Recognition of Early Emphysema by Pulmonary Function Tests*. **

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Chronic obstructive emphysema has been fully accepted as an increasingly common pathologic condition of the lungs. Though well recognized, this disease has given rise to diverse theories concerning its origin. The proposed etiologies run the gamut from congenital lack of elastic fibers, diminished circulation, chronic bronchitis, bronchiectasis, silicosis, tuberculosis, asthma and chemical irritants to smoking. The pathology seems confused by lack of definition, and difficulty in quantitating degrees of emphysematous impairment. The physiologists have studied far advanced emphysema extensively and have amply documented the gross changes such as obstruction of airways, uneven distribution of inspired air, increased lung volume, abnormal ventilation blood flow ratio, reduction in vascular bed, poor diffusion and altered blood gases. This paper is concerned with the application of pulmonary function tests in the detection of early emphysema.

Recognition of early emphysema is essential for the proper study of the natural history of this disease. If we are, indeed, to incriminate such items as chronic bronchitis, and smoking, the disease must be evaluated throughout its course. Those who wait for physiologic tests to indicate far advanced disease will miss the most crucial phase of the disease, namely the onset. As a general principle, little is learned about a pathologic condition by studying the late stages of disease. Furthermore, from the point of view of control of emphysema, one must ameliorate the condition before dyspnea becomes a prominent symptom.

How does one recognize early emphysema by pulmonary function tests? First, we will examine the tests used for recognition of far advanced disease and determine whether or not they are applicable to the problem. Emphysema, when most advanced, causes CO₂ retention and respiratory acidosis, but in the earlier stages this does not occur. Likewise, arterial blood oxygen unsaturation is a late finding. Bates, Knott and Christie¹ and others have reported that reduced diffusing capacity is a poor prognostic sign but again this finding is observed late in the course of the disease. Most often an increase in residual volume has been considered essential for making a diagnosis of emphysema,² but this too is a late manifestation. By a process of elimination we are now reduced to a discussion of the several ventilatory tests. Such a battery might be particularly useful clinically because ventilatory tests are easy to perform. To use many of these may be misleading because of their variability in emphysema.³ Those who treat patients with asthma, for instance, recognize that the ventilatory tests may revert toward normal as the dis-

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ease improves. Is it possible to selectively choose ventilatory tests which will minimize these objections?

The vital capacity (VC) is the best known of the ventilatory tests. In emphysema, it may be normal in the early stages, increased in the moderately advanced stage and only significantly decreased in the late stage. However, this relationship is not a constant finding and the vital capacity is not considered discriminatory in early disease.

From the standpoint of physical examination one of the prominent features of emphysema is the prolonged expiration time. This can readily be measured by timed vital capacity (TVC). This test should be included in our proposed battery of tests. The maximum breathing capacity (MBC) closely correlates with TVC in the obstructive type of breathing and therefore will add little except in the interpretation of the spirogram. The MBC has a limitation similar to the VC because it also may be in the normal range in early emphysema.

The air trapping indicated by elevation of the MBC spirogram E, has received little emphasis in physiologic literature, perhaps because the cause of this phenomenon remains obscure. Whittenberger ascribes the air trapping to increased resistance in the airways which causes a step like increase in trapping "until lung volume equilibration occurs at a point when the added pressure drop (resistance) is counter balanced by the increased potential energy of the lung at the end of inspiration." Figure 1a shows a typical MBC spirogram with progressive air trapping to hyperinflation level. On the other hand, many patients when asked to breath rapidly and deeply, as during exercise or performing the MBC, will first hyperinflate the lungs, to the limit of their inspiratory capacity as illustrated in Figure 1b. Even patients with early emphysema, custom-

FIGURE 1: Maximum breathing capacity spirograms. (a) Step wise elevation to hyperinflation level. (b) Abrupt rise to hyperinflation level.
early take one or more deep breaths before beginning rapid breathing, just as though about to plunge into a cold pool of water. The reason for this maneuver of hyperinflation is not clear. Perhaps, it is a habit acquired at an early age, or the psychosomaticist might suggest an anxiety phenomenon. More likely this maneuver improves the mechanics of the lung by placing the elastic tissue on the stretch, improving compliance and reducing airway resistance. This phenomenon of air trapping is a constant early finding in emphysema and is not abolished by administration of bronchodilators. Generally, the more rapidly the MBC is performed the higher the level of hyperinflation up to the limit of the inspiratory capacity. It should be noted that a few patients with very low inspiratory capacity may be unable to trap air.

The normal lung has remarkably uniform gas distribution, but the emphysematous lung has uneven ventilation. When one inspects the freshly cut section of an emphysematous lung (Fig. 2) or the whole lung section prepared by the Gough technique, one can detect with the unaided eye the diffusely enlarged alveoli or confluent spaces formed by the breakdown of alveolar septi. These spaces vary in size and have communicating ducts of diverse sizes. It seems reasonable to expect, therefore, that the distribution of gases within such lungs may be abnormal. The single breath of $O_2$ test (SB) described by Comroe and Fowler is recommended for measuring uneven ventilation within the lungs and is included in our proposed group of tests.

Thus, three simple ventilatory tests are available, each measuring a different facet of the complex pathologic physiology of the emphysematous lung. The TVC gives information on the degree of obstruction of the air flow. The elevated MBC spirogram reveals evidence of air trapping within the lung. Finally a rising alveolar nitrogen curve after a single
breath of O₂ suggests the presence of uneven distribution of gases within abnormally large alveolar spaces. A preliminary study from this laboratory showed that when a combination of each of these three tests which measure three different parameters of the lung are abnormal, then the presence of early emphysema may be diagnosed with considerable accuracy. The investigation concerning the detection of early emphysema was carried out on 328 consecutive patients who had pulmonary resection. The specimens removed varied from single segments up to complete pneumonectomies. The purpose of the present study was to enlarge our experience by correlation of these tests with the pathologic findings in 150 patients undergoing lobectomy for removal of tuberculous lesions.

**Material and Methods**

One hundred and fifty tuberculous patients in whom lobectomies may be considered to yield "ideal biopsies" were selected. Patients in whom the entire lobes were destroyed by disease or compressed under thoracoplasty or plombage were excluded because such specimens do not offer representative samples of lung tissue. The fresh lung specimens were inflated to normal size with formalin solution and several days later cut in slices approximately 1.0 cm. in thickness. Emphysema was considered to be present when generalized diffuse enlargement of the alveoli was apparent to the unaided eye. Colored photographs were taken and slides made which demonstrated diffuse emphysema (Fig. 2) with great clarity when projected on a large screen. In contrast, (Fig. 3) shows a section of lung with focal emphysema at the apex, the remaining portion appears to be normal lung tissue. Histologic confirmation was not attempted. Emphysema in conjunction with tuberculosis has received little attention from pathologists and usually in far advanced cases. There seems to be agreement, however, on two forms of emphysema; one generalized emphysema which may or may not be related to tuberculosis and secondly focal which is closely associated with tuberculous lesions. The latter type may involve lung tissue surrounding the distortion caused by disease or appear peripherally in which case bullae also may be noted.

![](http://journal.publications.chestnet.org/pdfaccess.ashx?url=data/journals/chest/21344/)

TABLE 1 — COMPARISON OF NONEMPHYSEMA WITH EMPHYSEMA PATIENTS BY DECADES IN RELATIONSHIP TO VENTILATORY TESTS

<table>
<thead>
<tr>
<th>No</th>
<th>Av. WL</th>
<th>Av. Hc</th>
<th>Av. TLC</th>
<th>Recommended Screening Tests</th>
<th>Av. MBC per cent</th>
<th>Av. VC per cent</th>
<th>Av. TR per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>No Emphysema</td>
<td>21</td>
<td>71</td>
<td>159</td>
<td>93</td>
<td>0.7</td>
<td>16</td>
</tr>
<tr>
<td>Years Emphysema</td>
<td>5</td>
<td>70</td>
<td>138</td>
<td>72</td>
<td>2.0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>30-39</td>
<td>No Emphysema</td>
<td>42</td>
<td>69</td>
<td>156</td>
<td>87</td>
<td>1.2</td>
<td>21</td>
</tr>
<tr>
<td>Years Emphysema</td>
<td>13</td>
<td>69</td>
<td>150</td>
<td>80</td>
<td>2.8</td>
<td>4*</td>
<td>9</td>
</tr>
<tr>
<td>40-49</td>
<td>No Emphysema</td>
<td>20</td>
<td>69</td>
<td>155</td>
<td>84</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Years Emphysema</td>
<td>20</td>
<td>69</td>
<td>148</td>
<td>72</td>
<td>2.4</td>
<td>2**</td>
<td>18</td>
</tr>
<tr>
<td>50 or More</td>
<td>No Emphysema</td>
<td>10</td>
<td>68</td>
<td>149</td>
<td>83</td>
<td>1.1</td>
<td>10</td>
</tr>
<tr>
<td>Emphysema</td>
<td>19</td>
<td>67</td>
<td>139</td>
<td>71</td>
<td>3.1</td>
<td>1</td>
<td>18</td>
</tr>
</tbody>
</table>

*2 had low inspiratory capacity
**1 had low inspiratory capacity
See text for symbols.
Each patient received pulmonary function tests within two weeks before lobectomy. Ninety-four of the 150 patients were available for testing at an average period of six months postoperatively. Vital capacity was performed on a 13.5 liter Collins respirometer by the method of Baldwin. Timed vital capacity was carried out on a 7 liter Collins vitalometer fitted with a potentiometer to transcribe the record on electrocardiographic paper. Maximum breathing capacity was determined on a 13.5 liter Collins respirometer by the method of Baldwin and the spirogram was inspected for evidence of air trapping. The single breath $O_2$ test for uneven ventilation was carried out by our modification of the method of Comroe. Residual volumes (RV) and index of intrapulmonary mixing by the open circuit method were determined in 20 patients with grossly abnormal screening tests.

**Results**

Data on the 150 tuberculous patients are presented in Table 1. The patients are divided into decades and each decade is subdivided into two groups according to whether or not emphysema was noted in the gross lung sections. As might be expected, there are more patients in the older age groups who have emphysema. Two factors may be operating here: it is recognized that the incidence of emphysema increases with age and the older patients have had pulmonary tuberculosis for greater lengths.
of time. The patients in each decade who had emphysema have a significantly lower weight than the nonemphysematous patients. In the emphysematous groups the VC and MBC tend to be lower but are not satisfactory for the detection of emphysema because of the wide range of values in the nonemphysematous group due in part to the variation in the pulmonary involvement with tuberculosis. Average vital capacity is 102 per cent, range 61 per cent to 142 per cent. Average maximum breathing capacity is 101 per cent range 48 per cent to 153 per cent. It may be seen in Table 1 that elevation of the MBC spirogram, on the other hand, gives a rather sharp demarcation between the normal and abnormal, particularly in the older age group. Timed vital capacity behaves in the reverse manner, namely better discrimination occurs in the younger age groups where the average 2 second TVC for the nonemphysematous in the age 20-29 is 93 per cent but reduced to an average of 83 per cent in the age group 50 or over. It is demonstrated that the single breath test does not significantly increase with age in our nonemphysematous groups. This finding is not in accord with the results of Comroe's studies, but comparison may not be entirely valid because our patients were not normal subjects. Finally, the terminal rise (TR) values are not discriminatory because in nonemphysematous patients there may be elevation in a variety of conditions such as open cavities, blebs, bronchiectasis, pleural adhesions and impaired function of the diaphragm. It may be seen, nevertheless, that in general the emphysematous patients have a higher TR as previously reported.

Figure 4 shows the results of the combination of the three screening tests, TVC, elevation of MBC spirogram and SB. The criteria used in detecting emphysema in these 150 tuberculous patients were: 2 second TVC of 90 per cent or less, elevation of th MBC spirogram above the resting expiratory level, and SB test of 2 per cent or greater. It may be seen that there are 93 patients without demonstrable emphysema in the sections of removed lobes. There were two patients in whom the combined tests indicated emphysema, although none was demonstrated pathologically. Fifty-seven patients had emphysema shown by the "ideal biopsy." The results of the combined function tests correctly indicated emphysema in 49 and failed to be definitive in eight of these patients. The three ventilatory tests were correct in indicating whether or not emphysema was present in 93 per cent of the patients.

Discussion

It is well known that the use of ventilatory tests to indicate emphysema in the asthmatic patient may be unreliable unless the examinations are made when the

<table>
<thead>
<tr>
<th>TVC</th>
<th>Best TVC Cut Off Values</th>
<th>TVC Per cent Correct</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 second</td>
<td>73 per cent</td>
<td>Emphysema</td>
<td>91 per cent</td>
</tr>
<tr>
<td>2 second</td>
<td>89 per cent</td>
<td>Emphysema</td>
<td>93 per cent</td>
</tr>
<tr>
<td>3 second</td>
<td>93 per cent</td>
<td>Emphysema</td>
<td>91 per cent</td>
</tr>
</tbody>
</table>

No Emphysema per cent | 50 per cent | 73 |
| No Emphysema | 52 per cent | 89 |
| No Emphysema | 54 per cent | 93 |
patient is in an asthmatic free period and has achieved maximum improvement with
effective bronchodilator drugs prior to testing. Similarly it might be argued that as
the tuberculosis becomes inactive the three recommended screening tests might revert
to normal. It should be noted that these patients were, for the most part, x-ray stable
and under antibiotic therapy for many months before being subjected to lobectomy—
some, however, had cavitary type of resection and still had positive cultures for acid
fast bacilli (AFB). Information regarding the reversibility of the tests may be ob-
tained by follow-up studies. Ninety-four of these patients were available for retesting
at an average period of six months following lobectomy. There were six patients in
the non-emphysematous group who, after surgery, appeared to develop emphysema
by these tests. One reverted from a false positive to negative. In the emphysematous
group, two patients had negative results on preoperative pulmonary function testing
which became positive after operation. Only one patient in the emphysematous group
reverted back to normal tests after surgery. Thus it becomes quite clear that reversi-
ibility of the tests is infrequent in patients with stable tuberculosis lesions.

In the previous study, the 2 second TVC was selected as showing better discrimina-
tion than the 1, or 3 second tests. Bernstein11 has demonstrated that there is no
advantage of one particular time over another since they all arise from similar curves.
He showed that correlations between 1, 2 and 3 second timed vital capacities were
equally good when compared with MBC. Tabulation of TVC data from these 150
patients tends to confirm Bernstein's concept. Table 2 shows that the cut off values
between emphysema and nonemphysema fall at the level of 73 per cent for 1 second,
89 per cent for 2 seconds, and 93 per cent for 3 seconds. Using these cut off points,
the 2 second TVC was slightly higher in discrimination. When the median values for
the TVC for emphysematous and nonemphysematous groups were calculated it was
found that the 2 second TVC provided values slightly farther apart and thus produced
better discrimination. The differences are slight between the 1 second, 2 second and
3 second but the results of this study again favor the 2 second with 89 per cent as
the level at or below which emphysema may be suspected.

Tabulation of the values for the single breath test show that the best cut off level
is at 2 per cent. Values above this level are also considered to be abnormal by Comroe.7

**FIGURE 4**

EFFECTIVENESS OF A COMBINATION OF 3 FUNCTION TESTS
IN DETECTING EMPHYSEMA AS JUDGED BY "IDEAL" BIOPSY.

(Elevation of MBC spirogram, 2 second TVC and SB)
The ratio of residual volume over total lung capacity (RV/TLC x 100) is thought to be abnormal if above 35 per cent although this value increases with age as was demonstrated by Gilson. Baldwin has stated that the diagnosis of emphysema should not be entertained unless the ratio of RV/TLC x 100 is 35 per cent or greater. In our study the ratio was determined in 30 patients having the most abnormal screening tests. SB values were above 35 per cent. The highest value was found in a 68-year old man who had moderate emphysema on pathologic section. It is again concluded that this ratio has poor discriminatory rating in early emphysema.

One of the striking findings in the present study is the relatively large number of smokers. The non-emphysematous patients in the total group of 150 patients was 43 per cent, which is similar to that reported by others. A high proportion of emphysema was also demonstrated in our previous communication. Bell found emphysema in a high percentage of rabbits chronically infected with human tubercle bacilli. If all patients with pulmonary tuberculosis may be assumed to be potential candidates for emphysema then it is permissible to review our young non-emphysematous group for the earliest signs of emphysema. Considering abnormalities in the three screening tests, elevation of the MBC spirogram seems to occur most often. The infrequent occurrence of prolonged TVC in the young age group and the widely scattered values in the older patients makes this a less valuable sign of early emphysema. The positive single breath test appears at a later age but an abnormal test is highly discriminatory at all ages.

An attempt to classify emphysema into stages would appear to be worthwhile in order to elucidate the progression of this disease as revealed by ventilatory function tests. The earliest sign may be the elevation of the MBC spirogram to the hyperinflation level persistent after maximum improvement is attained under treatment especially with bronchial dilators. Under conditions of maximum improvement, early emphysema may be suspected with reasonable certainty when the three screening tests mentioned above become positive. Based on these tests 39 patients had early emphysema. Moderately advanced emphysema is present when in addition to the positive ventilatory tests, the SB is 4 per cent or greater and the ratio of the residual volume/lung capacity x 100 is greater than 35 per cent in the young and 55 per cent in those over 50 years of age. At this stage the MBC is usually reduced below 70 per cent. Ten of our emphysematous patients fell into this group. Far advanced emphysema may be considered when the three screening tests are grossly abnormal, the MBC is in the range of 45 per cent or less, and the ratio of residual volume/lung capacity is over 50 per cent. In the later stages the diffusing capacity becomes reduced.

If arterial $O_2$ unsaturation occurs, pulmonary artery pressure rises above normal first after exercise and later may be permanently elevated. CO retention and respiratory acidosis complete the picture of pulmonary decompensation. Death occurs from recurrent pulmonary infection, respiratory insufficiency, cor pulmonale, or spontaneous pneumothorax.

**SUMMARY**

One hundred and fifty tuberculous patients received pulmonary ventilatory tests prior to lobectomy for removal of residual disease or cavity. Patients were selected whose removed specimen yielded an "ideal biopsy" of the lung. The presence or absence of chronic obstructive emphysema was determined on the basis of gross inspection of the cut lung. The most sensitive indication of early emphysema was a combination of positive findings on all three ventilatory tests, TVC of 90 per cent or less, elevation of the MBC spirogram to hyperinflation level and single breath $O_2$ test of 2 per cent or greater. It was possible to predict correctly whether or not generalized emphysema was present in 93 per cent of the patients examined. A follow-up study on 94 of these patients showed no significant reversibility of the three ventilatory screening tests within an average period of six months postoperative. Only six patients appeared to develop emphysema within the six months following lobectomy.

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**RESUMEN**

Se hicieron pruebas ventilatorias en 150 enfermos previamente a la realización de lobectomías para resecar enfermedad residual o cavidades. Se escogieron los enfermos cuyo espécimen rindió un reporte de una "biopsia ideal" del pulmón.

La presencia o ausencia de enfisema crónico obstructivo se determinó por la observación macroscópica del corte de pulmón. La indicación más fina de enfisema temprano fue la combinación de hallazgos positivos de las tres pruebas de ventilación: TVC (Capacidad Vital por Segundos), elevación del espirograma de la MBC (Capacidad Máxima Respiratoria-CMxR) al nivel de la hiperinflación y la prueba simple de Oxígeno de 2 por ciento o mayor.

Fue posible predecir correctamente si había o no enfisema generalizado en 93 por ciento de los enfermos examinados.

Un seguimiento de 94 de estos enfermos no mostró reversibilidad de significación de las tres pruebas ventilatorias mencionadas dentro de un término de seis meses después de la operación. Sólo seis enfermos parecieron desarrollar enfisema dentro de seis meses después de la lobectomía.
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RESUMÉ

150 malades atteints de tuberculose furent soumis aux tests ventilatoires avant lobectomie pour éxérèse d’une lésion résiduelle ou d’une cavité. Les malades choisis furent ceux pour lesquels la pièce enlevée représentait une “biopsie idéale” du poumon. La présence ou l’absence d’emphysème obstructif chronique fut déterminée sur la base d’un examen macroscopique du poumon coupé. L’indication la plus sensible de l’existence d’emphysème précoce fut une association de constatations positives portant sur les trois tests ventilatoires: test de la capacité vitale à 90% ou moins, élévation de la ventilation maximale à un niveau hyperélevé et test de la simple respiration oxygénée de 2% ou plus. Il fut possible de prévoir correctement s’il exis tait ou non un emphysème généralisé dans 95% des malades examinés. Un contrôle sur 94 de ces malades ne montra aucune réversibilité marquée des trois tests ventilatoires pendant une période moyenne de six mois après l’opération. Six malades seulement semblèrent développer un emphysème pendant les six mois qui suivirent la lobectomie.

ZUSAMMENFASSUNG


REFERENCES