

# nuclear techniques in transplant surgery

Progress towards a clearer understanding of many problems in transplant surgery was reported at an Agency meeting in Budapest during June.

Radiation for sterilizing purposes can play

an important part in this branch of medicine.

The experts selected by the Agency from nine countries, as well as one from the World Health Organization, recommended a programme of research into the possibilities of preserving tissues and organs in a living state.

Radiosterilization of medical equipment such as syringes, cat-gut and oxygenators has become a routine procedure in many medical institutes throughout the world. The use of radiation in sterilizing and preserving live tissue for human transplant operations is relatively new, but it appears a logical development of research already carried out.

Two years ago the IAEA and the Hungarian Government joined in organizing a symposium in Budapest on the sterilization of medical supplies and equipment by radiation exposure. It was therefore an appropriate centre for a panel meeting to discuss "The Use of Ionizing Radiation for Sterilization and Preservation of Biological Tissues". The twenty-one participants, as well as Mr. K. Ostrowski representing the World Health Organization (WHO), who attended concurred in recommending that further research be encouraged.

## Major Problems of Transplant Surgery

Until fairly recently human transplant surgery faced two major obstacles. One was the tendency of the recipient patient to reject the transplanted tissue unless the donor was a blood relative. The second was the absence of reliable methods of sterilization and their negative effect on the cell function of the transplanted tissue. Areas in which progress has been made have been particularly in the transplanting of human bones, cartilage, heart valves, nervesheaths and tendons.

The panel meeting was opened by Professor Ilia Zedginidze, Director of the IAEA Division of Life Science. He was followed by the Scientific Secretaries, Dr. Ferenc Antoni and Professor Viktor Agranenko of the Agency's Radiation Biology Section, who presented information and data showing ways in which nuclear techniques can contribute to tissue transplantation and implantation. They mentioned specifically the influencing of the immune or rejection response, the radiosterilizing and preserving of tissue grafts, and the use of the isotope tracer technique post-operatively to study interaction between the tissue grafts and the recipient organism.

Dr. K. Little of the Wantage Research Laboratory in the United Kingdom defined the present stage of development. She said that homografts and heterografts (transplant tissues from humans or animals) used in surgery are of two main types. In the transplantation of skin and organs such as the kidney and heart a basic requirement is that cells shall remain alive and functioning. The other type of graft consists of dead tissue, so that cell survival presents no problems. It is in the second type of transplant that the aid of ionizing radiation has so far proved particularly successful.

However, it was predicted that even in the first type of surgery - that of living organ transplants - the future holds many possibilities. Dr. Christian Barnard (South-Africa), who performed the world's first successful human heart transplant operation, suggested in unofficial talks to newspapermen that because ionizing radiation alters the antigen character of the transplanted organ, making it less liable to rejection, animals may in the future be bred specifically as donors for organ transplants. The animals might be irradiated over a period of time before removal of the organ to be transplanted, thus beneficially influencing the antigen character of the organ making it less liable to rejection after an operation while it is functioning. Such a process would not inactivate cell function completely, as occurs in radiation of transplant organs from cadavers, though it would presumably still inhibit the antigen character. If this theory should prove feasible, the problem of preservation of cell function - at present damaged by irradiation sterilization - might be solved.

Concerning the second type of transplant, that of tissue which need not be alive and functioning because it acts rather as a sheath or bridge. Dr. J. B. Campbell, Research Professor of Neurological Surgery and Director of the Milbank Research Laboratories of the New York University School of Medicine, told of the way in which he and his colleagues have developed methods of transplanting irradiated dead tissue into a living human being. Dr. Campbell and his colleagues have used irradiated and frozen bone for skull transplants since 1954.

#### Preparing skull bone for Storage

Before a bone segment is enclosed in the moisture-proof, air-tight plastic envelope in which it is to be stored, a number of holes 4 mm in diameter are drilled through the surface at two centimetre intervals. These holes are used later for the implantation of chips of non-irradiated and living bone tissue, often taken from the thigh bone of the recipient shortly before the operation.

This process is known as "seeding". The living bone fragments are able to accept nourishment and continue functioning and, in time, to permeate the larger inert graft tissue with living cells.

As early as 1954 irradiated frozen and stored strips of split rib and hip bone were used for filling skull apertures, interspersed with fresh implants from the patient's own thigh. This technique was eminently satisfactory, Dr. Campbell said, in transplanting bone where the patient's defective cranial area was relatively flat.

#### Living Evidence

A recent development has been that larger pieces of calvarium or cranial bone from the curved surfaces have been used with the seeding

method. In such operations the irradiated bone segment, being hardened by irradiation, must be fitted into the aperture. Dr. Campbell stated that the irradiated bone piece must not be more than two millimetres thick or nutrition cannot permeate the living bone chips.

It is usually difficult for surgeons to know how successful transplant surgery has been as long as the patient is "feeling all right". However, Dr. Campbell reported that in one patient they were able to obtain proof of the efficacy of the method. In 1962, an emergency operation had been carried out for the removal of a brain clot. Three months later a skull bone transplant seeded with bone from the patient's own body was carried out to fill the gap made by the first operation. Later, the patient developed a disfiguring keloid (a non-malignant growth). The operation to remove the growth required the lifting of a skin flap 13 months after the original transplant and revealed the presence of living new bone.

### Effects on Cells

Dr. László Révész of the Karolinska Institute of Stockholm, in discussing the effects of radiation sterilization upon cell multiplication, stated: "The particular property of radiation-sterilized cells of continuing the performance of vital functions to a normal extent for a considerable period after treatment enables them to influence the growth of a graft". A series of model experiments investigating the biological mechanism underlying this influence indicated that irradiated tissues are capable of enhancing as well inhibiting the growth of a graft in a host organism depending upon a number of variable factors. "It is conceivable", Dr. Révész said, "that these effects can be profitably utilized for the increase of the radiocurability of neoplasms (malignancies and tumours) and the prolongation of normal graft survival".

Dr. H. Frischau of the University of Vienna Department of Medicine gave details of experiments conducted with the co-operation of the Agency's Seibersdorf Laboratory. He and his associates studied the effect of gamma ray exposure on blood plasma proteins with particular attention to its influence upon fibrinogen, a clotting agent, and upon the hepatitis virus. It was found that irradiation has little or no harmful effect upon fibrinogen if the dosage is given at  $-70^{\circ}\text{C}$  when the fibrinogen preparation is in a dry state. Inactivation or "killing" of the canine hepatitis virus, a more stubborn problem which required on occasion doses up to three times higher than for routine sterilizing, is particularly important as transfusions and plasma applications can infect the recipient.

Ebbe Ahrensburg Christensen of the Statens Serumsinstitut of Copenhagen presented results of an investigation on the varying resistance of microorganisms to sterilization by irradiation. He said that for the most resistant microorganisms the lethal dose is proportionately 10 000 times greater than for mammals. His findings led him to suggest that emphasis should be placed on bacteriological control before sterilization.

### Research and Training Needed

At the end of the five-day meeting the panel recommended that the Agency should promote further research and that research records be

kept on the methods of collecting and preparing graft tissue for sterilization; on the type of radiation source used, dose rate, packaging, temperature, etc; on the actual surgical use of the prepared tissue; and on the post-operative follow-up.

It was also recommended that close liaison between WHO and IAEA be maintained, that a manual be prepared and published on methods of radiosterilization of biomedical products and that regional training courses be organized to acquaint surgeons and specialists with techniques of sterilizing and preserving biological tissues for human transplants.

## **power reactors - a correction**

A note in the last issue of the Bulletin (Vol. 11 No. 3, page 26) stated that for reasons of economy the experimental fast breeder reactor at Dounreay, UK, which had been operating and producing 12.5 megawatts of electricity since 1959, had been closed down.

To quote the words of Mark Twain on seeing an account of his death, this report was much exaggerated. The facility affected was the Dounreay Materials Testing Reactor, a 22.5 MW tank type reactor, which had been in use since 1958. The original fast breeder reactor is still functioning, and close to it a prototype is under construction to produce 250 megawatts of electricity. It is due to start operating next year.