Meningoencephalitis after measles-mumps-rubella vaccine

Str,—Altogether 124 health districts in this country have now achieved 90% coverage for measles-mumps-rubella (MMR) vaccine. Against this background, there have been several reports of meningoencephalitis temporally associated with the administration of MMR.1,2 The adverse publicity such cases generate and their potential seriously to harm a vaccination programme must not be underestimated. We would like to describe one suspected case which, despite subsequent exoneration of the vaccine, had an immediate impact on MMR coverage.

An 11 year old boy was admitted to hospital with a 72 hour history of vomiting and headache. He had received MMR vaccine 10 days before the onset of symptoms. On arrival he was afebrile and nonfocal but immediate investigations (including microcopy of the cerebrospinal fluid) were unremarkable. He was started on acyclovir and on examination but died 48 hours after admission. The cause of death was thought to be vaccine induced mumps encephalitis and this was quickly disseminated on the state medical and nursing network.

Immediately after the child's death the local director of public health convened an action committee. A press statement was released to the effect that there was no evidence to implicate the vaccine as the cause of death. Investigations subsequently revealed serological evidence of past mumps infection. No mumps virus was demonstrated on direct polymerase chain reaction of brain tissue. The only virus isolated was an echovirus type 25 from nasopharyngeal secretions. The committee therefore produced a further press statement confirming that there was no link between the vaccine and this child's death.

Professional and parental anxiety led to a sharp fall in MMR vaccine uptake that has only been restored after six months of considerable efforts by district staff. This case illustrated the importance of thorough investigation of a suspected vaccine reaction and ensuring a coordinated district response. We advise caution in labelling such an incident as vaccine related until conclusive evidence is obtained.

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LETTERS TO THE EDITOR

A new syndrome of congenital hypoparathyroidism, severe growth failure, and dysmorphic features

Str,—We were interested to read the paper by Dr Sanjad and colleagues1 as we previously described an identical group of patients in this journal.2 (1) The patients in our paper were from several parts of the Middle East and were not exclusively from Kuwait. This would suggest that the gene frequency is widely distributed throughout that region, and is not confined purely to Saudi Arabia as suggested by Sanjad et al in their paper.

(2) No comment was made relating to the skeletal surveys of these patients and we would be interested to hear whether the skeletal abnormalities described in our paper were present in these children.

(3) Although the patients in the paper by Sanjad et al were quoted as having normal T cell function, we note that four of their patients died during the first year of life, possibly because of intercurrent infections.

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Dr Sanjad and colleagues comment:

We appreciate Drs Richardson and Kirk's interest in our paper on congenital hypoparathyroidism, recently published in the journal.1 In our original description of the syndrome in 1988 we described the clinical and laboratory findings in five infants with severe intrauterine and postnatal growth retardation, congenital hypoparathyroidism, and dysmorphic features.2 (1) We do not deny that the gene for this syndrome may be widely distributed throughout the Arabian peninsula but were intrigued by the fact that almost 60% of the patients in our series originate from the western province of Saudi Arabia. (2) Skeletal surveys were performed in eight of our 12 patients. They revealed delayed bone age and varying degrees of demineralisation but no medullary stenosis of the long bones as described by Richardson and Kirk. (3) Cellular immunity, measured in five patients (and in another two, subsequent to our publication), was found to be intact—both quantitatively and functionally as detailed in our paper. While two of four deaths among our patients were attributed to infections, factors other than cellular or humoral immune deficiencies would have to be invoked. Again, this is in contrast to Richardson and Kirk's experience where four of their patients died without having reduced number of T lymphocytes.

In summary, the dysmorphic features and severe growth retardation in Richardson and Kirk's patients are indeed similar to the ones we have described. The skeletal and immune abnormalities in their patients probably represent additional variants to the same syndrome.


Gonadal function after allogeneic bone marrow transplantation for thalassaemia

Str,—De Sanctis et al in their paper on gonadal function after allogeneic bone marrow transplantation for thalassaemia observed gonadal damage in 80% of their girls with raised gonadotrophins and unmeasurable oestradiol concentrations.3 In contrast all the boys had gonadotrophin concentrations within the normal range with variable gonadotrophin responses to an intravenous dose of gonadotrophin releasing hormone. They concluded that the chemotherapy used as a preparative regimen for bone marrow transplantation in prepubertal life led to a higher incidence of gonadal toxicity in girls than boys.

We disagree with the conclusions of the authors. There is a body of evidence to suggest that the germinal epithelium of the testis is more vulnerable to cytotoxic damage from either chemotherapy or radiation than the Leydig cells of the testis or the ovary.2 Furthermore although it may be difficult to diagnose gonadal damage in prepubertal life, the age range of the two sexes at the time of the study was similar.

We would suggest that the results presented by De Sanctis et al do indicate a sexual dimorphism in thalassaemic children, not in terms of their gonadal response to chemotherapy damage, but rather in the persistence of gonadotrophin deficiency after iron deposition in the hypothalamic–pituitary axis. The question to ask is why the thalassaemic boys failed to mount an appropriate gonadotrophin response to gonadal damage in the presence of similar ferritin concentrations to those seen in the girls, whose gonadotrophin responded appropriately.

Incidentally, the testosterone concentrations quoted both for the thalassaemic boys and the controls are incorrect. The normal adult male range for testosterone is 10–30 nmol/l.

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Dr De Sanctis and Galimberti and Professor Lucarelli comment:

We thank Drs Oglivy-Stuart and Shalet for their interest in our paper and for their criticism.


Drs Ogilvy-Stuart and Shalet suggest that our results indicate a sexual dimorphism in thalassaemic children in terms of persistence of gonadotrophin deficiency secondary to iron deposition in the pituitary. The aim of our study was to assess whether conditioning treatment before bone marrow transplantation (BMT) with busulphan and cyclophosphamide may cause gonadal damage in thalassaemic patients, which would have a deleterious effect on the quality of life. While our data did not demonstrate obvious gonadal damage in prepubertal boys, it did so in girls. As a consequence, the discussion was focused on this last aspect, which was crucial to the aim of the study. However, we did recognize the possibility that the reduced gonadotrophin response after gonadotrophin releasing hormone in prepubertal thalassaemic males may be a consequence of iron overload which could conceal germinal epithelial damage. There is no doubt that long term follow up studies are necessary to demonstrate if the gonads of male thalassaemic patients are damaged by cytotoxic drugs.

This possibility is an additional reason for considering gonadal damage when discussing the pros and cons of BMT and this aspect was emphasised in our discussion. We agree that the patterns of gonadotrophin in response to gonadotrophin releasing hormone, found in prepubertal thalassaemic males, suggest a higher sensitivity to iron overload. However, we feel that other studies must be made to explain this dimorphism in thalassaemic patients, because this hypothesis is not supported by the findings of a multicentre study on endocrine complications in 3200 thalassaemic patients followed up in 41 Italian hospitals. The result of our survey has shown an absence of puberty in 41% of the males and 39% of the females, over the age of 15 years (V De Sanctis et al, unpublished data). We thank Drs Ogilvy-Stuart and Shalet for pointing out that the serum testosterone values reported in table 2 and in the text are not correct. We are very sorry for this mistake, which was caused by the change made from ng/ml to nmol/l. The values given should be reduced by a factor of 100.

**Computerised information systems**

WeIR.—I read with interest Dr Spencer’s recent article on neonatal information systems.1 While admirable covering large topic few pages, there were two points that I feel warrant greater emphasis.

1 ‘Local’ databases that are set up by enthusiasts—and I have been involved in four such systems in different hospitals—often fall into relative or absolute disuse after a period of time. While this may be due to fundamental weaknesses in the systems, it is more commonly due to one of two factors.

Firstly, the enthusiast who initiated the project may well move to a different hospital. This leaves a void, often with direct control passing to someone who was not immediately involved in the development. Any problems that later arise (and they will!) may be difficult to fix, and further development of the system often ceases.

Secondly, and associated with the first point, is the importance of clear documentation. Dr Spencer mentioned this in his last sentence as ‘an asset’, but this understates its crucial role. Interest in the database is likely to wax and wane with time, as workload alters, research fellows come and go, and as the deadline for yearly reports comes round. Without comprehensive and clear documentation for a system, including details of trouble shooting and support available, the system will gradually deteriorate. Clear manuals must be an essential aspect of any computerised system.

**Equipment requirements for community based paediatric oxygen treatment**

SIR,—The bare list of ingredients required for domiciliary oxygen treatment is of little value without accompanying instructions on how they should be assembled.1 Deficiencies in the current system of provision for community based oxygen treatment need to be tackled by national recommendations and the provision of appropriate devices for young children on prescription.

To this end, a Working Party on Domiciliary Oxygen Therapy for Children was convened under the auspices of the Committee for Thoracic Medicine of the Royal College of Physicians (London) in order to provide the Department of Health with the concerted recommendations of a number of organisations. It met in January and its recommendations have been submitted to the Department of Health.2 Briefly the document recommends the types of equipment that are needed, the means whereby the equipment should be supervised, and the level of clinical support for families receiving domiciliary oxygen treatment. The responsibilities of health professionals within and without the hospital and the role of the equipment industry were addressed.

It is hoped that these recommendations will provide the basis for the provision of domiciliary oxygen treatment for children to match the system which has evolved over a number of years for adults with chronic obstructive airway disease.

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2 *Members of the working party represented: Royal College of Physicians, Royal College of General Practitioners, Medical Gas Industry, Cystic Fibrosis Trust, British Paediatric Association, British Association of Perinatal Medicine, Royal College of Nursing, Department of Health, and British Thoracic Society. Copies of the recommendations are available from Dr Silverman on receipt of an A5 stamped, addressed envelope.

**Septicaemia and adenral haemorrhage in congenital asplenia**

SIR,—The incidence of congenital absence of the spleen is said to be one in 2000, according to the one postmortem series.3 Dyke et al report five cases of asplenia including two otherwise normal infants.1 We have recently seen a 1 year old infant who, in first year of life, had pseudoneumococcal meningitis twice and osteomyelitis (culture negative) once. Several ultrasound scans and a technetium labelled sulphur colloid scan failed to reveal a spleen. Numerous Howell-Jolly bodies were present in the erythrocyths. He has no other apparent congenital abnormalities; immuno-globulin, white cell, and complement studies are normal. We concur with Dyke et al that congenital asplenia is an under recognised entity, and recommend the use of pneumococcal and Haemophilus influenzae vaccine at diagnosis, despite the lack of demonstration of efficacy in infants less than 24 months. The potential of vaccination appears to outweigh possible adverse effects. Surely these infants need not wait until aged 18–24 months for potentially preventative immunisation?

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**Case report**

A white girl aged 2 months was taken late at night to a country hospital with a three day history of breathing difficulties and cough. Apart from a non-prescription cough medicine no other medication had been given before admission. The initial investigation showed that she had a temperature of 38°C and was tachypnoeic with laboured respirations. A provisional diagnosis of pneumonia was made and a single dose of intramuscular penicillin was given. After admission she appeared to settle initially but was found dead in bed four hours later. Her body was transferred to the Adelaide Children’s Hospital for postmortem examination with a provisional diagnosis of death from pneumonia or possible sudden infant death syndrome.

At postmortem examination there was situs inversus of thoracic and abdominal organs with dextrocardia but no other significant cardiac abnormality. There was no spleen but two splenunculi (combined weight 3 4 g) were found in the right upper quadrant. Both adrenal glands were appreciably haemorrhagic. The lungs were atelectatic but there was no evidence of pneumonia. Bilateral otitis media was evident. Microbiological cultures including blood culture and culture of lung and middle ears were negative, but penicillin given before death may well have eliminated a sensitive organism.

This case further emphasises the points made by Dyke et al of the need to look for