Bone marrow transplantation today

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Abstract Today, bone marrow transplantation (BMT) is an established therapy. This statement is best verified by the number of BMTs performed. Between January 1990 and December 1992, 172 European teams in 26 countries carried out a total of 14,334 transplants. There were 6,642 allogeneic transplants: 5,513 BMT from an HLA-identical sibling donor, 370 from a non-identical family member, 88 from an identical twin donor and 671 from an unrelated volunteer donor. There were 7,692 autologous transplants: 6,577 autologous bone marrow, 777 peripheral-blood stem-cell and 338 combined bone-marrow and peripheral-blood stem-cell transplants. Indications were: leukaemias in 52% (7,479), lymphoproliferative disorders in 29% (4,125), solid tumours in 11% (1,540), aplastic anaemia and thalassaemia in 3% (487) and inborn errors and miscellaneous disorders in the remaining 5% (703). The results of these transplants are not yet known. From previous analyses it can be expected that more than 50% of patients will be alive and well 10 years after BMT. The main factors influencing outcome are known; they depend on type, subtype, stage of disease at time of transplant, the time from diagnosis to transplant and the conditioning regimen for all transplants. For allogeneic BMT, donor source, donor and recipient age, sex, donor/recipient sex combination, donor and recipient viral status, graft-versus-host disease prevention method and region are additional factors. Knowledge of these factors enables us today to estimate the potential risk and adjust the therapy for an individual patient.

Key words Bone marrow transplants · BMT data

Introduction

First attempts at bone marrow transplantation (BMT) date back several decades, but they lacked a pathophysiological background. The modern era of BMT began after the experiments of Jacobsen and Lorenz [14, 15]. They were the first to demonstrate the protective effect against otherwise lethal irradiation by the shielding of the spleen or by the intravenous infusion of bone marrow. It was unclear initially whether this protective effect was provided by a humoral or cellular factor. Only in 1956 could it be shown by genetic markers that colonisation of the recipient bone marrow was performed by donor cells [21].

Recognition of the importance of the major histocompatibility complex, development of methods for supportive care and introduction of modern immunosuppressive agents had tremendous impact. Bone marrow transplantation has evolved over the last two decades from a rare experimental undertaking to common procedure [20]. Up to 1980, fewer than 200 transplants were performed annually [3]. One decade later,
the total number of BMT carried out worldwide is expected to exceed 10 000 per year. These numbers will probably continue to increase in the immediate future for two main reasons.

Allogeneic BMT has been recognised as an accepted therapeutic modality for certain diseases that cannot be cured by conventional treatment. For a long time it had been restricted to patients with an HLA-identical sibling donor. Today, BMT from unrelated volunteer donors has become possible and more than 1.2 x 10^6 potential donors are registered worldwide. National coordinating centres are active in North America, most West European countries, Australia, New Zealand and Japan. International cooperation and exchange are being practised and standardised through recommendations made by the World Marrow Donor Association [2, 6, 19].

Autologous stem-cell transplants, derived from bone marrow, peripheral blood cells, or from both, have become standardised routine practice [4]. Their use need not be restricted to curative attempts. They are a highly efficient tool in supportive care to shorten the aplastic phase following intensive radiochemotherapy. Better purging techniques and the probability of perfecting positive stem-cell selection will enhance the applicability to patients not in complete remission at the time of harvest. New strategies in combination with growth factors will include patients with tumours not treatable by current chemotherapeutic strategies [4, 17].

### Patients and methods

**Survey on transplant activity**

Members of the European Group for Bone Marrow Transplantation (EBMT) are invited to report on a survey sheet the number of transplants performed each year according to indication and donor source [9, 12]. The numbers of transplants performed between the years 1990 and 1992 are listed in Table 1. The number of teams reporting for each year is shown in Table 2. Figures reported for 1992 are lower than those for 1991. This is due to the fact that data entry for this manuscript was closed on 15 January 1993, and the list is not yet complete.

**Data collection**

The EBMT registries have been collecting data from participating teams for a subgroup of patients on an annual basis since 1979. These data are updated annually. The survey sheets cover several areas of interest, which are:

- Investigator information
- Recipient information: name, age, sex
- Primary disease: type, subtype, stage, date of diagnosis, date of remission, organ involvement, markers of disease
- Donor information (allogeneic BMT): histocompatibility, age, sex, relationship
- Transplant procedure: date, number of cells, in vitro manipulation
- Conditioning: drugs, total-body irradiation, dose, fractions, lung shielding
- Graft-versus-host disease (allogeneic BMT): prevention method, onset, maximal grade
- Complications: interstitial pneumonitis, veno-occlusive disease, infections, haemorrhage, cataract, secondary malignancy, cause of death
- Relapse: date, site, origin
- Survival status: actual status, Karnofsky performance

### Results

A total of 14344 transplants were performed in Europe during the 3-year period 1990, 1991 and 1992 (Table 1).

**Distribution by donor**

There were 6642 allogeneic and 7692 autologous transplants in total. The allogeneic BMT were made available from an HLA-identical sibling donor (5513), a non-identical family member (370), a twin (88) or from an unrelated donor (671). The majority of the autologous transplants were bone-marrow-derived (6577), 777 were peripheral-blood stem-cell transplants and 338 were combined peripheral-blood and bone-marrow stem-cell transplants. The relative proportion of each donor source is illustrated in Fig. 1.

**Indications by disease**

The individual diseases are listed in Table 1. There was a total of 5198 transplants for acute leukaemias (2961 allogeneic, 2237 autologous), 2281 for chronic leukaemias and myelodysplastic syndromes (2029 allogeneic, 252 autologous), 4125 for lymphoma and myeloma (469 allogeneic, 3656 autologous), 1540 for solid tumours (21 allogeneic, 1519 autologous), 487 severe aplastic anaemia and Fanconi's anaemia (486 allogeneic, 1 autologous) and 703 BMT for congenital disorders and miscellaneous indications (676 allogeneic, 27 autologous).

**Changes over the years**

Although numbers for 1992 are still incomplete, there has evidently been an increase in reporting teams (Table 2). There has been a significant rise in the number of unrelated BMT and in autologous and peripheral-blood stem-cell transplants. Indications with an upward trend are myelodysplastic syndromes, chronic lymphocytic leukaemia and myeloma for allogeneic transplants, and myeloma and breast carcinoma for autologous transplants.