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. We considered this to be a reflection of the amino acid composition of Vamin 9 and an idiosyncratic reaction as the pattern recurred consistently, and was much more evident when a modified solution containing less phenylalanine was used. One factor which Mcintosh and Mitchell did 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, 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 nutri-
tion on which plasma amino acid profiles were measured, the figures given for mean energy fed in both infants receiving Vamin 9 and those fed with MB233 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 MB233 group. Moreover, individual amino acid concentra-
tions 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, consist-
tent 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 concentra-
tions of phenylalanine and tyrosine measured every two weeks in a child with gastrochisis receiving total parenteral nutrition with a constant nitrogen intake: phenylalanine 149, 500, 200, 49, 63, 983, and 260 μmol/l and tyrosine 95, 60, 80, 58, 86, and 145 μmol/l. The concentration of MB233 is of interest, but it remains to be seen whether or not this new solution offers any advantages over alternative preparations.

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 ente-
raly. We agree with them in 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 solution and Mitchell would seem to therefore be a ‘non-successor’ to suggest the high concentra-
tions 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 concentra-
tions in 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 aminograms in the reference range of cord blood aminograms makes it an attractive alternative to Vamin 9 glucose where the aminogram at five days approach the values of infants with untreated phenylketo-
nuria and hereditary tyrosinaemia.

Virological investigations of acute encephalopathy in India

Str.—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 hydro-
phobia 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 al2—a could it have accounted for some of the cases among the 40% in whom they found no cause?

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4. Wadia RS, Makache CN, Kelkar AV, Grant KB. Focal epilepsies in India with special reference to lesions showing ring or disc-like enhancement on contrast computed tomography. J Neurol Neurosurg Psychiatry 1979;42:1298–301.

Auditing community screening for undescended testes

Str.—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 had their undescended testes detected and oper-
ated on.

In the Netherlands during the period from 1976 to 1986 about 3% of boys born in the ages of 0 and 14 underwent orchidopexy.3 Because this percentage is higher than the generally accepted estimate of the prevalence of truly non-descended testes (about 1%) we are not 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 localisa-
tion, in some parts of The Netherlands a card for the testes registration was introduced. On this card the localisation of the testes is regis-
tered 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 orchi-
dopexy was reduced to an acceptable level.

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

1. Kumar R, Mathur A, Kumar A, Sethi GD, Sharma S, Chaturvedi UC. Cystercerosis in India is not uncommon and parenchymal involvement, the most common form in children, may present acute encephalopathy. Acute diffuse parenchymatous disease presents with generalised cerebral oedema 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.


4. Wadia RS, Makache CN, Kelkar AV, Grant KB. Focal epilepsies in India with special reference to lesions showing ring or disc-like enhancement on contrast computed tomography. J Neurol Neurosurg Psychiatry 1979;42:1298–301.


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dopexy was reduced to an acceptable level.

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 retraction of the testes.

In 1989 a retrospective cohort study concerning the localization 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 (ESPAGAN) for the diagnosis of coeliac disease,1 emphasis has shifted from the need for repeated biopsies to the response to a 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. 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 a gluten challenge indicating that the practice of diagnosing coeliac disease by repeated biopsies had already lapsed. (3) The increased number of biopsies in 1990 reflected a more aggressive diagnostic approach. (4) Excision biopsies were often commenced in the absence of characteristic histological criteria. With the new criteria these children would require gluten challenge. It is therefore 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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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, lymhophcytosis on bronchoalveolar lavage, increased superoxide anion production from activated 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 colonis biopsies from patients with both Crohn's disease and ulcerative colitis, and have found raised serum concentrations of TNF-α in patients with relapsed colonic disease;3 we consider that chronic TNF-α elevation may contribute to anorexia and growth failure. TNF-α has also been implicated in granuloma formation;4 granuloma epithelial 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 so that chronic elevation of serum TNF-α might lead to TNF-α production by tissue based macrophages. Pulmonary alveolar macrophages are known to have high levels of TNF-α on stimulation than do circulating monocytes,6 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 microenvironment.

It is now clear that TNF-α can cause lung damage, and it is therefore an important mediator in the adult respiratory distress syndrome (ARDS), which frequently supervenes in conditions such as sepsisema where serum TNF-α concentrations are grossly raised. Alveolar lavage fluid contains considerable TNF-α of pulmonary origin in ARDS.8 Lesser elevation of serum TNF-α produces a more subtle derangement of pulmonary function demonstrated in many patients with chronic 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 for the first time in patients with chronic lung involvement in patients with life threatening toxic dilatation, where serum TNF-α may be much higher.


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VIDEO REVIEWS
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Arch Dis Child 1991 66: 560-561
doi: 10.1136/adc.66.4.560-d

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