CARBON MONOXIDE DIFFUSION

EXPERIENCE WITH, AND MODIFICATION OF AN OFFICE PROCEDURE

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To estimate the diffusion of gases across the alveolar-capillary membrane, one needs to know the partial pressure of the gas in the alveoli, its partial pressure in the blood, and the volume of gas transferred from alveoli to blood per minute. A gas such as carbon monoxide (CO) has a negligible partial pressure in blood.

Two methods exist for estimating CO diffusion: In one, rebreathing of CO in small concentrations until a steady state exists in the alveoli, is employed, and in the other a single breath which is held for approximately 10 seconds. The various criticisms which have been applied to these two methods need not be fully considered here.[1] The main difficulties are to obtain a representative alveolar pCO in abnormal subjects by the first method, and the fact that disappearance of CO is not truly exponential in the second method and that $D_{L_{CO}}$ so calculated tends to decrease with the time of breathholding.[1]

The first method seems to be most commonly used, and results are expressed either (*i*) as the percentage of CO removed or extracted from inspired gas mixtures, when only the CO concentrations of inspired and expired gases need be known, or (*ii*) as the diffusing capacity of the lungs $D_{L_{CO}}$, when in addition to the above measurements, the alveolar CO concentration, as determined in end-tidal samples, should be known.

McNamara *et al.*[2] have already compared these 2 measurements and found that percentage CO extraction and $D_{L_{CO}}$ are both of equal value in differentiating between normal and abnormal diffusion. They[2] also compared these results with the measurement of conductance of the lung (C_L), a term which they borrowed from Dornhorst.[3] Conductance gives 'an accurate measure of gas transfer from air to pulmonary capillary blood at the time of the test' and serves 'as an index of the efficiency of the whole conducting pathway'.[2] It does not, however, discriminate as effectively between normal and abnormal diffusion as $D_{L_{CO}}$ or CO% extraction.[2]

The infrared CO analyser gives reliable results in determining the CO concentrations in the various gases. The capital outlay required for an infrared CO analyser precludes this technique from being used in most hospitals, and in South Africa even the pulmonary physiology units of the larger teaching hospitals do not have such facilities.

The recent description of a technique by Milledge,[4] in which a pallado-sulphite detector is used for estimating CO concentration, has made diffusion studies an office procedure. It also allows such studies to be carried out at the bedside of severely disabled patients. This technique has been employed to measure the CO percentage uptake. CO percentage uptake, however, falls on exercise, while D_L and C_L increase as a larger surface area for diffusion, and an increase in pulmonary blood flow are established. The fall in CO percentage uptake on exercise could be explained on the basis of the fact that ventilation is not taken into account. Hyperventilation increases the volume of gas absorbed, but lowers the percentage of the gas removed from the inspired air.[2] As it is confusing to express an increased function by a decrease in the determined values, it seems advisable to use C_L when the palladosulphite technique is used for determining diffusion capacity in exercise studies.

This paper records our experience with Milledge's[4] technique in 18 normal subjects and in patients with emphysema and fibrosis. The C_L was done at rest and during exercise in normal subjects and in patients, and the results are compared with those of other workers using an infrared CO analyser.

* This work was carried out in association with the Degenerative Diseases Group, CSIR.

METHODS AND MATERIAL

The first few cases were done exactly as described by Milledge.[4] Subsequently, a larger bag was used for the inspiratory gas mixture, and a gasometer has been added to measure the expired minute volume. Fig. 1 illustrates the apparatus used,

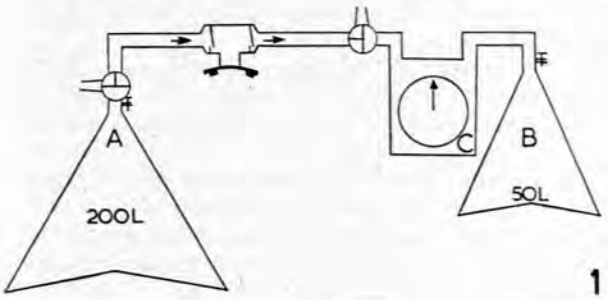

Fig. 1. Diagram of apparatus used. Bags A and B are 200- and 50-litre Douglas bags.

and the following description refers to the bags A and B as shown in this diagram.

Bag A is prepared by charging it with 200 litres of oxygen and approximately 520 ml. of coalgas. The CO concentration is measured by means of the pallado-sulphite detector and is approximately 0·04%. The patient breathes room air through the two-way taps until accustomed to mouthpiece-breathing through the one-way valve. The two taps are then turned so that the patient inspires from Bag A and expires into bag B through the gasometer C. After exactly one minute, as timed on a stopwatch, the taps are closed and the CO concentration in bag B measured. The gasometer gives the minute volume of breathing. For exercise studies the same procedure is carried out after the patient has commenced stepping on a 22 cm. step at approximately 15 steps per minute. The barometer reading and temperature are noted.

$$\text{CO uptake } \% = \frac{F_{ICO} - F_{ECO}}{F_{ICO}} \times 100$$

$$C_L = \frac{MV_I\, F_{ICO} - MV_E\, F_{ECO}}{F_{ICO}\ (BP - WVP)}$$

where MV_I and MV_E are the minute volumes (inspiratory and expiratory respectively) F_{ICO} and F_{ECO} are the inspired and expired concentrations of CO. BP = barometric pressure in mm. Hg and WVP = water-vapour pressure at room temperature. As the difference between MV_I and MV_E is small (0·1 litre per 10—20 litres ventilation) the results are not materially influenced by measuring only the one or the other,[2] in our case MV_E.

Nine normal male and 9 normal female subjects were studied. These were members of the resident staff, technicians, typists, and nurses. All were free from any respiratory complaints and most of them had repeated pulmonary-function tests performed on them, falling within the limits of normal. The patients were referred for pulmonary-function tests and the diagnosis of emphysema rested on clinical and physiological data. They ranged from patients with early emphysema to a severely disabled patient with cor pulmonale.

The patients included under the term 'fibroses' consisted of 3 with diffuse pulmonary fibrosis and 3 with a fibrosis involving a sufficiently large portion of one or both lungs to show a restrictive abnormality in the lung volumes.

RESULTS

The results of CO percentage uptake are presented in Fig. 2.

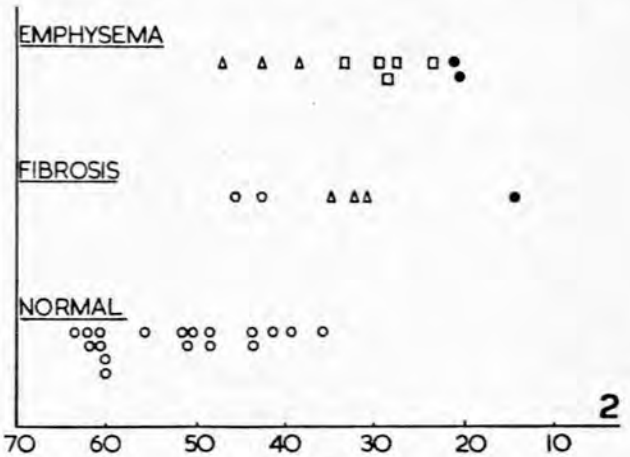

Fig. 2. Percentage CO uptake. Results in normal subjects and patients with emphysema and fibrosis.

○ No dyspnoea.
△ Grade I dyspnoea.
□ Grade II dyspnoea.
● Grade III dyspnoea.

The patients' degrees of dyspnoea are indicated. The results of C_L at rest and during exercise in 9 normals and 8 patients are shown in Fig. 3.

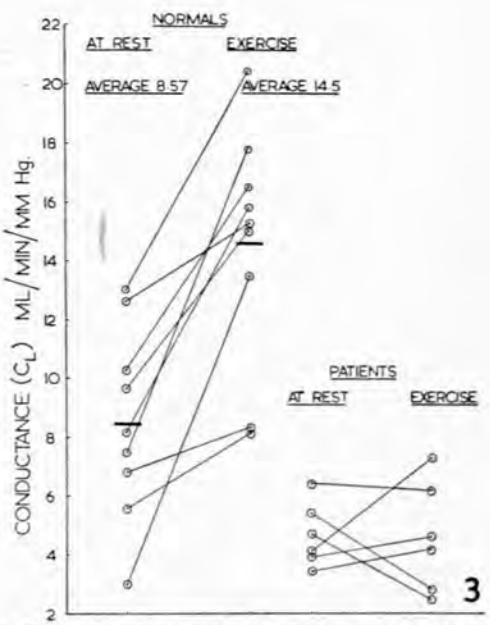

Fig. 3. Conductance at rest and during exercise in normal people and patients (same scale applied to both).

Not having an infrared CO analyser, our results are compared with those of other workers using such an analyser.

Our average value for normal subjects (52·5%) is similar to those of Milledge for 14 subjects (52%). It is also comparable to the results obtained on 21 cases (51·1%) and 10 cases (53·0±2·24) studied by McNamara *et al.*[2] and Bates[5] respectively. The last-mentioned two series were studied by means of an infrared analyser.

Normal persons with an unexpectedly low D_L or CO percentage uptake were found to be hyperventilating in McNamara's[2] series, and they consider it advisable to state the ventilation when reporting such values. The ventilation was, however, not recorded in the 2 normal subjects, with unexpectedly low values in this study. Fig. 2 also illustrates, as those of the other workers,[3,4] the difference between normal and abnormal subjects. The general correlation with the severity of the condition was also demonstrated (Fig. 2).

Our average C_L of 8·54 ml./min./mm.Hg compares favourably with that of McNamara *et al.*[2] (6·5±1·66), and the average during exercise (14·5) is comparable to their values (15·4±2·5) during a comparable exercise load (20 cm. step at approximately 15 steps per minute).

DISCUSSION

Bates[6] summarizes the clinical applications of diffusion studies as follows:

1. Pulmonary emphysema, where the overall diffusing capacity gives an indication of the state of the lung parenchyma. This information is not obtained from any of the ventilatory tests.

2. Obscure pulmonary infiltrations, where the impairment of diffusion will forecast the alveolar changes that the pathologist will demonstrate and that the radiologist may have difficulty in showing.

3. It may be used in the study of cardiopulmonary phenomena such as left ventricular failure, where diffusing capacity may be a sensitive indicator of change in pulmonary congestion.

We found this test of value when used in conjunction with qualitative methods for diffusion capacity (as commonly employed in the absence of a more specific method for CO diffusion). Qualitative methods are the estimation of O_2 saturation and pCO_2 in arterial blood. Owing to the fact that CO_2 has a greater solubility (and thus diffusion constant) than O_2, impaired diffusion may present as arterial hypoxia with a normal or low pCO_2. Probably not always appreciated by the clinician, is the fact that marked ventilation/perfusion defects can cause the same abnormality, viz. arterial hypoxia and normal or low arterial pCO_2. In lobar pneumonia, where more than 30% of the parenchyma is involved, arterial hypoxia ensues. Because of reduced compliance, the work of breathing increases and the resulting tachypnoea lowers the pCO_2 by hyperventilating the normal 70% of lung parenchyma. The functional shunt of blood through the unventilated consolidated 30% causes hypoxia which, however, cannot be corrected by the increased ventilation in the normal part of the lung.[7] Arterial blood-gas studies (van Slyke for O_2 and Astrup method for pCO_2) are carried out as a routine on all patients referred to the pulmonary-function laboratory, and arterial hypoxia with normal or low pCO_2 may often erroneously be assumed to be specific for diffusion defects.

A 'pure' impairment of diffusion, such as may occur in the Hamman-Rich syndrome, sarcoidosis, etc., does not cause arterial hypoxia until diffusing capacity is reduced to about $\frac{1}{3}$ of normal.[1]

Rankin[1] found diffusing capacity to be one of the most valuable tests of pulmonary function, while Bates *et al.*[5] have concluded that $D_{L_{CO}}$ is the most sensitive guide to prognosis in emphysema. McNamara *et al.*,[2] showing that CO uptake provides 'an estimate of diffusing capacity of the pulmonary alveoli no matter how the results are expressed' (i.e. as CO% uptake or $D_{L_{CO}}$), make the simplified procedure of Milledge[4] a most useful and economic procedure. An overall accuracy of ±10% could be obtained in Milledge's study, as compared to the infrared analyser.

The expendable pallado-sulphite tubes retail at 69c in South Africa. By using a 200 l. bag a number of tests can be performed using 2 tubes to check the CO concentration in the inspiratory bag. We found that this stays the same throughout the day, but tends to fall if left for longer periods. By using the tubes from both ends, a duplicate estimate can be made at a cost of 69c per patient.

If this test is carried out in a large number of patients, the tests can become expensive. For larger institutions the choice seems to lie between a small capital outlay and ever-increasing expendable costs, or a large capital outlay and relatively low maintenance costs.

OPSOMMING

1. Die ondervinding met 'n eenvoudige sykamer-tegniek vir CO-diffusie, soos beskryf deur Milledge,[4] word bespreek. Goeie korrelasie is verkry met die resultate van ander werkers wat 'n infrarooi CO-analiseerder gebruik.[2,5] Daar kan doeltreffend onderskei word tussen normale en abnormale persone; ook is 'n breë verhouding tot die graad van dispnee in die pasiënte gevind.

2. 'n Geringe modifikasie van die tegniek word beskryf om die toets bruikbaar te maak tydens oefeningstudies.

3. Die kliniese waarde van die toets word bespreek.

I wish to thank Prof. A. J. Brink for advice and facilities to carry out this work and Dr. R. L. M. Kotze, Superintendent of the Karl Bremer Hospital, for permission to publish the material reported here. The technical assistance of Messers. H. J. B. Joubert and M. J. Theron is acknowledged.

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