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PERIPHERAL BLOOD STEM CELLS (PBSC) AS A SOURCE FOR HEMOPOIETIC RECOVERY FOLLOWING AUTOLOGOUS BONE MARROW TRANSPLANTATION (ABMT) IN CHILDHOOD MALIGNANCY.

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In an attempt to improve hemopoietic recovery after ABMT, 16 children awaiting ABMT underwent 50 PBSC harvests. Age 12 months - 19 years weight was 9-84 Kg. They underwent 2-6 PBSC harvests each, primed by chemotherapy and GMCSF. PBSC harvest was carried out using the Fenwall CS 3000 plus. Total nucleated cells per collection ranged from 0.35-5.62x10E8 cells per Kg, and the number of CD34+ cells was 0.23-1.1X10E6/Kg. The number of CFUGM varied in these heavily pretreated patients between 0-5.3 CFUGMx10E4/kg per collection. Most of the CD34+ cells were found to be CD38+, CD33+, or CD33-. Low coexpression of CD34+ CD71+ cells may correlate to the low proliferating capacity of PBSC as compared to the BM cells. We conclude that PBSC harvest is a feasable and safe procedure in small children, and can be successfully performed, resulting in substantial yield even in heavily pretreated patients, and may replace ABMT.

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AUTOLOGOUS BONE MARROW TRANSPLANT (ABMT) IN ACUTE NON-LYMPHOCYTIC LEUKEMIA. Ortega J.J.Hospital Universitario M-Infantil Vall d'Hebron.Barcelona.Spain.

The question of which is the best post-remission induction treatment for children with ANL continues to be controversial.Although its real role in therapy of ANLL in children has not yet been established ,several studies have shown that ABMT performed after intensification therapy gives similar results to al-BMT in firt remission (CR-1) and is superior to chemotherapy in patients in CR-2.In this context we report the results of 3 studies:the first is an update of the EBMTG;the second is a comparative study between ABMT and al-BMT in CR-1 performed in 5 Spanish paediatric units;the third is a prospective study of treatment of ANLL with post-induction intensification therapy followed by ABMT or al-BMT performed in our centre.1.EBMT registry data (Update:Dec 92). 243 children received an ABMT,176 were in CR-1 and 67 in CR-2.In CR-1,DFS was 0.45±0.05 at 5 years;in patients receiving marrows treated with mafosfamide DFS was higher (0.54 *vs* 0.41).DFS and relapse probabilities in patients in CR-2 were 0.41 and 0.53,respectively.Transplanted related mortality (TRM) was approximately 10%.2.Spanish working party study.73 children in CR-1 received BMT as post-consolidation therapy between Oct 82 and Nov 91;in 38 it was an al-BMT and in 35 an ABMT.Patients' characterisitics in both groups were similar as was the mean time in remission (4 months) before transplant and conditioning treatments.DFS at 3 years was the same in both groups:0.59±0.07 *vs* 0.58±0.08).Only 1 patient in the ABMT group relapsed after 15 months and no patient receiving an al-BMT relapsed after 24 months.3.Prospective one-centre study.After 2 post-induction intensification treatments (HD Ara-C *plus* mitoxantrone and HD-Ara C *plus* AMSA) al-BMT (patients with HLA-identical donor) or ABMT (the rest) were performed.19 patients received an ABMT with purged marrow and 9 an al-BMT upto Dec 92.DFS at 3 years was 0.75 for both groups of patients and the overall survival for all patients included since diagnosis was 0.61 at 3 years. **Conclusions.**1.ABMT after intensification consolidation therapy seems to have similar effectivity to al-BMT in ANLL in children.2.ABMT appears superior to chemotherapy in treatment of patients in CR-2. 3.A prospective randomized study including many patients could answer the question of wether the results of ABMT are superior to those obtained by intensification chemotherapy alone.

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ROLE OF ABMT IN STAGE IV NEUROBLASTOMA OVER ONE YEAR OF AGE AT DIAGNOSIS

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Based on the LMCE 1 LMCE 2 and LMCE 3 studies a 10 years prospective experience will be reviewed and major questions isolated.

These questions will be then reviewed using 600 ABMT from the European Bone Marrow Transplant Group and using univariate and multivariate analysis.

A subgroup without metastasis after induction therapy is curable in 50 % of the cases.

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AUTOLOGOUS BONE MARROW TRANSPLANTATION IN CHILDREN WITH SOLID TUMORS.

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Between 1986 and 1992 154 children with solid tumors received ABMT in one of the 10 Centers of the AIEOP-TMO Group. There were 93 males and 61 females. The age at ABMT ranged between 1 and 19 years (median 4 years). Underlying disease included neuroblastoma in 109 children, Wilms' tumor in 14 children, Ewing sarcoma in 10 children, soft tissue sarcoma in 13 children, other tumors in 8 children. Marrow ablative therapy (MAT) included TBI associated to melfalan or to other drugs in 99 cases. Transplant-related mortality was 10%, progression free survival (PFS) at 5 years was 28.4%. According to underlying disease, PFS was 30.5 % for neuroblastoma (44% for the 51 children grafted in 1st CR, and 17.4% for the 58 children grafted in more advanced disease, p = < .01); 25.4% at 2 yrs for Wilms tumor; 20% at 12 months for Ewing and soft tissue sarcoma.

Supported in part by Istituto G. Gaslini, contract 9307002F and by Centro Nazionale Ricerche (CNR), contract 92.02315.PF39 .

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THE PRO'S AND CONTRA'S IN CHILDREN OF DIFFERENT MODES OF BONE MARROW TRANSPLANTATION.

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Bone marrow transplantation (BMT) in children is available since the end of the seventies. Three different types of BMT can be discerned according to the origin of the graft; i.e. allogeneic, autologous, matched unrelated. Allogeneic BMT is only available for 30% of the children, as HLA-identity still is needed. Graft-versus-Host disease (GvHD), infections (caused by the prolonged immunedepression), rejection and relapse are major obstacles. T-cell depletion is influencing the rejection rate and relapse rate tremendously.
In autologous BMT GvHD is no problem however a GvHD like syndrome, with minor clinical symptoms can be induced by stopping cyclosporin A medication. As relapse is a major problem after autologous BMT; this GvHD like syndrome is under study for its graft-versus-leukemia effects.
The use of purged graft in autologous BMT remains a field of investigation; although there is a tendency in favour for purging. BMT with marrow from matched unrelated donors is only available (after a search period) for a limited number of patients. During the presentation further comparisons are made in relation to the original diseases.

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ROLE OF AUTOLOGOUS BONE MARROW TRANSPLANTATION IN CHILDREN - ACUTE LYMPHOBLASTIC LEUKEMIA.

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The cure rate of acute lymphoblastic leukemia (ALL) in childhood with conventional chemotherapy is rather high. There is also accumulating evidence that children with a relapse of their ALL have a second chance of cure depending of the time point of the relapse. The best chance of survival in these cases results from allogeneic bone marrow transplantation (BMT). In contrast to that the role of autologous BMT is much less clear. 20 to 30 % disease free survival rates have been reported with this approach. However the same magnitude of cure rates can be obtained also with conventional chemotherapy. It is possible but not extractable from the literature that it is the same group of patients which can benefit from both either autologous BMT or chemotherapy. There is also a long discussion about the role of purging of the marrow with various methods before autologous BMT. To our opinion the value of autologous BMT in children with a relapse of their ALL is very limited. The pros and contras will be discussed.