also negotiating an agreement with the Commission for Technical Co-operation in Africa.

In addition the Agency has granted consultative status to nineteen non-governmental organizations, and is considering applications from a number of others. The nineteen are as follows:

European Atomic Forum
European Confederation of Agriculture
International Air Transport Association
International Cargo Handling Co-ordination Association
International Chamber of Commerce
International Commission on Radiological Protection
International Committee on Radiological Units and Measurements
International Confederation of Free Trade Unions
International Co-operative Alliance
International Council of Scientific Unions
International Federation of Christian Trade Unions
International Federation of Documentation
International Federation of Industrial Producers of Electricity for Own Consumption
International Organization for Standardization
International Union of Inland Navigation
International Union of Producers and Distributors of Electrical Energy
Japan Industrial Forum
World Federation of United Nations Associations
World Power Conference

NEUTRON EFFECTS ON LIVING THINGS

Scientific interest in neutrons and protons - two fundamental particles of the atomic nucleus - has grown in recent years as the technology of peaceful uses of atomic energy has progressed. Such interest also has increased because both protons and neutrons are encountered in outer space. However, only recently has a thorough study of the biological effects of neutrons and protons become possible, as a result of progress in making physical measurements of the radiation dose absorbed in biological systems (of plants and animals, for example). Reports of work in that field were presented in December 1962, when IAEA sponsored at Harwell Laboratory in the United Kingdom the first international symposium on detection dosimetry (measurement) and standardization of neutron radiation sources.

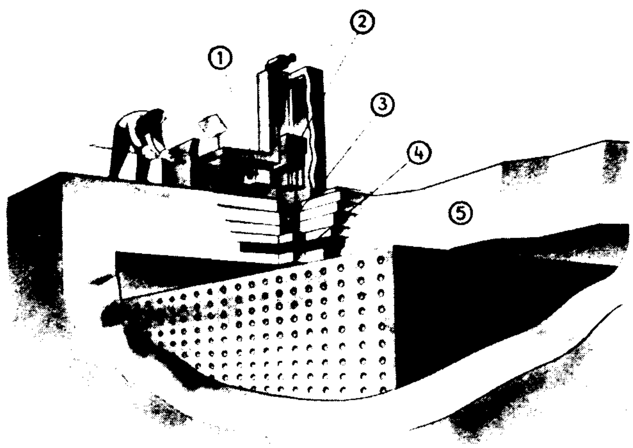
The Harwell meeting was followed in October 1963 at Brookhaven National Laboratory, Long Island, New York, by the first scientific meeting sponsored by IAEA in the U.S. Entitled "Biological Effects of Neutron Irradiations", the Symposium continued the review of problems of measuring radiation absorption in living things and provided in addition for several reports dealing with the effects of radiation on living organisms - plant, animal and human - and with delayed consequences of exposure to radiation, such as: change in life span; tumour incidence; and fertility. Eighteen countries were represented.

Although much has been learned about X-ray and gamma-ray effects, comparatively little is known about the biological effects of neutrons, and therefore many of the Symposium papers reviewed the various aspects of neutron experimentation. Similarly, since there is increasing interest in the biological effects of protons, papers were given on that related subject.

Measurement Problems

The principal topic discussed at the Symposium was methodology for comparing absorption in tissue of different types of radiation. There seemed to be general agreement among the participants that the approach most commonly used in recent years, namely Relative Biological Effectiveness (RBE), can hardly be considered adequate by itself as a method. The term RBE has been defined as the ratio of a "standard" dose of X-radiation to the dose of test radiation required to produce an equivalent biological effect. The standard dose is the amount of energy absorbed by a given volume of plant or animal cells from the incoming X-rays. The test dose is the amount of energy absorbed from incoming neutrons. For example, if a test dose of one rad* of neutrons produces the same biological effect on the cells in question as a standard dose of three rads of X-rays, the RBE of the neutrons is three.

* *rad: unit of the amount of energy absorbed by material exposed to radiation.*



Column used for biology experiments on top of nuclear reactor at Brookhaven. A container of plant seeds is pushed into an elevator with a long rod. It is then lowered to the bottom of the column, halfway through the five-foot concrete shield which surrounds the reactor. Some slow neutrons penetrate part way up the shield; a slab of bismuth filters out gamma rays. 1. Seed container; 2. elevator; 3. neutron exposure cavity; 4. bismuth slab; 5. shielding. (Photo. Brookhaven National Laboratory)

RBE values for neutron exposure were stated in many of the scientific papers presented at the Symposium. These values were also discussed at length in a panel on biophysical considerations in neutron experimentation. J. S. Krebs and R. W. Brauer, of the U. S. Naval Radiological Defense Laboratory, San Francisco, described recovery by cells in mice of full reproductive function after exposure to neutrons at short-spaced intervals; the investigators noted that recovery after X-ray exposure is incomplete. They reported that destroyed cells are replaced by division of the remaining cells when irradiations are spaced over long intervals of time. They conclude that knowledge of rate of recovery from large doses of neutron irradiation is more difficult to come by than for any other form of radiation, yet seems essential if differences between effects caused by neutrons and X-rays are to be interpreted significantly. They conclude:

> "The discoveries in the past few years about the kinetics of accumulation of radiation injury by cultured mammalian cells have made possible a more unified view of the process of injury accumulation in whole mammals, with the reconciling of many once divergent experimental viewpoints. With this new unity of view there is now the prospect of increasingly better understanding of the process of accumulation and repair of radiation injury in mammals."

Interplay of Particles

Another methodological concept discussed at length was linear energy transfer (LET). This term refers to the pattern of distribution of energy as it is absorbed in a given material, such as animal cells. The term originates from pioneer work by physicists who study the lines or tracks left by nuclear particles as they penetrate photographic emulsions. When the film is developed, these tracks identify incoming particles which interact with the atoms of which the emulsion is composed. Nuclear particles which penetrate the cell itself produce secondary particles, which actually travel not just in a linear pattern, but three-dimensionally, penetrating various parts of the cell. The interplay of incoming nuclear particles (neutrons or protons) with particles which make up the cell prompts measurements by biologists assisted by physicists. Resultant data are intended to help determine how radiation affects the life process in living cells. Similarly, data are collected on related experiments on tissue or organs or, to a more limited extent, on biological systems such as the nervous system, the endocrine system, etc.

LET was cricitized as being a "unidimensional" concept. Dr. H. H. Rossi, Department of Radiology, Columbia University, for example, has argued that investigators can indeed identify a cell track left by an incoming nuclear particle, but it remains difficult to interpret the inconsistencies in data resulting, in part at least, from numerous variations found in different cells of the same basic type. Actually, because of difficulties in "mapping" the trails left in the complex transfer of energy, measurements generally are made in gases stored in metal spheres of different sizes. The gas-filled spheres serve as scale models of corresponding volumes of tissue. The density of a gas is generally of the order of some 1/1000th that of animal and human tissue. Thus most LET data are based on a multiplication of measurements actually made in gases, rather than in living human or animal cells, in which technological control is difficult. Some of the participants pointed out that there is only limited scientific value in measurements of the amount of radiation necessary to kill a single living cell. Emphasis was placed on the importance of mounting experiments in which new data can be collected on the effects of radiation on the various life processes which take place in the cell. J. C. Moskalev, of the Institute of Biophysics of the Academy of Medical Science in Moscow, advocated even more extensive investigation of organs and biological systems. He expressed the view that the functioning of cells together in the performance of a biological function is more significant to man's understanding of radiation effects than is the functioning of a cell as a single entity.

Measuring LET

The use of "phantoms" or material containing chemical elements identical with those found in human beings, mice, dogs and guinea pigs was described by S. Snyder of Oak Ridge as part of a study of LET distribution of neutron dose. When the cylindrical "phantoms" are exposed to neutrons, the latter displace nuclei of atoms in the cylinder, or interact with these nuclei to produce secondary neutrons and protons. The LET of these recoil and secondary particles was analysed by means of a computer for neutrons of differing energies, and types of "phantoms" compared.

V.I. Ivanov of the USSR Institute of Engineers and Physical Science, Moscow, presented evidence of the utility of a new universal radiation dose unit in standardizing measurements taken in various countries, and reported on work by investigators at the Joint Institute of Nuclear Research at Dubna in using a synchrotron to produce a proton beam suitable for irradiation of experimental animals and "phantoms".

A "phantom" representing the human body at Brookhaven Laboratory. It is used to determine the rate at which neutrons travel in various parts of the body. The head, placed near the port of a medical research reactor receives the neutrons. (Phot. United Nations)

A group of scientists from the Biophysics Branch of the Kirtland (New Mexico) Base of the U.S. Air Force explained a series of experiments for measuring the neutron energy absorbed by the tissue of sheep, namely, the tissue volume between the hide and the abdominal cavity. The investigators inserted in the cavity a small sphere containing strips of metal, some of the atoms of which were made radioactive by incoming neutron beams to which the animals were exposed. Measurement of the radioactivity of the metal permitted determination of the energies of neutrons which had penetrated to that point, energies which could then be compared with the energies of neutrons which had entered the hide at the outset of the experiment.

Laboratory Safety - and Outer Space

While most of the papers presented at the symposium dealt with experiments intended to shed light on the basic mechanisms by which neutrons and protons produce effects in living things, there was also occasional mention of the potential value of such work in connection with maintaining health and safety procedures in laboratories and other installations where these two fundamental nuclear particles are produced. For example, protons are accelerated by cyclotrons and other types of high energy particle accelerators in dozens of universities and research organizations in various parts of the world. Neutrons are used in experiments in connection with over 400 nuclear reactors now in operation. Also, safe management of neutrons in larger reactors used for electricity generation is a problem in a growing number of nuclear power plants.

Still another field of practical application of new knowledge of biological effects of neutrons and protons is in connection with man's conquest of outer space. As pointed out in a paper by J. F. Spalding et al. of the Los Alamos (New Mexico) laboratory of the University of California:

> "The unusual radiation environment that man may encounter during future space ventures from such sources as primary cosmic rays, solar flares*, natural radiation belts circling the earth, and nuclear propulsion systems designed for extended space flights is cause for concern and a need for a better understanding of radiation effects. This is particularly true with regard to dose rate effects of ionizing agents of different qualities."

These authors then went on to say that the RBE for fission neutrons (such as those which an astronaut might encounter) did not vary with dose rate, but ranged from 3.5 to 4.5 in mice. In other words, the extent of injury was similar, whether the same radiation dose was administered over relatively short or long periods of time. These experiments imply that the total amount of neutron exposure of an astronaut is all-important, a corroboration of evidence from other forms of radiation down through the years.

Dr. J. Schaefer of the U.S. Naval School of Aviation, Pensacola, Florida, described biological effects of laboratory-produced protons of energies comparable to those generated in solar flares. Such high energy nuclear particles would be encountered by astronauts who pioneer cosmic areas beyond the Van Allen belts, areas which have not yet been penetrated by man. Dr. Schaefer pointed out that, since biological experimentation with protons in space is costly and difficult, the question arises as to how to develop instrumentation for measuring the absorption of incoming protons in tissue. He also dealt with questions of the additional biological effects of protons and neutrons dislodged in the tissue itself. These "by-products" or secondary particles he calls "enders" - that is, particles coming to rest in a specific volume

* *Radiation generated in cosmis eruptions on the sun.*

of tissue. He suggested that the density patterns of "enders" permit inferences on the variety of energies present in a beam of protons used to bombard tissue. He based his preliminary measurements of such effects on earlier work by cosmic ray physicists in analysing the scattering of protons in photographic emulsions exposed to high energy particles in the upper atmosphere.

A study of the extent to which protons of energies ranging as high as 730 MeV damage the tissues of the eyes of monkeys was described by S. C. Rexford-Welch of the Royal Air Force. He described work undertaken at the U.S. Air Force School of Aerospace Medicine, Brooks Air Force Base, San Antonio, Texas. He reported that cataract formation was common at that proton energy level, but not at lower energies. He noted that the onset of cataracts and other biological damage at specific energies may make it possible to infer from clinical observations the energy of radiations to which an organism has been exposed.

J. I. Moskalev of the Institute of Biophysics, Academy of Medical Sciences, Moscow, reported on experiments conducted with two colleagues, I.K. Petrovich and V.N. Streltsova. Results were given on comparative experiments on the effects of 500 MeV protons on 490 white rats as well as similar experiments with neutrons on an even larger colony. One of the findings is that the average life expectancy of rats irradiated with fast neutrons does not depend on sex. It was also noted that the over-all incidence of tumours in females is two to three times higher than in males. The report states:

> "The minimum tumour dose for the mammary glands with neutron irradiation is apparently rather less than 42.5 rad. The maximum incidence of tumours of the pituitary is found after irradiation with a dose of 42.5 rad.
>
> "With proton irradiation, the minimum tumour dose for haemopoietic (blood forming) tissue and the thyroid gland is in the neighbourhood of 250 rad, for the testicles 300 rad, for the prostate, the pancreas and the subcutaneous tissue 100 rad. After irradiation with fast neutrons the incidence of tumours of the testicles, the large intestine, the kidneys and the liver is increased at doses between 42.5 and 85 rad. The same is true for tumours of the skin and subcutaneous tissue at a dose of 85 rad. With fast neutron irradiation tumours appeared at approximately three to five times lower radiation doses than with proton irradiation."

C. A. Tobias reported for himself and several colleagues that the Lawrence Radiation Laboratory of the University of California at Berkeley conducted experiments in which white mice were exposed to 730 MeV protons as compared with exposures in other experiments involving X-rays. Part of the work, reported by Dr. C. A. Sondhaus et al., will consist of measuring the distribution of radiation dose from protons from a 184 inch cyclotron beam, scattered and degraded in energy to simulate solar flare radiation.

Mathematical techniques were used to express the scattering of radiation in "phantoms" or chemical substances containing the same chemical elements as make up the human body. Data from the computations were analysed with the assistance of a computer.

Dr. Tobias also summarized studies made by Dr. J. K. Ashikawa et al. of the injury suffered by mice exposed to high energy protons. These investigators noted that previous work showed that neutrons inflict more severe damage on the intestines and cause earlier death than do X-rays. The California group considers that such differences in biological effect may be ascribed to a difference in distribution of radiation dosage in tissue, X-ray exposures inflicting more severe damage to bone marrow.

Pathology of Neutrons

The pathology of injury caused by neutrons or protons was discussed and such injury compared with that inflicted by X-rays. Capt. M. A. Quaife of the Kirtland Base described clinical findings in sheep exposed to either neutrons or X-rays. Sheep were chosen because their tissue volume approximates that of man. Neutron exposures caused earlier death from damage to the gastrointestinal tract than did X-rays, but in similar experiments with dogs it was found that this species exhibited more disruption of iron metabolism in the blood, due rather to exposure to X-rays than to neutrons.

Dr. E. J. Ainsworth et al., of the Naval Laboratory in San Francisco, used neutrons from a research reactor to irradiate mice, rats and dogs. After comparing such exposures with comparable effects from X- or gamma-rays, the investigators determined that neutron-irradiated animals recovered more rapidly during the first five days following exposure than did animals exposed to X- or gamma-rays. They noted that this finding is at variance with earlier observations by other investigators who suggested a slower recovery in neutron-irradiated than in gamma-irradiated mice. They explained as follows the need for the work to shed light on this contradiction:

> "It is clear, therefore, that no unanimity of opinion exists in terms of relative recovery patterns of neutron-, X- or gamma-irradiated mice. Furthermore, our data at 9 and 14 days after a neutron-conditioning dose indicate significantly more injury than was detected at five days, the pattern being that of an apparent increase in injury at 9 days which is followed by further recovery by 14 days.
>
> "Such bimodality is unprecedented, at least at the time intervals involved here, and is particularly perplexing. We plan to explore these

recovery patterns in greater depth by the addition of intermediate recovery points, and by seeking some functional basis for the bimodality observed with the neutron-irradiated animals. The fundamental question is what type of damage, what form of recovery or, more simply, what is being measured."

Dr. H. J. Curtis, Chairman of the Brookhaven Biology Department, and two of his colleagues reviewed data from various laboratories on the differences of the effects of neutron- and gamma-rays on the shortening of the life span of mice. They expressed the view that accumulated data indicate that, in terms of chronic irradiation, very small doses of neutrons are proportionately just as effective as large doses, whereas for gamma-rays, smaller doses are proportionately only about one-fourth as effective as large doses. They also stated the view, based on a study of chromosome damage in irradiated liver cells undergoing the process of regeneration, that, for relatively large radiation doses, neutrons produce about twice the chromosome damage as do gamma-rays.

Dr. L. J. Cole of the Naval Laboratory in San Francisco reported on mouse experiments which he conducted with Dr. P. C. Nowell of the University of Pennsylvania Medical School. They concluded that neutrons produce greater damage at the cellular level than do X-rays; also that the production of tumours by neutron irradiation may decrease as the damage increases. Their explanation of the latter finding is that such doses presumably kill off or permanently sterilize large fractions of the cell population of a given tissue. They note that this "therapeutic effect" of high doses of radiation with regard to leukaemia incidence and lung tumours had previously been observed by other investigators.

Dr. D. K. Bewley of the Medical Research Council cyclotron unit of Hammersmith Hospital reported on work which he carried out in collaboration with Dr. S. Hornsey, a Hammersmith radiopathologist. The data confirmed the sensitivity of the intestines to neutrons. As a result, they called attention to "irrecoverable damage" to the intestines at given neutron energy levels, and issued a word of caution concerning the use of neutron radiotherapy to any area of the body near the intestines.