

Transplantation®

SPECIAL LECTURES

INTRODUCTION OF GEORGES MATHÉ

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Professor Georges Mathé, a man of literature as well as science, was born in 1922 in the village of Nieure and received his medical degree from the University of Paris in 1950. The theme of his professional life has been the use of immunity to treat neoplastic disease. These efforts began in 1958 when he obtained evidence in a mouse leukemia model of a graft-versus-tumor effect of transplanted hemolymphopoietic cells (1).

The risk of graft-versus-host disease in humans from bone marrow transplantation was not known at the time. In 1959, Mathé was presented with the possibility of determining this risk after a Yugoslavian nuclear reactor accident in which six workers were exposed to 4 to 8 Gy of total body irradiation. The patient with the largest dose promptly died, whereas the one with 4 Gy spontaneously recovered. The other four were rescued by Mathé with bone marrow cell infusions from non-related donors (2). The donor cells engrafted long enough to allow recovery of the native bone marrow without causing graft-versus-host disease (GVHD).

The experience, which defined an irradiation dosage window from which spontaneous recovery could occur, influenced the next step of organ transplantation. All six of the world's first long-surviving kidney recipients treated in Boston and Paris had sublethal total body irradiation in the 4 to 6 Gy range. Mathé's role is evident from his co-authorship of the classical report by René Küss (3).

Mathé's next seminal contribution was reported in 1963 in the *British Medical Journal* (4). Thirty-six years later, the article was designated a milestone at the University of California, Los Angeles, consensus development conference, which was convened to identify the major landmarks in the history of clinical transplantation (5). The 11-person consensus panel consisted of nine Medawar Prize recipients and three Nobel laureates and included the bone marrow transplant pioneers Donnall Thomas and Robert Good.

The committee's description read: "World's first prolonged engraftment of human allogeneic bone marrow in an adult recipient with leukemia conditioned with supralethal total body irradiation. Died without disease recurrence after 20 months, probably from complications of GVHD." The report

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was, in essence, the clinical fruition of Mathé's 1958 mouse leukemia experiments.

Mathé now sought a less dangerous and less histocompatibility-dependent approach to bone marrow transplantation. In his new strategy, patients were treated with large daily doses of antilymphocyte globulin (ALG) for 1 to 2 weeks before receipt of bone marrow cells from human leukocyte antigens mismatched and matched donors. As in the irradiated Yugoslavian patients of 1959, prolonged but unstable mixed chimerism was produced without evidence of GVHD (6). Mathé concluded that the risk of GVHD is directly related to the degree of recipient cytoablation. His advocacy of conditioning with ALG presaged the nonmyelotoxic strategies of pretreatment in tolerance induction protocols currently under extensive evaluation in several centers.

After 1970, Mathé fixed his attention on cancer immunotherapy by means other than transplantation. He has been recognized in many ways, including receipt of numerous prestigious European and American awards for cancer research. However, with the passage of time, the significance of his preeminent pioneer contributions to transplantation has become increasingly apparent.

Today, he receives the highest distinction of the Transplantation Society. I am gratified and honored to present to you, in absentia, Professor Georges Mathé: Commander of the French Legion of Honor, Grand Officer of the French National Order of Merit, recipient of the Grand Humanitarian Prize of France, and now a 2002 Medawar Laureate.

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