0031-3998/94/3502-0259$03.00/0
PEDIATRIC RESEARCH

Vol. 35, No. 2, 1994
Printed in U.S.A.

EUROPEAN SOCIETY FOR PAEDIATRIC RESEARCH

Selected Abstracts for the 1993 Annual Meeting
September 12–16, Edinburgh, Scotland, U.K.

IMMUNOLOGY

1

COW MILK ANTIGENS IN INFANT DIET SIGNIFICANTLY INFLUENCE THE DEVELOPING IMMUNE SYSTEM

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The concept of oral tolerance is based on work in experimental animals, but data demonstrating its hypothesized existence in humans is scarce. We enrolled 25 healthy term newborns with nonatopic heredity to a prospective study, during which scheduled visits took place at 3, 6, and 11 mo of age. Diet was determined at each visit. Gut humoral immune response was approximated with the ELISPOT assay of circulating antibody secreting cells, and serum IgM, IgA and IgG antibodies to cow milk antigens were measured. At 3 mo of age, despite low levels of serum IgA antibodies, cells secreting specific IgA to cow milk antigens were detected in the formula fed group, but not in breastfed infants. The number of these cells decreased between the 6 and 11 mo visits, remaining at a measurable level. The total number of IgA secreting cells increased with age ($p=0.001$). The milk in the infant's diet influenced this development: the age related increase was significantly greater in the formula fed group ($p=0.04$). The results indicate that diet significantly affects the developing immune system. Further, healthy infants, unlike those with cow milk allergy, are able to produce a local antigen specific immune response to dietary antigens. This could be crucial in attaining clinical tolerance of such antigens.

2

A MECHANISM FOR MATERNAL MODIFICATION OF INFANT IMMUNITY?

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Colostrum is known to contain large numbers of maternal immune cells. We set out to establish whether chemokines, or cytokines with chemotactic activity, were involved in recruitment of these into the milk. Very high concentrations of the chemokines Rantes (median 1.9ng/ml, range 0.3-13ng/ml) and IL-8 (median 0.8ng/ml, range 0.4-3.6ng/ml) were observed in the milk of 25 mothers on D3 of lactation; these decreased by D18. Chemokines appear stable for over 24 hours in the milk, and resistant to pH changes of pH3-8 of the milk. Monoclonal antibodies and mRNA in situ hybridisation data suggest that the chemokines are secreted by breast epithelium rather than the immune cells; this is supported by *in vitro* culture of breast epithelial cells activated by prolactin. Why are such high concentrations of chemokine present? We hypothesise that these molecules facilitate both movement of maternal cells into milk, their adhesion to the infant bowel, and their migration into infant immune tissues. This hypothesis would explain observations of non-inherited maternal influences on their children.

CARDIOLOGY

3

DIAGNOSIS OF CONGENITAL HEART DEFECTS BY MEANS OF TRANSTHORACIC 3-DIMENSIONAL ECHOCARDIOGRAPHY WITH A COMPUTED TOMOGRAPHY IMAGING PROBE (ECHO-CT).

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A prototype tomographic ultrasound system: Echo-CT was evaluated 71 patients aged 4 days to 17 years with normal heart (n=1), ventricular septal defect (n=14), subaortic stenosis (n=10), mitral valve anomalies (n=9), atrioventricular septal defect (n=9), aortic stenosis (n=5), atrial septal defect (n=4) and various other congenital heart defects (n=20). The transducer is a 5 Mhz device with 64 elements mounted on a sliding carriage. The transducer is driven by a computer-controlled stepper motor in steps of .5-1.3 mms and acquires parallel tomographic slices of the heart perpendicular to the position of the probe. The transducer moves from the outflow tract to the cardiac apex. With ECG and respiration gating a complete cardiac cycle is recorded at each tomographic level. 50 to 130 slices per patient were acquired. Position of the probe on the chest varied in each patient. In 7 newborns the probe was used from the subcostal position. Image acquisition took 3-7 minutes. Data are stored as three-dimensional datasets in the imaging computer. Out of those data sets up to 5 different two-dimensional views in different planes can be constructed, so that the heart can be viewed from multiple planes without changing the probe position on the chest. In all but 2 patients we could also reconstruct the heart three-dimensionally from different views, which took 20-90 minutes per patient. Views similar to the ones a surgeon has at operation can be genenerated. We conclude that this preliminary study demonstrates the feasibility of the tomographic three-dimensional reconstruction technique, which yields additional information on the morphology of septal defects, tricuspid, mitral and aortic valves and complex malformations.

CEREBRAL BLOOD FLOW MEASURED BY NEAR INFRARED SPECTROSCOPY (NIRS) IN CHILDREN UNDERGOING OPEN HEART SURGERY.

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A new non-invasive method for repeated estimation of cerebral blood flow (CBF) in infants and children during non-pulsatile cardiopulmonary bypass (CPB) is described. The method is derived from the Fick principle, using oxyhaemoglobin (HbO_2) as a non-diffusible tracer. A sudden change in O_2 flow into the oxygenator causes a change in arterial saturation (SaO_2) which is measured by an optical oximeter, and in cerebral [HbO_2], which is detected by NIRS. CBF is calculated from the expression:

$$CBF = k.\Delta[HbO_2](t) \Big/ [H].\int_0^t (SaO_2)dt$$

where k is a constant reflecting the molecular weight of haemoglobin and tissue density, [H] is the arterial haemoglobin concentration. CBF was measured on 16 occasions in 6 children undergoing CPB, median age 5.3 (range 4-62) months. Near-infrared light was transmitted from and returned to the spectrometer by fibre optic cables applied to the head. After a stable baseline of 88-96% SaO_2 (median 94%) had been achieved for at least 10 seconds, a rise in SaO_2 of 2-10% (median 5%) was induced. Values for CBF of 9-54 $ml.100g^{-1}.min^{-1}$ were obtained. Preliminary data from two children showed that at full pump flow median CBF was 47 (range 41-54) $ml.100g^{-1}.min^{-1}$ and at half flow was 23 (range 22-29) $ml.100g^{-1}.min^{-1}$. The method warrants further study but suggests that routine, repeated and non-invasive measurements of CBF during CPB may now be possible.