FORCED EXPIRATORY VOLUME AS A TEST FOR SUCCESSFUL TREATMENT OF ASTHMA

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This paper describes a method of interpreting measurements of "forced expiratory volume" so that they can be used not only as a quantitative measure of change in asthma but also to determine when maximum benefit from treatment is obtained and whether the patient is likely to have underlying emphysema.

Forced Expiratory Volume

Definitions and Terminology

In asthma the maximum amount of air that a patient can breathe per minute ("maximum breathing capacity," or M.B.C.) is reduced. The severity of asthma is often assessed by measuring the vital capacity (V.C.), but this is unsatisfactory because the defect in asthma is mainly obstruction to air flow rather than restriction of chest movement, as in pulmonary fibrosis, etc. Thus a patient with asthma may have an almost normal V.C. if the exhalation is made very slowly, yet be able to exhale very little air quickly. It is therefore not surprising that measurement of the volume of air which can be exhaled in a given time (usually either three-quarters or one second) during a rapid and forced expiration following a maximum inspiration—in other words during a "forced vital capacity" (F.V.C.)—has been found to be more closely related to the M.B.C. than is the V.C. (Tiffeneau *et al.*, 1949; Kadlec and Vyskocil, 1950; Gaensler, 1951a; Kennedy, 1953). This volume will be called the "forced expiratory volume" (F.E.V.) qualified by the time in seconds over which it is measured.

There are a number of ways of measuring it in use. Usually the measurement is from the start of the F.V.C., and this is implied unless otherwise specified. Thus, when the time interval is 0.75 or 1 second, the abbreviations F.E.V._{0.75} and F.E.V.₁ are used. The volume exhaled over a second, after 0.25 second has elapsed from the start of the F.V.C., would be the F.E.V._{0.25-1.25}. This terminology, recently recommended for general use by the Thoracic Society (Gandevia and Hugh-Jones, 1957), avoids the specific terms which have been applied to the measurement taken over the different time intervals; the differences between them are of little significance for most clinical purposes, and the different terms are becoming confusing.

Apparatus and Methods

Recording the F.E.V. is far less tiring for the patient and simpler for the physician than measuring the M.B.C. directly by getting the patient to hyperventilate maximally and collecting the total amount of air exhaled over 15 seconds. The apparatus required is a simple spirometer with a light bell, similar to the type described by Bernstein *et al.* (1952), into which the patient delivers the F.V.C. through a mouth-piece or mask. The F.E.V. is measured either by taking a tracing (Fig. 1) on a fast kymograph of the movement of the spirometer bell during an F.V.C. test, from which the time and volume can be measured with a suitable scale, or by an automatic timing device (Gaensler, 1951b). The latter was used for the routine measurements presented in this paper, though in general we prefer a tracing, since it is hardly any more trouble and provides a permanent record with more information.

For clinical tests we record the F.E.V.₁ with the patient seated. After preliminary practice, the mean of three readings is taken. Perhaps rather surprisingly, the measurement is not very sensitive to the patient's co-operation (McDermott and McKerrrow, 1956), provided a full inspiration is insisted on before the forced expiration. Thus the variation between the three readings is small.

Interpretation

The F.E.V. represents a reasonably fixed part of the cycle of breathing (D'Silva *et al.*, 1953) during maximum ventilation, and the M.B.C. can be predicted with great precision— $r=0.9$ approximately (Gaensler, 1951a; Kennedy, 1953)—by multiplying the F.E.V._{0.75} by a factor of 40 (Kennedy, 1953) or the F.E.V.₁ by a factor of 37 (Cara, 1953). For the F.E.V.₁ the simpler factor of 35 is commonly used, the resulting systematic error in the predicted M.B.C. being negligible.

This whole procedure of multiplying the result by a constant has no merit, and the values of the F.E.V. itself should be used. The only justification is that often the normal values for the M.B.C. are familiar, whereas those for the F.E.V. are not.

The F.E.V.₁, like the V.C. and M.B.C., has a wide range of normal values depending on the age, sex, and size of the patient. However, expressed as a volume per second it is a measure of mean air flow, so the change in it in an individual is a simple measure of the effect of treatment in asthma, independent of the problem of its normal value.

FIG. 1.—Tracings recorded when measuring the forced expiratory volume, showing comparison of the normal (A) with those from patients with purely "restrictive" (B) and mainly "obstructive" (C) chest lesions. (Note: As the spirometer rises during expiration the pen falls, so that the volume expired is traced downwards.)

Significance of the F.E.V.%

The F.E.V. is not only a simpler practical measure than a direct record of the M.B.C., it also provides more information. The F.V.C. is recorded at the same time, and the proportion of the latter that the F.E.V. represents (usually expressed as a percentage, and abbreviated here to "F.E.V. %") is held to be of diagnostic importance. In normal subjects the F.E.V.₁ is greater than 70% of the V.C. (Tiffeneau *et al.*, 1949; Gaensler, 1951a; Pemberton and Flanagan, 1956); in subjects with a purely restrictive defect of ventilation (as in ankylosing spondylitis, some cases of pulmonary fibrosis, etc.), both the F.E.V. and V.C. are reduced proportionately, so that the F.E.V. still forms more than 70% of the V.C. (Fig. 1); in subjects with obstruction to the air-flow, however, the F.E.V.% may fall to very low values, of the order of 30–50 (Gaensler, 1951a; Drutel and Dechoux, 1952).

When the obstruction to the air flow is wholly or partly reversible, as in asthma, it might be expected that the F.E.V.% would increase with administration of effective bronchodilator drugs, yet from a series of routine clinical tests the impression was gained that an increase in the F.E.V.% did not, in fact, occur in spite of an increase in the absolute value of the F.E.V.₁ and obvious clinical improvement. Below we present results which show this paradoxical lack of change in F.E.V.% during routine tests, and then some trials on individual patients which demonstrate the circumstances in which the F.E.V.% does change

towards the normal value and the significance of recording F.E.V.% for the assessment of the effectiveness of anti-spasmodic therapy and help in diagnosis.

Effect of Treatment on Change in the F.E.V. Relative to the V.C. in Asthma

Acute Response

The records were studied of 38 consecutive patients with severe asthma who had shown a definite response to a three-minute inhalation of a 1% isoprenaline aerosol, as shown by an increase of at least 10% in the absolute value of F.E.V.₁. There were 26 male and 12 female patients, their ages ranging from 13 to 72 years. On clinical grounds 25 of them had bronchitis or emphysema as well as asthma, the remainder being considered to simply be suffering from asthma with otherwise functionally normal lungs. On comparing the F.E.V.% before and after treatment (Fig. 2) the

Fig. 2.—Comparison of the F.E.V., as a percentage of the F.V.C., before and after three minutes' inhalation of isoprenaline aerosol. Figures from 38 asthmatic patients who showed a definite response to this treatment in the increase in their absolute F.E.V., of: group A, 10 to 25%; group B, 25 to 50%; group C, more than 50%.

results confirmed our impression that this percentage showed hardly any change, the points scattering closely to and on both sides of the 45-degree line, representing no change. Moreover, this lack of change seemed independent of the magnitude of change in the F.E.V. itself, as shown by the symbols representing grouped results in Fig. 1. In these patients the F.E.V. was expressed as a percentage of the F.V.C. rather than as a percentage of the V.C. measured from a full, unhurried, and steady expiration, which gives a more reliable reading, especially in asthma and emphysema (Gilson and Hugh-Jones, 1949; Scarrone *et al.*, 1955). However, subsequent records, in which both the F.V.C. and the V.C. were measured, showed that the use of the F.V.C. as a point of reference did not account for the results.

The failure to observe an appreciable increase in F.E.V.% results from proportional increases in both the F.E.V. and the F.V.C. so that the ratio between them remains constant. Although at low initial values of the F.E.V.₁ the response to the administration of a bronchodilator aerosol is known to be incomplete (Lowell and Schiller, 1953; Hume and Gandevia, 1957), the results were surprising to us, since it might be expected that if some of the obstruction to the airways was removed there would be a relatively greater increase in F.E.V. and thus a rise in F.E.V.% towards the normal value of more than 70%. Thus special studies of the serial changes in individual asthmatic patients were made to see in what circumstances the normal percentage could be obtained.

Serial Response

Two groups of patients were compared. In the first there were four patients (two female and 2 male, aged 24, 27, 31, and 57 years respectively) who were thought clinically to have uncomplicated bronchial asthma, without other structural damage in the lungs. In the second group there were three patients (males aged 37, 57, and 60 years) in whom asthma was thought, clinically, to complicate bronchitis and emphysema. All had been admitted to hospital with status asthmaticus, and the F.E.V.₁, F.V.C., and V.C. were measured on them, at first twice daily and later daily, both before and after three minutes' inhalation of isoprenaline aerosol, during their recovery. During this time they received other treatment such as antibiotics, steroids, long-acting antispasmodics, breathing exercises, etc., which was thought appropriate clinically.

An example from each group which is representative of the others in the group is shown in Fig. 3, where the absolute values for the F.E.V.₁ are plotted against the

Fig. 3.—Serial changes in the F.E.V. and V.C. recorded daily during recovery from status asthmaticus, showing comparison of a case of "pure" asthma (A) with one where the asthma was a complication of severe emphysema (B). The arrows indicate the initial values on admission to hospital. —●—●=Change after three minutes' inhalation of isoprenaline aerosol.

V.C. The arrows indicate, in each case, the initial values obtained on admission to hospital when the patients had severe asthma and had low absolute values for F.E.V. and V.C. The values for the points before and after the aerosol are joined by lines whose length therefore indicates the extent of the acute response and whose slope indicates the change in the F.E.V. relative to the V.C.—that is, change in F.E.V.%.

It is apparent that there is always an incomplete response to single aerosol inhalation, a point emphasized by Lowell and Schiller (1953) and by Hume and Gandevia (1957). However, as the patient improves with treatment there is a difference in the response in the two groups of asthmatics. In each, both the F.E.V. and the V.C. initially increase proportionately, and where the asthma complicates emphysema

this proportionate increase continues until no further improvement in either is obtained and the F.E.V. as a percentage of the V.C. remains low. In the asthmatic patient whose lungs are otherwise normal, however, both the F.E.V. and the V.C. increase until the latter reaches a maximum value (which is presumably the normal for the patient), and the F.E.V.₁ continues to increase with further treatment and the lines of acute response to aerosol inhalation become steep, so that the F.E.V.% then, and only then, reaches its normal value of over 70%, when no further change takes place and treatment is complete. We have subsequently found this curvilinear response, obtained by serial readings of the F.E.V.% during treatment, to be typical of patients with uncomplicated asthma that we have investigated, and it is shown by two patients followed by Hume and Gandevia (1957) at the Brompton Hospital. It is not seen in patients whose asthma complicates emphysema; in them the F.E.V.% remains consistently low despite good response to treatment of their asthma, as shown by an increase in the absolute values of the F.E.V.₁ and V.C.

Discussion and Conclusions

Other workers (Dulfano *et al.*, 1953; Lowell and Schiller, 1953) have reported that at low initial values the F.E.V.% tends to remain constant after an inhalation of a bronchodilator aerosol. Dulfano *et al.* studied 36 patients with asthma and remarked that "the ratio of the first second to the total vital capacity" appeared to be remarkably constant for a given patient. They suggested that the constancy of the ratio might indicate a "fixed state" of the bronchial tree. However, they made single observations on patients rather than serial readings, and it is evident from our results that a low F.E.V.% which does not change after the single administration of a bronchodilator aerosol can either mean that the patient is an insufficiently treated asthmatic and that eventually the percentage will increase, or that he has permanent structural damage in the lungs, and then it will remain low in spite of any improvement shown by an increase in the absolute F.E.V.₁. Serial readings will help to decide between these alternatives if other lung-function tests are not available. The explanation for the finding of a constant F.E.V.% after a single administration of a bronchodilator aerosol in our patients (Fig. 1) is that these patients were all referred during an exacerbation of their disease, and had a low initial F.E.V. and F.E.V.%. Thus, whether they had underlying emphysema or were merely suffering a relapse of bronchial asthma, they were on that part of the curvilinear change in F.E.V.% shown in Fig. 3 where the F.E.V.% is low and does not change after the administration of bronchodilator spray.

Because of the limited nature of our investigations we do not offer any explanation for the curvilinear form of the change in F.E.V.% obtained in the cases of asthma, but the results are presented because we have found serial readings of the F.E.V., together with calculation of the F.E.V.%, to be of value in the practical treatment of patients with asthma, and we draw the following conclusions about them:

1. Serial recording of the F.E.V.₁ (or possibly some similar variation of it, easily got from the tracing, such as the mean mid-expiratory flow of Leuallen and Fowler (1955), etc.) is one of the simplest and most valid methods of assessment of treatment in asthma so far available. Changes in F.E.V. continue until asthma is removed, whereas the V.C. shows marked change only at the stage of moderate to severe disability with low initial values of the V.C.

2. Since the F.E.V.₁, like the V.C., has a wide range of normal values, even after allowing for the effects of age and sex, it is difficult to tell when an individual patient has reached his own normal value. Herein lies the particular value of calculating the F.E.V.%, since when this reaches its relatively narrow limit of normal—about 70–85% (Drutel and Dechoux, 1952; Pemberton and Flanagan, 1956)—one can then presume, provided the V.C. is within the normal range, that treatment is complete and the F.E.V.

unlikely to show further change. It is important to note that the wheeze may have disappeared from an asthmatic patient examined at rest some time before this happens.

3. Failure of the serial value of the F.E.V.% to increase beyond about 50% on continued and intensive treatment is highly suggestive of a patient whose asthma is complicated by emphysema. We cannot agree with Cara and Sadoul (1953) that a low percentage (25 to 55%) is itself diagnostic of emphysema, taken on a single reading. Other more complex lung-function tests are necessary to distinguish between the two conditions. But where such tests are not available the finding of a persistently low F.E.V.% in spite of vigorous and continued treatment, and increase in the absolute values of the F.E.V. and V.C., is highly suggestive of underlying emphysema.

Summary

The volume of air that a normal subject can exhale in one second from the start of a rapid forced expiration, following a full inspiration (the one-second "forced expiratory volume" or "F.E.V.₁") is about 80% of his vital capacity (V.C.). A reduction in the percentage expired (F.E.V.%) implies obstruction to the airways, and is found in both asthma and emphysema.

Data on 38 consecutive patients with moderate to severe asthma who showed marked benefit from three minutes' inhalation of isoprenaline aerosol, as measured by the increase in the absolute value of their F.E.V.₁, demonstrate that in these circumstances there is no change in the percentage expired. This is because both the F.E.V. and the V.C. increase proportionately. However, repeated observations on six asthmatic and three emphysematous subjects during daily treatment showed that: (1) in asthma, the F.E.V.% tends to remain constant until the V.C. approaches what is presumably the normal value for the patient, and only then, when the F.E.V.₁ increases further on continued treatment, does the F.E.V.% reach its normal value of about 80%; and (2) in emphysema, this disproportionate increase in the F.E.V. does not occur, so that the F.E.V.% remains low despite continued treatment and initial benefit from an increase in the absolute F.E.V.₁.

Measurement of the F.E.V.% is a simple test for clinical use. A low value suggests that the patient either has insufficiently treated asthma or emphysema as well. Serial readings help to distinguish the two. If when the V.C. is within the normal range the F.E.V.% reaches its normal value no further benefit can be expected from treatment.

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