Expiratory Carbon Dioxide Concentration Curve
A Test of Pulmonary Function*

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Carbon dioxide retention is part of the pathophysiology of pulmonary emphysema, and therefore the measurement of the lung's ability to remove this gas is essential in the evaluation of this disease. Fractional analyses of expiratory air have been made on both emphysematous and normal subjects. Continuous carbon dioxide analysis during respiration was made possible through the use of rapid-response infrared carbon dioxide analyzers. The utilization of such an analyzing system has been applied to the study of continuous carbon dioxide concentration changes during expiration in patients with pulmonary emphysema.

METHODS

All subjects in this study were selected from the men in a general hospital. The ages ranged from 26 to 73 (mean 53.7) years. Preceding the pulmonary function testing, a clinical evaluation was done, including history and physical examination, basic laboratory studies, ECG, and inspiratory and expiratory chest x-ray films. The pulmonary function testing included: vital capacity, 3-second and total; maximum voluntary ventilation, 20-second testing period; residual volume by helium dilution; maximum expiratory flow rate; end-expiratory carbon dioxide concentration; MVV carbon dioxide removal (effect of the MVV test on the end-expiratory carbon dioxide concentration); and expiratory carbon dioxide concentration curve classification.

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All tests were performed with the patients rested and seated. Predicted values for VC and MVV were calculated. MEFR measurements were taken from tracings of the best of several efforts, using a double cone pneumotachograph.

The end-expiratory carbon dioxide concentration and the carbon dioxide expiratory curve were obtained by having the subject exhale directly through an infrared gas analyzer using a breathe-through type cell. There was a minimum dead space between the patient's mouth and the breathe-through cell. The patient was encouraged always to make a forceful and maximal expiration. The recorded expirations were started from a maximal inspiration, i.e., vital capacity, and from a tidal inspiration, i.e., expiratory reserve volume. A strip chart recorder, operating at a speed of 12 in. per minute, traced the changing carbon dioxide concentration in the expired gas. This tracing was termed "the expiratory carbon dioxide concentration curve." The concentration at the terminal segment of the curve was termed "the end-expiratory carbon dioxide concentration." The curve was then transferred onto a piece of clear film and identified by number only. Using these curves, the subjects were divided into four groups, based only on the configuration of the first portion of the curve.

An arrangement of valves in the collecting system for the MVV test was such that the end-expiratory carbon dioxide concentration could be measured before and immediately after the period of rapid breathing. The change in the end-expiratory carbon dioxide concentration immediately following the MVV test was called "the MVV-CO₂ removal."
The response time of the gas analyzer system was approximately 90 per cent in 0.1 second. Accuracy of the response of the carbon dioxide analyzer was assured by frequent standardizations with known concentrations of carbon dioxide in oxygen. No correction was made for moisture content of the expired gas.

The statistical analysis of the results was made by the non-paired method and null hypothesis was rejected at 5 per cent level.

Discussion of Results

As the subject exhales through the carbon dioxide analyzer-recorder system, a curve is described relating changing carbon dioxide concentration to time ('Fig. 1). This curve is influenced by the flow rate of the expired carbon dioxide, the intrapulmonary mixing, and the alveolar carbon dioxide concentration. As the subject is encouraged to exhale with maximal effort, the contour of the curve under these conditions reflects the effectiveness of voluntary forced expiration.

In the "normal" curve (Fig. 2, Type I), the characteristic is a rapid change to a constant concentration early in expiration. This results in a near right angle configuration with the remainder of the curve a plateau representing little change in concentration. The terminal segment of the curve represents that period during inspiration when no gas is moving through the analyzer cell.

In the most abnormal type of curve (Fig. 2 Type IV), the change in concentration of carbon dioxide is more gradual, rising throughout expiration and never attaining a constant composition. This results in a curve that is wider with a high end-expiratory carbon dioxide level. A plateau of constant composition may not be described because the carbon dioxide concentration is still changing at the end of expiration. In all subjects, the expiratory carbon dioxide curves are reproducible when recorded under the same conditions of testing. It has been noted that the shape of the carbon dioxide expiratory curve shifts to a more normal contour in patients improving under treatment.

The carbon dioxide concentration at the cessation of flow represents the alveolar carbon dioxide concentration in the normal subject. In the abnormal subject, it cannot be definitely concluded that this concentration is the alveolar carbon dioxide concentration because of the effect of trapping, disturbed intrapulmonary mixing and emptying. End-expiratory carbon dioxide

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*Testing with our analyzer showed no significant difference in comparing CO₂ in air and CO₂ in O₂.
concentrations are also reproducible in each individual if testing conditions remain the same. In measuring the end-expiratory carbon dioxide concentration, a lower value is obtained if a maximum inspiration precedes the measurement. This probably reflects the increased dilution by the greater volume of inspired air. However, a maximum inspiration has little effect on the contour of the first portion of the expiratory carbon dioxide curve.

There is no established single test or criterion for the diagnosis of pulmonary emphysema. Some pulmonary function test results may fall within limits of normality in mild emphysema while severe emphysema may present abnormal results in all phases of pulmonary function evaluation. The contour of the carbon dioxide expiratory curve is related to several aspects of pulmonary function and would be expected to vary with the severity of the disease. In addition to the clinical evaluation, the parameters for severity of our emphysema patients were the number of abnormal pulmonary function tests and the degree of abnormality of these tests.

The separation of the carbon dioxide curve into four arbitrary groups according to curve contour was done without knowledge of the diagnosis of the subjects. When these four groups were analyzed, all but one of the subjects tested as "normals" were in the Class I curve group. Clinically, the most severely debilitated and disabled subjects were in Group IV.

A summary of the pulmonary function test results of each group is presented in Table 1. An intergroup comparison is presented in Table 2. With respect to those tests done, separation of Group I from Group II was statistically significant except

<table>
<thead>
<tr>
<th>Table 1—Showing Mean and Standard Deviation of Pulmonary Function Test Results in the Groups of Patients Separated Only by Expiratory Curve Type</th>
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</thead>
<tbody>
<tr>
<td>Group I Mean</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>3 sec. VC/Tot.(%)</td>
</tr>
<tr>
<td>Tot. VC/Pred.(%)</td>
</tr>
<tr>
<td>MVV/Pred.(%)</td>
</tr>
<tr>
<td>RV/TC (%)</td>
</tr>
<tr>
<td>MEFR (L/min.)</td>
</tr>
<tr>
<td>Max. Exp. CO₂ (%)</td>
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<tr>
<td>CO₂ Removal—MVV (%)</td>
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In Figure 2, the typical expiratory curves are shown.
for one test, the end-expiratory carbon dioxide concentration. Carbon dioxide retention is probably not present to any degree in mild emphysema, but it certainly occurs in the more severe stages of the disease. The individuals with curves in Group II represented mild pulmonary dysfunction (refer to Table 1), and therefore the end-expiratory carbon dioxide concentration would not be expected to be different from Group I. The end-expiratory carbon dioxide concentration was significantly different only in the comparison of non-adjacent groups.

In patients with more severe pulmonary dysfunction, the carbon dioxide curve contour was not as discriminating in separating the groups. Group II differed from Group III in only two tests. Group III differed from Group IV only by the MVV test. Patients in Group IV had severe emphysema and their inability to perform the physical work associated with the MVV test may be the factor in the test’s ability to differentiate these two groups. There is a smaller difference between the mean values for the MVV test for Groups II and III, as compared to the difference between the other adjacent groups. No other reason is evident for the failure of the MVV test to separate Group II from Group III. These groups are separated by the RV/TC ratio and 3 second VC.

Carbon dioxide expiratory curves recorded before and after the MVV test are identical in contour. In the normal and mildly emphysematous patients, the end-expiratory carbon dioxide level following the MVV test was significantly lower. We believe this reflects the relative removal of carbon dioxide from the lungs during the period of forceful ventilation. In the severely emphysematous patient, little lowering of the end-expiratory carbon dioxide concentration was evident, and in some patients the expiratory carbon dioxide level was higher than the level measured before the MVV test. This is probably a reflection of the mobilization of carbon dioxide from poorly ventilated areas of the lung. Certainly in the severely emphysematous patient, the MVV test tends to aggravate the obstruction with more air trapping and less efficient ventilation. In these individuals, the performance of this test results in gas stagnation in a large portion of the lung, while the patient moves only tidal air. Thus, the MVV test paradoxically increases the dysfunction, and this is reflected in the increased level of carbon dioxide

<p>| TABLE 2—STATISTICAL RELATIONSHIP BETWEEN GROUPS SEPARATED ONLY BY CURVE TYPE AND PULMONARY FUNCTION TESTS PERFORMED ON THESE GROUPS |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>3 sec. VC/Total. per cent</th>
<th>I vs II</th>
<th>II vs III</th>
<th>III vs IV</th>
<th>I vs II</th>
<th>II vs III</th>
<th>III vs IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total. VC/Pre. per cent</td>
<td>t-8.6</td>
<td>p-0*</td>
<td>p-1.2</td>
<td>t-8.8</td>
<td>t-12.9</td>
<td>t-11.8</td>
</tr>
<tr>
<td>MVV/Pre. per cent</td>
<td>t-6.8</td>
<td>p-0*</td>
<td>p-0*</td>
<td>t-8.2</td>
<td>t-13.4</td>
<td>t-11.8</td>
</tr>
<tr>
<td>RV/TC per cent</td>
<td>t-9.6</td>
<td>p-0*</td>
<td>p-0*</td>
<td>t-11.8</td>
<td>t-13.7</td>
<td>t-11.8</td>
</tr>
<tr>
<td>MFER (L/Min.)</td>
<td>p-60</td>
<td>p-0*</td>
<td>p-0*</td>
<td>p-0.45</td>
<td>p-2.5</td>
<td>p-0.45</td>
</tr>
<tr>
<td>Max. Exp. CO₂ (per cent)</td>
<td>p-2.7</td>
<td>p-0*</td>
<td>p-0*</td>
<td>p-1.2</td>
<td>p-2.0</td>
<td>p-1.2</td>
</tr>
<tr>
<td>CO₂ Removal (MVV)</td>
<td>t-8.6</td>
<td>p-0*</td>
<td>p-0*</td>
<td>t-10.8</td>
<td>t-0.12</td>
<td>t-0.12</td>
</tr>
</tbody>
</table>

*Significant at 5 per cent level or better.
after the test. The maximum forced expiration was very difficult to elicit from this type of patient following the MVV test because of fatigue, coughing, and apprehension. The results of the MVV test in the severely emphysematous patient must be considered with this in mind.

Adequate intrapulmonary mixing of the helium is essential for the accurate determination of RV/TC. Although seven to ten minutes rebreathing were allowed for this test, it is possible that incomplete mixing in the severely emphysematous lungs occurred. This influenced the accuracy of the test and the correlation of the curves in separating Groups III and IV.

No single pulmonary function test was valid in separating all groups of emphysema patients of varying severity. Some tests were useful for separating the normal group from the mild emphysema group; others for separating the severe emphysema group from the moderately severe. The data support the concept that at present there is no good single pulmonary function test. A broad spectrum of physiologic abnormalities occurs when the respiratory organs are affected by the emphysema process. Unfortunately, too many of the tests depend on patient cooperation and motivation, and this becomes increasingly difficult to obtain as the patient becomes more debilitated. The patient with severe emphysema does not care about his performance in the MVV test. Even at rest his minute volume may approach his MVV. Many of these patients have a highly apprehensive emotional overlay, so strong that the pattern of respiration is poorly coordinated and highly variable. These patients are also poor subjects for the residual volume determination, and the other basic lung volume studies, giving poor test performances in spite of education and practice. Tests which can be accomplished with minimal cooperation are better tests for these individuals. The value of the carbon dioxide expiratory curve is the ease with which it can be obtained in any patient, and that it varies with the severity of the emphysema process.

CONCLUSIONS

1. A test of pulmonary function based on the configuration of the expiratory carbon dioxide concentration curve is described.

2. This curve is obtained by having the subject exhale directly through a rapid-response infrared gas analyzer using a breathe-through type cell and a strip chart recorder.

3. The test is effective in separating subjects with normal pulmonary function from patients with pulmonary emphysema of varying degree.

4. The respiratory carbon dioxide concentration curve is a valuable test of pulmonary function because of the ease with which it can be obtained.

CONCLUSIONES

1. Se describe una prueba de la función pulmonar basada en la configuración de la curva de la concentración de la expiración del dióxido de carbono.

2. Se obtiene esta curva haciendo que el sujeto exhale directamente a través de un analizador de gases rápido, usando un tipo de celda de exhalaición completa y un registrador de gráficas en cinta.

3. La prueba es efectiva pues sirve para separar los sujetos con función pulmonar normal de los que padecen enfisema de grados varios.

4. La curva de la concentración del dióxido de carbono es de valor para estimar la función pulmonar, por la facilidad con que se obtiene.

RESUME

1. L'auteur décrit un test de la fonction pulmonaire fondé sur l'aspect de la courbe de concentration expiratoire de gaz carbonique.

2. Cette courbe est obtenue en permettant au sujet d'expirer directement dans un appareil rapide d'analyse des gaz utilisant une cellule particulière et un enregistreur à rouleau.

3. Le test est efficace, car il permet la séparation des sujets qui ont une fonction pulmonaire normale des malades atteints d'emphysème pulmonaire à des degrés divers.

4. La courbe de concentration respiratoire de gaz carbonique est un test précieux de la fonction pulmonaire à cause de la facilité avec laquelle il peut être obtenu.
**ZUSAMMENFASSUNG**

1. Beschreibung einer Prüfmethode für die Lungenfunktion, basiert auf der Form der Kohlendioxyd-Konzentrations-Kurve in der Ausatmungsstufe.


4. Die Kohlendioxyd-Konzentrationskurve in der Atemluft ist ein wertvoller Test der Lungenfunktion wegen der Leichtigkeit mit der sie sich ermitteln läßt.

**REFERENCES**


**VECTOR ANALYSIS OF rS IN LEAD V₁**

Derived vectorcardiography has been performed in 25 patients with the rS pattern in V₁. In one patient, R and S waves were identical. In 20 patients, the vectorcardiographic patterns correlated with necropsy findings. The rS pattern was observed in right ventricular hypertrophy, combined ventricular hypertrophy and in myocardial infarction, which later may be (but not necessarily) associated with ventricular hypertrophy. The vectorcardiographic analysis of the rS pattern in V₁ renders it possible to differentiate right ventricular hypertrophy from the other conditions. Its value in the differential diagnosis of combined ventricular hypertrophy is smaller. This latter diagnosis should always be borne in mind if the central and terminal portions of the loop in the horizontal plane are displaced somewhat to the right and to the posterior segment. Similarly, attention should be given to the discrepancies between the form of the loop in the horizontal and in the frontal planes. According to their experience, the value of vectorcardiography in the diagnosis of myocardial infarction is very small, especially in comparison with electrocardiography.