ADVERSE REACTIONS TO ALTHESIN

Sir,—The precise mechanisms of adverse reactions to Althesin remain unclear and the value of a preliminary test dose debated (Radford, Lockyer and Simpson, 1982). Data from the following case report may usefully add to the available information.

A fit woman in her twenties, satisfactorily premedicated with lorazepam, presented for debridement of a chronically infected wound. She gave no history of atopy but had received Althesin, uneventfully, 2 weeks previously. Ninety seconds after receiving a test dose of Althesin 0.0025 ml (1 ml of a 1:400 dilution) she became flushed initially and then deeply cyanosed. She developed an irritable cough with salivation, a slight wheeze and a tachycardia of 110 beat min⁻¹. Her arterial pressure was unchanged and there was no urticaria or oedema. No treatment was necessary apart from supplementary oxygen for 5 min. She experienced moderate central abdominal pain some 30 min later which spontaneously resolved. Subsequent anaesthesia with thiopentone was uneventful.

Analysis of blood samples taken at the time of the reaction, and at 30 min and 16 h after the reaction, showed that there was no significant change in the concentrations of IgE (at 90 unit per ml), C₃, C₄, or total haemolytic complement. No immune complexes were detected (personal communication, Dr Denman, Clinical Research Centre, Northwick Park, Harrow).

The signs described are qualitatively the same as those previously reported to be the result of adverse reactions to Althesin, but were relatively mild. There are several pertinent points.

These signs are also compatible with those of direct histamine release (Lorenz et al., 1981) and it is worth emphasizing that, despite previous exposure to Althesin, there was no activation of the complement pathways, contrary to the expectations of Radford and her colleagues. A test dose 1/100th of that used by Scott (1979) may be of value in avoiding severe adverse reactions in the absence of true classical allergy, but this requires confirmation. The suggestion by Beamish and Brown (1981) of an association between chronic infection and complement pathway activation with adverse drug reactions is not supported.

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PREVENTION OF THE OCULOCARDIAC REFLEX
IN CHILDREN UNDERGOING SQUINT SURGERY

Sir,—I was interested in the paper by Mirakhur and colleagues (1982) which demonstrated that neither atropine nor glycopyrrolate i.v. always prevented the oculocardiac reflex during squint operations. Previously we showed that hyoscine butylbromide (10–20 mg i.v.) administered during the induction of general anaesthesia totally suppressed the reflex (Fry and Hall-Parker, 1975.) Since then we have studied many of these operations, on patients of all ages, without obtaining evidence of the reflex (as defined by a decrease in the heart rate by more than 10 beat min⁻¹ for any period, or the appearance of nodal rhythm or extrasyntoles). Hyoscine butylbromide has a good antischlaguan action (Fry, 1975) although it is of too short duration for routine use. However, we suggest that hyoscine butylbromide should be the anticholinergic drug of choice during squint operations.

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I.M. ATROPINE AND REGURGITATION

Sir,—In spite of the diminished use of anticholinergic drugs for premedication, 62% of anaesthetists in Great Britain still use these drugs routinely and of these, 73% recommend the i.m. route for this purpose (Mirakhur et al., 1978). It is well known that atropine produces a decrease in lower oesophageal sphincter pressure (LOSP) and barrier pressure (BP = LOSP minus gastric pressure) and it has been suggested that this may predispose to regurgitation (Brock-Utne et al., 1976). Metoclopramide produces an increase in LOSP and it has been recommended that this drug be used to antagonize the effects of atropine (Brock-Utne et al., 1976). However, all previous studies on this subject have utilized the i.e. route of administration of both atropine 0.6 mg and metoclopramide 10 mg (Cotton and Smith, 1982).

Because anticholinergics are generally administered as premedicants by the i.m. route 1 h before induction of anaesthesia, we have assessed the effects of this pattern of use on the LOSP. At the same time, if metoclopramide were to be recommended to decrease the tendency to regurgitation, it would be appropriate to examine the effects of a standard dose of 10 mg given i.e. at the time of induction of anaesthesia, that is 1 h after the i.m. administration of atropine 0.6 mg.

We have studied 10 healthy volunteers (seven male; age range 24–35 yr), free from gastrointestinal, respiratory or cardiovascular disease. All the subjects had taken part in our previous investigations of the effects of i.v. anticholinergic agents on the LOSP (Cotton and Smith, 1981). None was receiving any concurrent medication. After fasting for 6 h each subject swallowed a silastic tube containing three miniature transducers. Measurements of LOSP, gastric pressure (GP) and barrier pressure were undertaken as described previously (Cotton, Smith and Fell, 1981).

Following control measurements, each subject received atropine 0.6 mg i.m. and pressure measurements were made at 5-min intervals for a period of 60 min. At this time metoclopramide 10 mg was given i.e. and further measurements made 5 min later. Data were analysed using analysis of variance.

There was no significant change in barrier pressure during the 60 min following administration of atropine 0.6 mg i.m. In addition, the subsequent administration of metoclopramide 10 mg i.v. produced a small but non-significant increase in BP and LOSP 5 min following injection (fig. 1).
This study shows that, in contrast to the i.e. route, atropine 0.6 mg i.m. has no effect upon the LOSP or BP. In addition, this manoeuvre can substantially block the effects of metoclopramide 10 mg i.v.

Previous investigations on the combined effects of atropine and metoclopramide on the LOSP have utilized i.v. routes of administration. Brock-Utne and colleagues (1976) demonstrated that the effects of metoclopramide 10 mg were equally antagonistic with those of atropine 0.6 mg. However, Cotton and Smith (1981) showed that, in the same doses, atropine exhibited a predominant effect upon LOSP irrespective of the order of administration of the two drugs and also that this persisted for at least 40 min after the administrations. Laitinen and colleagues (1978) found, in a canine experimental preparation, that the influence of the combined administration of these two drugs on the LOSP was dependent on the order of administration. Thus, each drug produced the anticipated change in LOSP, but completely antagonized the effects of subsequent administration of the alternate drug.

The purpose of this study was to simulate the manner in which anticholinergic premedication is prescribed in routine clinical practice. From the results presented above, we conclude that atropine i.m. in standard clinical doses has relatively little effect on the LOSP and should not therefore change any propensity to regurgitation. However, if anticholinergic agents have been used for premedication, the administration of a standard dose of metoclopramide immediately before induction of anaesthesia is unlikely substantially to diminish any tendency to regurgitation.

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