# 23

LEUKEMIA IN GREEK CHILDREN

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Two hundred children with leukemia ,aged 3 months to 14.5 years were examined during the 5 year period January 1972- December 1976. Hundred seventy five children had acute lymphoblastic leukemia (ALL) and 25 had : AML (12), APr.L(7) ,acute myelomonocytic (3) and chronic myelocytic (3). Male:female ratio was 1.47. Forty per cent of the patients were 2 to 5 years old.

Intensive treatment (AL6B 71-11) was applied to 96 of the 175 patients with ALL. Of these 13 did not respond to initial treatment and died during the first 3 months. Of the remaining 83,about 30% are in their first remission more than 3 years, and only one developed leukemic meningitis so far.

Twenty-two of the 25 children with non LL received intensive care. Eleven (50%) died during first trimester. Four are in first remission for 24,28,32 and 33 months (2 AML, 1 APr.L, 1 Ch.ML).

Two of the 200 children developed diabetic coma while on l-asparaginase treatment.

# 24

THE POTENTIAL OF THYMUS HUMORAL FACTOR (THF) TREATMENT OF IMMUNODEFICIENT PATIENTS

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Therapeutic trials with THF in cellular immunodeficient patients were attempted. Peripheral blood lymphocytes (PBL) were separated on Ficoll isopaque gradients and tests of in vitro T-cell functions were performed: 1. E rosette formation 2. Microcytotoxicity of goat anti-human thymic antiserum (ATS) on PBL 3. Leucocyte Migration Inhibition Factor (LIF) production, after challenge with phytohemaglutinin (PHA), Concavalin A (CON A), PPD or Monilia antigen (MON) 4. $^{3}$H-Thymidine uptake after stimulation with PHA and CON-A 5. Intracellular CAMP levels prior to and after stimulation of PBL with trypsin 6.Dermal delayed hypersensitivity reactions in response to PHA, PPD or MON. Treatment was instituted in patients, whose T-cell parameters were reconstituted in vitro by THF, at the dosage of 1 mg/Kg/d for 2-4 weeks: 3 Down's syndrome (D.S.) patients suffering from severe gastrointestinal and respiratory infections; in 2 with Ataxia Telangiectasia (AT), the first having Varicella with pneumonitis, and the second with progressive bronchopneumonia; in 1 child with Acute Lymphatic Leukemia of Childhood (ALC), and life threatening Varicella; in 1 patient with partial Combined Immune Deficiency (CID), and 1 child with Systemic Lupus Erythematosus (SLE), complicated by autoimmune hemolytic anemia. In all patients, T-cell functions were completely or partially reconstituted. Nevertheless only 3/8 patients benefited clinically, including: IDS case, AT with Varicella, ALC with Varicella. It is concluded that THF is a promising immunostimulant in some cases of partial T-cell deficiency, having sufficient T-precursors.

# 25

ACUTE LYMPHOBLASTIC LEUKAEMIA: CORRELATION OF CELL 'MEMBRANE MARKERS' WITH CLINICAL FEATURES AND WITH PROGNOSIS.

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Samples of blood and marrow from 94 newly diagnosed children with ALL were investigated for the presence of cell 'membrane markers'. Four types of ALL were recognised: Group I (75%) common ALL (anti ALL+, Greaves et al. 1977), Group II (12%) T cell, Group III (2%) B cell, Group IV (11%) 'null' cell. The white cell count at diagnosis was $\geq 20 \times 10^9/l$ in 36% of children in Group I but in over 90% of children in the other groups. Massive mediastinal enlargement was a feature of Group II (9/11 patients) and Group IV (4/10 patients). Remission induction was easier in Groups I and II, than III or IV.

Preliminary follow up shows that the initial white cell count influences prognosis in common ALL (Group I) but that children in Group I with a high white cell count have a relatively better prognosis (median complete remission 86 weeks) than children in Group II (median complete remission duration 30 weeks).

Reference
M F Greaves et al., 1977. Membrane phenotyping: diagnosis, monitoring and classification of acute 'lymphoid' leukaemia in Immunodiagnosis of Leukaemias and Lymphomas. Verlag Munich, 1977.

# 26

IN VITRO STUDIES OF BONE MARROW STEM CELL FUNCTION IN URAEMIC STATES

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Anaemia is a frequent symptom in children with chronic uraemia. There is only few information about haemopoietic committed stem cell functions in renal insufficiency. Therefore we tested the ability to form granulopoietic and erythropoietic cell colonies in vitro in children with chronic uraemia.

Following separation of mononuclear cells from bone marrow aspirates by Ficoll Isopaque gradient centrifugation granulopoietic precursor cells were stimulated in soft agar gel using feeder layers of normal human leukocytes as source of colony stimulating factors. Erythropoietic precursor cells were stimulated in plasma clots by erythropoietin. The cells were identified by staining methods (Pappenheim respectively Lepehne) and counted.

Quantity and proliferative capacity of isolated granulopoietic and erythropoietic stem cells were not suppressed in the tested children. Under in vitro conditions the responsiveness of erythroid precursor cells to erythropoietin seemed to be normal. After adding autologous serum different degrees of inhibition of colony formation of erythropoietic stem cells resulted. The observed existance of inhibitory activity in sera of uraemic children may be one important factor in the pathogenesis of anaemia in chronic renal failure.

# 27

THE BERLIN-WEST ALL STUDY AFTER 7 YEARS AND ITS 3 YEARS' CONTROL IN MÜNSTER/WESTFALEN AND FRANKFURT/MAIN.

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In sequence 141 children and adolescents with previously untreated ALL (78 males, 53 females, 1 month to 16 years, median age 5 10/12 years) entered this cooperative study between Oct. 70 and Sept. 76. All patients (Berlin group 73, Münster/Frankfurt group 68 pts.) were treated according to the Berlin-West induction protocol (Riehm et al., Klin. Päd., 189: 89 (1977)). Maintenance therapy was applied in two modifications (Berlin: cyclic sequential application, Oct. 70 - May 76; Münster/Frankfurt: combined application, Oct. 74 - Sept. 76). 134/141 pts. achieved complete remission (CR), 7 were non-responders or died within 4 weeks. Death in CR occurred in 8/134 pts., all within 4 months after diagnosis. As to July 1st, 77, 92/126 pts. are in continuous complete remission (CCR) between 9 mths. and 6 9/12 yrs. The cumulative index for 7 yrs. CCR calculated by the life table method is 0.59 with as yet no difference between the two groups with different maintenance therapy. 34/126 pts.(27%) relapsed between 4 and 59 mths. after diagnosis (19x bone marrow, 10x CNS, 3x bone marrow/CNS, 2x testis). In pts. with WBC at diagnosis $< 25$ G/l the 7 yrs. cumulative index for CCR is 0.70 (66/77 pts. in CCR) and in those with WBC $> 25$ G/l 0.41 (26/49 pts. in CCR). 104/141 pts. survive (74%), the cumulative index for survival after 7 yrs. is 0.67. For comparison, the 3 yrs. cumulative indices for CCR (126 pts.) and survival (141 pts.) are 0.69 and 0.74 (Berlin) and 0.76 and 0.71 (Münster/Frankfurt).

# 28

LYMPHOCYTE MEDIATED CYTOTOXICITY AND BLOCKING SERUM ACTIVITY AFTER BONE MARROW TRANSPLANTATION FOR SEVERE APLASTIC ANEMIA IN CHILDREN.

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Studies were done to investigate whether peripheral blood lymphocytes, obtained from children who had received a successful bone marrow transplantation show an in vitro cytotoxic effect towards target cells of the recipient, to see if such cytotoxicity can be blocked by serum factors from the recipient and to test the possible correlation between the degree of lymphocyte cytotoxicity, the presence of blocking serum factors and the occurrence of graft versus host disease.

Lymphocytes and serum, collected from 7 patients with regular time intervals before and during 1 year after transplantation, were kept deep frozen and tested in one experiment. The test system used was the Takasugi-Klein microcytotoxicity assay using fibroblasts as target cells. Results show clearly that after successful bone marrow transplantation, lymphocyte cytotoxicity is present towards recipient antigens, which cannot be blocked by recipient serum. There appears to be no correlation between the degree of cytotoxicity and the occurrence and severity of graft versus host disease. In all patients cytotoxicity subsides after some time, ranging from 3 till 8 months after transplantation. Additional studies indicate that the occurrence of cytotoxicity towards recipient antigens cannot be explained by assuming the absence of suppressor cells. The difference between the in vivo and in vitro situation cannot yet be explained.