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 adrenoceptors 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.

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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 infancy[1] when the British 1990 growth reference[2] 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.

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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.

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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