IMMUNOBIOLOGY OF BONE MARROW TRANSPLANTATION

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PIERRE L'ESPÉRANCE (1940–1974)

Pierre L'Espérance, M.D. (1940–1974)

R. A. Good

DR. PIERRE L'ESPÉRANCE, returning from Jerusalem to New York, was a passenger on the TWA flight that crashed in the Ionian Sea on Sunday, September 8, 1974. This abruptly ended the life of a creative young scientist, friend, and colleague.

Pierre was born in Montreal, Canada, on November 20, 1940. He took his Bachelor of Arts degree at Ste-Marie College, Montreal, and studied for the Doctor of Medicine degree at the University of Montreal. Shortly after acquiring his medical degree, he went with his wife Louise, a nurse, to serve for 2 years as a medical officer for the Canadian Public Health Service at an arctic frontier, Fort Chimo. During this period in the arctic he constantly faced the problems of serious infectious disease, especially in the very vulnerable childhood population. His experiences in the arctic led to his desire for further training in pediatrics and kindled his interest in the study of immunity to infection and host-defense mechanisms. Between 1969 and 1971 he trained in clinical pediatrics at Hôpital Ste-Justine in Montreal. There his initial clinical research concerned the role of the intestine in immunologic defense.

In 1970 on a visit to the University of Montreal and the Hôpital Ste-Justine, a case of combined immunodeficiency disease was presented to me by a young pediatric resident named Pierre L'Espérance. After considering the patient's history, laboratory data, histologic material, and examination findings, we were forced to conclude that this patient could not be treated definitively by marrow transplantation, since at that time no matched sibling donor was available. After the case presentations, L'Espérance told me about his work on the intestine and immunity and said that he would like to come to study in my clinics and laboratories. We had an active training program in clinical immunobiology in Minneapolis and, because of our proximity to Canada, we had the good fortune of having many Canadian trainees. Consequently, I invited Pierre L'Espérance to join our team in Minneapolis.

In the late summer of 1971, L'Espérance came to Minneapolis to study, and almost immediately he was launched in vigorous investigations of clinical immunobiology, immunodeficiency disease, bone marrow culture, and marrow transplantation. In March 1972, I made the difficult decision to move to New York and to the Memorial Sloan-Kettering Cancer Center. L'Espérance selected himself to be the advance scout. Indeed, in the summer of 1972 he was the first to move to the Sloan-Kettering Institute, set up a laboratory, and facilitate plans and preparations for an immunodeficiency clinic and bone marrow transplant program. By early spring, 1973, we had launched our clinical investigations with L'Espérance, Smithwick from Downstate, and Siegal from Rockefeller University. Later, O'Reilly joined us from Boston, Dupont from Copenhagen, and Hansen from Minneapolis. By November 1973, we opened a Reverse Isolation Unit for bone marrow transplantation in the new Memorial Hospital. L'Espérance worked closely with Hansen, Dupont, O'Reilly, and Smithwick in developing the immunodeficiency disease clinic, the marrow transplantation program in the Memorial Hospital, and the tissue typing and experimental hematology laboratories in the Sloan-Kettering Institute. Thus, it was natural that he should be the one chosen to

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present our studies on congenital neutropenia and our new data on mixed leukocyte culture reactions as an approach for marrow donor selection at the conjoint meeting of the International Hematology and Transplantation Societies in Israel in the late summer of 1974.

Because of his formal religious training (Pierre had studied for the priesthood of the Roman Catholic Church in Quebec) he was especially joyous about his impending international travel. He was tutored in Hebrew by some of his laboratory colleagues. He had steeped himself in the biblical history of the Holy Land and, of course, he knew its symbolism for the major religions. L'Esperance was truly a man of peace; he was ecumenical in his religious attitudes and compassionate for all suffering mankind, especially when suffering was consequent to human strife. It came thus as an especially ironic and tragic event that he should not return from his first adventure in the mideast.

We have mourned his death and our loss.

But today we begin a celebration of the work in which he participated. In meeting together, we are making the best possible effort to advance our endeavor. It is fitting and proper that we should dedicate this First International Symposium on Bone Marrow Transplantation to Pierre L'Espérance.

We welcome Pierre's widow, Louise, to our deliberations and ask her to join us in making our scientific discussions and festivities appropriate to Pierre's memory.

INTRODUCTION

Bone Marrow Transplantation Conference, November 10, 1975

L. Thomas

THERE could not be a better time for a conference on this particular subject, since its outcome will provide a sort of model that will answer some of the major criticisms now being leveled at the whole enterprise of biomedical science. This subject is particularly suited for setting straight several large misconceptions, upon which some of the policymakers in Washington seem to be relying for crucial decisions concerning the long-range direction science should be taking in this country.

For instance, it is being said in some circles of high influence that biomedical science is a nearly perfected enterprise, so near to perfection that from now on it must yield ever-diminishing returns. According to this view, medicine is already a high science and it has come almost its full, achievable distance. We know everything, or nearly everything, and our trouble is that we are lagging in the practical application of this knowledge. Therefore, we should now be cutting back on basic research in order to expend more of our limited resources on applications. The scientists should be reexamining their notebooks and reaching back on laboratory shelves for all those usable pieces of scientific facts that they have been neglecting all this time.

The truth, of course, is quite different, and it can be glimpsed by simply scanning the program of this conference. Biomedical science is still in its earliest, most primitive stage of development. It has not yet reached a level of real certainty for any of its most important problems. There are no forgotten, neglected bits of truth, lost in our notebooks or gathering dust on the backs of our shelves. Indeed, if we have any trouble in this regard, it is that we tend to try to apply our experiments to human problems *too* quickly, before there is enough real certainty.

It is also said that biomedical science is a disorderly undertaking, badly organized and in need of more precise and closely directed planning. Already, in response to this criticism, we have seen the proliferation of centrally placed committees, charged with the responsibility of laying out the future and calling the shots in detail. The special logic of systems analysis, and the techniques of operations research, are being urged as the answer to our confusion. But what is not recognized or acknowledged—and I hope it will be one of the by-products of this conference—is the high degree of pure uncertainty that characterizes our most important problems. How can committees lay out plans for research when the next set of experiments, at every stage, must be governed by events that can only occur in the mind of the individual investigator? It is surprise that must be sought, if the research is to get anywhere. When things that we assumed as axioms suddenly turned out to be wrong, when observations are made which don't seem to fit with anything, when someone in the laboratory says, "but that is absolutely impossible!", then you know that the work is going well. A committee, by its very nature, cannot plan this kind of event; committees are programmed to prevent astonishment.

Finally, it is being said that we have all become overspecialized in our reductionism; we know more about less; our ap-

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proaches have become too narrow. The printed program for this conference is itself an answer. If you want to learn about bone marrow transplantation, you must cast a wide net. All of immunobiology is involved in the problem, and a good deal of cellular genetics, developmental biology, and the special forms of molecular biology that immunologists have recently commandeered, plus the latest in membrane biology. If the work goes as well as now seems the case, you could end up discovering the mechanism of rheumatoid arthritis or multiple sclerosis, or new ways of destroying cancer cells selectively, or new approaches to virus infection, before you reach the goal of successful marrow transplantation.

This kind of science depends on unpredictable observations, accidents, surprises, and outrageous stretches of the individual, solitary human imagination. If you want to plan work of this kind, you must plan to have the brightest people with the most agile and open minds doing the work, leading themselves down their own garden paths, running into snags, tripping over things, being amazed. This is, in real life, the way the system works, and it is my hope that this conference will provide us with a handy model for describing it.

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