SCLERODERMA LIKE GRAFT VERSUS HOST DISEASE (GVHD): A LATE CONSEQUENCE OF BONE MARROW GRAFTING: Märtti A. Siimes, Eija Johansson and Juhani Rapola, Children's Hospital, University of Helsinki, Helsinki, Finland.

This 10-year-old boy with unremarkable medical history developed aplastic anemia of unknown etiology in December, 1974. He received a bone marrow infusion from his sister whose leukocytes were HLA-identical and nonreactive in MLC. The transplantation was carried out without major complications and the patient spent normal life during the first year although he presented with mild skin lesions compatible with GVHD. During the second year after the graft the patient gradually over a period of about 4 months developed a severe, progressive scleroderma-like skin and joint involvement with markedly limited range of motion. His hemoglobin, blood cells counts, exclusive work-up of blood and urine and serum immunology showed values within the normal range, except the serum concentration of IgG gradually rose up to 3.6 g/l. In accordance of the clinical picture the skin histology was typical for the scleroderma. The patient was treated with i.v. methotrexate (12mg/m²) once and subsequently twice a week. During the follow-up period of about 10 months the severe skin lesions have gradually subsided, first in the area of face and shoulders and then in that of arms and upper trunk and the skin biopsy from the healed area showed normal histology. At present the patient is left with flexion contractions and slowly recovering skin lesions in the lower extremities. The history of our patient indicates the possibility of unpredictable long-term consequences after initially successful bone marrow grafting.

AN ANALYSIS OF ACUTE LYMPHOCYTIC LEUKAEMIA IN CHILDHOOD IN THE NETHERLANDS AND THE RESULTS OF TREATMENT; 1973 - 1977.

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Details of 215 children with acute lymphocytic leukaemia (ALL) are given with respect to age at diagnosis, sex, initial leukocyte and platelet counts. The results of intensive treatment have been analysed in relation to these characteristics.

A prospective study was undertaken to see if the addition of cyclophosphamide to maintenance therapy with 6-mercaptopurine and methotrexate altered the results of treatment.

Maintenance therapy with these three drugs did not effect the relapse rate in patients with initial leukocyte counts less than 50.000/mm³, but more lethal infections were seen in this group. Here the best results were obtained with maintenance treatment with two drugs (6-mercaptopurine and methotrexate).

For patients with initial leukocyte counts higher than 50.000/mm³ these two drugs were insufficient and better results were obtained using all three.

PURINE NUCLEOSIDE PHOSPHORYLASE DEFICIENCY ASSOCIATED WITH CELLULAR IMMUNODEFICIENCY: FOLLOW UP DURING TREATMENT.

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A female patient, at the moment 2½ years old, with a purine nucleoside phosphorylase (PNP) deficiency showed a gradual decrease of T cell immunity during the first year of life whereas B cell immunity developed normally (1). Later on in life some disturbance of B cell immunity also developed as could be concluded from the appearance of homogeneous immunoglobulins in the serum from the decrease in the synthesis of specific antibodies. Earlier studies (1, 2) have shown that an inherited PNP deficiency existed in two older sisters of the patient, both suffered from the same immunodeficiency and have died. The oldest sister has been treated with several thymus transplants, resulting in a partial and transient restoration of T cell function. However the most obvious therapeutic approach of these patients would be correction of the consequences of the metabolic defect. Therefore, the patient under study was treated by oral substitution with uridine and purines and afterwards with several transfusions of irradiated red cells and plasma. The former treatment was rather unsuccessful, the latter resulted in a remarkable change in the metabolic state of the patient and some improvement of in vitro immune functions. In contrast to findings of Polmar et al. (3) in a ADA deficient patient, complete immunological restoration could not be achieved by this treatment until now.

References:

1. J.W. Stoop et al., New Engl.J.Med. 296 (1977) 651-655
2. J.W. Stoop et al., Clin.Immunol.Immunopath. 6 (1976) 289-298
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PROGNOSTIC VALUE OF "PREDIAGNOSTIC PERIOD" IN CHILDREN'S ACUTE LEUKAEMIA.

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"Prediagnostic period" /PP/ is arbitrarily defined as the interval from the onset of complaints and/or symptoms till the definite diagnosis of acute leukaemia /AL/. Duration of PP may be connected with the rapidity of the disease, and - according to our hypothesis - a shorter PP is an indicative of poor prognosis.

Data were collected from 163 AL children registered in 1971-1973 and treated at Departments belonging to the Hungarian Children's Leukaemia Study Group. Duration of PP was variable /from days to months/, cases were put in two main groups: with a PP shorter respectively longer than one month. By means of the chi-square test comparison was made between the number of cases in these groups according to various disease characteristics.

We found in the shorter PP group a greater number of cases with poor prognosis, failures, complete remissions of shorter duration and shorter survival time as well. Our results indicate a prognostic value of PP in children's AL.

NEUTROPHILIC FUNCTION IN GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY.

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Cytochemical investigation by the NBT test was performed in view of determining the neutrophilic function in G6PD deficiency. The material consists of 25 children and adults with G6PD deficiency, 13 heterozygotes and 150 adult controls. The G6PD activity was determined by means of test-reactives prepared by Boehringer. The NBT test was applied according to the method of Peigün and Park. The G6PD activity was found to be 1.3±1.6 UI/10¹¹ ery. in the patients, 11.2±5.8 in the heterozygotes and 15.4±2.9 UI/10¹¹ ery. in the controls. A significant difference in activity was observed between all the groups: p<0.001.

The number of formazan positive neutrophils determined by the NBT test was 32.1±15.5% (1624.3±1123.3/mm³) in the G6PD deficiency cases, 35.7±16.9% (1618.5±1087.7/mm³) in the heterozygotes and 20.1±12.2% (980.787.6mm³) in the controls. The number of formazan positive neutrophils is significantly higher in the G6PD deficiency cases and heterozygotes than in the controls: p<0.001. The difference in the number of formazan positive neutrophils after stimulation by endotoxine, is not significant, the data obtained being 42.3±12.1% (2119.7±1063/mm³) in G6PD deficiency, 50.8±10.3% (2215±1017.8/mm³) in the heterozygotes and 35.8±12.6% (1684.9±900.8/mm³) in the controls.

According to the results obtained by means of the NBT test, it can be concluded that individuals with G6PD deficiency with a higher sensitivity to infections do not show neutrophilic dysfunction.

GRADUAL ESTABLISHMENT OF SPLIT (AUTOLOGOUS B, HOMOLOGOUS T) IMMUNOLOGICAL RECONSTITUTION FOLLOWING TRANSPLANTATIONS OF STEM CELL ENRICHED BONE MARROW FRACTIONS IN A PATIENT WITH C.I.D..

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The diagnosis of C.I.D. with immunoglobulins was made at the age of 15 months in a girl with a positive family history, who suffered from recurrent pulmonary infections and moderate failure to thrive. The number of blood T cells (E. rosettes) was below normal (x̄ 1100 per µl). The in vitro response of the peripheral blood lymphocytes was absent to mitogens and decreased (x̄ 21% of controls) to allogeneic cells. The delayed hypersensitivity skin tests were negative and a skin graft was not rejected. The number of B cells (sIg pos.) was above normal (x̄ 1600 per µl). Serum Ig levels were either normal (IgM, IgG) or increased (IgA, IgD) and of restricted heterogeneity. Isohemagglutinin titres were normal (anti A 1/8, anti B 1/64, bloodgroup O), but antibody formation to protein antigens was lacking. The human serum thymic factor (SF) was normal. Neither excess of suppressor nor lack of helper T cells could be found by in vitro stimulation tests or mixtures of the patient's lymphocytes with lymphocytes of her SD and LD identical brother. Treatment with thymic humoral factor at 22 months of age when the patient's SF level was very low, was unsuccessful. A first transplantation at 27 months of age with a stem cell enriched PHA-negative bone marrow fraction 3 (alb.gradient) of her SD-LD identical brother (bloodgroup A) restored only the cellular immune capacity; also SF levels became normal. A second transplantation at 33 months of age with stem cell enriched PHA-positive bone marrow fraction 4 (alb.gradient; kept at -196°C) restored also the humoral immune capacity. B cells, however, remained of receptor type, as well as the serum Ig allotype, whereas T cells were of donor type (quinacrine Y chromos. staining); anti A isohemagglutinins were no longer present in the serum.