Bone Marrow Transplantation Conference

(Conference Held in Atlantic City, N. J. on April 13, 1959; Alexander Hollaender and C. C. Congdon, Co-Chairmen)

Bone marrow transplantation in man.—Georges Mathé (Paris) opened the discussion by reviewing the Yugoslavian reactor accident and discussing the clinical management of the exposed individuals. Adult homologous bone marrow or homologous fetal liver was used to treat five of the victims. One man died and the others survived with evidence of temporary transplantation of red blood cell-forming elements. In all the cases treated with bone marrow there was a delay of three to four weeks in giving the marrow. In the discussion that followed Mathé’s report it was brought out by Ferree and Mathé that they thought delay in bone marrow transplantation after irradiation was warranted and possibly desirable if the patient could be controlled for a time by symptomatic treatment. A 10 day delay was mentioned. Andrews commented on the Yugoslavian cases and compared them to the Y-12 accident victims. He thought that all the Yugoslavian patients received more irradiation than the most heavily exposed victim in the Y-12 accident. No bone marrow was given to the Y-12 cases, and all have shown satisfactory recovery from the acute radiation syndrome.

Mathé also reported experimental studies on bone marrow transplantation in irradiated leukemic mice. His best results in mice were obtained when he irradiated the mice and treated them with homologous bone marrow at a time when they had the fewest tumor cells. He felt that a graft against tumor cell reaction was most effective when it had the fewest tumor cells to react against. He described two cases of acute leukemia in children treated during remission with radiation exposures of about 900 rads. Fresh homologous adult bone marrow was given some days after the irradiation. In both patients about 45 days after the bone marrow transplantation a secondary disease-like process developed with weight loss, gastrointestinal disturbances and fever. It cleared up with symptomatic treatment. In both patients serotyping technics showed a persistent level of donor-type erythrocytes indicating a “take” of the homologous marrow. The two patients were still in remission about 80 days after the radical therapy.

McGovern (Boston) described a case of acute leukemia in a child from whom he had taken bone marrow during a remission. Later, when drug therapy failed, 600 r of total-body irradiation was given and the preserved autologous marrow was reinfused. A remission of about 88 days was obtained before death from a transfusion complication. Two other cases mentioned by McGovern were given about the same amount of radiation and treated with homologous bone marrow; however, there was no beneficial effect.

Ferree (Cooperstown, N.Y.), pointed out that in the treatment of acute leukemias by whole-body irradiation in the exposure range of 200 to 1000 r the duration of remissions in most patients surviving the radiation was usually about two to three months. This is about the same as that seen after similar
treatment of leukemia in animals. This time figure applies to patients treated during a relapse or where there was an obvious tumor present. A figure is not yet available for acute leukemia treated by total-body irradiation during a hematologic remission. The two cases treated by Mathé should provide the first duration of remission figure on this important point. Thomas (Cooperstown, N.Y.) reviewed his experience on bone marrow transplantation after total-body radiation treatment of leukemia and discussed the total program of care and hematopoietic-tissue handling technics used by the Cooperstown group. In two sets of identical twins, each with a normal twin and one having acute leukemia, relatively quick hematologic recovery was seen in the leukemic individuals after radiation exposures of approximately 800 and 1000 r. Isologous bone marrow transplantation was given in each instance. He also thought they were getting successful adult bone marrow homotransplantation in a patient given 900 r.

Burchenal (New York) asked whether all leukemics in hematologic remission should have autologous bone marrow removed and preserved for possible future use. Kurnick (Long Beach, Calif.) said that in his practice they were preserving autologous bone marrow from patients with many kinds of cancer. Thomas said they had taken marrow for preservation from 15 patients during remission. He was somewhat pessimistic about its value, but said he would probably, after radical therapy, give first homologous bone marrow and if, that did not take, he would use the autologous marrow. Mathé emphasized a potentially important point that blood transfusions before irradiation might sensitize the patient to common antigens in the later bone marrow transplant.

Merrill (Boston) described a case of successful skin and kidney homotransplantation in human fraternal twins. The sick twin accepted a skin graft from the healthy twin, but the reverse transplant did not survive. Subsequently the sick twin was given small doses of total-body irradiation and then a kidney homotransplantation. The transplanted kidney began functioning immediately and continued to function during an 82 day period of observation before discharge. Merrill considered an antigen excess phenomenon as explanation for these results.

Radiation and chemical dose values to sterilize tumor cells in an animal.—Rough estimates on orders of magnitude of radiation or chemotherapy necessary to sterilize a disseminated leukemia in a mouse were given by Burchenal. It may vary from 3000 to 12,000 r depending on the type of leukemia. For nitrogen mustard the sterilizing values were three to five times as great as the LD₅₀ dose of the drug. Folic acid antagonists would not sterilize a transplantable leukemia with doses 100 times as great as the LD₅₀ value. Congdon pointed out that these rough estimates were very important in gaining insight into the magnitude of the problem of curing an advanced cancer. He thought this kind of information should be accumulated on all chemotherapeutic agents and types of radiation.

Preservation of marrow.—Preservation of bone marrow was discussed by several investigators. Congdon mentioned the work of M. A. Bender and L. H. Smith, who have undertaken the glycerol preservation of isologous mouse bone marrow for extended periods at three temperatures (−30°, −70 and
1256

Periodic testing in lethally irradiated mice is being made. Some new additives such as mannitol have been found using the mouse bone marrow assay system.

Large animal experiments.—Young (Austin, Tex.) reported that two monkeys of about 15 survived 900 r with homologous bone marrow therapy. McAlpine (Detroit) described homologous and autologous bone marrow therapy in irradiated monkeys. Autologous marrow was quite effective at 900 r, but it was not clear that much success was being obtained with homologous marrow. Mannick and Ferrebee obtained survival in the dog after a 1500 r exposure and autologous bone marrow transfusion.

Secondary disease and other topics.—Uphoff (Bethesda) found that a second small dose of irradiation for secondary disease in mice was not particularly effective in alleviating the disease. Dammin (Boston) said there was nothing new to report on the work of Wilson, who used a second small radiation dose in rabbits for secondary disease. Trentin (Houston) reported that in six homologous combinations fetal liver had not proved to be particularly advantageous as a donor material for circumventing “homologous disease.” Cristofanini (Philadelphia) described attempts to make the donors tolerant to homologous bone marrow by treating them at birth with the intended recipient cells. Some small effects on secondary disease were seen. Cole (San Francisco) reported on immunologic aspects of parent to F₁ bone marrow experiments. He found that parental blood leukocytes showed immunologic capabilities. Medawar (London) described the current status of chemical studies on the tissue-transplantation antigens. Polysaccharide-like substances are still implicated as an important lead.