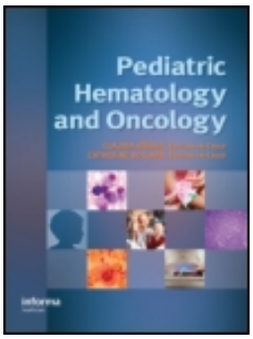

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Editorial

PEDIATRIC HEMATOLOGY AND ONCOLOGY IN FRANCE

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The contribution of French authors to pediatric medicine dates back to the end of the eighteenth century, but the hematologic and oncologic specializations in this branch of medicine are recent, dating from the 1950s.

At the beginning of the 20th century, the *French Cardiology Review* was called *Archives des Maladies du Coeur, des Vaisseaux et du Sang* (*Archives of Heart Diseases, Blood Vessels and Blood*). The first to describe polycythemia was the great cardiologist Henri Vaquez; this occurred at a time when hematology was becoming an independent scientific entity, with the foundation by P. Chevalier of the journal *Le Sang* (*Blood*) and the constitution in Paris in 1931 of the Société Française d'Hématologie (French Haematology Society), the world's first hematology society.

Research in pediatrics developed considerably since, and one of the great achievements of Robert Debré was that he encouraged his young collaborators to specialize in various branches of pediatrics. This was how Odile Schweisguth, who started as a cardiopediatrician, came to found *Paediatric Oncology*, and Jean Bernard to found *Paediatric Haematology*.

PEDIATRIC ONCOLOGY

When Schweisguth began dealing with the problem of cancer in children, it was essentially treated by surgeons and to a lesser degree by radiotherapists. Mortality was high and the work was difficult and required great courage. She started by opening an outpatient department and then recruited a small team of workers at the Pavillon Milhit at the Paul Brousse Hospital in Villejuif. Until 1970, this was the only French center of Pediatric Oncology. Schweisguth helped to set up a large num-

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ber of pediatric cancerology units in anticancer and university hospital centers. All pediatric oncologists are to some extent her students. In the 40 years since this specialization came about, the proportion of children's tumors cured has risen from 10% to 70%. Jean Lemerle later continued the work of Schweisguth. Twenty-seven years ago, she founded the Société Internationale d'Oncologie Pédiatrique (SIOP), which held its first meeting in Madrid in 1968. It was started with just a few members from France, Holland, Belgium, Spain, the United Kingdom, and the United States, and has grown considerably; its last congress in September 1994 (SIOP 26) in Paris was attended by 1,400 participants from 63 countries. France has had the honor of having three presidents of SIOP (Schweisguth, Raybaud and Lemerle) and of organizing three of the congresses (Lyon in 1970, Marseille in 1981, and Paris in 1994).

The Société Française d'Oncologie Pédiatrique (SFOP) was founded in 1984 at the instigation of Lemerle. Its pediatric oncology teams fulfill the specific training criteria for pediatricians. This Society includes clinicians, pediatric surgeons, radiotherapists, and pathologists in close touch with biologic research laboratories. Certain teams from this group also perform bone marrow transplantations. The SFOP includes 10 specific committees for each type of tumor. These committees activate pilot studies and phase I, II, and III trials. Especially worth mentioning are the treatment protocols for non-Hodgkin's lymphoma (LMB 84 and LMB 89), which have given the world's best results and are used as models by European teams outside France and by American teams, in particular the Cancer Children Study Group (CSG). French teams have also contributed to the progress made in treating nephroblastomas, bone tumors, and mesenchymal tumors, as well as to the development of intensive chemotherapy with bone marrow autografts to treat neuroblastoma, Ewing's sarcoma, and brain tumors in infants (Figures 1–3). The problems of late effects have always been a matter of concern, and these problems justified the creation of the therapeutic tapering protocol (eg, in Hodgkin's disease). Two regional registries for childhood cancer were established in 1983, in Lorraine and in the Provence Alpes Côte d'Azur area.

PEDIATRIC HEMATOLOGY

The first remission during acute leukemia in children was obtained in November 1947 by Jean Bernard and Marcel Bessis, thanks to exsanguination transfusion. Six months later, Sydney Farber opened up the way for chemotherapy with the discovery of aminopterin, the first folic acid antagonist. Two new lines of treatment were developing, one leading to the modification of environmental factors, and the other aimed at de-

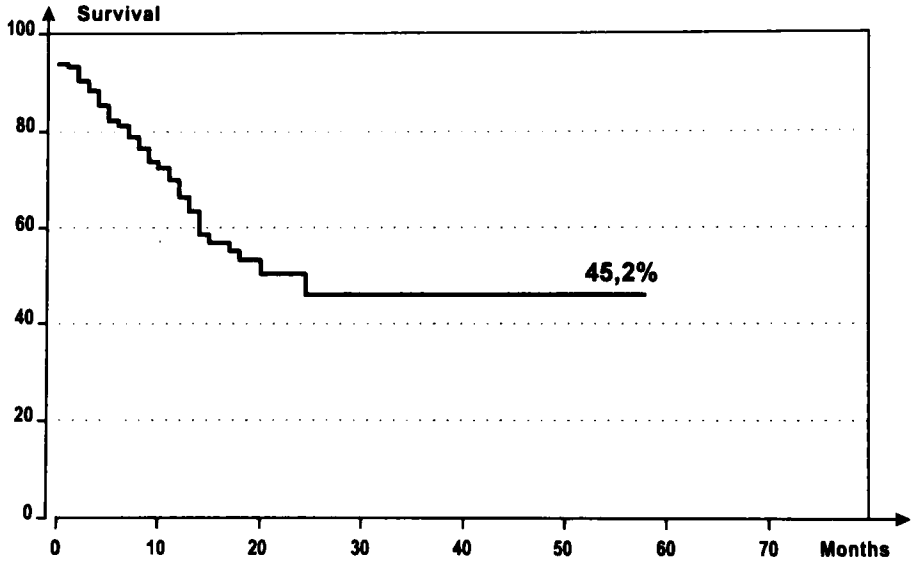

Figure 1. Survival following autologous bone marrow transplantation in stage IV metastatic neuroblastoma in children over 1 year of age (n = 126). Mean follow-up was 240 days.

stroying leukemic cells. More than 40 years later, it is the latter possibility that has proved useful. Acute leukemia was first treated using French or American protocols of the Acute Leukemia Group B until 1971. It is important to stress here the part played by Claude Jacquillat, who in 1974

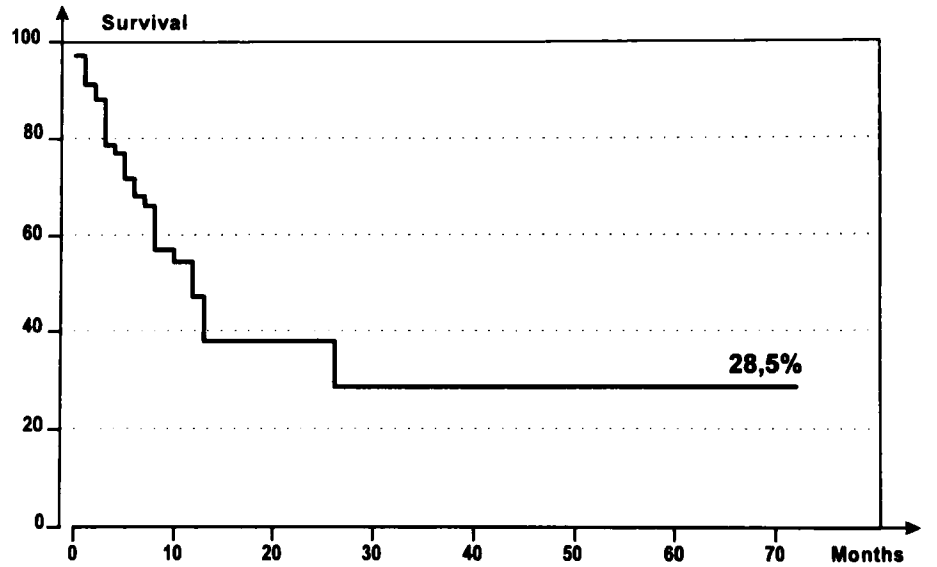

Figure 2. Survival following autologous bone marrow transplantation in metastatic Ewing's sarcoma, (n = 69). Mean follow-up was 210 days.

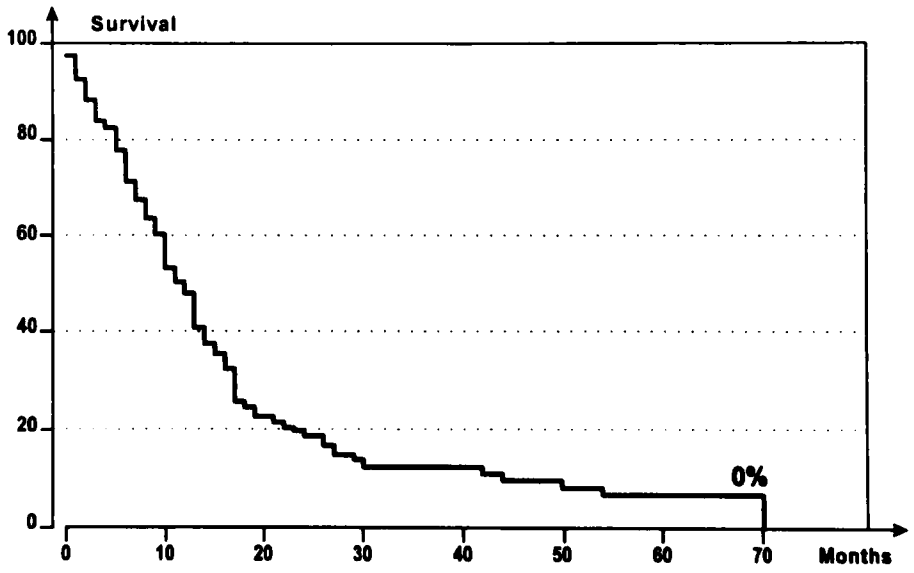

Figure 3. Survival following autologous bone marrow transplantation in brain tumors (n = 220). Mean follow-up was 330 days. Survival is 40% for medulloblastoma.

was responsible for three achievements: 1) persuading the French to accept the need for treatment protocols; 2) showing the importance of pulses in prolonging remission, and 3) adapting the treatment to the gravity of the initial disease. It is true that the first trials only took into account factors that were easy to determine, such as the number of white blood cells, tumoral mass, and patient age, but these trials made it possible to improve results for the more severe forms of leukemia. This improvement proved useful for drafting the VIRCALL (Very Increased Risk Children's Acute Lymphoblastic Leukemia) protocol, the first to be designed for particularly serious forms. Since then, all French protocols have taken into account these prognostic factors. In France, there are two groups for the treatment of lymphoblastic leukemia: the Fralle Group and the group attached to the European Organization for Research and Treatment of Cancer (EORTC). In addition to clinical data, the French protocol Fralle 93 for the treatment of acute leukemia takes account of the aspects of the disease concerning immunology, cytogenetics and molecular biology, sensitivity to treatment, and especially of residual disease.

The strong links between hematology and immunology led to the creation in 1969 of the European Society for Paediatric Haematology and Immunology (ESPHI), whose founding members were Shafer, Hitzig, and Seligman. One of their aims was to organize cooperative protocols. Unfortunately, in contrast to what occurred with SIOP, few such proto-

cols saw the light of day. In 1989, ESPHI held a meeting in Paris under the presidency of Gerard Schaison.

In 1986, the Société Française d'Hématologie et d'Immunologie Pédiatrique (SHIP) was founded by Claude Griscelli, Daniele Sommelet, and Schaison. Its twice yearly meetings attract hundreds of specialists in these disciplines. This society includes working groups on different types of leukemia, myelodysplasia, thrombopenic purpura, Diamond-Blackfan syndrome, and AIDS.

BONE MARROW TRANSPLANTATION

Bone marrow transplantation is an important link between hematology and oncology. In France, it was first performed in 1973 at the Saint Louis Hospital by Eliane Gluckman, who had been trained by Ed Thomas. In the same hospital, the laboratory of Jean Dausset, a winner of the Nobel Prize for Medicine, provided a great deal in the achievements of transplantation. The Saint Louis Hospital is the largest center of its kind in Europe, with 44 steriles rooms for children and adults undergoing allografts or autografts. To date, 940 allografts have been performed at this hospital, one third of them in children. The indications for transplantation include leukemia, acquired bone marrow aplasia, constitutional aplasia (44 cases of Franconi's disease have been transplanted),

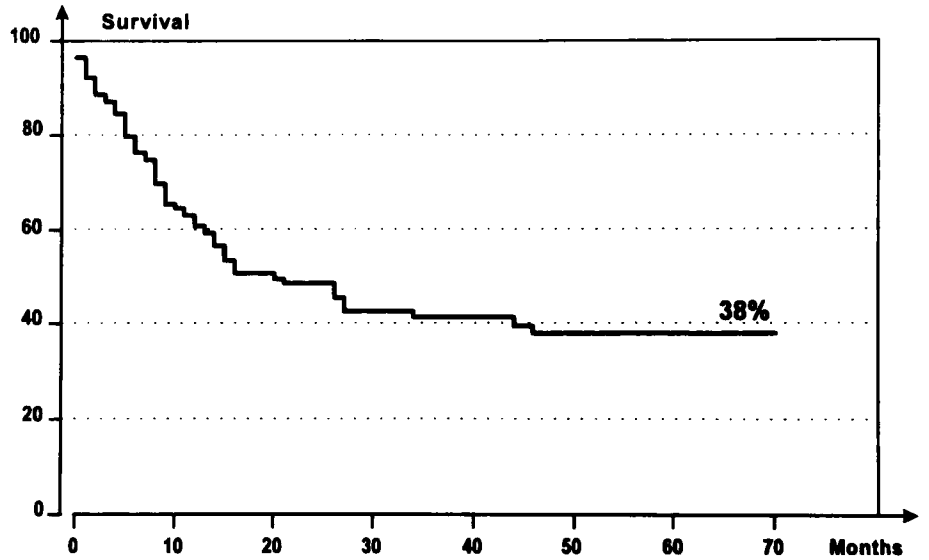

Figure 4. Survival following autologous bone marrow transplantation in acute lymphoblastic leukemia (n = 215). Mean follow-up was 270 days.

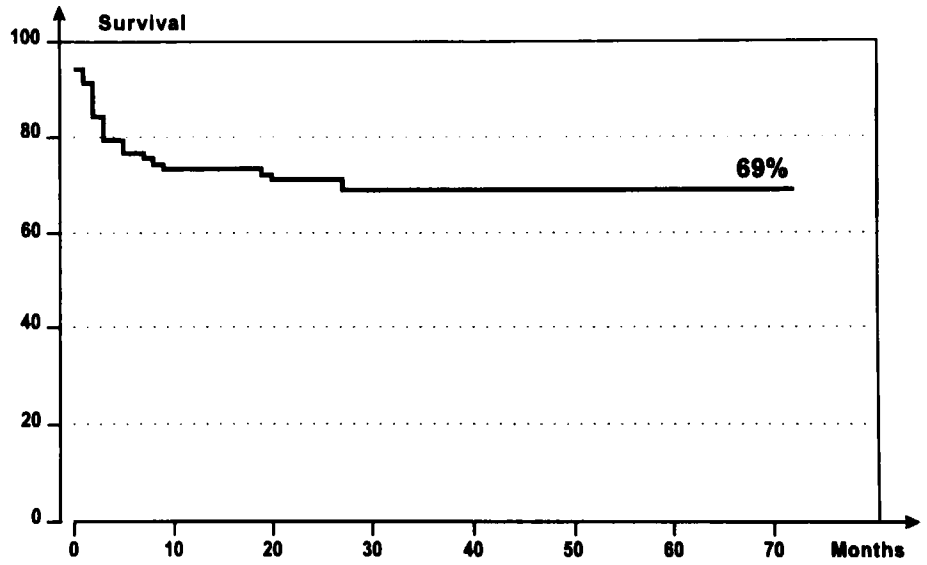

Figure 5. Survival following allogenic bone marrow transplantation in poor-prognosis acute lymphoblastic leukemia in first complete remission (n = 105). Mean follow-up was 630 days.

constitutional diseases, thalassemia, Gaucher's disease, and osteopetrosis, among others.

The first transplantation, using umbilical cord blood, was performed at the Saint Louis Hospital in 1990 in a child with Franconi's disease who

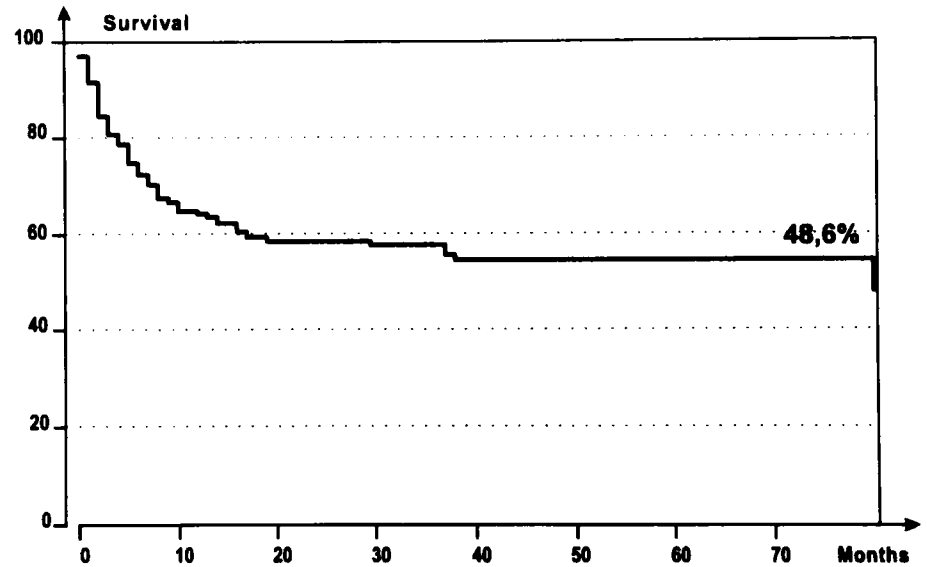

Figure 6. Survival following allogenic bone marrow transplantation in acute lymphoblastic leukemia in second remission (n = 223). Mean follow-up was 480 days.

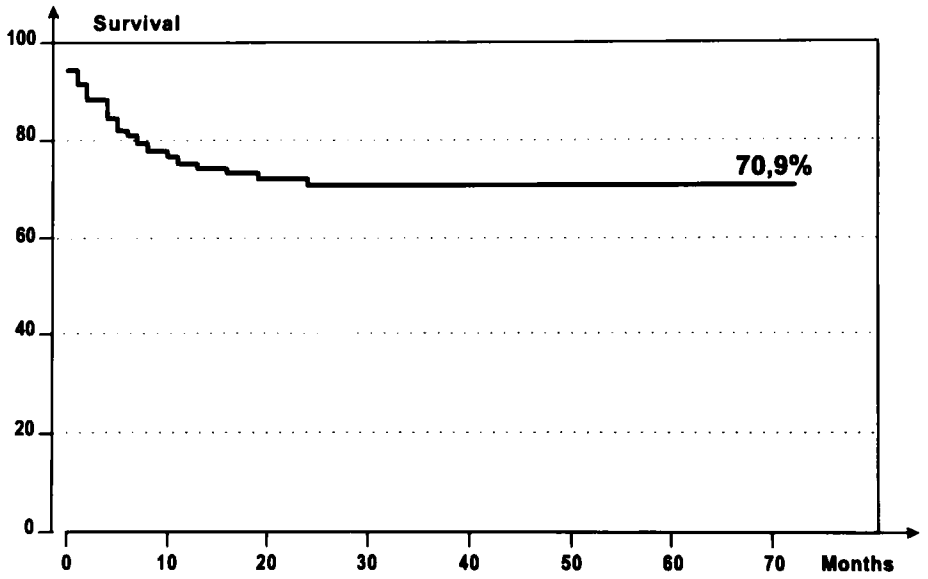

Figure 7. Survival following allogenic bone marrow transplantation in acute myeloblastic leukemia in first complete remission (n = 138). Mean follow-up was 600 days.

is currently cured. Since then, about 10 grafts have been performed with cord blood, and a cord blood bank was set up in 1993. The other large French transplantation centers are at the Necker Enfants Malades Hospital in Paris, which specializes in immune deficiency grafts, and the pediatric hospitals in Nancy, Lyon, Villejuif, and Marseille. Allografts are now carried out in 13 pediatric centers in France. In 1993, 581 such grafts were performed, 201 of them in children, and 1,522 autografts were performed, 295 of them in children. The autografts are done either with bone marrow or peripheral stem cells. Transplantations with CD34+ cells started a year ago.

Of the 1,033 allografts performed in subjects under 15 years of age that are listed in the registries, the overall survival rate is 51.8% at a maximum follow-up of 10 years. Details of the grafts performed in France are given in Figures 1 through 7. Figures 1 through 4 show the results of autografts for the various types of neuroblastoma, Ewing's sarcoma, brain tumors, and acute lymphoblastic leukemia, and Figures 5, 6, and 7, show the results for allografts for lymphoblastic leukemia during the first or second remission, and for myeloblastic leukemia during the first remission. (The curves were kindly supplied by the Société Française de Greffe de Moelle-[French Society for Bone Marrow Transplantation]). The registry for autologous bone marrow transplantation was started in 1992.

CONCLUSION

The recent history of pediatric hematology and oncology is one of cooperation among clinicians and research scientists. The discipline is truly clinicobiologic. The rarity of certain children's diseases fully justifies cooperation among the world's pediatricians involved in this branch of medicine. The great progress in biology, and above all the contribution of molecular biology, has revived interest in our discipline and has found a field of application, especially in constitutional diseases. At the dawn on the 21st century, will gene therapy be capable of correcting them?