EMPHYSEMA produces more widespread disturbances of lung function than any other disease. Thus, it is of particular importance to the anaesthetist.

Modern techniques of respiratory physiology have only been applied in clinical medicine during the last decade or so; but, in this short time, they have increased our knowledge of the disturbances in lung function enormously. The anaesthetist need not know details of the physiological techniques themselves or of the lung function tests used, but it is becoming increasingly obvious that an understanding of the functional changes in the lungs, and hence of the significance of function test results, is essential if anaesthetics are to be given safely to patients with emphysema. The subject is, however, so large that only a brief review is possible in this symposium.

Appreciation of the functional changes in emphysema will help the anaesthetist to recognize and assess emphysematous patients before operation, deal with complications which arise during and after anaesthesia, help him decide when it is advisable to postpone operation (and the benefit to the patient that can be expected if this is done), or to decide when anaesthesia, and operation, should be abandoned. Suggestions for the clinical assessment of lung function of patients with emphysema are given at the end of the article, together with some of the simpler tests which the anaesthetist, in hospital practice in this country, might reasonably ask for, to help with difficult cases.

DEFINITION OF EMPHYSEMA

Before describing the functional changes, we must decide "What do we mean by emphysema?" This somewhat irritating, but nevertheless pertinent, question nearly always arises in any discussion of the subject. And there is usually no real agreement as to the answer! Yet it is essential for us to be clear about what clinical entity we do refer to, so it is considered in some detail here.

The trouble seems to be that emphysema is defined from morbid anatomy and histology, in terms such as overdistension and disruption of alveoli, but owing to practical difficulties of lung biopsy, this pathological change can hardly ever be directly verified in life. From its Greek derivation, the word "emphysema" simply means "over inflation"; but the usual convention in pathology is to include in the definition only those cases in which there is some destruction of alveolar walls and their capillary blood vessels, though some pathologists have added overdistended but otherwise intact lungs, within their definition as one form of emphysema (Reid, 1958a).

Sometimes emphysema is very localized or, if generalized, of such a mild degree as to cause no detectable functional change in life and is only recognized post mortem. Such cases are naturally of little concern to the clinician or the anaesthetist; to them emphysema is really a functional diagnosis (Stuart-Harris and Hanley, 1958) in patients where a history of excessive breathlessness on exertion, without other cause, together with certain physical signs (see the clinical section of this symposium by Dornhorst (1958)), is assumed to have been caused by this pathological process. And most clinicians are of general agreement as to what they mean by emphysema though the physical signs are imprecise (Fletcher, 1952; Schilling et al., 1955) and the correlation with pathological diagnosis at subsequent autopsy not very high (Christie, 1944; Monroe, 1951; Hugh-Jones, 1958).

Although the meaning of emphysema clinically...
could, and should, be reasonably well defined, the
term is often used very loosely and added, almost
gratuitously, about any breathless patient who
has bronchitis, by the phrase "Bronchitis and
Emphysema". In this country, where bronchitis
is common, most patients with emphysema also
have bronchitis and it may well be that chronic
bronchitis gives rise to emphysema (Oswald,
1958; Stuart-Harris and Hanley, 1958). But many
patients only have excessive bronchial secretion,
with or without secondary asthma, and do not
have the features of emphysema. They tend to
be generally more fit than those with emphysema
and hence are less often seen in hospital. They
present the anaesthetist with a different and much
less serious problem. In contrast, there are a few
patients who appear to get pure emphysema with
no accompanying bronchitis and no history of
ever having had it. Such patients are probably
more common in the United States, where
chronic bronchitis seems to be less prevalent than
here (unless the diagnosis is simply less often
made). This difference between the two countries
may have added to the confusion over the term
"emphysema". But it is the vague use of the
word to cover almost any form of chronic chest
disease that is the most serious cause of con-
fusion.

In practice we are concerned with a condition
that produces changes in lung function rather
than anatomical changes that can be consistently
detected in life, except in extreme cases when the
diagnosis is usually obvious. Thus, there seems to
be much to be said for defining it in terms of
functional as well as morbid anatomical change.
Quite a good parallel is diabetes, which, with
the advance of biochemistry, has come to be
defined in terms of change in chemical function
in the body, and morbid anatomy plays a minor
role. In an early textbook of medicine (Marryat,
1758) diabetes was defined as "a preternatural
discharge of urine", with the patient feeling
thirsty; there was no comment on the mechanisms
of the lesion because biochemistry was not avail-
able and many cases were confused with urinary
disorders. Emphysema might similarly be defined,
clinically, as "a preternatural output of air from
the lungs on slight exertion, with the patient feel-
ing breathless". This clinical definition would be
misleading, and imprecise. But just as the ex-
cessive urine production in diabetes was later
understood, and the condition diagnosed precisely
from other conditions causing this symptom by
biochemical tests of blood and urine, so the cause
of the symptoms of emphysema can be under
stood from the application of biophysics and
biochemistry. When the tests, many of which are
at present too complex for routine use, are sim-
plified and further advanced, it is highly likely
that a precise diagnosis of emphysema, and its
extent, will be possible in life. In fact, it is
only in this condition that lung function test
have a real diagnostic value—apart from rare
exceptions like the diagnosis of alveolar-capillar
block (Cournand, 1952).

We shall therefore call "emphysema", in this
symposium: "a disease causing specific change
in lung function (described later) which is
associated with specific morbid anatomical find-
ings" (described by Reid (1958b) in the patholog-
section). Specific functional changes are diag-
nosed from clinical history and findings, asso-
ciated with functional tests (as in diabetes!).
Thus we exclude from consideration those
patients whose lungs are merely overdistended
(because of the pathological definition), as well a
those who have pathological findings which pro-
duce no demonstrable effect in life.

We may summarize the problem by comment-
ing that (1) it is essential for the clinician (or
anaesthetist) to be familiar with the functional
changes revealed by complex tests if they are to
interpret any purely clinical assessment with
some change of success, (2) that emphysema is
usually seen in this country with accompanying
bronchitis and secondary asthma, though it can
occur alone, and (3) that some patients with it
show more disturbance of the mechanics of ven-
tilation with attendant dyspnoea as their mos
obvious feature, while others show a greater pre-
ponderance of disturbance of gas-exchange in
their lungs, with cyanosis more obvious. It may
well be that a subdivision of patients into definite
functional types will later be possible. But in al
patients most aspects of lung function are af-
fected, and it is this which is pathognomonic
like the characteristic widespread disturbance of
the nervous system in disseminated sclerosis.
A plea is made for an attempt at precise
diagnosis of the presence and extent of em
physema, with the aid of lung function tests when available, and against the loose usage of the word to include any chronic chest condition.

DIFFERENT ASPECTS OF LUNG FUNCTION

What are the many different aspects of lung function which are changed in emphysema? Unfortunately, clinical discussion often suggests that they are not commonly known, so they will be briefly reviewed as a basis for the description of the changes in emphysema.

The primary function of the lungs of any animal is to maintain the oxygen and carbon dioxide tensions in the arterial blood between narrow normal limits, in spite of large changes in these gas tensions after the blood has been utilized in different organs and returned by way of the veins. This constancy of arterial blood-gases, at all levels of muscular activity and oxygen usage, demands close contact, over a large surface area, between the blood pumped to the lung capillaries by the heart, on the one hand, and the medium surrounding the animal on the other, if rapid gas exchange is to take place by diffusion.

In fish, the interface between blood and the surrounding water is easily maintained so long as the heart pumps the blood through the gills. But in land-living animals the problem is much more complex. The lungs themselves have to take on a secondary function as an air pump, activated by movements of the chest wall, in order to bring fresh air into contact with the blood in the lung capillaries.

Thus there are really three main divisions of lung function:

1. Those of the air pump (ventilation).
2. Those of an air-blood interface (gas distribution and exchange).
3. Those of being part of the blood pump (pulmonary circulation).

These three divisions are closely interlinked. It is, however, important for clear thought, and for practical testing, to deal with them separately. Thus, there is no satisfactory single "test of lung function" any more than there is a single test of liver or kidney function, which will deal with every case.

It so happens that patients notice, and therefore complain of, inadequacy of ventilatory function more than the others, because of the sensation of dyspnoea it produces. It is also the simplest function to measure. Hence tests for it are the only ones that have been at all widely used in clinical medicine. Defects of distribution of lung gases or circulation are rarely painful, though they may contribute to dyspnoea. Moreover, defects in these aspects of lung function may be advanced before their clinical feature, cyanosis, is detectable. Tests for these aspects are more complex and therefore less familiar than those for ventilation; nevertheless, they are of great importance in anaesthetics and are markedly abnormal in severe emphysema.

In the past, human respiratory physiology has often stopped short of descriptions of changes in lung volumes, and many medical students still learn "lung function" from preclinical studies only in terms of vital capacity (V.C.), complementary and supplementary air! Even most of the names are archaic (Pappenheimer, 1950). Although measurement of the total volume of the lungs (and its subdivisions) is often useful, it is really an anatomical measurement of size. Its main functional importance is when a reduced V.C. means a diminished stroke volume for the air pump, or there is a greater residue of air left at the end of the stroke.

The important concepts of ventilation are first, the ventilation (or "air output" and intake) required for a given amount of activity or oxygen usage. This is comparable to thought in terms of cardiac output or urinary output in other branches of medicine. The second concept is the maximum that the "air pump" can deliver, or maximum breathing capacity (M.B.C.) (which is the greatest amount of air that can be breathed per minute) as an indication of the ventilatory reserve available for exertion.

The last concept of ventilation is in terms of the mechanics of breathing which is concerned with the force needed to expand the lungs and to drive air in and out. Excessive force, giving rise to an increased work of breathing, is probably important in producing the sensation of dyspnoea (Marshall et al., 1954; Davis et al., 1956). There are two main components of the force required; the first is the change in intrathoracic pressure to produce a given change in the volume of the lungs (measured when air flow has ceased). This measures how stiff the lungs are,
though the results are usually expressed as the reciprocal of stiffness, that is, the compliance, or how “easy” it is to increase their volume (volume change per unit pressure change). The second is the extra force required during movement to overcome the friction of air flow in the bronchial tree (and partially from movement of intrathoracic viscera). This is the nonelastic resistance (pressure per litre/sec of air-flow). At the beginning of inspiration, before air flow begins, the intrathoracic pressure drop is zero; it reaches a peak at the maximum rate of movement of the lungs, and then decreases to zero at full inspiration when movement stops. This extra intrathoracic pressure drop required during lung movement for nonelastic work thus depends both on the rate of breathing and the resistance offered to movement, mainly as “airways resistance”.

Coming to the second main division of lung function, one realizes that not only must the total ventilation in the lungs be adequate for a given level of activity, but the air must be distributed evenly to the myriad of alveoli in the lung through which the blood is flowing, if the primary purpose of the lung in maintaining the normal gas tensions of arterial blood is to be fulfilled. Thus we are concerned with any inequality of gas distribution. Since the pioneer work of Rahn (1949), Riley and Cournand (1949) and other “clinical respiratory physiologists”, mostly in the United States, it has been realized that the significance of maldistribution of gas depends on the relative distribution of blood. To take an extreme case of all the ventilation going to one lung and none to the other; the patient is not seriously incapacitated if the unventilated lung has no blood flow, he simply has a “pneumonectomy”; but if normal blood flow continues in the unventilated lung, he has serious disturbance of the gas tensions in his arterial blood and, at the other extreme, if the air flow goes to one lung and the blood flow to the other, he would be dead! Such lack of balance between air and blood flow may occur in individual alveoli. Ventilation of unperfused alveoli means wasted ventilation or increased “physiological deadspace”; perfusion of under- or unventilated alveoli means some “venous admixture” or total “shunt”. Thus it is different ventilation-perfusion ratios throughout the lung which really matter, rather than maldistribution of gas. Provided overall ventilation is adequate and there is no barrier to the diffusion of gas in the form of a thickened alveolar membrane, then the summation of different ventilation-perfusion ratios throughout the lung alone determines the gas tensions in arterial blood when mixed venous blood of a given composition has traversed the lung.

Finally, in this second main division of lung function, there is the problem of any interference with gas diffusion, because of change in the structures which lie between the alveolar gas and the blood; namely, alveolar membrane, capillary wall, plasma, and red-cell membrane. Any interference with diffusion is measured by the diffusing capacity of the lung. Since gas flow to or from the blood into alveoli by diffusion simply depends on whether the gas is at a higher pressure in blood or alveoli respectively, and since the rate of flow depends on the magnitude of the pressure difference between the two, the diffusing capacity for any gas, is that quantity which passes per minute from alveoli into blood for each mm Hg pressure difference across the interface. But this quantity, for the whole lung, will depend not only on the resistance to diffusion at the interface, but also on the size of the interface which represents the surface area of the lung available for diffusion; this is a function both of the size of the lung itself, and of any lack of balance between ventilation and perfusion which may effectively reduce the interface. Thus, the overall diffusing capacity of the lung which is measured in practice, is a rather mixed, though useful measure of “the gas exchange capacity of the lung”.

The third main division of lung function, that of the lung circulation, entails concepts of cardiac output and pulmonary artery pressure. These concepts have already become, in “cardiology”, an accepted part of clinical medicine, unlike those of the other two divisions.

Table I summarizes this discussion of lung function, by showing the seven aspects which can, and should be tested, in the full functional assessment of a patient with respiratory disease. For reference, the methods used are indicated in parenthesis in the table. They, like their theoretical basis, are almost all fully described in the excellent book on the clinical physiology of the
TABLE I
Some Aspects of Lung-Function which can be tested in a full Investigation of a Patient with Emphysema or other Respiratory Disease.

(A) THE LUNG AIR-PUMP FOR VENTILATION
(1) Total Lung Capacity and Subdivisions.
(By closed circuit spirometry, with helium dilution technique; or by open circuit nitrogen wash out; or whole-body plethysmograph.)
(2) Ventilation at Rest and Standard Exercise (or known Oxygen Consumption).
(Using low-resistance gas-meter, or "anemometer", to measure ventilation and standard step-test, bicycle ergometer or tread-mill.)
(3) Maximum Breathing Capacity.
(4) Mechanics of Breathing:
(a) Compliance.
(b) Nonelastic Resistance.
(By relating intra-oesophageal pressure, as a measure of intrapleural pressure, to change in lung volume and air flow; or whole body plethysmograph; or air flow interruptor.)

(B) THE LUNG FOR GAS DISTRIBUTION AND EXCHANGE
(5) Inequality of Gas Distribution.
(From analysis of a single expiration using rapid analyzer for inert gas, e.g. nitrogen meter or mass spectrometer; or from multiple breath washing-out of lungs.)
(6) Ventilation-Perfusion Relationship.
(From analysis of arterial blood gas tensions, using the bubble syringe technique; or from alveolar gas tensions using a mass spectrometer.)
(7) Diffusing Capacity at Rest and Maximum diffusing Capacity on Exercise.
(For carbon monoxide either by a single-breath or multiple-breath "steady-state" method; or for oxygen using low oxygen breathing and analysis of arterial blood gas tensions.)

lungs by Comroe et al. (1955), to which the reader is referred for details. The list in table I is not exhaustive, other tests (such as bronchospirometry), and other methods than those listed, are used for special purposes; but it will serve as a framework for the description of the changes in emphysema. Those of pulmonary circulation itself are omitted; not because they are any the less important, but because they usually come within the sphere of cardiology.

The reader is referred to the previous postgraduate educational number this journal (Campbell, 1957) for definitions of any of the standard terminology and symbols which will be used.

CHANGES IN EMPHYSEMA

Total Lung Capacity and Subdivisions.
Observations. In most subjects with emphysema, but not all, the total lung capacity is increased compared with a normal man of the same age. A more constant feature is an increase in both the resting volume of the lungs or functional residual capacity (F.R.C.) and the volume of air that remains in the lungs at the end of a forced expiration (residual volume) (see fig. 1). The residual volume is not only increased absolutely, but it forms a greater percentage of the total lung capacity, compared with normal.

FIG. 1
Histogram showing the average values for the total lung capacity, and its subdivisions, in a group of five subjects with advanced emphysema (average age 54 years) contrasted with a comparable group of ten normal subjects (average age 54 years). Coefficient of variation approximately 20 per cent for all readings in both groups. (From Gilson and Hugh-Jones, 1953.)
In this country the closed-circuit method using helium as the indicator gas, is usually used to measure the total lung capacity. Its results agree fairly well (Gilson and Hugh-Jones, 1949) with the open-circuit method often used in the United States. During its use a tracing of resting ventilation (spirogram) is usually recorded together with the V.C. Such tracings are fairly characteristic in severe cases of emphysema (fig. 2). Not only is the V.C. reduced but the time taken to record it is much prolonged, thus, the tracing has a curved appearance, especially at the end of the expiration, when a long time is taken to expel the last small volume of air. Further, the original relaxation level (resting respiratory level) is not reached again until after a number of breaths, especially after measurement of the inspiratory capacity ("trapping", see later).

Clinical and pathological significance. In normal breathing with the subject at rest, inspiration is the only muscular action. Expiration is passive and occurs by use of the elastic energy that was stored in the lung when it was stretched in inspiration. Expiration continues until the elastic recoil of the lungs, tending to pull inwards, balances the tendency of the thoracic cage to spring outwards. (If a hole is made in the chest wall these forces no longer balance; the chest wall springs out and the lungs continue to retract, resulting in a pneumothorax.) Thus the lowest points on a spirometer tracing of normal breathing lie along a line, since the lungs return to the same resting respiratory level (R.R.L.) determined by this balance at each breath, and the F.R.C. remains constant. The upper points on the tracing depend on the muscular contraction applied for a given breath and are less regular (fig. 2) Tidal ventilation is increased on exercise mostly by increasing the depth of active inspiration, though there is some active muscular expiration so that the R.R.L. may change. The V.C. is some indication of the maximum available stroke volume of the lungs as an air pump.

In emphysema, much of the elastic recoil of the lungs is lost; this raises the R.R.L. and increases the amount of air in the lungs at the end of expiration (F.R.C.). When the thorax is opened the lungs will not collapse as far and the patient's chest is held in inspiration and may become "barrel-shaped". However, many patients with gross emphysema have thin chests, and the increased F.R.C. cannot easily be appreciated without measurement.

The V.C. is reduced, but even then it gives a falsely large impression of the maximum effective stroke volume, because of the length of time required to expel the full capacity. This and the trapping of air (discussed more fully later), which is seen on the spirogram, are why the V.C. is an unsatisfactory estimate of the ventilatory reserve in emphysema.

Although these changes in lung-volume measurements are characteristic of emphysema they are not, of themselves, diagnostic. A patient with spasmodic asthma, who has no emphysema at all, will give practically the same results on spirometry. Some differentiation between the two conditions will be seen by repeated tests after antispasmodic treatment, and emphysematous patients will also show changes in other aspects of lung function as well, which are not characteristic of asthma. Taking a raised value for the residual volume, expressed as a percentage of the total lung capacity, as being synonymous with emphysema (Motley and Lang, 1948) is erroneous. This percentage is raised in emphysema, but it bears no relation to the severity of the condition and correlates badly with general lung function (Baldwin et al., 1949). Further, it is raised, not only in asthma, but in many fibrotic conditions of the chest (which are functionally...
entirely different), not because of an increase in absolute residual volume but because of a reduction in inspiratory capacity and total lung capacity (Gilson and Hugh-Jones, 1955).

Ventilation Required for a Given Oxygen Uptake.

Observations. The group of five patients with advanced emphysema, shown in figure 1, had an average resting ventilation of 9.5 l./min. The corresponding group of normal subjects had an average resting ventilation of 8.4 l./min. When each group exercised at the same rate of work (350 kg.m/min) for 5 minutes they required a ventilation of 30.8 and 27.6 l./min respectively—the exercise ventilation quoted being "standardized" (Hugh-Jones and Lambert, 1952) to minimize the effects from some of the subjects being unable or unwilling to complete the full 5 minutes of exercise. These figures, in spite of the inaccuracy and difficulty in making such measurements (see later), fit in with the experience of most workers that even at an advanced stage of emphysema the patient's resting ventilation is only slightly increased above normal in spite of dyspnoea or breathing distress. Only at the most advanced stage, with marked cyanosis on exercise, is the exercise ventilation much increased.

Comments. It must be appreciated that the significance of any measurements of ventilation, particularly at rest, is always doubtful because the use of mouthpieces, valve-boxes or spirometers, may promptly cause psychological hyperventilation. However, the comparison of measurements made under the same conditions, between corresponding groups of emphysematous and normal subjects is probably valid even though the absolute values are less reliable.

Normally, the lung alveoli are ventilated with fresh air in sufficient quantity to dilute the carbon dioxide produced so that its partial pressure is 40 mm Hg (within narrow limits).

This fundamental relation is expressed by the equation:

$$P_{CO_2} = \frac{0.863 \times V_{O_2} \times R}{V_A}$$

where the constant 0.863 is simply the correction factor for temperature, pressure, and water vapour, and the product $V_{O_2} \times R$ (oxygen consumption × respiratory quotient or R.Q.), is the carbon dioxide produced per minute which, for a given R.Q., depends on the patient's activity as reflected by his oxygen consumption. Thus the alveolar carbon dioxide tension ($P_{CO_2}$) varies directly as the oxygen consumption but inversely with alveolar ventilation. If alveolar ventilation is increased, as in voluntary overbreathing, without an increase in metabolism, the arterial $P_{CO_2}$ falls. Increase in ventilation accompanied in this manner is defined as hyperventilation. Conversely, reduced alveolar ventilation without a decrease in metabolism, as in obstruction to breathing, causes hypercapnia and hypoventilation.

There is no pressure gradient between alveolar and end-capillary carbon dioxide in any alveolus; the respiratory centre is very sensitive to changes in arterial carbon dioxide tension ($P_{A CO_2}$) and readily adjusts the ventilation accordingly. The critical amount of this ventilation is the fresh air entering the alveoli and not that entering the nose or mouth. About a quarter or a third of the latter goes no further than the upper respiratory passages where no gas exchange takes place ("anatomical deadspace"). In emphysema this deadspace effect is increased, and an abnormally large proportion of inspired gas takes no part in alveolar gas exchange, because of ventilation of unperfused alveoli.

Thus, when a patient with severe emphysema has a total ventilation at rest but little raised compared with a normal subject, it is often found that this alveolar ventilation is inadequate and is raised above normal. If the $P_{A CO_2}$ is, say, 60 mm Hg, his alveolar ventilation is only two-thirds of that required to maintain the normal 40 mmHg. In other words a "normal" figure for ventilation may mean hypoventilation in an emphysematous subject whose physiological deadspace is raised. This is most important for the anaesthetist and physician to remember, especially when using artificial mechanical ventilation.

Some emphysematous patients do increase their ventilation for a given state of activity enough to overcome the increase in deadspace caused by the lack of balance between ventilation and perfusion of their lungs. They ventilate excessively, compared with normal subjects, and tend to complain of dyspnoea. Others, as it were, give up the struggle of dyspnoea and "settle" for inadequate ventilation and a raised $P_{A CO_2}$ even at
rest. This would suggest that their respiratory centre becomes rather insensitive to carbon dioxide (Donald and Christie, 1949; Prime and Westlake, 1954). However, recent studies (Cherniack and Snidal, 1956) show that introduction of some obstruction in the airways of a normal subject decreases his response to carbon dioxide; vice versa, relief of respiratory obstruction increases the response to carbon dioxide in emphysema. A major factor in the failure to increase the resting ventilation adequately, with the enlarged physiological deadspace in emphysema, is probably the altered mechanics of the chest. Increased ventilation would necessitate excessive work of breathing and there are stretch receptors for the lungs which provide signals related to the work of breathing (Davis et al., 1956). It seems that the “discomfort” from excessive stimulation of stretch receptors may be greater than that from excessive stimulation from carbon dioxide! However, the role of the stimulus to the respiratory centre by carbon dioxide and anoxia is important, and its significance relative to mechanical factors (Fishman et al., 1955) is still under review (see Nunn (1958), under Carbon Dioxide Narcosis).

There appears to be less ventilation on exercise in those emphysematous patients who have a raised alveolar and arterial carbon dioxide at rest than in those where it is normal (Donald, 1953). Usually, the increase in exercise ventilation in emphysema is small compared with the enormous increase which occurs in patients with various types of pulmonary infiltration which produce a reduced diffusing capacity for oxygen. For example, on the standard exercise test cited previously, two patients with xanthomatosis of the lungs had standardized ventilation of 69 and 76 l./min respectively, compared with the normal of about 27 l./min and more than twice that of subjects with advanced emphysema. Exercise ventilation is really excessive only in severe emphysema, with marked exercise cyanosis, and then it causes great distress because of the small maximum ventilation that the subject with emphysema can produce (see later).

In summary, hypoventilation occurs in many emphysematous subjects, even at rest, largely because of mechanical obstruction to breathing. This hypoventilation is often present when the total ventilation from the nose or mouth is normal or even increased, for a given metabolism. This is because there is extra “alveolar deadspace” (total physiological deadspace minus relatively constant anatomical deadspace of upper airways) caused by the presence of alveoli which are ventilated but not perfused with blood.

**Maximum Breathing Capacity.**

Observations. When the group of our five subjects with advanced emphysema were asked to breathe in and out both as deeply and as fast as possible for 15 seconds, the depth and rate being recorded in such a way as to ensure the optimum combination to produce the maximum ventilation (direct method of recording the M.B.C. by maximum voluntary ventilation test), their average “best” was 25 l./min compared with an average of 120 l./min for the normal group of men of the same age.

The results of this test are not, as might be expected, largely a function of the patient’s incentive to do the test. With a competent observer, the results are reasonably repeatable, and any defect in repeatability (compared with a V.C. test) are repaid in the big differences there are to measure between normal and diseased subjects. It is like using a coarse ruler to measure a long distance, rather than a fine one for a short distance.

But the performance of maximum voluntary ventilation is an uncomfortable and possibly dangerous procedure, especially in ill patients. One breath is very like another and the relation of inspiratory pattern to expiratory pattern is sufficiently fixed (Bernstein and Kazantzis, 1954) for it to be found that the M.B.C. can be predicted with remarkable accuracy from the volume of gas exhaled in a given time during a single forced expiration; the correlation between the two being of the order of r=0.9 (Tiffeneau et al., 1949; Kennedy, 1953; Kadlec and Vyskocil, 1950). The measurement of this volume is a very simple procedure for the subject; it merely entails taking in as deep a breath as possible and exhaling it as forcibly and rapidly as possible into a suitable spirometer. The volume exhaled in a given time, usually 1 second from the start of the expiration, is then recorded either from a spirometer tracing or by an automatic timing device
The functional pathology of emphysema (Gaensler, 1951). This volume is known as the forced expiratory volume in 1 second, or F.E.V.₁₀, in the terminology agreed in this country (Gandevia and Hugh-Jones, 1958). The F.E.V. in litres, when multiplied by a suitable factor (which is 35 for the F.E.V.₁₀) gives an indirect measure of the M.B.C. in litres/minute. This multiplication of the test results by a constant factor is, of course, unnecessary, and the F.E.V. itself is as good a measure of the patient's maximum ventilation as this indirect M.B.C.; the only justification for it is that the normal values for the M.B.C. are more familiar to most clinicians.

Measurement of the F.E.V. has been described in detail because it is a test simple enough for routine use by anaesthetists, for helping them to assess a patient before operation. A typical tracing from a patient with emphysema (fig. 3) contrasted with that from a corresponding normal subject, shows that although the vital capacity is fairly reduced the F.E.V.₁₀ is reduced by a disproportionately great amount, and forms only 30 per cent of this reduced vital capacity, compared with a normal value of about 80 per cent when there is no obstruction to air flow. Thus a low F.E.V.₁₀ as percentage of the V.C. means air-flow obstruction. In diseases where there is restricted chest movement, but no air-flow obstruction, as in ankylosing spondylitis, the F.E.V.₁₀ is reduced, and hence the M.B.C. is reduced, proportionately to the reduction in V.C., and the shape of the expiratory flow curve is normal.

Thus in emphysema, there may be gross reduction in the M.B.C.

Clinical significance and comments. Even in normal subjects a sensation of distress in breathing comes on with increasing ventilation on exercise; it becomes acute in most subjects, as the ventilation exceeds about 60 per cent of their M.B.C., though there is a wide threshold of distress. Emphysematous patients, then, have a lowered ventilatory reserve for exercise, because of their reduced M.B.C. When this drops to levels below about 20 l./min, they can do no more than walk very slowly on the level, and even this produces severe dyspnoea.

This low M.B.C. results from having a small stroke volume of their "air pump" as well as obstruction to air flow, particularly on expiration. Most patients who have emphysema have some bronchitis, and asthma as well; in them some of this air-flow obstruction is asthmatic "bronchospasm", and this can be relieved by antispasmodics. The F.E.V.₁₀ will then increase if it is remeasured after 5 minutes inhalation of an aerosol containing isoprenaline or adrenaline and atropine compound (B.P.C.). But much of the air-flow obstruction in emphysema appears to be caused by the loss of elastic recoil in the lungs and bronchial walls; it is therefore permanent (see later, under Mechanics of Breathing). In patients with pure emphysema without secondary asthma, there will be no change in the F.E.V. after aerosol or other antispasmodic treatment.

It is important to note that the forced vital capacity tracings of a patient with spasmodic asthma, and no emphysema, will, during an attack, be identical with those of a patient with emphysema. If after continued antispasmodic treatment.
treatment, the F.E.V. as a percentage of the V.C. rises to normal levels (greater than about 75 per cent), the patient has no emphysema, but other tests than the F.E.V. are needed to distinguish emphysema from asthma, which is resistant to treatment, when the F.E.V. percentage remains low. Even in spasmodic asthma the F.E.V. percentage may not initially increase during successful treatment, in spite of marked improvement in the absolute F.E.V., because the V.C. increases concurrently and the percentage remains the same (Thompson and Hugh-Jones, 1958).

In patients with asthma the inspiratory flow is reduced as well as the expiratory flow so that the difference between the forced inspiratory volume, in a given time, and the F.E.V. will be less than in patients with pure emphysema, in whom there is relatively little inspiratory air-flow resistance compared with that in expiration (Campbell, 1958a). A very low F.E.V. percentage means either untreated asthma or emphysema; an F.E.V. percentage persisting very low despite energetic treatment of asthma is highly suggestive of emphysema. Measurement of the F.E.V. is of great use to the anaesthetist in the assessment of ventilatory capacity in emphysematous patients before operation and in the detection of asthma.

Mechanics of Breathing.

Observations. When changes in intrapleural pressure (which, in practice, are usually measured as changes in oesophageal pressure) are plotted against change in volume of the lungs during quiet breathing the type of curves obtained for normal and emphysematous subjects are shown in figure 4. At the instants of air-flow reversal, at full inspiration (Y) and expiration (X), the airflow is zero, so the slope of the line X–Y represents the compliance of the lungs or the static volume change per unit change in intrapleural pressure. If measured during slow breathing there is often little change in this in emphysema, though there is a tendency for the lungs to be more compliant, that is the line X–Y is steeper than normal. In other words, the lungs tend to increase in volume more than they normally would for a given pressure change and, conversely, for a given volume of distension they exert less recoil pressure (Mead et al., 1955; Campbell, 1958a).

In practice, with the rapid breathing which is
often present in emphysema, some parts of the lungs fail to fill in the time available. The points of air flow reversal, X and Y, are not those of zero flow and the line X–Y does not represent the true static compliance line for the whole lung. In these circumstances the lungs appear to get stiffer, the faster the breathing rate at which "compliance" is measured (Cherniack, 1957) as the volume change which has taken place by the time of flow-reversal, for a given pressure change, is less than it would be had a long time been available. The "compliance" measured in such circumstances is called "dynamic", rather than the true "static" compliance.

Work is represented as areas on the pressure-volume diagram, and the extra force (above that required to hold the lungs at a given volume) which is needed to move the air into the lung is shown by the hatched area on the side of the line X–Y. It increases as flow rate increases, so that the loop gets wider as breathing becomes faster. From these curves, pulmonary flow resistance can be expressed as the pressure necessary to produce a given rate of flow. During quiet breathing Mead et al. (1955) found the resistance in emphysematous patients to be especially increased in expiration, with the well-known prolongation of the expiratory phase of breathing. In their example (fig. 5), the patient accomplished a flow of 0.2 l/sec, early in expiration, at a cost of little more than 2 cm of water, but later it was vastly increased compared with normal. On hard breathing this patient had tremendous airways resistance: "while applying a pressure difference of more than 80 cm of water to his lungs and airway, the rate of flow was only 0.5 litres or of the order of magnitude encountered during normal resting expiration where the resistance pressure would be less than 1 cm of water in normal individuals".

Comments and clinical significance. The increased compliance reflects the loss of elastic recoil. But it is the enormous expiratory resistance which is the main problem and this is bound up with the loss of recoil. Expiration is normally passive and the recoil pressure of the lungs, as it drives the air up the airways, maintains the pressure in them above that of the surrounding intrapleural space (Campbell, 1958a). This recoil is largely lost in emphysema. Any increase in intrapleural pressure from the use of expiratory muscles in an attempt to accelerate the air flow, simply narrows the airways and tends to produce "trapping" (Attinger et al., 1956). It is this which results in the enormous expiratory flow resistances seen on forced expiration. Campbell et al. (1957) have measured the maximum intrathoracic pressure which produces the maximum flow and found it greatly reduced in emphysema compared with normal subjects.

Thus, the flow resistance in emphysema is not bronchospasm. It is a different mechanism from that in asthma where the resistance is raised in inspiration as well. Trapping does occur in normal subjects but only at the end of a forced expiration, which it limits. In emphysema it tends to occur at the very start of expiration, when the chest is still high in the inspiratory position, if the slightest effort is made by the subject to increase his rate of airflow by the use of expiratory muscles.

The work of breathing may become so great in severely emphysematous subjects that the oxygen consumption of the respiratory muscles may be a high proportion of the total (Campbell et al., 1957), and any increase in ventilation or exercise would mean an oxygen cost of breathing greater than the extra oxygen intake. If such patients perform hardly any exertion their breathing distress is appalling.

Perhaps it is not surprising, considering the
mechanics of their lungs, that emphysematous subjects often do not maintain the alveolar ventilation required to avoid carbon-dioxide retention, especially with their increased physiological dead-space. To make matters worse, some elderly subjects with emphysema may have increased stiffness of their chest walls which we have not considered, since the intra-oesophageal balloon only enables us to measure lung compliance. The inspiratory muscles then contract against a relatively rigid wall and produce a small change in intrapleural pressure. Finally, the static lung compliance, after being increased, may eventually become reduced in emphysema, when cor pulmonale sets in; and the lungs become turgid with fluid (Cherniack, 1956).

All these mechanical factors are of importance, not only in understanding the functional lesions of emphysema, but to the anaesthetist in practice. For example, in artificial mechanical ventilation of an emphysematous patient with extreme hypoventilation and carbon dioxide retention, the ventilation may have to be very slow, and as deep as practicable to achieve the required alveolar ventilation, and the negative pressure phase used with care if trapping and dangerous resistance to air flow is to be avoided.

Lastly, the inequality of gas distribution in emphysematous lungs, which is described below, is probably largely dependent on their mechanical properties (Otis et al., 1956); and ventilation at different rates will alter this gas distribution by a mechanism illustrated in figure 6. Pask (1958) has recently produced a model to demonstrate this point.

**Inequality of Gas Distribution.**

*Observations.* It has long been known that it takes a much longer time to “wash out” all the nitrogen from the lungs, by breathing pure oxygen, in patients with emphysema than it does in normal subjects. Thus after breathing oxygen for 7 minutes, a patient with emphysema may have about 7 per cent of nitrogen in his expired gas instead of about 2 per cent as in normal subjects. This is partly because of the large functional residual capacity of emphysematous patients; but by following the pattern of washing out of the nitrogen it can be shown that uneven distribution of gas to the different regions of the lung contributes to this slow process of gas replacement in emphysema (figure 7). Were the inspired oxygen evenly distributed the breath-by-breath changes of expired alveolar nitrogen concentration would be on a straight line when they were plotted on a logarithmic scale against the number of breaths, on a linear scale. The slope of this line is dependent on the tidal volume and F.R.C. In normal subjects the points nearly do lie on such a line; in emphysema they are markedly curvilinear, the lung behaving as if the nitrogen is replaced in some parts of the lung more rapidly than in others (Fowler, 1949; Gibson and Hugh-Jones, 1955). A similar principle can be used with a closed-circuit spirometer to give an index of “mixing efficiency” (Bates and Christie, 1950).

An alternative and simpler procedure, when a rapid-recording automatic nitrogen analyzer is available, is to observe the change of concentration of alveolar nitrogen per unit volume exhaled following a single inspiration of oxygen (Comroe and Fowler, 1951). At the end of a normal expiration the subject simply inhales one deep breath of oxygen. He then exhales and the gas is continuously analyzed for nitrogen content. The nitrogen-free gas comes from the anatomic deadspace; then a plateau of alveolar gas is se
A is a record of the process of "washing-out" the nitrogen in the lungs by breathing oxygen. The concentration of nitrogen in the expired gas leaving the lips (measured with a mass-spectrometer) is followed, after the start of breathing oxygen at the point marked by the arrow. B is the results from A, in an emphysematous compared with a normal subject, with the expired alveolar nitrogen concentration plotted logarithmically against the number of breaths. The straight line (P) would be followed in perfectly even gas distribution, with the particular tidal volume and F.R.C. of the subject. (From Fowler and Hugh-Jones, 1957.)

on the tracing. Well-ventilated alveoli, in which the nitrogen has been well diluted with oxygen, empty early in expiration, and poorly ventilated ones, whose nitrogen concentration will be higher, empty late. In normal subjects there is little change in nitrogen concentration between the beginning and end of the alveolar plateau. But in emphysema there is a steep rise in alveolar nitrogen, thus revealing the uneven ventilation in emphysema from the different dilution of nitrogen by the oxygen in different groups of alveoli.

The principle of this test should be clear from curve 3 of figure 8, which is the same test "in reverse". The patient inhales a single breath of air containing argon (which is inert) and the subsequent long exhalation is continuously analyzed for its argon content by using a recording mass-spectrometer.

Comments. Marked inequality of gas distribution may be seen in emphysema and it is helpful diagnostically. Its functional significance depends on the relative distribution of the blood (see later). It should be noted that the single-breath method detects the regional inequality of ventilation only in so far as groups of alveoli with different ventilation empty consecutively. If all emptied simultaneously, throughout expiration, the alveolar plateau would be flat, whatever the regional variations in gas dilution. In practice, the emptying is asynchronous, the well-ventilated alveoli emptying before the poorly ventilated ones, and the increase in nitrogen concentration
During the alveolar plateau, the barometric pressure (Pb) is less than 47 mm of water vapor.

Ventilation-Perfusion Relationship.

Observations. In normal subjects, air appears to be almost equally distributed to all the different alveoli, so that the ventilation of each is practically the same. We have shown that, in disease, the ventilation is uneven, then the significance of under-ventilation of some areas of the lung is negligible if the blood flow through those areas is reduced by exactly the same amount, compared with under-ventilation when the blood flow is normal or increased. In the former case the arterial gas tensions will be normal and the lung, in effect, will simply have lost some of its enormous surface area (and it has a large reserve for diffusion of oxygen in exercise), whereas in the latter case, the arterial blood gas tensions will be distributed; the body is thus much more affected by the blood and gas distribution being "out of step" in the lungs than by inequality of either, if the proportionate distribution of the two is the same. Just as the ventilation-perfusion ratio determines the gas tensions in the blood leaving an alveolus so it determines those in the gas expired. Any lack of balance can therefore be observed either from blood analysis or alveolar gas analysis.

The first approach to measurement of ventilation-perfusion inequality was largely through blood gas analysis (Riley and Cournand, 1949).

The principle is that alveoli with balanced air and blood flow were considered "ideal", and they had defined alveolar gas tensions and contributed arterialized blood to the pulmonary vein with normal tensions. If an alveolus has its ventilation-perfusion ratio reduced it takes up less oxygen than would be required to bring it to the "ideal" value. Its contribution to the arterial blood per unit time can be regarded as equivalent to X ml of "ideal" blood and Y ml of "shunted" mixed venous blood ("venous admixture" effect).

Now the gas-exchange ratio (R.Q.) relates the quantities of carbon dioxide excreted and oxygen absorbed in the alveolus, and the quantity of each is determined by the difference in amount between that in the inspired and that in the alveolar gas:

\[
\text{R.Q.} = \frac{\text{CO}_2 \text{ excreted}}{\text{O}_2 \text{ absorbed}} = \frac{\text{F}_x \text{CO}_2 - \text{F}_i \text{CO}_2}{\text{F}_x \text{O}_2 - \text{F}_i \text{O}_2}
\]

The fractional concentrations in this equation can be converted to tensions (by multiplying each F by the barometric pressure (Pa) less 47 mm of water vapor pressure at body temperature), the \( P_{\text{CO}_2} \) in inspired gas is negligible, thus:

\[
\text{R} = \frac{P_{\text{A CO}_2}}{P_{i \text{O}_2} - P_{i \text{CO}_2}}, \quad \text{so} \quad P_{\text{A O}_2} = P_{i \text{O}_2} - \frac{P_{\text{A CO}_2}}{R}
\]

Carbon dioxide, unlike oxygen, has an extremely high rate of diffusion, and there is virtually always equilibrium between alveolar and arterial carbon dioxide tensions. Riley and Cournand showed that if the arterial \( P_{\text{CO}_2} \) is used for \( P_{\text{CO}_2} \), in this equation, then the "alveolar oxygen tension" calculated, knowing \( P_{i \text{O}_2} \) and the R.Q., was, even in abnormal subjects, very close to what the "ideal" alveolar oxygen tension would be if the subject had perfect balance of blood and gas flow. If the actual arterial oxygen tension is measured, then (1) the alveolar-arterial oxygen tension difference can be expressed and (2) the "venous admixture effect", in terms of what percentage of the cardiac output appears to be shunted through the lungs, can be calculated.

In a similar manner, relative over-ventilation of alveoli will reduce the proportion of carbon dioxide added to the expired gas. By relating the expired carbon dioxide to the arterial \( P_{\text{CO}_2} \) it is possible to extend the concept of physiological deadspace to give a measure of the amount of relative over-ventilation of some alveoli as if they were in the lung areas of alveolar ventilation, with absolute lack of perfusion, with the remainder of the lung having the "ideal" balance. This "dead-space effect" includes the anatomical deadspace together with the increased alveolar deadspace. It is usually expressed as a percentage of the tidal volume or total ventilation:

\[
\text{Dead-space effect (\%)} = \frac{P_{i \text{CO}_2} - P_{\text{A CO}_2}}{P_{i \text{CO}_2}} \times 100
\]

In emphysema, the alveolar-arterial oxygen tension difference may be 50 mm Hg, whereas in normal subjects it is less than 10 mm breathing air at normal atmospheric pressures. The venous admixture effect (perfusion of underperfused alveoli) may be over 30 per cent of the cardiac output; in normal persons it is never more than 5 per cent. The deadspace effect (including ventilation of underperfused alveoli) may become as high as 60 per cent of the tidal volume, compared with the normal 30 per cent caused by the conducting passage. It is this increase of "alveolar deadspace" in the disease that leads to most of the increased ventilation for a given oxygen uptake.

The alternative method of revealing regional lack of balance between alveolar blood and gas flow, entails rapid continuous analysis of expired gas so as to determine the actual gas tensions coming from different groups of alveoli. With a suitable mass spectrometer this can be done and a measure of the degree of regional ventilation-perfusion inequality in normal or diseased sub-
Continuous rapid alveolar gas analysis using a suitable mass-spectrometer. The record, copied from the direct-writing recorder, shows concurrent analysis for three gases and includes a single long expiration (starting at E) after an inspiration (at I) of air blended with argon. From the argon trace any uneven gas distribution can be demonstrated; from the CO₂ and O₂, the change in alveolar RQ is obtained, from which the variation in ventilation-perfusion relationship can be calculated. (C) represents clearance of apparatus deadspace by the inspired argon-air blend; (D) gas from upper respiratory deadspace; (A) Alveolar plateau for argon. (For details see West et al., 1957.)
jects becomes a rapid lung-function test, simple enough for clinical use because it only entails a single expiration from the subject (West et al., 1957).

The principle is similar to that for measuring regional inequality of ventilation by a single breath test, described previously, except that the expiration is analyzed for the change in oxygen and carbon dioxide tension in relation to the volume of gas exhaled (fig. 8). This enables the respiratory quotient from different groups of well-ventilated alveoli, which empty early in expiration, to be compared with that from groups emptying late. The minimum inequality of ventilation-perfusion ratios in different parts of the lung, which are needed to account for the observed change in respiratory quotient, is then calculated. In emphysema there may be over 40 per cent change in ventilation-perfusion ratio observed by this method, compared with an upper limit of about 10 per cent in normal subjects.

**Comments and Clinical Significance.** Lack of balance of ventilation and perfusion, together with hypoventilation are the major factors which produce the gross abnormalities of arterial blood gas tensions ("lung failure") which are seen in severe emphysema and probably determine the onset of the subsequent heart failure. The relation between these two factors is complex, and the reader is referred to the discussion in Comroe et al. (1955), Chapter 4, but as it is of great practical importance to the anaesthetist and clinician in the management and treatment of emphysema-tous patients, some of the main points will be discussed here.

A raised ventilation-perfusion ratio, in an alveolus, can hardly increase the oxygen saturation of the blood leaving that alveolus (because it is already nearly fully saturated with the normal ratio), but it will lower the tension of carbon dioxide. A lowered ratio will reduce both the oxygen and carbon dioxide tensions. Thus, if different ventilation-perfusion ratios occur in a subject previously normal (for example, by a patchy bronchopneumonia causing reduced or absent ventilation in many groups of alveoli where the perfusion is still normal), there will initially be a fall in Po₂ but a rise in Pco₂ in the arterial blood. The respiratory centre is stimulated and there is an increase in the overall alveolar ventilation. This hyperventilation of alveoli which were unaffected will lower the arterial Pco₂ but does little to raise the arterial oxygen saturation. Hence the common response to pneumonia in an otherwise normal patient: cyanosis, increased ventilation but a normal arterial carbon dioxide tension. An emphysemous patient often does not increase his ventilation adequately or at all, to compensate for the raised carbon dioxide because of the mechanic disturbance in his lungs, so that hypoventilation is added. Thus he has a raised Pco₂ and lowered Po₂.

Hypoventilation, alone, with no ventilation perfusion disbalance will lead both to carbon dioxide retention and a lowered Po₂. But owing to the shape of the oxygen dissociation curve when the Pco₂ is raised to about 60 mm Hg (at the Po₂ lowered to about 80 mm Hg with a R.Q. of 0.8) the oxygen saturation will be 92 per cent, and there is no cyanosis. Conversely, a disturbed ventilation-perfusion balance may lead to a fall of oxygen tension severe enough for cyanosis with little or no rise of Pco₂, compensatory increase in ventilation can take place. In emphysema, all combinations of ventilation-perfusion inequality and hypoventilation can be found, though in severe cases, especially with infection, both are usual, and cause severe "lung failure", a lowered arterial oxygen saturation raised carbon dioxide tension, and the low pH and high serum bicarbonate of respiratory failure.

Finally, it must be realized that although regional underperfusion is expressed as a "venous admixture" effect, there is usually no absolute shunt. On breathing pure oxygen the arterial blood becomes fully saturated.

**Diffusing Capacity.**

**Observations.** Bates et al. (1956) measured the "diffusing capacity of the lung" using the carbon monoxide steady state method. They found a severe reduction of diffusing capacity in advanced emphysema. Since the diffusing capacity increases on exercise in normal subjects, a phenomenon thought to be caused by opening up of blood capillaries with an increase in the area available for gaseous diffusion, the diffusing capacity for carbon dioxide or Dco₂ is often recorded on exercise to find its maximum value. Bates et al. (1956) stress not only the falling off in diffusing capacity at rest with advancing emphysema but the relative failure to augment the diffusing capacity on exercise, in this condition.
The alternative technique of measuring the Dco by a single breath inhalation (Ogilvie et al. 1957) shows a less marked decline in diffusing capacity in emphysema, though in occasional severe cases at rest, it can be reduced from the normal of about 15 ml/min/mm Hg down to less than half that value.

Carbon monoxide is used to measure the diffusing capacity largely because of simplicity and the difficulty of measuring it for oxygen. With carbon monoxide the mean tension in the lung capillaries is assumed to be about zero (because of the enormous affinity of carbon monoxide for haemoglobin), so that if the average alveolar tension can be measured at the same time, the Dco can be calculated.

With oxygen the mean capillary tension is not negligible and is difficult to determine, and any alveolar underperfusion also affects the alveolar-mean-capillary gradient for oxygen. However, these difficulties can be partly overcome, though the technique is complex and entails studies of oxygen uptake and blood gas tensions both when the patient is breathing a high and a low oxygen mixture. By this technique (Donald et al., 1952), the Dco was found to be reduced in some cases of emphysema, the impairment being most pronounced in those who had also had the largest combined venous admixture and deadspace effects.

Comments. Recent work on the difference between the results obtained from the single and multiple breath carbon monoxide technique suggests that much of the abnormality revealed by the latter may be accounted for by regional inequality of gas distribution in the lungs. Neither the histology, nor other functional studies, suggest gross change in the barrier to oxygen uptake per unit of surface area in the lungs. The significance of measurements of diffusing capacity in emphysema is at present controversial, but it seems likely that there is an effective reduction of surface area available for diffusion mainly because of the disturbed ventilation-perfusion balance, but that this reduction in effective surface does not become pronounced in its effects in limiting total gas diffusion till the condition is advanced. In other words, the disturbed lung mechanics and inability to ventilate set a limit to activity before that set by maximum oxygen uptake in most cases of emphysema.

SUMMARY OF THE FUNCTIONAL PATHOLOGY AND ITS CLINICAL SIGNIFICANCE

The nature of emphysema. We can now summarize the nature of the functional lesion in a patient with advanced emphysema. His chest is held in the inspiratory position (often, but not always with an increase in total lung volume) because of the loss of elastic recoil of the lungs and the marked tendency to trap air (airways collapse) if he attempts to use the muscles of expiration to compensate for this loss of elasticity. Consequently, he has a grossly diminished ventilatory reserve for exercise, partly from a small vital capacity, but more because of the narrowed airways causing a greatly increased expiratory resistance to air flow. The inspired air is unevenly distributed in the lungs; worse, there is lack of balance between air and blood flow resulting in an increased ventilatory requirement for a given oxygen uptake (which usually cannot be provided because of the mechanical difficulties), and hence there is both oxygen desaturation and carbon dioxide retention in the arterial blood. In the latest stages of the disease a decreased diffusing capacity may be added to the gross lack of balance between gas and blood flow, and heart failure—secondary to the primary lung failure—supervenes.

These combined functional changes are characteristic of emphysema. Other conditions may be similar in some features. For example, patients in a severe attack of spasmodic asthma have their chests held high in inspiration, with the attendant increase in F.R.C., and have an equally diminished ventilatory reserve. But they rarely have such a lack of balance between ventilation and perfusion so that gross change in arterial blood gas tensions are rare. The latter only occur in status asthmaticus from pure hypoventilation, largely because of airways obstruction by secretion. Moreover, there is no loss of elasticity and the obstruction to airflow is of a different nature. Although it is greater in expiration than inspiration, the inspiratory obstruction is greater than in emphysema.

The problem of diagnosis may be very great, especially when emphysema is combined with bronchitis and asthma. The only reasonably cer-
tain method of making a positive diagnosis in life, is testing for the specific changes described, taking account of test results in relation to the clinical findings and history.

**Relation of the functional lesion to progress.**

In spite of the gross and widespread functional abnormality in the advanced cases, which makes the emphysematous patient so difficult for the anaesthetist, the condition is often not quickly progressive and the amount of emphysema may go in infinite grades from nothing to the advanced stage, taking many years to develop. The rate of change seems to be related to the age of onset, again rather like diabetes, and definite emphysema in young subjects, while rare, is usually quickly progressive. Emphysema is common in the elderly, but then it is often only slowly progressive (Stuart-Harris and Hanley, 1957).

Some patients seem to have more of the purely mechanical ventilatory disturbance, some have more of the lack of balance between ventilation and perfusion, and have change in arterial blood gas tensions out of proportion to their ventilating defect. Some patients seem to "accept" breathlessness and maintain their arterial Pco₂, relatively normal by increasing their ventilation, while others seem to let their blood gas tensions become abnormal, hypoventilate and complain less of dyspnoea. However, the relation of function to different clinical and pathological types of emphysema and to the rate of progress of the condition is not yet worked out.

The onset of cor pulmonale possibly depends mainly on the degree of disturbance in blood gas tensions. There are three main reasons for believing this. There is evidence from animal and human experimental physiology that anoxia can produce acute increase in pulmonary vascular resistance and hence pulmonary hypertension. The onset of cor pulmonale and cyanosis (which means a markedly lowered Po₂) tend to occur concurrently. Finally, returning the grossly abnormal blood tensions (during periods of hypoventilation following infection) to normal by mechanical artificial ventilation appears to lower the pulmonary artery pressure.

A bout of infection is the commonest cause of sudden deterioration in the functional state. The emphysematous patient does not increase his ventilation in response to bronchopneumonic increase in ventilation-perfusion inequality like other patients, probably because of the extreme stimulation of stretch receptors and chronic insensitivity of the respiratory centre to carbon dioxide. The patient consequently has carbon dioxide retention, respiratory acidosis and increased cyanosis and often a rise of pulmonary artery pressure and heart failure. Giving oxygen which will relieve the anoxaemia, removes part of this respiratory drive resulting from anoxaemia the ventilation falls further and the arterial Pc rises, with consequent rise of cerebrospinal fluid pressure, and coma in extreme cases.

**The functional lesion and treatment.**

There is no known curative treatment of emphysema itself, but appreciation of the functional changes enables the physician to slow or prevent deterioration by removal of complication. The two main therapeutic measures are to improve the main functional defects—in overall ventilation and in the distribution of blood and gas. Nothing can be done to replace the loss of capillary bed and its contribution to loss of lung-diffusing capacity.

In the chronic state, treating superadded bronchitis and asthma is vitally important. Treatment of the former (by postural drainage, antibiotics, and omission of smoking) will keep air distribution as normal as possible. Treatment of the latter will remove what is often an entirely unnecessary added reduction in air flow and ventilatory capacity. Detection and treatment bronchospasm complicating emphysema is urgent and important.

In acute exacerbation from respiratory infection, oxygen is needed to relieve the anoxaemia and help heart failure. It should be given freely but this can only safely be done if any consequent hypoventilation is treated by frequent chemical stimulation of the respiratory centre (with nikethamide, aminophylline, or possibly amphetamine) or, in the few cases where this fails, by artificial mechanical ventilation using a cuffed tube as a temporary basis or tracheostomy for longer periods.

Effective increase in ventilation by intermittent positive pressure breathing in the conscious subject is difficult to achieve, and we have had rather less success with this measure than is claimed by some American work.
Radiographs: (A) Patient with extreme functional disturbance. Cyanosed, and bed-ridden by breathlessness, he died shortly after this photograph. (B) Patient with very good exercise tolerance ("could run for a bus") and lead a satisfactory life. (A) has emphysema and a gross lack of balance between ventilation and blood flow throughout the lungs. (B) has poor air flow to the left lung, from radiation fibrosis, but poor blood flow there as well.
Finally there is the place of surgery now and in the future. Removal of large bullae in emphysematous patients (or other patients for that matter) often improves the mechanics of the chest and helps to prevent air-trapping, though the choice of patients suitable for this treatment requires considerable skill. "Bullectomy" may also help in some cases by removing alveolar deadspace, though the significance of this effect is less certain. "Plexotomy" or, in a few cases, vagotomy alone may help by relief of dyspnœa, presumably by cutting the path of stretch receptors. Attempts have been made to remove the hypoventilation of advanced chronic emphysema (so as to improve arterial gas tensions and prevent pulmonary hypertension) by giving patients salicylates and other respiratory stimulants. In occasional cases this treatment meets with some success, but the patient may be rendered more breathless; possibly, if the stretch receptors could be cut, this treatment would be fruitful in halting the course towards cor pulmonale.

DIAGNOSIS AND ASSESSMENT BEFORE OPERATION
Most of the tests of lung function which have been mentioned are complex and only available at highly specialized centres. However, an understanding of functional lesions of the chest, from the results of these tests, greatly enhances clinical acumen and makes it possible to interpret history and physical signs so as to make a reasonably satisfactory functional diagnosis in many cases. But the chest radiograph, which is so much more helpful than physical signs, in the diagnosis of anatomical pathology (the recognition of lung cancer, tubercle, bronchiectasis, etc.) can be misleading in the diagnosis of function (fig. 9).

It is suggested that the anaesthetist, when he sees a patient with chronic respiratory disease before operation, should ask himself two sets of questions, concerned with an attempt at precise pathological and functional diagnosis, respectively:

A. Pathological diagnosis.
(1) Has the patient really got any emphysema, and if so of what degree?
(2) Has he chest infection?
(3) Does he get accompanying asthma?

B. Functional diagnosis.
(1) What is the ventilatory reserve of lungs? If a thoracic operation is contemplated what is it likely to be afterwards?
(2) Is the patient's resting ventilation adequate to maintain a normal arterial carbon dioxide tension or is he hypoventilating?
(3) Can the patient maintain a normal arterial oxygen saturation at rest or on exercise?

These questions may have to be attempted clinical judgment only. Some of the answers then be impossible to provide. A suggestion the use of simple lung function tests is there given. In either case the significance of these questions in relation to anaesthesia and postponement of operation is discussed.

Clinical Assessment.
This is discussed in the clinical section of this symposium (Dornhorst, 1958). It is sufficient to stress the importance of age and of a history of excessive breathlessness on exertion, with other apparent cause, in the diagnosis of emphysema. The breathlessness should be assessed terms of simple clinical grades as suggested Fletcher (1952). A history of the type and quantity of sputum for the diagnosis of bronchitis, of using a leading question about wheezing (preferably with a demonstration!) for the diagnosis of accompanying asthma, is likewise stressed.

On examination, stress is laid on listening asthmatic wheeze (often heard best by auscultation over the trachea) and of thinking in the of the probable M.B.C. when looking at chest movement, testing for air-trapping (see clir section), or considering a wheeze as evidence of air-flow obstruction. However, quantitative measurement of M.B.C. is far more satisfactory, the simple measurement of F.E.V. is excel for this purpose. An attempt can be made to evidence of hypoventilation from the presence of desaturation; and of exercise capacity, toge with exercise desaturation, from watching patient exercise (going upstairs). Again, how simple quantitative tests are more satisfactory

Simple Function Tests.
Of them all, the measurement of second F.E.V. during a forced vital capacity using a spiographic record or automatic time device, is the simplest and most informative
our purpose. This test should be freely available. The M.B.C. can be determined from it. Repetition of the test after an inhalation, adrenalin and atropine compound (B.P.C.) or of isoprenaline, from a suitable hand-nebulizer, will help to detect asthma and make the diagnosis of emphysema most unlikely if the F.E.V. forms a percentage of the V.C. greater than about 70 per cent (Thomson and Hugh-Jones, 1958).

If hypoventilation is suspected, the presence of a raised serum bicarbonate should be looked for. This is not pathognomonic without an arterial pH measurement because it can arise from a metabolic alkalosis rather than as a compensation for respiratory acidosis, though, in practice difficulty does not often arise.

These two tests should be available and their use, together with clinical appraisal, should deal with most problems. A standard exercise test using an ear oximeter is a useful adjunct to answer the last question suggested for functional diagnosis. But this is already getting beyond what is likely to be available. Unfortunately, many problems about the advisability of operation are highly complex in emphysematous patients, and are outside the scope of the anaesthetist himself. They demand close liaison between physicians, surgeons and anaesthetists, with access to all the various tests of lung function, if they are to be answered on a rational basis.

**Postponement of Operation.**

The presence of chest infection, asthma, or poor exercise tolerance associated with obesity, may make it advisable to postpone operation on functional grounds. Emphysema itself can be so severe in rare instances, as to make anaesthesia and operation dangerous and call for abandonment; postponement is only indicated if one of these three accessory factors is also present to interfere further with a lung function of an emphysematous patient.

If the M.B.C. is very low (less than 30 or 40 l./min, depending on age and sex), and especially if hypoventilation is present, then every effort should be made to treat any of these three factors that may be present. It is well worth postponing operation in an emphysematous patient judged to be a "poor risk", to clear purulent sputum by antibiotics and postural drainage, to relieve bronchospasm by the frequent use of a hand-nebulizer (with a demonstration of how to use it!) together with long acting antispasmodic tablets (e.g. choline theophyllinate), or to give time for dietary weight reduction.

F.E.V. measurements, before and after an antispasmodic aerosol, are invaluable in assessing the benefit likely to be obtained from postponement of operation and, if repeated during treatment, in measuring the actual benefit obtained.

**Abandonment of Operation.**

This is outside the scope of the anaesthetist. In chest surgery itself, lobectomy rather than pneumonectomy, or total abandonment in favour of, for example, X-irradiation, might be advisable on grounds of inadequate ventilatory reserve after operation or of possible excessive exercise ventilation after operation. But the problem is highly complex, often demands full functional assessment and even then the decision must rest with the surgeon or physician, who is given the facts; this is especially so in the case of malignant disease.

Finally, if thoracic surgery is undertaken to treat emphysema (in the way of removal of bullae) it is well to remember that success is often most apparent in the most severely disabled subjects who appear to be exceedingly bad anaesthetic and operative risks. In such subjects a distended bullae may behave like a tension pneumothorax, and its removal give striking benefit; a radiographically similar bulla, in a patient without obvious symptoms, may be functionally unimportant and its removal may produce most adverse effects. Such decisions about operation do not rest with the anaesthetist. But he must use all his skill and knowledge of lung function if a severely disabled emphysematous subject is to undergo surgery.

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