LETTERS TO THE EDITOR

Long term follow up of children born to mothers with periconceptional multivitamin supplementation

EDITOR.—Before recommending periconceptional folic acid-containing multivitamin supplementation universally for the prevention of neural tube defects one would also want to be sure that there was doing no harm. A UK study showed the over-representation of worries and anxiety among children at age 7–10 years born to mothers with periconceptional multivitamin supplementation. In our previous study based on a short term postnatal follow up of 3356 infants (mean age 11 months) born to mothers supplemented with multivitamin or placebo-like trace element in the period (30.6% vs 13.8%), the results of the tests of mental and behavioural development were similar in the two groups. However, at 6 years intelligence quotient was measured by the Brunet-Lezine method, and there was no difference neither in clinical symptoms, nor in the prevalence of failure to thrive between infants with and without periconceptional multivitamin supplementation.1

In conclusion, no adverse effect was observed in children whose mothers had received periconceptional multivitamin supplementation.

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Gastro-oesophageal reflux and cows’ milk protein allergy

EDITOR.—In their very stimulating paper, Cavataio et al reported their experience concerning gastro-oesophageal reflux (GOR) associated with cows’ milk protein allergy (CMPA). In a series of 47 cases of GOR, they found a very high prevalence of CMPA: 14 cases (30%) of these also assessed the possibility of recognizing these cases from characteristic ‘phasic’ pH tracing. We evaluated a series of 112 infants (65 boys and 47 girls; median age 3.7 months) with GOR documented by 24 hour pH monitoring. Using the results of an elimination diet followed by an open challenge test, we found CMPA dependent GOR in 18 patients (16%), a rate significantly lower than that found by the authors. We also stressed the importance of finding a characteristically oesophageal pH metric pattern distinguishing patients with CMPA from patients with GOR only: one out of 18 cases with CMPA dependent GOR showed the oesophageal ‘phasic’ pH monitoring reported by Cavataio et al, and this pattern was also present in three out of 67 cases with GOR only. It is difficult to explain the difference in these two sets of results. The increase in pH subsequent to feeding found by Cavataio et al (‘phasic’ tracing) may have been an non-specific event, evident for some reason only in those patients in whom CMPA was diagnosed. Besides, a high prevalence of CMPA in patients with GOR is truly surprising and has never been found by us or other authors in Southern Italy,1 by others in the USA,2 and without GOR disease (did any of these patients undergo oesophageal pH monitoring?).

Finally, it is noteworthy that another Italian group carried out a prospective study on GOR-CMPA association and found that 13/18 patients with GOR+CMPA and only 3/37 with GOR had a typical ‘phasic’ pattern of the pH-monitoring tracing.1


6 Di Stefano G, Violante M, Traverso G, Oddo S, Marino V, Catald F. Usefulness of 24-h
Chromosomal and clinical features in an infant with Hallermann-Streiff syndrome

**Editor,—** Hallermann-Streiff syndrome (HSS) is a disorder of unknown origin rarely diagnosed in neonatal period. The early diagnosis of HSS is important for management because many complications, that are often life threatening, may occur early in this syndrome.1 We report an infant with clinical and radiological findings of HSS, a spontaneous fracture of the left arm, and with chromosome variant 46, XX, 16qh+. She was a girl born at term after a normal pregnancy. Her family history was unremarkable. During pregnancy there was no exposure to known teratogens. Birth weight was 2700 g and length was 44 cm. Physical examination showed frontal prominence and cutaneous macrognathia, microphthalmia, and a cataract in the right eye. Arms and legs were short in comparison to the body. Abdomen, thorax, genitourinary examination, cardiac structure and function were normal. Skeletal radiography showed thin ribs, clavicles, and long bones (ulna and radius). Chromosomes were 46, XX, 16qh+ by R banding and C banding techniques. Because of micrognathia and macroglossia the infant was fed by gavage in the first weeks. No respiratory problems occurred in the first month of life. At the age of 3 months the patient had a spontaneous fracture of the left radius and at 10 months (fig 1) she returned to our department because of a severe pneumonia; examination revealed growth retardation (her weight was 4050 g), hypotonia, squatting, and a cataract in the left eye.

Few chromosomal anomalies have been found in HSS cases, with only Carones et al describing a del(Bp).2 In our patient we found a well known polymorphism of the long arm of the Y chromosome,3 and Balert et al describing a del(Bp).4 In these patients, we observed that the fracture of long bones should be considered a possible complication in HSS related to the bone abnormalities described in these patients.

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**Neutral lipid storage disease—response to dietary intervention**

**Editor,—** Neutral lipid storage disease (NLSD) is an autosomal recessive metabolic disorder characterised by a multisystem accumulation of neutral lipids (triglycerides). The patients with NLSD have congenital ichthyosis and variable systemic manifestations.2 The storage of cytoplasmic triglycerides in NLSD patients results either from a severe defect in the degradation of cytoplasmic triacylglycerols containing long chain fatty acids1 or rapid triacylglycerol resynthesis.3 Based on these biochemical data, one might expect that a low fat diet poor in long chain fatty acids could be beneficial to these patients. We report a boy with NLSD with emphasis on his response to dietary intervention.

**CASE REPORT**

An 8 year old boy was born as a collodion baby to unrelated parents. Examination at the age of 2 months revealed ichthyosiform erythroderma, hepatomegaly (11 cm below the right costal margin), and diffuse bilateral cataracts. Liver enzymes were raised (aspartate aminotransferase (AST): 177 IU/I, alanine aminotransferase (ALT): 179 IU/I, γ-glutamyltransferase: 42 IU/I). Liver histology showed gross fatty infiltration of the hepatocytes with lobular fibrosis. Leucocyte neutral lipid vacuolation was detected in the peripheral blood smears. Lipid thin layer chromatography from skin tissue showed increased accumulation of triglycerides.

The boy was put on a low fat diet (table 1) and at the end of the first year of treatment the size of the liver decreased by 50% and the liver function improved. The skin also became less erythematous and less scaly. At the age of 3.5 years the boy was operated for cataracts. At the age of 8 years, still on the special diet, his skin condition improved further and the liver size was normal (AST: 60 IU/I, ALT: 70 IU/I). There was no hearing or muscle power impairment and he made good progress in school.

In our patient a low fat diet, poor in long chain and enriched with medium chain fatty acids, led to regression of liver size, improvement of his skin condition, and possibly prevention of other organ involvement. In 1980 Angelini et al reported improvement in liver size with a medium chain triglyceride diet in a 5 year old girl with NLSD.2 As in other metabolic disorders the special diet did not restrain the progress of the patient’s cataracts.3 It is conceivable that by starting the special diet before or at the age of 1 year, this complication might be totally prevented. This observation indicates that in cases of NLSD, an early initiation of a diet poor in long chain fatty acids might improve the skin condition and prevent systemic disturbances.

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**Primary manifestation of Henoch-Schönlein purpura during immunosuppressive treatment**

**Editor,—** Although numerous investigations suggest an immunological process involving a disturbance of the regulatory mechanism for IgA synthesis,1 the aetiology of Henoch-Schönlein purpura are still unresolved.

We report a 4 year old boy who received a liver transplant at the age of 3 years after developing a fulminating liver failure due to intoxication with α-amanitin. After transplantation, immunosuppressive treatment with cyclosporin (Necoral, Sandoz) and prednisone was carried out. During later care the cyclosporin trough serum concentrations are maintained within the therapeutic range.

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**Table 1  Diet given to the patient with NLSD**

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Meal</th>
<th>Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequent meals (every 4-6 hours)</td>
<td>to avoid lipolysis</td>
<td>Normal protein (15% of total energy)</td>
</tr>
<tr>
<td>High carbohydrate (65-70% of total energy)</td>
<td>mainly in the form of starchy foods and one or two glucose 10% polymer drinks during the night (Maxijul, Scientific Hospital Supplies)</td>
<td></td>
</tr>
<tr>
<td>Low fat (20% of total energy)</td>
<td>18% derived from medium chain fat (MCT Oil, Mead Johnson) and 2% from essential long chain fat.</td>
<td></td>
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<td></td>
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</tbody>
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always exceeded 100 ng/ml while simultaneously the dose of corticosteroids was reduced to 1 mg/day. Eight months later, after a short minor infection of the upper respiratory tract, the boy developed the clinical signs of Henoch-Schönlein purpura with a typical purpuric skin rash and ecchymotic areas particularly on the lower legs and the feet, joint involvement with periarthritis, tender- ness and swelling, and abdominal pain with- out fever, but guaiac positive stools. During the subsequent course, renal involvement manifested with one episode of macrohaema- tocytosis and swelling, and abdominal pain particularly on the lower legs and the feet, joint inflammation renal transplantation. Nephrol Dial Transplant 1994;9:423-5.


Thyroid morphological findings in the mothers of infants with congenital hypothyroidism

Barlow—Little information is available on the aetiology of primary not transient congenital hypothyroidism due to thyroid malformations. It is considered to be a sporadic disease; however, to date, there are no reliable studies to identify some possible family risk factors for the disease.1 Therefore between April and September 1996, during therapeutic follow up of affected chil- dren, we examined the mothers of 19 consecutive infants with congenital hypo- thyroidism (group A) and through our regional newborn screening program (Emilia-Romagna, Italy) and 17 age matched volunteer mothers of unaffected children (group B). At the time of this examination the chronological age of the infants with congenital hypothyroidism was 5.5±3.8 years; in all cases the diagnosis of congenital hypo- thyroidism was confirmed and all had malforma- tions (15 ectopic thyroid glands, three athyrotic, one hypoplastic). All the mothers examined were resident in our region, clinically euthyroid, and had not previously had any thyroid investigations. In all subjects a thyroid ultrasound was performed by the same blind operator using a 10 MHz probe and blood samples were taken to determine serum concentrations of thyroid stimulating hormone, free triiodothyronine, and free thyroxine and antithyroid antibodies.

At the ultrasound examination three moth- ers in group A (15.8%) showed congenital thyroid abnormalities that were pathological asymmetries of the gland (agenesis of the left lobe and of the right lobe in one case and severe hypoplasia of the left lobe in the other two cases). Their incidence was 33.4% (1/3 cases) in the mothers of athyrotic children and 13.3% (2/15 cases) in the mothers of children with ectopic glands. None of the mothers in group B showed the same abnormalities. Thyroid enlargement on ultrasound examina- tion was found in 8/19 cases in group A and in 7/17 cases in group B; the percentage of nodular goitres was 75.0% and 85.7% respectively.

All subjects examined showed thyroid hor- mone values within the normal range: pos- itive antithyroid antibody titres were found in 2/19 subjects of group A and in 1/17 subjects of group B.

Congenital thyroid hemiagenesis is thought to be a rare developmental anomaly of the gland and its exact incidence is unknown as the data are usually skewed toward selected patients. The only data in literature from a large necropsy series re- ported a prevalence of 0.34%. The prelimi- nary results of our study seem to indicate that the ultrasound findings of a pathological thy-roid asymmetry represent a possible risk fac- tor for fetal congenital hypothyroidism. Fur- ther family studies are needed to evaluate the thyroid transcription factor-1 gene which is probably responsible for thyroid develop- ment. In our region (Emilia-Romagna, Italy) we have observed an elevated incidence of ‘asymptomatic’ goitres in women of fertile age. This disease, however, does not appear to be related to a higher risk for thyroid malfor- mation in the offspring.


Investigating children with mild to moderate learning difficulties

Editor—Dr Corrigan and colleagues ask important questions about the value of diag- nostic screening for children with mild to moderate developmental delay.1 Unfortunately, their study has many of the methodological weaknesses highlighted in a recent review on this field.2

The vital issue of clear case definitions is not adequately addressed mainly because no standardised cognitive or developmental as- sessment tools were employed. Furthermore to meaningfully evaluate the performance of the diagnostic tests examined in this study requires not only accurate prevalence data, but also a knowledge of the individual tests’ sensitivities and specificities.

Most of the known aetiological causes of mild to moderate developmental delay are of a low prevalence, limiting the usefulness of small studies. In the specific case of fragile X screening it is worrying that the authors con- clude ‘The failure of this study to detect any cases of the fragile X gene would suggest that until larger studies are completed on similar populations fragile X screening of children with mild to moderate learning difficulties should not be recommended’. The preval- ence of fragile X syndrome in the general population is currently estimated at around 0.2/1000 and in boys with learning dis-abilities near 5/1000.3 It is not therefore surprising that no cases of fragile X were detected in this study’s sample of 95 children. Perhaps a more appropriate conclusion would be that although they have not yet found any affected children, they should keep looking. DNA testing for fragile X has a high sensitivity and specificity, and testing is not only for the child’s benefit but also for the mother and extended family.

Choosing medical investigations in develop- mentally delayed children remains a diffi-
Increased incidence and prevalence of diabetes mellitus in Down's syndrome

Editor.—In 1968 Milunsky and Neurath reported an increased prevalence of diabetes mellitus in patients with Down's syndrome.1 However, the response rate in their survey was low (55%), and the authors did not distinguish between insulin and non-insulin dependent diabetes mellitus. In 1973, Jeremiah et al also reported an increased prevalence of diabetes mellitus in Down's syndrome patients.2 Their observations, however, were based on the presence of glucosuria.

In the second Dutch nationwide study on the incidence of diabetes mellitus type I in children, three cases of Down's syndrome were identified in the age range of 0–14 years were spontaneously reported. Taken into account a yearly incidence of 250 newborns with Down's syndrome, this results in an incidence of diabetes mellitus in Down's syndrome of 50/100,000 year (95% confidence interval (CI) 16 to 116/100,000/year), whereas in the general population the incidence during the same period was 12.4/100,000/year (95% CI 12.1 to 12.7/100,000/year). These data suggest a threefold increased risk of diabetes mellitus in children with Down's syndrome. We also estimated the prevalence in a population based study among 893 children with Down's syndrome aged 0–9 years born between 1986 and 1994. Three of them had diabetes mellitus, giving a prevalence rate of 335/100,000 (95% CI 87 to 980/100,000), which is higher than the prevalence of diabetes mellitus type I in the age matched general population (40/100,000; 95% CI 35 to 45/100,000).

Our data confirm the suspicion that children with Down's syndrome are more prone to develop diabetes mellitus. All children were insulin dependent. However, it remains to be investigated whether these patients have type I or type II diabetes mellitus as both autoimmunity and signs of premature aging in Down's syndrome could predispose towards type I and type II diabetes mellitus.3 As the symptoms of diabetes mellitus in Down's syndrome children may be more difficult to detect and there is an increased risk of complications such as hyperosmolar coma,4 special attention has to be taken to symptoms as polydipsia and polyuria.

UK paediatric clinical research under threat

Editor.—The message of your contributor(s) concerning prospects for clinical research in paediatrics was disturbing.2 Two aspects cause me concern.

First, that the author(s) requested anonymity. Was this through reticence or self effacement? There seemed little in the article to cause offence. If the author(s) thought that they or their departments might be censured by their universities or grant giving bodies, this would be a serious enough matter to be taken up by national academic and representative bodies. Academic paediatricians need visible, resolute leadership and the unequivocal support of non-university paediatricians.

Second, your contributor(s) offered no proposals to deal with the threat. It will not recede spontaneously and neither academic medicine nor clinical practice is immune from the laws of natural selection—adapt or perish. Those who lead our specialty and promote its academic underpinnings should be making plans individually and collectively (including other specialties) to meet and overcome the threat. These include your contributors, presumably, and our esteemed college Vice President who has declared his commitment to promoting paediatric research.

One tactic would be to expect that all trainees in paediatrics should undertake a period of research—not a series of audit projects. Some European countries specify that a number of papers in peer reviewed journals is required for the final certification process. The arguments for promoting research in the training of NHS consultants were set out by the President of the Royal College of Physicians a few years ago.5 Practising evidence-based medicine without knowing how the evidence was derived is absurd as managing asthma without knowledge of respiratory physiology.

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and into academic medicine. Another option would be for NHS trusts to take over the funding of HEFCE funded clinical lecturer posts, but this seems little more than a pipe dream given the existing difficulties of getting NHS trusts to fund ordinary training grade posts.

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Fashion victim: infective endocarditis after nasal piercing

EDITOR,—We report a case of infective endocarditis occurring after nasal piercing.

A previously well 14 year old girl presented three weeks after nasal piercing and metal stud insertion. After insertion she developed progressive ‘flu’ like symptoms with fever, myalgia, headache, nausea, and vomiting. Examination revealed a normally developed girl who was pyrexial (39.4°C) and uncomfortable, with suprapubic and epigastric tenderness.

Examination of her cardiovascular system demonstrated no abnormality. Investigations showed a neutrophil leucocytosis, a raised C reactive protein and erythrocyte sedimentation rate. Blood and urine cultures were taken. Because of her persisting abnormalities a laparoscopy and appendicectomy were performed and showed no abnormalities.

Despite treatment with flucloxacillin, ceftaxime, and metronidazole she proceeded to develop myalgia, headache, nausea, and vomiting.

Blood and urine cultures repeatedly grew Staphylococcus aureus despite appropriate antibiotic treatment.

Subsequently she developed signs of focal sepsis. An echocardiogram was performed, revealing a large vegetation on the anterior leaflet of the mitral valve with no evidence of valvular incompetence. The size of the vegetation and the blood culture results indicating the likely infecting organism to be S aureus. A diagnosis of infective endocarditis was made and she was treated with high dose flucloxacillin and vancomycin.

Subsequently she developed clinical signs of mitral regurgitation confirmed on echocardiography. She developed an allergic rash to flucloxacillin and treatment was changed to vancomycin. The girl was left with minor degree of mitral incompetence evident clinically and echocardiographically.

Infective endocarditis due to S aureus in the absence of an underlying cardiac defect is uncommon.1 In vitro studies have demonstrated the ability of S aureus to induce a tissue factor promoting adherence to valve endothelium, altering host responses and partially protecting from antimicrobial treatment resulting in a prolonged bacteraemia.

Initial treatment of infective endocarditis comprises intravenous benzylpenicillin and gentamicin. If staphyloccocal infection is confirmed then flucocaxillin is added and treatment continued for six weeks, using vancomycin in cases of penicillin allergy.1

Nasal carriage of S aureus renders piercing of this area more likely to result in infective endocarditis, however piercing of any mucous membrane may result in bacteraemia and infective endocarditis.

We report for the first time infective endocarditis arising after nasal piercing in a person with a structurally normal heart, and emphasise the importance in excluding this diagnosis in patients with a persisting pyrexia after recent invasive adornment.

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Needle injuries as a cause of non-accidental injury

EDITOR,—Carers of young children need to be aware of the wide range of possible non-accidental injuries so that they may be recognised and managed appropriately. The insertion of sharps into body cavities or soft tissues is an uncommon form of child abuse and we wish to report three cases presenting to us during a four year period.

Case 1—A 4 week old infant of Asian parent died before being admitted to the emergency department. A necropsy confirmed the cause of death as bacterial pneumonia. Examination of the scalp revealed a healed 1 cm laceration posterior to the anterior fontanelle. Tracts led to three broken sewing needles embedded within the occipital lobes.

Case 2—A female sibling to case 1 had previously presented at the emergency department with bruises, abrasions, and burns. A skeletal survey demonstrated four needles in the soft tissues of the head, neck, and forearm. These were removed surgically and found to be sewing needles.

Case 3—A baby boy was born at 25 weeks’ gestation after a concealed pregnancy in a young African mother. An abdominal radiograph at 3 weeks demonstrated two linear opaque objects in the abdomen. Repeat radiography after 10 days showed two further similar objects in the pelvis. At laparotomy four needles were removed.

The insertion of sharp needles through the skin or mucus membranes of young children is a rare form of non-accidental injury with only seven other cases having been described thus far.1–4 We are not aware that this is a recognised part of African or Indian culture and this must be considered and managed as child abuse.

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Acknowledgment and authors

EDITOR,—I share Dr Moncrieff’s irritation at the number of requests for information which I receive and replying to the first request for information often invites further trouble. I agree with him that researchers should do their own research.

I also agree with him about authorship but I would point out that in a department which supports a serious number of research fellows, the head of department is quite likely to have had the idea and written the grant application, as well as having a substantial hand in writing the abstracts and reports. This is hardly guest authorship and five or six research fellows can easily generate 10 to 20 papers in a year if they are consulting towards the end of their period of research.

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Height and weight achievement in cleft lip and palate

EDITOR,—We were interested to read the recent article by Lee et al.1 Of course, it is not surprising that children with cleft lip and palate have growth failure in infancy, especially with their feeding difficulties. However, follow up in this study was only to a mean of 25.5 months.2 Growth failure is common in children with cleft lip and palate and is related to the type of cleft, as well as age and sex.3 Some children with cleft palate and especially those combined with an additional midline cleft lip may be part of holoprosencephaly complex and have hypothalamic pituitary deficiency, there being no other dysmorphic features.4 However, growth hormone secretion has little influence on growth in early childhood.5 Growth may be normal in children with pituitary deficiency until approximately 2 years of age. In addition, children with midline defects may have evolving endocrinopathy with pituitary deficiencies only appearing in later childhood.6 Moreover, growth hormone deficiency has been described as 40 times more common in children with cleft lip and palate.7 We believe that although early catch-up growth is undoubtedly important, growth of children with cleft palate should continue to be monitored throughout childhood.

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1 A research culture that asks too much. Lancet 1997;349:515.

**Aetiology of asthma**

EDITOR,—Austin and Russell suggest that mobility of families may be more important in the aetiology of asthma than exposure to any one individual allergen or pollutant. This ties in with the finding of Hughes and Baumer, except that they failed to ask whether there is an emotional component to this. Most of us know that moving house is second only to divorce as a traumatic event in life, and considering the greater attachment that children have to their home (they after all spend more time there than adults as a rule), it is no surprise that this could be the mechanism of the effect these authors describe. In some cases the move may be due to family break up.

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