APPLICABILITY OF REBREATHING METHOD FOR DETERMINING MIXED VENOUS CO_2 IN CASES OF CHRONIC PULMONARY DISEASE

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(Received for publication September 24, 1934)

The carbon dioxide tension of oxygenated mixed venous blood has long been used, in normal individuals and frequently in subjects with various forms of disease, in the determination of cardiac output according to the Fick principle. The method of rebreathing mixtures of CO_2 and oxygen, for establishing equilibrium between the CO_2 tensions of the lungs and the incoming venous blood, and at the same time oxygenating this blood, was first described by Christiansen, Douglas and Haldane (1); later by Henderson and Prince (2) and others. In 1922 Douglas and Haldane (3) showed that the same arteriovenous differences in CO_2 content were obtained in a given subject, whether the rebreathing procedure equilibrated CO_2 tensions only and oxygenated the blood in the lungs, or whether this procedure equilibrated simultaneously both CO_2 and oxygen tensions of incoming venous blood with the rebreathed air. Field, Bock, Gildea, and Lathrop (4) showed that arterial blood drawn during the course of rebreathing a mixture of 6 per cent CO_2 and 94 per cent oxygen was fully oxygenated, and that the CO_2 tensions in arterial blood and in the rebreathed air were the same. Most workers have been able to demonstrate an equilibrium of CO_2 tensions by similar rebreathing technique; Hamilton, Moore and Kinsman (5), however, were unable to establish equilibrium or "plateau" levels of CO_2 during rebreathing in experiments with a small number of subjects. Richards and Strauss (6) in 1930 reviewed the numerous assumptions made in various rebreathing methods for estimating the values of the gases of the mixed venous blood. They showed experimentally that the same equilibria or "plateau" levels of CO_2 tension of oxygenated mixed venous blood could be regularly obtained in a normal subject after 15 to 20 seconds of rebreathing, with the use of initial mixtures in the rebreathing bag which differed in CO_2 tensions by 10 mm. or more. By constructing a nomogram of the subject's blood, and by plotting on this nomogram the CO_2 tensions (as obtained by rebreathing) of (*a*) oxygenated and (*b*) true mixed venous blood, these authors found that the (*a*) and (*b*) CO_2 tensions represented approximately the same CO_2 content of the blood.

It is of interest to inquire how far the method of rebreathing can be applied to the determination of CO_2 tensions in oxygenated mixed venous blood in cases with various forms of pulmonary disease. This inquiry forms the subject of the present paper. Specifically, answers have been sought, in each patient studied, to the following questions.

1. During the course of the rebreathing procedure can a constant or nearly constant ("plateau") level of CO_2 tension be demonstrated, which persists over a five second interval, or longer (e.g., from 15 to 20 seconds after the start of rebreathing)?

2. If this is the case, can the same plateau level of CO_2 tension be arrived at, in successive experiments, when the initial CO_2 tensions in the rebreathing bag differ by several millimeters?

3. When such a transient equilibrium of CO_2 tension in the rebreathed air is established, is there at the same time a close agreement between the tensions of CO_2 and oxygen in the air sample taken at the end of expiration ("alveolar" air), and the CO_2 and oxygen tension in the blood leaving the lungs (arterial blood)?

That the establishment of these three equilibria indicates that the plateau level of CO_2 tension is the same as that of the oxygenated mixed venous blood, may be argued as follows:

The complete oxygenation of the arterial blood

during rebreathing shows that all parts of the lungs which are perfused with pulmonary blood are at least partially ventilated. The close agreement between the CO_2 tension of the alveolar air with that of the arterial blood during rebreathing indicates that there are no large regions of the lungs in which the CO_2 of the regional, true alveolar air is appreciably different from the CO_2 of the "alveolar" (expired air) sample as measured. If there were such regions the arterial blood sample taken during rebreathing would have a CO_2 tension different from that of the "alveolar" sample as measured, except for an improbable or occasional situation in which regional variations in CO_2 tension of alveolar air or pulmonary capillary blood happened to result in a mean arterial tension identical with that in a sample of the expired air. If mixing of rebreathed air throughout the lungs and the rebreathing bag is complete, and if the same CO_2 tension after rebreathing is reached within the circulation time of the blood in successive experiments when the initial tension of CO_2 rebreathed in each experiment is different, there is no reasonable explanation other than that the excess of CO_2 has been carried away by the blood, or the needed deficit of CO_2 supplied by the incoming blood, and that the state of equilibruim means an essential identity between CO_2 tension in the alveolar air and in the oxygenated mixed venous blood. There may actually be certain small systematic differences, due to recirculation of small amounts of blood (such as that of the coronary circulation), or to continuous concentration of the rebreathed air due to absorption of oxygen; these factors have been discussed by Richards and Strauss (6) and need not be reviewed further. A false equilibrium or "plateau" level may also be obtained by the use of a very high concentration of CO_2 in the rebreathed air, as shown both on theoretical and experimental grounds by the same workers; but there would be in this case no identity of equilibrium with respect to CO_2 tensions, when different initial mixtures of CO_2 were used.

The equality of the levels of equilibrium on successive rebreathings also indicates that the individual studied is in a steady state with respect to his mixed venous blood gases.

In abnormally functioning lungs, the rebreathing process may not provide complete mixing between true alveolar air and that in the rebreathing bag, as for instance in a case with large volume of residual air, or one with a small or poorly distributed tidal air. Does the establishment of the three equilibria above mentioned indicate even in this case that the level of the plateau of CO_2 tension is the same as the level of CO_2 tension of the oxygenated mixed venous blood? With respect to the equilibrium which does exist between the CO_2 tension of the sample of expired or "alveolar" air, and the CO_2 tension of the sample of arterial blood drawn during rebreathing, the same argument that has just been given holds true: namely, that the CO_2 tension of the sample of expired air represents at least the resultant or mean of the CO_2 tensions in the pulmonary capillaries. If equilibrium with respect to CO_2, between incoming blood and alveolar air did not exist, there would be a general trend of change of CO_2 tension in successive samples of expired air, toward the level in the blood, though with incomplete mixture such a trend might be at times irregular. Thus, so far as concerns the successive CO_2 tensions of expired air, measured at 5 second intervals during rebreathing, it is quite possible that incomplete mixture might result in irregularities in the curve of change of these values, and that false "plateau" levels might appear in the curve. In this case, however, it is unlikely that such apparent equilibria would occur regularly over the same time interval; and still more unlikely that with different initial mixtures of CO_2 in the rebreathing bag, the same equilibrium should be thus reached in successive experiments over the same time intervals.

From the argument just given it seems a reasonable conclusion that if the three equilibria above outlined are established consistently in a given case, then the CO_2 tension so defined is close to that of the oxygenated mixed venous tension. The question of the magnitude of the error involved in the determination will be discussed after the data are presented.

It should be noted that in the process of equilibration by rebreathing for the determination of oxygenated mixed venous CO_2 tension, there is an inherent advantage not shared by a technique employing inhalation of a foreign gas; in that poorly ventilated parts of the lungs, during the process

of rebreathing, will be constantly receiving CO_2 from the incoming venous blood, as well as from the rebreathed air; and the CO_2 tension of oxygenated mixed venous blood is therefore more readily attained throughout the lungs, providing that ventilation is sufficient throughout to bring about complete arterial oxygenation. It is therefore possible that a method of rebreathing CO_2 may be valid in cases where a method using inhalation of a foreign gas is not.

The question may well be raised, why equilibration for oxygenated mixed venous CO_2 was attempted in the present investigation, rather than equilibration for mixed venous oxygen or for both true mixed venous CO_2 and O_2, as in the technique of Burwell and Robinson (9). The chief reason for our choice of method was the results of Richards and Strauss (6), who demonstrated both on theoretical and experimental grounds, in normal subjects, the difficulty of securing adequate equilibrium of rebreathed gases, with respect to oxygen. Presumably this difficulty would be increased in subjects with disturbed pulmonary function. Grollman, Friedman, Clark and Harrison (10), in a recent paper, have brought out some of the practical difficulties of oxygen-equilibration methods. Friedman, Clark and Harrison (11) have subsequently described an adaptation of the Burwell-Robinson technique, modified by the use of longer rebreathing periods, repeated samplings during rebreathing, and arterial blood samples also drawn during rebreathing. It may be that this method will be found applicable to certain cases of pulmonary disease.

An important assumption should perhaps be mentioned, which is made both by methods employing the Fick-principle and by most methods using inhalation of a foreign gas (6, 12); namely, that any change in blood flow produced by the hyperventilation of rebreathing, does not measurably affect the arteriovenous differences of oxygen or CO_2 within the time during which rebreathing takes place.

METHODS

The apparatus and technique were essentially the same as those employed by Richards and Strauss (6). A diagram is shown in Figure 1.

For the experiment, the subject was in the resting post-absorptive state, lying supine, with one pillow. Mouthpiece and noseclip were applied and the subject respired

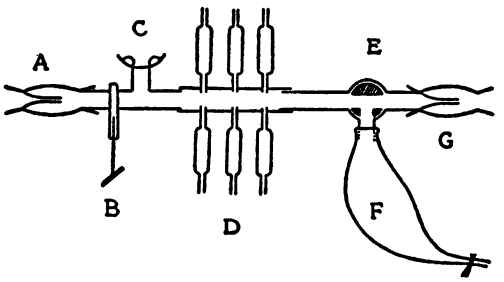

FIG. 1. DIAGRAM OF APPARATUS USED FOR OXYGENATED MIXED VENOUS CO_2 TENSION DETERMINATIONS.

A, intake flutter valve. *B*, shut-off slide valve. *C*, mouthpiece. *D*, evacuated gas sampling tubes. *E*, three-way valve, connecting with rebreathing bag *F*. *G*, outflow flutter valve. For cardiac output determination, the same apparatus was used, outside air being led in through valve *A*, and expired air from *G* collected in a Tissot spirometer.

through the apparatus for about ten minutes, so that a steady state might be reached. At a signal "blow," given at the end of a normal expiration, the subject made a complete expiration, while slide valve *B* was closed off. An alveolar sample was then taken into one of the evacuated tubes, and valve *E* then turned to connect the subject with the rebreathing bag. The subject then emptied and filled the bag completely, by successive respiration, a sample being taken into the evacuated sampling tubes every five seconds at the end of complete expiration. The rate of respiration varied with the subject; those with large vital capacities and slow resting respiratory rates made only four or five complete respirations in 20 seconds, those with small capacities and rapid rates rebreathed six or seven times in 20 seconds. The volume of air used in the bag for rebreathing also varied with each subject, from 1,500 cc. to 3,000 cc.; the volume being such that the subject could just empty the bag completely with a deep, rapid inspiration.

Several preliminary experiments were made during the first few days of the investigation of a given subject, with the double purpose of training him in the technique of rebreathing and of determining proper concentrations of CO_2 to be used in the rebreathing bag. The remainder of the gas mixture was, of course, pure oxygen. Usually one experiment with a very high (over 60 mm.) CO_2 concentration and one with a very low (less than 45 mm.) were performed to provide an approximate estimate of the level of CO_2 tension reached by the subject during rebreathing. In succeeding experiments, intermediate concentrations of CO_2 were used, and the upper and lower limits were thus determined within which the rebreathing procedure brought the CO_2 tension to a constant level.

For the exact determination of oxygenated mixed venous CO_2, two or more experiments were performed on the same morning, and the CO_2 tension of the mixture of CO_2 and oxygen in the bag, as measured just before the

TABLE I

Carbon dioxide tensions of expired ("alveolar") air during the course of rebreathing CO_2–O_2 mixtures of varying initial CO_2 tensions

Patient	Date	Initial CO_2 tension in bag	Expired air tension of CO_2 after rebreathing for					Remarks
			10 seconds	15 seconds	20 seconds	25 seconds	30 seconds	
		mm. Hg	*mm. Hg*	*mm. Hg*	*mm. Hg*	*mm. Hg*	*mm. Hg*	
E. S.	June 21	60.5	48.8	49.1	48.1	49.1	49.8	Before pneumothorax
		47.9		48.2	48.6	48.3	49.5	
	August 5	54.4		48.3	47.7			Left pneumothorax
		52.7		47.7	48.7			70 per cent collapse
	September 21	49.4		47.6	48.0			85 per cent collapse
		51.6		47.2	46.9			
M. P.	January 23	48.8	42 7	42.0	42.2	42.2		Right pneumothorax
		49.2	41.3	42.1	42.1	42.2		40 per cent collapse
	January 27	46.5		41.7				Same
		42.6		42.3	42.3			
	March 7	50.6		44.7	45.0	45.9		Complete re-expansion
		39.1		43.6	44.9	45.8		
L. P.	March 7	49.7		47.0	47.5	47.1		Spontaneous pneumothorax,
		53.3			47.7	47.8	48.3	80 per cent collapse, positive pressure
	April 11	54.2	47.4	47.7	48.1	49.0	49.4	Re-expansion to 40 per cent on
		51.6	46.5	46.7		47.0	48.5	March 17, followed by 2nd spontaneous pneumothorax
	April 12	49.5	44.3	44.6		46.1	46.9	to 85 per cent collapse
		50.9	46.2	46.3		47.1	47.1	
	April 14	49.4	46.4	46.4	46.6	47.2	47.5	On April 14, 75 per cent col-
		52.3		47.0	47.3	47.6		lapse
I. A.	January 30	52.1		49.4	50.0	50.8		Spontaneous pneumothorax,
		53.9		51.4	51.1	51.3		positive pressure, 85 per cent collapse
	February 1	54.3		51.3	51.8			Same
		55.3		51.3	50.8			
J. H.	December 15	52.0		49.0	48.9			Advanced bilateral tuberculo-
		58.2		49.1	49.2			sis
	February 3	54.3		49.9	50.0			Same
		48.4		49.7	49.7			
	April 20	48.9	47.6	48.0	48.8	49.5	49.6	Right pneumothorax
		50.8	49.0	49.8	49.8	51.4	51.9	60 per cent collapse
J. M.	December 21	53.6		46.1	46.6	47.7	47.8	Advanced pulmonary fibrosis
		51.9		40.7	41.9	41.9		
H. E.	October 3	46.2	51.2	52.2	53.2	53.8	53.9	Pulmonary emphysema
		55.5	53.1	54,2	54.8	54.6	55.6	
		60.9		55.0	55.2	55.4	55.9	
	October 25	61.7	53.8	55.1	56.0	54.1	53.2	
L. C.	October 5	42.2	44.6	46.0	46.6	47.3	48.3	Pulmonary emphysema
		56.6	46.4	47.2	48.5	48.6	49.6	
		58.1	47.6	48.7	49.2	49.7	50.1	

rebreathing, was kept within equilibratable limits previously defined.

In the experiments in which CO_2 tensions obtained by rebreathing were compared with tensions in the arterial blood drawn during the course of rebreathing, the same technique of rebreathing was used. The subject first applied mouthpiece and noseclip. The region of the brachial artery was injected with novocaine. The needle

was then inserted into the artery but no blood drawn. Usually a drop or two escaped into the syringe, occasionally as much as 1 or 2 cc.; for this error, an easily calculated correction was applied later. The arterial puncture was usually a nearly painless procedure, not affecting the subject's pulse or respiration; even if it did, however, this would not disturb the establishment of the particular equilibrium which was being investigated. As soon as the needle was in the artery the signal for the beginning of the rebreathing was given, and the procedure carried out as outlined above. From the 20th to the 35th second of rebreathing, arterial blood was drawn, usually from 15 to 20 cc. being obtained.

The blood was drawn into an oiled syringe and transferred under oil into chilled bottles containing minimal amounts of dried neutral potassium oxalate and sodium fluoride, sufficient to make final concentrations of about 0.2 per cent of the former and 0.1 per cent of the latter. These salts were used in preference to heparin because of the greater stirring of the blood necessary with the latter substance to produce a uniform anticoagulant effect. Samples of the same blood, one treated with the oxalate-fluoride mixture, the other with heparin showed the same level of the CO_2 dissociation curve of oxygenated whole blood. The blood bottle was kept stoppered and on ice until the gas analyses were made. Duplicate analyses of the CO_2 and oxygen contents of the whole blood were made using the Van Slyke-Neill apparatus. One point (occasionally two) on the CO_2 dissociation curve of oxygenated blood was determined, the technique of equilibration being essentially that of Austin, Van Slyke, et al. (7) with a few modifications (8, 6). Blood was equilibrated in a water bath for 20 minutes at 37.2° C., duplicate analyses of CO_2 and oxygen contents of blood and gas phases of the system then made. A small correction for lactic acid formation during equilibration was made in the blood gas values. The CO_2 tension for this equilibration was planned so that it would be as nearly as possible the same as that of the oxygenated mixed venous tension to be determined. The slope of the dissociation curve was obtained from previous (or subsequent) studies of the same patient's arterial blood.

Blood drawn from the artery of the arm from 20 to 35 seconds after the start of rebreathing is approximately the blood that has passed through the pulmonary capillaries 5 seconds earlier, and should therefore have the same CO_2 tension if equilibrium between blood and pulmonary air were complete. It was noted above that a few drops of normal arterial blood usually entered the syringe before rebreathing began. This necessitated a small and easily estimated correction of 0.1 to 0.3 volumes per cent, in order to obtain the actual arterial CO_2 dissociation curve and its tension compared with that of the alveolar samples obtained from 15 to 30 seconds after the beginning of rebreathing.

RESULTS

Two cases of artificial pneumothorax with relatively normal pulmonary function were studied, two cases of spontaneous pneumothorax with strongly positive intrapleural pressures, two cases of pulmonary emphysema, and one case of advanced generalized pulmonary fibrosis with dyspnea. Of numerous respiratory experiments on each of these subjects, a few typical results are given in Table I. The studies of the arterial blood drawn during the rebreathing procedure are shown in Table II. More detailed clinical de-

TABLE II

Comparison of CO_2 tensions of expired ("alveolar") air after rebreathing, with CO_2 tensions of simultaneously drawn arterial blood

Patient	Date	Initial CO_2 tension in bag	Tension of CO_2 in expired air after rebreathing for				Arterial blood drawn 20 to 35 seconds after beginning rebreathing			Condition
			15 seconds	20 seconds	25 seconds	30 seconds	O_2 saturation	CO_2	CO_2 tension	
		mm. Hg	*mm. Hg*	*mm. Hg*	*mm. Hg*	*mm. Hg*	*per cent*	*volumes per cent*	*mm.*	
E. S.	November 5	50.0	48.6	49.0	49.4	49.5	101	56.8	49.4	Artificial pneumothorax
M. P.	January 24	45.0	39.6	39.7	40.4	40.3	101	46.2	42.6	Artificial pneumothorax
	February 11	43.4	39.0	40.0	40.2	41.0	100	45.2	40.4	Same
I. A.	February 21	53.1	50.0		51.0	52.0	99	53.3	50.0	Spontaneous pneumothorax
J. H.	March 31	48.6	42.6	45.3	45.3	45.4	98	54.9	47.0	Bilateral tuberculosis, pneumothorax
J. M.	December 12	51.9	40.5	42.2	41.9		99	51.7	42.6	Pulmonary fibrosis
H. E.	October 25	61.7	55.1	54.0	54.1	53.3	90	57.6	51.3	Emphysema
	October 28	56.7	53.2	54.2	54.0	54.2	100	58.8	49.0	

scriptions of some of the cases are given in a subsequent paper.

E. S., an Italian-American youth of 17, with an early tuberculous lesion in the left upper lobe, was studied before and during the course of establishment of a left pneumothorax. He had, as shown in Table I, an excellent capacity for rebreathing to a constant level varying initial tensions of CO_2 both before and after his pneumothorax. Furthermore, there was a close agreement (Table II) between rebreathed CO_2 tensions in the expired air and the CO_2 tension of the simultaneously drawn arterial blood; this experiment was done at a time when the patient had a complete left pneumothorax. Similar results were obtained with M. P., an Italian woman of 22, with a small healed lung abscess and a partial collapse, which was later allowed to re-expand; with the exception of a rather poor agreement between the CO_2 in the lungs and the blood in the first experiment (Table II), although there was complete oxygenation of the arterial sample. In the second experiment a good agreement was obtained.

L. P. and I. A. were young men each of whom developed a spontaneous pneumothorax with positive pleural pressure (+ 4, +8 in L. P., + 5, + 13 in I. A.). Each one also had a partial re-expansion, then a second spontaneous collapse and a second re-expansion while under observation. L. P. showed (Table I) at first a satisfactory equilibration to constant CO_2 tension in the rebreathing experiments, then a period (experiments of April 11th and 12th) following his second collapse when equilibration of CO_2 was less satisfactory; followed in turn by a third period when positive pleural pressure was reduced and re-expansion progressing, during which satisfactory equilibration was again attained. No blood experiment was done with this patient. The arterial blood experiment on I. A., done when pneumothorax was still nearly complete and pleural pressure positive (+ 5, + 13), showed a fairly good agreement of CO_2 tensions in the lungs and the arterial blood, though oxygen saturation was not quite complete.

Patient J. H., with advanced bilateral tuberculosis, showed, nevertheless, surprisingly good capacity for bringing varying mixtures of CO_2 and oxygen to an equilibrium during rebreathing. He had at this time a slight arterial oxygen unsaturation. Following a partial pneumothorax, when arterial oxygen saturation was only 87 per cent, he was not able to equilibrate CO_2 tensions by rebreathing quite as satisfactorily as before (Table I, April 20th). At this time an arterial blood experiment showed incomplete arterial oxygen saturation, and an arterial CO_2 tension differing by 1.7 mm. from the corresponding CO_2 tension of the alveolar air sample.

J. M., a patient with pulmonary fibrosis, markedly dyspneic but without arterial oxygen unsaturation, or CO_2 " retention," had a good capacity for equilibrating a mixture of CO_2 and oxygen by rebreathing; and equilibrium between lungs and blood during rebreathing could also be demonstrated. His respiratory state was, however, most unstable; this is suggested by the widely different levels of equilibrium, in respect to CO_2 tensions, reached in successive rebreathing experiments (Table I). A large amount of other work on this patient being published elsewhere has given ample proof of this fact.

The last two cases, H. E. and L. C., had pulmonary emphysema. With the former it was usually possible in rebreathing experiments to establish an equilibrium in CO_2 tension; though in some experiments the results were quite irregular. It was not possible, in two arterial blood experiments (Table II), to demonstrate the existence of equilibrium between tensions of the rebreathed expired air and the arterial blood. H. E. had arterial oxygen saturation, usually between 85 per cent and 90 per cent. With patient L. C., there was not demonstrable any equilibrium or " plateau " level of CO_2 tension in the course of rebreathing; the curves of CO_2 tensions of rebreathed expired air, plotted against time, as illustrated in Figure 2, and in the last experiment of Table I, are characteristic of the behavior of this emphysematous subject.

In brief, the experimental material shows: that in two cases of simple artificial pneumothorax, with pulmonary function otherwise good, and in one case of spontaneous pneumothorax with positive pleural pressure, it was possible to determine CO_2 tensions of oxygenated mixed venous blood by rebreathing methods; that there was some doubt of the applicability of the method in one phase of a second case of spontaneous pneumothorax with positive pleural pressure; that the

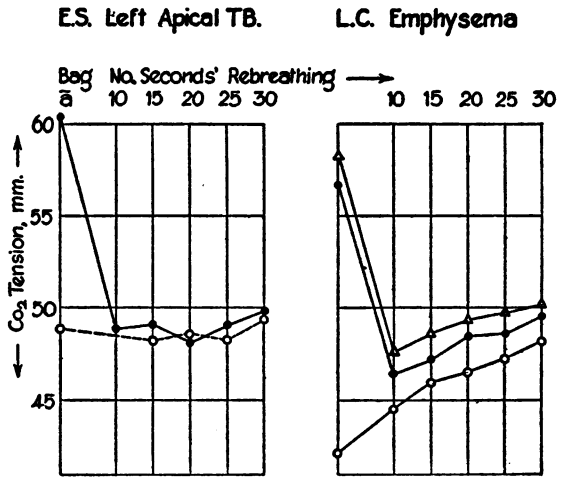

FIG. 2. CO_2 TENSIONS OF EXPIRED AIR DURING REBREATHING, SHOWING: EQUILIBRIUM REACHED BY E. S., ABSENCE OF EQUILIBRIUM LEVEL BY L. C.

First column (Bag $\bar{a}$) gives initial CO_2 tension in rebreathing bag, before rebreathing was begun.

method was shown to be unreliable in a case of advanced bilateral tuberculosis with pneumothorax, in a case of pulmonary fibrosis with marked dyspnea, and in two cases of pulmonary emphysema.

It is probable that the CO_2 tensions obtained are not the absolute values for the CO_2 of the resting oxygenated mixed venous blood; but that there are small systematic errors due to recirculation of small amounts of blood within 20 seconds, to the hyperventilation of the rebreathing procedure, and so forth. These factors have been discussed previously by various investigators. The method thus gives a relative rather than absolute measure of this function.

An estimate can be made of the limits of experimental error of the method. For our own purposes, in cases of abnormal pulmonary function (see subsequent paper (13)), these values of CO_2 tension are useful only in determining the actual CO_2 content of the mixed venous blood. It may therefore be well to estimate the experimental error of measurement of this latter function. A group of two properly conducted rebreathing experiments with a trained subject can be expected to give three of the four values of CO_2 tension at the 15-second and 20-second intervals agreeing within about 0.7 mm. or 0.8 mm. of CO_2 (see Table I). This difference represents about 0.3 volumes per cent of CO_2 content. In addition there is the experimental error of method in the level of the CO_2 dissociation curve on which these tensions are plotted; this is chiefly that due to the method of blood gas analysis, or plus or minus 0.1 volume per cent. These two sources thus constitute a considerable experimental error, of about 10 per cent in an ordinary determination of cardiac output, since the arterial arteriovenous differences of CO_2 with which one is usually dealing are only about 4 volumes per cent.

A final brief comparison may be suggested between the above method as applied to determination of cardiac output and the methods involving inhalation of a foreign gas. The errors of method are considerably less in the latter in cases with normally functioning lungs. On the other hand, it is probable that mixed venous CO_2 can be determined by rebreathing in certain cases of abnormal pulmonary function in which ventilation is not adequate for the determination of cardiac output by foreign gas methods. A further advantage of the technique which we have described is that it can determine the applicability or nonapplicability of the method in a given case. This advantage is also shared, however, by the Grollman technique (10), through the measurement of acetylene in the blood.

SUMMARY

1. The applicability of the method of rebreathing for determining CO_2 tensions of the oxygenated mixed venous blood in certain cases of pulmonary disease has been investigated.

2. The method required the demonstration of the same " plateau " levels of CO_2 tension in successive rebreathing experiments, when the initial CO_2 tensions of the mixtures in the rebreathing bag in the separate experiments varied by several millimeters; and the demonstration of equilibrium between CO_2 tension in the samples of expired air (during rebreathing) and the CO_2 tension in the simultaneously drawn arterial blood.

3. It has been found that the method gave satisfactory results in two cases of unilateral artificial pneumothorax; gave doubtful results in two cases of spontaneous pneumothorax with positive pleural pressures; and was unreliable in a case of advanced bilateral tuberculosis, a case of pulmo-

nary fibrosis with dyspnea, and two cases of advanced pulmonary emphysema.

4. By the technique described it can be determined in a given case whether the method of rebreathing is applicable or not.

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