also illustrated some of the difficulties in attempting comparisons of different amino acid solutions.

We have previously drawn attention to abnormal plasma amino acid profiles in Vamin 9 fed infants.² We considered this to be a reflection of the amino acid composition of Vamin 9 rather than an idiosyncratic reaction, as the pattern occurred consistently, and was much less evident when a modified solution containing less phenylalanine was used.³ One factor which McIntosh and Mitchell do not address in detail, but which may have considerable influence on plasma amino acid profiles, is the amount of enteral nutrition being given. In our original index case of hyperphenylalaninaemia,² small volumes of breast milk given as a supplement to parenteral nutrition produced large changes in plasma phenylalanine. The patients of McIntosh and Mitchell received either breast milk or preterm formula in addition to their intravenous nutrition. In fact, by day 5 of the study, the only day during parenteral nutrition on which plasma amino acid profiles were measured, the figures given for mean enteral feed in both infants receiving Vamin 9 and those fed with MB233G represent approximately 60% of the total nitrogen intake. It is therefore difficult to see how valid conclusions can be drawn about the suitability of either amino acid solution as a parenteral nitrogen source.

Although 68 patients were recruited to the study, some died, some were excluded, and some had inadequate blood sampling or blood taken on the wrong day. As a result, the data derive solely from a single plasma amino acid analysis, performed on only seven patients in the Vamin 9 group and five in the MB233G group. Moreover, individual amino acid concentrations are reported as mean (SD) suggesting normal distribution of data. However, the fact that -2SD would give a negative value for 50% of the amino acids measured indicates non-parametric distribution of results, consistent with similar studies.³ It would therefore be interesting to be able to compare mean (after log transformation to 'normalise' the data) and ranges of individual amino acids.

Finally, single measurements of plasma amino acid profiles may not allow adequate comparison of different solutions as plasma concentrations can vary considerably. This is illustrated by the following plasma concentrations of phenylalanine and tyrosine measured every two weeks in a child with gastroschisis receiving total parenteral nutrition with a constant nitrogen intake: phenylalanine 149, 500, 200, 49, 63, 983, and 260 $\mu\text{mol/l}$ and tyrosine 95, 60, 80, 58, 86, 86, and 145 $\mu\text{mol/l}$.

The theoretical basis for the formulation of MB233G is of interest, but it remains to be seen whether or not this new solution offers any advantages over alternative preparations.

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- 1 McIntosh N, Mitchell V. A clinical trial of two parenteral nutrition solutions in neonates. *Arch Dis Child* 1990;65:692-9.
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Professor McIntosh comments:

Drs Puntis and Booth suggest that the enteral component of nutrition may be important in the development of hyperphenylalaninaemia. They point out that on day 5 both groups of infants in our study received approximately 60% of their nitrogen intake enterally. We agree with this, as at this time the intravenous nitrogen intake was about 40% of the total! The point of difference in our two groups was the composition of the intravenous amino acid mixtures and it would seem therefore to be a 'non-sequitur' to suggest the high concentrations of phenylalanine, tyrosine, serine, proline, and asparagine were due to the enteral intake.

There were in fact 16 and 14 patients with 'good' samples for amino acid analysis taken on day 5—see original table 5. We accept that the results were not in a Gaussian distribution—this is why Wilcoxon's signed rank test was used when comparing amino acid concentrations the two groups.

We note the information in the last paragraph which we find very interesting.

We believe that the apparent ability of babies given MB233 to keep their plasma aminogram in the reference range of cord blood aminograms makes it an attractive alternative to Vamin 9 glucose where the aminograms at five days approached the values of infants with untreated phenylketonuria and hereditary tyrosinaemia.

Virological investigations of acute encephalopathy in India

SIR,—Rabies should be considered in the differential diagnosis of acute encephalopathy in children living in endemic areas. It may present as a non-specific encephalitis without the pathognomonic features such as hydrophobia and a clear history of exposure is not always present. It was therefore surprising that it received no mention in the series of Kumar *et al*¹—could it have accounted for some of the cases among the 40% in whom they found no cause?

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- 1 Kumar R, Mathur A, Kumar A, Sethi GD, Sharma S, Chaturvedi UC. Virological investigations of acute encephalopathy in India. *Arch Dis Child* 1990;65:1227-30.

Dr Kumar comments:

Rabies is endemic in the Indian subcontinent. It produces an acute encephalitic illness usually with a pronounced psychological component. We agree that occasionally none of these pathognomonic features may be found and therefore it may account for a few of the fatal 'unexplained encephalopathies' in this study. Although we have discussed other viral encephalitis as a cause in this group we have not specifically mentioned rabies. We therefore appreciate Dr Hall's comment.

SIR,—Dr Kumar and his colleagues in reporting their investigations into the cause of acute encephalopathy in children in Lucknow have not considered the possibility of cerebral cysticercosis in their differential diagnosis.¹

Cysticercosis in India is not uncommon² and parenchymal involvement, the most common form in children,³ may present acutely. Acute diffuse parenchymatous disease often severe enough to cause an acute rise in intracranial pressure with deterioration of consciousness and cerebral shifts. Acute focal parenchymal disease presents with localised patchy oedema often resulting in convulsions.

The diagnosis of cerebral cysticercosis may present difficulties. Serology is beset with the problems of poor sensitivity and specificity and cerebrospinal fluid changes are often non-specific and non-diagnostic. Computed tomography has improved diagnostic accuracy but it not always readily available in India. Where there has been the opportunity to perform enhanced computed tomography on Indian patients presenting with seizures, lesions suggestive of cysticercosis have been reported in 26% of cases,⁴ excision biopsy confirming the diagnosis in a further series of cases.⁵

A diagnosis of cerebral cysticercosis should be considered in all children presenting with 'acute encephalopathy' in India.

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Auditing community screening for undescended testes

SIR,—With interest we read the article of Tamhne *et al* about the screening for undescended testes. We were surprised by reported high cumulative rates of orchidopexy especially as the authors state that some of the children in the younger cohort would not have their undescended testes detected and operated on.¹

In The Netherlands during the period from 1976 to 1986 about 3% of boys between the ages of 0 and 14 underwent orchidopexy.^{2,3} Because this percentage is higher than the generally accepted estimate of the prevalence of truly non-descended testes (about 1%⁴) we are making efforts to reduce unnecessary orchidopexy.

As we have reason to believe that in the past the high orchidopexy frequency was related to inaccurate registration of the testes localisation, in some parts of The Netherlands a card for the testes registration was introduced. On this card the localisation of the testes is registered by the person who assists the delivery. If the testes are not scrotal at birth the boys are followed up. After introduction of this card in one region the number of operations for orchidopexy was reduced to an acceptable level.³

We chose registration soon after birth because the cremaster reflex is still absent at

that time. Because of this reflex we doubt the efficacy of screening boys for undescended testes at 1 year and at school entry. The figures from Tamhne *et al* confirm our opinion that too many boys will be operated on unnecessarily because of retractility of the testes.

In 1989 a retrospective cohort study concerning the localisation of the testes from birth until puberty of 853 boys born in 1973 and living in West Friesland (The Netherlands) was done. In this study, which has been submitted for publication, we found a considerable number of boys with one or two undescended testes, that when previously measured, had been registered as scrotal. In all these boys the testes had assumed a normal scrotal position at puberty. This supports our advice that if the testes were descended no further screenings are necessary.

We agree with Tamhne *et al* that there is a need to set clear guidelines for the diagnosis of undescended testes and for referral pathways. This is important especially to prevent unnecessary operations.

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Revised criteria for diagnosis of coeliac disease and medical audit

SIR,—In the recently published revised criteria from the European Society for Paediatric Gastroenterology and Nutrition (ESPGAN) for the diagnosis of coeliac disease,¹ emphasis has shifted from the need for repeated biopsies to the response to dietary gluten withdrawal, combined with initial histological appearance of the jejunal biopsy.

It might be thought that this could decrease the use of this unpleasant and time consuming diagnostic procedure. However this may not be the case.

As part of a medical audit programme the clinical and histological details of jejunal biopsies performed in the Royal Liverpool Children's Hospital between January and May 1990 were reviewed.

Analysis of the data showed: (1) Out of 46 attempted biopsies, 10 were initially unsuccessful. (2) Of the 36 children biopsied, only four biopsies were performed after a gluten challenge, the rest were for initial diagnosis. (3) The number of jejunal biopsies for the first five months of 1990 was similar to the whole of 1989 (36 v 39) yet proportionately more children started a gluten free diet (11/36 (30%) v 10/39 (25%)). (4) Children referred from an outlying hospital were more likely to have a biopsy specimen compatible with coeliac disease (50% v 25%). (5) Eleven children commenced a gluten free diet, but only six had the characteristic 'flat' small intestinal mucosa of coeliac disease.

It was concluded that: (1) There was a significant chance of procedural failure with jejunal biopsy in children. (2) Few biopsies were performed after gluten challenge indicating that the practice of diagnosing coeliac disease by repeated biopsies had already lapsed.² (3) The increased number of biopsies in 1990 reflected a more aggressive diagnostic approach. (4) Gluten free diet was often commenced in the absence of characteristic histological criteria. With the new criteria these children would require gluten challenge.

It is therefore to be hoped that the use of the revised ESPGAN criteria will reduce dependency upon multiple jejunal biopsies and the inappropriate use of gluten free diet as highlighted by our medical audit.

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- 1 Report of the Working Group of the ESPGAN. Revised criteria for the diagnosis of coeliac disease. *Arch Dis Child* 1990;65:909-11.
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Crohn's disease

SIR,—Dr Puntis and colleagues have reported in this journal the first case of granulomatous lung involvement in a child with Crohn's disease.¹ It is clear from many previous reports that pulmonary involvement is actually common in chronic inflammatory bowel disease, although only a minority of patients have symptoms or overt signs. Bonniere and colleagues have demonstrated, in 22 adults with Crohn's disease who had no pulmonary symptoms, reduced serum activity of angiotensin converting enzyme, lymphocytosis on bronchoalveolar lavage, increased superoxide anion production from activated alveolar macrophages, and abnormal pulmonary function tests.² They concluded that most patients with Crohn's disease have latent pulmonary involvement. After recent findings in this unit, we are now able to suggest a mechanism for this previously unexplained phenomenon.

We have demonstrated production of the cytokine tumour necrosis factor- α (TNF- α) by single macrophages in colonic biopsies from patients with both Crohn's disease and ulcerative colitis,³ and have found raised serum concentrations of TNF- α in patients with relapsed colonic disease⁴; we consider that chronic TNF- α elevation may contribute to anorexia and growth failure. TNF- α has also been implicated in granuloma formation⁵; granuloma epithelioid cells are in fact activated and transformed macrophages. TNF- α mRNA was found in large quantities within these experimentally induced hepatic granulomas and anti-TNF- α monoclonal antibodies caused both rapid granuloma regression and reduction of TNF- α mRNA content.

TNF- α production is actually increased by exposure of macrophages to TNF- α itself,^{5,6} so that chronic elevation of serum TNF- α might lead to TNF- α production by tissue based macrophages. Pulmonary alveolar macrophages produce several times more TNF- α on stimulation than do circulating monocytes,⁷ and we suggest that raised serum TNF- α concentrations in chronic inflammatory bowel disease could stimulate alveolar macrophages to produce more TNF- α , which

would then act within the pulmonary micro-environment.

It is now clear that TNF- α can cause lung damage, and it is viewed as an important mediator in the adult respiratory distress syndrome (ARDS), which frequently supervenes in conditions such as septicaemia where serum TNF- α concentrations are grossly raised. Alveolar lavage fluid contains measurable TNF- α of pulmonary origin in ARDS.⁸ Lesser elevation of serum TNF- α produces a more subtle derangement of pulmonary function, demonstrated well by the abnormal lung function tests found in patients treated for malignancy with recombinant TNF- α .⁹

We think that this mechanism would account for the activated alveolar macrophages found by Bonniere *et al*,² for the subtle lung function abnormalities found in many patients with active disease, for pulmonary granuloma formation, and for the more florid ARDS like picture found in many patients with life threatening toxic dilatation, where serum TNF- α may be much higher.⁴

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VIDEO REVIEWS

The Six Week Check of Infants. A video training package. Commissioned by: Nottingham Health Authority. Production Company: Chrysalis Television Midlands. Cost of training package (video and manual): £195; additional trainer's manuals £6 each. For details contact: Mrs B Whitchurch, Training Office, Notting-