41 THE EFFECT OF ASCORBATE ON SEVERAL BLOOD CELL FUNCTIONS IN THE CHEDIAK-HIGASHI SYNDROME.

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The Chediak-Higashi (CH) syndrome is an autosomal recessive disorder, issociated with oculo-cutaneous albinism, recurrent pyogenic infections, ieutropenia, increased bleeding tendency and the occurrence of a lymphoma-like accelerated" phase. Characteristicly, giant granules are ound in all granule-containing cells.

We have examined a patient with the CH-syndrome with defects in chemoactic responsiveness and bactericidal activity of the neutrophils (PMN), n the aggregation of the platelets and in the antibody-dependent lymphoytotoxicity. These defects may be explained by abnormal microtubule issembly and/or membrane fluidity. Administration in vivo or in vitro of iscorbate corrected the elevated cyclic AMP levels and the various funcions of the neutrophils, partially corrected the arachidonic-acid-induced latelet aggregation, but had no effect on lymphocytotoxicity. Clinically, dramatic reduction in the number of episodes with recurrent infections vas observed during ascorbate treatment.

42 POSSIBLE INVOLVEMENT OF AN ELECTRON TRANSPORT SYSTEM IN SUPEROXIDE GENERATION BY RESTING AND PHAGOCYTIZING HUMAN GRANULOCYTES.

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The role played by NADH and/or NADPH in generation of superoxyde nion in normal granulocytes remains a controversy. We studied yridinodependent O2-production and NADH/NADPH consumption in ubcellular fractions from resting and phagocytizing human polyorphs. O2-production was 1.5 to 2 fold higher in fractions from hagocytizing cells with both cofactors. It was 10 fold higher ith NADH than with NADPH. NADH was also more consumed by the ytem. Effects of several agents such as Cu++, Mn++, superoxyde ismutase, manitol, histidine and diéthyldithiocarbamate will e discussed. We studied more accurately the significance of ADH requirement for O2-generation. In entire polymorphs, otenone and antimycine A had a strong inhibitory effect on the uperoxyde formation in resting as well as in phagocytizing ells. In subcellular fractions, antimycin partially inhibited he NADH dependent O2-production while rotenone had no effect.

hese data suggest : 1) that the pyridinodependent O2-forming ystem could involve multiple metabolic pathways, 2) that the ADH dependent O2-production can be partly attributed to an lectron-transport system such as described by Boveris and anedas.

43 ANTIBODY TREATMENT OF MARROW GRAFT IN VITRO: A PRINZIPLE FOR PREVENTION OF GvH DISEASE.

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Graft-versus-Host disease (GvHD) is still a frequent complication in clinical marrow transplantation. Advances in immunology have delineated the causal role of thymus-derived (T) lymphocytes in GvH reactions. Attempts have been made to reduce T-cells by treating the bone marrow itself in vitro after reparation. Experimental studies of our group showed that in mice an in vitro treatment of incompatible donar cells with T-cell specific antibodies before transplantation could supress an otherwise lethal GvH-reaction completely. The GvH-reactive T-lymphocytes are removed by a specific xenogenic antiserum against T-cells which had been purified from antibodies cross reacting with hemopoietic stem cells by an extensive absorption procedure.

The present report will summarize the application of this principle to clinical bone marrow transplantation: A case of a 11 year old girl with a second relapse of common acute lymphoblastic leukemia was successfully transplanted after marrow incubation with anti-T-cell globulin.

44 THYMIC HUMORAL FACTOR (THF) THERAPY IN A PATIENT WITH DI GEORGE SYNDROME

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A total of 55 doses of THF (1.5 mg/kg/day) was given to a 5.5 month old male with Di George Syndrome.Skin tests (for PHA and Candida) were negative,E rosettes were low (24%),blastogenic transformation response to PHA and allogeneic lymphocytes were low prior to therapy. He had a low level of circulating thymic factor (5.0 pmoles/10^7 cells) and a marginal stimulation of target cells. E rosettes showed a 59 percent increase after incubation (in vitro) with THF. No side effects of THF was observed. Despite a clinical well being and weight gain,episodes of gastroenteritis and otitis continued. After THF treatment (at age of 10 months) percentage of E rosettes (56%) and in vitro lymphocyte response to PHA were increased; skin test for PHA became positive. But no improvement in in vitro response to candida and allogeneic lymphocytes was observed.

45 SPECIFIC IMMUNE CAPACITY IN CHILDREN WITH APLASTIC ANEMIA.

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The specific immunological capacities in 32 children, suffering from aplastic anemia were investigated at the time of diagnosis. The mean number of bloodlymphocytes was low i.e. 1.9 x 10^9/l; several patients had a lymphocytopenia. In 16 patients lymphocyte subpopulations in the peripheral blood were investigated: the absolute numbers of T cells were within the normal range; the absolute numbers of B cells were low. The serumimmunoglobulin levels for the different Ig classes were within the normal range. The in vitro response of bloodlymphocytes following stimulation with PHA and ALS, and following stimulation with allogeneic cells was normal. In contrast, the response of bloodlymphocytes to PWM and Con-A was significantly (α <0.05) dedreased, as was the stimulatory capacity in the MLC, in comparison with normal controls. In 13 children treated for their severe aplastic anemia with bone marrow transplantation these in vitro lymphocyte responses to mitogens were significantly (α <0.05) decreased in comparison with the data from their MLC identical bone marrow donors. A positive correlation between these findings and the absolute numbers of monocytes in the blood and in the in vitro cultures was found. An indication was present for a possible relationship between some of the immunological findings and the course of children with aplastic anemia, either on medical treatment or after bone marrow transplantation.

46 ELEVATED RED CELL ADENOSINE DEAMINASE ACTIVITY IN DOWN'S SYNDROME.

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The blood level of uric acid is in many studies shown to be elevated in patients with Down's syndrome. Lack of adenosine deaminase (ADA, E.C. 3.5.4.4) in red cells and lymphocytes is a regular finding in a form of congenital combined immunodeficiency. Lowered resistance to infections is also a characteristic of Down's syndrome. Tests measuring cell-mediated and humoral immune response have shown abnormalities.

We have studied ADA activity of erythrocytes in 29 cases of Down's syndrome and in 29 age- and sexmached controls. ADA activity was assayed kinetically by a coupled enzymatic system, in which adenosine is converted into inosine with uric acid as the final product.

The mean activity of ADA in Down's syndrome was 1883±463 mU/gHb (37°C) and 1361±294 in the controls. The difference is highly significant ($p < 0.001$).

The study indicates abnormal metabolism of purines in Down's syndrome. Further characterization of this abnormality is in progress.