It has been claimed [1] that disodium cromoglycate makes it possible to reduce the dose of long-term steroid therapy or even to withdraw it completely. This may prove to be its most valuable property. However, any reduction of the maintenance dose of steroid should be attempted only if patients are closely supervised, with regular measurement of forced expired volume in one second, or peak expiratory flow. The subjective relief which disodium cromoglycate undoubtedly confers in many patients may obscure the development of a potentially dangerous situation in which the patient is deprived of symptoms which otherwise might give warning of an acute relapse at a time when he is especially vulnerable by reason of the lowered dose of steroid. This seemed to be the only explanation of a recent case of very sudden death which occurred in a boy of 14 who was under the care of the outpatient department of this hospital.

The criteria for selection of patients for treatment with disodium cromoglycate are still far from clear. As your annotation points out, the drug appears to inhibit the effects of "certain antigen-antibody reactions" (type I). This suggests that in clinical use it should be most effective in allergic asthma, its action being more of a prophylactic than a therapeutic nature. My own experience of its use in a small number of carefully selected patients in both hospital and general practice confirms such a view. I have found it to be of great value in some patients, particularly children, who have chronic "extrinsic" asthma, whereas I have not found any significant benefit from its use in patients with non-allergic or "intrinsic" asthma. In the former group of patients its action appears to be one of maintaining a state of remission rather than of suppressing active asthma.

It seems likely that general practitioners will soon find themselves under increasing pressure to prescribe disodium cromoglycate. I hope that much more information about its action and use in clinical practice will be available before it comes to be prescribed widely and, possibly, indiscriminately.

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SIR,—We are grateful to Dr. Grant, who wrote last week (p. 282), for pointing out some obscurity in the description of our trial [6] of disodium cromoglycate. However, we believe that the situation is made clear three paragraphs later and also in the tables; and, indeed, Dr. Grant has correctly interpreted the design of the trial.

As we stated, our record card was of similar design to that of Smith and Devey,[7] but it was not identical. The difference is unimportant. We expected that purulence of the sputum might be important in assessing response and therefore gave lower scores to purulent than to non-purulent sputum. This increased the number of possible scores describing sputum production to seven.

The average difference between mean scores for active drug and placebo included, of course, those patients who showed no response or even deterioration. The facts are that the differences described as significant are normally accepted as such, and that when all criteria were used 10 of the 21 patients showed much improvement and 5 more showed some improvement on disodium cromoglycate. This is more than "an occasional case".

The discrepancy between the F.E.V.$_1$ results and other indices of improvement underlines the inadequacy of information both on the meaning of the F.E.V.$_1$ in asthma and on the mode of action of disodium cromoglycate. We claim only that our results suggest that disodium cromoglycate "will improve the general level of well-being of many patients with allergic bronchial asthma", not that it should be regarded as "a major advance". We do, however, believe, with Professor Pepys and his colleagues (July 20, p. 134), that it "promises to be a valuable tool for the study of immunological mechanisms of respiratory allergic disease."

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1. Altounyan, R. E. C., Howell, J. B. L., Proceedings of the 2nd International Symposium on Tuberculosis, Climate, Asthma and Bronchitis, Davos. *Medna Thorac.* 1967 (in the press). Morrison Smith, J., Devey, G. F. *Br. med. J.* 1968, ii, 340.
6. Moran F., Bankier, J. D. H., Boyd, G. *Lancet*, July 20, 1968, p. 137.
7. Smith, J. M., Devey, G. F. *Br. med. J.* 1968, ii, 340.

WHAT'S IN P.V.C.?

SIR,—In your annotation (July 6, p. 34), discussing the need for standards specifications for the use of plastics in medicine, you mention that Parkhouse and I [1] drew attention to this need several years ago. This seems an appropriate time to amplify that suggestion.

There are two main approaches to the problem. One is to provide a detailed recipe for the manufacture of each plastic, and the other to define a series of properties which those plastics which are used in medicine should possess. It is at once apparent that to specify in detail the composition of acceptable plastics, and issue these in the form of a "white" list, would hinder progress, and probably prevent the development of more suitable plastics for any particular purpose. There is already evidence that preliminary attempts in this direction have failed to take into account the properties required for each specific use. A silicone sponge, for example, intended for use outside the body succeeded in reaching approval as a "medical" grade, and has since been used for implants. On the other hand a carefully purified and prepared grade of silicone fluid, having been used in an obviously unsuitable manner with adverse results, has been rejected. So for more legitimate uses doctors are falling back on less well purified grades never intended for the purpose and therefore not subject to the ban.

The need, therefore, is for specifications of the properties which plastics must have, whatever their composition. But the properties which are specified need to be relevant to the problem. To take the example quoted by Dr. Duke and Professor Vane (July 6, p. 21), the tubing found to be unsuitable for their purposes did comply to a Food Packaging regulation which specifies the total weight of material which can be leached out. For reactions with tissues this is meaningless. A comparatively large amount of a non-toxic material could be tolerated, but not a much smaller amount of toxic material. You rightly point out that all tests should be performed after the same sterilising procedure as that which will be used in practice. One might doubt, however, the statement that irradiation "can render P.V.C. toxic by the formation of hydrochloric acid". In practice, for the uses to which polyvinylchloride (P.V.C.) is normally put, abrasion from filler particle seems to be the cause of a number of effects reported as "toxic". One grade of green tubing has produced chlorine during irradiation, but the manufacturers tell me this has now been withdrawn from production.

These examples taken from *The Lancet* of July 6 illustrate the two essential points to be remembered in devising a standards specification. One is that a particular plastic not only must be thought of as "suitable" or "not suitable" for general medical use, but also each plastic must be considered for the situation for which it is intended. The other is that the tests should be relevant. It can only induce a false sense of security if tests are adopted because "one ought to do something".

I would suggest that, as basic research reveals the properties that are genuinely meaningful, then tests should be devised to meet these situations as they arise. Thus with biological testing, the tissue-culture methods using fibroblasts and chick-embryo cells devised by W. L. Guess and J. Autian give a reliable indication of the toxicity of the materials under test. But subcutaneous and intramuscular implantation tests suffer from the disadvantages that both toxic materials and ones

1. Little, K., Parkhouse, J. *Lancet*, 1962, ii, 857.

with unsuitable surfaces produce cell reactions, so that the shape of the implant is important. Although they are invaluable methods for investigating the properties for which other tests must be devised, they are unsuitable for routine testing. The third type of biological test is the long-term implant, in the clinical situation required, to find out how the plastic itself withstands degradation by surrounding tissue fluids. Such tests need to be continued for periods up to 5 years, and there is at present no satisfactory chemical method for obtaining the information. Attempts are being made to devise a formulation such that so many hours exposure to a chemical brew will be equivalent to a number of months or years of implantation, but to do this there is a need to have plastics which have been in the body for a number of years (either human or animal) for comparison. If any of your readers, removing plastic devices at either operation or necropsy, were to send them here for evaluation of the plastic, it would be most helpful.

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RESTRICTIVE VERSUS OBSTRUCTIVE VENTILATORY IMPAIRMENT

SIR,—Dr. Prime and Professor Scadding[1] have aptly reminded us of the origin and definition of the terms "restrictive" and "obstructive" ventilatory impairment. They discuss the development of a lung-function defect with decreased F.E.V.$_1$ (forced expiratory volume in 1 second) and F.V.C. (forced vital capacity), but with a relatively normal F.E.V.$_1$/F.V.C. ratio, as a late consequence of obstructive lung disease. We wish to report data from a study on acute ventilatory changes in byssinosis which underline their comment, and which show that such "pseudo-restrictive" patterns may also be found in conditions of acutely induced bronchoconstriction.

Hemp-dust inhalation causes dyspnœa and decreased ventilatory capacity in workers in the industry as well as healthy subjects.[2] The accompanying table shows average results of function tests in 2 healthy men and 11 hemp-workers who were exposed to dust (45 minutes to 4 hours). These are all experiments, from a larger series, in which F.E.V.$_1$ decreased more than 0·20 litres during dust exposure. Tests were done before and after exposure, and again 30 minutes after inhalation of an isoprenaline-phenylephrine mixture ('Medihaler Duo'). The dust causes decreases of F.E.V.$_1$ and F.V.C. in about the same proportion, since the F.E.V.$_1$/F.V.C. ratio changes little. Since the dust effect is rapidly reversible by the bronchodilator treatment, and little or no sputum is raised in association with

ACUTE EFFECTS OF HEMP-DUST INHALATION ON PULMONARY FUNCTION
(% CHANGES FROM VALUES BEFORE DUST SHOWN IN PARENTHESES)

Time	F.E.V.$_1$ (L)	F.V.C. (L)	F.E.V.$_1$/F.V.C. (%)	P.E.F.R. (L/sec.)	Vmax at 50% V.C. (L/sec.)
Before dust	3·05	4·44	68·1	6·55	2·89
After dust	2·64 (−13·4%)	4·08 (−8·1%)	64·8	5·81 (−11·3%)	1·85 (−31·2%)
After bronchodilator	2·97 (−2·6%)	4·41 (−0·7%)	67·0	6·72 (+2·6%)	2·56 (−4·8%)

Average results in 13 men in whom F.E.V.$_1$ decreased more than 0·20 litre while exposed to dust. F.E.V.$_1$ and F.V.C. were measured during forced expirations into direct-reading spirometers. P.E.F.R. and Vmax at 50% V.C. were measured from maximum expiratory flow-volume curves (see figure).

this improvement, we believe that bronchial smooth-muscle contraction is the main cause of these changes. There is no evidence that any mechanism other than airway obstruction causes these changes in the men exposed to dust; yet these changes would presumably be described as "restrictive" in nature if one adheres to the criteria to which Dr. Prime and Professor Scadding object. Even if this airway obstruction would result in pulmonary collapse, one would presumably have to consider the defect an obstructive one, although in our view the definition then becomes a matter of semantic preference.

The nature of the pulmonary-function change becomes more clear if one measures maximum expiratory flow-rates at different lung volumes, from maximum expiratory flow-volume (M.E.F.V.) curves. We recorded such curves and measured both peak expiratory flow-rate (P.E.F.R.) and maximum expiratory flow-rate at a volume corresponding to total lung capacity minus 50% of the control V.C. (Vmax at 50% V.C.) (see accompanying figure). Total lung capacity (T.L.C.) did not change significantly after dust, nor again after bronchodilator, in these men. Therefore one may assume that the measurement of Vmax at 50% V.C. yields a measurement of maximum expiratory flow-rate at a constant degree of lung inflation. The figure and the table show that these flow-rates show more pronounced changes, both after dust and after bronchodilator, than flow-rates such as P.E.F.R., which are made at volumes near T.L.C. The decrease of F.E.V.$_1$ reflects the decrease of instantaneous maximum flow-rates throughout the first second of the forced expiration. The decrease of vital capacity reflects the fact that flow-rates are proportionally more depressed at low lung volumes, so that residual volume (i.e., the lung volume at which flow reaches zero) increases. Since in many of these men flow-rates are extremely low near residual volume, the end-point of the F.V.C. determination is often hard to define, in particular from a standard spirographic record. The more time the subject is able and willing to spend near residual volume, to expel the last bit of air, the larger the measured F.V.C. will be.[3]

A more complete report of our findings is in preparation.

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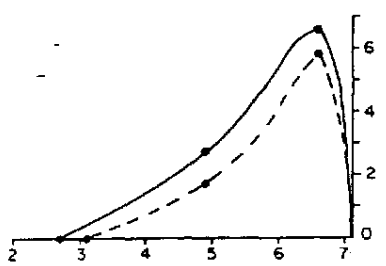
1. Prime, F. J., Scadding, J. G. *Lancet*, 1968, i, 1372.
2. Bouhuys, A., Barbero, A., Lindell, S.-E., Roach, S. A., Schilling, R. S. F. *Archs environ. Hlth*, 1967, 14, 533.



Average M.E.F.V. curves before (———) and after (- - - - -) hemp-dust exposure in 13 men.

Abscissa = thoracic gas volume (in litres); ordinate = maximum expiratory flow-rate (in litres per sec.). Curves begin at T.L.C. (7·1 L., right-hand side of volume scale). Vmax rapidly increases to peak values (P.E.F.R., black dots) and decreases thereafter. Vmax at 50% V.C. and residual volume (2·7 and 3·1 L.) both indicated by black dots.

BLOOD-GAS TENSIONS AND SPIROMETRIC FINDINGS

SIR,—Dr. Grant and Dr. Harris (July 6, p. 45) suggest that in our analysis of the changes in the forced expiratory spirogram and their relation to changes in arterial blood-gas tensions in patients with bronchial asthma[4] and chronic bronchitis,[5] partial rather than total correlation coefficients should have been calculated; they also ask for the "results of a multiple correlation procedure" on our data. Accordingly we

3. Leith, D. L., Mead, J. *J. appl. Physiol.* 1967, 23, 221.
4. Palmer, K. N. V., Diament, M. L. *Lancet*, 1968, i, 318.
5. Palmer, K. N. V., Diament, M. L. *ibid.* p. 1233.