Benign recurrent sixth (abducens) nerve palsies in children

N R Mahoney,1 G T Liu2,3

ABSTRACT
Sixth nerve palsy can occur as a result of elevated intracranial pressure, neoplasm or trauma. Reports from tertiary centres indicate that between 5% and 16% of referred cases have no ascribed aetiology and are classified as benign. Rarely, these benign palsies can recur. A retrospective chart review of a cohort of 253 paediatric patients with sixth nerve palsies was analysed and uncovered 30 cases of benign sixth nerve palsy, nine of which recurred. Our data and review of other studies on the subject imply that a new onset sixth nerve palsy presenting in children can be benign in approximately 13% of cases, so a thorough history and physical examination to evaluate for any other neurological symptoms or signs followed by MRI of the brain with and without contrast is recommended.

Identifiable causes of sixth nerve (abducens, lateral rectus) palsy in childhood include neoplasm, elevated intracranial pressure and trauma.1 2 Idiopathic or benign sixth nerve palsy in childhood may also occur, sometimes following viral infection, fever or vaccination.2 Uncommonly, children with benign sixth nerve palsies experience one or more recurrences.3 4 Prior reviews of paediatric sixth nerve palsies suggest that between 5% and 16% of cases are ultimately classified as “idiopathic”.1 3 However, some of the benign diagnoses are suspect because not all patients in previous series underwent modern neuroimaging. Inference from reported cases and series about the frequency of the rare recurrence of a benign sixth nerve palsy is likely to result in overestimation because of both over-publication of recurrent cases and referral bias in benign case series. Nonetheless, we report on the frequency of recurrent and non-recurrent benign cases among a cohort of paediatric patients with sixth nerve palsies seen by a paediatric neuro-ophthalmologist.

METHODS
After institutional review board approval, charts of children under the age of 18 seen by the Children’s Hospital of Philadelphia Neuro-ophthalmology Service between 1993 and 2005 with a diagnosis of sixth cranial nerve palsy were reviewed. Children with benign sixth nerve palsy, defined as an isolated unilateral abduction deficit (a) without ptosis, papilloedema or other neurological signs, (b) if allowed by the parents, with normal magnetic resonance imaging (MRI) of the brain with and without gadolinium, (c) with spontaneous improvement, and (d) without an infection, rheumatological or other systemic or neurological illness found, were identified. Recurrence was defined when benign sixth nerve palsy occurred again with (a), (c) and (d).

RESULTS
Benign sixth nerve palsy subgroup (with or without recurrence)
Of 253 children identified with sixth nerve palsy, 225 had only sixth nerve involvement. Aetiologies were ascribed in 90 (40.0%) of these children to neoplasms with or without neurosurgical intervention, in nine (4.0%) to inflammatory disorders, in 14 (6.2%) to an infectious aetiology, and in 25 (11.1%) to increased intracranial pressure; six (2.7%) cases were designated congenital, two (0.9%) were secondary to surgery not related to neoplasm, one (0.4%) was ascribed to radiation necrosis, 23 (10.2%) to trauma, and 10 (4.4%) to vascular disease.

Thirty (13.3%) cases were benign with a mean age of 3.08 years at evaluation. MRI with and without gadolinium was performed in 25 of these children (93.3%). The parents of the other two (6.7%) children (both aged 12 months) declined imaging, but these two patients were followed closely, did not develop new symptoms, and eventually recovered from their deficits. Only six (20.0%) children underwent a lumbar puncture; in each case it was normal. A cerebrospinal fluid examination was often deferred in the absence of meningeal signs or when the child appeared otherwise well. Eleven (36.7%) of these children had negative acetylcholine receptor antibody testing. Other frequent serum tests performed were Lyme antibody titres and, in cases evaluated more recently, anti-Gq1b antibody testing. A comparison of laterality, sex and age characteristics within the subgroup can be found in table 1.

Though extensive follow-up is not available for some cases that were improving but not completely resolved, only one child with follow-up at 3 years had some residual abduction deficit. Four children, including three in the recurrence cohort, had residual esotropia but full ductions, and all were referred for strabismus surgery.

Benign sixth nerve palsy subgroup with recurrence
Nine of these 30 (30.0%) children had at least one documented recurrence of symptoms and five of the nine (55.6%) had an office visit for a third or following recurrence. A description of these patients can be found in table 2.

DISCUSSION
Various aetiologies have been proposed as possible mechanisms responsible for benign sixth nerve palsy, including variant ophthalmoplegic migraine.
atypical myasthenia gravis, inflammation secondary to viral infection or an idiosyncratic vaccine response. The cause of cases with recurrence is unclear. It is of prognostic importance that the frequency of benign disease among children presenting with sixth nerve palsy in our study was 13.3%, which is well within the range of 5% to 16% reported in previous reviews. This is somewhat surprising given the consistent use of modern imaging techniques.

With such a low prevalence, the statistics of clinical presentations are difficult to interpret. Recently, Yousuf and Khan reviewed the clinical features in cases of benign sixth nerve palsies through a meta-analysis of prior reviews and reports. They found the mean age in the recurrent cohort to be younger than in the “non-recurrent” cohort. Also, they note a trend toward “non-recurrence” in boys, more pronounced in boys with right-sided palsy, and recurrence in girls, more pronounced in girls with left-sided palsy. Our review corroborates their finding that all patients who had a benign sixth nerve palsy temporally related to vaccination had at least one recurrence. Interestingly, one patient presented after varicella infection unrelated to vaccination and did not develop recurrence.

Yousuf and Khan also found that “all children who presented at 14 months of age or younger developed recurrence”. Our review, however, found seven such patients with reasonable follow-up, who did not develop recurrence. Perhaps this is a consequence of the authors’ suggested selection bias from previously reported cases and our benefit of reviewing all the cases presented to one specialist. Still, our study is nonetheless problematic having been conducted at a referral institution as both uncommon presentations of benign cases and the overall number of neoplasm and neurosurgical patients may be over-represented.

Referral bias could influence the frequency of recurrence in additional ways in this or any review of sixth nerve palsy in children. A parent with a child with a recurrent sixth nerve palsy, a prior negative work-up and previous quick resolution of symptoms might forego a visit to their physician for a first

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<th>Table 1</th>
<th>Laterality, sex and age comparison of recurrent and non-recurrent benign sixth nerve palsies in children</th>
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<td>Recurrent</td>
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<td>Non-recurrent</td>
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<td>Mean age (years)</td>
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<td>Range (years)</td>
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*One female presented with a right-sided deficit which recurred on the left and is only included in the total column.

Table 2 | Recurrence characteristics of benign recurrent sixth nerve palsy in nine children seen at the Children’s Hospital of Philadelphia by the Neuro-ophthalmologic Service from 1996 to 2005 |
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ACE, angiotensin converting enzyme testing; AchRAb, acetylcholine receptor antibody testing; ANA, antinucleic acid antibody testing; CT, computed tomography; DPT, diphtheria, tetanus, pertussis vaccination; ESR, erythrocyte sedimentation rate; HIB, Haemophilus influenzae B vaccination; LP, lumbar puncture; MRI, magnetic resonance imaging; PTE, prior to evaluation; RPR, rapid plasma regain testing; URI, upper respiratory infection.
recurrence and more probably for a second or third. Additionally, straightforward cases may be managed without referral to an academic centre where data reporting generally occurs and therefore may be under-reported and under-represented.

For a child presenting with new onset sixth nerve palsy we recommend a thorough history and physical examination to evaluate for any other neurological symptoms or signs followed by MRI of the brain with and without contrast. The decision to perform a lumbar puncture as well as serum myasthenia gravis testing, Lyme testing and anti-Gq1b testing should be made on a case-by-case basis. Parents should be instructed that the majority of cases of benign sixth nerve palsy do not recur. However, the minority of instances that recur are still benign.

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REFERENCES
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