Burkholderia cepacia and ΔΔ508 homozygosity in cystic fibrosis

EDITOR—Colony formation by Pseudomonas aeruginosa has long been recognised as a common trait in cystic fibrosis. Lately also Burkholderia cepacia, formerly known as Pseudomonas cepacia, has emerged as a common finding in cystic fibrosis as a significant, although not so widespread, pathogen. As it has been suggested that homoygotes for ΔΔ508, the commonest cystic fibrosis mutation, could be more often affected by B cepacia than by other bacteria, we decided to evaluate the correlation between ΔΔ508 homozygosity and B cepacia colonisation in cystic fibrosis.

All patients attending the Verona Cystic Fibrosis Centre between November 1991 and November 1994 were examined for B cepacia airway infection, and most of them genetically tested for ΔΔ508. B cepacia colonisation was considered chronic after at least two positive cultures a year for one or more years, or three consecutive positive cultures over a four to 12 month period. Fourteen out of the 40 (35%) chronic and eight out of 38 (22%) non-colonised patients were homoygotes for ΔΔ508. A significant difference in frequencies was shown between subjects chronically colonised by B cepacia who were homoygous for ΔΔ508 and patients chronically colonised carrying other genotypes (2×2 contingency table analysed by Fisher's exact test; p value = 0.0123; odds ratio = 2.468; confidence interval = 1.236 to 4.927). Clinical evaluation of patients showed in ΔΔ508 homoygotes no signs of a more severe pulmonary disease, which could have explained the different colonisation rates, and the comparison of two investigations showed no significant difference (forced expiratory volume in one second p value = 0.8985; x ray score p value = 0.7277). Furthermore we could not find any evidence of early colonisation by B cepacia in ΔΔ508 homozygotes: there is no significant age difference at B cepacia first isolation in the two genotype groups (two tailed p value = 0.2876).

Our data show how patients show a higher prevalence of B cepacia chronic colonisation, and have more than double the chance of colonisation, compared with those carrying different genotypes. Surely environ- mental factors influence the colonisation rate, but apparently genotype is involved as well. If further studies in different populations and environments confirmed these results, the determination of chronic colonisation by B cepacia could be extensively included in studies on the genotype/phenotype correlation, considering also mutations less frequent than ΔΔ508.

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Birth weight in phenylketonuria

EDITOR—The report by Verkerk et al of relatively low birth weight in Dutch infants with phenylketonuria1 agrees well with our earlier finding of low birth weights in phenyl- ketonuria in Ireland and west Scotland.2 In agreement with other workers in the USA,3 the UK,4 and Poland,5 we found that in our total sample of 62 infants with phenyl- ketonuria and 53 unaffected siblings, and within families, there was no significant difference between infants with phenyl- ketonuria and their unaffected siblings either in their unadjusted birth weights or in their birth weights adjusted for factors that affect this quantity. Moreover, the 115 birth weights in the combined sample lay on a normal distribution curve with no evidence of a bimodal or tridomal distribution. However, in 4 of 19 (21%) children and 84 out of 85 (51%) infants of the combined sample was 121 g less than the mean for a randomly selected sample of 819 control infants born in the same hospitals in the same years as the infants with phenyl- ketonuria and their siblings (p < 0.02); for the adjusted birth weights the difference between the means was 107 g (p < 0.02). We concluded that, as the reduction in birth weight was the same for both infants with phenyl- ketonuria and their unaffected siblings, the lower birth weight was not related to the pathogenesis of phenylketonuria or to the fetal genotype. It appears that the random loss of weight in birth was most likely due to the maternal genotype affecting the intrauterine environment and was a previously unknown effect of the phenylketonuria gene in single dose.


Dr Verkerk comments: Verkerk and Crockett hypothesise that the reduced birth weight in phenylketonuria as found in some studies may be the result of maternal genotype affecting the intrauterine environment. This interesting hypothesis is based on their own findings and on a qualita- tive review of the literature. According to their theory no differences should be found in birth weight between infants with phenylketonuria and their healthy siblings. However, the find- ings of the first study on the relationship between phenylketonuria and birth weight are not in agreement with this theory.1 The study by Saugstad found that mean birth weight of 49 infants with phenylketonuria was 356 g lower than mean birth weight of their 86 healthy siblings. After adjustment for differences in gestational age, the discrepancy in birth weight even increased to 530 g. I am therefore not yet convinced by the explana- tion offered by Woolf and Crockett. Perhaps a quantitative review of the literature (meta- analysis) may provide more information on this subject.


Diagnosis of mycobacterial lymphadenopathy

EDITOR—Clark and colleagues recently reviewed 17 cases of non-tuberculous mycobacterium (NTM) lymphadenopathy.1 As they conclude, it is important to differentiate mycobacterium avium complex (MAC) infection, although this is not always possible on clinical grounds alone. If mycobacterial infection is suspected, then definitive species group identification is essential, as the surgi- cal management, and the antibiotic sensitivi- ties, of NTM and M tuberculosis are very different.

Skin testing is a useful first line investi- gation of infective lymphadenopathy.2 Mycobacterium avium purified protein deriva- tive is available commercially in Australia (but not in the UK). Cross reactivity between this and the human immune test is common. However, if a NTM is the causative organism then the M avium hypersensitivity reaction is usually significantly larger than that caused by...
the human Mantoux. If skin testing is equivocal, or in cases of infection involving potentially vulnerable sites (such as the mastoid), when adjacent antimycobacterial drug treatment is given, then it may be helpful to have the surgical disease examined by the polymerase chain reaction. This allows differentiation between \( M. \) \textit{tuberculosis} and NTM infection, although the specificity and sensitivity of the polymerase chain reaction in this setting is not known. Thus appropriate antimycobacterial treatment can usually be given long before mycobacterial culture results are available at 2–3 months, and the choice of treatment does not rely solely on clinical features.

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Overnight oscillations of rectal temperature

EDITOR.—We have previously reported from New Zealand regular variations of overnight rectal temperature in infants. The periodicity is about one hour and the amplitude up to 0–3°C. These infant rectal temperature oscillations were found in 24 (80%) of 30 continuous overnight recordings. We have now examined a further 98 overnight recordings of rectal temperature that were part of a study by Wallen et al from Leicester. These recordings were classified by the infant’s state of health: ‘well’ (n=24), ‘incubating illness’ (n=44), or ‘unwell’ (n=30). Regular oscillations were observed visually in 68 (69%) of 99 overnight recordings, similar to the 80% reported from New Zealand. Using power spectral density and digital filtering techniques, confirmation, and measurement, of regular oscillations were found to be present in 55 of these 68 recordings. Temperature oscillations were seen equally in all three health groups of the infants. Also there was no change seen in the proportion of infants with oscillations with increasing age.

The mean period of oscillations in the Leicester babies was 59–2 minutes (range 46–5–73–2); this compares well with the 58 minutes as discovered by Brown et al. Well infant records had oscillations with a slightly longer period (mean 63–4 minutes) than unwell infant records (mean 57–2 minutes) (p<0.05) with those incubating illness in between (mean 58–6). The oscillatory period was significantly shorter for infants over 12 weeks (mean 57–1 minutes) than for infants under 6 weeks (mean 62–5 minutes), with infants 6–12 weeks falling in between (mean 59–2).

We have shown that the presence of overnight temperature oscillations is a consistent characteristic of early infancy, occurring both in health and illness.

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Compliance with growth hormone treatment – are they getting it?

EDITOR.—We previously reported that only 48–9% of our patients treated with recombinant human growth hormone (rhGH) complied in all aspects. We identified patient education and rhGH reconstitution as the major contributory factors and, as a consequence, offered a choice of rhGH preparation appropriate to their needs and a hospital based clinical nurse specialist to train them in its use at home. We have now administered the same questionnaire to a new group of patients.

Patients attending over a two month period were asked to complete a questionnaire if they were receiving rhGH. The questionnaire designed to assess level of understanding and compliance with treatment was accepted by 177 patients. Altogether 105 (59%) (group 1) had started treatment before the change in policy; 64 (36%) (group 2) had been trained by a clinical nurse specialist at home. Eighty one per cent of patients in group 2 had a good, 10% an adequate, and 9% a poor understanding of the therapeutic regime compared with 50%, 34%, 15% respectively before (p<0.01). Patients in group 1, who had started rhGH before the change in policy failed to improve their understanding of the therapeutic regime despite being seen at regular intervals at hospital visits by a clinical nurse specialist.

Compliance was assessed by questions designed to uncover the number of missed injections during a three month period. Fifty eight per cent of patients in group 1 complied with all aspects of their treatment, which was not significantly different from our previous experience; 84% of patients in group 2 complied with all aspects of their treatment (p<0.001).

Compliance in children prescribed rhGH treatment has improved considerably. Initial training of the patient and family at hospital appears to be the most important element in achieving compliance.

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Morbidity from excessive intake of high energy fluids: the ‘squash drinking syndrome’

EDITOR.—Following the article by Hourihan and Rolles on the ‘squash drinking syndrome’ we would like to take the opportunity to remind readers that excessive squash drinking can rarely be associated with serious side effects than failure to thrive. Recently a 22 month old girl presented here with a generalised afibril convulsion and hypotonia. She had previously been recognised elsewhere as failing to thrive, with her weight lying below the third centile. Her weight at presentation here was 8.7 kg. On questioning she was found to be drinking approximately two litres of squash a day, as she slept with a large jug of juice at the bedside.

Investigation revealed a serum sodium concentration of 114 mmol/l, potassium 4.0 mmol/l, urea 2.9 mmol/l, creatinine 54 μmol/l, glucose 5.2 mmol/l, and calcium 2.34 mmol/l with a simultaneous urinary sodium of 19 mmol/l and urinary osmolality of 128 mmol/kg. Serum sodium rose to normal concentrations simply with fluid restriction to normal fluid requirements of around one litre a day. A water deprivation test subsequently revealed normal renal concentrating ability excluding diabetes insipidus as a cause for her polydipsia. The parents were advised to restrict squash consumption.

There have been no further fits on follow up over one year. Squash consumption has varied, but a normal serum sodium has been maintained. However, weight gain has been better at those times when squash consumption has been less excessive.

We agree with Hourihan and Rolles that excessive squash consumption is an important cause of failure to thrive. Additionally the possibility of water intoxication, with all its complications, should be considered if squash consumption is excessive.

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The art of communication with children

EDITOR.—The need to communicate well with children and their parents is fundamental to paediatric practice. Most of us see our young children, including those sick children, as their doctors, but rarely do we get an opportunity to join them as normal adults with whom they can play and frankly discuss their problems. One way I learnt to understand children was to spend some weekends camping with the Woodcraft Folk, a recognised educational charity for children and young people. These camps are organised as