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NEW INSIGHTS INTO THE PATHOGENESIS OF APPENDICITIS BASED ON IMMUNOCYTOCHEMICAL ANALYSIS OF EARLY IMMUNE RESPONSE

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Although appendicitis is the most common condition requiring surgery, the pathogenesis of this disease is poorly understood. In this study we investigated in an animal model and in humans, the possibility that an effector immune response to local antigen stimulation could be a significant mechanism in the development of appendicitis.

Polymorphonuclear leukocytes (PMN), plasma cells and T-cell infiltration was measured in 24 New Zealand bred white rabbits following experimental obstruction of the appendiceal lumen for periods ranging from 30 minutes to 24 hours. T-cell infiltration was the most dominant earliest infiltrating cell type of the lamina propria occurring at 30 minutes after obstruction. Significant infiltration ($p<0.01$) of the remaining cell types occurred as follows: IgM and IgG plasma cells at 30 minutes after obstruction and IgA and PMN at 2 hours.

Lymphocyte infiltration was also seen as the earliest immunopathological event in a study of 15 acute suppurative appendiceal specimens and 5 specimens with only focal appendicitis compared to 5 histologically normal appendices. Equally significantly increased levels ($p<0.01$) of T_H cells, IL-2 positive cells as well as plasma cell isotypes IgG and IgA infiltration of the lamina propria was seen throughout the entire resected organ of patients with focal and acute suppurative appendicitis compared to histologically normal appendices. Significant PMN, monocyte and NK cell infiltration was only present in acute suppurative appendicitis. These findings suggest the probability of a specific immune response to lumen derived antigens as a triggering factor in acute appendicitis.

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The role of ionic transport in the respiratory burst activation in human polymorphonuclear granulocytes

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The role of ionic transport in the respiratory burst activation in polymorphonuclear granulocytes was investigated by measuring of superoxide anion production by the cells stimulated with 10^{-7} M FMLP varying the ionic composition of the suspending medium (KRPD).
It has been found that the external cationic concentration change had no significant effect on spontaneus and FMLP stimulated superoxide anion production of granulocytes measured continously by recording ferricytochrome c reduction. However inhibition of Na^+-K^+--pump by Ouabain in the concentration of 10^{-4} M resulted slight decrease in superoxide anion production of granulocytes stimulated with FMLP.
Replacement of external chloride anion with saccharose or blocking the chloride influx across the plasma membrane by Antracenum hydrochloricum in the concentration of 5×10^{-3} M resulted significant decrease of FMLP stimulated superoxide anion production measured by ferricytochrome c or nitroblue tetrasolium reduction.
It has been conclude that the extra- and/or intracellular chloride anion can influence on the respiratory burst activity of FMLP stimulated human neutrophil granulocytes.

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NEONATAL NECROTIZING ENTEROCOLITIS (NEC): PREVENTION AND TREATMENT IN LBW INFANTS BY ORAL IgG ADMINISTRATION.

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NEC represents one of the major causes of morbidity and mortality in LBW, preterm neonates. We evaluated the efficiency of oral monomeric IgG administration in its prevention and treatment. Twenty-eight newborns of birth weight less than 1500 g and gestational age of less than 34 weeks were randomly studied. According to the protocol used, 500 mg IgG divided in 5 doses was given per os for the first two weeks of life. None of the 15 treated infants developed NEC. In the control group, we had 3 cases of NEC ($p<0.05$), and 3 babies with GI-transit problems and intestinal distension requiring prolonged fasting. Eight neonates with NEC were randomly assigned to an oral trial of IgG for 15 days with a dosage of 500 mg per day for those weighing less than 1500 g, and 1000 mg for those more than 1500 g. None of the treated newborns needed surgery, all having a positive disease course, and no late complications. Of the four controls, two needed surgery and one abdominal drainage. No newborns in the study died.

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IMMUNE FUNCTION IN GROWTH HORMONE-DEFICIENT CHILDREN TREATED WITH BIOSYNTHETIC GROWTH HORMONE.

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Conflicting data regarding the immune function in growth hormone (GH) deficient children or changes in immunological parameters during substitutive GH therapy have been reported. We have looked at the immune function in 13 patients with GH deficiency, before and during treatment with biosynthetic GH (12IU/m2 b.s./week) at 6 and 12 months of therapy. We found that absolute number of total T and T-lymphocyte subsets (using monoclonal Ab as markers), Natural Killer cell activity (target K562) and response of lymphocytes to polyclonal mitogens (PHA, ConA, PWM) were all in the normal range and so remained after 6 and 12 months of treatment. Absolute number of B lymphocytes (monoclonal Ab) was in the normal range before treatment and after 6 months of therapy but dropped significantly ($p<0.001$) after 12 months of treatment. Serum immunoglobulins (IgG,IgA,IgM) did not show a parallel drop remaining normal throughout the whole study. Our data seem to confirm that,as evidenciated clinically by the lack of undue susceptibility to infectious agents in GH deficient patients, immune function is intact in these children and it is not suppressed by GH treatment. Although a drop in B lymphocytes was observed, the normal level of Igs and the normal functional response to PWM seem to demonstrate the maintenance of a normal specific humoral immunity.

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PRECISION OF CEREBRAL BLOOD FLOW (CBF) MEASUREMENT BY NEAR INFRARED SPECTROSCOPY (NIRS).

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We recently described a new method for the cotside measurement of CBF in sick newborn infants using NIRS (Lancet 1988;ii:770). The method is based on the Fick principle and uses small changes of inspired oxygen concentration to cause changes in cerebral oxyhaemoglobin concentration ($DHbO_2$). $DHbO_2$ behaves as an intravascular tracer which can be observed using NIRS. Measurements made on the adult forearm by this method and be venous occlusion plethysmography showed good correspondence (n=14, $y=0.91x+0.16$, $r=0.94$, $p<0.001$). (J. Physiol., in press.)

A computerised Monte Carlo simulation of the method predicts an intra-subject coefficient of variation (cv) of 16%. We have estimated cv from repeated measurements (4-10, median 7) in 8 sick but stable infants (gestation 26-29 weeks; age 1-12 days). Mean CBF ranged from 8 to 20 ml/100 g.min (median 17.5). The intrasubject cv ranged from 8% to 27%, mean 18%.

NIRS thus allows repeated, non-invasive measurements of CBF at the cotside with acceptable precision. It has the potential to be a practical clinical and research method.

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EFFECT OF SYMPATHETIC INNERVATION ON CEREBRAL BLOOD FLOW AUTOREGULATION IN THE NEWBORN PIGLET.

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To evaluate the role of the sympathetic nervous system (SNS) in cerebral blood flow autoregulation (CBF-AR) in the neonatal period, CBF was measured (microspheres) at different levels of mean arterial blood pressure (MABP) within the normal range for AR (blood withdrawal), following ablation of the right superior sympathetic ganglion in 6 piglets (1.5±0.3 g) and compared to 6 controls (1.6±0.1 kg).

In denervated animals, prior hypotension, CBF is significantly greater than in controls (table); during hypotension, for MABP above 50 mmHg, CBF and MABP are positively correlated showing a loss of AR [CBF (ml/min/100 g) =5.76 MABP (mmHg)-261, r=0.85, p<.001]. When MABP drop further, CBF remains stable showing the presence of AR as observed in control animals.

MABP (mmHg)		≤45	46-55	56-65	>65
CBF	Controls	58±20	49±6	64±19	51±4
(ml/min/100g)	denervated	49±7	37±9	97±38	176±34*

These data show a shift of the upper limit of the AR range in denervated animals which suggests a poor adaptation to high MABP. Because of the absence of differences between the two hemispheres, it is suggested that innervation is blunt only in large vessels supplying the willis circle; an immaturity of the innervation of the distal arteries could explain this finding.

M±SEM, $p<0.01$ vs controls.