PostScript

LETTERS

Determining the true prevalence of autistic spectrum disorders

We read with interest the January edition of *Archives* containing three thought-provoking articles on the autistic spectrum. The article by Harrison *et al.*,¹ which described the two source "capture recapture" technique as a means of determining "true" prevalence, provided an enlightened alternative to using conventional, "passive" ascertainment of point prevalence. We conducted an 18-month retrospective audit of our social communication clinic for children in Enfield. The primary aim was to compare our clinic with the recommendations set by the National Autism Plan²; however, it also raised issues on:

1. the difficulties in obtaining accurate prevalence and incidence estimates; and
2. the effect of changes in child health surveillance policy.

Cases were identified from the Enfield social communication clinic referral dataset for the referral period January 2004–June 2005. A total of 124 children were referred during this period, of whom 66 fulfilled the criteria for autistic spectrum disorder (ASD; using either International Classification of Diseases—10th revision or the Diagnostic and Statistical Manual of Mental Disorders—IV revision). The birth rate in Enfield is about 4000 children/year. The age-related incidence of ASD was calculated looking at chronological years. In the age groups 2–3 and 3–4 years, for which 40 patients were diagnosed over an 18-month period, we found an age-specific incidence of 33.2/10 000 children/year. This is considerably higher than the incidence rate of 8.3/10 000 reported by Powell *et al.*,³ who looked at preschool children being diagnosed in the West Midlands between 1991 and 1996. Published prevalence estimates are, however, highly variable as shown by the recent systematic review by Williams *et al.*,⁴ ranging from 3.3 to 121/10 000 children, largely dependent on diagnostic criteria, age of assessment and case-load location.

Enfield's Pupil Level Annual School Census records from 2005 show that the Local Education Authority (LEA) was aware of 255 children known to have a diagnosis of ASD (point prevalence of 46/10 000). Capture and recapture methods applied to special educational needs data and our records over a longer period of time would be expected to give a truer picture of the incidence and prevalence of ASD.

We were surprised by Harrison *et al.*'s data from Scotland, where only 5% of patients were <4 years of age. In all, 60% of the children diagnosed in our social communication clinic fell within the 2–4-year age group. We speculate that this is primarily due to our referral patterns (fig 1).

We found that 26% of our referrals came from health visitors after the 2-year checks. This suggests that routine surveillance is making a considerable contribution to the early detection of autistic spectrum disorders in Enfield. This has been documented by other

Figure 1 Source of referrals to Social Communication Clinic. ENT, ear, nose and throat; EP, educational psychologist; GP, general practitioner; HV, health visitor; OT, occupational therapist; SENCO, special educational needs coordinator; SLT, speech and language therapist; SN, school nurse.

investigators. Tebruegge *et al.*⁵ conducted a retrospective study of year 4 pupils attending 74 schools in Maidstone, and found that 68% of children diagnosed with ASD had been referred for further assessment as a consequence of routine 2–3 year checks. The uptake rate of the 2-year check offered by health visitors in Enfield is around 80% (Profit Impact of Marketing Strategies Data 2001); the 2-year check provides, and is a good opportunity for communication difficulties to be picked up in a culturally diverse area where questionnaire-based assessments are less effective. Unfortunately, the extent of this contribution to Enfield will only be clear when the current local practice is discontinued.

Clearly, barriers to sharing database information are found across agencies, but the ability to share such information would help ascertain not only the "true" prevalence of ASD but also local demographical needs, enabling comprehensive planning and provision of services.

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A survey of palivizumab for infants with cystic fibrosis in the UK

Palivizumab is a humanised monoclonal antibody to respiratory syncytial virus (RSV) that has been advocated as a potential prophylactic treatment in at-risk infants (ex-preterm).¹ Infection with RSV in cystic fibrosis may be a factor in the development of early lung disease and acquisition of bacterial pathogens. We aimed to determine the number of infants with cystic fibrosis in the UK who would be potential candidates for palivizumab prophylaxis and to quantify hospitalisation rates and mortality from RSV in this cohort. We conducted a national questionnaire study of 42 cystic fibrosis centres over the winter RSV season of 2005–6. Data were sought on patient population (number of infants born after October 2004), admissions with RSV infection and palivizumab use. Testing for RSV infection occurred where clinically indicated. Questions were asked on the likelihood of prescribing palivizumab, if funding were not an issue, and on the significance of RSV infection in the pathogenesis of early cystic fibrosis lung disease (scale: 1, not likely to 10, very likely).

In all, 34 centres responded (81%). A total of 143 infants with cystic fibrosis aged <1 year (mean 4.2 infants/centre) were identified. Of these, 70 infants were diagnosed by newborn screening (48.6%); 16 (11.2%) of the 143 infants were hospitalised owing to RSV infection; none required paediatric intensive care unit admission and none died; 14 (9.8%) infants received palivizumab between three cystic fibrosis centres, and one of these infants was subsequently hospitalised with RSV infection (other risk factors for this infant were not reported). Two of the three centres that used palivizumab had a local funding agreement negotiated into annual costings and offered RSV prophylaxis to all their patients <1 year of age. The likelihood of prescribing palivizumab if funding were not an issue was rated as a median of 6.5. The significance of the role of RSV in the pathogenesis of early cystic fibrosis lung disease was rated as a median of 5.0.

This survey highlights several issues regarding treating infants with cystic fibrosis using palivizumab. Subjectively, most respondents consider RSV infection important in cystic fibrosis lung pathogenesis and, if funding were not an issue, would prescribe palivizumab. However, there are no data from randomised controlled trials to support this,² and our data suggest that designing such a trial would require an unfeasibly large number of participants to show a clinically relevant reduction in hospitalisation. Given the importance doctors place on the long-term consequences of RSV infection in cystic fibrosis pathogenesis, reduction in hospitalisation may not be an appropriate outcome measure. Again, studies that evaluate longer-term outcomes that correlate with respiratory well-being are impractical. We are in a difficult situation; there is no national guidance on the use of palivizumab for infants with cystic fibrosis, and it is unlikely that

evidence of efficacy from well-conducted randomised controlled trials will become available to support its use, yet cystic fibrosis teams believe that prevention of RSV infection is intuitively a good policy, and a few have already organised local funding support under the umbrella of a "chronic paediatric respiratory illness". Engaging in RSV prophylaxis is a major undertaking for families of infants with cystic fibrosis, and our survey suggests that, given the current lack of an evidence base, only a minority of cystic fibrosis centres in the UK are advocating such a policy.

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A newborn screening programme for congenital toxoplasmosis in the setting of a country with less income

A well-established newborn screening programme for congenital toxoplasmosis has been reported in a European country with low prevalence¹; however, this programme has also been implemented in countries with lower income but with a higher percentage of newborn infected children. We conducted a study in 11 public health community hospitals in the Department of Quindío, excluding the capital (Armenia), in Colombia; about 4560 children are delivered in these hospitals annually. Infants born from August 2003 to December 2003 were enrolled in the study. Informed consent was obtained from mothers during sampling and results were reported in accordance with the resolution 008430 of 1993 of the Ministry of Public Health concerning medical research in Colombia. All serum samples were tested with the Platelia Toxo IgM Neonatal assay (Bio-Rad, Hercules, California, USA) as recommended by the manufacturer. In all, 322 samples were collected, including 106 dry paper samples from the heel, which about 25% of which were insufficient. Thus, 216 samples were taken in 5-ml tubes at the arm at the first medical check of the newborn (10-30 days after birth). All the poor-quality dry paper samples were taken again at the arm. Five samples showed positive Platelia IgM assay (one from a filter card and

four from the tubes). All positive samples were then confirmed on the same sample by testing immunoglobulin (Ig)M and IgA using the ISAGA assay (ISAGA Plus, BioMérieux, Marcy L'Etoile, France) and a commercial western blot assay (ID Blot Toxoplasma DPC Diagnostics, Los Angeles, CA, USA) was performed according to the manufacturer's protocol. Diagnosis of congenital toxoplasmosis was conclusive for two children (a dry paper sample in one case and a tube sample in the other). Both children showed the simultaneous presence of toxoplasma-specific IgM and IgA in ISAGA and western blot assays. Three children with negative ISAGA and ID Blot assays were considered not to be infected. Thus, the prevalence of congenital toxoplasmosis during this newborn screening programme in community hospitals in Quindío was 0.62% (95% confidence interval 2.2 to 0.19). The two infected children were asymptomatic and were treated with weekly doses of pyrimethamine-sulfadoxine for 1 year. Both children remained asymptomatic and without ocular signs or gross neurological problems at the end of the first year of life. Our results show that it is possible to carry out neonatal screening for toxoplasmosis and to identify congenitally infected but asymptomatic children.

We think that in countries such as ours, detection programmes for congenital toxoplasmosis should be established urgently. Newborn screening programmes would be an attractive strategy in countries with less income for two reasons. Firstly, the toxoplasmosis prenatal screening programmes are very costly. Thus, in Colombia, despite their proved effect on the health of Colombian children,²⁻⁴ the public and private health assurance companies are reluctant to implement these programmes. Secondly, a large number of mothers (10-20%) did not have prenatal care, and congenital infections can be detected only in newborns.

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Positive benefit of postnatal treatment in congenital toxoplasmosis

We read the editorial of Gilbert and Desateux.¹ In their analysis, they take into account some newborn screening programmes for congenital toxoplasmosis in developing countries such as Brazil and Mexico, with reported rates of up to a maximum of 20 cases/10 000 live births; however, they did not mention our recent report that found a prevalence of 0.5% in a reference hospital in Colombia.² This study found one child who died 1 week after birth. As we had information only on the frequency of deaths in a reference hospital, we carried out a study in a representative sample of all newborns from Quindío and found nearly the same prevalence: 0.6% (see letter in *Archives of Disease in Children* in response to the paper by Schmidt *et al*).³ Clearly, prevalence is higher in South America than in Europe, but in addition our cases are more symptomatic. In an analysis in 17 children congenitally infected and detected in prenatal and newborn screening programmes, 41% were symptomatic. Two children (11.7%) died before 6 months of age; in four of 13 (30%), there were retinochoroidal lesions with ophthalmological examination and in four of 11 (36%) there was neurological involvement with ultrasound examination.⁴ Although only eight children were followed until the first year of life (two died before 6 months of age, thus 7 were lost to follow-up), it is obvious that we did not need this period to conclude that our children are more affected than those reported by the group in Lyon (France), where 12% of children had ocular lesion during their first year of follow-up.⁵

We are concerned about the affirmation (and conclusions that can be derived thereof by paediatricians and parents of infected children) that there is no evidence that postnatal treatment is beneficial. This may be true with respect to preventing recurrences of retinochoroidal lesions after the first year of life, but we cannot agree that postnatal treatment and treatments with pyrimethamine and sulfanamids are not beneficial. The recent report of the National Collaborative Chicago-Based, Congenital Toxoplasmosis Study validates a 1-year treatment with pyrimethamine-sulfadiazine by comparing the outcomes with historical controls.⁶ As stated in the editorial to this work, a double-blind study, including an arm of untreated patients, was ethically contraindicated. We think that congenital toxoplasmosis is a clinical situation where, in the context of our historical and contemporary knowledge, we can reasonably accept that postnatal treatment is better than no treatment, yet there are no double-blind controlled trials. Particularly in our country, it is easy to obtain a natural history of what happens in cases of no treatment, which are in the majority. Thus, we can agree that more efficacious drugs are needed for postnatal treatment, but to advance new proposals for