



Chronic, non-malignant hypersplenism with lymphadenopathy, hypergammaglobulinaemia, and autoimmunity was first reported in children in 1967. The condition, now known as autoimmune lymphoproliferative syndrome (ALPS), is further characterised by an abundance of double-negative T cells (lymphocytes with  $\alpha\beta$  T cell receptors but without CD4 or CD8 surface determinants), and defective lymphocyte apoptosis. Most patients (about three quarters) have heterozygous, germline mutations in the Fas gene (*TNFRSF6*) that controls programmed cell death (apoptosis). These patients are said to have ALPS type I. A few have defects in the genes for caspase 8 and caspase 10—proteins also associated with the process of apoptosis (ALPS type II). In about a quarter of cases, however, no gene defect has been demonstrated (ALPS type III). Now six children with ALPS type III have been examined (*New England Journal of Medicine* 2004;**351**:1409–18, see also perspective article, *ibid*: 1388–90) and all six had *Fas* mutations in their double-negative T cells. In two of the children cells from skin and bucal mucosa were examined and they did not contain the mutation. It is therefore suggested that ALPS type III is associated with somatic *Fas* mutations in haemopoietic cells and these cases should be reclassified as mosaic ALPS type I or ALPS type Im. Lymphocytes with a *Fas* mutation resist apoptosis and therefore persist and become double-negative T cells.

Researchers in Bristol (*Gut* 2005;**54**:170–1) analysed breastmilk samples from four breastfeeding mothers who were taking mesalazine (5-aminosalicylic acid, 5-ASA) for chronic inflammatory bowel disease. They found low concentrations of 5-ASA in the milk (4–40 ng/ml) and calculated that the babies would receive a dose of between 0.0006 and 0.006 mg/kg/day—a very small proportion of the standard therapeutic dose. When they examined the N-acetyl metabolite of 5-ASA, however, they found breastmilk concentrations about 1000 times greater than the concentrations of 5-ASA. They argue that this means that 5-ASA is probably metabolised to N-Ac-5-ASA within breast tissue. N-Ac-5-ASA is an inactive metabolite and unlikely to be toxic so they conclude that it is probably safe to breastfeed while taking mesalazine. But the metabolism of drugs within the breast and the accumula-

tion there of high concentrations of drug metabolites could have wider implications for drug therapy.

In 2000–2002 ophthalmologists in Sweden (*British Journal of Ophthalmology* 2004;**88**:1362–7) examined 72 children adopted from eastern Europe (Poland, Romania, Russia, Estonia, or Latvia) between 1993 and 1997. They found ocular abnormalities in 56 of these children and 26 of 90 age and sex matched Swedish controls. Nineteen of the adopted children but none of the controls had a visual acuity in the best eye of 0.5 or less. Eleven of the adopted children and two controls were amblyopic. Hyperopia, myopia, astigmatism, and squint were all much commoner in the adopted children. Four adopted children had optic nerve hypoplasia, suspected in three cases to be due to maternal drinking in pregnancy. More than a third of the children had visuoperceptual problems. These children need detailed assessment including an ophthalmological examination on arrival in their new country. Previous studies have shown growth and developmental delays among children adopted from eastern Europe.

Children with Henoch-Schönlein purpura (HSP) have a leukocytosis in blood and there is perivascular polymorphonuclear infiltration. Interleukin 8 (IL8) can be produced by monocytes, epithelial cells, and endothelial cells, and promotes neutrophil release and infiltration. Now researchers in Taiwan (*Annals of the Rheumatic Diseases* 2004;**63**:1511–3) have shown that children with HSP have raised serum concentrations of IL8 and their serum induces release of IL8 from cultured human umbilical vein endothelial cells. The HSP serum did not, however, induce the expression of intercellular adhesion molecule-1 (ICAM-1) on the endothelial cells. They suggest that in active HSP there is a factor in the serum that stimulates endothelial cells to produce IL8 and that this could be a mechanism for inducing perivascular neutrophil infiltration.

All babies cry—some of them, especially younger ones, cry a lot; and some are abused. But, as *Lancet* commentators point out (*Lancet* 2004;**364**:1295–6), the baby is never to be blamed for the abuse. The fault lies in the abuser's response. Undesirable

responses are, however, fairly common. In the Netherlands (*ibid*: 1340–2) the parents of 3259 infants were interviewed after they had filled in a questionnaire. Substantial proportions of the parents of 6 month old infants admitted to having ever smothered (1.6%), slapped (1.9%), or shaken (3.4%) the infant in response to crying. One in 18 (5.6%) admitted to at least one of these responses. Unemployed, immigrant, and urban parents were more likely to admit to such behaviours, as were parents who worried about the infant's crying or considered it excessive. The presence in the home of a carer who was not a biological parent of the child was also a risk factor. Parents may need help to cope with their infant's crying.

Data from school records and national cancer registries in Denmark (*New England Journal of Medicine* 2004;**351**:1619–26; see also editorial, *ibid*: 1679–81) have shown that high birthweight, rapid growth in childhood, early and rapid pubertal growth spurt, and adolescent thinness all increase the risk of girls later developing breast cancer. The biological mechanisms at work are ill understood but, since most of these factors are associated with reduced risks of cardiovascular disease or diabetes in later life, interventions might prove hazardous.

Standard surgery for refractory gastro-oesophageal reflux disease (GORD) has been fundoplication, either open Nissen's fundoplication or laparoscopic fundoplication. An alternative operation, endoscopic endoluminal gastroplication, has become popular in adults and can be done as a day-case procedure. In London (*Gut* 2004;**53**:1745–50) 17 children (median age 12.4 (range 6–16) years, 12 girls) with medication dependent or refractory GORD underwent the endoscopic procedure in which gastric plications are created by inserting series of stitches into the stomach lining 0.5 and 1.5 cm below the gastro-oesophageal junction. Three patients needed a repeat procedure after 6 weeks. After an average follow up of 23 months 14 of the 17 patients remained off all antireflux medication. Six of nine patients had normal results on oesophageal pH monitoring one year after the procedure. The long term effects of this procedure in children are not known and randomised controlled trials will be needed.