

## HOW EARLY CHILDHOOD STRESS INFLUENCE YOUR IMMUNE SYSTEM

Suicide and depression are commoner in humans separated from their mother's at an early age and maternal separation has been used in animals to induce neurotic behaviour. The current study in this month's *Gut* used this model to show that early stress induces long lasting increases in both small intestinal and colonic permeability. This was associated with increased bacterial translocation and increased colonic myeloperoxidases, mast cells and inflammatory cytokine expression. The inflammatory response to a chemical injury (TNBS) was also increased. The authors argue that these changes are all secondary to altered permeability. Whether this is in turn due to increased endogenous steroid secretion or due to long term alterations in gut flora is uncertain. This finding has implications for many human diseases and their relation to psychiatric disorders, whose origins may well lie in early childhood stress.

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## HOW ARGININE HEALS THE WOUNDED MUCOSA

Repair of defects in the mucosal barrier is dependent on the migration of epithelial cells to cover exposed basement membrane. Enhancement of this process is an important goal of therapy in many conditions. Arginine, a widely available dietary amino acid, is a precursor of nitric oxide which itself stimulates epithelial cell migration. The present study used sheets of cultured cells which were wounded with a razor blade. The authors showed not only that Arginine stimulates migration at physiological contractions, but also that this effect can be substantially reduced by the nitric oxide (NO) synthetase inhibitor, NMMA. Arginine causes phosphorylation of focal adhesion kinase (FAK), an enzyme whose activation enhances cell migration. Using transfection studies to insert a defective FAK gene, the authors showed that such cells failed to respond

to Arginine indicating that FAK is critical to Arginine's effect. These studies are relevant to the nutrition of premature infants. Those that develop the catastrophic syndrome of necrotising enterocolitis (NEC) have very low serum Arginine levels. Arginine supplementation significantly reduces the incidence of NEC, possibly acting via the mechanisms shown in this paper to enhance intestinal healing.

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## MORE DETAILS ON LYMPHOCYTIC COLITIS

Last month's issue of *Gut* drew attention to the fact that lymphocytic colitis now accounts for a substantial proportion of unexplained diarrhoea, especially in the over 70's. The large patient cohort from the same research group, reported on page 536, provides some important new associations. Family history of colitis or celiac disease was found in 12% of 199 patients. Interestingly, while 1/3 had a chronic intermittent course, 2/3 described an acute, possibly infective onset with a relatively short lived illness, median duration 6 (4–11) months. They speculate that an unknown organism, such as was thought to be responsible for the outbreak of "Brainherd diarrhoea," might be the cause.

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## WHAT IS THE YIELD OF REPEATED SCREENING COLONOSCOPIES?

As national colonoscopic/flexible sigmoidoscopic screening programmes are starting to role out, data on the yield of repeated colonoscopies is of great importance, as it will influence recommendations on the frequency of such examinations. This month's issue contains a report from a cohort of 6 226 Japanese patients who had at least 3 colonoscopies over a 14 year period. Unlike previous studies, this one effectively eliminated artificially inflated incidence rates which occur when a missed lesion is counted as a new one on a second later examination, by calculating incidence rates from the results of a third colonoscopy after two negative ones. The authors report that subjects with no initial neoplasms showed an incidence rate of colorectal neoplasms (adenomas/carcinoma in situ/severe dysplasia) of 7.2% at the third colonoscopy and 0.21% per year developed advanced lesions (carcinoma in situ, severe dysplasia). These figures will be valuable in any cost benefit analysis of various proposed screening schedules.

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## PREVALENCE OF HEPATITIS C AMONG CHILD BEARING WOMEN IN SCOTLAND

The importance of hepatitis C virus and its long term implications for the health service are substantial. Accurate estimates of the true incidence are therefore vital. The authors of the current study utilise the fact that 99.97% of mothers allow their babies to be tested for hypothyroidism and other metabolic defects (Guthrie Test). This heel prick sample can be tested for passively transferred maternal antibodies to hepatitis C and when positive, indicate maternal infection. After irreversibly unlinking the Guthrie cards from patient identifiers, they were able to do some interesting epidemiological analyses. The seroprevalence rate was 0.3–0.4% depending on the precise criteria used. The incidence was clearly related to social and economic status and rose with deprivation. Somewhat disturbing, more than half of these infections had not been diagnosed prior to delivery. As expected, intravenous drug usage accounted for most of these cases. The anonymity of this study means that it is quite feasible to repeat this at intervals and in this way monitor the National incidence of Hepatitis C. This will provide much valuable information on the effectiveness of measures which attempt to reduce the incidence of this condition.

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