improve, and surgery be possible. Often, however, the recurrent bleeding produces a worsening of hepatic function and it becomes clear that the major feature is hepatocellular failure and surgery will be impossible. At this stage the apparatus should be withdrawn, as its further use increases the patient's misery and complications are likely. In some of these patients local surgical attack on the varices has been suggested, porta-caval anastomosis being performed later (Linton, 1953; Welch, 1957). This was attempted in six of our patients, but all died after the first operation, a reflection of their inability to support any form of surgical treatment.

Complications of intubation are common, and in one series of 50 patients treated with the Sengstaken tube

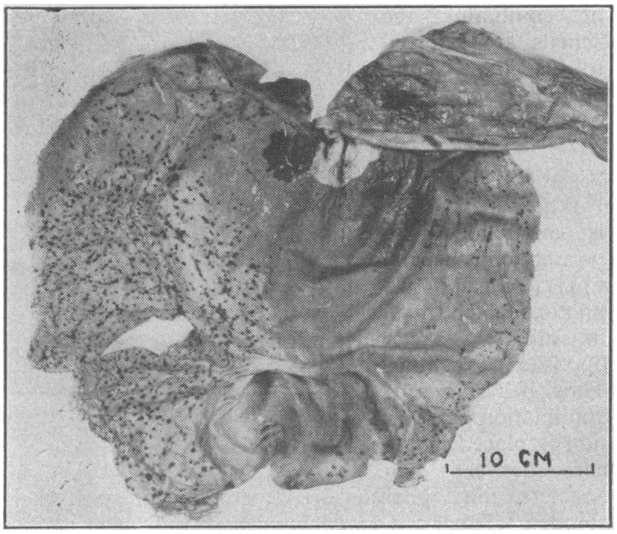

FIG. 7.—A cause of failure: diffuse haemorrhagic gastritis.

nine died as a consequence of its use (Conn, 1958). The most serious complication in this series was obstruction to the airway and regurgitation of blood and gastric secretions into the lungs. Our commonest complication was oesophageal ulceration. This was related to the duration of intubation and to the amount of traction. Nachlas (1955) believes that ulceration may be decreased by omitting the oesophageal tube and using a triple-lumen single gastric balloon tube. In our experience, however, this tube required more traction to keep it in position and the gastro-oesophageal ulceration rate was increased.

Summary

The Sengstaken oesophageal compression tube controlled the haemorrhage initially in 32 of 38 patients with portal hypertension and oesophageal varices. Only 10 survived to leave hospital, and only five of these were suitable for porta-caval anastomosis. The other 28 suffered recurrent bleeds and ultimately died in hepatic failure. Results are contrasted with a group of patients with good hepatic function and portal hypertension who also suffered haemorrhage but who recovered without the use of the Sengstaken tube.

Practical details of the intubation and management of the patient are described. Complications included ulceration of the oesophagus and/or pharynx (10 cases), respiratory complications (14 cases), mechanical difficulties with the apparatus (14 cases), and infective enteritis (2 cases).

The method is a useful one for controlling bleeding from oesophageal varices. Intubation should not be continued if bleeding recurs repeatedly and liver failure is obvious. Under these circumstances the patient is made miserable and complications are many.

We would like to pay tribute to the nursing staff of Hammersmith Hospital for their meticulous and sympathetic care of the patients reported.

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STUDIES OF REGIONAL LUNG FUNCTION USING RADIOACTIVE OXYGEN

BY

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The use of a radioactive isotope of oxygen provides a method of assessing regional variations of ventilation and blood-flow in the lungs without intubation of the patient.

This method has advantages over bronchospirometry, which has hitherto been used to compare the function of the two lungs, because in the latter procedure the passage of the catheter into the bronchial tree is unpleasant, the conditions are far from physiological, and it is not usually possible to measure local variations of function within either lung. Kipping *et al.* (1957) overcame some of these problems by using the radio-isotope xenon-133. They measured local variations in ventilation, in the detection of bronchial tumours, by observing the distribution of radioactivity over different parts of the chest during normal breathing of air containing the radioisotope.

If oxygen is used instead of xenon, local blood-flow as well as ventilation can be assessed. This has not been practicable until now because of the rapidity with which radioisotopes of oxygen decay; the longest-lived, oxygen-15, has a half-life of only two minutes. However, the cyclotron built by the Medical Research Council (Gallop *et al.*, 1957) was sited within a hospital for a number of reasons, one of which was to make available

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for medical purposes isotopes with a very short life. Oxygen-15 has now been prepared at Hammersmith Hospital with this cyclotron, and details of its preparation, purification, and preliminary use have already been published (Dyson *et al.*, 1958). The present paper describes the use of oxygen-15 for the study of regional lung function in different diseases.

Methods

Principles

Oxygen-15 decays with the emission of positrons. These are annihilated almost immediately by combination with electrons in surrounding matter, with the production of γ-radiation. By aligning scintillation counters in front of and behind the chest, the radioactivity of the oxygen-15 can be measured by counting the γ-radiation which arises from cores of lung tissue between the counters. Two pairs of counters are used, so that the radioactivity in two regions can be measured simultaneously.

In the usual test the patient is given a single breath of air containing a trace of oxygen-15 and holds his breath for about twelve seconds. Normally, the counting rate from any region rises rapidly to an initial peak, falls slowly during the breath-holding, and then falls more rapidly when the gas is washed out by subsequent breaths of room air (see Fig. 3). Because of the short half-life of oxygen-15 the activity in the body decays within a few minutes, and the test may then be repeated.

Measurement of "initial activity" allows the relative ventilation of two regions to be compared, and simultaneous records indicate the time relationship of the ventilation of these regions.

The fall of counting rate per second during breath-holding, which is defined as the "clearance rate," measures the uptake of oxygen-15 by the blood and is used to assess regional blood flow.

Preparation

The cyclotron accelerates deuterons (the nuclei of heavy hydrogen), which are available as an external beam. Atmospheric nitrogen (nitrogen-14) is used as the target material; when this is bombarded with deuterons a proportion (very small by ordinary standards) is converted to oxygen-15 by the (d,n) reaction—that is, the nucleus gains one deuteron but loses one neutron. The energy of the deuterons is 15 MeV, but by reducing this to about 3 MeV, using aluminium foils (or magnesium sheet, in which sodium-22 is produced as a useful by-product), the yield of unwanted isotopes is reduced.

Compressed air is passed continuously through a vessel provided with a thin aluminium window through which the deuteron beam is projected. The oxygen-15 labelled air is then passed over purifying agents to remove ozone and oxides of nitrogen. Details of the radiochemical contaminants and the method of purification were described in the preliminary communication (Dyson *et al.*, 1958). Another description of the preparation of the isotope is given by Ter-Pogossian and Powers (1958).

The gas is produced with an activity in the region of 100 millicuries per litre and is diluted about twentyfold with air. The activity of this diluted gas is continuously measured in a re-entrant ionization chamber connected to an amplifier and pen recorder.

Counting Methods

A single counter placed over the chest would measure radioactivity mainly from parts of the lung just under the chest wall. This is rarely useful, so the counters are aligned in pairs, fore and aft, and their signals are combined electronically by one of two methods in order to detect radiations from the whole core of tissue between the counters. The counters are supported on two gantries, and are provided with adjustments so that they can be positioned accurately with respect to the patient (Fig. 1).

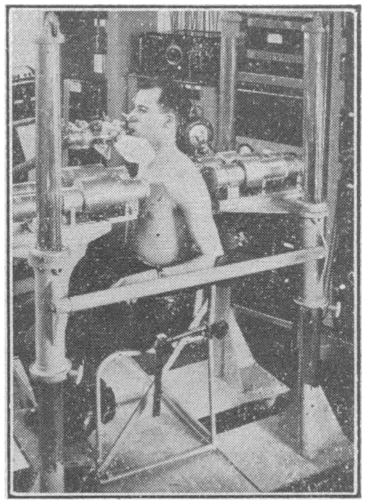

FIG. 1.—Photograph of patient about to inhale radioactive oxygen in air from "polythene" bag.

The two methods of combining the signals are referred to as the "coincidence" and the "parallel" methods.

Coincidence Counting

When a positron is annihilated the γ-radiation is usually emitted as two photons which travel in almost exactly opposite directions. Thus, if a source of annihilation radiation is placed in the core between two counters, some photons arrive simultaneously at each counter. These can be distinguished from other counts by using an appropriate electronic circuit which records only these simultaneous events. If the source is offset so that annihilations are no longer taking place between the counters, no coincidences will be recorded.

A number of problems in the use of the annihilation coincidence method are referred to by Dyson *et al.* (1958) and by Dyson (1959). A particular difficulty arises because of the random coincidences which occur when two unrelated photons, arising from annihilations outside the core, chance to arrive at the two counters at approximately the same time. Their number depends, among other things, upon the extent to which the electronic circuit can distinguish between truly coincident events and those which are close in time but not quite simultaneous. Within this limitation the random coincidences can be minimized and a correction automatically made.

Each detector over the chest consists of a sodium iodide crystal associated with a photomultiplier connected to a linear amplifier. Each pair is connected to a coincidence unit which detects the total coincidences and, independently, the random coincidences. These two outputs from the coincidence unit are applied to a circuit which subtracts them and yields a signal proportional to the real coincidence counting rate alone, and this is used to operate a pen recorder. The tracings are obtained at a speed of 6 in. (15 cm.) per minute, and the records from the two regions are displayed side by side.

Annihilation coincidence counting was used by Brownell and Sweet (1953, 1956) in the diagnosis and localization of brain tumours, using the cyclotron-produced positron-emitting isotope arsenic-74. The counting method has been developed in the present work, and gives a high degree of spatial resolution which enables a core of lung tissue only 4 cm. in diameter to be examined with no interference from surrounding regions. The effect of background radiation is negligible. The arrangement of counters and collimators, and a diagram of the iso-count curves for the system, are shown in Fig 2 (*a*).

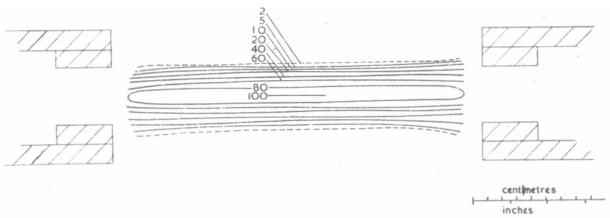

FIG. 2 (*a*)

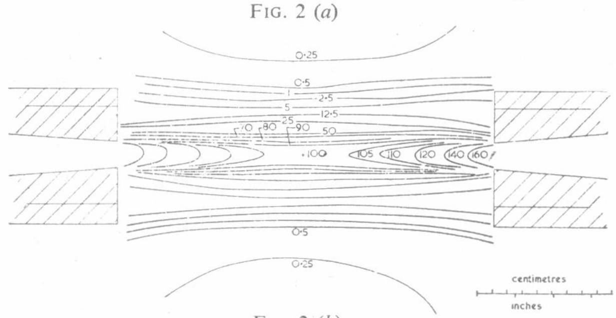

FIG. 2 (*b*)

FIG. 2.—(*a*) Iso-count curves for counters in coincidence (crystal separation 22 in. (56 cm.)). The figures show the relative contribution to the counting-rate given by a source at any point in the field. (*b*) Iso-count curves for counters in parallel (crystal separation 22 in. (56 cm.)). The field is wider and contributions are less uniform at different points along the core.

Parallel Counting

In this method the outputs from the two opposed detectors are simply added together and counted electronically and the resulting signals fed to the pen recorder. The spatial discrimination of this system is inferior to the coincidence system, and even when specially designed collimators are used the core is about 9 cm. in diameter. Because the counting-rates are higher for a given activity of oxygen-15, the parallel arrangement has been found specially useful for measuring clearance rate whenever the requirements for spatial discrimination can be relaxed. Background radiation produces an appreciable effect, for which allowance is made. The collimation of counters set for parallel counting and the iso-count curves for this system are shown in Fig. 2 (*b*).

Procedure and Calculations

The chair in which the patient sits has adjustable rests for neck, arms, and feet, because small lateral movements of the patient relative to the counters will alter the volume of lung between them. Before the test the areas to be compared are marked at symmetrical points to ensure accurate localization of the counters. When there is doubt, radiographs are taken, centred on opaque external markers, to define the underlying tissue and to check whether the counters are clear of mediastinum and heart. The counters are then brought up to the patient and positioned according to the markings. The patient is asked to breathe normally through the mouthpiece of a respiratory valve box.

In the usual procedure a polythene bag attached to the valve box is filled with gas of several millicuries activity and taps are turned during an expiration so that at the next inspiration the labelled air is taken. The patient is asked to hold this breath for about 12 seconds, after which normal breathing is resumed. The expired gas is taken to waste outside the room.

When particular attention is being paid to the time relation of the ventilation in two regions, tracings may be recorded during a slow inspiration, lasting 5 to 10 seconds, followed by normal breathing. In circumstances where a deep inspiration might produce spurious ventilation of abnormal regions, ventilation may be assessed at resting tidal volumes by administering the labelled air continuously during normal breathing.

Usually, duplicate assessments of both ventilation and blood-flow from different zones on each side of the chest can be made in four to eight breaths. The procedure takes 30 to 60 minutes.

For assessing ventilation, especially in small volumes of lung, coincidence counting is usually preferable. For assessing blood-flow, parallel counting is generally necessary, because the high counting-rates produce smoother curves. If this method is unsuitable because higher spatial resolution is required, coincidence counting may be used after moderate exercise, which increases the clearance rate and so gives steeper slopes that can be measured more accurately. For the exercise, the patient pushes on a pair of foot pedals against resistant springs for three minutes before the test breath, at a rate which approximately doubles the rate of body oxygen consumption.

"Initial activity," taken as the counting-rate at the beginning of inspiration, is obtained by extrapolating the graphs back to that time (Fig. 3 *a*).

The "oxygen-15 clearance rate" is calculated from the recorded slope during the 8 to 12 seconds after the peak value (Fig. 3 *b*). It is expressed as a percentage fall of the initial activity per second. Corrections must be made for the diminishing radioactivity of the isotope (0.56% per second, according to our determinations) and for instrumental errors if high counting-rates are used.

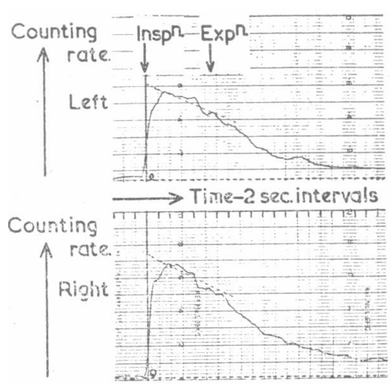

FIG. 3 (*a*)

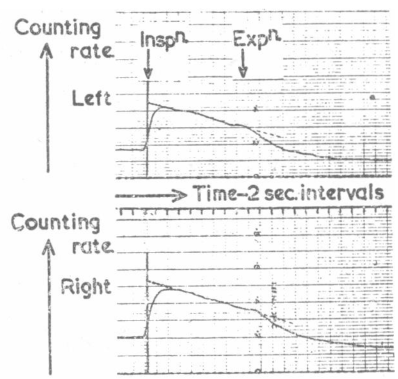

FIG. 3 (*b*)

FIG. 3.—Normal curves (*a*) in coincidence counting; (*b*) in parallel counting. In (*a*) the counting-rate is lower, so the curves are more irregular than in (*b*). In parallel counting, before inspiration, gas in the bag gives an appreciable background count, but when the bag is emptied the background falls to a low level.

Radiation Hazard

The absorbed radiation dose associated with the inspiration of air containing oxygen-15 depends mainly on the amount of activity inhaled and on the rate of washout from the lungs. In assessing hazard, the important absorbed doses are those in the lungs, blood (and blood-forming tissue), and gonads. Such doses have been calculated; those for a typical patient are shown in the Table.

Absorbed Doses of Radiation (in Millirads Per Breath) in Three Sites

Type of Radiation	Lungs	Blood	Gonads
β	36·9	9·4	1·7
γ	5·1	1·1	1·1
Total ($\beta+\gamma$) ..	42·0	10·5	2·8

Although on general principles the number of breaths has always been limited to the minimum necessary for obtaining useful results, it may be seen that the actual radiation hazard is small. The gonad dose of about 3 mr per breath must be compared with the dose of 100 mr delivered annually by natural background radiation. The dose to the lungs, some 330 mr altogether in eight breaths in this example, is comparable to that given in a chest radiograph and is much less than the 5–10 r per minute of chest screening.

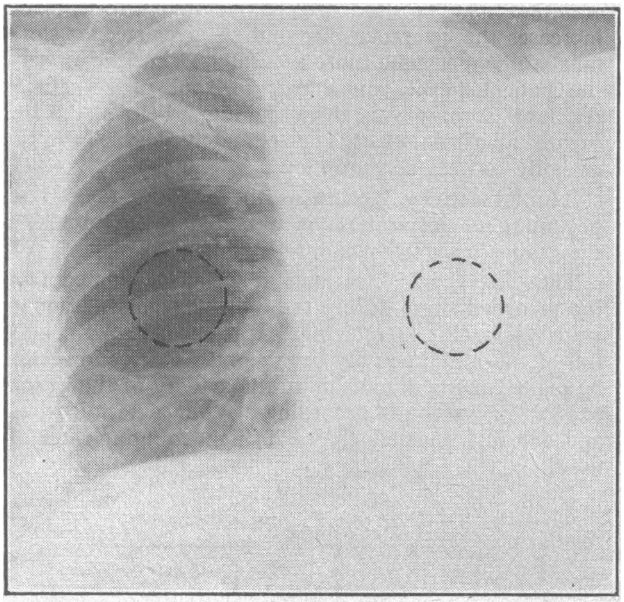

FIG. 4 (*a*)

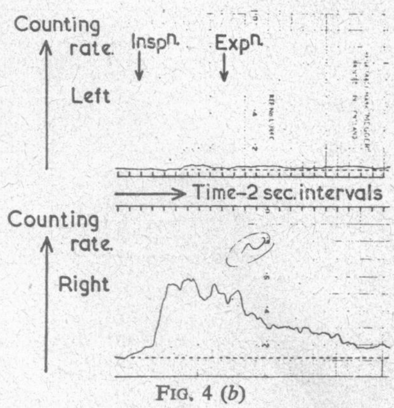

FIG. 4 (*b*)

FIG. 4.—Ventilation L.:R.=1:60. (*a*) Radiograph and (*b*) oxygen-15 tracings from a 60-year-old woman with extensive fibrosis of the left lung. Circles on the radiograph show the approximate regions studied. The lesions followed a pulmonary infection 40 years previously. The tracings show, as predicted, that there is no evidence of ventilation in this region of the abnormal lung.

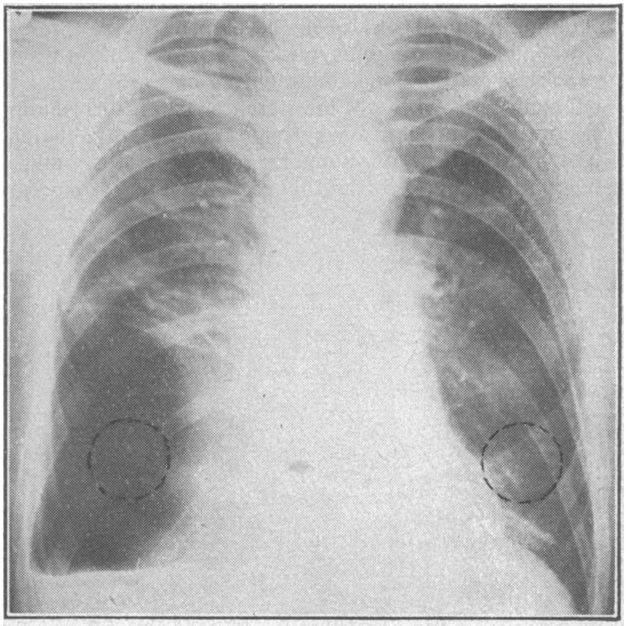

FIG. 5 (*a*)

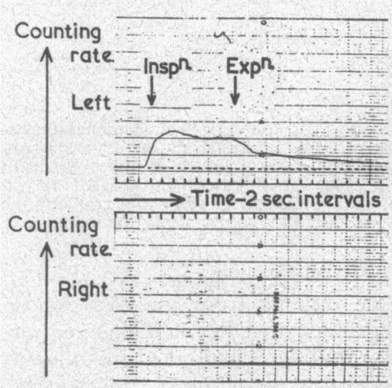

FIG. 5 (*b*)

FIG. 5.—Lower zone. Ventilation L.:R.>30 : 1. Clearance rate: L.=1.2% per sec.; R. = not measurable. (*a*) Chest *x*-ray film and (*b*) oxygen-15 recordings from the abnormal zone of a patient with a single lung cyst. The patient was a man aged 53, with no abnormal symptoms. The tracings show no measurable ventilation of the cyst. In the lung above it other tests showed greater ventilation than on the normal side.

Results

Tracings from a normal subject are shown in Fig. 3, which demonstrates typical features of records from coincidence and parallel counting. Normal values for comparative ventilation of symmetrical regions of the lungs have given a mean ratio of 1.0, with a standard deviation of 0.2 (in an individual observation). Duplicate measurements on the same subject agree within an average of 10% of their mean value.

Estimates of clearance rates in the upper zones of normal men, in the sitting position, have given a mean value of 1.0% per second, with a standard deviation of 0.4% per second. Duplicate measurements agree within an average of 30% of their mean value. In the lower zones the clearance rates are higher.

Some examples of the application of the procedures are shown in Figs. 4 to 10. Clinical details are given with the illustrations.

The first patients are those in whom clinical assessment was fairly complete, so that the results of the test could largely be predicted. The first case, illustrated in Fig. 4, is that of a woman with severe chronic fibrosis of the left lung. Tests with oxygen-15 showed no evidence of ventilation in this lung. Similarly, Fig. 5 shows the findings in a man with a large single cyst in one lung. This cyst was not ventilated, but the lung above it showed greater ventilation than that on the other side.

Some effects of changes in blood-flow are shown in Figs. 6 and 7. In the first case there is abnormally increased flow, and the test shows unusually high clearance rate. Conversely, Fig. 7 shows the graphs of a patient with pulmonary artery thrombosis. Over the abnormal lung, clearance rate is much reduced, but rises appreciably after exercise.

Thus in these examples tests with oxygen-15 gave the type of result predicted. In other instances the test gave results not available from other techniques. Thus Fig. 8 shows the findings in a man with an abnormally radiotranslucent lung. In the area of greatest abnormality it was possible to demonstrate reduced ventilation, no clearance during the breath-holding period, and slow washout in subsequent normal respiration. Inspiration of the abnormal lung was also delayed compared with the normal side. In other techniques these changes would have been obscured by the more normal function of the upper lobe. Fig. 9 shows the findings on a male talc-worker whose *x*-ray film showed unilateral shadowing, attributed to talc pneumoconiosis. It was suggested that one lung was radiologically clear because it was not ventilated. The test showed, however, that the lesser ventilation was on the side of the shadows; hence this was the abnormal side.

Fig. 10 illustrates a case of bilateral emphysema with gross bullous disease limited to the right lung. The investigation showed that both ventilation and clearance rate were only moderately reduced in the bullous lung.

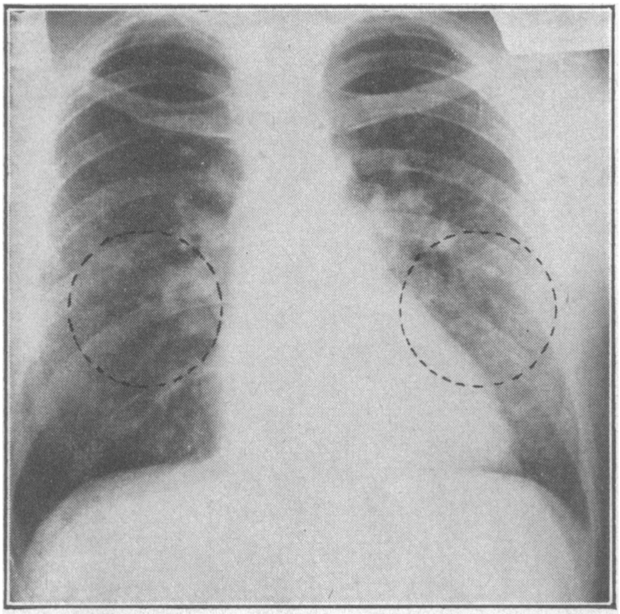

FIG. 6 (*a*)

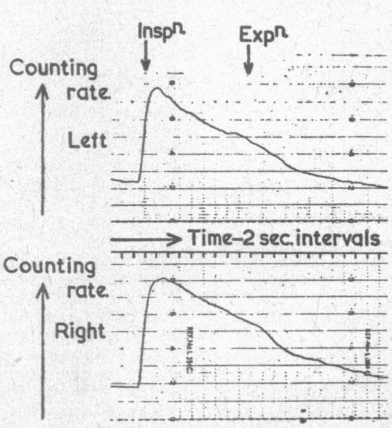

FIG. 6 (*b*)

FIG. 6.—Ventilation L.:R.=0.9:1. Clearance rate: L.=2.5% per sec.; R.=1.8% per sec. Recordings from a man aged 36, with high pulmonary blood flow of 15–20 l./min. This resulted from anomalous return of pulmonary veins to the superior vena cava. The patient had minimal symptoms. The *x*-ray film (*a*) shows large pulmonary vessels, especially on the left. Oxygen-15 studies (*b*) show ventilation approximately even, but unusually high rates of oxygen-15 clearance, especially on the left side.

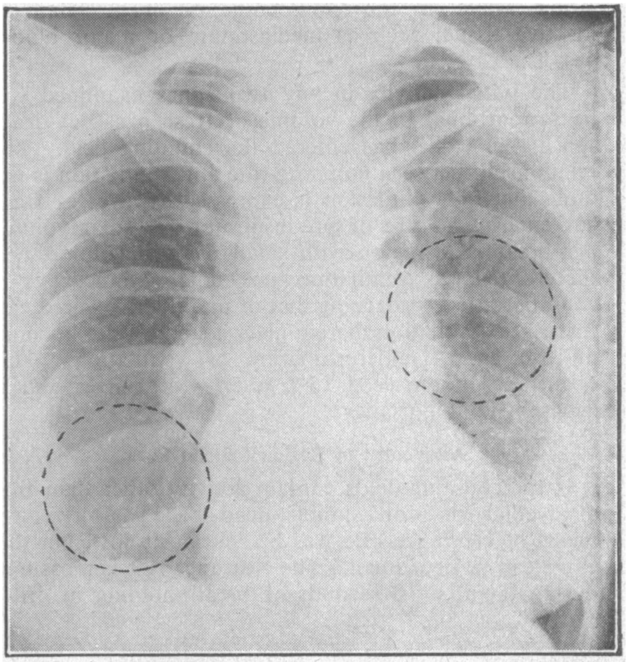

FIG. 7 (*a*)

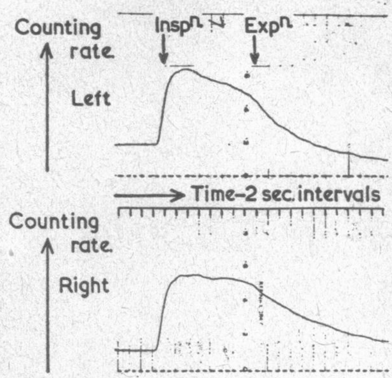

FIG. 7 (*b*)

FIG. 7.—Clearance rate: L. upper zone=1.4% per sec.; R. lower zone=nil. Recordings from a woman aged 45 with cardiac failure secondary to pulmonary thrombosis. *X*-ray films and angiocardiograms had shown large vessels in the left upper zone and almost no blood-flow in the right lower zone. Recordings from these sites (*b*), as marked on the *x*-ray (*a*) showed adequate ventilation but diminished clearance rate in the less vascular zone. (On exercise, clearance rate increased in both zones—to 3.1% per sec. on the left and 1.7% per sec. on the right.)

Discussion

Assessment of Relative Ventilation

To count repeatedly through the same tissue, or to compare recordings from opposite sides of the chest, it is essential to have accurate and symmetrical surface markings. Movement of the counters by only ½ in. (1.3 cm.), especially near the tapering lateral edge of the chest, can reduce the length of the core of lung tissue examined and thus the total counting-rate by up to one-third. A similar error in assessing ventilation arises if the core contains much relatively inactive tissue, such as mediastinum or major blood-vessels.

The initial activity in any two zones examined will be proportional to the volume of fresh gas (not dead-space gas) which has entered the counting field. The relationship between counting-rate and ventilation is not quite linear if ventilation is expressed as litres of fresh gas entering a litre of pre-inspiratory alveolar volume per breath. A region with small original volume, and therefore large ventilation per unit volume, has a counting-rate approaching that of undiluted inspired gas. Increased ventilation therein gives a smaller rise in count and so causes underestimation of ventilation. This error does not exceed 15% over wide ranges and is generally unimportant.

Assessment of Regional Blood Flow

If the counting-fields contain activity other than that of alveolar gas—for example, dead-space gas—measurements of clearance rate will be spuriously low, but this effect can be kept small. The clearance rate is measured during the first 10 seconds of breath-holding in order to prevent error caused by active gas in recirculating blood. In fact, the effect of recirculation on the slope of the tracing is seldom detectable, chiefly because of the small volume of blood in the counting-fields. As a further precaution patients are asked to relax during breath-holding, to prevent alteration of pulmonary blood-flow which might result from a Valsalva manœuvre, although in a few observations this has produced no effect.

The clearance rate as defined is faster for oxygen-15 than for the natural stable isotope oxygen-16. This is because molecules of oxygen are continually crossing the alveolar membrane in both directions as the blood moves along the capillary. Molecules move into the blood at a rate proportional to alveolar oxygen tension and move out at a rate proportional to capillary oxygen tension. Net oxygen exchange thus depends on the tension difference between alveolar and capillary oxygen—that is, the overall transfer of either radioactive or stable isotope is the difference between forward and backward flows. However, the ratio of forward to backward flow of oxygen-15 is initially much greater than that of oxygen-16 because of the appreciable

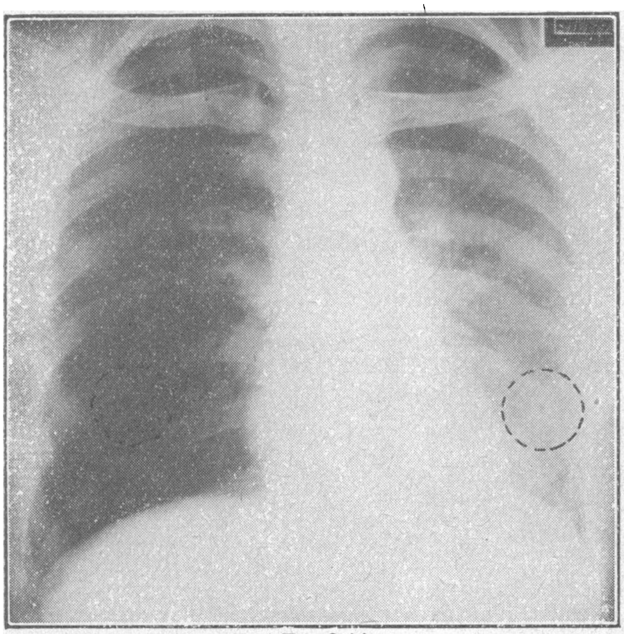

FIG. 8 (*a*)

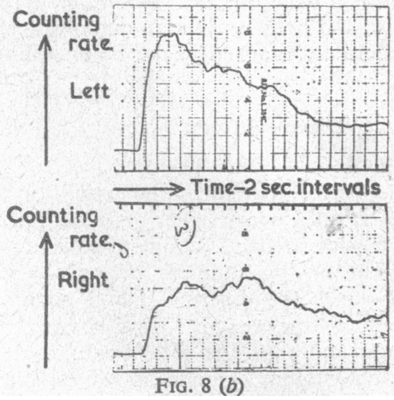

FIG. 8 (*b*)

FIG. 8.—Ventilation L.:R.=1.6:1. Clearance rate: L.=1.5% per sec.; R.=nil. Recordings from a 37-year-old miner. The patient suffered from moderate dyspnoea on effort. The *x*-ray film (*a*) shows that the right lung is significantly more radiotranslucent than the left. There was some doubt whether his left lung showed pneumoconiosis or his right lung was abnormally deficient in vessel markings. Oxygen-15 tests (*b*) in the upper zones showed less ventilation and clearance on the right side. In the lower zones, the tracings show that in the right lung there is moderately reduced ventilation but no oxygen clearance at all, and in subsequent normal respiration the radioactive gas is washed out abnormally slowly.

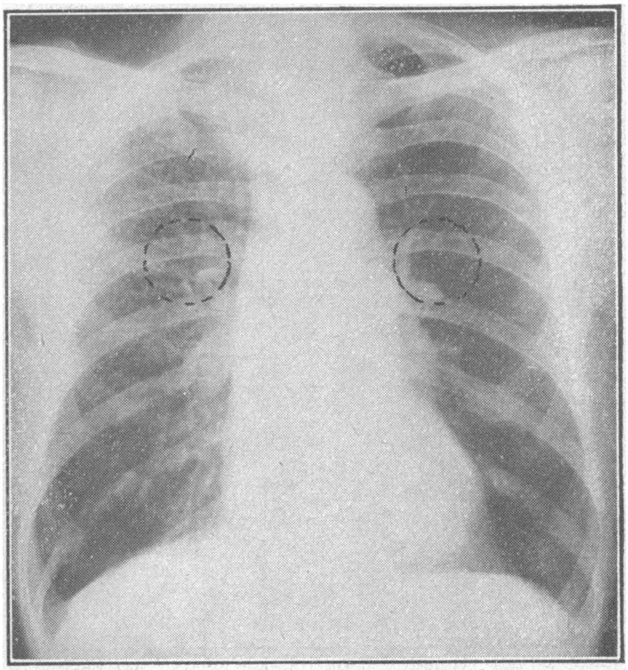

FIG. 9 (*a*)

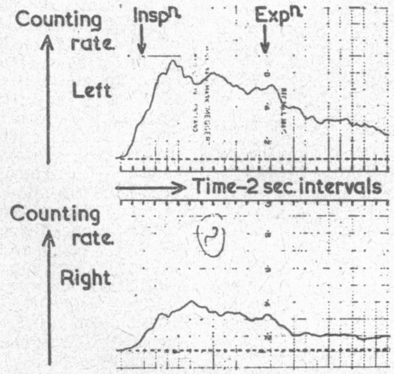

FIG. 9 (*b*)

FIG. 9.—Ventilation L.:R.=1.5:1. *X*-ray (*a*) and oxygen-15 recordings (*b*) from a man aged 41, with slight dyspnoea and suffering from recurrent lung infection. In the *x*-ray film there is abnormal shadowing in the right upper zone, which was attributed to industrial talc aspiration. The left lung was thought to be clear because it was not ventilated. In fact, the records show reduced ventilation in the region of the shadows, the left lung being better ventilated than the right.

partial pressure of oxygen-16 in mixed venous blood. Therefore the fractional transfer of oxygen-15 from alveoli to blood is greater than that of oxygen-16. This phenomenon has been studied in detail, and the results will be published elsewhere (Dyson, Sinclair, and West, in preparation).

The clearance of oxygen-16 in a small region of the lung is limited chiefly by the blood-flow ; the ventilation and diffusing characteristics of the tissue are relatively unimportant. In the same way, the clearance rate of oxygen-15 in any region depends mainly on local blood-flow. However, the oxygen-15 clearance rate may be high when the oxygen-16 clearance rate is normal—for example, in the presence of a high cardiac output with a low arteriovenous oxygen difference. An instance is the case of anomalous venous return illustrated in Fig. 6. Generally, clearance will increase when cardiac output increases—for example, in excitement and exercise ; while it will decrease with reduction of blood supply to a region. The clinical cases presented generally support these conclusions, and for most purposes oxygen-15 clearance rate gives a useful assessment of local blood-flow.

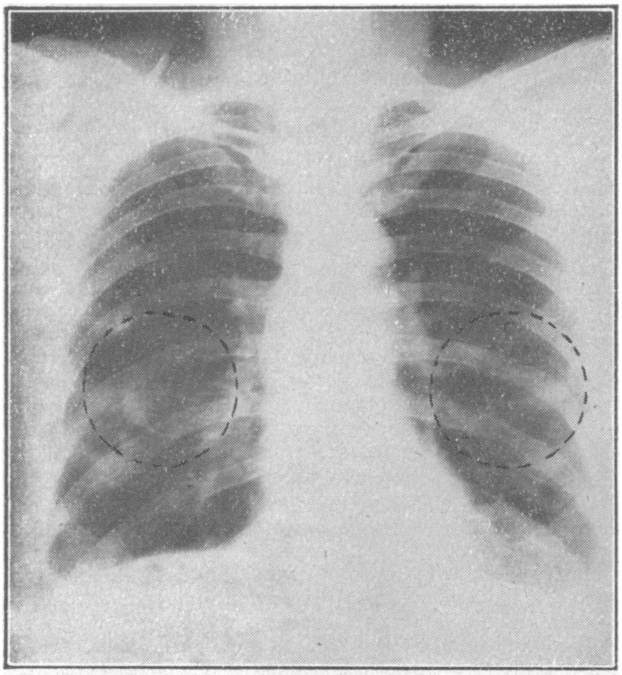

FIG. 10 (*a*)

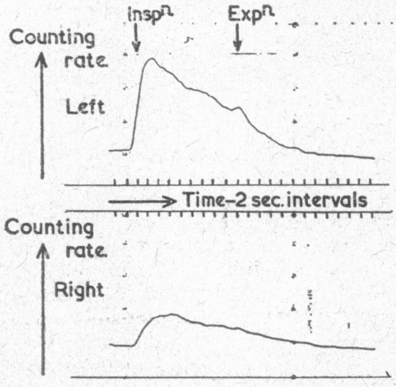

FIG. 10 (*b*)

FIG. 10. — Lower zone. Ventilation L.:R.=2.2:1. Clearance rate: L.=1.9% per sec.; R.=1.0% per sec. Radiograph (*a*) and recordings of oxygen-15 tracings (*b*) from a man aged 58 with bronchitis and emphysema. The *x*-ray film shows extensive bullous disease of the right lung. In the upper zones, ventilation had been shown to be approximately equal; in the lower zones it is reduced, as shown, on the right compared with the left. The clearance rate is also lower on the right.

Conclusions

The enormous advantage of being able to make regional assessments of ventilation and blood-flow, particularly without discomfort to the patient, needs no elaboration. In some 30 patients tested, informative data have been obtained. The test requires the simplest manœuvres from the patients, and the breath-holding is the only deviation from physiological conditions. In this, the test contrasts strongly with bronchospirometry, which requires intubation and local anaesthesia. Moreover, bronchospirometry cannot easily be repeated, whereas tests with oxygen-15 can.

The oxygen-15 test does not measure function of a definite anatomical lobe or segment, and in this respect the procedure compares less favourably with the studies of Mattson and Carlens (1955) and Clarke *et al.* (1958), who have sampled gas from the right upper lobe. Data obtained at bronchoscopy by regional sampling of expired gas from other individual lobes and segments (Hugh-Jones and West, 1960) are complementary to those obtained with oxygen-15.

In tests so far, function in any region has usually been assessed by comparison with function elsewhere. If conditions were rigidly controlled, absolute measurements in a single region should be meaningful. For the assessment of ventilation, the depth and level of inspiration, and the length of the core of lung tissue under observation would need to be known. For oxygen-15 clearance rate to give an absolute value of perfusion, it would be necessary to know more about the factors affecting local oxygen-15 and oxygen-16 uptake ; these factors are being further investigated. At present, the most useful information is that obtained from the comparative data of simultaneous records.

The test may not demonstrate generalized lung disease at all, for compensatory changes may maintain normal ventilation and clearance rates. In localized abnormalities such compensations presumably do not occur, and so the present scope of the test lies in the investigation of function within discrete pathological lesions of lung. Here it can provide unique information on the extent and timing of ventilation and on the amount of local perfusion.

Clearly a radioisotope with a half-life of two minutes can be used only at the place of its manufacture, and the work described has been possible because of the presence of the Medical Research Council's cyclotron in the hospital grounds. However, a cyclotron is not unique in its ability to produce oxygen-15 ; 3-MeV deuterons are necessary, and these can be produced by small pressurized electrostatic generators. Oxygen-15 can also be produced at low activities with electron accelerators of 20 or more MeV. The reactor-produced isotope oxygen-19 with a half-life of 30 seconds might also be used where a reactor is available.

Longer-lived isotopes can, if necessary, be used, especially when they are not absorbed in the body ; for example, ventilation has already been studied by Knipping *et al.* (1957) using xenon-133 (half-life 5.28 days), and krypton-85 (half-life 10.4 years) has been used in studies of circulation (Jaimet *et al.*, 1958 ; Sanders and Morrow, 1958). If the gas is absorbed in the body, the radiation hazard may be greater and serial tests more difficult because of the gradual build-up of activity. Nevertheless, methyl iodide labelled with iodine-131 (Jaimet *et al.*, 1958) and carbon monoxide labelled with carbon-11 (Tobias *et al.*, 1945) have been employed, again in circulation studies. The use of such gases, combined with external counting over lung, could be complementary to the oxygen-15 technique and broaden the approach to the clinical problems described in this paper.

Summary

The cyclotron-produced radioactive isotope oxygen-15, with a half-life of two minutes, has been used to study regional lung function. There is no intubation of the patient.

Pairs of scintillation counters placed on the chest wall have been used to measure radiation from two regions simultaneously. From observation of counting-rates during breath-holding following a single inspiration of active gas, the relative ventilation and blood-flow of the regions is assessed.

This paper describes the results obtained in selected patients with abnormal lung function.

We thank Dr. Constance Wood, Director of the M.R.C. Radiotherapeutic Research Unit, and the physicians of this hospital and elsewhere who kindly referred their patients for the investigations; Mr. D. D. Vonberg, the senior cyclotron engineer, and his staff; Dr. Ter-Pogossian, of Washington University, St. Louis, for early discussions on the preparation and use of oxygen-15; and Mr. P. Buckingham, Mr. L. E. Baker, and Mr. W. Verney for valuable technical assistance.

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The Indian Government's Central Drugs Laboratory in Calcutta has now found a permanent home, while a new building has been constructed to house an associated chemical laboratory, a library, and a reading-room. The Government has also been approached to provide an air-conditioned animal-house with facilities for keeping all species of animals. The routine analytical work of the laboratory greatly increased during the year under review. (*Annual Report of the Central Drugs Laboratory, April 1, 1955—March 31, 1956.* Ministry of Health, Government of India.)

INTERSTITIAL-CELL TUMOUR OF THE TESTIS IN A CHILD

REPORT OF A CASE AND A REVIEW OF THE LITERATURE

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The rarity of interstitial-cell tumour of the testis in children prompts the following report. The preceding history and the urinary steroid excretion were of particular interest, and these findings are discussed in relation to 25 previously reported cases.

Case Report

The patient, a boy aged 11 years, was referred to us in January, 1956, because of an enlargement of the right testis present for one year. The family history revealed that a female first cousin had an arrhenoblastoma of the ovary at the age of 15.

In November, 1950, when aged 6, he had been sent to the children's department of a psychiatric hospital because of backwardness at school. It was observed at this time that he was nervous and dreamy, disliked his school studies, and became involved in many fights. He had shown intense hostility to his younger brother, and on one occasion had pushed his perambulator in front of a tram. It was noted that the patient's language was aggressive and that he resented authority, but no precocious development was found on physical examination.

Apart from this he was apparently a normal child until the age of 9 years, when he began to develop rapidly and exhibit abnormal physical strength. He became difficult to manage at home because of precocious puberty, and was sent to a children's hospital. Here it was thought that the left testis was underdeveloped. Radiological examination of the skeleton revealed no abnormality, his bone age being in accordance with his chronological age.

From June, 1954, until January, 1956, he continued his abnormal development, but at no time were there any symptoms referable to the right testis, apart from gradual enlargement.

A week after being seen in our out-patient department, he was admitted as an emergency case because of abdominal pain. There were no physical signs of an abdominal lesion to account for this, and his symptoms rapidly subsided.

On examination the patient had the appearance of a rather aggressive youth of about 18 (Fig. 1) because he was very muscular and hirsute. The external genitalia were of adult proportions. The right testis was enlarged, firm, regular, and not tender. The left testis was small and soft. The prostate, as assessed on rectal examination, was considered to be normal. No abnormality was detected in the nervous, respiratory, and cardiovascular systems. The blood-pressure was 110/70.

Investigations.—Radiology: Bone age, approximately 17 years (Fig. 2). Haemoglobin, 17.6 g./100 ml.; packed cell