

LETTERS TO THE EDITOR

Prevalence of asthma and wheeze in the Highlands of Scotland

EDITOR,—In their study on asthma and wheeze in the Highlands of Scotland Austin *et al* performed exercise tests on children in six geographical regions between April and June 1992.¹ The prevalence of exercise induced bronchospasm was particularly high on the Isle of Skye which was one of the most rural of the areas studied. However, data from the weekly returns service of the Royal College of General Practitioners showed that new episodes of asthma in 5–14 year olds were almost three times greater in June compared with April in 1992. Both asthma and hay fever show annual and seasonal variation² and are partly affected by the severity of the prevailing pollen season.

Clearly, unless the exercise testing was carried out simultaneously in each region, comparisons are likely to be unreliable.

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- 1 Austin JB, Russell G, Adam MG, Mackintosh D, Kelsey S, Peck DF. Prevalence of asthma and wheeze in the Highlands of Scotland. *Arch Dis Child* 1994; 71: 211–6.
- 2 Fleming DM, Norbury CA, Crombie DL. *Annual and seasonal variation in the incidence of common diseases*. Occasional paper 53. London: Royal College of General Practitioners, 1991.

Drs Austin and Russell comment:

Drs Ross and Fleming raise an interesting point in relation to the exercise testing which we used to support our questionnaire survey carried out in March and April 1992. We know of no epidemiological study which has correlated the prevalence of bronchial hyperactivity to exercise with new asthma episodes, but it is reasonable to suppose that seasonal variations in general practitioner returns will be more closely related to variations in the prevalence of various trigger factors, including pollens, than to variations in underlying bronchial hyperactivity. Nevertheless, allergens are known to affect bronchial hyperactivity, and the prevalence of exercise induced bronchoconstriction might thus be influenced by the date of study.

We have therefore reanalysed our data to look for possible seasonal effects. If exercise tests performed in June are omitted, the overall prevalence of exercise induced bronchial hyperactivity rises to 9.6% compared with 8.9% when data for June tests are included.

Although weekly general practitioner returns for new asthma episodes in school aged children show a rise in late June/early July, this is small compared with the sharp rise in September.¹ In Highland Region, figures from one general practice suggest that there is little difference for out of hours consultations for childhood asthma between April and June, although the numbers are low (four calls in April, one in May, and two in June) (figures

courtesy of Ardlarich Medical Practice, Inverness).

We believe it is unlikely that pollen levels had any major influence on our results. In the north of Scotland the pollen count is low because of the climate (pollen tends not to hang in the air of the prevailing winds, and pollen production is lower and occurs later than elsewhere in UK) and the relatively sparse vegetation, especially in Skye. In any case, the tests in Skye were performed on 8th May 1992, too soon to be influenced by the seasonal effects proposed by Ross and Fleming.

- 1 Asthma Information Agency. *Seasonal variations in asthma*. Factsheet 93/4. Available from Department of Public Health Sciences, St George's Hospital Medical School, London. (Data 1987/92 quoted from Royal College of General Practitioners weekly returns service.)

Cardiovascular malformations in Turner's syndrome

EDITOR,—We were interested to read the findings of Gotzsche *et al* who reported the prevalence of cardiovascular malformations and karyotypic association in Turner's syndrome.¹ We have recently reviewed the karyotypes and phenotypes of 63 Turner's syndrome patients who have been referred to our department. Cardiovascular malformations have only been recognised in seven of them (2/14 45 X, 2/4 45 X/47 XXX, 2/2 45 X/46 XY, and 1/3 45 X 46 Xr(X) patients). Like Gotzsche *et al* we did not see cardiovascular malformations in any patient without a 45 X cell line and aortic valve abnormalities accounted for most of the cases. If, as Gotzsche suggests, around 26% of Turner patients have cardiovascular abnormalities then it is likely that some of our older patients who have not undergone routine echocardiography have as yet unrecognised cardiac problems. This is an important point, as minor aortic abnormalities may be associated with dissection of the aorta in Turner's syndrome adults² and this complication could be screened for in susceptible individuals.

Gotzsche *et al* concluded that 'no patient with structural abnormalities of the X chromosome had cardiovascular malformations'. This is true for their 13 non-mosaic patients but in fact 4/46 of their patients with cardiovascular problems did have a cell line containing a ring or iso (X) chromosome. It is likely that these four individuals began life with a non-mosaic karyotype and that a 45 X cell line arose later as the abnormal X chromosomes were lost during cell division. It seems, therefore, that it is the presence of a 45 X cell line at an early stage of development that might influence whether a cardiovascular abnormality is likely to be present or not.

Why should this be so? It has been suggested that a gene which is present on both the X and the Y chromosome and which escapes X inactivation may be responsible for the somatic features of Turner's syndrome.³ An individual must possess two functioning copies of this gene in order not to manifest Turner's syndrome characteristics. Structurally abnormal X chromosomes may still express this gene which is proposed to lie on the long arm of the X at Xq13, close to the centromere and the X inactivation centre. Only a single copy of this gene can be expressed in cells which contain a 45 X cell line. This gene may have a primary role in the causation of cardiovascular malformations or a secondary role because its absence gives rise

to lymphoedema.⁴ In our study lymphoedema was documented in 79% patients with only a 45 X cell line and in 33% patients with structural X chromosome abnormalities.

We are in agreement with Gotzsche and other authors who have suggested an increased prevalence of cardiovascular malformations in Turner's syndrome patients with a 45 X karyotype. However, although the incidence of cardiovascular abnormalities is low in patients with non-mosaic structural abnormalities, patients who are mosaics for ring (X) or iso (X) with a 45 X cell line or who have X chromosomes or markers lacking the Xq13 region may still be a significant risk of heart problems and should be screened for these.

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- 1 Gotzsche C-O, Krag-Olsen B, Nielson J, Sorensen KE, Kristensen BO. Prevalence of cardiovascular malformations and association with karyotypes in Turner's syndrome. *Arch Dis Child* 1994; 71: 433–6.
- 2 Price WH, Wilson J. Dissection of the aorta in Turner's syndrome. *J Med Genet* 1983; 20: 61–3.
- 3 Watanabe M, Zinn A, Page D, Nishimoto T. Functional equivalence of X and Y-encoded isoforms of ribosomal protein S4 consistent with a role in Turner syndrome. *Nature Genetics* 1993; 4: 268–71.
- 4 Clarke EB. Neck web and congenital heart defects: a pathogenic association in 45 XO Turner's syndrome. *Teratology* 1984; 29: 355–61.

Growth hormone and hypophosphataemic rickets

EDITOR,—There has been some interest in the use of growth hormone in children with hypophosphataemic rickets who have short stature as a consequence of their metabolic bone disease. In addition to its growth promoting role there is the theoretical advantage that growth hormone by increasing the tubular reabsorption of phosphate may lead to a reduction in phosphate supplement requirements which have been linked to the development of nephrocalcinosis.

We would like to report our observations on the changes in renal phosphate handling and markers of bone turnover in a 7 year old girl with hypophosphataemic rickets treated with growth hormone over an initial seven month period. She was originally referred for an endocrine assessment because of her short stature. Although she was exceedingly short for her age (height SD score -3.9), there was no evidence of deformity of her legs and no active rickets. An insulin tolerance test with adequate hypoglycaemia demonstrated a peak growth hormone response of 7.5 µg/l (15 mU/l). In view of this and her short stature it was decided to give her a therapeutic trial of growth hormone in a dose of 0.6 IU/kg/week increased to 0.75 IU/kg/week after three months given as six daily injections/week.

Over a seven month period she gained 4.4 cm in height, her height SD score improved from -3.9 to -3.7 and height velocity SD score from -1.8 to -0.1. On the same doses of phosphate and vitamin D her plasma phosphate rose from 0.99 mmol/l to 1.37 mmol/l at three months and then dropped to 1.02 mmol/l at seven months. The level of TmPO₄/glomerular filtration rate increased