## 35 THE MAJOR ALLERGEN, Der p I, OF THE HOUSE DUST MITE IS A SECRETORY PRODUCT OF THE MITE ALIMENTARY CANAL.

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Der p I has been described as the major allergen from the house dust mite (Dermatophagoides pteronyssinus). Its major source is the mite faecal particles. Little is known about its natural synthesis and nothing about its site of production within the mite. It could be present in the faeces either as a bi-product of food degradation in the alimentary canal or as a result of synthesis and secretion by the alimentary or excretory systems.

Pure cultures of mites were grown on bovine serum albumin (BSA). Cultures were examined at 1, 3, 7, 14 and 21 days after $^{125}$I-BSA was introduced to the cultures. The proteins were separated by chromatofocussing and characterised by immunodiffusion and electrophoretic techniques. Counting of protein fractions with an LKB rack gamma counter demonstrated that the Der p I protein peak only acquired significant radioactivity from the 14th day. If the protein was a digestive product, it would probably have appeared earlier. The mite body allergens became radioactive after a similar lag.

The slow incorporation of the radiolabel suggests that Der p I is synthesised and secreted by the gastro-intestinal or excretory tracts.

## 36 IgG subclass antibody production to milk and egg antigens during infancy.

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The type of antibody produced to foods during infancy may predict or influence the subsequent development of food intolerance and atopic disease. We therefore studied IgG antibody production to two common food antigens in 191 unselected healthy term infants. IgG1,2,3 and 4 subclass antibodies to bovine casein and to ovalbumin were measured by an enzyme linked immunosorbent assay on sera collected at 7 days, 3 months and 1 year of age.

Antibodies to casein were detected in all IgG subclasses. They were low at 7 days [mean IgG1 261, IgG2 52, IgG3 54, IgG4 125U/ml] and had risen by 3 months [mean IgG1 2325, IgG2 95, IgG3 130, IgG4 376] with similar levels at 1year. In contrast ovalbumin antibodies were restricted to IgG1 & 4. The levels on day 7 [mean IgG1 1001, IgG4 716 U/ml] had fallen by 3 months [mean IgG1 287, IgG4 108] but had risen again by 12 months [mean IgG1 836, IgG4 135]. The predominant subclass to both antigens was IgG1.

We have investigated the relationship of IgG antibody production to maternal antibody levels and to infant feeding practice. Seventeen infants showed defective yeast opsonisation, an abnormality associated with atopy. IgG subclass production in these infants was similar to the group as a whole and to matched controls.

## 37 Intestinal transepithelial passage of bovine milk protein antigens in vitro.

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In bovine milk intolerance β-Lactoglobuline (β-Lg) is more allergenic than α-Lactalbumine (α-La) and β-casein (β-cas). We studied the two major limiting steps to the transfer of the milk protein antigens to blood, i.e. hydrolysis and epithelial permeability. Methods : In vitro pepsin-trypsin hydrolysis was measured by disappearance of protein antigens (ELISA) and appearance of α-NH2 residus. The transepithelial fluxes for antigenic determinants (ELISA) and degraded products (isotopic measurment) were performed in isolated stripped rabbit ileum in Ussing chamber in vitro. Results : Pepsin-trypsin hydrolysis showed an increasing resistance in the order β-cas < α-La < β-Lg. The rate of intracellular hydrolysis was in the same order (β-Lg the most resistant to hydrolysis). The fluxes of antigenic determinants across the epithelium was β-Lg > α-La > β-cas, i.e. 412, 135 and not detectable ng/h.cm$^2$ respectively. These results indicate a selective intestinal mucosal permeability for milk protein antigens. This selectivity may play a role in allergenicity.

## 38 Enhancement of leukotriene C4 (LTC4) production on peripheral polymorph-onuclear (PMN) cells form children with asthma

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Leukotrienes have been demonstrated to play a major role in mediating allergen induced asthma. We assessed the contribution of macrophages and PMN in the production of LTC4 in 11 patients with extrinsic or mixed type asthma, aged 3 to 15 years, and 10 healthy non allergic children , aged 4 to 15 years. Cells were separated by percoll gradient centrifugation and . Monocytes were further separated by adherence. Cells were stimulated with 2μM A23187. LTC4 was quantitated by an RIA of the supernatant. Granulocytes of asthmatic patients generate significant higher ($p<0.001$) amounts of LTC4 (range from 0.75 to 19.10 ng/ $10^6$ cells, geometric mean 10.57 ng /$10^6$ cells) than controls (range 0,21 to 5.86 ng/$10^6$ cells, geometric mean 1,95 ng/$10^6$ cells) whereas monocytes of the same patients produce amounts of LTC4 comparable to controls. The reason for the higher production of LTC4 by PMN of asthmatic patients might be the higher proportion of LTC4 producing eosinophils or an in vivo prestimulation of the eosinophils of these patients.

## 39 PREDICTING THE COURSE OF ASTHMA IN CHILDREN

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4000 cases of childhood asthma attending our ambulatory clinic for the first time before December 31,1981,were examined. 45 children were selected: they all had to have an actual age >15 years and at least 3 physiologic evaluations of pulmonary function performed before 10 years of age,in interval phases,that is between episodes,of their illness and in a period > 6 months.On the ground of this specific selection,we defined "persistent asthma" the cases who had a persistent residual alteration of forced expiratory volumes ($FEV_1$ <85% and FEF 25-75 < 80% of the "expected values")verified at least for 3 times in "interval phases"(asymptomatic) before 10 years of age. 39 subjects were entered into the study :13 (gp.A) were asymptomatic by the age of puberty;26 (gp.B),on the contrary,had had at least an asthmatic attack in an age > 13 years.Age at onset of asthma (gp.A:2.9 yearsvs.gp.B:3.2 years) did not affect the prognosis,nor sex of the patients, family history of atopic diseases (gp.A:60% vs.gp.B:55%)or asthma (gp.A:31% vs.gp.B:46%).Immunoterapy for a period ≥ 3 years had been performed in 70% cases of gp.A and in 85% cases of gp.B.Similarly there was no significant difference between the two groups with regard to the IgE levels in the serum and to the generic prick test positivity (100% positive in both groups)or to the positivity to specific allergens (foods,pollens,H.D.M).Furthermore frequency and gravity of the asthmatic attacksat the age < 10 years did not differ between gp.A vs.gp.B.The 2 groups showed a significant difference in terms of actual pulmonary functions:an abnormal FEF 25-75 was registered in only 2 patients of gp.A and in 20 of gp.B (15% vs.77%:p <0.001),(p<0.01 for $FEV_1$ values).The presence of associated persistent eczema (over the first 2 years of age)was associated significantly to the gp.B ($p<0.05$),while the long term breast feeding (>3months)clearly improved the long term prognosis (gp.A:70% vs. gp.B:35%)but values were nearly significant.An highly significant difference between the two groups was found for the spirometric alterationes proved < 10 years ($p= 0.002$):70% of patients of gp.B could be designed as having "persistent asthma"in that age,vs.15% of patients of gp.A.When assumed $FEV_1$and (particularly) FEF 25-75 assessed at the age 7-10 years in the "interval phases" of the illness the best "marker" of our 2 groups(A vs.B),we evaluated the prognostic value of this parameter:only 10% of the cases who < 10 years of age showed variationes in their airflow obstruction without ever reverting to normal lung function (persistent asthma) "grow out"of their illness after puberty (spirometric and clinical recovery).On the other hand,only 2/19 of the cases who before 10 years showed "intermittent asthma" had not remission after puberty.

## 40 DEPOSITION OF ACTIVATED COMPLEMENT COMPONENT COMPLEXES IN ACUTE APPENDICITIS IN CHILDREN.

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Immunopathological events in acute appendicitis are poorly understood. It is well known that activation of the complement system plays an important role in mediating inflammatory reactions. Using monoclonal and polyclonal antisera we have investigated the role of complement activation in the pathophysiology of appendicitis in children. Frozen and paraffin embedded tissue specimens were examined immunohistochemically with anti $C_3$, $C_4$, Factor B and a monoclonal antibody (AE11) to a neoantigen on $C_9$ in 20 inflamed suppurative appendices, 6 gangrenous appendicies, 8 perforated appendices and 10 normal appendices. Deposits of $C_9$ of the terminal complement complex (TCC) were uniquely present at subendothelial sites in submucosal arteries in inflamed appendices. In addition complement activation products were present in germinal centres of 72% of inflamed appendices. A strong correlation was seen between the number of $C_9$ positive arterioles and clinical degree of disease activity based on histology ($p<0.01$). These results indicate a previously unrecognised important role of complement activation in the pathogenesis of appendicitis.