation.

Now, besides the humoral factors concerned with protection or treatment, we have also been concerned with cellular factors, and these chiefly were antibody-producing cells. As is well known, young tissue, especially from the liver and spleen, seems to be especially effective in protection against radiation injury. Studies show, for example, that infusion of rabbit tissues into rats or mice exposed to lethal doses of radiation, will protect against radiation injury and that these animals later on exhibit cells from the different species. However, when cells from rodents are transferred into rabbits exposed to lethal doses of radiation, although the rabbits survive, we have yet been unable to demonstrate that heterologous -- that is rodent -- cells survive in the rabbit.

Now, as regards the harmful effects of radiation, I am sure you are well acquainted with the work of Dr. C. Phillip Miller which concerns the enhancement of an infection that occurs in animals that are exposed to radiation.

Long-term or chronic effects of radiation are under study by Dr. Hasterlik, who is studying over 100 persons, who were treated in the earlier years, 1913 or 1915 to 1931, with radium salts.

More recently Dr. Dwight Clark has completed studies suggesting that radiation to the upper respiratory tract and the lower respiratory tract may have something to do with the development of cancer of the thyroid. Thank you, sir.

Dr. Bernard Altshuler, New York University - Bellevue Medical Center:

The research programs that I am going to speak about are those of the Institute of Industrial Medicine of the New York University-Bellevue Medical Center, directed by Dr. Norton Nelson.

We have done some basic studies in pulmonary physiology which are related to problems of environmental hazards from radiation. These deal mainly with the deposition of dust particles in the lungs, with particular emphasis on the place in the lungs where these particles are deposited. This question of regional deposition of dust particles in the lungs is very pertinent in assessing the risk of bronchogenic cancer from inhaled radioactive particles.

One important project that has been going on which is of special interest to this conference is concerned with bronchogenic cancer. We have had a program under way with respect

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to many materials for the induction of cancer in the lungs in experimental animals.

One technique that has been developed successfully is to implant a pellet in a major bronchi. Pellets that have been plated with radioactive material (Ru-106) have been in rats for more than a year. These have consistently produced squamous cell carcinoma.

Dose levels were from about .01 to 10 microcuries n. The smallest time in which they have produced cancers has been about eight months. The range of doses has been in the order of a thousand rads to the order of a million rads. The highest doses produced something like 80 percent incidence of carcinoma.

This technique is particularly valuable because it gives a very definite quantitative relationship with the absorbed dose to the tissue which is responding.

Another program with which we are concerned is centered on the fact that we expect soon to have use at the Medical Center of a whole body radioactive counter, a joint use with the Health and Safety Laboratory of the Atomic Energy Commission. With this facility, the general program is to relate internal radioisotope burden and disease, to study clinical status and internal burden, and also uptake, localization and turnover of trace elements and fission products. In addition we expect to investigate acute local exposures, excessive exposures, that might occur in the geographic area and that are available to us.

I should say that the primary emphasis at our Institute is mainly with chronic exposure, rather than large, acute exposure. I would also add that we are developing a strong interest in an epidemiological study of biological effects arising from low-level radioactive hazards.

This, then, summarizes the program as it is in our Institute. Thank you.

Dr. Cannan: Could I ask if Dr. Altshuler would give us a little more information on these epidemiological studies?

Dr. Altshuler: These have not been well delineated. I don't know that I am able to yet.

Dr. Cannan: You haven't found your population yet?

Dr. Altshuler: That is right.

Dr. Cole: Could I inquire about the bronchogenic carcinoma. I am curious about the doses that were required. I was wondering whether one million rad was the dose required.

Dr. Altshuler: That is the highest level -- not the dose required. These pellets that have been im-

planted in the major bronchi are fixed there with a kind of hook, and they are kept in one place. Now, the order of time that is involved for it to produce is in the order of a year. The smallest time is eight months.

The total dosage that we calculate is delivered to the basal epitheliem. We have given many different levels of radioactivity, ranging from thousandths -- let us say a hundredth of a microcurie to ten microcurie. This dose that is delivered over this period of time has ranged from, I think, around 1500 rads to about the order of a couple of million. I am talking about dosages which have produced carcinoma. These are calculated dosages, the reliability being a factor of two -- something like that.

Dr. A. C. Andersen, Director, AEC Projects 4 and 6, School of Veterinary Medicine, University of California:

I might start by saying that we at the Veterinary School, University of California, Davis, are engaged in studies involving large numbers of dogs. We have two projects under way, and for the sake of clarity, I would like to first explain Project Number 4.

Project Number 4 deals with the effects of whole body irradiation in relation to work capacity and longevity in the dog. This project began in 1951 and is still continuing. The average age of the dogs is now about five and a half years post-radiation exposure. Approximately 418 beagles are in this experiment. I have slides, or this afternoon I could show a movie, which will give you a perspective of the size of the kennel and facilities.

The facilities of this project have been designed primarily to ascertain the late or long-term effects of radiation. I might just mention that the kennel is four acres in size, with about five and a half miles of fencing, maintaining about four and a half tons of dogs.

We raise our own dogs, and have whelped over 450 litters. Females are being used for the experiment proper. The dogs are raised and when ten to twelve months of age are given a specified exposure. The experiment includes fourteen different levels, the lowest being 25 r, 28-day interval, totaling 100 r and the highest being a single bilateral exposure of 300 r.

We have spent considerable time during the past four or five years evaluating the environmental conditions of our dogs, and I might mention in retrospect, of our kennel conditions. Some 225 beagles have been released throughout the State of California. This study has given us a somewhat accurate record on what happens to the beagle under natural conditions. We are using this as a control for

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evaluating our environmental factors in the kennel.

Such aspects as kennel sociology, kennel epidemiology, etc., have been included in our studies. We have gone to great length to evaluate the workload of the kennel, and so forth. I think it can all be summarized by saying we are trying to obtain a complete history of each and every animal throughout her lifespan. This is, by and large, being accomplished by examining each dog every 10 to 14 days. These data are tabulated on IBM cards and include such things as body weight, the estrous cycle, general appearance of the animals, or any defect that we may be able to detect.

We started, for instance, with some physiological measurement, and settled on reproductive fitness. I would like to briefly describe this study, because I think the study has definite merit and explains why we have been using female dogs. Half the population is bred and given an opportunity to produce two or more litters before reaching four years of age. This study is now in process of statistical analyses.

Besides our routine examination twice a month and reproductive studies, we do conduct an annual examination on each dog, with special emphasis based on tumor formation, cataracts, and any other observable pathological syndromes.

Each animal is bled at least three times a year. To date, we have obtained several thousands of complete blood counts from the colony. This is largely directed toward evaluating the acute or immediate effects of irradiation as versus some latent effects; namely, leukemia. We have not seen leukemia as yet.

Now, presenting this project would hardly be complete if I did not mention an intra-vascular substance that we have found in those dogs receiving the highest whole body exposure. It is a polysaccharide material. We feel quite sure that we have recently isolated the substance, and it is certainly not a hoax, because we have found it in 52 animals. Also, the substance has been found in other species, and we feel reasonably certain that it should be present in man. This material is related apparently to the acute radiation syndrome. It does not occur before signs of radiation sickness, that is, in large amounts. After signs of radiation sickness have passed, the substance has not been found.

Presently, we are directing our attention toward using this material as a diagnostic means if we have some luck in developing some kind of precipitant reaction.

I think that about concludes Project Number 4, except one of our biggest problems has been to establish normal values to evaluate critically the effects of radiation.

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The next Project, Project Number 6, has actually been under way for two and a half years. It deals with the effects of Strontium^{90} administered orally during the growth period of the dog. Although we have been engaged in this project two and a half years, the activities have largely been confined to construction and preliminary experiments. The experiment as now designed will include between 850 and 1000 dogs.

The oral strontium treatment will involve seven dose levels, ranging from two-tenths to 27 microcuries per kilogram of total body weight, when the dog is 18 months of age. Administration will begin with the parent stock. Progeny will be carried until 18 months of age at a specific dose level. When 18 months of age, the dogs will be "cooled off" and then placed in large outside runs. We also are including a single Strontium 90 injection program as well as Radium 226 treatment.

To date, our activities have been involved with experimental procedures for maintaining or keeping a large number of dogs under strontium treatment. We have satisfactorily, we feel, completed the program and our building is ready for occupancy. Our parent stock are ready, and within the next few months we hope to get the Strontium 90 administration program under way.

In regard to preliminary experiments, we have conducted several trials on acute toxicity by the oral route. We have found that about one millicurie as a single oral dose will cause death within 30 days. Above one millicurie Sr-90, death occurs within six to seven days. On autopsy these cases reveal massive hemorrhage, and here we have again found the intravascular polysaccharide material.

In relation to the chronic effects, we have not succeeded in bringing six dogs through an 18-month dosage of 20 rc Sr-90 per day. Two of the six dogs died during treatment from malignancy (reticulo-sarcoma), and the other dogs are still cooling.

During the next year we hope to proceed uninterruptedly with the program, and we hope to have some results by 1960.

Dr. Parrino: Any questions for Dr. Andersen?

Question: I am not clear where he finds his polysaccharide material.

Dr. Andersen: It is always found intravascularly, except in areas of hemorrhage and in these areas the material is extravascular.

Question: You find it in the wall?

Dr. Andersen: No, within the blood vessels themselves, that is, the lumen. We could go on for quite some time on this subject, We think it is very interesting.and offers

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promise.

Dr. Parrino: May I ask what factors went into selecting the beagles as the type of breed for this type of work?

Dr. Andersen: Well, the beagle, we feel, represents at least these features: moderate in size, medium length of haircoat, in two or more colors, and, even disposition. We are very well satisfied with the beagle dog as an experimental animal. When one considers dealing with hundreds of animals, every ounce even makes a difference. For example, examining a colony that weighs four and a half tons, you have to consider the weight, size, behavior, etc.

As a matter of fact, I might mention for those who are interested that in our routine examinations we can examine 100 dogs an hour.

Question: Has leukemia been observed in the nonexposed beagle?

Dr. Andersen: No, we have not seen it, as yet. We have been very patiently sitting around for eight years looking for leukemia, but we have not seen it. That is one thing -- it requires really patience and low blood pressure in conducting these experiments.

Dr. John L. Tullis, New England Deaconess Hospital, Cancer Research Institute, Boston, Massachusetts:

I am presenting this report on behalf of Dr. Shields Warren, the Director, and also the members of the staff of the Cancer Research Institute of the New England Deaconess Hospital in Boston. We in this Institute have been interested for a long time in radiation problems and in radiation medicine. It is impossible to go into a discussion of all of our projects at this time. However, I do want to talk about a few of the things which are of particular interest in civil defense matters.

There has been considerable interest in determining the effectiveness of chronic low-level exposure to ionizing radiation in shortening human life span. In the developmental period of radiology and radiation therapy in this country, the inherent dangers of the new modality and the advantages of protective methods were not fully understood by all physicians. Estimates of accumulated exposures to the pioneer radiologists range from 1000 to 4000 r, and that is a tremendous amount of radiation. This comes from a study made by Braestrum at Columbia University College of Physicians and Surgeons, New York City.

It has been shown that radiologists in the past have had a higher incidence of leukemia and certain other diseases than do non-radiologists or the lay public. It has also been noted that radiologists as a group die earlier than the corresponding male population over 25 years of

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age. The difference in life span was as much as five years on the average in the earlier days, the period before World War II. It has decreased since then to about two and one-half years difference in the 1956-1957 period.

The improvement in longevity of radiologists is considered to be due in part to an increased awareness of the dangers inherent in their occupation and associated with unnecessary exposure to radiation. Also it is due concurrently to the improved concept of radiation protection and improved means of protecting against radiation exposure. These steps have been much more clearly defined in modern radiation practice, and the radiologists have taken active steps to follow the dictates of good practice.

A study by Court Brown and Doll in England of the life span and cancer mortality among the British radiologists is somewhat different than our own figures here in the United States. They have found no nonspecific life shortening or shortening of life expectancy in a study of 1377 male radiologists during a 60-year period from 1897 to 1957. There was an excess of cancer deaths in those who entered the practice of radiology before 1921, but none is apparent after that date.

In discussing with these authors the discrepancies in the two reports, it has been determined, or it is thought, that the most likely reasons for these discrepancies appear to be the nature of the control group used in the British study and the fact that effective protection devices were adopted in England much earlier than they were adopted in this country. The use of effective protection devices, would contribute materially to the health and welfare of the radiologists.

It is generally agreed that the British were aware of the occupational hazards earlier than the American radiologists, and they also adopted steps to take on the protective measures, which their American colleagues did not do at so early a date. The gap is now being closed. As I pointed out, the two and one-half year life expectancy difference in the late figures as compared with the five years difference in the earlier figures in the American radiologists, is an indication of that.

The control group of the British radiologists is listed as the "socio-economic class 1." It is difficult to define this particular control group. It is felt by American students of the subject that the arbitrary selection of a control population may introduce a bias which might lead to a false conclusion. We think it would be very interesting if the British would repeat their study, using as a control group, physicians who are not ordinarily exposed to radiation in the normal practice of their profession.

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Another group of experiments in progress at our Institution is designed to clarify the role of radiation in carcinogenesis. We have used Slonaker rats and Ajax mice. They have been subjected to total body radiation in increments of 100 r per week ranging from doses of 100 r total to 1000 r total. In general, it can be stated that fairly high levels of radiation are required to produce tumors in any appreciable number.

Many disease processes play a part in shortening the life span of the mice. Chief among these are leukemia, sepsis, lung tumors, which are both benign and malignant, and a scattering of other tumors in other organs and glomerulosclerosis. It is interesting that leukemia and sepsis become prevalent in mice that receive about 300 roentgens, but doses greater than this amount do not increase the incidence of leukemia. On the other hand, doses in the range of 500 roentgens produce bronchiolar and alveolar epithelial metaplasia beginning about 20 weeks after exposure. This is greater than the leukemia dose requirement.

Metaplasia in the respiratory epithelium was found in nearly all the mice that received 500 roentgens or more of radiation and that survived for 50 weeks. It first appears at 20 weeks, but practically all the animals have it after 50 weeks. In the control animals, this change is rare at any age and is particularly so before the age of 50 weeks. Mice that have received irradiation in amounts greater than 500 r develop lung cancers with increasing frequency, beginning about 30 weeks after exposure. Adenocarcinoma of the lung is often seen in mice dying 40 to 50 weeks after irradiation, while in the controls, simple adenomas were very rarely seen before 50 weeks, and carcinomas were uncommon, even in very old mice. Glomerulosclerosis is a common finding in the older irradiated mice and is not seen in the control animals.

The acute pathologic and physiologic changes following irradiation of the central nervous system in adult laboratory animals, especially rats and mice of known genetic background, have been studied during the past nine years.

High points are:

(1) The various elements in the brain are differentially affected by various doses and especially different intensities of radiation. To illustrate by extremes, 200 r of conventional x-rays produces virtually no measurable effect; 1500 r conventional x-rays kills a few oligodendroglia cells; and 20,000 r, a few neurons. If the 20,000 r are given in a few minutes or a few seconds, severe brain damage with acute destruction of cerebellar granule cells, cortical neurons and even white matter, occurs.

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(2) Very high intensity radiation -- that is to say 35,000 rad in one second of 3 Mev electrons -- which penetrates through a mouse's brain may kill it instantly.

We are fortunate in having available to us a great deal of high-powered equipment at the Massachusetts Institute of Technology Radiation Laboratory. We are therefore able to get these massive doses in a brief period of time. The site of action in this massive dose experiment is shown by shielding to be the lower medulla. However, sharp differences exist between the genetic strains of mice in respect to this instant death as well as the pathologic response of the cellular elements. These have only in part been related to peculiarities of brain metabolism of the mice.

(3) A third point, an interesting new lesion has just been seen in mice exposed to the foregoing high intensity radiation which survive a day or two -- which an occasional mouse will do. The lesion is characterized by symmetrical bilateral large regions of necrosis in the brain stem, cerebellum, midbrain or hypothalamus.

The fourth project which I would like to mention is the one dealing with acute pathologic effects and the mechanisms of malformative development that follow exposure to ionizing radiations. We have done this both in rats and mice and a few other laboratory animals during the past nine years. The high points of this study include the fact that x-rays in doses ranging from a threshold of 30 r to about 300 r selectively destroy primitive differentiating embryonal cells. Doses higher than 300 r are much less selective.

Malformations are the result of the developmental processes disturbed by this selective destruction, and they parallel in principal what happens in lower vertebrates when similar cells are extirpated mechanically in experimental embryology. Irradiation of embryos and fetuses is now used not only to study how radiation malformations come about but as a tool for experimental mammalian embryology.

Special attention is being given to using this new experimental tool to learn how the nervous system, especially the cerebral cortex develops. Also, because the malformative patterns in the nervous system are highly reproducible, animals so affected are being studied behaviorly to relate the development of structure to function.

Dr. Dearing: What was your control on the American radiologists study? You referred to the question of the control of the British studies.

Dr. Tullis: Other physicians.

Dr. Dearing: You used other

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physicians.

Dr. Tullis: Yes, we used physicians who were not radiologists and were not routinely exposed to stray radiation in their practices as controls for radiologists. There have been objections to that study, but the fact that we have more leukemia in radiologists today than we have in physicians who are not radiologists is firmly established. This is difficult to get away from.

Question: Is there any evidence that damage to the CNS contributes to the acute deaths of mice given the dosage of LD 100 -- say 1000 or 800 r?

Dr. Tullis: No, there is very little evidence of CNS damage at that level.

Dr. Chamberlain: I am Chamberlain of the Veterans Administration. I hope this won't seem that I am starting a controversy. It isn't that. But I think you said your information about the British radiologists studies was sort of hearsay, and that it was the result of conferences with the authors --

Dr. Tullis: It has been published, sir. But we tried to iron out the differences by discussion and examination of the facts. The principal authors agreed that the reasons given above might explain the discrepancies in the results of the two investigations.

Dr. Chamberlain: I wanted to bring in a personal experience, because I think it is of some significance. I spent the year 1918 in Scotland as a member of the Armed Forces, U.S. Navy Base Hospital No. 2. I got the impression that they were far behind the American radiologists in their development of an understanding of the harmful effects of irradiation and the dangers. They were undertaking things that were causing a great deal more damage to patients than the American radiologists were, during those years. I began practice in 1916, and while I was rather young in the field, I had a good deal of responsibility at the University of California and at Stanford University from 1916 to 1930, and then later in Philadelphia.

Well, now, in this contact with the British, there was not any question but what they were operating with much less protection than we Americans. We saw the new deep therapy machines, the 200 KV machines, that began to come in in 1919 and 1920, were being installed there with inadequate protection.

In fact, W. Ironside Bruce, one of the famous radiologists of the era that I knew so well, died of aplastic anemia. It was not until a good many months had gone by that the cause was found in the fact that the more tired he got, the more time he spent on a couch separated from a deep therapy installation by a one-inch thick wooden tongue-grooved

partition. These things -- it could be just anecdotal, except I made a very great study of injuries to patients and of the attitudes of radiologists in England and Scotland during 1918 and was appalled at the lack of respect which they had for the rays.

Now, as I say, I have studied these things and have read the articles that have come out about it. I have tried to understand why we Americans had a different experience. I cannot help having this personal opinion that it is tied up with the fact that in the early years of radiology the men that went into radiology chose it as a specialty in large numbers, because it represented a possibility of getting out of pushing doorbells and doing night work. They were often people who had had tuberculosis, who wanted to take it easy, who had high blood pressure, malignant hypertension, or something of that sort. They felt that radiology offered them the opportunity to cut down the workload and to govern their workload and that sort of thing. Now, I just cannot see any other way of explaining it, because to my mind, the early men here -- it is true we had our markers, as they did over there -- but those were somatic effects -- the men got their hands burned when they used the hand to study the hardness of the ray, with their hand fluoroscopes and things of that sort. There were many things that happened very early, but you can count those -- they have been pretty well documented. There are only about 25 of those radiologist markers in the United States, and, as I say, those were many times local effects. Now, the leukemia picture I think we cannot question at all. But the British have found an increase in the leukemia incidence in their radiologists, haven't they?

Dr. Tullis: Just before 1921.

Dr. Chamberlain: Before 1921?

Dr. Tullis: Not since 1921 -- they divided the population in two groups, up to 1921 for one group and after 1921 for the second. Since 1921 the incidence of leukemia among British radiologists has been no greater than the incidence of leukemia in socio-economic classes.

Dr. Chamberlain: I thought they had had some experience along the lines of ours. I think we cannot question the fact that leukemia is more frequent in the radiologists here than in nonradiologist medical people. But I just brought up the question of this matter of longevity, because it is awfully hard for me to feel that the British took better care of themselves protection-wise than we did. At the time I observed the work they were very careless indeed and seemed not to appreciate the importance of protection.

Dr. Tullis: Well, that is very interesting, Dr. Chamberlain. It is good to get your point of view on

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this thing as a first-hand observer. In any study like this, it is difficult to reconstruct in retrospect the conditions as they might have existed and apply the results to a whole population of physicians.

Dr. Chamberlain: I realize that what counts is the whole picture, and I could not have had the whole picture. At the same time when you brought this out, I had to give you my impression.

Dr. Tullis: We do have this knowledge, that the radiologists or radiation societies were established much earlier in Great Britain than in this country. They were organized into unions, if you will, and had discussions about their problems, and must have understood some of the difficulties connected with it perhaps a little before we did in this country.

Dr. Chamberlain: Well, if you read the American Journal of Roentgenology for the years 1910 to 1930, you will find an awful lot of work was being done by committees here also.

Dr. Tullis: Even today, for example, a few practicing radiologists in this country sometimes do fluoroscopy examinations without protective gloves.

Dr. Chamberlain: That is an interesting thing. I would like to point this out. I do not advocate that exactly, but it just happens that every bit of ray that reaches the radiologist's hands has been through the patient. The amount of ray that reaches the fluoroscopic screen is amazingly small. I myself feel that the wearing of the gloves is rather unimportant. I did not wear gloves and I did an awful lot of work. It is this whole body radiation you have to be worried about -- not what you get on the hands. What gets on the hands, you can see the somatic effects, of course. I happen to have psoriasis of the fingernails, but the only roentgen or radiation injury that can be demonstrated on me is the thumb -- opposing surfaces of thumb and index finger, because I foolishly, during the last two or three seconds of preparing a radium applicator, would invariably grab the thing and wind up the adhesive -- or that sort of thing. I thought I could get away with that. It is amazing how little it takes of that to produce an atrophy that makes my fingerprint look like sandpaper. Even that only affects those two fingers of each hand.

I would like to emphasize the fact that what we are really talking about is whole body radiation -- whether you wore rubber aprons, had protection around you, good lead in the fluoroscope, etc. I do believe that as much attention -- and in my book, more attention was paid to those things in the early days in the United States than was paid in Great Britain by the men who were practicing. Those are the men I saw.

Dr. Parrino: Along that line, I

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would like to add if there are any studies of longevity of German radiologists, they would be interesting. I had the same observation you did. I was a long time in Germany and we started to hire a German roentgenologist. We were appalled, as you say, by lack of respect -- he would not wear gloves nor aprons. Also I did not know what the relative leakage was on the very large machines -- Siemons Electric, as compared to ours. It was quite a worry to some of us that we could not get these people to wear gloves.

Dr. Chamberlain: I can say a word about the Siemons equipment. It has always been very carefully built and extra fine and well protected. I was really going back earlier than the Siemons equipment, to the days when a good deal of the equipment in the British Isles, particularly, was homemade, to say the least.

Dr. Parrino: Any other questions for Dr. Tullis? We learned of some very interesting basic research that is being done at the Cancer Research Institute of the Deaconess Hospital. Any other questions? Thank you, Dr. Tullis.

Dr. E. P. Laug, Food and Drug Administration:

There are a number of problems associated with exposure of foods and drugs to radiation. Our activities to date have been chiefly concerned with developing what these problems might be. They are divided roughly into two aspects: (1) Effect of prompt radiation; (2) Effect of fallout.

In 1953 we conducted experiments using about forty of the drugs most commonly used and evaluated these after exposure to prompt radiation. The exposure was close to ground zero within what is commonly known as the area of total destruction, about half or three-quarters of a mile in radius. Within this distance, activation of elements in the drugs by neutrons produced radioactivity, the chief element so affected being phosphorous. As far as effects on quality are concerned, there was deterioration of Vitamin B-12 and about 15% deterioration of 40-unit insulin. There were no others except the visible effects on all glass containers, that is to say, a darkening or smokiness of the glass, which turns out to be a very convenient "built-in" dosimeter.

With respect to foods, we had a large participation in 1955, "Teapot" Series, in which a variety of foods -- canned, frozen, fresh meats, vegetables, beverages, and so on -- were exposed, again to prompt radiation. Our chief findings here were, again, induced radiation with phosphorous the chief element involved. This radioactivity continued to be significant for a period of 4 to 6 weeks.

There was also taste deterioration

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in some foods. An attempt was made in our laboratories to trace down the cause for the off-flavors. In the case of meats we believe this may be caused by the formation of carbonyls.

In addition to this, foodstuffs were made up into diets and fed to animals in our animal colony. We had a series of rats which received a synthetic diet -- half of which was exposed to prompt radiation and half not. We studied the usual effects on animals, such as the weight, the blood chemistry, etc., and counted also the longevity. Although the statistics are rather poor because we hadn't nearly enough animals, there was some indication that the animals that ate the foods that had been irradiated had a somewhat shorter longevity.

In 1957 we participated again. This time we focused our attention on the contamination of foodstuffs from fallout. The most interesting outcome of this experiment was a very practical problem of contamination of a large element in our food -- wheat. Wheat, because of its great surplus, is commonly stored now sometimes in unprotected dumps. So we exposed wheat at about 4-inch thickness on large tarpaulins. We got it thoroughly contaminated as we could from fallout, 25 miles distance from ground zero. After this the wheat was shipped to an experimental mill in Manhattan, Kansas, and milled in accordance with the usual methods that are used. The milled stream was then sampled at thirty different points to determine where, if any, the radioactive contamination would be separated. We found (a) that the chief separation of the radioactive contamination was, as you might have anticipated, in the bran; (b) that wheat exposed to the degree that we were able to obtain here produced flour which had an extremely low radioactive contamination.

Finally, since we are attempting to keep abreast of these problems, we initiated three years ago, a program to determine to what degree the Nation's food supply was becoming contaminated by fallout. We examined approximately 2500 samples, half of which were collected before the advent of man-made contamination and the other half since. Using the pre '45 data, we made the comparison between modern and the old foodstuffs. Radioactivity measured was total beta.

Our findings so far are that the fruits and vegetables up to the year 1956 do not show a significant increase in radioactivity. But the seafoods, particularly fish and shellfish, showed a significant increase and, also the dairy products, such as cheese and dried milk and fluid milk. And finally the most interesting one which has given us much cause for thought has been tea. This has occurred twice in our control activities -- once in 1956 and

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again this summer when vessels laden with tea came through New York Harbor. In the last case, there was a very significant increase in total beta activity, so much so that there was some thought that might have to be detained. Our measurements have indicated that while the activity of the tea was quite high, the brewed tea carried only about 20% of the total radioactivity.

There have been several other instances. For example, there was a radioactive smog in Los Angeles about November 1, 1958. Our inspection staff picked up leafy vegetables grown in this area, and we found that lettuce, spinach, and celery stalks were, in fact, significantly contaminated. However, this is early fallout and we have at present no indication that this involved any of the long-term materials. A calculation indicates that the maximum concentration of strontium 90 that could have been in this material would have been approximately 300ths of one percent.

I might also say that in this summer's program there were collected a large number of agricultural products. The most significant was alfalfa. In almost every case, the alfalfa assumed activities which were about as great as that of the tea. We found, anywhere from 100 to 150 dep per gram, potassium corrected. We believe this may account for some of the activity that has been found in cow's milk. There was hardly any increase in the radioactivity of ensilage. As far as our future activities are concerned, we believe further examination of the tea is indicated. The tea plant has a high mineral content -- consequently it may translocate radioactive minerals from the soil. There is no data yet to indicate whether this activity we found is due to a direct contamination of the leaves or whether it represents such translocation.

I might say that a rerun of the values obtained in August from this tea has indicated only about a 10 to 15% deterioration in the total beta count. So we must assume that the material is of a longer-lived variety. This does not necessarily give us a clue whether the material is translocated or not, but there would be some indication in that direction.

The other activity will concern itself with seafood, since it has been indicated from our preliminary studies that the shellfish, particularly oysters and clams, carry a greater burden of total beta activity. The fish, also, and there is some chance that dried fruits, since many of them are produced under conditions of maximum exposure to air, might be very good "sticky-gatherers" for radioactive dust.

Obviously, the most important part of our activities, which we hope will come, is the characterization of individual isotopes. The measure-

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ment of total beta activity is a very quick and easy way of appraising what kind of a problem you have. Then, when you do find significantly high activities, it is, of course, necessary to characterize what the isotopes are. This is the problem that we will be immediately engaged in.

Dr. Parrino: Thank you Dr. Laug. Someone raised the point about deterioration of meat, radiation of foods, etc.

Dr. Laug: Well, we weren't able to go very much further. They are carbonyl compounds which probably contribute to the off-flavors and they are very small quantities, and it is necessary to process a large amount of meat. Of course, this isn't peculiar of prompt radiation. We can get the same effect by exposing it to gamma radiation or electrons.

Dr. Parrino: Any other questions?

Question: Do you have any idea why the rats eating the irradiated food did not live as long as the controls?

Dr. Laug: We don't know what it is sir. We made up a diet composed of the grains and milk powder, all except the mineral additives, that is to say that phosphorous, calcium, and the usual mineral additives we did not expose those. We made up a diet of these products. There were about ten of them: wheat, corn, milk powder, etc., and these were exposed and half of them were not exposed. They were all transported to the Test Site so that we felt at least they were all subject to the other variations that might have affected quality. I say guardedly that the statistics were poor, but nevertheless when you plot you get a clear indication that the rats eating this type did not live as long. It would have to be repeated and also a very much larger number because I think there were about 25 of the two-year age group. Now that's, of course, poor statistics.

Question: Could effect be due to radioactivity of the diet?

This has nothing to do with residual radioactivity because by the time the diet was made up, several months had elapsed and the only possible items that could have been there would have been phosphorous 32 and that would have gone through at least five or six half-lives. But we don't think that is significant. This may have something to do with deterioration of quality.

Joe W. Howland, M.D., Chief, Medical Division, School of Medicine and Dentistry, University of Rochester (Projects submitted - Not read at the Conference):

Summaries were submitted of the following Atomic Energy University of Rochester projects:

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1. Acute Effects: Rate of Recovery in the Dog (S. M. Michaelson; J. W. Howland)

2. Protective Effects: Drugs. Failure of S, β-Aminoethylisothiuronium, Br. HBr. to Protect Against Lethal Total Body X-Irradiation in Dogs (S. M. Michaelson; J. W. Howland)

3. Delayed Effects: Rate of Recovery in the Dog (S. M. Michaelson; J. W. Howland)

4. Therapy for the Radiation Syndrome in Dogs (M. P. Coulter; R. W. Miller; S. M. Michaelson; J. W. Howland)

5. Influence of Starvation on the Endocrine Control of Carbohydrate and Protein Metabolism (S. R. Glasser)

6. The Differential Response of the Rat Thyroid to 500 and 800 r X-Rays (S. R. Glasser)

7. Influence of X-Radiation on the Physiology of Placentation (S. R. Glasser; A. P. Casarett)

8. Influence of X-Radiation on the Developmental Physiology of the Chick Embryo (S. R. Glasser; F. T. Brayer)

9. Binucleate Lymphocytes as Indicators of Radiation Exposures in the Tolerance Range (M. Ingram)

10. Studies of Phagocytosis and Other Aspects of Leukocyte Physiology (M. Ingram)

11. Leukocytapheresis Studies (M. Ingram)

12. Clinical and Biochemical Studies of the Irradiated Dog (W. B. Mason)

13. The Effects of Ionizing Radiations on Endocrine Glands. I. Thyroid (F. T. Brayer; S. R. Glasser)

14. The Effects of Ionizing Radiations on Endocrine Glands. II. Adrenal (F. T. Brayer; A. P. Casarett; S. R. Glasser)

15. The Role of the Adrenal in Post-Irradiation Physiology (A. Casarett; F. Brayer; T. Noonan)

16. Effect of X-Irradiation on the Aging Process in the Rat (J. B. Hursh)

17. The Cause and Prevention of Acute Radiation Deaths in Rabbits (L. T. Steadman)

18. Research on the Biological Effects of Radioactive Strontium (L. W. Tuttle)

19. Effects of Daily Low Total Body Doses of X-Rays on Spermatogenesis in Dogs (G. W. Casarett)

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Dr. Karl Z. Morgan, Director Health Physics Division, Oak Ridge National Laboratory:

It has been requested that I say something about our health physics training and education program at Oak Ridge. This is a job that we have inherited perhaps because we have been in this training business; the training of health physicists, longer than any other group. We keep in contact with most of our graduates in the field of health physics. Unfortunately, we are not able to meet all the demand for health physicists. But to those of you that are needing health physicists, I will say we are interested in hearing of your needs and contacting those health physicists that are available and helping you to employ these individuals if possible.

I would like to begin by saying it is my understanding that the purpose of this conference is to review the programs that hold promise of preventing, minimizing, and treating the effects of nuclear radiation. The Health Physics Division at Oak Ridge National Laboratory plays an important role in these programs. I will outline very briefly our various programs that relate to these interests.

First of all, Figure 1 gives the organization chart in our Health Physics Division. This organization chart indicates the various research activities we have in our Division.

As you know, a health physicist is a man that is dedicated to radiation protection. He is educated in physics, mathematics, radiobiology, engineering, etc. and he applies this information in the measurement and interpretation of absorbed dose of ionizing radiation. He is a man that anticipates and prevents radiation accidents rather than tries to cure them or do something about them once they occur.

One of our most important programs as it relates to your interest here is that of education and training of health physicists. Of course, Oak Ridge National Laboratory has training programs for other groups, but our biggest and most important assignment in this field is the training of competent health physicists.

We think this program has been rather successful. During the past fifteen years we have trained many of the health physicists for the various Atomic Energy Laboratories, for the Army, Navy, and Air Force, U. S. Public Health Service, and for private industry. A large number of these personnel have received some or all of their first health physics training in our Division.

Perhaps the most effective, and successful training program that we have had has been the so-called health physics or radiological fellowship training program. Most of you know that this is an arrangement by which one or more

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universities is paired with one of the National Laboratories, and in this manner, we give both the basic and the applied training. In our own case, for example, Oak Ridge National Laboratory is paired with Vanderbilt University. At the University the students take the courses leading to a Master's Degree in Physics. At our Laboratory they take the applied training and we offer them the specialized courses in health physics. It is our feeling that perhaps these programs should be extended and enlarged - - we should begin in meeting the demand by enlarging something we know has been successful.

The next activity, the radioactive waste program (see Figure 1), is divided into a number of components and some of these relate to your interests. We have in the past done work in the treatment of sewage for the removal of radioactive materials. We have had several projects on treatment of radioactive wastes and potable supplies of water. We have had projects in which we have tested military devices for purification of water and removal of radioactive contaminants. We have a very energetic program studying the disposal and permanent fixation of high-level wastes, and, oddly enough, one of our most important programs in this activity is ecology. We group our ecological work with the radioactive waste disposal program because the primary objective is to determine what level of radioactive waste is permissible, i.e is acceptable in the environment.

We hear a great deal about the genetic effects of radioactive contaminants in the environment, but we know little or nothing about the ecological effects of radioactive contamination. We don't know, but we believe there is a possibility that the ecological effects of the fallout material and other waste radioactive material in the environment may set the limiting factors in disposal or the distribution of radioactive wastes.

What I have in mind here is that, in our environment, we have a very carefully balanced system, a balance between the arthropods, the fungi, the bacteria, the mammals, the fish, worms, etc. It has been known for many years that it takes large doses of ionizing radiation, say 10^5 or 10^6 rads, to destroy these organisms immediately. But more recent experiments have indicated that it takes relatively low doses -- a few hundred to few thousand rads -- to affect the reproduction of these organisms, or to hinder them in their environment as they seek their food supply. Also experiments during the past few years have indicated that there are factors of selective absorption or concentration of certain of the radioactive materials in some of these organisms. Therefore, it is quite conceivable that these relatively low doses of a few hundred to a few thousand rads may

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seriously damage these organisms and with factors of concentration of many orders of magnitude, levels of radioactive contamination in the environment that are of no consequence from the standpoint of direct damage to man, may indirectly affect his food supply or may affect his natural resources, his recreational facilities, and may be a limiting factor in the disposal of radioactive wastes. In any case, we have the responsibility to investigate these effects and get some basic and applied information.

Another of our activities that is shown in Figure 1 is applied health physics. I won't take your time to describe this here, except to say that in the neighborhood of our laboratory, we have perhaps the world's largest area contaminated with fission products. We are not particularly proud of this radioactivity "hot" White Oak Lake bed but we believe that this presents an opportunity for unique research in studying the distribution and the uptake of the fission parts from the natural environment. This applied group is studying the distribution of radioactive materials in the river, in the mud, and in the plants and in many organisms. We are studying the fallout material from our stacks, as well as from the weapons tests, the accumulation in milk and other food elements in the environment.

The next study shown in Figure 1 is our internal dosimetry program. We have concentrated during the past several years on studies of enriched uranium. These studies began in cooperation with Dr. W. H. Sweet of Massachusetts General Hospital. We studied terminal patients and the distribution of enriched uranium in the various body tissues. These studies are being extended to dogs and to other animals and to other radioactive materials, e.g. thorium and some of the more hazardous fission products.

I would like to indicate with the aid of a few slides, some of our specific activities in this field of health physics. We have seen this morning some very interesting animal work going on in various laboratories. We readily admit that for many years to come we will have to depend on these animal experiments for obtaining the effects of radioactive material in man. But a basic thesis of the health physicist is that we must obtain as much information directly on man as we possibly can. We must determine the damage from a known distribution of radioactive materials in man.

It so develops that one of our best sources of information on the distribution of radioactivity in man has been a spectrographic study of the trace elements in human tissue. In this program, we have collected human tissue from over 300 autopsies from many States of the Union and from many countries of the world. We have examined this tissue for the distribution of

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approximately 35 trace elements in 35 different organs of the body. From this study we have gained information on the uptake, the distribution, the biological half-life, many other parameters of these particular elements, and applied this information to the associated radioisotopes of these elements. Figure 2 is a typical chart showing the distribution of some of the more common tract elements in the human liver.

In using such data of the normal element distribution in the body we are able to obtain information useful in the assignment of maximum permissible concentrations of radioactive materials in our environment.

This chart of the periodic tables (Figure 3) summarizes some of our efforts. The black squares indicate the isotopes presently assigned maximum permissible concentration, MPC, values. There are 86 of these listed in the old edition of the ICRP-Handbook ("Recommendations of the International Commission on Radiological Protection" British Journal of Radiology, Supplement 6, 1955.) There will be over 240 in the new handbook that is about ready for publication. The new values that have been added in the new publications are indicated by the cross-hatched squares and the squares with circles indicate the radionuclides for which no MPC values have been determined. (K. Z. Morgan, Chairman of the Committees on Internal Dose of the National Committee on Radiation Protection, NCRP, and of the International Commission on Radiological Protection, ICRP, submitted the new handbooks for publication in Dec. 1958. Pergamon Press, Inc., London, England, will publish the handbook for the ICRP and the NCRP handbook will be available as a NBS-handbook, Superintendent of Documents, Washington 25, D. C.)

In our spectrographic studies of the distribution of the elements of the body, we hope to obtain other parameters by combining this information with a study of the human diet, e.g. studies of what goes into the body, the autopsy material, and the excreta. After obtaining this information for individuals of various ages, sex, weight, race, etc. we will be able to get correction factors that can be applied to specific cases.

For example, during the Windscale incident in England, we were impressed with the fact that it is very desirable that we have in hand information that is directly applicable to accident situations in which large numbers of people are involved. Here it was not possible to take the MPC value for radioiodine-131 and apply it directly to their problem. Rather, they had to use certain correction factors that were applicable to the situation. We hope in these studies to get information, not only applicable to the occupational exposure of the individual, but also applicable to the infant, to the old-aged person, to the fat and

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to the slim that may be exposed to ionizing radiation.

In the Windscale incident to which I refer, radioiodine was the principal problem. Here they very quickly determined that the limiting factor was the young individual, the child, the infant. This individual was the limiting person in the population, because of the high-radiosensitivity of the tissue, the greater intake of milk containing the radioiodine and the smaller mass of the thyroid. In this particular case, instead of taking the thyroid as having a mass of 20 grams (that of the average adult man) they took a mass of 1.5 grams. In this case instead of taking a dose of 30 rem that is permitted each year to the thyroid of an occupational worker they decided that they would allow 20 rads during this interval of exposure. So from these figures (i.e. mass of the organ, dose permitted to the organ, milk consumption, etc.) they were able to arrive at permissible concentrations of radioactive material in the vegetation. One of the criticisms that they directed at their own program during the accident at Windscale was that there was a delay of several days before they arrived at acceptable MPC values for the emergency situation. We are convinced that we must concentrate on some of these studies in obtaining figures ready in hand to use, when and if we have a Windscale accident in our own country.

The new limits of occupational exposure are shown in Figure 4. The maximum permissible RBE dose to the skin or thyroid is 30 rem per year; it is 12 rem per year (maximum) to the gonads or total body but the average RBE dose in this case must not exceed 5 rem per year.

The average to the bone is 5 rem per year but may be six times this in local areas of the bone. The RBE dose limit to the hands, forearms, and feet is 75 rem per year and for all other body organs it is 15 rem per year.

Of course, the values in figure 4 are for occupational exposures. When we talk about permissible exposures to large groups of people we are thinking of average values that are much smaller; values such as those given in Figure 5. There are no official exposure limits for the population at large but the ICRP has suggested these values to serve as a guide (see revised report of ICRP for detailed information - - - publication reference given previously). The United Nations Scientific Committee and a number of geneticists have recommended that the RBE dose to the gonads of the average man to the age of 30 should not be more than 10 rad from man made sources. From Figure 5 it can be seen that if the average RBE genetic dose from medical sources is 4.5 rem, the RBE genetic dose suggested by the ICRP from other man made sources is 5

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rem. Only 1.5 rem of this is alotted to internal exposure from man made radioactive contaminants in the environment.

In case of an emergency much larger RBE dose must be considered. Again no official values have been selected but Figure 6 indicates some values our health physics emergency teams plan to use if we have a serious emergency. The NCRP and ICRP have stated that in emergency situations 25 rads can be taken once in a lifetime; but I think we have to have these other figures in mind in case we have major accidents; in case we have to assist in rescue operations such as drag people out of accident areas. The permissible concentrations in air and water under these situations are 10^4 and 10^5 times higher than for occupational exposure.

Perhaps we can set acceptable MPC values for various situations following use of atomic weapons. We want to introduce some rather simple functions similar to the curve in Figure 7 that Dr. C. P. Straub of the U. S. Public Health Service and I set up emperically a number of years ago. Certainly in the early period following the detonation of a weapon the permissible concentration of the fission products can be quite high--a few microcuries per cc (as shown in upper part of the curve in Figure 7). But when we talk about lifetime exposures, we must get exceedingly low levels (as shown in lower portion of curve in Figure 7). During emergency situations; when we have accidents such as they had at Windscale; or atomic weapons are used the critical tissue during the early period is probably the thyroid, the lungs or the GI tract. Figure 8 shows the levels used in the emergency areas of England following the Windscale accident when iodine-131 and strontium-89 and 90 presented problems for serious consideration.

Figure 9 shows the sort of calculations that some of our personnel have made to obtain the dose in the case in which the GI tract is the critical organ. With radionuclides such as strontium, we have an initial insult to the stomach; then the dose rate gradually decreases as the Sr^{90} passes through the small intestine, because there is considerable absorption of the strontium from the small intestine. The sudden rise in the dose is the consequence of a smaller mass in the upper and lower large intestine and a longer time spent there. In a case like Ra^{228} there is a rapid rise in the dose as the material leaves the stomach and enters the small intestine. This results from the growth of the radioactive daughter Ac^{228}. This is followed by a sharp rise because of the smaller volume in the GI tract and the longer time spent in the lower and the upper large intestine. In other cases, such as with the short-lived radionuclide Pr^{144}, the dose is limited essentially to the stomach. These are the sort of

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problems one must keep in mind in applying permissible levels to civil defense problems.

In a study made some years ago ("Maximum Permissible Concentration of Radioisotopes in Air and Water for Short-Period Exposure" Geneva Paper 1955 by K. Z. Morgan, W. S. Snyder, and M. R. Ford, Proceedings of the International Conference on the Peaceful Uses of Atomic Energy, Vol. 13) we tried to list the radionuclides according to the hazards that they present to man under various situations e. g. as a result of various types of exposure. One surprising thing to some of us was that certain radionuclides (indicated in colors in Figure 1) appear among the first of the list, regardless of the assumptions we made. Thus there are certain radioactive materials that you would expect to be the most hazardous whether you take them by inhalation, ingestion, or through the skin and regardless of whether or not they are in the soluble or insoluble form.

The last group in our division (see Figure 1) that is doing work associated with your interests here is engaged in dosimetry; and we have many programs in radiodosimetry that should be of interest and concern to civil defense. I'll mention only a few of them. For example, we have basic studies of dosimetry. These studies are of importance, first of all in the improvement of devices for measuring the dose. In these basic studies we are finding out something about the mechanisms of damage from ionizing radiation. This basic information is useful in obtaining an understanding of radiation damage.

Some of these parameters which we are studying are W, the electron volts required to produce an ion pair, the stopping power, the attachment coefficient, drift velocity, relative biological effectiveness, the degrading of ionizing energy to low velocity electrons before it is finally converted into heat; the application of information theory to the state of organization within the nucleus -- all of this basic information provides a mechanism of understanding the sort of damage that those assembled here are studying and working with.

Some of our more practical dosimetry studies of this group (shown in Figure 1) in the past have had to do with the development of monitoring equipment that can be airborne. For example, during the earlier period (about 12 years ago), we developed the direct ion collectors that could be used and may still be used by the Air Force to obtain a rapid indication of airborne radioactive contamination. Then we developed the scintilation counters that were used by the Geological Survey. I believe the two DC-3 aircraft we equipped with this automatic equipment are still being used for survey programs.

Dr. J. S. Cheka from our health physics division (appearing later on the agenda) will discuss the program

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of dosimetry for mixed radiation and its application. We believe that the situation in Hiroshima and Nagasaki offers our best opportunity to apply this development in dosimetry in order to relate human damage from ionizing radiation to the dose received. Dr. Cheka will describe in more detail our contribution in dosimetry of mixed radiation to this very fine program under the direction of Dr. R. Keith Cannan of the ABCC. We are very proud to be a part of this program, in trying to determine with greater accuracy the shattering of the radiation, the shielding parameters and the dose that the people of these two cities have received.

Figure 11 is to remind us that one of the big problems of health physics is the study of accidents themselves in developing various techniques and dosimetry devices to determine the dose received by individuals in the various radiation that we have had. Here we have the opportunity of making a study of the direct relationship between known dose to man and the biological effects.

We had the unfortunate experience in the Y-12 area of Oak Ridge sometime ago (June 16, 1958) to have an accident in which eight persons received exposures ranging from about 20 rads up to 360 rads. This Figure 11 gives the distribution of the doses received by these individuals. We are setting up a program to study various means and mechanisms of determining dose in case of such accidents.

It turns out in this particular Y-12 case that the best dose measurements were obtained by a study of the activation of sodium in the blood of the exposed individuals. We plan to study the activation of other radionuclides in the body and examine the use of various types of dosimeters.

We have a group set up in our laboratory, Drs. G. S. Hurst and R. H. Ritchie, together with several of our consultants, Dr. G. E. Toma of St. Louis University Hospital, Dr. Neil Wald of University of Pittsburgh, and Dr. W. T. Ham of Medical College of Virginia to make a special study of radiation accidents and the dosimetry associated with them. They will study the accidents at Oak Ridge, at Los Alamos, at the Argonne National Laboratory, at Chalk River, and the recent accident in Yugoslavia, and try to gather in one report all of the information required to evaluate the dosimetry, and to relate the biological effects to the dose received.

I close this discussion by saying that it is our belief that none of the research programs in radiobiology and in medicine can give information of greater reliability than the reliability of the dosimetry. Your radiobiological results can be only as good as the dosimetry that goes along with it. And one of the most urgent needs is to get more trained men in health physics to work with you determining dose, its distribution, linear energy transfer, and other factors.

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Mr. Joseph Cheka, Health Physics Division, Oak Ridge National Laboratory:

Ladies and gentlemen, I am going to touch upon two applied dosimetry problems that Oak Ridge has recently worked on. The first is a problem of ascertaining the radiation hazards from various types of contaminants, as well as shielding properties of structures.

We collaborated with the FCDA, the National Bureau of Standards, and the University of California, and Tracerlab, Western Division. Our main object was to determine shielding from the fallout on the ground plane, shielding from fallout on the roof, and the effectiveness of various modifications that could be done simply and inexpensively, and what information we could gather on the dependence on energy and the feasibility of the use of reciprocity.

Now, of course, we could not spread fallout, but it could be simulated by distributed sources. Our sources consisted of 400 Cobalt-60 pellets, which had been activated at Oak Ridge. We found 400 of them were within $\pm$ 5% of 4.15 millicuries per source. These were put into a plastic tube and anchored at two-foot intervals with tygobond cement. These tubes apparently stretched somewhat when in the field. They were attached to wires so that the spacing would remain the same.

For the ground surface, we took radii such that the circumferences were even multiples of 100.

There was also a two-curie Cobalt-60 source. For a lower energy of approximately 0.66 Mev, there were 20 120-curie Cesium-137 sources. These were in double stainless steel capsules.

The buildings used were those that were left on the Nevada test site by a previous FCDA project in 1955. They consisted of five types of buildings. One was a reinforced masonry house. One was a precast concrete house. Others were: a wood frame rambler, a two-story brick house, and a two-story wooden frame house. These houses were used because they were available and were far from habitation. It would not interfere with any people. They were far enough apart so that measurements could be taken simultaneously because radiation from one location wouldn't affect the others.

The detectors used were the Victoreen pocket ionization chambers. They are energy independent except at the lower energy ranges.

Previous work at the laboratory showed that this could be eliminated down to 20 kilovolts by use of 40 mils of tin by covering one quarter the length of the meter at the cap end. It was found in the field, however, that the energies we were using of 1.1 Mev and 0.66 Mev made this not necessary.

Now, to get a base line, we

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constructed what was called a phantom house. First slide, please. This was done on Yucca Lake bed. It is quite flat. The framework was made of thin wall aluminum tubing, 1/2 inch in diameter. The various distances, i.e. various radii, were laid out, and measurements made. There was also a grid laid out on the floor of the phantom house to simulate the roof exposure. There was not much difference between the reflection of radiation from below or from above. This established the radiation from roof sources.

Next slide. This shows the precast concrete house. The reinforced masonry house turned out not to be of sufficient uniformity because it appeared that some of the blocks were filled with concrete and some of them were not, so it was not used. This particular picture shows one of the modifications that I mentioned where a doorway and a window were covered by four inches of four-inch concrete block.

Next slide shows the inside of this building and shows the setup to which the ionization chambers were placed.

Next slide. This is the reading at a 3-foot level, where the radius of the circle is 42-1/2 feet. This normalized to 2 millicuries per foot or 1 4-millicurie source per 2 linear feet. Measurements were taken at the 3-foot level in all the house and at the 5-foot level in some cases.

This slide shows the wood frame rambler which has been mentioned previously. This is the wood frame rambler showing the inside, showing the settings of the ionization chambers. This is the two-story brick house which was measured in the basement, the first floor, and the second floor. The wood frame house is very similar so one measurement would serve for both.

These are figures of the first floor of the two-story brick house with the source radius of 42-1/2 feet.

This is the wood frame house in which all the first floor and the roof measurements were made, also the window wells for the basement. Blocking these wells was one of the modifications used to prevent radiation coming in at the windows.

Here is another modification where a double thickness of four-inch concrete block was put on a wooden table and there is another shelter structure in the basement.

Next slide. This is the figure at the three-foot level, second floor of the wooden frame house at the source radius of 63.7 feet.

Incidentally, to get the ground level radiation here without shielding, a bulldozer was passed around to at least 65 feet from the house so the ground was smooth to at least that distance.

This shows how the lines were laid out. In that particular case we have a fill-in of sectors where the radius

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was too small to complete the ring. You see the stakes set out for the larger circles.

This is a reciprocity exposure. Incidentally, for reciprocity instead of having the detectors on the inside and the source outside, the 2-curie sources were used inside and the detectors outside.

I show this because it shows how the circles went when we were evaluating the ground radiation.

The next slide shows the shielding factors observed. A wood frame house offers a factor of 2 on the first floor, while a brick house gives a factor of 7 at the same level. A basement yields a factor of 50 to 100 without modification, and up to approximately 1000 when 8" concrete blocks are placed on a table for a shield.

A detailed report on this exercise is being prepared by C. Eisenhauer of NBS.

The other problem concerned the measurement of prompt gamma and neutron radiations from nuclear weapons.

Gamma radiation measurements were made with chemical dosimeters by Edgerton, Germeshausen, and Grier of Las Vegas. Our part of the problem comprised the evaluation of neutron radiation by means of threshold detectors. These give, not only total neutron dose, but also a rough breakdown of the spectrum of neutrons producing the dose. The method has been described in the literature. (P. W. Reinhardt and F. J. Davis, "Improvements in the Threshold Detector Method of Fast Neutron Dosimetry," Health Physics 1, 169 (1958).

The measurements made included air dose, angular distribution, and attenuation by structures.

These measurements were made as a part of what we call the "Ichiban Project." The Ichiban Project is an attempt to evaluate the radiation doses sustained by survivors of the Hiroshima and Nagasaki bombs. In this we work in cooperation with the Atomic Bomb Casualty Commission (ABCC).

The ABCC has done a monumental job in collecting case histories on these survivors. These histories are chiefly medical, although they include details of location at the time of the burst. Such information can be made more valuable if the symptoms noted can be correlated to doses received. Such information would also be valuable in the case of nuclear warfare, or in case of a nuclear accident.

The structures used were constructed to simulate Japanese dwellings of three characteristic sizes. This type of experiment is feasible because of the great uniformity of Japanese dwellings. These houses had substitute wall materials rather than the clay of the true Japanese dwellings. The substitute material,

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transite, was chosen after extended tests at our Laboratory of various building materials in sheet form. Transite was found to have relative gamma and neutron attenuating characteristics very similar to that of a Japanese wall section.

The first slide shows the collimators, on a 1000-yd. radius, which were used to measure angular distribution of radiation.

The next slide shows the inside of one house with the detectors attached to cables forming a three-dimensional grid. The cables were pulled out of the structures after the shots.

We had seven houses, and exposed them to three shots, since the structures had not been demolished by the first two, but were usable after some repair. The houses were placed so as to check effects of orientation and mutual shielding. The next slide shows the arrangement for the first shot.

The next slide shows the rearrangement for the second shot.

The next slide shows the arrangement for the third shot, using six houses, as one was beyond repair. This is looking toward Ground Zero.

The last slide shows the type of data obtained. These results are from a previous test during Operation Plumbbob, when only two houses were used.

The recent data have not yet been analyzed.

Dr. Niel Wald, University of Pittsburgh, School of Medicine and Graduate School of Public Health:

In accordance with the Chairman's somewhat unanticipated request, I will discuss briefly the type of radiation health training and research program upon which we are embarking, in common with at least three other institutions - Johns Hopkins and Harvard Schools of Public Health, as well as New York University College of Medicine.

This program was instituted under the auspices of the Medical Education and Public Health Division of the Rockefeller Institute, which is headed by Dr. John Bugher. Need was felt for a type of training which would enable medical and public health personnel to deal with the various health problems which arise out of nuclear technology, the increasing applications of nuclear power, and nuclear propulsion, for example.

It was felt that the people trained in the medical specialties were not too well equipped to deal with the physics side of the problems, whereas those with the education and training in the physical sciences were not too well equipped to deal with the health problems.

Our training program, which will take its first students next September, is designed, as are the others, I presume, to fill this particular need. We are planning on a program of at least ten years' duration in an

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exploratory sense, to see how this sort of project can be developed.

The basic training is properly located in the School of Public Health. It includes general instruction in handling public health and occupational health problems in some detail, as well as some more specialized training in radiological and radiobiological matters.

For the field experience, in Pittsburgh we are rather fortunate in that our location's vicinity includes cyclotrons; a power reactor at Shippingport, Pennsylvania; the Bettis plant of Westinghouse which produces the nuclear submarine engines; and the materials test reactor complex, also of Westinghouse, at Waltz Mills nearby. In addition, as research facilities we are using those that are present not only at the School of Public Health, but also at the Medical School and the affiliated hospitals of our Health Center. I think this in general will give you some idea of the type of program that we are trying to develop.

I have some leaflets which give this in a general way, and also a sample curriculum, if anyone is interested. These will be made available to the secretary for the Proceedings.

To support this type of training program, we must also have a research program. This brings me into the research activities at the University of Pittsburgh, which I was planning to mention briefly.

I should point out that these activities are not centralized, as is the case at some university campuses - Rochester or California, for example - and therefore, the efforts are not always complementary or supplementary, but go into many directions.

In the field of acute effects, there are some studies going on under the direction of Dr. Max Lauffer, "Correlation of Radiation Effects with Physical and Chemical Changes in Viruses." These studies are on a fundamental level and deal with changes in the RNA core of the tobacco mosaic virus which they have been able to demonstrate. They have also been able to show that RNA breakage and virus inactivation occurred after radiation in a one-to-one ratio, implying that the core is a single chain. Further studies are going on along these lines.

There are some other basic studies concerned with hydrogen peroxide toxicity, and its significance for biological effects of ionizing radiation - again, on the biochemical level.

Concerning the late effects, there is a rather large program at the School of Public Health, which deals with lung hazards from inhaled radioactive particulate matter. It is quite similar to that which was described earlier this morning in the work at the N. Y. U. - Bellevue Medical Center.

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This program demonstrated in rats at the outset of this study that intrapulmonary radioactive particulates are carcinogenic. This research has gone on to examine some more specific aspects. The duration of radiation, as well as the absolute absorbed dose, turned out to be crucial in the occurrence or production of bronchogenic carcinomas. The type of materials used were radioactive dust particles by intratracheal insufflation, as well as radioactive beads of the type that were mentioned earlier. The radioactive materials included barium sulphate, thallium-activated clay particles, Strontium^{90} beads, and radioactive cerium flouride.

Another study concerning the late effects of radiation is one that we are carrying on in investigating the cytogenetic changes of the white blood cells after irradiation and in leukemia itself. This is an attempt to determine whether the changes in the genetic configuration of the white blood cells occur gradually with variations in chromosome number and type, or whether they occur in an explosive manner all at once. This, of course, has bearing on whether or not a threshold is present for leukemogenesis, secondary to radiation.

There are some other studies pertaining to chronic effects on a cellular level - a study of aging, for instance, carried on by Dr. Ralph Buchsbaum, using a mouse cell tissue culture which is living but nondividing. This is necessary in order to show aging effects, since cell division results in production of new, young cells.

A study which concerns both genetic and somatic effects of low level exposure is currently being embarked upon at the School of Public Health by Dr. C. C. Li, Dr. Thomas Parran, Dr. Antonio Ciocco and myself. A preliminary survey will be conducted soon concerning the feasibility of study of the monozite sand dwelling Brazilian population for genetic and somatic effects of long-term, low-level radiation exposure. As you know, the basic physical measurements have already been made and presented to the U. N. Radiation Committee. It appears that there is a population of at least 50,000 people who are living and have lived for generations in a relatively high background radiation area. It is of interest to determine whether or not one can demonstrate any effects of this repeated lifetime and generation-after-generation exposure to low-level radiation.

There are some additional features of our program which are similar to those already mentioned at the Bellevue Medical Center. We are planning to institute the use of low-level, whole-body radioactivity counting, both for the detection and medical management of radiation overexposure, if and when it occurs in the populations of industrial workers in our area, and also for the further understanding of the metabolism of various tracer elements and radioactive materials which may present problems in the environment of the nuclear technology employee.

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The other large problem which is going on at our University concerns the effects of radiation on the immune response, under the leadership of Dr. Frank Dixon. These studies have gone on for many years now, and are quite complex. Very briefly, they have shown that there are both radiosensitive and radioresistant phases in antibody production in the mammalian organism. Also, they have shown that radiation will affect the antibody-producing cells not only directly but also indirectly, if one transplants such cells, for example, into a radiated host.

There are many studies under the departments of radiology at the various hospitals which comprise the University of Pittsburgh Health Center. I will not attempt to review all the isotope applications in both diagnostic and therapeutic work which is going on.

That, in general, summarizes the programs at the University of Pittsburgh. A more detailed listing of participants, projects and publications has been given to the secretary of this meeting for inclusion in the written proceedings.

Floor: I was wondering how you maintain the mouse tissue cultures in the nondividing state and for how long?

Dr. Wald: That has been the main problem of that particular project of Doctor Buchsbaum up to this time. I am not qualified to give you the details of the technique. I can only refer you to Dr. Ralph Buchsbaum. I think this is fairly new work. That will be Dr. Ralph Buchsbaum at the University of Pittsburgh, Division of Natural Sciences.

Floor: This study of people living on radioactive sand - is it in progress?

Dr. Wald: The preliminary survey team will visit Brazil shortly after the beginning of next year (1959) to develop the actual plans. Up to this point it has been a matter of correspondence to determine whether even a preliminary team visit is justified, and it appears to be well justified.

Floor: The Indian government has such a project.

Dr. Wald: Yes, there is a very similar project with a larger population, and perhaps cleaner, in the sense of the population staying in one place. There are complications in these studies from a political or geopolitical standpoint. It is possible that the Brazilian one may be more easily developed than the Indian one. But both are being actively examined. These are, I think, the two largest population groups presently known in which the dosimetry of the situation has been explored sufficiently.

Dr. Parrino: I would like to ask exactly what your study on the depression of immunity entails? Are you also doing some work, for example, on the relative effectiveness of antibiotics in the irradiated as opposed to the nonirradiated animals?

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Dr. Wald: No, this has not been explored. This work of Dr. Dixon's group is a series of studies which are presently well limited to the fundamental problems of the immune response as it is affected by x-irradiation, without adding any additional unknowns.

Frank A. Todd, D.V.M., Assistant to the Administrator, Agricultural Research Service, Department of Agriculture:

In the Department, all of our projects in this field are carried out in cooperation with the Atomic Energy Commission. Most of the research effort carried out by the Department of Agriculture deals with the contamination of soils and crops. We do have the one project that Dr. Comar mentioned this morning. We also have one field operation in which we are using atomic energy as a means for disease eradication.

Project One: AEC Contract AT(49-7)-1. Accumulation and Movement of Fission Products in Soils and Plants (ARS)

The behavior of nuclear fission products in soils, their availability to plants and their direct absorption and distribution within plants, are investigated by laboratory, greenhouse, growth chamber, and field experimentation. The redistribution of deposited fallout by rain and erosion and methods for the decontamination of agricultural land are studied in the field. Attention is centered on the long-lived fission products, expecially strontium-90 and cesium-137.

The extent of movement of radiocesium and radiostrontium under leaching was measured recently. Present soil studies include the absorption sites of radiostrontium on clay surfaces and the possibility of fixation of strontium in nonexchangeable states. The effects of natural exchangeable calcium and of lime on the uptake of strontium by plants remain under study.

Project Two: AEC Contract AT(49-7)-2. Collection and Preparation of Samples of Soils, Plants, and Animals for Calcium and Strontium Analyses (SCS)

The objectives of this project are to determine the worldwide distribution of strontium-90 in soils, plants, and animals, and to contribute to an understanding of the meteorological factors determining the distribution of radioactive fallout. Emphasis is given to soil characteristics and landscape features that determine the retention of strontium-90 in place or subsequent movement after deposition. At a number of locations the relation between soils, plants, and animals is followed on a continuing basis. Interpretation of the data is made in terms of significance of strontium-90 in the food chain of man.

Project Three: AEC Contract AT(49-7)-1527. Equipment and Methods for Decontamination of Agricultural Lands Contaminated by

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Radioactive Fallout (ARS)

Feasible procedures for the large-scale economical decontamination of agricultural lands with power implements are investigated. These might entail the removal of standing crops, crop residues, or of a layer of the soil itself. In the last case, a successful method must not reduce drastically the depth of the productive surface soil. Various types of crops, soils, land surface conditions, and equipment are compared. Commercially available machinery is used wherever possible, and adapted or modified as required. The use of materials for consolidating fallout with the soil surface prior to removal, such as asphalt emulsions, is investigated. The criterion of effectiveness of a procedure is the percentage of the applied quantity of radioactive contaminant remaining on the land.

Project Four:

Dr. Comar mentioned very briefly the work being carried out at Cornell University in cooperation with the Agricultural Research Service and the Atomic Energy Commission. This project includes a study designed to determine the extent to which radioactive strontium ingested by dairy cows and goats becomes incorporated into their milk.

Studies to date have included the collection and correlation of data on laboratory and domestic animals in regard to tumor induction, nutritional management, and natural and artificial radioactivity and will serve as a basis for understanding and investigating the implications of radioactive contamination of the food chain.

This work includes the study of incorporating into the diets of selected dairy cows and goats tracer amounts of radiostrontium and radiocalcium designed to establish the similarity of radioactive isotopes in cows and goats as related to their quantitative residual appearance in milk, blood, feces and urine. This would also include determining the fate of the radioactive materials in the metabolic processes of animal tissues with particular emphasis on the quantitative residual appearance.

Project Five:

This includes the application of atomic energy as a means of disease eradication. This project is being conducted in the southeastern part of the United States and is specifically for the eradication of the screwworm.

The screwworm fly is estimated to cost the livestock industry in the southeastern United States approximately $20,000,000 annually. Entomologists have studied the life cycle of the male and female screwworm flies and have learned, among other things, that the female fly mates only once in its life span and - equally important - that this proclivity is not characteristic of the male fly. Thus male flies are artificially reared in large numbers, up to 50

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million per week or more than 2-1/2 billion per year, and irradiated with gamma rays from cobalt-60 sufficient to cause sterility. The sterile flies are liberated by air at carefully timed intervals in sufficient numbers to blanket the area. When these males are allowed to breed with the female flies, it results in no fertile eggs.

The project of eradication of this disease appears to be successful and it is hoped that the disease will be eradicated in about two years. It is estimated the entire cost will be about ten million dollars.

The results of the project to date are indicated by the fact that last year many thousands of cases of infected cattle were reported as compared to less than 100 cases this year. This project stimulates our thoughts to new approaches to insect control using this new weapon of atomic energy.

Mr. Kenneth J. Nicholson, Food and Materials Requirements Division, Commodity Stabilization Service, Department of Agriculture:

I'm not directly concerned with research; so I have no research to tell you about. Dr. Frank A. Todd covered that yesterday for USDA. My concern is with defense mobilization planning, and particularly with what resources we might have in food and agriculture after a nuclear attack.

My work is largely done directly with the National Damage Assessment Center, which is operated by OCDM. Now I must tell you that one of my main concerns in this work is about something that I've heard little about here as yet. Possibly something has been done about this problem that has not been told, and if so, I hope we'll hear something about it. My problem deals with livestock. It is easy to forget that a very large part of our food is taken as livestock products.

We would, of course, be very much concerned postattack with the feeding of the people. The first line of food supply might be the livestock that are remaining on farms and are directly accessible. But one of the things that we do not know enough about is how much of this livestock will be available, at least alive and usable either for meat or to produce milk.

Dr. Weber, I think it was, mentioned something here just a few moments ago that was very much to the point. He said we might find internal radiation problems to be the limiting factor, postattack, rather than the external radiation. We have suspicions that may be true in livestock. A very large part of our livestock is grazing livestock, and would be in a position where it would immediately be taking up isotopes that might be the limiting factor, possibly radioactive iodine,

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cesium or other isotopes that I know not enough about. It is true that most of our thought and concern has been in terms of trying to determine what livestock we would have available to use for food on the basis of external gamma radiation dosage alone. But is that really the true problem? Possibly grazing livestock will die from internal radiation before external gamma dosage becomes critical. I know that Mr. Forrest Western of AEC has been concerned with some of these problems of internal radiation. I believe he really feels that it is an area to which we ought to give a lot of attention, even including non-grazing livestock, and still more especially in the dairy cattle.

It is my understanding that the experience at Windscale, possibly other experiences as well, would point to virtually no milk to be consumed by human beings from any area that has had any radiation at all, possibly up to say, two or three r per hour, which is virtually nothing under attack conditions. If that is true, we would have a tremendous problem in this Country in supplying the milk needed during the first 30 or 60 days after attack.

Possibly there are other areas here, closely associated with what I have just touched on, that would be worthy of consideration by you people who are directly active in research. If these answers are already known, I hope you will use your offices to pass the information along to us who are concerned with trying to assure a food supply postattack. I think that one of your greatest problems is to develop a plan which will assure a wider spread dissemination of the results of research, especially to the planners and the action agencies where it can do much good.

Dr. Parrino: Thank you, Mr. Nicholson. Any questions?

Dr. Straub: With respect to the last point Mr. Nicholson just raised, the present data, resulting from the analysis of human tissue vs. animal tissue, drawn from similar neighborhoods or nearby areas, does indicate clearly that the level of strontium-90, for example, in cattle may run 20 to 40 strontium units while those humans in the same neighborhood would run less than one. You can hazard guesses as to why this is true; I suppose it's because of grazing and quick uptake of polarly deposited fission products in contrast to the relatively fine foods that humans consume. And I think this could be used as a guide, perhaps not as a scaling factor, but as a guide to what the prospect might be in case of massive fallout. This could also be true as to cow's milk vs. human milk. We have some data on this.

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Dr. W. Edward Chamberlain, Special Assistant to Chief Medical Director for Atomic Medicine, Veterans Administration:

There will be a documentation on projects which will take care of details. It is not yet ready and I think you might appreciate why when I tell you that at the end of FY 1957, we reported to Congress 6,370 individual medical research projects at VA hospitals. These projects are abstracted in "Medical Research in VA," House Committee Print No. 188, 85th Congress, 2nd Session, May 6, 1958, which is available.

Now, a great many of these represent contributions of individual doctors practicing in Veterans Administration Hospitals, investigating sometimes at their own expense, but at any rate, on VA money, if no outside granting agency is involved. A great deal of support comes to these investigators from the granting agencies that we have been speaking of in general terms, largely from the National Institutes of Health.

The NIH has done us the honor of pointing out that sometimes the research that they are interested in and would like to support had to be done somewhere where there were a lot of patients and that is one thing the VA has -- a great many patients. These patients are available for follow-up purposes and with the help of the National Research Council we have an excellent program of follow-up.

You are, perhaps, familiar with the follow-up machinery which has been established at the National Research Council for long-term follow-ups. And that, of course, is one of the things which is usually not so well accomplished in a free democracy. But we have a kind of control over our patients which is benign and at the same time effective.

The VA doctors are doing a good job these days. Since 1946 we have had a great deal to be proud of in the kind of medical care given to patients, wards, beneficiaries, of the Veterans Administration setup. The patients tend to come back and, at any rate, we have access to them through their disability checks and their pensions.

With so many research projects to deal from, I thought today I would only pick out a few that seemed to be illustrative of what can be accomplished or what can be brought out in this kind of program.

Our whole program is extraordinarily decentralized. That seems to me to be a very good thing for the purpose for which our research program is supported. The men in the field at field stations are working on their own particular research programs. We do not sit at the Central Office

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and say there shall be research done in this field or that field by this man or that man. Nothing of that sort ever happens. We are there to make it possible for these men to do research, to create the facilities for them.

The dividend which the VA gets is that you have a more scientifically higher type of doctor working on VA patients because of this research program. It is very easy to prove that, and, as the history of the research program shows, it has had a profound effect in making that possible for us to recruit a higher type of physician for the VA's medical service and in putting the doctors already in the VA on their tiptoes. It has increased their interests and has in every way improved the service to the patients. The particular projects which I have selected to talk about are these. We have a good deal of interest in total body radioactivity measurements. Now that sort of thing is going along in several places in the country, but we have patients with whom that becomes a big problem. We are happy in the fact that at one of our field stations, the facilities are available for whole body radioactivity measurements, with the proven high efficiency of the order of 90% in Dr. B. A. Burrows' low level external body counting device up in the VA hospital at Boston.

Another project which had attracted a great deal of attention at Central Office is the one by Dr. Rex L. Huff out at Seattle. Dr. Huff did some of his best work in this particular project sitting at his desk and thinking. He was struck by the fact that the most sensitive radiation cells in the animal body are situation inside the tubular long bones protected from something by a bony cortex. He remembered that there is a certain amount of soft radiation coming from K-40, the radioactive isotope of potassium, which has a natural prevalence of something like one atom per 25,000 atoms of stable potassium.

Dr. Huff surmised that perhaps the location of these radiation sensitive bone marrow cells might be produced in the way that evolution produces things, by the necessity for protection against the soft radiation of $Potassium_{40}$. With the help of the Atomic Energy Commission, he got some potassium which had its K-40 components reduced by a factor of 80%. He made culture media for tissue cultures from the normal, natural potassium that has its normal and natural prevalence of K-40 and also from this specially produced potassium which had a depleted K-40 component. To his amazement the tissue cultures are very tight and particularly the leukemia-cell cultures and things of that sort grew luxuriantly in the culture media that had potassium in form of the specially low radioactivity status.

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I think the only other project I thought I would mention at this moment is that about the training at Long Beach Veterans Administration Hospital, Long Beach, California. Dr. N. B. Kurnick learned how to freeze bone marrow removed from a living patient in glycerol and preserve it for indefinite periods of time, with a salvage of as high as 85% of the cellular components after restoring it to its natural state by warming it up. His proof of viability is satisfactory to all of us. He has been carrying out this experiment on selected cases in which large parts of the body had been irradiated with very large doses.

He has succeeded in improving the lot of the cancer patient having to undergo a great deal of heavy therapy, by preserving this bone marrow from the patient and giving him the autogenous transplant of his own bone marrow after irradiation had depleted his white count and had done away with his hematopoietic tissues to a very great extent.

The big question comes up, of course, as to how many cancer cells might be preserved in the glycerol freezing process, but usually patients have some marrow spaces where the likelihood of cancer being present is very small -- at least that is the hope. But it has interest, of course, to us on account of the possibility that someday we may obtain a source of bone marrow cells that will stand transplantation into the human beings on a larger scale. Now I think that's all unless somebody has some questions. Thank you.

Stella Leche Deignan, Ph.D., Director, Bio-Sciences Information Exchange, Smithsonian Institution:

The Bio-Sciences Information Exchange is a unique clearinghouse for current research in the bio-sciences. It embraces basic biology, medicine, and psychology, but does not include physics, chemistry, or engineering except in those areas related to medicine and the bio-sciences.

The Exchange began in 1946 when the government initiated its peacetime support of research in schools of medicine and the life sciences, in order that the supporting agencies would not unknowingly duplicate each other; but was formally established as an interagency unit in 1950.

The primary function of the Exchange is to inform granting agencies of the amount and sources of support of investigators, institutions, and fields of research. Its knowledge of fields of research comes from summaries of research problems written by the investigators carrying out the work. The staff of the Exchange indexes these summaries in great detail and as a result is

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enabled to provide the scientific community as well as granting agencies abstracts of work in progress.

Although supported wholly by seven government granting agencies, the programs of the national fund-raising agencies and of the major private foundations are also registered with the Exchange. In addition the intramural research of several government groups and some research, not grant supported, in universities and other institutions has been recorded with the Exchange.

Twenty thousand active research projects comprise the body of current information in the Exchange. As problems are registered when they begin and as the summaries are revised annually, the summaries frequently precede publication by several years. Further, the abstracts of terminated projects provide a source of direction to negative or unpublished results.

It has been amply demonstrated that there is often a close relationship between the problems of men in totally different disciplines and in totally different fields. People with widely diverse scientific interests do not often meet in professional societies nor communicate through journals. The Exchange bridges this gap, for it aims to put men in direct communication with each other. It does this by providing pertinent summaries of research in response to individual requests. It welcomes registration by scientists and it provides information without charge to research men associated with recognized institutions.

The Exchange provides information on the amount of support only on that research supported by national granting agencies. In this group you may be interested to know that of the 12,410 awards made by national granting agencies in the Fiscal Year 1958 (July 1, 1957 - June 30, 1958), 9993 were from government agencies and the remainder from nongovernmental ones. Of these 12,410 awards, 528 were for research in radiation effects and usage. The overwhelming number of these, 475, were supported by government grants and contracts.

Radiation studies are indexed in a variety of ways and in great detail with and without reference to radiation effects. From the former standpoint they are categorized to show the direct effects at the tissue level; the direct effects on genetics, reproduction, immunity, etc.; the environmental effects on soils and plants, air and water, etc.; and the uses of radiation in sterilization, therapy, diagnosis, etc.; protection against and treatment of radiation injury; and a number of other approaches. This should present a partial outline of the Bio-Sciences Information Exchange coverage of research in the field of radiation biology.

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In closing, the Exchange will welcome registration of other work in this field and will be happy to receive inquiries on specific research problems.

Dr. Parrino: Any questions on the Exchange?

Dr. Taylor: I am glad to hear of this as I was unfamiliar with the Exchange. Would you explain the figures on the numbers of projects - 12,000 supported by granting agencies and others. What are the others?

Dr. Deignan: Research in industry and industry supported research has not been registered with the Exchange, nor has the intramural work of the AEC, the laboratories of the PHS, nor work in universities not supported by granting agencies. Exclusive of industry, I believe that the Exchange has 90 percent of the research supported by grants and contracts. It is my personal opinion that almost every laboratory is receiving some support from national granting agencies.

Dr. Taylor: I just want to remind you that it is too bad that the Exchange doesn't have this other information too.

Dr. Deignan: It is unfortunate that, although we have national conferences on documentation and the need for rapid communication, investigators cannot all see that we have an effective means of communication that can be used freely and which takes from the research man only the time necessary to write a 200-word summary of his problem.

Further discussion centered on the number of requests for information handled by the Exchange and the time involved in answering them.

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Dr. N. F. Barr, Sloan-Kettering Institute:

Dr. John S. Laughlin, Chief of the Biophysics Division, has asked me to outline those projects now in progress at the Sloan-Kettering Institute which might be of interest to this conference.

We are doing fundamental studies on the synthesis of DNA in irradiated normal and neoplastic tissues in tissue culture as well as an investigation of the oxygen effect in virus-infected bacterial cells. We have a continuing program on the relative biological effectiveness of the various radiations we use for a variety of biological test systems. But of more direct interest to this conference is, perhaps, the secondary dosimetry studies which are being undertaken in conjunction with these and other more applied studies. At present we rely very heavily on chemical dosimetry in these radiobiological studies and in particular on the Frucke ferrous sulfate dosimeter, and accept as a consequence of this (along with all of the advantages of this type of dosimetry) its principal disadvantage, its relative insensitivity.

We have, however, in the past few months developed aqueous systems which are based upon the destruction or production of fluorescence in aqueous solution which increases greatly the sensitivity of chemical dosimetry. With these systems we are at present able to measure, in completely tissue equivalent material, absorbed doses of the order of 5 RADS with a precision of 5%. We can very easily detect absorbed doses of 500 millirads. Since we are convinced that it will be very easy to increase this by factor of 10 or 20 in the near future, we are very close to an objective of ours, that is a completely tissue equivalent dosimeter which is easily read and manipulated and which will measure absorbed doses of the order of few millirads.

Recently completed work at the Institute has made available for dosimetry studies a cylindrical miniature condenser ionization chamber with a completely flat exposure dose response over the entire range of diagnostic x-rays. This is extremely convenient to use. I have the completed report of this work which I will turn over to the Committee.

In the miniature dosimeter field we have been working with the rods mentioned yesterday by Dr. Comar - these are silver activated phosphate glass, and while their quality response leaves a great deal to be desired, we have found that the variation of sensitivity with depth for various radiations is not so spectacular, and that we might be able to use these for certain types of in vivo measurement.

Now in all of these secondary dosimeter measurements we rely very heavily on primary calibration which is based upon a direct calorimetric measurement of the absorbed dose. We have made these direct calorimetric measurements of absorbed dose

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with 22 Mev x-rays and with Cobalt^{60} gamma radiation in tissue equivalent plastic, and are now making the measurements with softer radiation in a variety of low atomic number metals and with pure carbon. We use all of these secondary dosimeters either singly or in combination in a program we have in progress in the determination of total body dose, of marrow dose, and of fonadal dose associated with therapeutic and diagnostic procedures involving both external beams and implanted radioisotopes. For this purpose we have available several phantoms which consist of unit density pressedwood in which is inserted a complete human skeleton. We duplicate the marrow space with beeswax and the lung volume with low density cork.

In addition to this, we hope that these secondary dosimeters will also prove to be of some utility in the types of studies that Dr. Glicksman will now talk about, the clinical studies which are in progress in the Division.

Dr. A. S. Glicksman, Sloan-Kettering Institute for Cancer Research, New York, New York:

Dr. J. J. Nicleson would like to express his regrets for not being able to attend this meeting personally, and has requested that I present to the group the studies in progress in the section of Radiobiology at the Sloan-Kettering Institute that would be of interest to you.

One of our major activities has been the investigation of the biochemical, physiologic, and clinical effects of total body radiation in humans. To date we have studied approximately 40 patients. The dosage that we have used has been between 25 and 150 r. The radiation has been delivered either through a 1 Mev x-ray generator or through Na^{24} as an internal emitter.

These patients all have cancer. We attempt to select them in such a way that they do not show biochemical, hepatic, renal or pulmonary dysfunction. Bone marrow must be normal and they must have no evidence of secondary anemia or bizarre metabolic disorders.

The studies on these patients are rather diversified. We have done hematologic studies and have looked and are continuing to study the formed elements. We have documented a rather characteristic fall in the platelets between the 28th and 35th day which subsequently rise. Of interest also has been a fall in the lymphocyte count during the first week and interestingly enough this rarely returned to the pre-radiation level.

A word about the bone marrow morphology involved at these times. We have seen on a few occasions an apparent inconsistency in that there has been hyper-plastic marrow at times when there has been maximum depression of circulating platelets and white blood counts. We are interested now

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in looking at more kinetic studies of bone marrow, including the tritium labeled thymidine corporation at various times following the total body radiation.

Other aspects of the hematologic problems that we looked at in some detail have been the blood clotting factors. We have followed silicon clotting, prothrombin time, prothrombin consumption time, Factor V, Factor VII, thromboplastin generation, AC globulin concentration, PTC concentration (Christman Factor), platelet function studies, capillary fragility studies - all of which have been essentially normal during the total body radiation. However, on three occasions we have had patients who have all of these normal and who have shown a bleeding diathesis. Although these studies were normal, the injection of protamine sulfate dramatically stopped the bleeding. The significance of this is still under investigation.

The biochemical studies that we have been interested in have included lipoproteins. These have been done in cooperation with Dr. M. Petermann and Dr. M. Backley. We have seen an increase in the clearing factor in those patients who have shown clinical bleeding. Patients without clinical bleeding have shown no clearing factor increase, despite thrombocytopenia of a very severe and sustained nature.

In other biochemical studies, we are currently documenting an increase in the urine creatine/creatinine ratios of whole body radiation. This has been reported in animals previously. We believe there may be an increase in creatine/creatinine excretion in humans between the 7th and 9th day post-irradiation.

Other studies include urine pentoses which appear to increase between the 4th and 8th day post-irradiation.

The possibility of altering membrane permeability, or enzymatic effects of membrane exchange, is also under investigation. We have followed glucose utilization curves following total body radiation and have seen a trend toward a decrease in membrane permeability. Similarly, using K^{42} transfer, this same type of decrease in membrane transfer (in a four compartment system, between the second and third compartment) has been noted.

In terms of immunologic study, we have noted in two out of three patients that there has been a significant increase in properdin immediately following total body radiation. This work has been done in cooperation with Dr. Chester Southern.

We are continuing this aspect of the work and are trying to add further to this list of parameters to define in more detail the physiological and biochemical alterations involved in the post-radiation syndrome. We would like now to continue this with more finite dosimetry than we have had before as Dr. Barr has mentioned. These studies have been supported in part by the Armed Forces Special

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Weapons Project.

Another aspect of the work in the Radiobiology Section has been an interest in the modification of late radiation changes. The characteristic pattern of radiation damage to each tissue has been documented for at least forty years. That this exists in a static state seems improbable; if it is in a dynamic state, attempts to modify this might prove worthwhile. In a clinical setting it was observed by members of the Memorial Center that the skin of patients who had had previous radiation and for one reason or another had modification of their thyroid status, that this skin seemed to alter with the modification of their thyroid status. With the availability of 3.5.3' L-tri-iodothyronine, we undertook a clinical study to see if this was a true situation.

The advantages of tri-iodothyronine are its rapidly built-up blood levels and its rapidity of excretions. Should there be toxic manifestations, they could be overcome very rapidly.

There are inherent difficulties to any evaluations of late radiation changes, so that it became very obvious that we had to have a double blind study. I would like to show a few pictures of some patients that we have studied in a double blind setting. This patient is a 67-year-old female who had carcinoma of the cervix treated approximately 30 years ago. She developed an ulceration in the left hip area that is shown here; approximately two years after radiation and when she was seen in 1955, this ulceration extended to, but did not include, the joint capsule. You may be able to see in the left-hand corner of the slide some of the old pinchgraph scar that had failed previously.

May I have the next slide please. Following the T_3 for approximately eighteen months, the lesion has healed completely and has remained so.

The next slide indicates some of the type of measurements that we have taken with this. The pinchmeter pictured here we have used to measure the elasticity of the overlying skin. In this setting there has been an improvement in the elasticity. You'll notice that the control level was very low. This patient started off at a weight of 97 pounds and she was practically moribund. With the correction of the infection and the ulceration, the patient gained approximately 40 pounds, the tensile strength, the elasticity of her skin improved, and as you see, two years after the onset of this form of therapy, both the affected and control factors were potentially equal. Off medications for four months, it was the same. And now I can say that off medication for a year and one-half, it has remained constant.

The next slide please. The next patient showed an ulceration due to previous radiation R_x for a lymphangioma in the left temple area. The ulcer had been present there for approximately thirty years. The

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measurements are listed and, as you see, in approximately 34 weeks the ulceration had healed and one year following the cessation of drugs, had remained healed.

The next slide. This was a woman who had had radiation at another institution, for what was considered to be osteogenic sarcoma. It proved not to be so, but she did develop a fibrosis of the right knee due to the intensive course of radiotherapy given. On medication she showed this excellent improvement. She has remained cured for the one year following cessation of drugs.

May I have the next slide please. This is a demonstration of the placebo in our double blind study. The ulcer attempted to heal and then it broke down again. This type of waxing and waning of ulceration is what we have seen as characteristic of these late radiation injuries. This patient currently is on active medication and has almost completely healed.

The next slide is another measurement in this patient showing the ankylosis of the shoulder and in this case there was absolutely no change in the patient's ability to move her shoulder.

May I have the next slide please. This summarizes our experience up into October of 1958. (Table I.) We had 75 such patients and somewhere about 60% of them had shown good to excellent effect of the triiodothyronine. Of major interest to us was that 22 of these patients were lost to follow-up for one reason or another, but the major reason was the development of persistent neoplasm. It may very well be that the tri-iodothyronine in its metabolic effect also increased the metabolism of the few with residual cancer cells which then became active. The tri-iodothyronine in the doses we have used is a pharmocologic dose but by slowly acclimatizing the patient to this dosage, it has been possible to carry almost all the patients at these rather large doses for as much as two years. Only five patients became toxic so that we could not continue the medication.

The possibility that other thyroid analogues might be advantageous in this system is being explored. Triiodothyropropionic acid and triiodothyroacetic acid are currently being investigated in the clinical setting. However, it is apparent that we need a laboratory system in which we can evaluate drugs in an impartial manner, in an easily duplicated system. We could then go from the animal to the human to study a drug. Although Serendypity gave us the first compound, we certainly cannot depend upon this for future compounds. We, therefore, have explored the use of the delay in wound healing following irradiation as a test system.

May I have the next slide please. This is essentially the setup. A surgical wound in a previously irradiated area is made down to the

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peritoneum; then it is closed by 3-wire sutures, and at stated intervals after the surgical procedures, a balloon is put into the abdomen and the pressure that is necessary to disrupt this wound is measured. In our laboratory this can be easily accomplished and gives us a quantitative measure. T_3 obviously was the first drug that we used in this system.

May I have the next slide. As you see, there was a moderate but significant increase in the tensile strength of the x-rayed wound with the T_3. The upper two lines are the control and T_3 alone tensile strengths.

The next compound that we investigated was T_3P, or tri-iodothyropropionic acid, and as you see, this was much more effective in improving the tensile strength of the irradiated wounded area.

On the other hand, thiouracil, the next slide, showed absolutely no effect.

The last slide is a summary of some of the drugs that we have used. (Table II). We have evaluated these drugs in terms of a "healing coefficient," which is a figure that we use to put an "order of magnitude" to the effectiveness of the drug and, as you see, T_3, T_3P, improve the situation while thiourea does nothing. Interestingly enough, actinomycin D plus x-ray in the first two experiments shows a delay in wound healing apparently potentiating the x-ray effect. When the actinomycin D had deteriorated, it was not effective in the system. These studies are currently going on. We're using ascorbic acid, and other hormones, in evaluating this system.

Question: And what dose of radiation do you use for the wound healing experiment?

Dr. Glicksman: In the wound healing experiment we are using a two by three centimeter field. We deliver 1960 r tissue dose. This is one exposure.

Question regarding increase in properdin.

Dr. Glicksman: This increase in properdin, of course, is a transient one that occurs following the irradiation. It is the two to threefold increase which we feel to be significant. It comes back to the baseline in approximately a week. The third patient who did not show an increase in properdin had zero properdin before the irradiation and remained at this level.

Dr. Parrino: You mention ascorbic acid for example, that cabbage and onions are protective of the ascorbic acid content.

Dr. Glicksman: Well, we haven't completed the laboratory work on the wound healing effect of ascorbic acid but the first ten days of these experiments show that ascorbic acid does nothing to increase the tensile strength of radiation wound. But

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these are still not completed studies.

Question unable to be heard.

Dr. Glicksman: In the cases that I mentioned, the bleeding occurred in the fourth week post total body irradiation. The appearance of petechiae alone is not considered a very severe bleeding diathesis. One patient developed severe naso pharyngeal bleeding, required both anterior and posterior packing. Another one developed a vaginal hemorrhage. And the third one also had bleeding of the oral cavity. These are severe bleedings, not just the transient petechiae. These three patients had normal blood clotting factors. Despite the fact that we could find no evidence of any of these factors being off, the use of protamine sulfate stopped the clinical manifestations of bleeding. This is interesting in light of some previous publications of Jacobson and Allen in 1948.

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TABLE I

Effect of Triiodthyronine on Late Post-Radiation Changes

Type of Change	No. of Cases	Excellent	Good	Fair	No Change	Worse	Lost
All Cases	75	14	26	7	5	1	22
Ulcers	46	10	18	4	-	1	13
Fibrosis	24	4	7	2	3	-	8
Pulmonary Fibrosis	5	-	1	1	2	-	1

Excellent - Complete healing; no residual changes
Good - Steady progressive healing; minimal residual changes persist
Fair - Slower progressive healing; some residual changes persist
No Change - Essentially no healing or change
Worse - Further progression of the changes
Lost - Not available for evaluation-persistant neoplasm, surgical intervention, or on no active drug in double blind study

TABLE II

Effect of Drugs on Wound Healing in Rats - 1 Week Post-Irradiation

Drug	Dosage	Healing Rate	Healing Coefficient
X-ray		11.3	27.1
T_3 + X-ray	40 μg/day	14.5	44.5
T_3P + X-ray	500 μg/day	24.0	96.4
Thio + X-ray	.05% - 14 mg/day .1% - 28 mg/day	11.4	27.6
Act. D + x-ray	(1) .4 mg/Kg (injected)	5.5	11.1
	(2) .4 mg/Kg (injected)	5.0	11.4
	(3) .4 mg/Kg (injected)	14.0	49.0

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Dr. Lauriston S. Taylor,
Chief, Atomic and Radiation Physics Division, National Bureau of Standards; Chairman, National Committee on Radiation Protection and Measurements, NBS; and Chairman, Advisory Committee on Civil Defense, National Academy of Sciences:

I. National Bureau of Standards

The National Bureau of Standards is not engaged in any direct research activities in the field of radiobiology or radiation medicine. However, it is deeply involved in certain contributory researches relating to the physical problems involved in the application of radiation in biology and medicine.

Physical standards of dosimetry have been established and maintained at the Bureau over the past 30 years. These include the standards of x-ray dose expressed in terms of the roentgen. In spite of the roentgen being an old and well established unit of dose, there are still outstanding problems when it comes to the application of this unit over the entire energy range that is being utilized today. Precise standards are available in the energy range of about 50 Kev up to slightly over 1 Mev. Research efforts are presently being directed to a better understanding of the dosimetry problems in the energy regions below and above these limits.

The service aspect of the Bureau's program includes its standing ability to calibrate instruments or other dose measuring devices that may be used in radiobiology and medicine. These services are limited, in the main, to the calibration of working standards that would be used by laboratories or institutions. It does not include the routine calibration of instruments for ordinary clinical use; these calibrations can be effectively performed by commercial organizations.

In the field of radioisotopes the Bureau is responsible for the development of standardized sources of radionuclides. Some two dozen of the more commonly used radionuclides have been standardized up to the present time, and research is being directed to the extension of this list. Here also we are trying as rapidly as possible to turn this work over to private commercial laboratories once the basic research has been completed.

In addition to the work directly associated with standards, the Bureau has for many years been conducting a variety of studies relative to radiation shielding and the shielding properties of materials. Beginning over ten years ago, our theoretical group has been developing a basic approach for the solution of problems of

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radiation penetration and diffusion in matter. This work now has been carried to the point whereby it is possible to compute the shielding characteristics of most physical situations.

For the past three years this group has been working actively on problems of shielding relative to nonmilitary defense. The work has been supported in the main by OCDM and in part by AFSWP and the AEC. This group has also been collaborating closely with the National Academy of Sciences Advisory Committee on Civil Defense, which I will mention later. The special task at the moment is providing the theoretical background and support for the OCDM study of the shielding characteristics of buildings subjected to radioactive fallout. It is also preparing a technical manual on the analysis of such shielding problems.

II. National Committee on Radiation Protection and Measurements

The National Committee on Radiation Protection and Measurements was established in 1928 through the cooperative effort of the medical and radiological organizations in this country and the National Bureau of Standards. Throughout the past 30 years it has endeavored to provide the basic guidance and philosophy in the matters of radiation protection for use in this country. It has a close but informal working relationship with the International Commission on Radiological Protection. There is considerable overlap of membership between the two groups so that there are no serious differences in the points of view between the national and international bodies.

I should point out that while a substantial amount of the effort going into the NCRP is supplied by the NBS, the committee is not a NBS committee nor does it carry any official relationship or sponsorship by the Bureau or the Department of Commerce. This is a fact that is frequently misunderstood and it is for this reason that I mention it. The Bureau's participation in this work is considered to be part of its public responsibility and the relationship is similar to that between the Bureau and many other committees of a nongovernmental nature. I might also mention that in addition to the support by the Bureau the NCRP also receives some support from the AEC and OCDM.

The NCRP has been responsible for setting the basic permissible exposure levels for occupational exposure to radiation in this country. Its recommendations have been included in some dozen and a-half Handbooks prepared over the past 25 years, and revised from time to time. In all, the NCRP operates with a structure of an Executive Committee,

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a Main Committee, as well as 18 subcommittees having a total membership of the order of 150 technical people.

The NCRP program of most direct concern of the groups meeting here today is that of Subcommittee 14 dealing with the subject of Radiation Exposure under Emergency Conditions. This committee is endeavoring to prepare a handbook outlining the problem of emergency exposures such as might be encountered in nuclear warfare or a large-scale nuclear disaster. The recommendations are being designed to assist planners and to provide background information that would be used in making command decisions in the event of a nuclear attack.

The development of these recommendations has been underway for two or three years. The slowness in the production of the report is occasioned not so much by any basic disagreement as to the approach as by the difficulty of presenting the material in a form that would be useful to a large number of people having only secondary knowledge in the field of radiobiology and radiation medicine. In the meantime the general philosophy of this group has been informally fed into OCDM in a manner sufficient to make interim planning possible.

III. The National Academy of Sciences Advisory Committee on Civil Defense

This committee was established by the National Academy of Sciences about four years ago as a result of a specific request from FCDA. The committee has had broad latitude as to its scope and areas of interest but briefly it can be described as a committee that reviews the OCDM research programs and gives advice on their direction and adequacy. At the same time it has the responsibility for looking at the overall nonmilitary defense picture with the purpose of determining where new areas of research should be opened. A considerable amount of the work of this committee has been communicated to the OCDM in the past through informal discussions. Although some reports have been written and others are presently in the course of preparation.

The most recent report of this committee is entitled "The Adequacy of Government Research Programs in Nonmilitary Defense." This report which was originally for limited circulation is being supplemented by a more complete report that will be better suited for general consumption.

The basic NAS committee is kept small in size but is designed too that it can be easily expanded to consider special problems. A recent extension of the committee's activities has been the

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establishment of an Ad Hoc Subcommittee to study the overall physical problem of community shielding against fallout radiation.

This committee is made up of representatives from some half dozen or so major organizations in this country working on the problem. It is expected that through the work of this subcommittee the research and development ideas of the various government departments in this particular field will be adequately drawn together and coordinated at the working level. So far it appears to be a highly satisfactory operation.

It is part of the "Modus Operandi" of the Academy Committee that additional subcommittees of this type can be established in other fields when and as the situation demands. For example, consideration is being given at the moment to the establishment of a group to evaluate the radio-medical problems that would be involved in the performance of the functions of the OCDM. This group will probably be built around the group that prepared the biomedical part of the report on government research programs that I mentioned earlier.

In the very brief outline that I have just presented I have covered three types of operation including the NBS, the NAS and the NCRP. While I have to some extent separated these operations, I should point out that there are such close working relationships between all of the groups that it is difficult to draw any line between where the activity of one ends and another begins. It is typical of a very small part of the whole problem. Within the three areas that I have mentioned above, coordination and collaboration is brought about to a major extent by overlapping of individuals between the three kinds of activity. On the whole this has proven to be an operation that conserves rather than wastes manpower. Through these relationships which, for the most part are fairly informal, it seems possible to produce a maximum amount of productive effort with a minimum expenditure of man hours. It is to be hoped that similar working relationships can be established in other areas than those which I have specifically mentioned.

Government at its best is complicated almost beyond imagination these days. The problem of coordinating research is recognized repeatedly in many ways and each time it is tackled anew there is a tendency to establish some new coordinating group. Now coordination in itself is about the most frustrating experience I can think of; particularly when carried out with a high degree of formality. I hope that as a result of some of the presentations and discussions during the course of these meetings, we will somehow see our way clear to providing the neces-

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sary degree of knowledge as to what is going on, with the result that the activities can be sufficiently interrelated as to prevent the further dilution of our limited manpower capabilities. Thank you, sir.

Dr. George Lefevre, Jr., Program Director for Genetic Biology, National Science Foundation:

The National Science Foundation, unlike some other Federal granting agencies, does not operate any research laboratories of its own. It does not have any intramural research program. Furthermore, in general, it does not initiate research by contract arrangements, and, due to the nature of its operation, it does not support research in the field of clinical medicine or in applied areas in general. Relatively little radiobiological research is supported by the National Science Foundation. We support projects only when investigators apply to us and, in general, people in the field of radiobiology turn first to the AEC and perhaps second to the NIH. We get very few applications, therefore, from people in radiobiology.

In investigating our support in this area, I find that out of well over a thousand currently active research projects there are fewer than two dozen research projects that I would classify as radiation biology. More than half of these are in radiation genetics. I am not sure that any of our projects pertain precisely to the interest of this meeting -- that is, research that holds promise of preventing, minimizing, or treating effects of radiation. Of course, some of the projects in radiation genetics are concerned with problems such as the modification of the radiation-induced mutation rate through the simultaneous addition of drugs or changing the oxygen tension. Perhaps of interest among this kind of project are those where attempts to reduce protein synthesis after irradiation did affect the production of mutations to an appreciable extent. One such drug -- chloramphenicol -- is being used in a couple of projects to see how the production of mutations is affected by the inability to synthesize protein. Whether research of this sort eventually make it possible to prevent the production of mutations by radiation in any practical way is perhaps debatable at the present time.

Research of this kind is obviously necessary to gain a basic understanding of the mutation process before practical applications in such organisms as humans could ever be possible. In addition to a number of such genetic projects, there are a few supported by the National Science Foundation studying radiosensitivity of living organisms or organ systems, assessing the degree of radiosensitivity, and attempting to identify factors that can influence

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radiosensitivity. But our support of projects in this area is very limited. I daresay that no one who calls himself a radiobiologist derives his full research support from the National Science Foundation.

It has occurred to me that perhaps a large number of people use radioisotopes in biochemical research, though not in the field you would properly call radiobiology. There are a surprisingly large number of people who are trained in the use of radiation equipment and are knowledgeable about the facts of radiation and the techniques of handling radioactive material.

It seems plausible to me, at least, that the OCDM would be interested in knowing who in the country is fully capable of monitoring radiation, dealing with radiation, so that in the event of emergency, teams of competent individuals could be quickly assembled. Therefore, I made a survey on our projects to see how many individuals are competent in handling radioactivity. Here, instead of a dozen or two projects, perhaps ten per cent or so of all biological research supported by the Foundation involves the use of radioactive isotopes in one way or another. I have prepared a list of these people, should you have any interest. I regret that the Foundation is not a significant supporter of radiation biology and that such support as it does offer is not in the area particularly pertinent to this conference.

Dr. Lauriston Taylor (NBS): I gather from what you've said that if the Science Foundation received a creditable request for support for radiobiological research you would probably entertain it.

Dr. Lefevre: Yes. We do not rule out any projects except those which are in the field of clinical or applied research. These we do not support.

Colonel John E. Pickering, Division of Radiobiology, Randolph Air Force Base, San Antonio, Texas:

The program at the School of Medicine is maintained by contracts to civilian institutions and in-house programs. For the purpose of discussion today, I have divided these into three areas which I choose to call the fundamental, clinical, and applied research areas.

In the fundamental areas, primarily by contract, work is going on in studies of basic mechanisms. One of these studies is free radical formation and reactivity of water with various solvents involving radiation, conducted by Dr. C. Pomer at University of Texas Medical School, on tissue culture studies using glial cells

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and neurons radiated by neutrons, gamma rays, or x-rays are being studied. This is being extended to proton and electron radiation at the present time.

In the clinical area, there has been a study progressing for approximately five years with the M. D. Anderson Cancer Hospital, Houston, taking advantage of certain patients that had been receiving therapeutic radiation. Doses extend from 25 roentgens to 200 r. We have had the opportunity of working pre-radiation and post-radiation with these patients, observing them in clinical follow-up and doing some Psycho-motor tests. Many of the tests administered were comparable to the stainine tests given during pilot training, in determining whether or not there were performance breakdowns in the patients following radiation.

This study has been extended, perhaps as some of you know, by one of the members of the staff, Dr. Gerstner, to look at the response of these 263 patients and compare them, where possible, with the accidental exposures from those few AEC accidents, from among the Marshallese, and from among the Japanese. This has been reported as the "Clinical and Military Effects Study of the Acute Radiation Syndrome."

The study then progressed into the applied field from the clinical application in conjunction with the work reported by Dr. Morgan and Dr. Cannan yesterday during Operation Plumbbob. An attempt during the angular distribution studies mentioned by Dr. Morgan was, at the same time, to endeavor to expose small primates at comparable distances to the dosimetric measurements, as well as the Japanese houses; then to look at the clinical response following bomb radiation. In this particular study, we were able to look at the clinical effects immediately following radiation as well as long-term effects. We have approximately 85 that are now 18 months post-radiation for long-term follow-up.

In that same regard, two large-scale programs have been under way for approximately eight years. These have applications more specifically of a military nature, but perhaps they are of interest to this group. I have divided them, for this summary, into the acute and the chronic studies.

There is probably now in existence almost a thousand Rhesus Monkeys in our colony. Around 250 of them have undergone various types of acute exposure to ionizing radiation. The initial intent was to study cataractgenic threshold. Animals have been exposed to 14 Mev fast neutrons; another series had been exposed to thermal neutrons; and a third series, to cobalt gamma radiation. They have been followed for either vacuoles or mature cataracts if this be the endpoint;

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we have RBE studies for several endpoints.

Complementing these few studies a long-term chronic program has been developed again using the Rhesus Monkey in which the experiment actually is divided into three distinct sub-experiments. One group of animals was exposed to mixed radiation, neutrons, and gamma radiation using polonium-beryllium neutrons and Cobalt^{60} gamma. They are exposed at three different dose rates, quarter of a rep per hour, half a rep per hour, or one rep per hour. Two different intervals were used. Exposures every fourth day or every twelfth day for 40 or 20 times. Again the endpoints are cataracts, leukemia, and ultimately shortening of the life span.

The second follow-up of this program was to repeat the experiments using only neutrons, the same three dose rates, the same intervals, and the same endpoints. The third experiment uses only gamma radiation. All these animals have accumulated into a long-term follow-up which is essentially now eight years post-radiation. Perhaps of interest in the acute studies, we did develop mature cataracts at certain dose levels. In the chronic studies we have not developed cataracts. There is no evidence of leukemia and at the present time the animals are being watched for the longevity aspect.

Continuing in the applied area, work has been going on using radiation and so-called other stresses that may be of importance in Air Force operations. One of these has been the investigation of low level radiation conducted by Dr. Carlson, at the University of Washington, wherein he has used about 8/10 r per day Cobalt^{60} gamma radiation and studied animals at five degrees, 28°, and 35°, with an endpoint of radiation and its effect on metabolism.

Perhaps an interesting note with respect to these low levels of exposure, at the present time Dr. L. Carlson's exposed animals are outliving his control animals. I understand other individuals are finding this to be true in certain of the low levels of exposure. As a matter of fact the contract was extended to wait for the radiated animal to die.

Complementing the mixed neutron studies in the monkey, a program is in being with the University of Chicago Radiation Laboratory under the direction of Dr. K. P. DuBois. He is using the mouse, the same radiation parameters, polonium-beryllium neutrons and Cobalt^{60} gamma radiation, three dose rates, 1/3, 2/3, and 1 rep per hour. Again these animals are being followed for the three endpoints, cataract, leukemia and longevity. His overall program is further divided into a protective compound study, specifically in the various compounds

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which presumably may be of interest in radiation. Thirdly, he is looking at biological dosimetry, particularly in the enzyme systems.

I think in general that about summarizes our program.

Dr. Lauriston Taylor: I am interested in the remarks you made at the last, Dr. Pickering, about the longer survival of slightly irradiated animals compared with some of the controls. This keeps bobbing up. Is it being looked at systematically? Do you believe your results?

Colonel Pickering: I believe Dr. Carlson's results, yes sir. May I say just this -- I am sure there are others who have opinions on this, but there are several experiments of which I am aware where, as you say, it has bobbed up continually. One in particular which Dr. Gerstner in our own laboratory conducted, a bit different from this. Namely, if one administered one large dose of radiation and measures the survival, and then complements this experiment by administering a small dose to a second group of animals followed by a second large dose, it takes a larger dose to produce the same mortality than in the first experiment.

I am certain that this has been demonstrated by Dr. Lautit, and I am sure Col. Hartgering has some words on this. I do not know other than our own small attempt whether this is being systematically followed.

Dr. Taylor: Well, it seems fairly important to me. The thing that kind of worries me is the fact that the people keep seeing these results and keep saying, "Well, there must be something wrong with it." I hope something is being done to really peg this down and find out what it means.

Col. Pickering: In our own association with the Los Alamos group, Dr. W. H. Langham, and now with Dr. J. B. Storer, who has left Los Alamos, we have small groups who are interested in this thing.

Floor: Question about fractionated doses and cataracts.

Col. Pickering: Yes sir. Very definitely. In the mixed irradiation group, the highest dose was approximately 616 rep. We used 560 r of gamma and 56 rep of neutrons on the assumption that the RBE may be about 10. I seriously doubt it will be this high. These are, by the gradings of Dr. D. V. Brown (who has the same as with Dr. Christenberry), plus 1. These are 3-300 vacuoles by their definition. I think I should go on to say, these animals are being followed in terms of visual acuity. They make discriminations equally well as those that have not been exposed.

Dr. Taylor: In your concern with

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cataractogenesis from gamma rays, has anybody thought of the possibility of using the Army as the source of information for dental x-rays? The Army procedure is like the civilian procedure, I suspect it is not too different. I even get a complete irradiation for every film that is taken of the teeth, that is every single film, not just one irradiation for examination. There are probably records of large numbers of people who have had repetitive full mouth x-ray examinations. I think this would be a very fruitful source of information.

Col. Pickering: I would like to say this and then let Colonel Hartgering comment later. It would be our opinion, Dr. Taylor, that in terms of the cataract studies the dose required in the monkey, and I think Dr. Cogan would probably substantiate this from his experiments, that the dose required to produce cataracts probably is very close to LD 50-30 dose in gamma radiation.

Floor: I would think that maybe among Army personnel and Veterans Administration might be a chance to really get some information about this question.

Colonel Carl F. Tessmer, Chief, Radiation Injury Section, Division of Pathology, Armed Forces Institute of Pathology:

Editor's Note: Col. Tessmer's remarks made at this point have not been received due to the need for clearance and other causes. Should his statement be received before this document goes to press, it will be included in an appendix at the end of these Proceedings.

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Colonel Carl F. Tessmer, Chief, Radiation Pathology Branch, Armed Forces Institute of Pathology:

The Armed Forces Institute of Pathology (AFIP) is a tri-service organization, administratively supported by the Office of the Surgeon General of the Army. The directorship rotates among the three services with a deputy from each of the remaining services. The present Director is Captain W. M. Silliphant, U.S.N. The Institute functions basically as a consultant in pathology with additional activities in the area of training and research. There are numerous working relationships with a large number of civilian and government agencies.

In line with the discussion here today, I suppose it might be said that research at the AFIP has been a part of its activities since it was organized close to the Civil War days. But it has been only recently that work in experimental pathology and in certain basic sciences has been possible with, as some of you know, the enhanced facilities. Subjects range very widely in this work and I think it is best to select a few that might be pertinent to the subject of this meeting; those dealing with some phase of radiation or obviously related to it.

Cosmic ray effects have been under study by the Neuropathology Section. It seems to me that many of their efforts have been an attempt to define a problem. This has been done by active collaboration with the Air Force research groups, and other agencies.

There have been extensive studies in the Neuropathologic Section of radiation damage, as many of you know, by Dr. Webb Haymaker, Chief, Neuropathology Section, AFIP, and his colleagues.

There are other explorations along the biologic preparation for, I suppose the best term is, space activities. One of these that excites interest, although I do not know the present status of it, was reexamination of the matter of goldfish. Some of you recall the reports by Dr. F. Ellinger, Naval Medical Research Institute, NNMC, Bethesda, Maryland, and others of the pigment response to radiation, presumably as a central nervous system activity. This shows in pilot studies at AFIP a complex time dose relationship that has actually not been worked out completely.

One of the reasons for exploring the use of goldfish is the idea that they can be readily sealed in a plastic container and are rather resistant to cold.

In the Radiation Pathology Branch we have carried out Co-60 point source exposures in line with one of the major interests in the tissue changes. These are often quite revealing; for example, we have observed what appears to be repopulation by lymphocytes of areas under intense radiation when ordinarily we have a concept that

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lymphocytes are quite sensitive to radiation. In other circumstances, it is quite important to examine an organ such as the kidney, where basically radiation changes are very confused by the systemic factors. As many of you may know, one of the relatively early changes in radiation nephritis is an irreversible hypertension, which then overrides much of the morphologic picture. This can be avoided by the use of a local point source of radiation.

Another aspect of the work relates to a subject which was discussed earlier in this meeting, the matter of humoral factors in radiation protection. Using methods employed in the isolation of erythropoietic factors, studies have been followed using a similarly derived substance in animals that had been conditioned to trauma. Now the hypothesis here, of course, is that if one can obtain a factor which protects the animals against trauma, it is obviously a good thing to explore as an agent against radiation damage. This shows some promise, and an initial report was made at a recent meeting of the Reticuloendothelial Society.

Another area that relates to the remarks of Dr. Cannan earlier in the meeting points up the function of the Armed Forces Institute of Pathology as the central area for human radiation material. Beginning with the Joint Commission data and studies in early '46 until the present time, there has been gathered a significant amount of human radiation material. Now I think I am safe in saying that there is more human radiation material at AFIP than anywhere else; on the other hand, it is by no means complete. One of the current projects for analysis is a rather detailed study of approximately 90 leukemias that are associated with exposed and control Japanese population.

Another aspect of this radiation material is a function as a registry. Obviously if we consider certain levels of continued exposure, there have already been predictions of a certain incidence rate of leukemia. In order to evaluate this, I think first of all one needs a baseline and of course, secondly, a strict pattern on review of such cases. This has been the fault of many leukemia surveys. The diagnosis really has not been established beyond doubt or has been subjected to variable interpretations.

I would like to show you some of the work of AFIP which relates to field activities. Through the cooperation of the joint task force medical group which studies the Marshall Islanders at yearly intervals, we have been given the opportunity to review human material from individuals exposed to radioactive fallout. We have endeavored to assemble such case material at AFIP, and make it available as teaching preparations. This is a four-week lesion in the anticubital space of the Marshall Islanders due to fallout, and I think it is

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well to study this because it initially was apparently not recognized. It is a raised lesion which was highly pigmented. We have made some efforts to study this lesion and other ramifications of it. Six months later, the patient represents a clinical recovery. We have reproduced the essential features of this lesion of the skin experimentally in Hormel swine. This animal was selected because of relatively small size, known response of the skin in a fashion similar to humans, and a variable pigment pattern. Several of the energies occurring in radioactive fallout were chosen and these exposures were provided at several dose levels. Monochromatic electron exposures were provided by Dr. Howard L. Andrews, Ph.D., National Cancer Institute, National Institutes of Health, Bethesda 14, Maryland, utilizing a Van de Graaf generator at several energy levels. Utilizing 0.6 Mev electrons, the pigmented portion of skin showed a reaction of the pattern seen in the Marshall Islanders. In the lightly pigmented areas, a faint skin reaction was obtained which resembled that of the few Caucasian responses reported. The latter were not immediately recognized as fallout lesions.

The experimental lesion produced by 0.6 Mev at approximately one year later shows evidence of significant damage to underlying structures. This occurred without ulceration and breakdown. The full comparison of this experimental lesion with fallout conditions is not yet possible.

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Dr. John B. Youmans, Technical Director of Research, U. S. Army Medical Research and Development Command, Department of the Army

As might be expected, the Army has a very considerable interest in radiobiology and radiation medicine. It has a program of research, both basic and applied, and both in service and by contract. I believe that covers nearly all of the areas which are listed in the notice of the meeting which you received, with the possible exception of genetics. I do not think there is anything directly on genetics, but it may touch on it indirectly.

Colonel Hartgering is going to talk to you a little later, or he is scheduled to talk to you. He is the Director of the Division of Nuclear Medicine and Chemistry at the Walter Reed Army Institute of Research. He also has a knowledge of our general program. I am going to ask for your permission if he may present not only his own work, but a review of the program as a whole.

Lt. Col. James B. Hartgering, Director, Division of Nuclear Medicine and Chemistry, Walter Reed Army Institute of Research

This is a tough job for a few minutes. I tried to select two or three things from our contract program that might be of particular interest in view of the discussion of the last couple of days. We have a contract with Overman at the University of Tennessee on macro-fractionation of dose rather than micro-fractionation, and I'll refer to that a little bit later. We're obviously interested in the whole problem of dose fractionation and in its effects on man.

Operating with the Armed Forces Special Weapons Project, we have three contracts on the total body radiation of man. These are at the Universities of Pennsylvania, Baylor University, and Memorial Hospital in New York City. Some 200 patients have been radiated over the past five years, at generally the dose levels that Colonel Pickering talked about, on the order of 25 to 200r. The next move probably will be to use total body radiations in divided doses at 25r, then perhaps 50. This has already been done at daily and weekly intervals on a few patients.

At Texas A&M Research Foundation, we have a fairly extensive contract on wound healing and fracture work. Dr. S. Levenson will discuss something of the work that he's been doing at Walter Reed in the healing factors and wounds.

Also, there is a contract in the area of anesthesia and analgesia at the Yeshiva University in New York. There is surprisingly little literature on this subject.

One of our large interests in the past few years has been the influence of radiation on infections. We have not been very successful in encouraging contract work. The only outstanding contract we have at the present time

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is with Wisseman at Maryland who is studying the effect of radiation on living types of vaccine. As you know, Zinnser's classic work in this field was with richettsia. The question is if you have to vaccinate troops or civilians after a nuclear disaster, what is the effect of giving a living vaccine such as might have to be used with typhus?

In the very near future the laboratories at Fort Detrick will study the relation of infection and radiation. They have a new million volt GE generator. It is my personal feeling that we do not know very much about the influence of radiation on infectious problems and common diseases that require hospitalization, the GI upsets, the upper respiratory infections, etc. I personally feel that a lot more work needs to be done in this area. The literature is not very helpful.

Most of you know about our laboratory at Fort Knox; Dr. Krebs has the Radiobiology Section there. He has been working on fractionated dose problems and trying to evaluate the practicalities of the grid idea that has been used by clinical radiologists for years, i.e. the problem of the damaged vs. undamaged tissue. They will get some new equipment in May of this year from a College in Oregon. This will allow ultrafractionation to a 1,000th of a second, so that he can deliver a dose and shut it off in a microsecond. The delivered dose in this period of time will be 20r, so this may be a useful tool to study fractionation problems.

At Walter Reed, where we have our largest inservice program, we have been involved in the past two years in extensive field tests in Nevada. About 1200 animals were exposed at Operation Plumbbob. Col. MacDonald was the project officer, and in the recent series, Hardtack, about 600 animals. Col. Moncrief was project officer.

One of the results of the second study that is of some interest is the evaluation of Na^{24} as a biological dosimeter. This was discussed by Dr. Morgan yesterday. He used it on the Y-12 accidents. This works very well in the field. The pigs, of course, had activated sodium in their blood. This had a reasonable coagulation of biological effects.

The Division of Nuclear Medicine at Walter Reed for the past several years has been involved in studying worldwide fallout. Most of you know that originally we did this by collecting urine specimens from military personnel in the three services stationed throughout the world. More recently we have put into operation a total body counter. I can show a couple of slides for those of you who haven't seen it. We have both a total body liquid scintillator and a sodium iodide crystal. In the liquid scintillator the counting times are very short, on the order of 200 seconds. This results in good accuracy on potassium 40. We can also readily determine the cesium present as a result of fallout.

Particularily useful is our fortunate

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location at Walter Reed, in the Washington area. We have access to a large number of people, both from this Country and foreign Countries. We have a constant stream of visitors through from other lands and most of them have been quite willing to be counted. Our first thousand patients have been counted. The cards are now at IBM for analysis. I think we can over the period of next year gain a good feel for exactly what gamma emitting isotopes are present in man.

The sodium iodide crystal is familiar to many people here. This permits localization and identification.

We have initiated in the last year a preprotection chemical program. Captain David Jacobus is working at Walter Reed and has a movie that is self-explanatory. For the first time we have been able to protect a large animal against a LD-100 dose of radiation.

Sound movie, "Preprotection of the Dog Against Lethal Radiation."

Obviously, these chemicals are not new. They have been known for a good many years, but to the best of our knowledge, this is the first attempt to combine previously known effective chemicals in large animals. Captain Jacobus was able to avoid some of the toxic effects and still get protection. However, he was operating at near toxic levels. We think that there are a family of chemicals which do offer some promise. I think we are a long way from a pill for the soldier or the civil defense worker, but I think there is some definite hope in this area, and we feel it is worth a great deal of research effort. Thank you.

Stanley M. Levinson, M.D., Chief, Surgical Metabolism & Physiology, Walter Reed AIR:

I can tell you very briefly about a few additional studies going on at Walter Reed. The first is concerned with the response of the germfree animal to radiation. This work is done collaboratively by the Division of Nuclear Medicine and the Germfree Department.

Some of you may not have yet had the opportunity to see a germfree laboratory. I brought a couple of slides of that. Basically, our laboratory is based upon that designed by Professor Reyniers of Notre Dame. As you can see from the first slide the animals are kept in large steel autoclaves which are fitted with neoprene gloves and an additional autoclave lock; the basic principle of getting items in the tank and/or handling the animals is as in any isolator procedure.

Now, the first experiment which was done concerned itself with the radiation response of the chick. This was done because it is much easier to get a large number of germfree chicks than of germfree mammals.

This slide illustrates the basic technique of getting a germfree bird. Fertilized eggs are obtained, washed

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thoroughly, then immersed in a germicidal solution for a period of time, long enough - statistically at least - to kill the surface organisms, but not enough to kill the embryos. Then they are introduced through a sterile germicidal trap into the tank where they are allowed to hatch.

This next slide shows you how food and other materials are gotten in and out of the tanks. Attached to the main tank is a second autoclave. For entry, the door leading from the main tank to the small attached autoclave is shut, the food is placed in the small clave, and sterilized. While the outer door of the "food clave" is still shut, its inner door is opened, and the food taken into the main tank. The inner door can then be closed, etc.

The response of the germfree animals was significantly different from that of the conventional. The survival time and the incidence of mortality following x-ray irradiation was studied in germfree and conventional 10-day-old White Leghorn chicks. At a dose rate of about 35 to 40 roentgens per minute, at doses below 800 roentgens, the germfree chicks showed a better survival compared to conventional bacterially contaminated chicks raised in the identical circumstances. The enhanced survival is indicated by the fact that about two to three times as many germfree chicks survive as do conventional controls. At doses above 800 roentgens, while the ultimate survival is identical with that of the conventional control chicks, the survival times of the germfree chicks are longer.

Now one other area of study which I would like to mention to you is the effect of whole body radiation on wound healing. We are studying the wound healing response of the irradiated animal as a biologic indicator of what may be happening to the animal as a whole; this is part of a series of comprehensive metabolic studies of the effects of various types of injury.

We have avoided the laparotomy wound because of the multiple layers which one goes through; we have gone to a simple skin incision of the dorsum of the rat's back. The incision is 5 cm. in length. Some simple stainless steel wire sutures are put in place; the wound is not dressed; it is allowed to heal spontaneously. At the time of sacrifice the length of the wound is measured. It is then placed on a brass cutting block, and with a multiple guillotine set-up is sectioned into five 1 cm. strips. One or more of the strips is sent for histologic observation, the tensile strength of the other strips is tested on a machine which gradually pulls the skin apart. The point of rupture of the wound is recorded automatically. We have observed that the wounds of male rats weighing around 250 grams exposed to 500 r whole body radiation (250 k.v. x-ray machine) heal differently from those of unirradiated controls. This particular slide illustrates our findings in rats wounded three weeks after irradiation; one week and

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fourteen days after the incision, the animals were sacrificed and examined. As you see, the wounds of the radiated animals were significantly weaker than those of the unirradiated controls. This is true whether the wounds are made at the time of the whole body radiation or one, two or three weeks later.

Now the reason I asked Dr. Glicksman about the histology of the wounds in his experiment is that we have examined these wounds histologically. We can detect no difference between the wounds of the two groups of animals, using the usual type stains, etc. So we have the problem that histologically we see no difference between the wounds of the unirradiated and irradiated animals, but by our tensile strength measurements there is a striking difference. This is not too surprising, since we may be measuring quite different facets of the healing process. We are studying the biochemistry of the healing process now to see if we can find a chemical basis for our findings.

Now one other problem which I would like to mention is the question of the effect of irradiation on the response of mammals to other injuries. This is a problem which interests the military greatly, I am sure it has much implication for the OCDM. There have been occasional reports to the effect that an irradiated animal is more sensitive to various shock-producing procedures than unirradiated controls. We have tested this with mice, rats and guinea pigs using either thermal injury or tourniquet shock as the stressing agents. The mortality of these procedures was low in the unirradiated controls. If animals are subjected to the shock procedure within the first few days following irradiation, we find no "sensitization" - the mortality is still low. But if one waits until the 9th or 10th day after radiation, then there is a significant increase in the 24-hour lethality of the shock procedure for the irradiated animal. We are looking into the mechanism for this. The levels of x-irradiations we used were 200 r for the guinea pigs, 350 r for the mice and 500 r for rats.

Finally I should like to describe briefly some metabolic studies. We have studied dogs and swine. For the latter the x-irradiation, 800 r whole body, was carried out after an 8-day control study period. All animals were fed 2 hours prior to irradiation; to control the possible effects of different food intakes, the unirradiated animals were pair fed according to the intake of their respective irradiated partner.

The animals under metabolic study were offered daily, for a fixed period of time, a constant quantity of a commercial swine food adequate for (slight) growth; the amounts ingested were recorded. The daily ration when completely consumed supplied 16 grams of nitrogen, 64 mEq of sodium and 102 mEq of potassium. Unlimited amounts of water were offered 3 times daily at 1000, 1400 and 1600 hours and the

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quantities consumed were measured. Body weights were taken each morning prior to feeding. The general appearance and activity of each pig were noted during the day and changes recorded on individual control cards as they occurred. Similarly, the occurrence of diarrhea, blood clots in stools, bloody urine and other evidences of bleeding were recorded. Autopsies were performed on most of the animals that died.

The following biochemical measurements were made:

Food: On random aliquots, nitrogen, sodium, potassium and chloride.

Urine: Total nitrogen, creatinine, urea, sodium, and potassium daily.

Feces: Total nitrogen, sodium, potassium and chloride in aliquots of 4-day pooled specimens.

Blood: Urea, sodium, potassium and chloride were measured on fasting serum specimens.

In selected animals, plasma volume was measured by T-1824, red cell mass by Cr^{51}. Blood cultures were taken in some. In no irradiated animal were two positive cultures obtained on the two days cultures were taken (days 8 and 10 post-irradiation).

The pig has turned out to be suitable for balance-type studies. Some control serum chemistries are listed.

These are similar to those previously observed by us in the Duroc pig; both are similar to those of men. These pigs, growing, were in distinct positive nitrogen balance, about 4 gm/24 hrs. The fecal nitrogen, relative to intake nitrogen, is similar to that of the dog, and about twice that of man. Theoretical K balance, based on N retention, 11 mEq k; observed K balance, 11 mEq/K/24 hours.

On the day following irradiation, all pigs ate their complete ration. However, during the next 4 days, the appetites of most of the irradiated animals were poor, their food intakes low, and many vomited. Their appetite returned by the 6th post-irradiation day and remained good until shortly before death when their food intakes dropped again. Diarrhea began in almost every animal on the third day, but persisted for only a few days. Thereafter, their stools were normal. Only slight melena was noticed; terminal hematuria was seen in two pigs.

During the second week after irradiation, the pigs became sluggish and weak and spent most of the time lying inertly on the floors of their cages unless disturbed. When disturbed, they were very irritable and routine handling (such as necessary for weighing and blood drawing) seemed to be very painful.

In about half of the animals there was some increase in fecal nitrogen following irradiation. This increase amounted to about 1 gram per day. There was a tendency for an

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increased urinary nitrogen excretion by the irradiated animals, particularly from the 5th and 8th days. In about half of the irradiated animals nitrogen balance was negative. The increased urea production by some irradiated animals is masked (in terms of urinary N output) by urea retention.

The largest net loss of nitrogen by an irradiated animal (compared with his control) was about 54 gm. in 10 days. This, theoretically, might derive from about 1.7 kg tissue (fat-free). Actually, this animal lost 2.8 kg more than his control.

During the last few days there was a tendency for a slight weight loss in most irradiated pigs.

There is a transient rise in the serum urea nitrogen of the irradiated animals beginning the 3rd day after irradiation but this was never very considerable, the highest value recorded being about 25 mg %.

In about half of the animals, there was an increase in fecal potassium following irradiation. There was also an increase in the urinary potassium excretion with a consequent negative potassium balance beginning with the 6th day in unirradiated animals.

In the majority of the irradiated animals there was striking sodium retention beginning on the 2nd day after irradiation and lasting about 3 days.

In general, in both the control and irradiated animals, urine output paralleled closely water intake. There was generally little difference between the two groups of animals in these parameters.

In the pigs dying following 800 r irradiation, the most striking gross finding was the presence of multiple pin point petechial hemorrhages and evidence of gross hemorrhages in the pleural cavities, kidney pelves, and bladder, subcutaneous tissues, peritoneal cavity, and pericardial cavity, in that order of frequency. In one, spontaneous bleeding resulted in acute cardiac tamponade. The histologic examinations have not yet been reported.

In collaboration with the Surgical Research Service of the Medical College of Virginia, certain aspects of the metabolic response of dogs to thermal burns and radiation, singly and in combination, have been studied. The burns were produced by repeatedly holding a burning iron of constant temperature (60° C.) against the clipped skin for one minute. The area of the burning iron was 25 cm. using a standard surface area formula, separated burns involving 20% or 30% body surface were produced with the dog under nembutal anesthesia. The burns were deep second degree. The irradiation was whole-body, single dose (100, 200 or 300 r) from a 1000 k.v. beryllium window tube. Half the calculated exposure was given to one side of the dog; the dog was then turned and the other side irradiated equally. When a single dog was both burned and

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irradiated, the irradiation immediately preceded the burn (previous work in our laboratory has shown no influence of the order in which these two injuries are given in the time intervals, 10-30 minutes, used).

All dogs were offered a fixed diet (2.5 grams protein, 50 calories/kg. body weight) daily. This is sufficient to maintain them in slightly positive nitrogen balance and at relatively constant weight. After a one-week adaptation period, a control period of two or more weeks followed. The injuries were then produced, and the animals were followed for several weeks, or until death. Only an occasional animal with 20% burn alone died, while the 20% burn plus whole-body irradiation was fatal in almost every case.

In general, most burned dogs promptly went into negative nitrogen balance and lost weight after injury, despite constant food intakes. These parameters were little affected by irradiation, alone or when added to the burn. Diminished food intake occurred only as a terminal event; there was no diarrhea. Most dogs became anemic; the burned dogs developed leukocytosis; the irradiated developed leukopenia and thrombocytopenia. None became jaundiced or azotemic.

In summary, it seems that the so-called "Metabolic Reaction to Injury" which regularly occurs after all sorts of trauma is relatively slight after uncomplicated irradiation injury. The increased urinary nitrogen and potassium excretions, the hyponatremia, the rapid burning of body fat so characteristic of the wounded, burned, fractured, or surgically treated are much less evident in the irradiated, even those fatally irradiated. This difference in response to traumatic and irradiation injury has led us to formulate a hypothesis for the basis of the metabolic response to injury; this will be put to experimental test, using as one tool, germ-free animals. Thank you.

Kenneth P. DuBois, U. S. Air Force Radiation Laboratory, University of Chicago (Paper, Research Program on Radiobiology, submitted in absentia. Not read at conference.)

The research program of the U. S. Air Force Radiation Laboratory consists of the three phases which are briefly described below. Two of these projects may be classified as applied research since the immediate objective is the finding of a practical means of treating radiation injury or the accumulation of data on the chronic toxicity of neutron and gamma radiation. The third project consists of basic research aimed at extending knowledge of the mechanism of radiation injury. All of the programs are of the type which seem worthy of continuation on a long-term basis.

Chronic effects of neutron and gamma radiation in experimental animals. A research program on the effects of chronic exposure to low levels of gamma and fast neutron irradiation on the life span of mice is being conducted.

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Two large populations of chronically irradiated mice of the same age, sex, weight and strain are being used for the comparisons. An evaluation of the effects of variations in dose rate, total dose, fractionation and protraction of the radiation dose on the amount of injury produced by gamma and fast neutron irradiation is being made. The onset, progression and incidence of cataract formation, as well as the occurrence of leukemia, are being studied. It is expected that these experiments will provide some information on the comparative injurious effects of gamma and neutron irradiation at dosage levels lower than those being used in similar experiments in other laboratories.

Screening of chemical agents for prophylactic and therapeutic activity in acute radiation injury. Drugs and miscellaneous chemical compounds are being screened for therapeutic and prophylactic value against radiation injury. Mice are being used for this program and a single dose of 800 r of x-ray is employed. Some compounds are being synthesized in this laboratory but most of them are being obtained from pharmaceutical and chemical companies. All of the agents are tested by administration before and after irradiation. Special emphasis is being placed on sulfur-containing compounds in an effort to find agents which exceed in effectiveness those already known to protect against radiation lethality. Over 600 compounds have been examined to date in this screening program.

Studies on the effects of ionizing radiations on the biochemistry of mammalian tissues. Research on the influence of ionizing radiations on the biochemistry of mammalian tissues consists of a search for radiation-induced changes in the activity of various enzymes and alterations in the levels of other chemical constituents of animal tissues following acute and chronic exposure to neutron, gamma and x-irradiation. Attention is also being given to the mode of action of sulfur-containing protective drugs and to intermediary sulfur metabolism in animal tissues. Possible practical application of radiation-induced biochemical changes are being explored in connection with possible usefulness in estimating the relative biological effectiveness of ionizing radiations and for the biological estimation of radiation dosage.

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Lt. Col. Sven A. Bach, Armed Forces Special Weapons Project Department of Defense:

We support research having to do with the effects of atomic weapons. So our interest in radiobiology is obvious. Our program is directed toward getting the clinical data on whole body radiation in relatively high dose ranges -- Colonel Hartgering has mentioned this to you already -- on protection against and treatment for radiation injury. We are interested, in general, in both acute and chronic radiation exposure.

We concentrate on effects of immediate military consequence. I think we could say that these are the effects that would happen to a person within a period of about a year. None of our biomedical research is directly administered. We furnish funds to various agencies who in turn let contracts. In many cases there is joint funding. For this reason, the details of most of our projects are included in much of the material that you have heard or will hear. I would like to emphasize the importance of dosimetry, since we are all interested in this problem.

First of all, it is hardly likely that the evaluation, and I am speaking of individual dosimetry now, it is hardly likely that the evaluation of man's response to a complex radiation environment can be performed by any single, simple system. Any source of individual dosimeters should have as a minimum a guaranteed radiation exposure history to be the same as that of the person exposed. The implication is obvious that we must look for something in the body which alters and is readily measured, since assorted body fluids and parts usually go the same places. Any such changes must be relatable to the dose, as a minimum, the physical dose and much more preferably, to the individual subsequent clinical course. Not the least advantage of a clinical test of this sort is the economic one, which, in the case of your problem, would be a tremendous one. You would avoid the purchase of gadgets, you would avoid the tremendous administrative load of issuing, checking, and recording. Thank you.

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Dr. A. T. Krebs, Director, Radiobiology Division, US Army Medical Research Laboratory, Fort Knox, Kentucky:

(Editor's Note: Since the tape with his remarks was inaudible, we are using the attached notes and statement which Dr. Krebs was kind enough to submit.)

Project: Biological and medical aspects of the effects of ionizing radiations.

Approach: In 3 dose ranges (massive, medium, low) on the cellular, organ and whole-body level.

Work:

1. Special emphasis on fractionation problems.

a. Fractionation in time:

The goal is to push normal fractionation procedures in the short exposure time, highly pulsed irradiation range, with exposure times in the range of microseconds and less, pauses of similar magnitude, different exposure-time-to-pause-time ratios, several thousands-and-more frequencies per second.

Experiments done so far with rotating-sector-method and exposure-times down to 2×10^{-5} seconds show the effect to be a function of exposure time, pause time, exposure-time-pause-time ratio, frequency.

The biological response goes through a minimum with shortening of exposure time, showing a dip for a certain frequency, characteristic for the studied object.

At present, pulsed, high energy x-ray equipment is under construction to allow more flexibility as to variation of exposure time, of pause time, of exposure time-pause time ratio, and pulse frequency.

Experimental tubes, based on the field-emission principle, have given so far outputs of 20 r per microsecond pulse at 300 kv. Apparatus available to AMRL in May 1959 will give a still higher output at still shorter exposure time.

The F-T tubes will be operating at 300 kv at currents of up to 3000 amperes per microsecond pulse.

These time intervals should come close to the times in which the primary events, recovery and repair mechanisms in irradiated systems occur. They may help to get an idea about the time-of-existence and the life-span of radiation-produced free radicals, intermediates and chemical substances.

It is agreed that these experiments should give some insight into basic fundamental mechanisms and be of practical importance in connection with therapeutical questions and present discussions on the construction and use of pulsed reactors.

b. Fractionation in Space:

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Total-body irradiation through grids (sieves); influence of open-to-closed area and of hole-size on the protection afforded by this partial body shielding procedure.

Mechanism of this protective action is not yet known. It is assumed to be caused by the beneficial effect of healthy, unirradiated tissue on irradiated damaged tissue. Experiments of interest in connection with basic fundamental questions on radiation-produced "diffusible" substances, exchange- and interchange-dynamics between healthy cells and radiation damaged cells and tissues; possible practical application in shielding procedures, such as body armor, etc. Present work tries to study existing conditions for milli- and micro-hole grids; use and advantage of woven materials in protective measures.

2. Routine Activities of the Normal Radiobiology Research

a. Massive dose range

Effect on central nervous system; Protection by pentobarbitals and tranquilizers.

b. Medium dose range

Chemical protection by:

Cysteine:

(1) protection of nucleic acid (DNA) - syntheses against radiation damage (Hevesy effect) in intestines of the rat (1953);

(2) protection of mitotic process in rat cornea;

(3) protection of mitotic process, (number of mitotic figures, number of chromosome aberrations) in intestinal mucosa of rat.

Cobalt:

Protection with oral administration before and after irradiation; feeding cobalt results in production of polycythemia, which causes the protection. Earlier experiments 1951 and 1952 with pitressin and serotonin are continued and taken up now in combination studies.

Triphenyl-Tetrazolium Chloride:

Protector against radiation damage, probably on account of being a hydrogen-acceptor.

Physical means of protection:

Grid shielding experiments; Fractionation, ultra fractionation procedures.

Physiological means of protection:

Continuation of earlier studies on the protection afforded by bone marrow homogenate, and by embryo homogenate, in connection with studies on the antibody formation and immune titer reaction of the irradiated animal.

c. Low dose range:

Adaptation phenomena;

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Cosmic ray effects in connection with low dose-long time irradiation problems;

Biological dosimeter based on the use of fallout products (fission isotopes I-131, Cs^{137}): Uptake and distribution of fallout products under different stress conditions, so far studied for I-131 and Cs^{137}, planned for strontium-89.

I restricted myself intentionally to our fractionated dose studies: fractionation in time and fractionation in space. As to fractionation in time where we go into the millisecond and microsecond exposure time with pauses of the same magnitude in between the exposure, I reported on the data we have gotten with the pulsed x-ray equipment early this year; namely, an output of 20 r per microsecond pulse.

You may be interested to hear that a machine is underway for use next spring which will operate with 3000 amperes at 300 kv per microsecond pulse with an average energy of up to 300 Megawatt. The equipment, based on the field emission principle, will be built under contract with the Surgeon General of the Army by the Linfield Research Institute in Oregon.

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Colonel Edward J. Dehne, Commanding Officer, U. S. Army Environmental Health Laboratory, Army Chemical Center:

I wish to tell you about the Army Environmental Health Laboratory which is a service agency of the Army Medical Service. Mobilizing for World War II, it was recognized that some of the industries engaged in by some of the Armed Forces would be quite hazardous. The Army Industrial Hygiene Laboratory was established to assist in controlling health hazards related to work activities. Later this Laboratory moved to the Army Chemical Center at the end of World War II. It is a Laboratory staffed by a hundred military and civilian scientific personnel, who are under the direction of the Surgeon General of the Army and work within the Health Service of the Army.

In this respect the Army can be compared to a large industry engaged in developing and producing weapons. Of course the work changes very rapidly with the weapons. You mentioned World War II, we would be interested in the old-fashioned ones, the ordinary explosives and things. After World War II, with the advent of the nuclear weapons, we ventured into new activities that dealt with radiological health hazards.

A new division, radiological hygiene division, was organized in the Laboratory. At the time the Radiological Hygiene Division was established we were thinking of nuclear weapons effect. When we started to staff for a radiological surveillance capability in the Army it was found that the main job ahead of us, was supervision and control over the operation of our Army Medical Service x-rays.

Our objective is to apply the things that we have developed as early as possible to protect people working with hazardous materials. We also do a considerable amount of "shoe-leather" epidemiology related to employees' claims against the government. The Bureau of Employees Compensation deals with us quite a lot. If they receive a claim against the Government in an alleged exposure, they often turn this over to us to report on the potential exposure the claimant had received. We investigate the work exposure after the facts since we have up-to-date hygiene surveys of all the Army operations.

In this connection I might mention that the Armed Forces now do have a medical 201 file on every individual, so that when he has an x-ray of his teeth, chest, etc, the report goes in that file. From this one may make a summary of all of his exposures. Actually the file is not intended for that, but it does contain valuable information on radiographic exposures as well as occupational exposures to radiologic substances. We are interested in other types of exposures as well, such as noise (the loss of hearing) and many chemical hazards in the work environment. This is a brief introduction, I should say, to our Laboratory.

The Army Environmental Health Laboratory supports the occupa-

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tional health service of the Army. Occupational health programs are actively developed Post level. Support of these programs by the Army has been provided at the Continental Army level in the United States. At the Continental Army level there are many preventive medicine consultative services available to the posts. There is also operated an Army area laboratory which provides epidemiologic laboratory services to assist the occupational health programs at post level. At the Department of the Army level the Surgeon General initiates policies, prepares directives and provides technical advice on all matters pertaining to radiological exposures. The Surgeon General also maintains the Army Environmental Health Laboratory to support the occupational health service through the provisions of field and laboratory services in environmental hygiene, sanitation and occupational health. The Army Environmental Health Laboratory conducts special studies, surveys, investigations in the fields of occupational health, industrial hygiene, industrial hygiene chemistry, industrial hygiene engineering, radiological hygiene, sanitary engineering, toxicology and entomology. So you see we provide a very broad coverage for preventive medicine.

Now to go back to radiological hygiene, we operate this program very much like we do the others by furnishing special studies, investigations, and consultive services. In addition to this the Army Environmental Health Laboratory provides at approximately annually intervals a survey of all work activities on each Post. A biennial survey is conducted of all radiologic exposures. The actual operations in which radiological materials are handled in the Army are: (1) The medical diagnostic x-rays, therapeutic x-rays, (2) the medical radioisotopes, (3) the research isotopes, (4) a large number of large industrial x-rays, (5) several betatrons, (6) the power reactor, and lastly, (7) the nuclear warheads may eventually be distributed to local levels.

Another function of the Army Environmental Health Laboratory, within the U. S. Army, is similar to that of the Atomic Energy Commission in the United States. Every application for a source by Army agencies goes through the Surgeon General's Office and that application is screened by the Army Environmental Health Laboratory to determine whether applicant, the user of the source is qualified to use it safely, to protect himself and to protect others. The objective is to see if he has a proper plan for its use, a plan for its disposal, proper waste disposal, and suitable dosimetry. In many cases before the source is delivered, a health physicist from Army Environmental Health Laboratory will be present to supervise or maintain surveillance over the delivery and handling of the source at the time it arrives.

There is another project that might be related to research that is quite important. The Laboratory spent about two years surveying Army Hospital x-ray facilities for the National Bureau of Standards and provided a rather comprehensive report on the controls used and the measured exposures.

About a year and a-half ago, there was a story published in several

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newspapers which claimed that armored personnel of the Army who operated the "Canal Defense Tanks" during World War II had been exposed to an extraordinary radiation and that some of them had turned out to be sterile. We looked into this very carefully. There was a tank which was equipped with a strong arc-light, it had no radiologic hazards. We consulted the industry that manufactured the lights and many other agencies which had used similar or much stronger lights of the type under study. It was found that no radiation occurred. There is this problem of microwaves from powerful radar equipment. The Laboratory is now working with a committee to determine if there is any real health hazard or would help to determine the health hazard. Action is being taken to develop instrumentation to measure microwave exposure from powerful radar sets. There is no chance of radiation related to these radar microwaves. Thank you, sir.

Dr. Leonard J. Cole, Head, Experimental Pathology Branch, U. S. Naval Radiological Defense Laboratory:

What I would like to do this morning is to first present to you a list of various projects and programs. This is a list of publications and reports from the Biological and Medical Sciences Division of the Laboratory which have been categorized in 11 categories, as suggested by Dr. Parrino -- categories such as dosimetry, acute effects, recovery rates, delayed and late effects, genetic effects, protective efforts, therapy, hazards from ingested radioactive material, combined effects of radiation and burns, use of isotopes, effects of radiation on immunity. These comprise approximately 230 titles. So much in the way of an introduction.

Then I would like to give you a very broad outline of the type of work going on in the Biomedical Division of the Naval Radiological Laboratory in terms of the breakdown of types of projects. You must bear with me in this because I would like to give you a broad picture first and then, perhaps, more specifically discuss matters of more direct interest to OCDM.

Here we have a breakdown into such categories as these: diagnosis and treatment of radiation injury, effects of ionizing radiation on intermediate metabolism and nutrition, biological and chemical factors which influence radiation injury, internal radiation hazards, biological effects of penetrating radiation, acute effects of partial body exposure. This gives you a general idea of the scope and of the type of Laboratory work going on covering this very wide range of areas. In all these areas direct laboratory experimentation is going on. Now first, in connection with the

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more specific interests of OCDM, I would like to state some questions that we have in mind; questions which provide the general framework upon which our contracted work with OCDM is related.

What is the relationship of the acute radiation damage and late effects? Does the exposure to ionizing radiation induce in the survivors the sequence of changes and a course of aging which differs not only from the normal but also, and especially, from those which follow exposure to other stresses? This is one question.

Secondly, are there specific biochemical, physiological, or pathological changes demonstrable in the post-radiation subject which can be correlated with the reduced life expectancy or the enhanced morbidity characteristic of the delayed radiation syndrome?

Three - what is the role of inherent or superimposed infection as well as of exposure to a variety of adverse external conditions in the development of the delayed radiation syndrome?

And is it possible, number four, to alter and in particular to minimize the development of this debilitation and the reduction of life span in the post-radiation subject by measures aimed at the acute radiation episode and also by more general measures such as specialized dietary regimes? Obviously this covers a very wide variety of things and so with this general framework I would like to proceed.

But first, as a basic aspect of work going on, we are very much interested in the effects of radiation at the, what you might call, biochemical level; that is, the biochemical-subcellular level. In other words, since we know, or it has been shown in many places, that exposure of cells, particularly radiosensitive cells, in organs of the whole animal or in isolated cell systems, that ionizing radiation very markedly and drastically inhibits the biosynthesis of the group of substances which are required to cell division. This, of course, results in the very well known inhibition of mitosis.

One present approach of this problem is a study of the incorporation of tridium labelled thymidine into DNA (deoxyribonucleic acid) in isolated, in cell-free systems. That is to say we are now in the process of studying the biosynthesis of DNA in enzyme systems and this has been shown to be possible; that is to say, one can show the net biosynthesis of DNA in extracts of certain tissues. And one of our objectives is to study this system in vitro as a radiation object. Thus we feel very strongly that at least at the fundamental level of radiation effects, the understanding of this reaction is basic.

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Now, getting to the whole animal, we are studying the acute effects of radiation, using very specific end points as a measure of effects. For example, Fe^{59} uptake into the bone marrow as a functional test of effect of radiation on bone marrow. The total DNA content of radiosensitive tissues; such as bone marrow, spleen, lymphoid tissues in general, and intestinal mucosa, gives a quantitative chemical measurement of the number of cells; and the dose response curves which have been obtained are very reproducible and show the inherent time course of the effect, depending upon the dose, of course, the effect and recovery in the acute period of the first thirty days.

This is also being extended now to fractionated doses, because we feel quite strongly that the time course of events, if you follow the specific end points, such as iron incorporation, or the DNA content of these sensitive tissues, the course of recovery as to fractionating dose is not predictable from the single dose effect. This has to be worked out empirically at this point, in order to be able to follow up with the late effects study which I will mention later.

Another side product of the acute effects of radiation are the biochemical studies to be used as diagnostic indicators for radiation damage. These, as I mentioned briefly before, are studies of urinary excretion of taurine, an oxidation product of sulfydryl-containing compounds, presumably cysteine in the body, and also the purines which are known to be breakdown products of nucleic acid catabolism. At least the taurine excretion is related to the now well-known effects of breakdown of the macro-molecular nucleic acids in the radiation-sensitive tissues following exposure to radiation.

For example, it can be shown that within two to four hours after whole body exposure to lethal doses of x-rays, the DNA content of the spleen drops very markedly and is accompanied by an increase from zero levels in the normal case -- an increase in a soluble DNA-like breakdown product, from initial DNA-protein in the tissue. We have every reason to believe that the further breakdown of this compound, by enzymes presumably, leads to the observed excretion of the taurine which is seen in the urine. As I mentioned before, up to 250 r, this excretion of taurine is dose-dependent. Beyond this point, the effect is not dose-dependent. At the present time, we cannot say that this is a diagnostic tool for radiation injury. However, studies in this direction are being pursued.

Now with respect to delayed effects of radiation here are the effects which occur, the phenomenon which may occur, at some delayed period, say second, third, fourth,

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fifth month, after exposure to various doses of radiation. Here we have attempted to study the nonrecuperable injury; that is to say, following the recovery after the acute phase, how can one assay the state of the tissues following this exposure.

There are several procedures that are being employed to detect this nonrecuperable fraction of injuries, so-called nonrecuperable. This is being studied by Fe^{59} uptake into the bone marrow. It is a functional test and there is definite evidence that there is a nonrecuperable fraction. That is to say, the incorporation of iron into the bone marrow following, say, six months' exposure is not normal. This is now being studied as a response to dose. Another means for studying nonrecuperable injury is the regrowth potential of rats which have been hypocalorically reared; that is to say, rats which have before radiation been reared on diets which are low in calories. They're highly restricted. These animals grow at a very slow rate. The regrowth potential following putting these animals on normal diets is used as a criterion for assaying or evaluating the nonrecuperable injury.

Another measure is the challenge of the animal with a subsequent dose of radiation, so that the change in the LD_{50} gives you a measure of the residual injury.

Another measure is susceptibility to superimposed infection.

And finally, two other measures of this nonrecuperable injury, the ability of these animals to grow on marginal diets; such as diets which are deficient in pantothenic acid.

Now, getting to the late effects of radiation. Here the attempts to observe the late effects relate then to the acute damage. Now, knowing what we do about the acute radiation damage, and this applies to x-rays, gamma rays, and fast neutrons as far as we know, at least in mice, we know that the limiting factors in survival of animals in the lethal, single, acute dose, is the status of the bone marrow and the lymphoid tissues. I group these together; they're very much related, actually, and we'll just say that bone marrow and lymphoid tissue.

We know that animals given bone marrow injections following a certain lethal dose will survive. We know also that the one difference that one can detect between such animals, that is one animal given lethal radiation and bone marrow transfusions after the exposure; the difference that one can detect is the rate which the bone marrow and spleen regenerate after this treatment. That is to say, in the animals which are radiated and given no treatment, the total DNA content of the bone marrow drops very sharply and stays down until the animal dies. The animal given bone marrow infusions, has an

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initial drop which is indistinguishable from the growth of control animals, and then by four or five days, we begin to see a very sudden and rapid, sharp increase in the DNA content, which is a measure of regeneration of bone marrow. This effect can be picked up both by the total DNA content of its tissues and by radioactive incorporation studies in this DNA. We are going on the supposition that limiting factors of survival in acute radiation damage is the bone marrow picture.

Now the late lesions that we have seen and other people have seen in mice, in populations of mice which have been kept for the total life span and observed, can be characterized by actually two or three specific lesions. Well, let me get more specific here.

We have examined the late effects of radiation in several groups of mice given various treatments. One group of mice received a single dose of 690 r x-rays, 250 r x-rays. This was the LD_{30} and we studied the survivors of this dose. Then we gave the same total dose, in various fractionated schedules -- I will just talk about the one fractionated schedule -- namely, the 85 r given eight times, the same total in which the 85 r was given once, once a week. And then we had control groups of normal nonirradiated animals.

We have kept these animals their life span and the results are rather interesting. We have another group in which we gave 690 r and the animals were given bone marrow therapy after the exposure and also followed. First of all we find that the life span reduction was greatest in the animals given the 85 r times eight, fractionated dose; that is to say, in specific numbers the normal median life span of the normal animals was 27 months. Among the animals which received 690 r, single dose, for survivors the median life span was 21 months. Those that received 85 r given eight times 15 months median life span.

Now looking at the pathology of these animals, we find that the largest single cause of death in the animals that got the 690 r was the nephrosclerosis which was mentioned earlier yesterday as a late effect and, which we have found very, very regularly in our long-term animals. This is a vascular lesion in the kidney which was found in this particular dose, in the order of 60% of the animals. In the previous study we found 100% of the animals which had gotten a super lethal dose of x-rays and were followed by bone marrow treatment.

The group that received the 85 r times 8, exposure fractionated dose, showed essentially no nephrosclerosis. That is to say, the level is precisely the same as seen in the normal nonirradiated animals, on the order of 5%, which is the background value.

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However, looking at the leukemia incidence in these groups, and this strain of mice happens to be of a relatively high leukemia incidence strain, let us say high spontaneous incidence, we find that the highest leukemia incidence was seen in the group that received the 85 r times 8 fractionation, and the group the received the 690 r alone actually have a lower leukemia incidence than the normals did. So here we have two endpoints of late effects, in which we have an opposite effect of the fractionation, and also in effect the opposite consequence of the high single dose. We feel that these two endpoints, at least in this strain of mouse, are the two major late effects. The other late effects seen are gastrointestinal hyperplasias, which I will not go into right now, except to say that with x-rays the gastric-hyperplasia observed (it is a late effect), seems to go along with the vascular changes in the submucosa.

Now, to go back to one of the questions that we asked. One of the questions was, what is the relationship of the acute radiation damage to late effects? Well we have an additional clue to this question by studying the effects of fast neutrons on mice, and studying again the late lesions and life span. Now as is quite well known by now, fast neutrons, the one that we use, are 2 Mev neutrons or 8 Mev. Fast neutrons have a high LET for acute damage to the gastrointestinal tract -- of the order of 2 to 3 as compared to x-rays in mice. This can be demonstrated by histological criteria on the gastrointestinal epithelium, also by weight depression of the intestines.

Now we find that if we keep animals that have been exposed to fast neutrons for their life span, this is sublethal doses of fast neutrons, we find that these animals have a relatively short life span on the order of median life span of about 12 months as compared to 27 months for the control animals. These animals show a very high incidence of gastrointestinal carcinomas.

Now the comparable group of animals that received an LD_{100} dose of x-rays followed by bone marrow transfusions, these animals show essentially no, zero, incidence of gastrointestinal carcinomas. This is for a full life span.

Now, to follow this up, we have very recently finished a study of a group of mice which had received a super-lethal dose of x-rays, that is to say, doses in the order of 1100 r as compared to 800 r being LD_{100}. With this dose, we are approaching gastrointestinal acute effect -- acute gastrointestinal syndrome as far as x-rays are concerned. With such doses we can only save a relatively small percentage of animals with bone marrow treatment. But we can save in the

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order of 30% of these animals. These are the animals the survivors of which we have studied.

Now in this group we find, in keeping them for their life span, a very high incidence in the order of 30% gastrointestinal carcinomas. So here we have, I think, a very direct trend of answer to the question raised, namely, the specific influence on the occurrence of GI neoplasms; that this late effect is related to the acute damage seen both with fast neutrons in mice and also with much higher doses of x-rays in mice, as related to the acute effect.

Now one consequence follows from these studies, and I think from other studies of literature, that we ask the question as to the relationship to the acute radiation damage to late effect. We know that if you fractionate a dose of radiation, a given dose, the acute damage is definitely less. Now if we now follow these animals for their life span, we might make the hypothesis that we consider two types of late effects, one being degenerative effects and the other being neoplastic effects. The data that we have at the moment, at the present time, seems to fit the hypothesis that fractionation of dose of radiation dose will cause a decrease in the degenerative late effects, in other words, in this case, we can say that the animals receiving fractionated dose shows much less nephrosclerosis, much less vascular damage in the stomach submucosa, and also much less graying of the hair. In fact you cannot distinguish these animals from the normal animals of the same age, so far as the graying is concerned, so these are what you might call degenerative diseases, or degenerative phenomena. These are decreased with increased fractionation. Now with respect to neoplastic transformation, in other words, cancer or leukemia, this is definitely not the case, at least under the circumstances of our experiment. That is to say, fractionation of the dose here does not decrease the incidence -- if anything, in our group of animals, leukemia has occurred earlier than they did in the normals. But in any case, it did not decrease the incidence of leukemia. And also, fractionation did not decrease the incidence of mammary carcinoma of these animals. So this is the hypothesis we are dealing with. Also this is related to another phenomenon; namely, the fact that we saw very much less leukemia in the group that received the single high dose (690 r). Now here one might speak of the effect as therapeutic. So that one way of looking at it might be that this deletion of a large number of cells which are destined to become leukemic (you see, this is a relatively high leukemic strain of mice), resulted in a lower leukemia incidence.

This same kind of thinking actually has been applied to some other studies that had been done in our

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Laboratory by Davis & Alpen on skin tumors resulting from localized beta radiation in rats. Here the incidence of skin tumors as related to the dose, goes through a maximum and then drops, as the dose increases. You can apply the same kind of reasoning there that the higher doses of beta radiation actually killed off so many cells that the incidence of the neoplastic transformation is lower.

Now the other question that was of interest is the question of modification. Is it possible to alter or modify the post-radiation syndrome? Here again, we can relate modification of the acute effects with consequent modification of the late effects. Here we come into the bone marrow picture again, where it is well known by now that either if you shield the bone marrow through the exposure, at least to x-rays (lead shielding), or if you give transfusions of bone marrow, and this is now true in dogs, as well as in mice and rats, in the case of dogs one has to give more bone marrow but nonetheless the principle still holds. If you give transfusions of bone marrow, the animal survives, otherwise LD_{100} dose and in the case of mice, these surviving animals show a very low incidence of leukemia and this again we feel is related to the fact that in the acute phase, after the transfusion of the bone marrow cells you get very dramatic and drastic regeneration of the bone marrow and lymphoid tissues.

Incidentally, in this connection, one of the major obstacles to bone marrow therapy following radiation in humans, has been the observation that, at least up to recently, one has to give either autologous bone marrow or so-called isologous bone marrow, that is, bone marrow from the same strain of mouse, in order to provide this protection. And if you gave bone marrow from another strain of mouse, in effect, a different genetic combination, then although you would get temporary protection with bone marrow in the first 30 days, this so-called secondary disease phenomen would occur; namely, the animals would die off the second, third, and fourth month from the syndrome which is really not radiation because the bone marrow had recovered already, but something else, the difference being immunological in nature, actually. I don't have time to go into that now, but I think it of interest to say here now that in recent months, pasf six or eight months, it has been shown both in our Laboratory and in England and also NIH that it is possible to prevent the secondary disease with homologous bone marrow treatment; that is to say, from two different strains, by using spleen or liver as hematopoietic cells from newborn or fetal donors. By use of such material, we can completely prevent the secondary reaction, and at least in our Laboratory we now have animals which have been alive for almost a year following injection of

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hematopoietic cells from foreign donors; foreign in a genetic sense, different strains of mice. So that if one were to think about applying this to humans at this stage of the game, I think the question now is really a question of logistics and procurement rather than of principle.

Now as to some other aspects of late effects, we are very much interested in knowing whether this nephrosclerosis which is seen in animals and mice and rats after single high doses of radiation is due to a direct effect on the kidney of the radiation per se or, is it also influenced by indirect effects on the rest of the animal. Here, as was mentioned previously, I think this morning, we are interested in localized radiation of the kidneys and in following up such animals.

Now another large area of study of late effects is the question of interaction of the late effects syndrome with the nutrition of the animal, of the population. And this, of course, is something we feel that should be pursued and is being pursued now in our Laboratory, because the studies I have mentioned up to now are situations in which the diets are, so to speak, standard, the animals are standard, and this is so we can control the situation. The question comes up as to whether these late effects would be modified or changed, or the level of incidence changed in populations with different nutrition. Of interest in this respect is the fact that has been shown in our Laboratory recently that the dose response curve, that is, the dose mortality curve for a population of rats which ordinarily is quite steep (you have a S-shaped curve if you plot the per cent 30-day mortality vs dose). It is entirely modified if you do a dose response curve on the hypocalorically reared rats. Their slope is much, much more gradual, in fact the slope is of the order of 1/5th of that of the normal population of animals. This means that a test to pin down LD_{50}, of a population, depends at least in part, upon such factors as nutrition. This is a very extreme situation, of course, but nevertheless it's a possibility. I think that this will hold. I think looking into the situation of the Japanese population would be quite pertinent, because there, of course, the diet is not up to optimal or maximal or of optimal caloric intake.

Another question most specifically relates to the effect of diet as regards, for example, the presence of the high unsaturated fatty acids, the level of cholesterol, aspects of estrogens, of thyroid hormone, in the diet environment of the animal as relates to the expression of the late effect syndrome.

In more general terms, then, we can say that the things we are interested in with respect to late effects have to do with the mechanisms of injury fixation of the late effects

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syndrome, particularly at the cell level. Also the question of carcinogenesis with respect to somatic mutations, which is one of the theories involved, of course. In this framework, the question is what happens when you change the population of the cells, which is what the acute radiation is doing. You are knocking out some of the stem cells, for example, and you are changing the population. Some of the effects that we see of the long term must be related to this change in the population, for example, in the bone marrow, in the spleen, and in the liver, and kidneys too. Also the whole question of healing process, as has been mentioned early this morning. One other problem is what you might call the population which I have alluded to already, is the question of the genetic makeup of the population, whether it is an example of inbred population, for example the type that we have been studying, or the people in the laboratory study, or when you talk about heterogeneous population, genetically speaking.

Finally, we would like to know whether, when you get to much lower doses of radiation than what I have been discussing, whether the effects there are the normal aging which has been accelerated, or are they something different again? Here again we have another problem and the effects obviously are very, very much more subtle than they are at the high single doses.

I think I will stop at this point. Are there any questions?

Floor: Question relating to the finding of late radiation effects in kidneys.

Dr. Cole: We are aware of the direct effects to the kidney, but how much of the syndrome observed might be the results of a feedback mechanism from irradiation of the rest of the body.

Dr. Paul S. Parrino: I would like to ask Dr. Cole in reference to this work on the low caloric-bred rats as a measure for non-recuperable injury and I believe you did some other work on irradiating skinny rats and fat rats in general, as far as extrapolation of humans, what does it look like now -- that fat people or skinny ones will be able to take radiation better?

Dr. Cole: I cannot answer that question, but what the implications here are is that we have to look closely at the nutritional status of a given population with respect to defining the dose mortality curve for that population. It might not necessarily be the usual steep sigmoid type of curve that one sees in the usual experimental groups. So that if this is an extreme situation, we would have two types of LD_{50} curves to examine and the generalized population might be between these two extremes. So that the LD_{50} changes also, and is not a

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fixed constant, necessarily.

Dr. Paul S. Parrino: Some of the results seems like there is some conflict. Sometimes overweights are better protected and other times, the underweight.

Floor: Question relating to the relative effects of fast neutrons.

Dr. Cole: Well, we have a report being written up right now on the fast neutron work in mice. The picture looks like this. So far as the RBE, gastrointestinal, hyperplasia and carcinoma, we can say that the RBE as compared to 250 KV x-rays is of the order of over two (between two and three). Because we obtain the same effect by comparing fast neutrons (about 300 or 400 rad) and 1100 r of x-rays giving comparable late effects of hyperplasia and intestinal carcinoma. Also, we can say that it seems from our data that the 2 Mev neutrons have a greater carcinogenic effect on GI tracts than do the 8 Mev neutrons.

This is what might be expected, I think, from considerations of LET (linear energy transfer); and it shows that direct carcinogenic action on cells occurs; and incidentally, these fast neutron irradiated animals, showing the hyperplasia of the stomac show no evidence or no indication of any vascular degeneration in contrast to the x-ray effect. Also with respect to nephrosclerisos, the RBE, again, is only the order of one -- the typical x-ray effect. We have a differential here between two soft tissues -- kidneys and the gastrointestinal tract, with respect to fast neutron effects.

We do not feel these RBE values should be taken for large animals, such as dogs, because of the changes in the nature of the neutron irradiation as it passes through the tissues of the large animal, and being converted to gamma radiation.

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Commander F. W. Chambers, Jr., MSC, USN, Naval Medical Research Institute, National Naval Medical Center:

The efforts at the Naval Medical Research Institute have been directed primarily towards the acute effects of external ionizing radiation. This does not mean that we are not interested in chronic and genetic effects, but we do not have facilities to hold the larger animals we are using for some of our studies. We hope to develop a collaborative effort with another group having such facilities that will be of mutual benefit in this field. We are also interested in activation analysis as it is associated with induced radioactivity from neutron exposure. We expect to have facilities to pursue this line of investigation in the near future.

I would like to mention the fact that we are very fortunate in having the collaboration of not only our own clinical group but also that of groups in other laboratories in the Department of Defense, other Federal agencies, and, through some of our former Naval Officers, in universities.

When we were confronted with the problems of ionizing radiations from nuclear detonations, past experience in the clinical application of ionizing radiation proved to be very valuable in understanding the problems involved.

We immediately concerned ourselves with measuring the dose at various depths in unit density material as well as determining the air dose. The data we obtained in several field tests are now partially declassified, and I would like to present as much to you as I can as a basis for presenting our research endeavors.

Note: Slides were shown at this point in the presentation.

Miniature ionization chambers were used throughout phantoms made of approximately unit density material. These chambers had a wall thickness of 60 mg/cm^2, a voltage gradient of 10,000 volts/cm and were energy independent down to 30 KV.

Depth dose curves were obtained for the initial gamma and fallout radiation. First, with regard to the initial radiation, a comparison of laboratory source data with field data indicated that a 10 Mev Betatron at Naval Ordnance Laboratory closely approximated the field source.

There is another problem associated with the initial radiation; the presence of a neutron component under certain conditions that can be of considerable significance. Good depth dosimetry data are needed in this area. We are developing a miniature tissue

equivalent plastic ionization chamber filled with a tissue equivalent gas, based on the work done by Rossi at Columbia, which we hope will permit better correlation of biological effects of mixed radiations with physical measurements.

As soon as we feel we have satisfactory dosimeters, we will start preliminary studies with small animals in our hospital reactor and hope that in the not-too-distant future a large pulsed reactor that will permit the use of high dose rates to large animals will be available.

On page 11 of the AEC publication, "Some Effects of Ionizing Radiation on Human Beings," depth dose curves for the initial radiation and an early fallout field are shown. I would like to point out that, with regard to the fallout radiation, the ratio of the rapidly absorbed component, I use this term because it appears to be a combination of high energy beta particles and low energy photons, to the high energy gamma component changes with time. Where one might find a 10 to 1 ratio in the first twelve hours after detonation the ratio will fall to 2 or 3 to 1 on the third day. This is important because it is my feeling that if the Marshallese had received the same integrated gamma dose in the first 12 hours after detonation as they did over the period for which they were exposed, the damage due to the readily absorbed component could have been considerably greater. Another fact to be considered is that the radiation from a fallout field is coming from a large planar source and, as can be seen from the curve, gives a more uniform dose throughout the body which would mean that it might be more effective per air roentgen than the initial gamma radiation which comes from a unilateral source.

We are studying the effects of different energies and geometries on various species at the present time, and again we hope to obtain equipment that will permit us to more nearly approximate the sources found in the field. At the present time a 2500 curie source of cobalt providing a 4π field of radiation is being used as well as X-ray generators ranging from 1000 to 2,000,000 volts.

Of interest in this connection, Dr. Ellinger has obtained different mortality curves for AP, PA, lateral and bilateral exposures for the same energy and air dose in several species. This leads to the question of critical tissues which, in turn, leads to an interesting project being carried out by Dr. Bland Williams. He is studying the basic mechanisms involved in recovery of certain tissues from the effects of total body radiation. He started with the small bowel epithelium of the rat because it was found that the effect was a direct one uncomplicated by a significant humoral

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factor. Plans for studying other tissues have been formulated. Along with the tissue recovery studies, he is studying the effects of fractionation and protraction of dose which is critical to the evaluation of both weapons' effects and the therapeutic use of ionizing radiation. He has been able to demonstrate that it is possible to separate experimentally the effects of ionizing radiation upon cell populations in interphase in the small bowel epithelium, and to distinguish those changes that are most critical to recovery of this tissue.

In the field of protection, Doctor Ellinger is working on a cell-free spleen extract. This material does not appear to cause any secondary complications as some of the other agents do. It did not lose its effectiveness over a period of three months and an investigation is under way to determine how long it will remain effective. Another important fact concerning the substance is that in tests that have been carried out up to the present time it has been shown that mouse spleen extract will protect both the mouse and guinea pig and that guinea pig spleen extract will protect the guinea pig. Further studies are being made and planned. A very active program for isolation and identification of the protective spleen factor by chemical and physical chemical methods is in progress.

Captain E. R. King, Chief of Radiology, U. S. Navy Hospital, National Naval Medical Center:

Whatever I have to say will be very general and extemporaneous. Before I mention this new Facility, I would like to mention a couple of projects that are under way at the Naval Medical Center. One is a joint project at the Tissue Culture and Tissue Bank with the Department of Nuclear Medicine regarding a study of possible methods of preserving bone marrow. The Tissue Bank has had several years' experience in freeze-drying various tissues and are going into this study. I am not very well acquainted with it, so I cannot answer any questions if somebody wants to ask them about this particular project. As Mr. Chambers mentioned, at our Hospital we have a small Aerojet-General AGN 5-watt power reactor with a rather low neutron plug. In addition to the project that he is working on regarding dosimetry, we have for several months been carrying on a project involving neutron activation analysis of biological specimens, primarily tissues, blood and urine from patients.

We also have a project connected with the reactor involving the production and clinical evaluation of short half life isotopes, but this project probably has nothing to do with the content of meeting.

The new Facility that has been

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mentioned has been approved. The work will probably start on it in the near future. It will entail a small two-story building with its own laboratories; tissue, chemistry, and hematology laboratories, its own radioisotope laboratory facility, a very small space for patients, and four steel low background counting rooms. These rooms will have eight inches of steel on all sides. They will be used for low background total body counting. The exact counting equipment that will be utilized in these rooms has not yet been decided upon. Although it will probably have something similar to what Walter Reed has at the present time. This Facility is to be available for any casualties that may result from any type of peace-time accidents in the Navy or Marine Corps. Of course it will be available to anyone else if they desire to use it for such work. It is designed so that we can bring patients into this Facility and do all types of clinical,hematological, blood chemistries, and so forth, as well as counting procedures, including total body counting, and a study of internal emitters that might have gained access into the patient's body.

It will also be used to do baseline studies and follow-up studies on Navy crews who are in the engineering spaces, or near the engineering spaces, of our nuclear-powered ships. These studies are quite necessary, we feel, and have not been carried out to date.

During the routine operations, the Facility will be used for various types of projects similar to those mentioned here in the last few days. It is hoped that by constant use of the laboratories in clinical research projects, that the crews that will man the Facility will be available and ready at any time in case an accident may happen aboard one of our nuclear-powered ships or involving an aircraft. Thank you.

Edwin G. Williams, M.D., Radiological Safety Consultant, Division of Hospital and Medical Facilities, U. S. Public Health Service:

We, in the Bureau of Medical Services, do not have at the present time anything under way which could by any stretch of the imagination be called radiobiological research.

We do have under consideration and negotiation with OCDM, certain studies with regard to hospital activities, hospitalization facilities, and medical care facilities of the shelter program. This undertaking will be, in my definition of the word research, no more than fringe research, although it will involve very important parts of organizational, operational, managerial planning for a shelter utilization program.

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There is another field in which we might become active and which we would probably do in conjunction with the American Hospital Association. It is the general analysis or systems analysis of the conduct of what we now call hospitalization in a disaster period. This I submit is one of the most needful studies that could possibly be undertaken.

Dr. Francis J. Weber, Chief, Division of Radiological Health, PHS, D/HEW

Now I take it that my appearance on the program at this point is not to present details on any research projects of the type that you've been hearing about. The Public Health Service does, however, have representatives who later in the program will be able to give us such details, notably Dr. Straub of our staff, as well as Dr. Zubrod of the Cancer Institute.

I would like to say in the beginning, however, that, since one does form impressions while listening to the descriptions of the projects being presented here, one is that I can't help feeling, particularly as an official in the field of public health administration, that the work being described is of extreme importance to decision making by those public health administrators who are being confronted with these problems to an increasing degree.

I think it is true also that those of you who lay a patient seige to the truth in your laboratory must feel at times that your efforts sometimes go unrecognized. If you require any reassurance on that point, I can tell you that they are certainly taken into account when attempting to deal with the problems of the magnitude of this one.

Now today I am prepared to offer a few remarks which will attempt to describe in rather general terms some of the research problems which appear to be of practical importance to us in the Public Health Service; problems which, at the same time, are related quite intimately to the civil defense field.

Therefore, I feel I should begin by saying a word about our own Radiological Health Division which I represent, and how it may relate to the problems that we are discussing at this meeting. Now this particular Division is a part of the Bureau of State Services of the Public Health Service, the latter one of three operating Bureaus. You have just heard from Dr. Williams who represents the Bureau of Medical Services and you will hear later from the other Bureau, the National Institute of Health. Now this particular Bureau of State Services is an arm of the Service dealing with problems of direct public health significance, in which both the Service and the States are involved. Therefore, it concerns itself primarily with large scale threats to health, whether those threats are in the form of biological or physical agents, the latter of which we are

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discussing these two days.

Consequently any research program that this particular Bureau operates is one of the applied sort, and is directed toward problems of public health significance. I believe this to be of particular importance to civil defense, because the respective programs are bound to touch one another at several points. The main differences that I can see between the two are one of time and place, if we think of the contrasting situation of peace versus war.

In considering the need for research to serve the interests of both the Public Health program per se, as well as the Civil Defense program, it would appear at first view that we really face an infinity of new problems in this field. It might be that the word "problems" is not the best term, since it might be more accurate to say that what confronts us is a paucity of facts, to sum up what we have heard in these last two days.

It is certain that the collection of basic facts which are so badly needed could conceivably lead to establishing some useful conclusions of importance both to public health and civil defense in the solution of many of these so-called problems. Therefore, I believe that one of the principle aims in the radiological health research field at this time is concerned with the establishment of facts calculated to enable public health administrators, who are subject to questions all the time about what to do, to be in a better position to exercise sounder judgment in establishing rational procedures in this whole field. I won't go into those particular program activities that are affected thereby, for the simple reason that time on this occasion is sufficient only to talk about research.

Now in the applied research effort in radiological health of the Public Health Service, and in which it is beginning to move in certain directions, I think for purposes of convenience that this program interest can be described in the following three separate phases. In the first, we are interested in the measurement of dosages, both external and internal. This is a primary step, of course, in any epidemiological procedure, whether we are dealing with biological or physical agents.

Number two, and also in the classical tradition, is the interest in the manner in which biological organisms absorb both external and internal radiation, to which the technical term of this field, "biological uptake," is applied.

Number three, naturally, is the effect of that uptake. In this particular case we are interested in those effects expressed as certain somatic as well as genetic conditions, developed both over the short-term and long-term.

Now in discussing these three phases of the effort very generally, an attempt will be made to indicate

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what the Public Health Service is now doing or would like to do in the public health aspects of this field; how this particular research effort relates to civil defense; and the gradual development of a trained corps of fallout monitors, as the latter have come to be called.

The Public Health Service has now developed a corps of trained and experienced monitors which gives us a nucleus about which a fairly rapid expansion of the work can be effected. This also lends itself to a broader participation by the inclusion of other interested groups.

In addition, an intensive effort is under way by means of special techniques, about which I hope we can hear more later, to monitor foods and waters, utilizing such means as measurement of decay of fission products, the determination of monitoring of alpha contamination, and the evaluation of suitable methods to remove radioactivity from water supplies.

In another phase, where the concern is with short and long-term effects, it is hoped to get under way, with financial support provided by the Atomic Energy Commission, a study aimed to determine the body burden accumulated as the result of ingestion of radioactive material in the hope of pursuing this to a point where the contribution of internal emitters to the total radiation picture can finally be determined.

In the area of special effects, the Public Health Service, fortunately, through its arrangement to help the Atomic Bomb Casualty Commission secure medical officers, is improving its position to learn more about results of radiation effects in populations subject to wartime bombing.

In addition, it has begun to initiate a study with the National Office of Vital Statistics to determine the effects of x-radiation of pregnant women in terms of their offspring. This is an item of some practical significance for exposed populations, including those who are exposed in the course of any enemy-fired thermonuclear attack.

Now to take up more specifically the matter of the relevance of this work to civil defense. First, I think it should be emphasized that no matter the source of radiation, the same type will have the same type of biological effect. Therefore, it seems to those of us engaged in pursuing investigations involving low levels of radiation during peace-time can rather confidently expect that findings as are developed will prove of value in estimating certain effects during the time of civil defense disaster.

Through epidemiological studies, for example, in which we, AEC, and other Federal and State agencies have a great interest, it should be possible to add considerably to techniques of field investigations, which can then be applied advantageously to any of the effects of exposure under civil defense

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operations.

Finally, to consider future areas of radiological health research, if we are to assist in both the peacetime effort as well as any war effort, there is need for much more extensive and intensive work in the field of radiation research. Some of the needs to emphasize in this future should be: (1) The development of more adequate instrumentation which is both economical and of sufficient accuracy in its performance to be dependable during the course of disaster operations.

(2) The need for intensified efforts to find ways for removing fallout from water supplies and other media, or otherwise making the same potable.

(3) A more precise understanding of the effect of radiation upon the public health picture as it would occur during a thermonuclear disaster or the determination of the contribution of internal emitters to the total radiation hazard. This is an area in which the information is still scanty and unclear despite the obvious importance.

(4) There is a great need for the adequate training of persons in the various aspects of radiation monitoring, especially fallout. This is an area in which we are notably deficient in view of the comparatively small cadre of well-trained people.

(5) We see the necessity to develop good triage methods in the evaluation of combined injuries on which some good work has been done, but in which much more is needed in order to gain a practical understanding.

(6) The development of adequate monitoring programs, since the present effort, owing to budgetary and other limitations, is one grossly deficient in terms of managing the radiation problem, if one thinks in terms of this civil defense disaster.

Now in the event, let us say, of a thermonuclear attack, we can institute certain procedures founded on the considerable amount of information in relating to external radiation of high levels. Therefore, this puts us into position to make certain statistical predictions in these terms, based on the nature of the attack and population exposed. It is believed, however, that in the months following any nuclear attack, the major fallout hazard could well be one posed by internal emitters rather than just external radiation. Now owing to the conditions under which we have had to do monitoring to date, we have been able to obtain comparatively little information, although there is some. I believe this to be extremely significant because the population that survives is the one in which we must depend to mobilize the remaining resources of the United States for effective countermeasures against the enemy. Consequently we need to do work on these problems while there

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is still the opportunity to do so.

Due to the unsettled international situation, it is natural that in the haste to develop weapons, the latter will get priority. Thus while fundamental problems concerning weapons use are rather rapidly solved due to the concentration of resources in their support, the same is not exactly the case in preparing for proper defense against their effects, radiological or otherwise. Yet, this seems to us to be of equal importance. In point of fact, it requires even a vaster administrative and scientific organization, if results comparable to weapons development achievements are to be realized.

With respect to radiological health, all activities in that field, civil defense as well as others, are intimately related. This indicates, therefore, that the need for the closest collaboration of all agencies represented here today is urgent, if this particular program is to be managed successfully.

C. Gordon Zubrod, Clinical Director, National Cancer Institute, NIH

My responsibility is to tell you about the radiation research that is going on at the National Institutes of Health (NIH), the research arm of the U.S. Public Health Service. This is rather a large task as in looking over the various project headings listed, the NIH program encompasses most of the headings in the outline. I think the use of radioactive isotopes at NIH in the study of disease and the study of normal physiology is particularly extensive.

NIH does not have any extensive coordinated program with respect to the radiation casualty situation, but a number of individual scientists in several of the Institutes are engaged in work related to radiation injury. I have chosen to talk a little about the program at the National Cancer Institute. Here, our chief interest, of course, is the study of radiation in relation to causation of cancer and its usefulness in the treatment of cancer. I have selected a few illustrative examples, however, of pieces of research which have some bearing upon the subject of this Conference.

With regard to the problem of the modification of radiation injury, we turn first to the use of bone marrow. The late Dr. Egon Lorenz, chief of our radiation branch, was one of the first to undertake and show that bone marrow could be used to protect against radiation damage in animals. The interest that the National Cancer Institute has continued since Dr. Lorenz's death now centers around the problem of the homograft reaction. I think our present feeling about the usefulness of bone marrow in the treatment of radiation injury in man is shown now in the first slide.

The small mouse on the right is moribund from the homograft

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reaction. Both of these mice have received 800 r total body radiation. The one on your left has received isologous marrow. The one on the right has received co-isologous marrow, that is, the donor was almost identical with the mouse that gave the isologous marrow, differing from it, however, only in a single gene.

It is our feeling that if this severe fatal homograft reaction is going to arise because of single gene difference of the donor, that the problem of administering the bone marrow as a practical agent to man is one on which we are going to have considerably more new research findings before this can be accomplished. Thus we have not engaged in the use of bone marrow in man, but have preferred to do work on basic level, trying in some way to obviate this homograft reaction.

Our present efforts in this area, are to study the use of fetal tissues, as well as to alter host reactivity by means of drugs and by means of other metabolic alterations in the host - particularly in the area of antibody synthesis.

We have also been interested in the problem of drugs which can be used prophylactically against radiation injury.

Dr. Kelly at NCI has been doing work with AET. These are the chemical groups that have been developed at Oak Ridge, and we have worked somewhat with Dr. Doherty at Oak Ridge who has supplied us with compounds for study.

This next slide shows some confirmation of Dr. Doherty's results in terms of protection by AET against total body radiation in mice. In other words, we conclude that the AET given in large doses to a mouse, approximately cuts in half the effect of tatal body radiation.

This is true not only of total body radiation but it protects against radiomunetic drugs. This next experiment shows some of the protective effects against nitrogen mustard.

Under the influence of increasing doses of the AET, one sees that the toxicity to the host of this dose of nitrogen mustard is at least cut in half.

We have taken these drugs over in an attempt to find out their toxicity to man. However, shortly after starting it became apparent that while this was a wonderful drug to use in the mouse, it is reasonably toxic to man, and at doses at 20 mg. per kilo, we have some symptomatic toxicity and it seemed unwise to proceed further. So we never were able to get up into the range of 100 to 200 mg. per kilo, where one might think of AET as a protective agent against radiation.

We are particularly interested in this, because of the fact that while the AET protects the host against the damaging effects of radiation,

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and the damaging effects of nitrogen mustard, it does not protect the tumor. This occurs because of the difference in the pharmacological disposition of the compound. More compound gets into the normal tissues of the host than gets into the tumor, so that one can achieve considerable therapeutic benefit from the radiation or from nitrogen mustard in the mouse when that mouse is protected with AET. We would like very much to be able to do this in patients with cancer; I don't think AET is the drug which can do it. We're continuing our work with a series of similar compounds and hope that we may be able to find others which are less toxic to man.

Now the other topic I wanted to review for you was the kind of patients we see at the National Cancer Institute which are suitable for the study of some of the problems that arise concerning radiation injury. We do not see many patients, of course, who have extensive radiation exposure, but we do see large numbers of patients with the problem of bone marrow failure. We have a big program in acute leukemia and the other diseases related to it. These patients, partly because of their disease and partly because of the drugs that are used to treat the disease, are very frequently in the state of partial and sometimes complete bone marrow failure. We have a very extensive program in NCI in the study of bone marrow failure. We are faced every day, and have a number of research projects going, in the field of infections which occur in bone marrow failure. As one small example, we have seen at least 25 patients in the last two years with pseudomonas septicemia, a situation fairly common in the animal suffering from total body radiation. This is presumably a septicemia which would be common in patients who have had severe total body radiation.

We are interested in the hemorrhagic problem that occurs with bone marrow failure and a number of programs are going with respect to its mechanism and management.

We also see an occasional patient who has received in the remote past a large dose of some internal emitters, such as radium dial painters, occasionally we get a patient who has had a large dose of thortrast, and we study them largely for their relationship to the production of cancer.

We also more recently have been deliberately giving to patients a large dose of Sulfa 35, because of its localization in certain tumors containing cartilage. I want to show you a little part of the work with regard to it.

May I have the next slide, please. This slide shows two rats, littermates, this one in the foreground has received a large dose of S-35 early in life; the other is a normal control. Because of the localization of the S-35 in the cartilage, there are effects on growing bones which results in diminished skeletal growth.

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Next slide, please. In addition to its localization in the cartilage, S-35 is localized in chrondrosarcoma. In this logarithmic scale is shown that the traces of S-35 in this patient was concentrated almost ten-fold in the chondro-sarcoma as compared to its concentration in the skin and in many other tissues. Because of this favorable concentration of the S-35, a large dose of S-35 was given this patient.

Next slide, please. He received one curie of S-35 in three divided doses, and this shows the blood levels of the S-35 at 3 doses.

Next slide. This had a very considerable effect upon the peripheral blood elements, as shown on the dropping of all of the elements almost down to zero. By way of treatment, he was given nothing but a little fresh blood at the very lowest point, because he did start to have some slight bleeding. He was not given antibiotics and suddenly and dramatically repaired his peripheral blood counts. The S-35 did localize in the tumor and there was considerable beneficial effects in terms of tumor regression.

We are continuing such studies with chondro-sarcoma and it does give us some opportunity to study in addition to the effect of the tumor, the problem of total body irradiation.

Finally, there's the problem of accidental exposure, and in conjunction with some of Dr. Taylor's specimens this morning, I wish to report on a piece of work of Van Scott of NCI. That has to do with the effects of radiation on the hair roots and whether or not this could be developed into some measure of how much radiation the patient has received. We believe that this biological effect is dose-dependent and we are pursuing the study further.

Next slide, please. This shows the normal hair root with a scalp, with a plus-40 magnification. When 300 r radiation has been applied to the scalp, one sees this effect upon the hair root which is very easily discovered under a microscope (next slide).

If one pulls a hundred hairs from the scalp and examines them, one can chart the percentage of dysplastic hairs against time. One can see that in a range of 50 to 225 r there is dose dependency.

Our work is continuing in terms of trying to find earlier effects histologically and with microtechniques on the chemistry of the hair root, changes that might be localized within the first day following radiation, in which case it might be of more practical use as a dose dependent biological effect of radiation.

Finally, we do occasionally see a patient with an accidental exposure to radiation. This slide shows the skin of the abdomen of a scientist who was accidentally exposed to about 3500 r electron burn from a Van der Graff. For the first week there were very few changes except a slight reddening of the skin. This

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shows a picture at 35 days. We watched him for four months during which time there were continuous changes. At that time we were forced to skin graft because of the loss of hemoglobin and albumin from this large surface. Even at that, however, there was continuous undermining at the edges of the graft and continuous breakdown out at the edges for another several months. But he finally was successfully grafted and now 2-1/2 years after the surgical therapy, he was doing very well.

As for the future, about our research at Cancer Institute, I think we are concentrating on four general areas. One is the circumvention of the homograft reaction in animal experimentation, using the procedures I have mentioned. Secondly, is to continue attempts to find some new drug which can protect man against the effects of radiation. Thirdly, is the more precise use of this hair-root technique in quantitating exposure to radiation. And finally, and perhaps most important, would be a study of the kinds of patients I've outlined above, for intensive examination of the effects of total body radiation. This will specifically include studies of metabolic changes, in which very little has been done; a study of the bone marrow failure problem; of thrombocytopenic bleeding, of the altered host resistance to bacterial infection, and of poor immulogic response. We would certainly agree with Dr. Morgan's statement yesterday that all those who are accidentally exposed to irradiation in this Country from whatever source, should be intensively studied; not only as he suggested for the problem of dosimetry, but also for the parameters just mentioned. We would be happy to collaborate with any of the groups working on the problem in this Country in terms of specific examination of this problem of bone marrow failure and to admit selected patients to NIH for intensive study and treatment.

Dr. Parrino: Thank you, Dr. Zubrod; is there any discussion of this very interesting work going on at NIH? Dr. Cole?

You mentioned the problem of the alteration of protein synthesis and I didn't quite get the point you made there.

Dr. Zubrod: In the same sense that a patient with agammaglobulinemia can accept a graft of donor skin, I think there are many situations in cancer patients, particularly chronic lymphocytic leukemia, myelonia, and so on, where it might be possible because of the failure of production of gamma globulin to undertake similar studies. We are studying similar problems with regard to gamma globulin synthesis under a variety of circumstances and the effect of diminished synthesis on accepting and tolerating homografts.

Dr. Conrad Straub, Chief.

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Radiological Health Unit, Robert A. Taft Sanitary Engineering Center, Cincinnati, Ohio

Dr. Parrino, Ladies and Gentlemen:

The work at Cincinnati is directly concerned with the determination of the levels of radiation in the environment. Because of our tie-in with the other programs at the Center, namely air, water, milk and food, we are looking at the actual levels of activity in these particular media. Where initially we were primarily concerned with measuring gross activity, we soon found that in terms of trying to evaluate the potential hazards, or even making a comparison of the levels of activity in the various media, we had to find what specific radionuclides were present. This has been the direction of a good bit of our research effort.

We have tried to develop procedures that were applicable to the wide variety of media in which we have an interest and concern. In this, actually, we combined the optimum features, let's say, of radiochemistry and of instrumentation, to the wide variety of media studied. Perhaps the medium about which you have heard most recently has been milk, which is felt to be representative of foods. Here, in addition to strontium-90 and total strontium, we have also measured the amounts of iodine, barium, and cesium. These were the radionuclides encountered in this particular medium.

To our surprise, or perhaps not so much to our surprise, we found out that iodine itself could be a very significant contributor, particularly when one encounters a source where there is constant release of this particular material into the environment.

This is not actually the case from weapons, but it could be the case from, let us say, the operation of a fuel reprocessing plant. This is a factor which is of considerable interest to us.

The milk studies have also indicated to us that there are areas in the Country in which higher levels are found than in other areas. We are now planning a more intensive study of these areas, to determine which of these particular environmental media are basically responsible for this higher level of activity in the milk supply in these regions as compared to other regions.

The purpose of all these studies is quite obvious in that we are trying to determine what the body intake of the radionuclides of particular interest to us is. It is hoped that this information will be helpful in evaluating potential hazards to the general population; also it will focus attention on the particular environmental medium which is basically responsible for the maximum contribution of the radionuclide in which we have an interest. Furthermore, it may also provide some basic information which would be useful to the National Committee

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on Radiation Protection, or the International Commission on Radiological Protection, on the actual levels of these materials in the invironment and perhaps something of their significance.

Dr. Robert L. Smith, Public Health Service

While we're continuing this thought of divisions in the one service, we have a couple of other people here, and Public Health Service recently organized a new division, of which all of you know - Dr. Robert L. Smith. Bob, would you like to tell the group something about your new division and what's going to be your new relationship to radiobiology?

Dr. Smith: Well, I would like to just straighten you out that there is not a new Division as yet. There is contemplated a broader delegation in the area of health from OCDM than there has been in the past to D/HEW-Public Health Service; and the Division to discharge those responsibilities, when it is established, will be established in the Bureau of State Services. I'm in the Bureau of State Services at the present time, doing some ground work for the establishment of that Division. The Division Director will be Dr. Carruth J. Wagner, whom some of you know. I haven't any more of a report than that.

Marlow Stangler, Physical Sciences Office, Research, OCDM

This is going to be rather off the cuff. I might start out by saying that civil defense requirements for instrumentation, and particularly operational dosimetry, are based on the philosophy that the instrument itself does not offer the protection but that the information provided by the instrument while being in the radiation field, can be used to protect yourself.

The information from the dosimeter reading can be used to either in turn prevent over-exposure or give a good idea of what the individual's exposure is. The dosimeters we now have are very good as far as accuracy, having an error of less than plus or minus 10% over their range. The variation due to energy response from 80 KEV up to about 2 MEV is within about 20%. The leakage character is very good, in the order of 1/2% of full scale per 24 hours.

For operational purposes we really come to the requirement of having a self-reading ionization chamber dosimeter. The scale ranges that we presently use are 0 - 20 roentgens and 0 - 100 roentgens. These cost us slightly under $5. The 0 - 100 roentgen one is being replaced with dosimeters of 0 - 200 roentgens range, mainly because of the better insulators, and production techniques that are available today, and the increased possibility that doses exceeding 100 r will be required in certain instances. Also, this is about the upper dose range at which widespread sickness is produced. If scheduled missions,

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and we would hope they would not, would have to exceed this dose for something that is very important, you may do the mission, and (1) not worry about recording the excess dose, (2) recharge your dosimeter, or (3) we do have some high range dosimeters - phosphate glass type non self-reading which in some instances could be used. Our operational dosimeters are charged with a charger which uses a D-cell flashlight-type battery and is transistorized, again costing us about $5 apiece.

Regarding the emergency permissible exposure levels that are set up, I don't think really rigid limits can be set up for everything, and that they will apply all the time. You have to use them as guidelines depending upon the hazard you are concerned about, whether it is sickness and mortality, or whether you are thinking in terms of genetic effects, or others. I think guidelines are needed for planning purposes, for exercises, emergencies, etc., and agree with Dr. Morgan that the best possible numbers or figures should be established now, for possible emergency use, even if only tentative.

As for our other instruments for monitoring purposes, we have the medium-range survey meter which would be the civil defense workhorse. It has 3 ranges: 0-.5 r/hr, 0-5 r/hr, and 0-50 r/hr full scale. It is gamma sensitive only. We do supplement this with a higher range instrument which has a 0-500 r/hr range on it, and it is beta-gamma discriminating. Our survey meters cost us about $20 each.

For food and water monitoring and personnel monitoring, decontamination, etc., our present instrument is a geiger counter with a range from 0-50 mr/hr. It is also beta-gamma discriminating. The available standard for water contamination measurement compares the beta activity in the lid of a can with that of the water being measured.

As for the training program, we have the radiological defense school located at Battle Creek. An Eastern training school in New York City was established last June. I know they have had one or two courses. There is going to be another one there the 2nd week in December. The plans are for two more schools located throughout the Country. The purpose is primarily to train monitor instructors, who in turn will go back and train other monitors how to operate and use this equipment. We also have a higher level course called the Radiological Defense Officers Course. Another course that is concerned with just general aspects of radiological defense is designed and taught to acquaint administrative-type people with the radiological problems. Equipment is available to State and local civil defense personnel for training purposes.

Another training program is the high school instrument program which I think that most of you have heard about. A kit with instruments

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is being distributed to at least 6000 high schools at the present time and this number will increase as we procure more instruments. Essentially a complete set of instruments, one of each, are included. We hope to promote science education, particularly nuclear physics aspects of it, and in turn get young people both interested in science and also possibly interested in radiological defense. They may even work up enough interest to interest their parents. We do not plan to make monitors out of high school students. Certainly the information they learn may be useful in protecting themselves and others, and in future generations, they would be a very well-trained nucleus with which to start.

We are also training and providing Federal agencies with equipment to develop their radiological defense capabilities. In addition, we have a beginning on a Federal network of monitoring reporting stations. Anything else I haven't covered?

Dr. Parrino: No, I think you hit the high points. Any questions?

Question: I would like to know how you service these instruments.

Mr. Stangler: This is a big problem. We are hoping to do this from the Federal level. I am not sure that this will be entirely possible. We do have eight instrument technicians located throughout the Country in our warehouses. We can repair all of the Federally-owned equipment. There is some question as to whether we can repair instruments that are either granted or loaned to States, as they have agreed to maintain them when they were delivered.

At present the maintenance is on a matching funds basis. OCDM will allow up to so many dollars per instrument per year for upkeep and repair. It is the responsibility of the person with the instrument or the State civil defense group to keep the instrument in operating condition. This amount also includes replacement of batteries.

Question: These instruments do not go back to the warehouse?

Mr. Stangler: Not the ones that are going into high schools. Under the distribution of radiological equipment and radioactive sources to States for training monitors, some will be returned. A large kit is designed for use with each course. A small number of instruments, a few of each kind, are to remain with the local groups that are trained. These are to be used in refresher training. The large kit is to be returned either to the State for additional use within the State or returned to OCDM.

Question: If a large number of survey meters are issued out to organized civil defense units for operational purposes, any idea of what the fraction of those instruments would be operational six months after they are issued?

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Mr. Stangler: We don't have too good data available on that. The instruments that are shipped around by our Radef School to the various courses presented throughout the Country are generally sent by railway express. Actually we find that we have less than 10% of these that are inoperable, even after the course is completed. I can't vouch for the accuracy of the calibration or that it is going to be as good as it should be, but these instruments do have a zero adjust and circuit check which allows us to at least check the operability of the battery complement and all working parts except the ion chamber and high meg-ohm resistors. Therefore, you can be fairly certain the instrument is in working condition. There is a factory setting on the calibration adjustment so that if this is not changed, the instrument would give you a very good idea of what the dose rate is.

It may not be absolutely accurate but would certainly be relatively correct.

If these instruments aren't shipped around too much, I think that they stand up very well. With time, we will have much better data on it.

Question: I think it would be worth a little effort to try to just pick out a couple of thousand instruments and see what percentage is surviving.

Mr. Stangler: As I was mentioning, the instruments used in the school get much more wear and tear than is normally expected. Of the instruments that are shipped only once, and they are in good condition when received, little trouble should be experienced with them except for occasional battery replacement. To verify this, we have 20 large 120 curies cesium sources to be distributed throughout the Country. In addition, we may have a smaller check source available for each county in the Country before too long. Trained personnel could then keep check on their own instruments.

There are some other instruments that we have or are developing. One is a fixed station remote indicating instrument operating off either AC or battery. It is designed to measure the external dose rate and to be read out inside a shelter.

The other is an aerial survey instrument for rapid ground survey from aircraft. In the interim, our CD v-710 medium range ion chamber survey meter can be used. We are working quite closely with the AEC and industry on instrument development. NBS is doing our instrument testing and some development work on a dosimeter charger. We will be glad to know of any new instrument developments. If there are any other questions, I will try and answer them.

Dr. K. Z. Morgan: I'm glad to know that you are developing this airborne equipment. It was pointed out in Great Britain that although they did find the light aircraft very useful, it was several days later that they attempted this. Also, in interpreting the data, they had difficulty because

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of lack of background surveys.

There are many situations where the Civil Air Patrol are extremely anxious to get into this; in fact, the only things they need are sources and survey equipment. They are well equipped - they have planes and other facilities that go along with it. And one man in an airplane properly equipped with two-way radio is worth more than several dozen in automobiles. At Oak Ridge we have plans that would get planes in the air within an hour after an accident.

Mr. Stangler: I've seen the flight plans they have. We have worked with the CAP and others in this connection. Fred Rehm had an aerial survey project out at Operation Plumbbob at the NTS in 1957. We performed some further testing this fall but found we do need a little bit more development on the aerial instrument, but the medium-range ion chamber, I think, can be used quite well for an interim, aerial survey instrument.

Dr. Parrino: We are running a little low on time. Suppose we take a break and then if the panel in the meantime will assemble, we will decide how the panel will function. We hope everybody can return, but if you go now, make sure that everyone has been registered. If your name is not down here and you haven't registered, leave your name.

Dr. Dunham: I have been asked to say a word about a little romp session that the Evaluation Panel just had here. We agreed that at this point the mass of material presented here in the last two days did not lend itself to definitive discussion. The suggestion was made that the transcript of this meeting be made available to the members of this Panel, to Dr. Taylor, who is a member of the panel, and to the Radiobiology Sub-group of the National Academy of Sciences Advisory Group on Civil Defense. When the next meeting of this Sub-group is held, I believe around the 20th of January, the Panel and the Sub-group can use the transcript of this meeting as a basis for discussion. They can then attempt to identify specific areas where considerably more emphasis needs to be placed in order to assist OCDM in fulfilling its mission.

Dr. Parrino: We will have quite a little job getting transcripts to the Panel. Then we will decide if we should have a joint meeting with Dr. Taylor's committee.

I emphasize again that if there is any material that you would like to submit showing any work going on in your respective agencies, we certainly would like to have it. We hope to put out this transcript as soon as possible and especially the many references, so that people will know where to find more

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detailed information on the work that you are doing. We certainly appreciate not only that all of you came but that you have stuck to the bitter end.

Today, this was somewhat of an innovation, having so many people present statements at 15-minute intervals.

I think in general this Conference has worked the way that we had planned - this was a general summary of what people are doing, with no great detail on any one particular project.

Question: Will these transcripts be made available?

Dr. Parrino: I think first we will get the transcript to the Panel, which will evaluate it and make some recommendations. Then we will get the final proceedings to everybody. If you think of any other suggestions for future meetings, make sure you communicate with me or with the Panel. Again, we thank everybody for being with us and hope you got something out of it.

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