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Where are all the babies? Paediatric risk of mortality score in meningococcal disease

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Sir: We read the paper of van Brakel et al. [3] with great interest, but are intrigued by the composition of the study population. In that study [3], the mode age of the population was 3 to 4 years old. In our experience, as in several other reported studies, the peak attack rate is in the under 1 year-old age group [1, 2]. Our data show the highest number of Paediatric Intensive Care Unit admissions being in the under 1 year-old category (Fig. 1), as do the studies from Melbourne, Australia [2] and Western Norway [1]. The number of admissions then falls rapidly towards the age of 5 years old. There is a well-reported secondary peak, in the early teenage years, which we also found.

Does the higher mode age of admission in meningococcal disease in the Dutch study reflect a different pattern of meningococcal disease acquisition? Alternatively, does it reflect the fact that the younger age groups do not survive to be admitted to a Paediatric Intensive Care Unit in the Netherlands, or are they cared for elsewhere?

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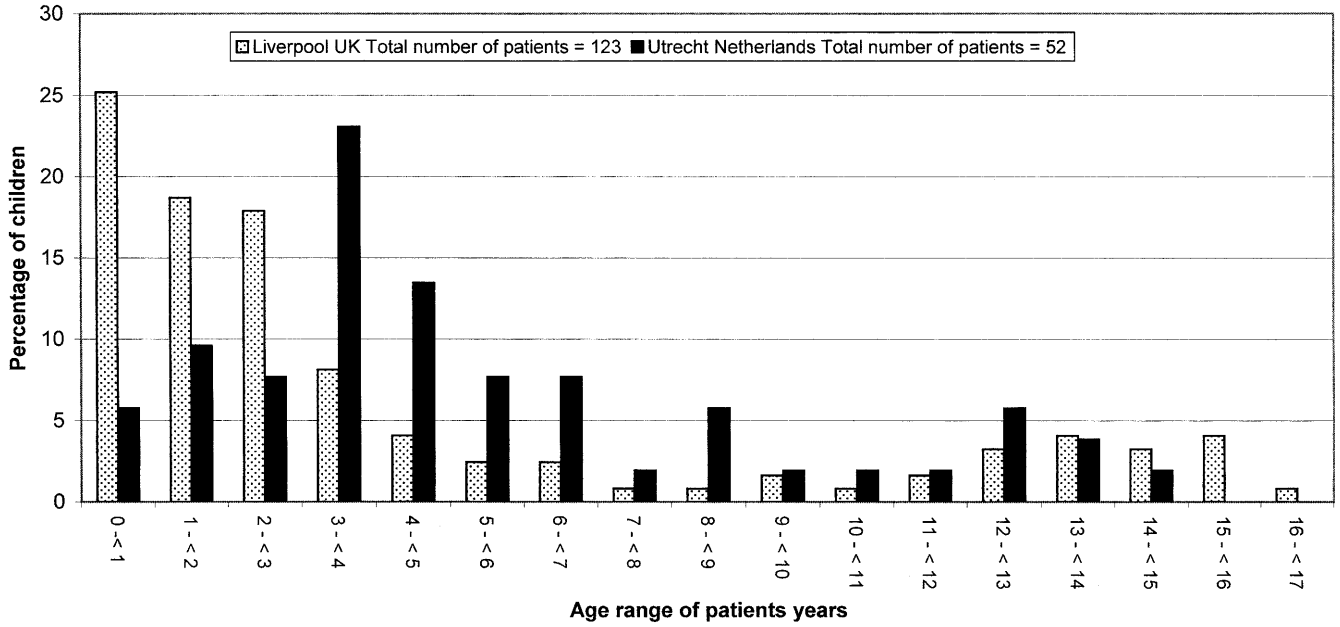

Fig. 1 Graph depicting the percentage of each age group admitted to two Paediatric Intensive Care Units with a diagnosis of meningococcal disease

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Successful treatment of phenylketonuria with tetrahydrobiopterin

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Sir: Worldwide newborn screening for phenylketonuria (PKU) and early dietary treatment of patients with impairment of the enzyme phenylalanine hydroxylase has resulted in prevention of mental retardation in more than 3000 patients [3]. However, a small number of patients with increased blood phenylalanine (Phe) levels have a defect of the coenzyme tetrahydrobiopterin (BH_4) which leads to hyperphenylalaninaemia (HPA) and neurotransmitter deficiency. They are treated by BH_4 and neurotransmitter supplementation [1]. Up to now, no patient with a defect in the apoenzyme was found who can simply be treated by supplementation of BH_4. One of our PKU patients responsive to BH_4 supplementation was found in the newborn screening programme with blood Phe levels of 96 μmol/l (reference range 36–108 μmol/l) and at 14 days of age of 885 μmol/l. BH_4 loading (20 mg/kg body weight) resulted in a decrease of blood Phe to 67 μmol/l 8 h post-loading. Under normal feeding with a breast milk adapted formula, plasma Phe levels rose again to 934 μmol/l. With a daily supplementation of 10 mg/kg of BH_4 (Dr. Schircks Laboratories, Jona, Switzerland), blood Phe levels dropped again and remained between 84 and 222 μmol/l. Surprisingly, there was no BH_4 coenzyme deficiency (normal values for neopterin and biopterin in urine, normal dihydropteridine reductase activity in red blood cells, and normal neurotransmitters and pterins in cerebrospinal fluid). However, mutation analysis of the phenylalanine hydroxylase gene revealed the two mutations IVS10G^{-11}A in intron 10 and E390G in exon 11. The first one creates a zero activity of the enzyme, the second one is a missense mutation, together resulting in a phenotype with mild PKU [4]. The patient is now at 10 months of age on 10 mg BH_4/kg per day and developing normally. We speculate that there may be more mutations resulting in a K_m-variant of the phenylalanine hydroxylase enzyme in which enhancement of the residual activity can be achieved by supplementation of BH_4 as recently also found in hyperphenylalaninaemic patients in Japan [2]. Our observation strongly emphasises the necessity of the BH_4 loading test in the newborn period and further DNA mutation analysis in hyperphenylalaninaemic patients responsive to BH_4 supplementation. BH_4 supplementation instead of a low Phe dietary treatment may be possible in at least some patients with PKU or mild PKU. In these cases, treatment compliance with coenzyme substitution may be much better in adulthood.

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Bartonella henselae bacteraemia in patients with cat scratch disease

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Sir: We read with interest the article on cat scratch disease (CSD) by Del Prete et al. [1]. They suggested that PCR-DEIA assay provides a rapid and specific test for CSD. To our knowledge, the prevalence of bacteraemia among patients with CSD is not known. We report here the prevalence of *Bartonella henselae* bacteraemia detected by PCR among CSD patients.

Between July 1996 and June 2000, 229 sera and 67 peripheral blood cells from 229 patients (155 children and 74 adults) suspected of having CSD were sent to us for serological and PCR diagnosis [2, 3]. Of the 229 patients, 82 (62 children and 20 adults) were serologically positive for *Bartonella*, whereas 147 were serologically negative. The PCR, performed in 26 of 82 patients with serological diagnosis and in 41 of 147 patients without serological diagnosis, was positive in 5 of 26 (19.2%), and in 2 of 41 (4.9%), respectively. Altogether, 7 of 67 (10.4%) patients gave a positive PCR. The sequence of the amplicons was identical to that previously reported for *B. henselae*.

Three possibilities could explain that 2 of 41 patients without serological diagnosis were PCR positive. First, PCR contamination occurred in the patients; however, we believe the possibility is remote because of careful laboratory procedures to prevent contamination, and the use of positive and negative controls. Second, PCR demonstrated bacteraemia in the initial stage of illness before the significant rise of antibodies to *Bartonella*. It was hard to prove this possibility because convalescent-phase sera were unavailable in these patients. Third, the immune response of these patients was not enough to produce antibodies to *B. henselae* even if bacteraemia was present.

Our findings suggest that bacteraemia may not be rare in immunocompetent healthy individuals with CSD. PCR analysis combined with serological studies may be recommended for early detection and immediate intervention of *B. henselae* bacteraemia.

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