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, associated with oculocutaneous albinism, recurrent pyogenic infections, neutropenia, increased bleeding tendency and the occurrence of a lymphoma-like accelerated phase. Characteristically, giant granules are found in all granule-containing cells.

We have examined a patient with the CH-syndrome with defects in chemotactic responsiveness and bactericidal activity of the neutrophils (PMN), in the aggregation of the platelets and in the antibody-dependent lymphocytotoxicity. These defects may be explained by abnormal microtubule assembly and/or membrane fluidity. Administration in vivo or in vitro of ascorbate corrected the elevated cyclic AMP levels and the various functions of the neutrophils, partially corrected the arachidonic-acid-induced platelet aggregation, but had no effect on lymphocytotoxicity. Clinically, a dramatic reduction in the number of episodes with recurrent infections was 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 superoxide anion in normal granulocytes remains a controversy. We studied pyridinoddependent O₂-production and NADH/NADPH consumption in subcellular fractions from resting and phagocytizing human polymorphs. O₂-production was 1.5 to 2 fold higher in fractions from phagocytizing cells with both cofactors. It was 10 fold higher with NADH than with NADPH. NADH was also more consumed by the system. Effects of several agents such as Cu⁺⁺, Mn⁺⁺, superoxide dismutase, manitol, histidine and diethyldithiocarbamate will be discussed. We studied more accurately the significance of ADH requirement for O₂-generation. In entire polymorphs, rotenone and antimycin A had a strong inhibitory effect on the superoxide formation in resting as well as in phagocytizing cells. In subcellular fractions, antimycin partially inhibited the NADH dependent O₂-production while rotenone had no effect.

These data suggest: 1) that the pyridinoddependent O₂-forming system could involve multiple metabolic pathways, 2) that the ADH dependent O₂-production can be partly attributed to an electron-transport system such as described by Boveris and Cadenas.

43 ANTIBODY TREATMENT OF MARROW GRAFT IN VITRO: A PRINCIPLE 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 donor cells with T-cell specific antibodies before transplantation could suppress 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/10⁷ 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. A.M.P. Koolen, L.J. Dooren and J.M. Vossen.

The specific immunological capacities in 32 children, suffering from aplastic anemia were investigated at the time of diagnosis. The mean number of blood lymphocytes was low i.e. 1.9 x 10⁹/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 serum immunoglobulin levels for the different Ig classes were within the normal range. The in vitro response of blood lymphocytes following stimulation with PHA and ALS, and following stimulation with allogeneic cells was normal. In contrast, the response of blood lymphocytes to PWM and Con-A was significantly ($\alpha < 0.05$) decreased, 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 ($\alpha < 0.05$) 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 sex-matched 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.