

November 3, 1971

UCCM/RCC1.958060.001

EVOLUTION OF BONE MARROW TRANSPLANTATION  
IN TOTAL BODY IRRADIATION STUDY  
AT THE UNIVERSITY OF CINCINNATI

Because of radiation-induced hematologic depression, autologous bone marrow storage was instituted in 1964. Employing the method of Kernick (Transfusion 2: 178-183, 1962) marrow was removed from the posterior iliac crest under local anesthesia, averaging approximately 300 cc in volume. It was mixed with Osgood-glycerol medium and stored at  $-83^{\circ}$  centigrade after programmed temperature reduction  $1^{\circ}$  centigrade per minute. Prior to infusion dextrose was added, and then the marrow was given intravenously, initially without filtration, at a rate of 50 to 60 cc. per minute. The first two patients who received a marrow transfusion in our study, numbers 051 and 053, were infused with frozen marrow 24 and 19 days post irradiation respectively, at a time when the marrow sinusoids were relatively empty of precursor cells, with the expectation that there would be more room for the transplant to take. Marrow viability in these two procedures was 55% and 57%. Further details of these two infusions can be found on page 34 of our report to the Defense Atomic Support Agency, May 1, 1967 through April 30, 1968 in Table 5.

Patient number 051 experienced moderate hemoglobinuria not seen in patient 053 after infusion. Marrow was given in both cases 2 to 3 weeks post irradiation; hence it was impossible to distinguish spontaneous marrow recovery from successful marrow autotransfusion.

Because hemoglobinuria had been noted a triple filter system was developed and marrow autotransplantation on patient 070, 077, 078, 087, 090, 091, 095, 098, 099, 107 and 111 have all been performed employing this filter system. The technique has been described in our report to

the Defense Atomic Support Agency (DASA 01-C-69-0131) for May 1, 1970 through April 30, 1971, pages 19-42.

In marrow transplants of patients 070, 077, and 078 the delay between the removal of marrow and transfusion was 11, 2 and 0 days respectively. The platelet count of patient 078 never fell below 125,000 per cubic millimeter, but the white blood count dropped as low as 900, suggesting possible effectiveness of the technique for the first time.

For the next 8 patients the technique was therefore modified so that a larger volume of marrow (500 cc.) was removed from the patient under general anesthesia. The patient was then irradiated and the marrow replaced intravenously on the same day as it was removed. Table 3 of the Defense Atomic Support Agency report May 1, 1970 through April 30, 1971 indicates the success attendant on the modification of this procedure. Furthermore, our patients now require hospitalization for 4 to 5 days in total, after the first patient transplanted with our new technique (patient 087) was followed in the Clinical Research Center, Cincinnati Children's Hospital, for over 6 weeks without any evidence of illness.

The three failures in the revised transplantation technique have been patient 090, 099 and 107. Patient 090 suffered a cerebrovascular accident unrelated to her tumor or her radiotherapy. The latter two patients (099, 107) had had widespread radiotherapy which had affected the reticuloendothelial framework necessary for stem cell development, and preliminary cell aspirates in allegedly unirradiated areas, did appear hypocellular. Patient 107 appeared to possess normal granulocyte reserves, one of our marrow screening parameters, only because we were given an incorrectly high body weight on which

to base our etiocholanolone dosage, thus falsely elevating the marrow and granulocyte reserves. From this unfortunate experience we now insist that a candidate for marrow autotransplantation have a normal iliac marrow aspirate histologically, a normal bone marrow scan employing technetium 99m sulfur colloid, and normal granulocyte reserves measured with etiocholanolone (after we weigh the patient) as indicators of normal marrow function. At autopsy, patient 099, who died on day 31 post radiation, had widespread carcinoma of the pancreas. Patient 107 survived her pancytopenia without any evidence of sepsis.

The marrow transplantation technique developed at this Medical Center has been further evaluated in two marrow allotransplantation attempts in two women dying of aplastic anemia with septicemia. In the first patient, transfused while she was in shock secondary to Gram-negative septicemia, there were no cardiovascular sequelae of the transplantation, but the patient died of her infection two hours after infusion of the marrow. Post mortem examination indicated no bone, fat, or fibrin emboli in the lungs. The second woman, also in shock secondary to Gram-negative septicemia, had impressive clinical improvement post-transplantation with normalization of body temperature and recovery from shock, but died from intracerebral hemorrhage on the 4th day post transplantation.

It should be noted that patient 111 has not been included in the analyses of marrow transplantation contained in our DASA report covering May 1, 1970 through April 30, 1971, because her marrow autotransplantation occurred May 19, 1971. This patient continues to do well however, and her hospitalization lasted only 4 days.