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CHRONIC GRANULOMATOUS DISEASE (CGD): ISOLATED DEFECT OF THE NADPH-OXIDASE ACTIVITY IN NEUTROPHILS.

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CGD is characterized by deficient membrane bound NADPH-oxidase activity in phagocytes. These patients suffer from severe recurrent bacterial and fungal infections. In a boy with typical clinical history of CGD, investigations of his total leukocytes showed reduced cytochemical nitrobluetetrazolium (NBT)-reduction (30-48 % NBT-positive phagocytes), decreased O_2^--production in response to the phorbolester PMA and low glucose oxidation. Because in typical CGD-patients at least 99 % of the phagocytes are NBT-negative, we suspected a variant of CGD. Extensive examinations in pure (> 98 %) preparations of polymorphonuclear leukocytes (PMN) gave results compatible with classical CGD: absent production of chemiluminescence and oxygen metabolites (O_2^-, H_2O_2) after stimulation with PMA and opsonized zymosan, low glucose oxidation, decreased bactericidal capacity and 99 % NBT-negative PMN. However, in monocytes of the patient, a nearly normal PMA-induced O_2^--formation has been found (11.4 nmole O_2^-/h/2x10^5 cells, controls 18.2±2.3). The same was true with H_2O_2-production. In addition the patient's macrophages, cultivated in a long term culture, similarly released oxygen metabolites after stimulation of the respiratory burst with either PMA of opsonized zymosan. We demonstrate here an isolated defect of the NADPH-oxidase activity in neutrophils of a patient with CGD.

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PRENATAL DIAGNOSIS OF X-LINKED SEVERE COMBINED IMMUNODEFICIENCY (SCID) BY FLOWCYTOMETRIC INVESTIGATION OF FETAL BLOOD

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Prenatal diagnosis of SCID has until now been limited due to the inability of obtaining sufficient fetal blood volumes for immunological investigation. - We report the diagnosis of X-linked SCID at 19 weeks of gestation by using 200µl fetal blood for flowcytometric evaluation. Amniocentesis was performed in the 17th week of pregnancy on a 36 year old woman with positive family history for X-linked SCID. Chromosome analysis revealed a normal male caryotype. To confirm the suspected diagnosis of SCID a fetal blood sample was taken by puncturing the umbilical cord vein under sonographic control at 19 weeks of gestation. 300µl were used to perform chromosome analysis, the remaining 200µl were prepared for flowcytometry. Whole blood was stained with a combination of phycoerythrin and fluorescein-conjugated monoclonal antibodies to leukocyte surface antigens (Leu2, Leu3, Leu4, Leu7, LeuM3, HLA-Dr). Simultaneous two color flowcytometric analysis showed virtually no T-cells consistent with a diagnosis of SCID. Pregnancy was interrupted and the diagnosis confirmed after fetal autopsy. - Our data demonstrate that flowcytometry provides a reliable tool for early prenatal diagnosis of immunodeficiencies requiring minimal blood samples.

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ELEVATED LEVELS OF TUMOR NECROSIS FACTOR (TNF) IN ADOLESCENTS ON HEMODIALYSIS (HD)

TNF is a cytokine released by activated monocytes exerting a number of reactions that may occur during HD (fever, neutropenia, monocytopenia, vascular endothelial lesions). We measured serum levels of TNF in 6 adolescents aged 14-21 years undergoing regular HD 5 min before and 15 min after start of the procedure with cuprophane membranes. Before HD TNF could not be detected in measurable amounts. In contrast, 5 of 6 sera taken after start of the HD session we found significant amounts of TNF (1045-7000 pg/ml serum). Our results suggest that TNF is released by HD. Therefore the above mentioned side effects of HD may be related to the action of TNF. The high TNF levels may also contribute to the development of autoantibodies or the persistance of cytotoxic antibodies in HD pts.

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Aerosol Challenge of Sensitised Rats increases the Permeability from the Lumen in Life.

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Aerosol challenge of sensitized rats leads to an apparent increase in permeability of the fixed trachea (Clin Exp Immunol 1986; 65:647). The present study was undertaken to show that this increased permeability occurs because of increased porosity of the luminal surface in life. Rats were sensitized with DNP_{19} ovalbumin (DNP-OA) or saline. There were exposed to an aerosol of DNP-OA plus lanthanum nitrate for 1 hour. Tracheas were processed immediately after challenge. The elemental lanthanum concentration was measured by X-ray microanalysis with KeVex 5,000 A/6,000 spectrometers. The lanthanum penetrated between the cells. Its concentration was greatest at the airway surface and decreased progressively towards the cartilage. More lanthanum was present in the epithelium of 6 DNP-OA sensitized rats (42.9 ±6.0 counts/100 sec) compared to 6 controls (11.9 ±1.5 counts/100 sec), ($P<0.01$, Mann-Whitney). The DNP-OA sensitised group showed a more severe response on body plethysmography. There is an increase in permeability of the luminal surface of the trachea on challenge with aerosol antigen, probably as a result of the opening of the intercellular junctions. (Wellcome Trust Supported).

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Clinical data of 1318 asthmatic crises treated in the Pediatric Emergencies Service of Hospital de Ntra. Sra. del Mar (Barcelona) between January 1st. 1983 and December, 31, 1985, have been examinated.

Age, sex, number of hospitalised cases related to the total emergencies have been analysed, and a correlation is established with air pollution, meteorological data and pollen levels. The highest incidence of bronchoespastic processes has been observed in autumn. No significant relation is observed between asthmatic attacks and meterological data or pollen levels. During the highest contaminated days the number of asthmatic attacks does not increase, but there is a significant association between asthmatic crises in children over 3 years old and the SO_2 level ($p= 0.003$).

Bronchoespastic processes in children under 3 years old are influenced by temperature ($p< 0.0001$), february is the coldest month and the highest incidence occurs.

These results must be considered with caution. Only the continuity of the study in the next years can provide definitive conclusions.

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The effects of major surgery on lymphocyte subsets in infancy and childhood

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A study was designed to test the hypothesis that the lymphopenia caused by surgical stress in children may arise through selective depletion of one or more lymphocyte subsets.

Blood samples from 18 children were taken pre- and post-operatively and 6, 12, 24 and 48 hours after surgery. Lymphocyte subsets were identified and counted using monoclonal antibodies and indirect immunofluorescence.

By 6 hours post-operatively, the mean total lymphocyte count had fallen by $2.04x10^9/l$ ($p<0.01$); this was largely due to the fall in helper T-cells ($1.70x10^9/l$, $p<0.01$) and both counts remained depressed for at least 48 hours. The helper:suppressor ratio also fell, from 3.19 to 2.16 ($p<0.01$), but had recovered by 48 hours. The changes were independent of age.

Major surgery in infants and children causes a selective reduction in helper T-lymphocytes with a corresponding decrease in the helper:suppressor ratio, suggesting a reduced immune competence in the immediate post-operative period. The duration of this and its relationship to infection are not yet known.