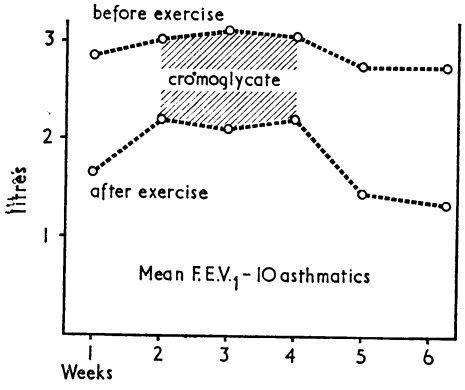
as histamine, SRS-A, or bradykinin; and (3) changes in hydrogen-ion concentration due to lactic acidaemia, which stimulates ventilation and results in hypocapnia during the recovery period. Attempts to block the exercise effect by an antihistamine have been unsuccessful,[1] but this does not exclude the possibility of a local release of histamine. Disodium cromoglycate is said to prevent the release of histamine from mast cells following an antigen-antibody reaction, and we thought it was possible that it might also interfere with the local release of histamine on exercise resulting from hyperaemia and the mildly traumatic effect of increased ventilation.

A trial was made on 10 asthmatic subjects who all complained of asthma following exercise. In five of them this was quite troublesome and occurred after fairly ordinary activity such as hurrying after a bus or washing a car. There were nine males and one female with an average age of 28 years (range 17–48 years). Eight had positive skin reactions to one or more antigens and five had an eosinophilia of more than 400/cu. mm.

Experiments were carried out on six occasions at weekly intervals: before cromoglycate, after the inhalation of one Spincap containing 20 mg. cromoglycate without isoprenaline; one and two weeks after three such Spincaps per day; and one and two weeks after stopping cromoglycate. No bronchodilator was allowed within three hours of the test, but otherwise there was no restriction in treatment. During the experiment the F.E.V.$_1$ was measured at three to five minute intervals for 15 minutes before exercise and up to 45 minutes after exercise. Exercise took the form of running up and down stairs for three to four minutes and was kept as constant as possible for successive studies on each patient. In most patients the maximum fall in F.E.V.$_1$ occurred within 10 minutes of the cessation of exercise, and the lowest value occurring during this period is used to calculate the exercise effect.

The average fall in F.E.V.$_1$ after exercise before, during, and after cromoglycate is illustrated in the Figure. The experiments fall naturally into two groups, those carried out during cromoglycate therapy and those carried out before and after. The mean fall in F.E.V.$_1$ was 0·935 litre during therapy and 1·34 litres without, and an analysis of variance shows that this is a statistically significant difference ($0·01 < P < 0·05$). In all but one patient, in whom the data are incomplete, cromoglycate offered some protection from exercise by inhibiting the fall in F.E.V.$_1$ by 30% on average.



These results are rather less dramatic, but in accord with those reported by Davies[2] who found a marked inhibition of the exercise effect following the inhalation of 1 Spincap of cromoglycate. This rapid effect of cromoglycate, which to some extent we have also found, is analogous to the inhibition of the immediate asthmatic reaction following the inhalation of antigen which has been reported by Pepys *et al.*[3] It is interesting that steroids do not protect asthmatics from the effects of exercise, and the partial success of cromoglycate suggests that histamine release may be one of the mechanisms involved.

The question arises as to whether the degree of protection justifies the use of cromoglycate in asthmatics who complain of the adverse effects of exercise. Previous studies have shown the beneficial effect of isoprenaline and other sympathomimetic drugs in this situation[1 4] and Crompton[5] found atropine to be very effective in one subject. We do not therefore feel justified in recommending cromoglycate when exercise-induced asthma is the sole or main complaint.—We are, etc.,

F. G. WARD.
S. GOMES.
R. S. MCNEILL.

Department of Therapeutics,
Maryfield Hospital,
Dundee.

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SIR,—It may not be generally recognized that, although the airstream sucked from a Spinhaler will deposit agglomerates when directed on to a microscope slide, this technique does not allow collection of the finer particles in the cloud. Provided properly designed apparatus is used this principle can be used to estimate the extent of inhalable particles in a powder cloud.[1] Thus, using an impactor designed[2] to allow all particles less than 13 μ to pass through a membrane filter gave values of approximately 5 mg. of disodium cromoglycate from a single capsule. Furthermore, laser holography—that is, three-dimensional photography of a portion of the moving Spinhaler cloud—has clearly shown numerous discrete particles less than 5 μ.[3] Particle size analysis using a Hexhlet dust sampler[4] has shown that 1–2 mg. of the drug is likely to penetrate to the alveolar region. In addition to these fine particles the cloud contains larger particles and agglomerates, which are, of course, retained in the upper airways.

The size range ensures that deposition occurs over a wide area of the bronchial tree, and we believe, until more is known about the anatomical location of the allergic reaction, such a distribution is desirable. Preference has been expressed for aqueous sodium cromoglycate solutions (14 June, p. 696), and therefore we feel it is important to record our results with a 5% w/w solution. To achieve a comparable dose to the Spinhaler (1–2 mg. alveolar penetration) would require approximately 200 actuations of a hand-operated nebulizer.—I am, etc.,

J. S. G. COX,
Director of Research and Development,
Fisons Pharmaceuticals Ltd.
Loughborough, Leics.

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Dangers of Certain Appetite Suppressants

SIR,—I read the letter sent by Dr. D. A. Cahal (3 May, p. 316), reporting that certain appetite suppressants "might cause pulmonary hypertension," with some alarm. I have under my care many patients afflicted with chronic chest diseases who are breathless, and among them are some who are grossly overweight.

It has seemed desirable to encourage such patients to lose surplus fat by simple dietary measures, aided in a few instances by the administration of an appetite depressant. The drug used has been fenfluramine. I have also been investigating the effects of prolonged airways obstruction upon cardiopulmonary function, and by chance have obtained measurements of pulmonary artery pressures at rest and during exercise upon six of them who have been taking fenfluramine. These patients had been on the drug for periods varying from two weeks up to three months before being investigated. On looking through the data collected from these cases to see whether there was any evidence of pulmonary hypertension I was unable to find any such evidence. This failure does not prove conclusively that fenfluramine never causes pulmonary hypertension, particularly as the patients had been taking it for only very short periods of time.

Nevertheless, the available pharmacological evidence[1–3] suggests that fenfluramine may not produce pulmonary hypertension in human subjects.—I am, etc.,

F. J. PRIME.
Institute of Diseases of the Chest,
London S.W.3.

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Management of Unconscious Poisoned Patients

SIR,—In your otherwise excellent and timely leading article on management of unconscious poisoned patients (14 June, p. 647) you refer to "short-" and "medium-acting" barbiturates. The continued use of this traditional classification of barbiturates, based on apparent duration of therapeutic action, still confuses the toxicological situation. "Short-" and "medium-acting" bar-