Discussion

There are several points which are unusual. The presence of recurrent respiratory symptoms in association with a gradual fall in weight against the mean over a period of years suggest that achalasia may have been present from a very early age. It is most unusual, in view of the fact that severe achalasia was present radiologically, that there were so few gastrointestinal symptoms, although achalasia presenting with weight loss or respiratory symptoms alone is recognised.⁵ Of particular interest is the fact that the achalasia was present in association with foreign body obstruction of the oesophagus. The history of actual weight loss was relatively short and as the patient gained weight steadily after the removal of the foreign objects, without further treatment, it would seem that it was the obstruction superimposed on the underlying pathology of achalasia of the oesophagus which was responsible for the rapid deterioration.

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Adverse drug reactions in medical inpatients

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SUMMARY Fifteen of 268 children admitted to a general medical ward suffered a definite or probable adverse drug reaction to their treatment. In 6 of these children the reactions were preventable. Anti-convulsants were the most common cause of an adverse reaction.

Several studies (mostly American) have investigated the extent of adverse drug reactions in paediatric inpatients and factors that predispose to drug reactions.¹⁻³ This study determined the extent of the problem in a British hospital and to what extent the reactions were preventable.

Subjects and methods

Over a 6 month period 268 children were admitted for medical care to the Royal Liverpool Children's Hospital via their general practitioner or casualty department. There were no referrals from other hospitals requiring a specialist opinion. All the children were suffering from illnesses of a general

medical nature, although there was a slight bias towards patients with neurological disorders (mental handicap and epilepsy) due to the interests of one of the consultants. Poisonings were excluded.

A record was kept of all drugs given in hospital, both on the ward and in the casualty department. A drug was arbitrarily defined as a substance that had to be prescribed by a member of the medical staff, with the exception of intravenous fluids and oxygen which were excluded from the survey. Drugs given before hospital admission were determined by (1) history from the parents, (2) the referral letter, and (3) a questionnaire sent to the general practitioner asking specifically about treatment before admission.

Drug reactions were looked for prospectively by medical and nursing staff on the daily ward round. An adverse drug reaction was defined as any undesired or unintended response to medication. These were classified according to the criteria originally used by Seidl *et al.*⁴

(1) Definite; directly attributable to a drug, having a clear temporal relation to drug administration and confirmed by positive rechallenge or

laboratory investigation, for example abnormal blood values.

(2) Probable; occurring with a clear temporal relation to drug administration and improving on withdrawal of treatment.

(3) Possible; having some temporal relation to drug administration, but the effects could have been due to the basic illness.

The validity of each reaction was discussed with an independent consultant (FH).

Results

Fifteen children suffered a definite or probable adverse drug reaction to hospital treatment (Table 1); boys and girls were similarly affected. Drowsiness, ataxia, diarrhoea, vomiting, and tachycardia were the most common side effects. Two children suffered from two reactions each (drowsiness and ataxia in both cases). Seven children had their medication discontinued. There was also one probable drug reaction due to medication from the general practitioner (oral monilia due to amoxycillin).

There were 7 cases of possible drug reaction (three due to hospital medication, three due to treatment from general practitioners, and one due to self medication).

Six of the 15 drug reactions could have been avoided. In three children the dosage prescribed was too high (cases 5, 8, and 9) and in one the treatment was not necessary (case 1). Application of pharmacological principles would have prevented a further two reactions—in case 7, the induction of chloramphenicol metabolism by phenobarbitone could have been predicted by previous work⁵ and in case 13 the theophylline concentration was not determined be-

fore an intravenous bolus despite the child being on regular oral theophylline.

The type of drug used affects the incidence of drug reactions. In the children studied, anticonvulsants were the group of drugs most likely to cause a detectable adverse drug reaction (Table 2).

Discussion

Previous American studies^{1,3} have reported a high drug usage (4.2 drugs per patient in Florida and 7.6 drugs per patient in Boston) and a high adverse drug reaction rate (10% in Florida and 16.8% in Boston). Both our drug usage (1.5 drugs per patient) and our adverse drug reaction rate (5.6%) were similar to those of Whyte and Greenan in Glasgow² (2.3 and 6.5% respectively).

The adverse drug reaction rate is probably directly related to drug usage. There are, however, difficulties in making direct comparisons between studies. The sort of patient studied affects both the number and type of drugs used and also the likelihood of a drug reaction. All previous studies have been based in referral centres and have included oncology patients who have a four times

Table 2 Type of drug and adverse drug reactions

	No of patients receiving drug	No of adverse drug reactions	Incidence of adverse drug reactions (%)
Anticonvulsants	51	9	17.6
Antibiotics	71	5	7.0
Bronchodilators	68	3	4.4
Antipyretics and analgesics	132	0	0
Topical	31	0	0
Miscellaneous	55	0	0

Table 1 Definite or probable drug reactions to hospital treatment

Case No	Age (years)	Drugs	Drug reaction
1	1	<i>Anticonvulsants</i>	Drowsiness
2	5		Drowsiness
3	2		Drowsiness and ataxia
4	3		Drowsiness and ataxia
5	9/12		Drowsiness
6	2		Hyperactivity
7	1		Induction of metabolism of chloramphenicol
8	1	<i>Antibiotics</i>	Vomiting
9	1		Vomiting
10	1/12		Oral monilia
11	11/12		Diarrhoea
12	7/12		Diarrhoea
13	7	<i>Bronchodilators</i>	Tachycardia
14	3		Tachycardia
15	5		Paraesthesiae

*Medication discontinued.

higher incidence of drug reactions than other patients.³ The different surveillance systems used (nurse monitors in Boston and Glasgow and a pharmacist in Florida) are likely to affect both the type and number of drug reactions detected. Although definitions of drug reactions are consistent between studies, the definition of what constitutes a drug is rarely given. Also, in determining total adverse drug reaction rates, possible reactions are sometimes included alongside definite and probable reactions.

In this study anticonvulsants were the group of drugs most likely to cause a detectable drug reaction. This is probably related to the narrow therapeutic range of anticonvulsants. It may also be partly explained by the bias towards patients with neurological disorders in the study. These children were more severely ill than other children and thus at greater risk from a drug reaction.²

That 6 of the 15 adverse drug reactions were preventable suggests that doctors need to be more careful in the drugs they prescribe—asking themselves whether the drug is necessary or not, whether the dosage is correct, and whether any drug interac-

tion is likely. The results suggest that if these simple measures were carried out, fewer iatrogenic problems would arise.

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Cleft palate and gonadotrophin deficiency

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SUMMARY A boy who had previously had a cleft lip and palate repaired and bilateral orchiopexies presented at 16 years of age with delayed puberty. Isolated gonadotrophin deficiency and testicular hyporesponsiveness to human chorionic gonadotrophin were found. The possibility of bilateral cryptorchidism due to gonadotrophin deficiency should be considered in boys with either cleft lip or palate, or both.

Case report

A 16 year old boy was investigated for delayed puberty and short stature. He was born in July 1967 with a cleft lip and palate which were repaired at the ages of 3 months and 15 months respectively. The only details of his previous growth available were a height of 131 cm (25th centile) at 9.8 years and 140 cm (25th centile) at 11.5 years. He developed

moderately severe asthma at 8 years of age and because of acute exacerbations required brief admissions to hospital on three occasions. His only exposure to corticosteroids was a 10 day course of hydrocortisone and prednisone during each of the latter two admissions to hospital. Bilateral cryptorchidism was not diagnosed until 9 years of age; right and then left orchiopexies were performed at ages 10 and 12 years. A nasal septoplasty was necessary at 15 years of age. He has been asymptomatic apart from occasional rhinitis and wheezing for which he has continuously taken bronchodilators and sodium cromoglycate. There is no family history of short stature, delayed puberty, or atopy.

Physical examination showed a short prepubertal boy of normal habitus and intellect with both height (156.5 cm) and weight (45.4 kg) below the third centile. He had bilateral, partial nasal obstruction and some degree of hyposmia. He seemed neurologically intact; his optic fundi, visual fields, and colour vision were normal. There was no physical