E. Donnall Thomas
Twenty-eighth Chief Resident Physician
1952-1953
1949: Surviving Lethal Radiation by Lead-Shielding of Spleen

INTRAVENOUS INFUSION OF BONE MARROW IN PATIENTS RECEIVING RADIATION AND CHEMOTHERAPY

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COOPERSTOWN, NEW YORK, AND BOSTON, MASSACHUSETTS

AFTER a lethal dose of radiation in rodents,¹ canines² or primates,³ the destroyed bone marrow may be repopulated by intravenous infusion of cellular suspensions of marrow taken from healthy isologous, homologous⁴ and, in some cases, heterologous⁵ donors. Effective cells for these infusions may be stored by the Polge technic of freezing to −80°C in glycerol.⁶ Hosts seeded with donor marrow have some of the immunologic characteristics of the donors, and in some circumstances will take and hold homografts of other organs from them.⁷

Since cases of radiation disaster may occur, and since bone-marrow deficiency from radiation or chemotherapy does occur in the normal course of clinical medicine, an effort has been made to determine the availability and usefulness of bone-marrow infusions for the treatment of these conditions in man.

up for visual estimate of rate of synthesis by autoradiography.¹⁰

CLINICAL INVESTIGATION

Intravenous Infusion of Fetal Bone Marrow

Case 1. A 44-year-old man had had chronic myelogenous leukemia for 4 years, treated with x-rays, busulfan (Myleran) and 6-mercaptopurine. He went downhill rapidly in the last month of his life, with fever, anemia, bleeding, infection and finally coma. On the 21st, 22d and 23d hos-

Per Cell

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Human Bone Marrow Transplants from 1958 to 1967 (n=200) (Bortin, 1970)

# Reported Cases

Seattle Team in 1965

Don Thomas

Rainer Storb

Bob Epstein

Dean Buckner
Allogeneic Marrow Engraftment Following Whole Body Irradiation in a Patient with Leukemia

By C. Dean Buckner, Robert B. Epstein, Robert H. Rudolph, Reginald A. Clift, Rainer Storb and E. Donnall Thomas

The demonstration of a transient marrow graft in a leukemic patient in 1956, and the treatment of victims of an irradiation accident in 1958, initiated a number of attempts to utilize allogeneic marrow grafts in patients with marrow failure or with leukemia. Recent reviews of those attempts show a notable lack of success with death due to failure of engraftment or to graft-vs-host disease. Survivors showed a transient engraftment with reversion to host marrow, with the exception of the one long-term engraftment reported by Mathé et al. These previous attempts to transplant marrow in man may have failed because (1) donors were not selected on the basis of histocompatibility testing, (2) patients were terminal at the time of transplantation in most cases, and (3) isoimmunization against transplantation antigens had been induced by multiple prior transfusions.

Extensive studies in outbred dogs have demonstrated the correlation between histocompatibility, graft survival and severity of the graft-vs-host reaction. In addition, studies in dogs and in monkeys have shown that the graft-vs-host reaction may be ameliorated by immunosuppressive therapy. Recent rapid advances in human histocompatibility typing have provided in-
Results in First 70 Acute Leukemia Patients

Figure 2. Survival Curves in 70 Patients with Acute Leukemia Given a Marrow Graft from a Major-Histocompatibility-Complex-Matched Sibling (Open Circles Indicate Living Patients).

1 Thomas et al. NEJM 292:841, 1975
Result in First 19 CR1 AML Patients

Figure 1. Kaplan–Meier Product-Limit Estimates of Percentage Surviving in Patients Given Transplants during Remission.
Day 0 is the day of marrow transplantation. The open circles indicate living patients.

1 Thomas et al NEJM 301:598, 1979
Malignant Diseases Treated with Marrow Transplantation

- Leukemia
- Lymphoma
- Myelodysplasia
- Multiple Myeloma
- Selected Solid Tumors
  - Testicular
  - Neuroblastoma
Non-malignant Diseases Treated with Marrow Transplantation

Aplastic Anemia
Hemoglobinopathies
Immunodeficiency states
Autoimmune disorders

Isolation Room
Transplantation Activity Worldwide
1968 - 2014

Transplants

Autologous
Allogeneic
Relapse Following Allogeneic HCT for Leukemia
1. Stimulation with EBV/CMV peptide

2. Transduce with TCR\textsubscript{C4} Lentiviral supernatant

3. Sort on virus- and WT1-multimer\textsuperscript{+} cells

4. Flask expansion

5. Bioreactor expansion

Total production time: ~5 weeks
CART / TCR Trials Planned or Underway

ALL
Non-Hodgkins lymphoma
AML
Sarcoma
Lung cancer
Breast cancer
Melanoma
Pancreatic cancer
E. Donnalll Thomas
1920 – 2012

Dorothy E. Thomas
1923 – 2015