

VENTILATORY TESTS IN BRONCHIAL ASTHMA

EVALUATION OF VITAL CAPACITY AND MAXIMUM BREATHING CAPACITY*

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REDUCTION of the vital capacity during an acute attack of bronchial asthma has been known for many years.¹⁻⁵ Relief of bronchospasm with bronchodilator drugs can be demonstrated by repeated determinations of the vital capacity, although the remarkable clinical improvement obtained from such drugs is much greater than might have been expected from usually small increases in vital capacity.⁶⁻⁸ Vital capacity measurements are also used to estimate the severity of asthma induced by the administration of histamine, methacholine, and aerosolized allergenic extracts.⁹⁻¹¹ Finally the protection afforded by adrenergic, anticholinergic, and antihistaminic drugs is generally estimated by serial vital capacity measurements.⁹⁻¹⁵

Baldwin and associates¹⁶ have aptly divided pulmonary function into a ventilatory component, concerned with the "mass displacement of air between the outside atmosphere and the interior of the lungs" and an alveolorespiratory component, concerned with "respiratory gas distribution in the alveoli and alveolo-capillary gas diffusion." It is the ventilatory component which is chiefly of concern in following the moment-to-moment changes of the asthmatic lung.

The vital capacity, one of the methods of evaluating ventilatory function, has been generally accepted in studies of asthma because the required apparatus is simple and inexpensive, the use of the spirometer is readily taught, extensive literature is available concerning normal standards, and the test is performed by the patient with little effort. Nevertheless, it is being recognized increasingly that vital capacity measurements alone are inadequate and often misleading tests of ventilatory function, particularly in any disease causing reduction of air-flow velocity. The great limitation of the vital capacity is that it is a measure of a single maximal ventilatory effort, irrespective of time. A patient's degree of dyspnea depends on the total volume of air which he is able to move in and out of his lungs during a given period of time, and not on the volume which he is able to exhale during a single maximal effort, irrespective of time.

Hutchinson,¹⁷ who first defined and measured the vital capacity in 1846, realized that ventilation involved not only the vital capacity or volume, measured with his spirometer, but also what he called "inspiratory and expiratory power," which he measured with a tube filled with mercury and connected to the patient's nostrils. The rise of the mercury, noted during forceful expiration, was the first attempt to measure something resembling air velocity. Since then many tests have been devised which include the time element or the velocity of air flow.

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The oldest of these is the candle test whereby the patient is required to blow out a candle placed at some distance from the mouth. Rotameters, designed to measure the speed of air flow, are occasionally used but are unreliable in the absence of a steady flow of air because of their inherent inertia. Spirometric tracings represent integral curves of ventilation and differentiation would be required to obtain air velocity. An approximation of the velocity at any given point can be obtained by drawing a tangent to the curve. Pneumotachographs record differential curves of ventilation and, therefore, air velocity can be read from them directly.^{18, 19}

The maximum breathing capacity is at present the most frequently used test of ventilatory function involving a time element. It is defined as the largest volume of air which can be moved voluntarily in and out of the lungs during a given period of time.²⁰ This test has been used on many thousands of patients and adequate standards for prediction of normal performance are available.¹⁶

METHOD

Vital Capacity (V.C.).—Patients were instructed to inhale as deeply as possible, and then to exhale as deeply and rapidly as possible into the mouthpiece of a water spirometer. During the last phase of expiration patients were encouraged to continue their effort. The best of 3 consecutive determinations was recorded and readings were corrected to 37° C. Predicted values were calculated according to age, sex, and height.¹⁶

Maximum Breathing Capacity (M.B.C.).—Patients were asked to breathe as deeply and rapidly as possible into the mouthpiece of a high velocity respiratory valve. Air was collected in a Douglas bag fitted with a 3-way gas cock.²¹ The volume in the bag was measured in a chain compensated Tissot spirometer. Expired air was collected for 30 seconds and the best of 3 efforts was recorded. Results were reported in liters per minute at 37° C. Predicted values were obtained from the age, sex, and body surface.¹⁶

Selection of Patients.—Patients were selected from a group referred to this laboratory for study of dyspnea due to unknown causes, evaluation of chronic emphysema treated with pneumoperitoneum,²² and for routine study prior to surgery for a variety of pulmonary lesions.²³ A number of asthmatics were referred for study before and after pulmonary plexus resection.

RESULTS

Detection of Nonclinical Asthma.—The first patient in whom function studies drew our attention to a discrepancy in ventilatory function as measured by V.C. and M.B.C. gave no history of intermittent dyspnea.

H. P., a 37-year-old single man, was referred for evaluation prior to thoracoplasty. He had far-advanced pulmonary tuberculosis which had progressed for 7 years in spite of pneumoperitoneum treatment. He was afebrile and appeared physically well. Bronchoscopy failed to show endobronchial disease.

A striking discrepancy between a M.B.C. of 43 liters per minute, or 38 per cent of predicted, and a V.C. of 3,550 c.c., or 84 per cent of predicted, disappeared after inhalation of isopropyl norepinephrine (1:200) aerosol (Fig. 1). Tests repeated 10 minutes after treatment showed a M.B.C. of 72 liters per minute, or 81 per cent, and a V.C. of 3,590 c.c., or 85 per cent of predicted. Actual ventilatory function was therefore doubled but as measured by V.C. it increased only 1 per cent. The patient volunteered that the "inhalation treatment" had improved his breathing and on repeated questioning he admitted occasional dyspnea accompanied by wheezes particularly during the summer.

Evaluation of Severe Asthma.—No previous diagnosis of bronchial asthma had been made in this patient. An "asthmalike" episode, which responded well to epinephrine, was noted after topical anesthesia prior to a previous bronchoscopy.

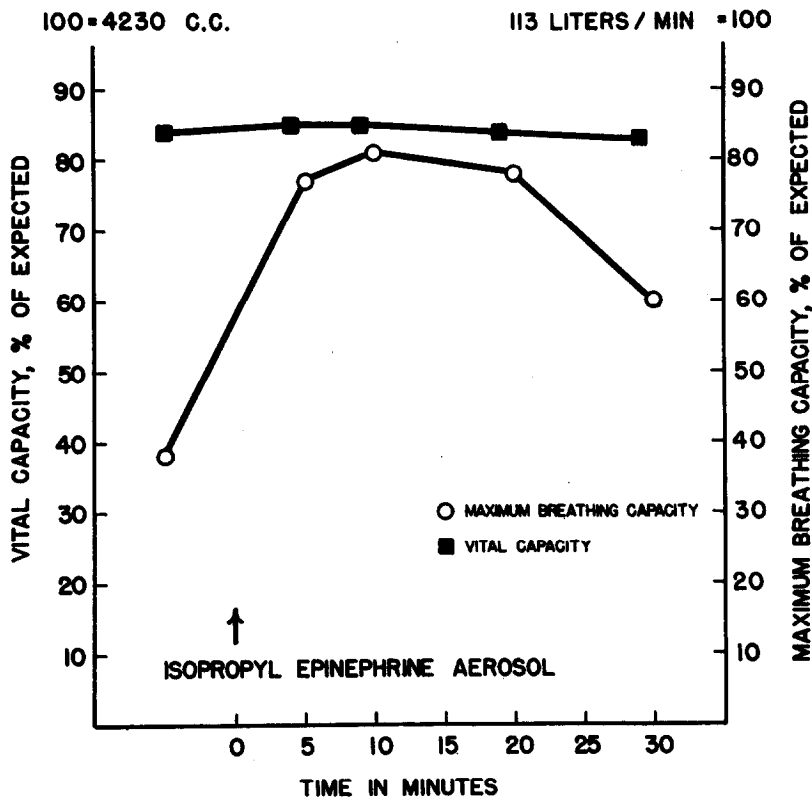


Fig. 1.—Graph of a 37-year-old man with pulmonary tuberculosis. Asymptomatic bronchospasm detected by discrepancy in pulmonary function as expressed by vital capacity and maximum breathing capacity. Relief with isopropyl norepinephrine aerosol.

I. N., a 57-year-old housewife, was referred from the Boston City Hospital with a chief complaint of intermittent shortness of breath of 10 years' duration. This was thought to be due to atelectasis of the right middle lobe, visible on roentgenogram of the chest and due to chronic emphysema as evidenced by a barrel-shaped chest and flattening of the diaphragm on the chest roentgenogram taken on expiration.

When first seen this patient was not dyspneic but many wheezes were heard over both lung fields posteriorly. M.B.C. was 32 per cent of predicted and V.C. 68 per cent. Here again inhalation of isopropyl norepinephrine resulted in marked improvement of M.B.C. to 84 per cent, but unlike the last patient there also was some increase of V.C. to 92 per cent of predicted (Fig. 2). After 50 minutes the effect of the sympathomimetic had almost disappeared and

the patient was given a spray of 2 per cent Pontocaine to the back of her pharynx prior to planned differential broncho spirometry. Severe asthma developed shortly and 10 minutes later the M.B.C. was only 8 liters per minute, or 13 per cent of predicted. This was less than her previously recorded minute ventilation at rest. She became cyanotic and, 13 minutes after the spray, arterial blood was obtained which showed only 72 per cent oxyhemoglobin saturation. The fall in V.C. during this time from 78 to 61 per cent of predicted in no way mirrored her respiratory distress at that time. Subcutaneous epinephrine 0.5 mg. promptly doubled the M.B.C. and oxyhemoglobin saturation 12 minutes after the epinephrine was 92 per cent. During this time the V.C. increased by only 3 per cent.

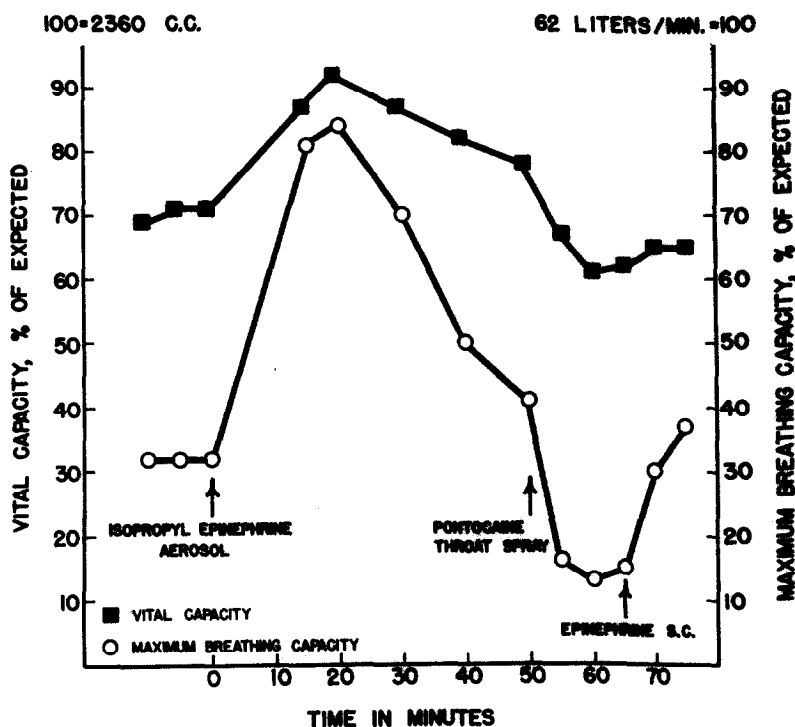


Fig. 2.—Graph of a 57-year-old woman with atelectasis of middle lobe of right lung. Relief of asymptomatic bronchospasm by isopropyl norepinephrine aerosol. Severe asthma induced by Pontocaine throat spray was relieved by epinephrine.

Timed Capacity Measurements.—A time element was introduced to the usual vital capacity test by inserting a 3-way gas cock between the mouthpiece and the spirometer bell. A V.C. was first determined in the usual way to familiarize the patient with the technique. One minute later another test was made but the stream of air was shunted from the spirometer to room air by means of the cock 6 seconds after onset of the deep expiration. One minute later this was repeated but the cock was turned after 3 seconds. Finally, one minute after that the M.B.C. was determined.

A. K., a 21-year-old single Canadian girl, was referred for evaluation prior to resection for bronchiectasis. She had been sensitive to a variety of foods since childhood. Reactions consisted of urticaria and occasional mild asthmatic attacks. She also suffered from hay fever. For the past 2 years asthmatic episodes had become more frequent and relationship to foods could no longer be traced. She began to have many colds and raised much sputum. Cylindrical bronchiectasis, limited to the lingular branch of the left upper lobe, was

demonstrated by bronchography. Culture of the sputum revealed a predominantly gram-negative flora and streptomycin aerosol therapy was started. After the second treatment she noted urticaria, wheezing, and some dyspnea which was relieved after some time by oral administration of an antihistaminic drug.

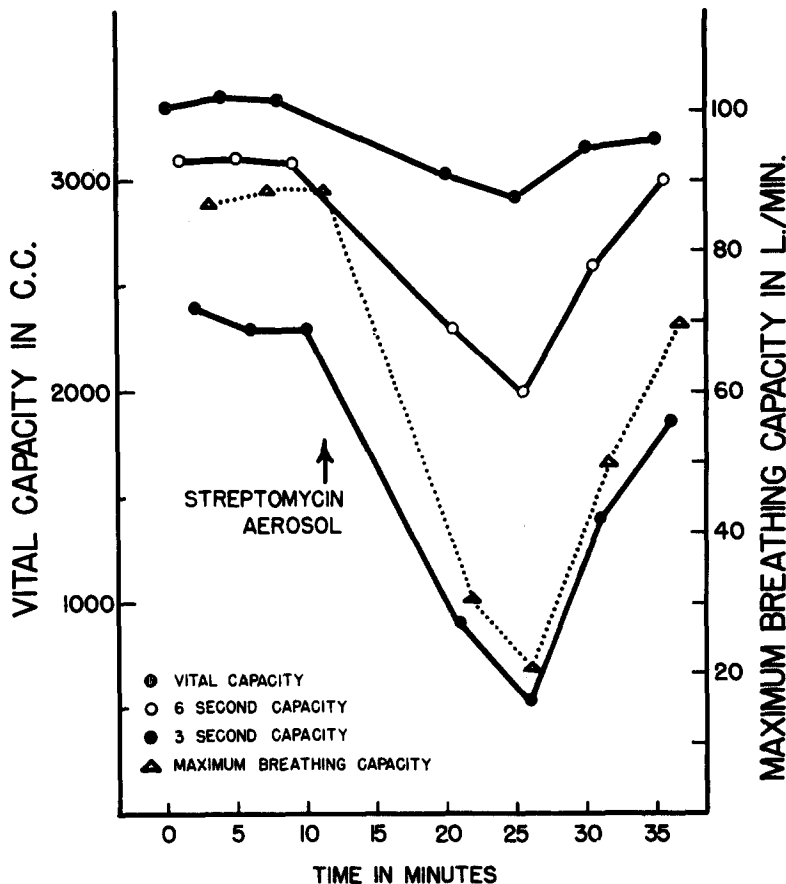


Fig. 3.—Graph of a 21-year-old woman. Asthmatic attack induced by streptomycin aerosol. Comparison of vital capacity, 3-second capacity, 6-second capacity, and maximum breathing capacity.

Function studies showed no striking ventilatory insufficiency. The M.B.C. was 89 liters per minute. V.C. was 3,360 c.c., the 6-second capacity 3,100 c.c., and the 3-second capacity 2,300 c.c. Three control determinations varied by no more than 3 per cent (Fig. 3). She was then given one single aerosol inhalation of a 10 per cent solution of streptomycin without being told what the nebulizer contained. Tests were repeated 8 minutes later, after clinical signs of asthma became apparent, and continued every 5 minutes after that. The peak reaction occurred 13 minutes after the inhalation. The M.B.C. showed the familiar sharp dip from 89 to 21 liters per minute, a 76 per cent drop. Again, as in previous cases, there was little change in V.C. which decreased 420 c.c., or 13 per cent. The 6-second capacity retained the shape of the V.C. curve but showed a larger response than the latter with a 1,100 c.c., or 39 per cent drop. The 3-second capacity curve most closely resembled that of the M.B.C. response with a drop of 1,520 c.c., or a 66 per cent loss. These same 3- and 6-second values can be obtained from vital capacity tracings recorded on a rapidly moving drum.

Protection Studies.—The M.B.C., performed with a high speed value and Douglas bag, is not as readily applied to protection studies as the V.C. Frequent repetition of a 30-second M.B.C. at short time intervals is not possible

because of the necessary rest periods after each test. Reduction of the time of voluntary hyperventilation to 15 seconds or performance of the test with a recording spirometer makes it more adaptable to this type of study. An occasional patient is encountered where attacks of asthma are induced by M.B.C. determinations. Decrease of the V.C. with successive tests is also occasionally noted in such patients. A typical protection study is illustrated in Fig. 4.

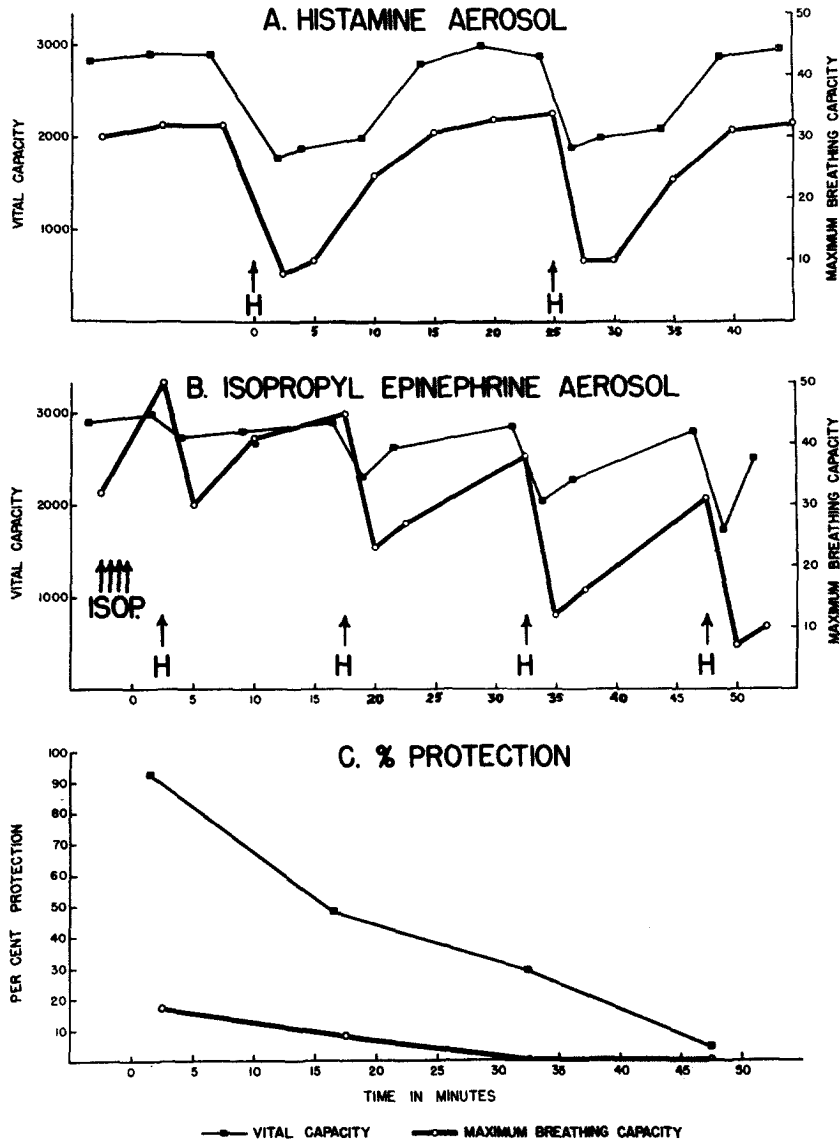


Fig. 4.—Protection of isopropyl norepinephrine against histamine-induced asthma.
 A. Asthma induced by histamine aerosol (H) with spontaneous relief.
 B. Reaction to histamine aerosol (H) after protection with isopropyl norepinephrine aerosol (ISOP.).
 C. Per cent protection during same time interval calculated for vital capacity and maximum breathing capacity.

A. M., a 47-year-old salesman, was referred for study of bronchial asthma and chronic pulmonary emphysema prior to bilateral pulmonary plexus resection. He had been suffering from asthma since childhood with less and less relief from medical therapy. During the past 20 years he had never been entirely free from asthma except during a 2-year period in the Army. Attacks could not be related to external circumstances and a large psychic factor was recognized by the patient.

Function studies during a relatively free period showed a M.B.C. of 32 liters per minute, or 43 per cent, and a V.C. of 2,890 c.c., or 77 per cent of predicted. A brief but severe attack of asthma could be induced by a single inhalation of histamine aerosol. At the height of the attack, the M.B.C. was reduced from 32 to 8 liters per minute, and the V.C. from 2,890 to 1,750 c.c. (Fig. 4, A). Response to isopropyl norepinephrine was marked by a large increase

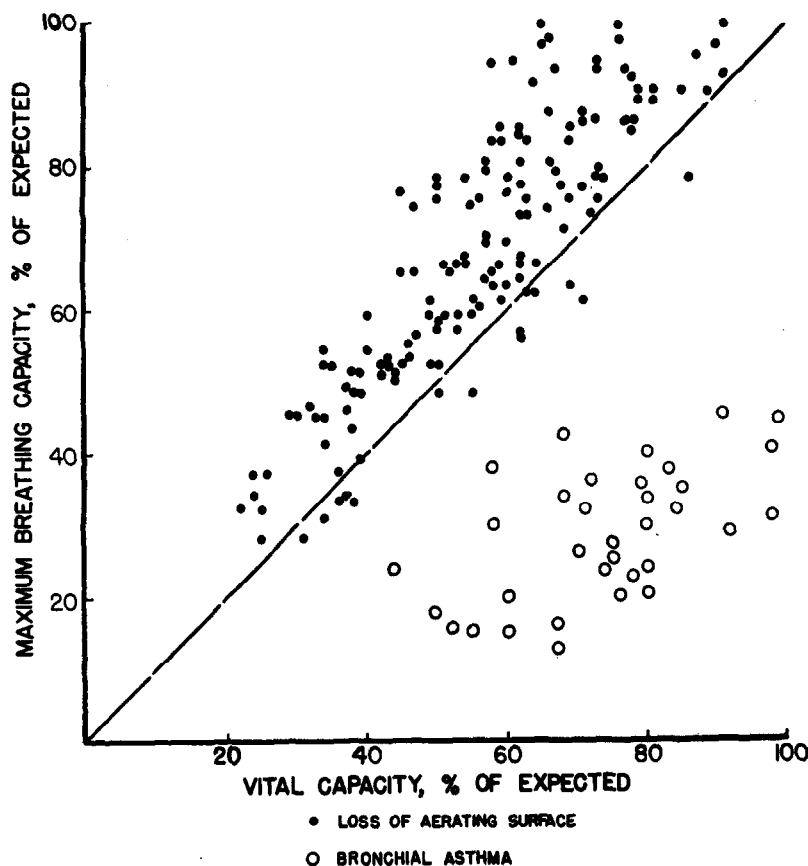


Fig. 5.—Comparison of the effect on vital capacity and maximum breathing capacity of pulmonary insufficiency due to bronchial asthma and to loss of aerated lung tissue. In bronchial asthma the vital capacity is relatively less decreased than the maximum breathing capacity.

in M.B.C. to 50 liters and a small increase of V.C. to 2,950 c.c. The effect of this drug as a protecting agent against histamine aerosol is illustrated in Fig. 4, B. In Fig. 4, C, the "per cent protection" was calculated and plotted for both the V.C. and the M.B.C. as a testing device according to the formula of Levinson, Beakey, Bresnick, and Segal.¹² It is evident that when the V.C. is used to determine bronchospasm, it appears that isopropyl epinephrine offers almost 100 per cent protection against histamine-induced asthma. The same formula applied to the M.B.C. as evaluation for bronchospasm shows only 17 per cent protection shortly after the protecting aerosol and no protection one-half hour later. The V.C., therefore, can be and has been successfully used for relative comparison of the effectiveness of

various drugs, doses, and routes of administration but it does not give a true estimate of the actual benefit or protection afforded the patient.

Relationship of Maximum Breathing Capacity and Vital Capacity: the Air Velocity Index (A.V.I.).—Since the V.C. is a measure of air moved irrespective of time, and M.B.C. is a measure of air moved during a unit of time, the relationship between the two must therefore be related to time, or the velocity of air flow. The relationship can be best expressed by the ratio

$$\frac{\text{per cent of predicted M.B.C.}}{\text{per cent of predicted V.C.}} = \text{A.V.I.}$$

where A.V.I. is the "Air Velocity Index" previously suggested by us.²⁴ Equal impairment of M.B.C. and V.C. will result in an A.V.I. of 1.0 irrespective of the degree of impairment. An index of less than 1.0 is found if there is relatively greater impairment of M.B.C. than of V.C. as in the illustrative cases of bronchial asthma. An index greater than 1.0 is usually found in patients with chronic ventilatory insufficiency due to reduced parenchymal lung tissue.²⁴

Fig. 5 presents this relationship graphically. Points were plotted for 34 patients with bronchial asthma and 150 patients with ventilatory impairment due to loss of pulmonary parenchymal tissue. Per cent of predicted M.B.C. was used as ordinate and per cent of predicted V.C. as abscissa. All points falling on the line drawn at a 45° angle have an A.V.I. of 1.0, points below that line an index of less than 1.0 and above this line, an index over 1.0. The average A.V.I. for the 34 patients with bronchial asthma was 0.36 with a range of 0.19 to 0.67. The average for patients with ventilatory insufficiency due to loss of aerated lung tissue was 1.23 with a range of 0.90 to 1.75. There was a good correlation between the A.V.I. and the severity of the asthma (Table I.).

TABLE I. MAXIMUM BREATHING CAPACITY, VITAL CAPACITY, AND AIR VELOCITY INDEX IN BRONCHIAL ASTHMA

CLINICAL SYMPTOMS	NO. OF PTS.	MEAN M.B.C.		MEAN V.C.		MEAN AIR VELOCITY INDEX
		LITERS PER MINUTE	PER CENT OF PREDICTED	C.C.	PER CENT OF PREDICTED	
Asymptomatic	9	53.9	41.2	3,300	82.5	0.50
Signs of bronchospasm, no distress	17	32.0	27.8	2,490	73.2	0.38
Dyspnea at rest	8	22.2	18.3	2,240	67.8	0.27

DISCUSSION

In the past, the vital capacity has been almost universally used for the quantitative estimation of ventilatory impairment due to bronchial asthma. The primary physiologic manifestation of asthma consists of a slowing of the expiratory phase of respiration due to a combination of bronchospasm, bronchial mucosal edema, and bronchial secretions. Since the vital capacity measures volume irrespective of time, it is an inadequate measure of ventilatory insufficiency if such insufficiency is partly or wholly due to a decrease in the expiratory air flow velocity.

Evidence from other sources than our own may be cited to emphasize this point. That certain patients appear short of breath despite a normal vital capacity was first noted by Hutchinson who attributed this to a lack of expira-

tory "power."¹⁷ Means²⁵ felt that dyspnea should become apparent when the vital capacity is decreased below the volume of resting tidal air (300 to 600 c.c.). This is in contradiction to the common finding of vital capacities of 2,000 c.c. or more in patients who are severely dyspneic. Curry and Lowell⁹ have noted that administration of histamine to asthmatics frequently results in respiratory distress without decrease in vital capacity. In such cases the expiratory slope of the vital capacity tracing became flattened without change in the height of the peak of the slope. Pneumotachographic tracings of patients with bronchial asthma show a marked prolongation of the expiratory phase.²⁶ Changes in such tracings due to treatment with epinephrine are chiefly characterized by a return to normal of the expiratory-inspiratory time ratio.²⁷

The maximum breathing capacity, an excellent measure of ventilatory insufficiency due to any cause, gives by itself no indication of air flow velocity, since a low M.B.C. may be due to both loss of functioning lung tissue and obstruction to the flow of air. Since vital capacity is significantly reduced only in the former case, a comparison of the two may give a hint as to the cause of ventilatory insufficiency. The maximum breathing capacity is also of great value in protection studies not only because it gives a more relevant picture of the actual protection afforded by a drug but also because a sufficiently large "control drop" of the vital capacity with a given bronchospastic drug can occasionally not be obtained without objectionable side reactions to the drug. The control drop of the maximum breathing capacity is invariably relatively larger for the same quantity of bronchospastic drug.

Study of the maximum breathing capacity, vital capacity slopes of spirometric tracings, pneumotachographic curves, and timed capacities are all of greater value in expressing the ventilatory insufficiency of bronchial asthma than the vital capacity.

SUMMARY

1. The vital capacity bears little or inconstant relationship to the ventilatory insufficiency of bronchial asthma while the maximum breathing capacity appears to reflect this insufficiency with a high degree of correlation.
2. Latent or minimal asthma and its response to bronchodilator drugs could not be demonstrated with repeated vital capacity determinations but could be shown with the maximum breathing capacity.
3. Introduction of a time element into the usual vital capacity measurement was of help in estimating the severity of asthma.
4. While vital capacity measurements are adequate for comparative study of the effectiveness of various bronchodilator drugs and various routes of administration, protection studies carried out in this manner were shown to give an erroneous impression of the actual protection afforded by a given drug.
5. The principal dynamic physiologic manifestation of bronchial asthma consists of a reduction of the rate of flow of the expiratory air stream. The vital capacity measures air volumes irrespective of expiratory time and is, therefore, an inadequate measure of the pulmonary insufficiency of bronchial asthma.
6. The dynamic expression of the "time-volume" relationship is exhibited by the air velocity index. The mean index for 34 patients with bronchial asthma

was 0.36, whereas the mean index for 150 patients with pulmonary insufficiency due to deficient parenchymal lung tissue was 1.23.

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