of total Dco by the single breath method and the membrane component using the single breath method at different O_2 tensions (Forster *et al.*, 1955). The membrane component of the Dco multiplied by 1·23 should give the same value as the membrane component of DO_2. I have not measured DO_2 so I have had to compare the Dco with the predicted values of DO_2 but a rough comparison can be made. The Dco and the membrane diffusing capacity for CO were measured at rest and the membrane Dco multiplied by 1·23 gives a calculated membrane diffusing capacity for O_2 ($D_{M_{O_2}}$) of 59 which is over twice the $D_{M_{O_2}}$ calculated from the predicted DO_2. On exercise sufficient to increase the O_2 uptake to 2·6 litres per minute the membrane Dco rises to 70 which gives a calculated $D_{M_{O_2}}$ of 86; this is in comparison with a predicted maximal DO_2 of 60 and a $D_{M_{O_2}}$ of 73 for a person of this size. At present we do not know the reason for these different results. One possible explanation is that the DO_2 measures the diffusion only into those capillaries through which blood is flowing at the time that the measurements are made; the Dco will measure diffusion into any capillaries containing blood irrespective of whether the blood in them is flowing or stagnant. If only about half of the capillaries have a normal blood flow through them at rest this could explain the different results obtained by the two methods; on exercise the blood flows through more capillaries and the two values approach each other.

To conclude, although the Dco does not give a direct measure of DO_2 the technical advantages of measuring the Dco usually outweigh the disadvantages, particularly since, in practice, the two methods usually run in parallel and for clinical purposes reduction in diffusing capacity can be shown quite adequately by measurement of the Dco.

The single breath method of measurement of the Dco gives the same results as the other CO methods and as it is the easiest method to carry out it is the method of choice for measurements made at rest. Measurements made on exercise minimize the technical errors of the steady state methods but except for this reason I know of no advantage to be gained from measurement of the Dco on exercise. The result depends on the rate of exercise and the maximum value for Dco is reached only at fairly severe rates of exercise in normal people.

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Oligopnœa [*Abridged*]

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THE term "oligopnœa" was purposely chosen to mean an inadequate output of air from the lungs, just as "oliguria" is used for an inadequate or scanty output of urine.

Some factors controlling ventilation.—Before giving clinical examples of oligopnœa, their diagnosis and treatment, it is helpful to consider the factors controlling the normal "air output", or ventilation of the lungs. It is generally taught that this is chiefly regulated by the tension of carbon dioxide in the arterial blood. A rise of carbon dioxide tension stimulates the respiratory centre and leads to an increase in ventilation, while a fall in either oxygen tension or pH has a similar, though much less marked, effect. All this is undoubtedly true, but it is becoming apparent that nervous impulses from stretch receptors in the lungs play an equally, if not more, important role. Just as proprioceptive impulses from joints determine posture, reflexly in relation to muscle stretch, so these pulmonary stretch receptors regulate ventilation according to the degree of movement of the lungs. In disease, disturbance of reflexes from these receptors may become the primary mechanism which regulates ventilation, and this disturbance is readily accompanied by the sensation of "dyspnœa".

The significance of stretch receptors can most easily be demonstrated by a very ingenious experiment designed by Fowler (1954) which was concerned with the breaking point of breath-holding. It was held that the limit to voluntary apnœa was the rise of carbon dioxide and fall in oxygen tension in the blood causing extreme stimulation of the respiratory centre, and a number of papers had been published which defined these arterial blood gas-tensions when the limit to breath-holding was reached. Fowler got a spirometer and filled it with an "air" mixture containing oxygen and carbon dioxide at the same tensions as these gases would be in the blood at the limit to breath-holding. He asked a subject to hold his

breath for as long as possible and then to breathe in and out of the spirometer. Of course the subject's carbon dioxide tension then went on rising and oxygen tension falling but instead of feeling worse, he felt relief! After a while the subject felt uncomfortable breathing from the spirometer in this way, and was then asked to hold his breath again; soon he could hold it no longer and again he was told to breathe from the spirometer, and so on, until the total "breath holding" period was much prolonged. But from our point of view, the important thing is that every time chest movement was restarted relief was experienced, showing it was the lack of impulses from stretch receptors and not gas tensions which was of prime importance in the discomfort of breath-holding. And you can do this experiment now by simply stopping breathing; it becomes uncomfortable at once, long before there is a significant alteration in the gas tensions in the arterial blood.

It appears that if the stretch receptors either send no impulses or if they send excessive impulses the sensation is unpleasant. Excessive impulses occur when inspiration approaches the maximum possible depth (which again you can try now by taking in as deep a breath as possible). Excessive stretch of these receptors may be one of the many factors which appears to be responsible for the sensation of "dyspnœa" when ventilation reaches a certain proportion of the maximum possible ventilation, or maximum breathing capacity (Hugh-Jones, 1952).

Just as it has been shown by Fowler's experiment that breath holding is limited by stretch receptors rather than by blood gas tensions so there is increasing evidence that in some circumstances impulses from the stretch receptors, rather than blood gas tensions, regulate ventilation. These receptors send impulses from the lungs which are related to the work of breathing (Davies, Fowler and Lambert, 1956) and in disease states, for example emphysema, where the mechanics of breathing are disturbed and a given intrapleural pressure change may be responsible for a diminished air-flow in and out of the lungs, the patient may maintain a ventilation determined by keeping the work of breathing as low as possible, with his abnormal lungs, at the expense of maintaining normal gas tensions in his arterial blood. This is a common finding in emphysema where the patient readily complains of breathlessness if his ventilation is stimulated in any way (usually by exertion) and where the arterial oxygen is low and the carbon dioxide high when the patient is at rest. Yet such a patient, at rest, can often put his carbon dioxide tension back to normal by increasing his resting ventilation on command. Such patients Dornhorst (1955) has considered to be "lazy breathers". They are, in fact, in a state of chronic hypoventilation or mild chronic "oligopnœa".

The effect of infection.—The importance of mild chronic oligopnœa becomes much more apparent when the patient gets an acute respiratory infection. Any patient with a patchy bronchiolitis or bronchopneumonia has some parts of his lungs underventilated or even entirely unventilated, yet with blood still flowing in these areas. Thus, there is virtual "shunting" of venous blood into the arteries, in these underventilated areas. As a result of the increased carbon dioxide in the arterial blood, ventilation is augmented so that those parts of the lung in which air still flows are excessively ventilated. From them carbon dioxide can be eliminated, but the blood in them is already being fully oxygenated so their overventilation can only compensate for the rise of carbon dioxide in the arterial blood but not for the fall in oxygen caused by the presence of those areas of the lung with a normal blood flow, but reduced, or absent, air-flow. Hence the familiar picture of a cyanosed patient with pneumonia, breathing rapidly. If, however, the patient has altered mechanics of his chest as well as his pneumonia then, either because of excessive stimulation of the stretch receptors, or in some severe cases because of greatly reduced maximum breathing capacity, the ventilation is not adequately augmented and the patient becomes not only cyanosed but retains carbon dioxide. In other words, he develops acute oligopnœa, with relatively severe underventilation compared with his needs, even though he may appear to be breathing rapidly and hard. In such a patient, whose respiratory centre is no longer responding normally to carbon dioxide, the administration of oxygen for his cyanosis removes the remaining factor of anoxia, which was tending to maintain the little ventilation he had, so that his ventilation falls even further and leads to such high levels of carbon dioxide as to cause a comatose state to supervene on the disorientation from the previous lack of oxygen.

Diagnosis.—Clinically, the diagnosis of acute oligopnœa may not be easy; the mental state can be mistaken for that of a primary neurological condition such as a cerebrovascular accident, and the respiratory hypoventilation can be overlooked especially if there is rapid shallow breathing.

Just as the rise of blood urea is a useful confirmation of uræmia in states of oliguria, so arterial blood gas analysis confirms the carbon dioxide retention of oligopnœa. Another useful adjunct in diagnosis is to measure ventilation, just as one normally measures the urinary output for the diagnosis of oliguria; we use the very suitable anemometer designed

by Dr. B. M. Wright of the M.R.C. Pneumoconiosis Research Unit. It is small, virtually free from resistance, and can be used even with severely ill patients to chart their minute ventilation instead of simply charting respiratory frequency, which is, of course, not necessarily a reflection of the ventilation at all. With readings from this instrument, and the respiratory frequency, the alveolar ventilation can be calculated using an assumed value for the upper respiratory dead space. Then, the effects of oxygen and other therapeutic agents on the alveolar ventilation can be observed.

Treatment of acute oligopnœa.—Just as in oliguria arising from sulphonamides it is desirable to ensure a free passage for urine by flushing out the ureters by ureteric catheterization, so a free airway is the first essential in oligopnœa. In the patient with bronchopneumonia, secondary asthma is usually present, which is a major factor to air-flow obstruction. It is usually best detected by hearing the wheeze by auscultation over the throat, and treated by continuous aerosol inhalation of adrenaline or isoprenaline. This inhalation can be given at the same time as the oxygen which these patients badly need. We have seen patients in whom adequate aerosol treatment given with oxygen was itself enough to treat the hypoventilation. In all patients with central cyanosis from acute respiratory failure we give oxygen continuously and at a flow rate that is needed to remove cyanosis; if, on this regime, there is a tendency to acute oligopnœa, carbon dioxide retention, and drowsiness, then ventilation must be stimulated—either chemically, or if that fails, mechanically.

Chemical stimulation of ventilation.—Aminophylline (10 ml.) is given intravenously. It is a most useful drug in that it both acts as a central stimulant to ventilation and as an "antispasmodic" and we repeat it far more frequently than is customary, often two-hourly if that maintains adequate ventilation to prevent drowsiness from the oxygen and the patient gets no nausea with it. An alternative is intravenous nikethamide in similarly "heroic" doses of up to 5 ml. about two- or three-hourly depending on the clinical response. These injections, an aerosol of isoprenaline, and continuous oxygen successfully deal with the majority of patients who have acute oligopnœa on top of a chronic chest condition and literally save life while antibiotics have time to deal with the acute respiratory infection which usually precipitates this functional state. Nevertheless these patients are a serious medical emergency and if chemical stimulation is not completely successful and especially if abundant purulent sputum, or viscid secretion from status asthmaticus, prevents the maintenance of an adequate airway then we have no hesitation in performing a tracheotomy and using artificial mechanical ventilation.

Mechanical ventilation.—Tracheotomy is done under cyclopropane or intravenous barbiturate anæsthesia with Flaxedil as a muscle relaxant. With the tracheotomy tube in, adequate suction of bronchial secretions becomes much more practicable and a mechanical pump is used to provide the ventilation the patient needs.

A film, showing the first patient we artificially ventilated in this way, was projected at this stage:—

The patient was literally moribund, with cold extremities and feeble pulse, after a previous phase of high output heart failure of cor pulmonale. His respiratory rate of no less than 70 breaths per minute was associated with shallow abdominal breathing and negligible chest movement, and his severe oligopnœa was reflected by an arterial oxygen saturation 42%, carbon dioxide tension 74 mm.Hg, pH 7·32. Half an hour after tracheotomy blood analysis showed he had been over-ventilated by the pump because his carbon dioxide tension was then only 32 mm.Hg and his pH 7·63. Such over-ventilation can be dangerous and result in a further fall of blood pressure, especially if inadequate time is given in the respiratory cycle for venous filling of the heart. But after giving the correct ventilation his arterial blood was returned to normal (Fig. 1) and he was up and about in three weeks' time.

We find full humidification of gas going to the tracheotomy essential to prevent "crusting" in the trachea. If this is done there is little trouble with the procedure and simply by maintaining the arterial blood gases at normal through artificial ventilation, the heart failure disappears with an apparent lessening of the pulmonary artery pressure.

Usually a few hours on an automatic pump is all that is required to restore the arterial blood to normal and treat the acute oligopnœa though the tracheotomy may have to be maintained for a few weeks, not only to assist the efficiency of the patient's own ventilation, by reduction of upper respiratory dead space, but also to provide a means of sucking out secretions in patients who are not adequately coughing.

While the patient is anæsthetized and relaxed, any automatic pump in which the frequency and stroke volume can be altered is adequate if a cuffed tracheotomy tube is used. Occasionally a patient-cycled respirator is useful to "boost" ventilation later when the patient recovers consciousness, though it is rarely necessary.

We have had less success in using a patient-cycled positive-pressure respirator in the conscious patient as some American workers have recommended (Sicker and Hickam, 1956)

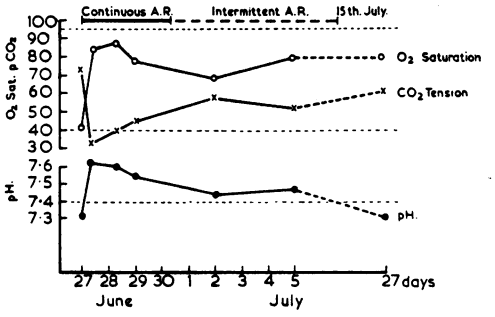

FIG. 1.—Arterial blood changes as the result of treating acute oligopnœa by tracheotomy and mechanical ventilation in a patient with advanced emphysema. (Continuous A.R.—automatic pump ventilation. Intermittent A.R.—patient-cycled ventilation.)

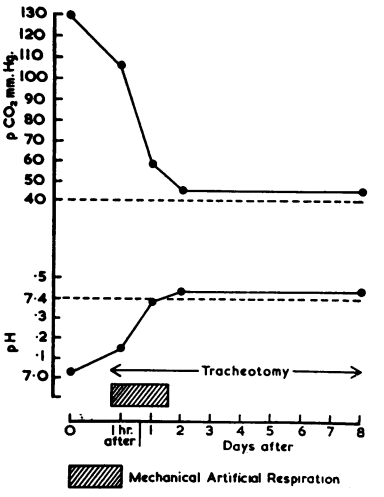

FIG. 2.—Arterial blood during treatment of acute oligopnœa from status asthmaticus.

for we find that oligopnœic patients do not tolerate a mask over their faces and, without a tracheotomy, their stomachs are inflated as well as their lungs! However, tracheotomy is a much simpler procedure than usually considered and really enables an adequate airway to be established. To "take over" a patient's breathing who is severely ill with respiratory failure by artificial ventilation under anæsthesia (when morphine or barbiturates can be given safely) is not only life-saving, but kind to a patient fighting for breath and oxygen.

Indications for treatment of acute oligopnœa.—An objection to the treatment of oligopnœa has been that it becomes merely a method of resuscitation of permanent respiratory cripples when it is applied in patients who may have chronic respiratory disease. Like using the artificial kidney in oliguria it is clear that mechanical ventilation with an "artificial lung" should only be undertaken for a temporary and potentially reversible condition. However, it is often extremely hard, if not impossible, to tell which patients have gross and irreversible emphysema when they are seen in oligopnœa from an acute respiratory infection. A demonstration of this is shown by an analysis made by Dr. W. B. Thomson of all the deaths over the last three years at Hammersmith Hospital clinically diagnosed as arising from acute respiratory failure in patients suffering from "emphysema" (Table I). Nearly a quarter had no material degree of emphysema at post-mortem examination, but died from a potentially reversible bronchopneumonia. Three or four years ago we resuscitated moribund patients with gross carbon dioxide narcosis from oligopnœa, who have had the subsequent years of comfortable and useful life.

TABLE I.—DEATHS FROM RESPIRATORY FAILURE IN HAMMERSMITH HOSPITAL

Year	Nos. dying with diagnosis of bronchitis and/or emphysema	Nos. dying from resp. failure	Pathology: little or no emphysema
1954	26	8	1
1955	25	10	3
1956	22	9	2
Totals	73	27	6

Thus, we tend to apply methods I have mentioned to all patients in whom there is even a slight prospect of relatively permanent success and then assess their lung function fully, as a guide to prognosis, on their recovery from the acute attack. Fig. 2 shows the progress of another patient who was admitted in status asthmaticus and who, after all the usual treatment had failed, including full steroid therapy, was referred to us by Dr. C. L. Cope. In her case the main problem was removing through the tracheotomy the almost

rubbery exudate which filled her bronchi; even after energetic suction quite a high pump pressure was needed to maintain her ventilation and reverse the severe oligopnœa which had caused such a dramatic change in her arterial blood gas tensions. But she made a complete recovery from this acute attack.

Treatment of chronic oligopnœa.—The treatment of mild chronic oligopnœa in emphysema is, like the emergency of acute oligopnœa, another worth-while field of therapeutic endeavour. Occasionally "lazy breathers" can be made to ventilate, with definite improvement in their mental well-being and a probable diminution of their chances of heart-failure from pulmonary hypertension, by the prolonged use of respiratory stimulants, including salicylates. But if such treatment is successful increased breathlessness from excess stimulation of their pulmonary stretch receptors may occur. There is probably a chance that our surgical colleagues could then help such patients by division of the nerve pathways in which these receptors run. But more research into the anatomical pathways of these nerves is much needed.

Conclusions.—The use of artificial mechanical ventilation in the ventilatory defects of poliomyelitis, tetanus, &c., is well established. We would like to see the treatment of acute oligopnœa in chronic respiratory disease become equally accepted. It is most rewarding. In fact tracheotomy and mechanical ventilation are rarely needed since energetic use of chemical stimulation of the respiratory centre together with antispasmodics deals with the majority of cases. But the diagnosis of acute oligopnœa must be made and adequate treatment given. We use oxygen in full amounts in all patients who need it and combat any tendency to carbon dioxide narcosis from oligopnœa by appropriate ventilation, achieved either chemically or mechanically.

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Mechanisms of Airway Obstruction in Emphysema and Asthma

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NARROWING of the airways, particularly during expiration, is the most important physiological defect in the asthma, bronchitis, emphysema group of conditions. This expiratory obstruction is responsible for the limited ventilation and total gaseous exchange of which these people are capable. It is also responsible for most of the physical signs and for the reduced performance in such tests as the Maximum Breathing Capacity, Vital Capacity and Forced Expired Volume. The nature of the airway obstruction is poorly understood. The term "bronchospasm" is commonly used to describe it. Although I doubt if many of the people who use the word really believe that spasm of the bronchial muscles is the explanation of the airway narrowing, nevertheless little thought has been given to the number of ways in which the airways may be narrowed. Unfortunately, the common simple ventilatory function tests, although they provide good estimates of the severity of airway obstruction, do not distinguish between the possible causes. The mechanisms may be grouped as follows:

(1) Reversible disease of the airway, e.g. increased bronchoconstrictor tone.
(2) Relatively irreversible disease of the airway, e.g. chronic inflammation.
(3) Loss of elastic support of the airways so that they collapse during expiration.

I want to describe some studies which shed more light on these mechanisms. They were performed on normal subjects, on patients with asthma, and patients with emphysema. A full description of these experiments has been published elsewhere (Campbell, Martin and Riley, 1957), therefore technical details will be omitted.

The basic observation which provided the starting point of this study and which is to be found in earlier work concerns sequence of changes in intrathoracic pressure and rate of air-flow during a forced voluntary expiration (Fig. 1). If intrathoracic pressure is recorded from the œsophagus and rate of air-flow is recorded at the mouth during a forced expiration the rate of air-flow rises to a maximum value and then decreases while the intrathoracic pressure continues to rise. This observation suggested to us that there may be a maximum