Propranolol is contraindicated in asthma

EDITOR,—The datasheet for Inderal (propranolol) states specifically that the drug is contraindicated in patients with asthma or a history of bronchospasm. Despite this, and despite the well known risks of non-selective β blockers in patients with asthma, over the past few years Zeneca has received a number of reports of cases in which an asthmatic patient died as a result of being prescribed propranolol.

Since propranolol was first marketed in 1965 the estimated exposure to it has been about 56 million patient years. The Medicines Control Agency has 51 reports of bronchospasm in its database of reports of adverse reactions to propranolol; 13 of the cases are recorded as having been fatal. Of more interest, however, are six reports in which it is stated that the patient had a history of asthma, bronchospasm, or wheeze; five of these cases were fatal. To help prevent further occurrences of this sort in asthmatic patients who might be prescribed propranolol erroneously, Zeneca has decided to highlight the warnings concerning asthma in the patient information leaflet for Inderal and related products. Pack labels will also carry warnings. Doctors should prescribe original packs so that a last line of defence against incorrect prescribing is not breached.

Current advice in the prescribing information for Inderal recommends that bronchospasm can usually be reversed with a β_2 agonist bronchodilator such as salbutamol, although large doses may be required and the dose should be titrated according to the clinical response. As β_2 adrenoreceptors are blocked by propranolol the advice will now be augmented by the statement that ipratropium and intravenous aminophylline may also be indicated.

We thank the Committee on Safety of Medicines for providing us with its information.

J M FALLOWFIELD
Medical adviser, product safety group

H F MARLOW
Senior medical adviser, clinical research group

Zeneca Pharmaceuticals,
Macclesfield SK10 4TG

Sex differences in weight in infancy

Published centile charts for weight have been updated

EDITOR,—Charlotte M Wright and colleagues report a discrepancy between the sexes in weight in infancy¹ when the British 1990 growth reference² was used to standardise the weights of infants in Newcastle upon Tyne. They suggest that this arises from a bias in the growth reference rather than a regional difference in growth.

We looked for a possible regional effect in a cohort of 7400 babies from West Sussex, who were measured between birth and 35 weeks (courtesy of Dr Ann Wallace). As in Newcastle, there was no sex difference in the standard deviation score for weight at birth, but thereafter the boys' weight centiles tended to exceed the girls' (by a mean score of 0.31, compared with 0.41 in the authors' study). Thus regional differences alone are unlikely to explain the finding, and a bias in the growth reference must exist. We believe that this bias arose during the fitting process, when several datasets were merged after adjustment for regional imbalances and secular trends. This process distorted the relation between the sexes, particularly in infancy.

We have now eliminated the bias by modifying the fitting process.³ We have also added data on a nationally representative sample of 1.5–4.5 year old children to the reference dataset.⁴ Compared with the original reference, the revised median weight for girls is reduced by a standard deviation score of up to 0.2 (180 g) at 9 months, while that for boys is unchanged. The line indicating a standard deviation score of –2.0 for girls (close to the third centile used by Wright and colleagues) is reduced by up to 0.3 (200 g), while that for boys is reduced by 0.07 (40 g), a net difference of 0.24. This accounts for about three fifths of the sex discrepancy in Newcastle and rather more in West Sussex. We are confident that the remainder is a genuine regional difference.

Wright and colleagues point out that the same imbalance between the sexes occurred with the 1966 British standards. The same is true of the 1980 Dutch standards,⁵ which were based on a large sample ($n = 8301$). This emphasises the variable nature of the sex difference in weight during infancy.

Length—often regarded as more important than weight for measuring growth—does not show the same sex discrepancy in infancy. The revised length centiles differ from the old by <4 mm, which is within measurement error at this age. The net effect on the sex difference is a score of <0.05.

These revisions have been incorporated into the published centile charts (version 1996/1) and the computer spreadsheet.

M A PREECE
Professor of child health and growth

Institute of Child Health,
University College London,
London WC1N 1EH

J V FREEMAN
Part time lecturer

Medical Care Research Unit,
Sheffield S1 4DA

T J COLE
Senior scientist

MRC Dunn Nutrition Centre,
Cambridge CB4 1XJ

- 1 Wright CM, Corbett SS, Drewett RF. Sex differences in weight in infancy and the British 1990 national growth standards. *BMJ* 1996;313:513–4. (31 August.)
- 2 Freeman JV, Cole TJ, Chinn S, Jones PRM, White EM, Preece MA. Cross sectional stature and weight reference curves for the UK, 1990. *Arch Dis Child* 1995;73:17–24.
- 3 Cole TJ, Freeman JV, Preece MA. British 1990 growth reference centiles for weight, height, body mass index and head circumference fitted by maximum penalized likelihood. *Statistics in Medicine* (in press).
- 4 Gregory JR, Collins DL, Davies PSW, Hughes JM, Clarke PC. *National diet and nutrition survey: children aged 1.5 to 4.5 years*. Vol 1. London: HMSO, 1995.
- 5 Roede MJ, Van Wieringen JC. Growth diagrams 1980. Netherlands third nation-wide survey. *Tijdschrift voor Sociale Gezondheidszorg* 1985;63(suppl):1–34.

Data from Sheffield support authors' findings

EDITOR,—Charlotte M Wright and colleagues describe differences between the sexes in the weights of infants in Newcastle upon Tyne compared with the British 1990 national standards.¹ Some support for this sex discrepancy is found in a longitudinal prospective study of failure to thrive in a socially disadvantaged group of infants in Sheffield that is currently in progress. Table 1 shows the mean weights at birth and 3 months in

these infants compared with the standards given by the national 1990,² Tanner (1965),³ and local Sheffield weight charts (1974).⁴ Although the selection of subjects precludes any direct comparison with the mean weights of the standards, it is interesting that there is a considerable discrepancy between the 1990 standard deviation scores of the otherwise homologous boys and girls in the study group at 3 months, which, as Wright and colleagues note, places more girls than boys below the mean.

J K H WALES
Senior lecturer in paediatric endocrinology
C P A KENNEDY
PhD student

Department of Paediatrics,
University of Sheffield,
Sheffield Children's Hospital,
Sheffield S10 2TH

- 1 Wright CM, Corbett SS, Drewett RF. Sex differences in weight in infancy and the British 1990 national growth standards. *BMJ* 1996;313:513–4. (31 August.)
- 2 Freeman JV, Cole TJ, Chinn S, Jones PRM, Preece MA. Cross sectional stature and weight reference curves for the UK, 1990. *Arch Dis Child* 1995;73:17–24.
- 3 Tanner JM, Whitehouse R, Takaishi M. Standards from birth to maturity for height, weight, height velocity and weight velocity: British children 1965. Part 1. *Arch Dis Child* 1966;41:454–71.
- 4 Carpenter RG, Gardner A. *Sheffield weight charts*. London: Foundation for the Study of Infant Deaths, 1978.

Confusion over whether new technologies should be regulated at European or state level

EDITOR,—In their editorial on the Safety and Efficacy Register of New Interventional Procedures, Trevor A Sheldon and Alex Faulkner discuss regulation of the new health technologies.¹ It is true that, if drugs have to be evaluated before their widespread use is permitted, one could expect the same requirement for interventional technologies and that, because this has not been the case, new technologies have diffused through health care systems despite lack of evidence of their safety, effectiveness, and cost effectiveness.

The creation of the register is certainly an important initiative to answer these questions. Since it will concentrate exclusively on safety and efficacy, however, two questions should be discussed.

Firstly, on 1 January 1995 a new set of European rules covering practically all non-pharmaceutical products became effective in the member states of the European Union for the marketing approval of implantable medical devices—namely, CE marking, which indicates that devices meet the essential requirements of the medical device directives. After 14 June 1998 all medical devices will have to bear the CE mark. To implement these directives some countries reorganised the relevant units within their ministries of health. Others delegated authority and operational responsibilities to independent organisations. Thus many of the member states of the European Union currently have their own notified bodies dealing with the marketing approval of new medical devices.²

The fact that the new register will concentrate on safety raises the issue of how it will share this responsibility with the notified bodies. It will be

Table 1—Standard deviation scores at birth and three months for male and female infants in study in Sheffield compared with 1990 and 1965 (Tanner) national standards and 1974 local (Sheffield) standards

	Boys (n = 63)			Girls (n = 56)		
	1990	Tanner	Sheffield	1990	Tanner	Sheffield
At birth	–0.07	0.01	0.01	–0.01	–0.01	0.00
At 3 months	0.06	0.13	0.11	–0.43	0.03	0.10