73 L. BUSINCO,F. LAURENTI,P. ROSSI,F.MARCHETTI,E. GALLI,C. MIDULLA,F. AIUTI. Department of Pediatrics and Internal Medicine III, CNR Centre for Respiratory Viruses,ROME,ITALY. Levamisole treatment in a case of Job's Syndrome: clinical and immunological results.

The clinical and immunologic features of a six-year-old girl with a lifelong history of severe atopic dermatitis, asthma, recurrent otitis media, staphylococcal infections and disseminated "cold" skin abscesses were reported. A cellular defect in neutrophil chemotaxis, hyperimmunoglobulinemia E, specific IgE antibodies against cow milk associated with T lymphocyte dysfunction were found. Moreover the patient lacked serum IgM and staphylococcal agglutinins. Other neutrophil functions as well as Complement fractions C_3, C_3PA and C_4 were normal. Levamisole therapy (2,5 mg/Kg three days weekly for three months) induced a markedly clinical improvement. The skin lesions and staphylococcal abscesses gradually resolved and the patient gained weight. After the therapy a significant enhancement of PMN chemotaxis and T Lymphocytic functions were demonstrated, while serum IgM and staphylococcal agglutinins were still absent.

74 T.Hovi[x], C. Holmberg[x], A. Ranki[x], P. Häyry[x], J. Rapola[x] and E. Savilahti[x], Department of Virology, Children's Hospital, Transplantation Laboratory, University of Helsinki, Finland. Combined immunodeficiency associated with adenosine deaminase enzyme with altered kinetic properties. (Introduced by Prof. Kari Launiala)

About one half of patients with severe combined immunodeficiency also have a hereditary defect in adenosine deaminase (ADA). We report a child with fatal combined immunodeficiency and erythrocyte ADA with altered kinetic properties. The patient developed normally until the age of 6 months. Since then she had chronic candidiasis, recurrent respiratory infections and pneumonias, and her growth retarded. No thymic shadow was seen in chest x-rays at the age of 13 months; slight abnormalities in the bones were noted. Serum levels of IgG, IgA and IgM were low and total lymphocyte counts were at times subnormal (2000-370/mm^3). The proportion of T lymphocytes was decreased (24-26%) while that of B lymphocytes was elevated (42%). Several mitogens were used to stimulate the lymphocytes in vitro but no responses were obtained. The patient died of protracted bloody diarrhoea and septic infection at the age of 15 months. In autopsy, the thymic lobuli were small with no Hassal's corpuscles and only scattered thymocytes. The specific activity of ADA in the patient's erythrocyte lysates was 3-10 times the mean of normal values in all three blood samples tested. The apparent Michaelis coefficient (K_m) for adenosine was higher than that of ADA of normal individuals (80μM vs. 35-40μM). This kind of enzymatic change might result in increased cellular synthesis of adenine nucleotides, as it happens in the absence of ADA.

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Cyclic AMP production in mouse lymphocytes in response to L-Norepinephrine.

Congenital athymic nude /nu/nu/,heterozygous /nu+/ and BloA 6 weeks old mice were used for studies on their response to L-Norepinephrine.In twelve experiments cell suspension of lymphnodes were prepared and the cells were incubated in culture medium containing 1.o or o.1 mM L-Norepinephrine./2-8³H/-adenine was used and net cyclic AMP production was measured after deproteinisation by thin-layer chromatography.Lymphocyte basal cyclic AMP content /expressed in pM cyclic AMP/1o⁷cells/ was 4.o±o.53 in the nu/nu group,17.75± 9.6 in the nu/+ lymphocytes and 11.12±1.3 in BloA animals.Incubation for four minutes with 1.o mM L-Norepinephrine produced an increase of 218 per cent /38.75±9.5/ in nu/+ and 586 per cent /65.25±12 / in BloA lymphocytes.o.1 mM L-Norepinephrine resulted in 3o2 per cent increase of cyclic AMP content /53.66± 16/ in nu/+ and 971 per cent /1o9.o±25/ in BloA animals.In contrast,athymic nude lymphocytes did not show any significant cyclic AMP content change in response to L-Norepinephrine at any concentrations.The results suggest,that primarily T cells are involved in the cyclic AMP response induced by L-Norepinephrine.

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Immunogenetic base of congenital malformations:association of HLA-B27 with spina bifida.

A random sample of 46 families with single and multiple cases of spina bifida has been selected from families referred to Institute Pediatrics for genetic counselling.This sample constituted a group of 92 parents and 102 offsprings /41 normal,48 with spina bifida and 13 with spina bifida occulta/.Routine HLA typing was perfomed in the parents and their children.Foreach case,13 HLA specifities from locus A and 15 from locus B were determined.Segregation analysis in families showed excellent agreement with the expected values.HLA gene frequencies in the affected children as compared with a control population of 240 normal adults,revealed significantly higher frequency for HLA-B27 allele:Chi square = 11.958, p /corrected for the number of alleles/ < 0.027.A significant relative risk of spina bifida development for a given HLA-B27 antigen was 2,7. In view of the presented results a routine HLA typing might be recommended for genetic counselling as a new tool for identification of high risk families.

77 Dependency of sulfatide synthesis upon Glucose and D-βOHbutyrate concentration in the medium of dissociated mouse brain cell cultures.

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Sulfatide Synthesis (SfS) serving as an indicator for brain cell development was assessed as $^{35}SO4$ incorporation into sulfatide of dissociated brain cells. These were gained at birth and cultured for 13 days at which age SfS is active in vivo and in vitro. SfS was expressed as dpm ^{35}S-sulfatide/mg cell protein. The effect on SfS of varying concentrations of Glucose and D-βOHbutyrate in the medium between 10 and 13 days in culture was studied and compaired to control cultures containing the usual Glucose concentration in brain cultures (27 mM). SfS was dependent upon Glucose concentration being 55± 24% of controls at 6.5 mM, 16± 7% at 4.2 mM and 7± 5% at 0 mM Glucose (all sign. different from controls, $p < 0.001$). D-βOHbutyrate (2.1 and 4.2 mM) was able to replace Glucose allowing a SfS of 19± 13% and 22± 10% (sign. different from 0 mM Glucose, $p < 0.005$). Addition of D-βOHbutyrate-3-C^{14} (specific activity 1 μCi/4.2 mM) yielded $^{14}CO2$ corresponding to an utilization of 4.5 μg D-βOHbutyrate/mg protein/3 hours through the Krebs cycle indicating that D-βOHbutyrate was used as a source of energy. This system of cultured brain cells may serve as a model to study the effect of various fuels on brain cell metabolism and development.

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Reduction of oxidized glutathione (GSSG) in azoester treated red cells of neonates and of adults.

The rates of GSSG reduction are compared in isolated red cells of neonates and adults after treatment with methyl phenylazoformate according to Kosower with the following modifications: Final azoester concentrations 2.7 and 6.8 mM, incubation with glucose at 22°C, measurement of GSSG at 0,25 and 60 min, graphic determination of the GSSG half time (t 1/2) on a semilogarithmic scale. t 1/2 in red cells of adults and neonates after addition of 2.7 mM azoester was 13.3 ± 3.1 and 14.8 ± 3.6 min, respectively ($n = 6$; $p > .40$). Significant differences between neonates and adults became evident, when using 6.8 mM azoester, by which not only the oxidation of intracellular GSH, but also an alteration of cellular membranes is produced: Whereas t 1/2 in adult red cells increased only slightly, to 19.6 ± 3.9 min, the increase in neonatal red cells was more marked, to 34.7 ± 8.7 min ($n = 13$; $p < .001$). The increase was less marked in young compared to old cell populations of neonates (26.6 ± 8.7 and 36.1 ± 10.9 min, respectively; $n = 5$; $p < .025$). The data provide further indirect evidence, that differences in glutathione metabolism between red cells of neonates and adults are due to different membrane properties rather than to differences in the intracellular metabolism.