The Journal of Clinical Investigation

# STUDIES IN CONGESTIVE HEART FAILURE XXII. A METHOD FOR OBTAINING “MIXED” VENOUS BLOOD BY ARTERIAL PUNCTURE

Ben Friedman, … , Gurney Clark, T. R. Harrison

*J Clin Invest.* 1934;13(4):533-546. https://doi.org/10.1172/JCI100603.

Research Article

# STUDIES IN CONGESTIVE HEART FAILURE

## XXII. A METHOD FOR OBTAINING "MIXED" VENOUS BLOOD BY ARTERIAL PUNCTURE

By BEN FRIEDMAN, GURNEY CLARK AND T. R. HARRISON

*(From the Department of Medicine, Vanderbilt University, Nashville)*

(Received for publication January 9, 1934)

### INTRODUCTION

Burwell and Robinson (1) devised a method for determining the cardiac output of man. These authors did not apply their method to patients with cardiac disease, for it was believed that in such cases diffusion of oxygen through the pulmonary membrane might be impaired, and hence the tension of oxygen in the rebreathing bag might be different from that of the venous blood. In an endeavor to overcome this possible cause of error we have developed a method in which "mixed venous blood" is taken from a peripheral artery while the subject breathes "venous air" which has been obtained by previous rebreathings. The technical details of our method are similar to those of the Burwell and Robinson procedure except for the final rebreathing, during which the blood samples are drawn. In the following pages data are presented which seem to indicate that the method allows one to obtain, from an artery, blood which has passed unchanged through the lungs.

### PRELIMINARY ADJUSTMENT OF THE AIR IN THE LUNGS

We found, as did Burwell and Robinson, that one can best obtain an accurate equilibrium by washing out the lungs with a low-oxygen high-carbon dioxide gas mixture, just before the subject begins to rebreathe from the bag. Unless this is done the bag is diluted at the beginning of each rebreathing with residual air which is so much richer in oxygen than the venous air that a true equilibrium cannot be obtained. In order to remove the excess oxygen from the residual air as rapidly as possible we prepared in a Tissot spirometer 60 to 80 liters of a gas mixture containing approximately 92 per cent nitrogen, 6.5 to 7.0 per cent carbon dioxide, and 0.5 to 1.5 per cent oxygen. Following a forced expiration the tap was turned so as to connect the subject to the valve and he then rapidly took two to four breaths from the spirometer, the expired air being discarded through the valve. In order to determine the optimal amount of "washing" necessary to bring the gas tensions in the residual air to approximately the venous level numerous analyses were made of alveolar air following varying amounts of " washing." The data are plotted in Figure 1.

Alveolar oxygen (black symbols) and carbon dioxide (hollow symbols) are plotted against the volume of the air breathed in the preliminary adjustment of the lung air before rebreathing from the bag was begun. The

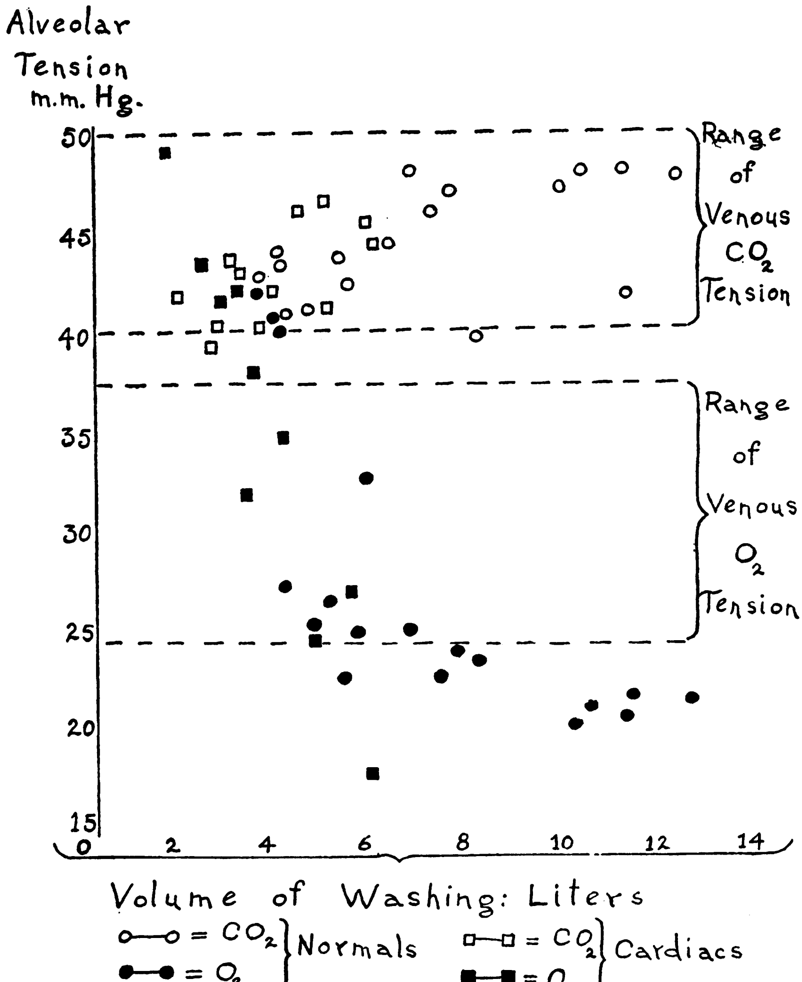


FIG. 1. PRELIMINARY ADJUSTMENT OF THE AIR IN THE LUNGS

gas mixture used in the adjustment contained about seven per cent carbon dioxide and one per cent oxygen. Almost all of the values for carbon dioxide fall within the range of the normal venous carbon dioxide tension. However, the oxygen values for both normal subjects (circles) and persons with cardiac disease (squares) tend to be above the venous oxygen tension when the volume of washing is less than three liters and below this range when the volume of washing is greater than seven liters. Values within the desired range are best obtained when the volume of air breathed is five to six liters, when the gas mixture has the composition described. This can be breathed in two breaths by normal subjects, whereas persons with cardiac disease require three to four breaths depending on the degree in which their vital capacities are reduced. In order to be certain that the volume of " washing " was approximately correct the spirometer scale was marked before each rebreathing, and the tap was turned into the rebreathing bag as soon as the subject had " washed " his lungs with the desired amount of gas. With well trained subjects the duration of this phase of the procedure was three to six seconds, leaving approximately twenty seconds for equilibration between the blood and the air in the bag.

### THE ATTAINMENT OF EQUILIBRIUM BETWEEN THE VENOUS BLOOD AND THE GAS IN THE REBREATHING BAG

The oxygen and carbon dioxide tensions of the " mixed " venous blood of normal persons are in the general region of thirty and forty-five millimeters of mercury, respectively. Consequently, we have prepared the rebreathing bag with about nine liters of a gas mixture of 4 to 4.5 per cent oxygen and 6.5 to 7 per cent carbon dioxide. In a large series of observations in which analyses of the contents of the bag were made after repeated rebreathings we found, as Burwell and Robinson did, that subjects with normal lungs will usually reach and maintain reasonably constant values, i.e., within two millimeters—for oxygen and carbon dioxide within six to eight rebreathings. Ten to twelve repetitions may be necessary in persons with mild cardiac failure. However, the fact that gas tensions become constant does not necessarily indicate that they are in equilibrium with the venous blood—for at the beginning of each rebreathing the air in the bag is diluted with the residual pulmonary air containing a gas mixture which, even though the " washing " has been correctly done, may be several millimeters different from the venous tension. Hence, if the volume of air used in washing the lungs and the duration of the rebreathing are constant one might obtain the same gas mixture in the bag at the end of each rebreathing, even though this mixture was not in equilibrium with the venous blood. In order to test this possible source of error a group of observations was made in which the subject rebreathed alternately from two bags of different oxygen content, one of them having less and the other more oxygen than the amount corresponding to the tension of the venous blood. It was found that in normal subjects and in patients with mild congestive failure the two bags reached the same oxygen content after repeated rebreathings. An example of such an experiment is shown in the broken lines of Figure 2. On the other hand, when the same procedure was repeated in cases with severe congestive failure, the two bags did not always reach the same oxygen content. Such a failure to obtain equilibrium occurred most commonly in persons with syphilitic aortic insufficiency. It indicates that the method is inapplicable to such cases.

During the final rebreathing it is necessary to exceed somewhat the minimum circulation time in order to obtain blood samples. The return of

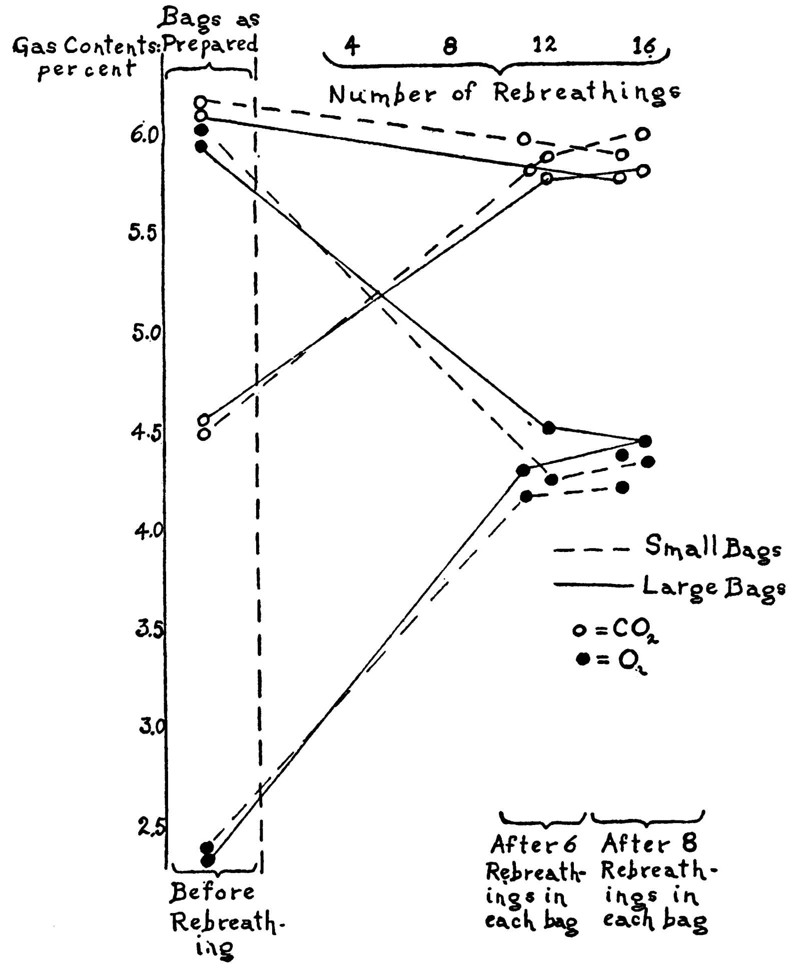


FIG. 2. THE ATTAINMENT OF EQUILIBRIUM BETWEEN THE VENOUS BLOOD AND THE GAS IN THE REBREATHING BAG

coronary or other blood will tend to lower the oxygen concentration in the bag, but this error will be less the greater the gas volume in the rebreathing system. In order to determine whether the volume of gas used makes any appreciable difference in the final tensions arrived at, experiments have been done in which each rebreathing period was divided into two parts, two different bags being used. After "washing" the lungs in the usual way the subject rebreathed from a bag containing nine liters. Twenty seconds after the beginning of "washing" from the spirometer the tap was turned into a second bag containing three liters, from which the subject rebreathed for five or six seconds longer. Such an experiment is plotted in Figure 2. The experiment was performed on a normal subject with a special five way tap to which four rebreathing bags were attached. Nine liters of a gas mixture relatively rich in carbon dioxide and relatively poor (as compared to the venous blood) in oxygen were introduced into a bag and three liters of the same gas mixture were introduced into a smaller bag. Another large bag and another small bag were filled with similar amounts of a different gas mixture, which was poorer in carbon dioxide and richer in oxygen than the tensions corresponding to the venous blood. After washing the lungs in the usual way, the subject breathed into the first large bag for 15 seconds and then into the first small bag for five seconds. The second rebreathing was similarly performed using the other two bags. For the third rebreathing the first two bags were used and so on. Gas samples taken from each bag after six and eight rebreathings into each of them were almost identical in composition, the maximum difference for each gas being about two millimeters.

The experiment illustrates the following points: (1) The use of gas volumes as great as nine liters in the rebreathing bag does not vitiate the results. (2) Constancy in the composition of the rebreathing bag probably indicates that the gas tensions represent those of the mixed venous blood, for the final gas mixture is independent of that put in the bag originally and is approximately the same whether arrived at from higher or lower tensions. (3) In normal subjects the desired equilibrium can be obtained in six rebreathings, after which there is no significant change in the composition of the bag. (This is true only if the "washing" procedure is properly carried out, as described in the preceding pages.)

In order to determine the cardiac output by the method under discussion it is necessary to know the time which elapses before recirculation of blood changes the composition of the gas in the lung-bag system. Numerous observations have been made on this point, the method used being that of alternate rebreathings with two different bags, the time allowed for one bag being constant, but the duration of breathing being different for the other bag. It has been found that under the conditions of our experiments, i.e., using bags containing nine liters of gas, prolonging the rebreathing time to twenty-five or even thirty seconds does not alter the final result. In order to obtain blood samples properly a somewhat longer period than thirty seconds is, however, usually necessary. Consequently, observations were made in which repeated samples of the lung-bag air were taken in evacuated sampling tubes during prolonged rebreathing.

The object of the experiments charted in Figure 3 was to determine the maximum duration of rebreathing before recirculation caused significant changes in the gas content of a rebreathing bag containing nine liters of "venous air." Repeated rebreathings, which did not last longer than twenty-five seconds, were done until constant values for oxygen and carbon

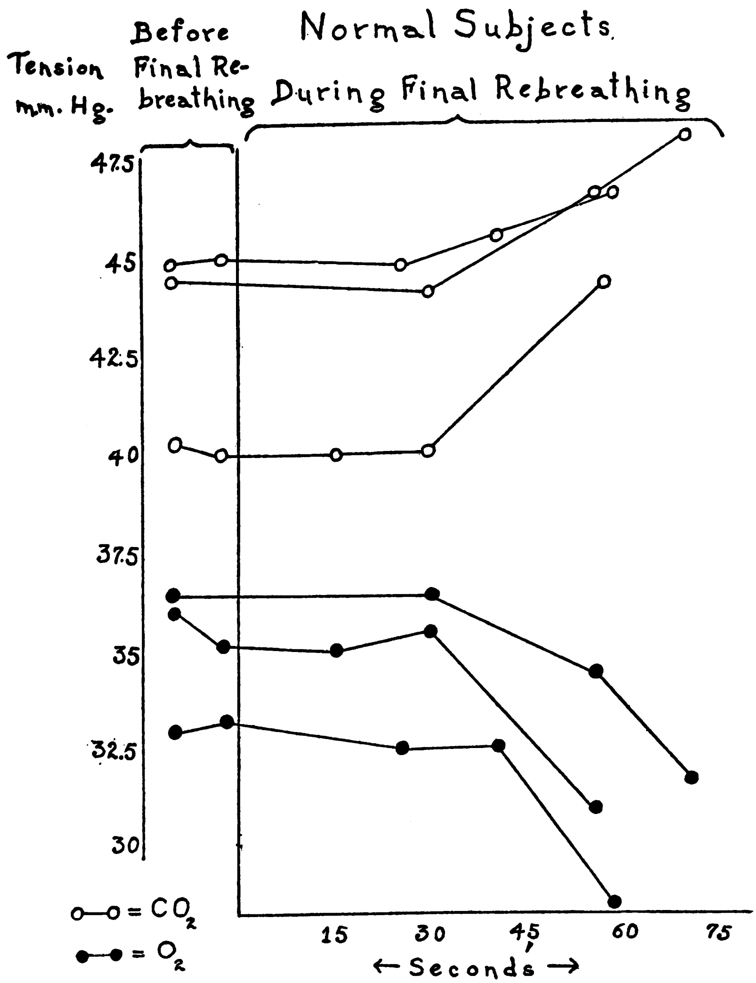


FIG. 3. INFLUENCE OF THE DURATION OF REBREATHING IN NORMAL SUBJECTS

dioxide were obtained in the bag. The effect of a prolonged final period of rebreathing was then observed. During and at the end of it gas samples were taken into evacuated sampling tubes. The observations indicate that in normal subjects recirculation does not cause significant changes in the oxygen and carbon dioxide contents until rebreathing is prolonged more than forty seconds.

The observations charted in Figure 4 were similar to those portrayed in the previous figure but the subjects used were patients with mild cardiac failure. The results show that when relatively large gas volumes, i.e., nine liters, are used in the bag, recirculation does not usually cause significant changes in the gas contents until rebreathing is prolonged beyond forty-five

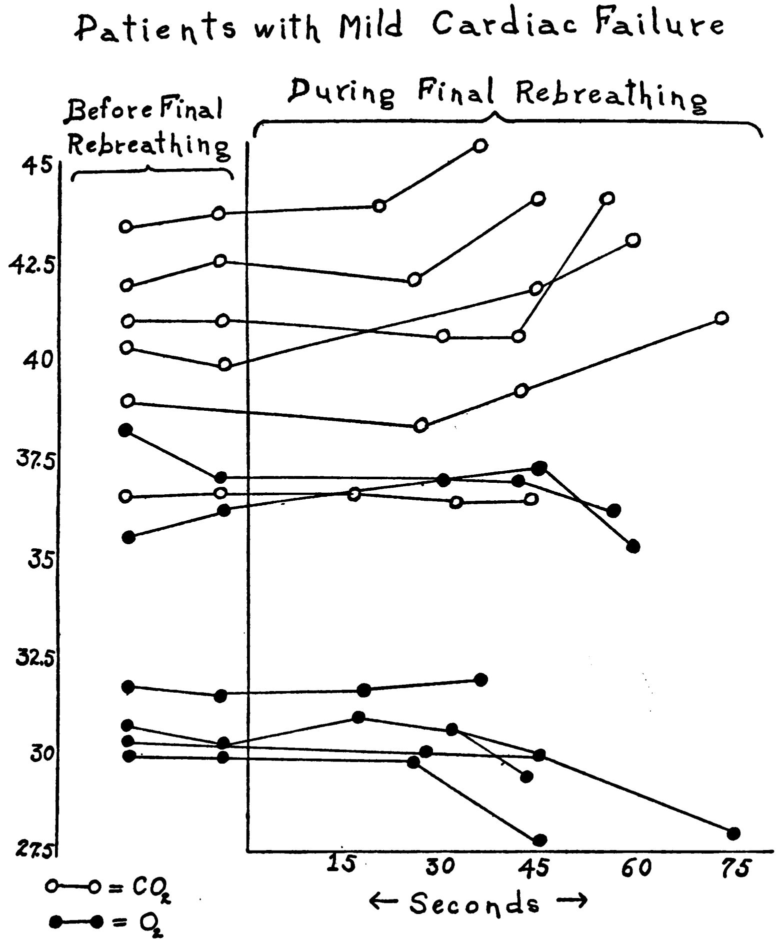


FIG. 4. INFLUENCE OF THE DURATION OF REBREATHING IN PATIENTS WITH MILD CARDIAC FAILURE

seconds. The data in Figures 3 and 4 indicate that both in normal subjects and in persons with mild cardiac failure, significant changes in the composition of the lung-bag air do not usually occur before 40 seconds when large gas volumes—nine liters—are used in the bag. After forty-five seconds recirculation causes sufficient change in the gas tensions to render the method inaccurate. Hence, the final rebreathing, during which blood samples are obtained, should not be longer than forty seconds in normal subjects or forty-five seconds in persons with cardiac failure. In all instances gas samples should be taken from the bag during and at the end of the final rebreathing. If the gas tensions in these samples do not agree, within one or two millimeters, with those obtained from the bag earlier in the rebreathing the entire experiment should be discarded.

## CURVES OF THE ARTERIAL OXYGEN DURING THE REBREATHING OF "VENOUS AIR"

After the preliminary rebreathings had been completed, arterial blood was obtained from the femoral artery while the subject breathed air. With the needle still in the vessel the lungs were "washed" and the final rebreathing was begun. The arterial blood, which maintained its bright crimson color for the first ten or fifteen seconds, became blue after about twenty seconds. As soon as the change in color was well marked sampling was begun and specimens were taken as rapidly as possible during the succeeding thirty seconds. When the oxygen content of these samples was determined, curves of the type illustrated in Figure 5 were obtained. After an initial lag, which is not shown in the curves, the oxygen diminished rapidly and then became constant for a time. This plateau usually occurred between the twenty-fifth and forty-fifth seconds after the subject began to breathe the low-oxygen mixture and was followed by a further decrease in the oxygen content of the blood.

Failure to obtain a plateau in the oxygen curve occurred in a number of instances and was usually due either to difficulty in getting the blood samples or to some error in the respiratory manipulations. Such experiments have been discarded. When a plateau was found it has been assumed, however, to represent the oxygen content of the mixed venous blood. This assumption has been based on the following considerations:

1. On theoretical grounds it appears likely that the lag in the decline of the blood oxygen is dependent on the time required for previously arterialized blood to pass from the lungs to the periphery. The initial decrease in the oxygen is probably due to a mixture of such blood with other blood which has been equilibrated with venous air. When all of the blood which had been exposed to air before the beginning of rebreathing has passed out of the arterial system the curve becomes flat until recirculation produces sufficient reduction in the oxygen content of the bag to cause a secondary decrease in the blood oxygen. The plateau in the curve probably represents venous blood which passes unchanged through the lungs.

2. Experiments were performed on dogs as follows: The animals were anesthetized with barbital and placed in a small Drinker respiratory apparatus, with a detachable top. The respiratory procedure was then carried out in the same way as in our observations on man, the lungs being "washed" with the nitrogen-carbon dioxide mixture and then several

breaths being taken to and from a rebreathing bag containing the gas mixture as used in observations on man. With suitable adjustment of the apparatus it was possible to produce large respiratory excursions. Because of the shorter circulation time of dogs the procedure was not prolonged more than fourteen or fifteen seconds. Following twelve or more repeated

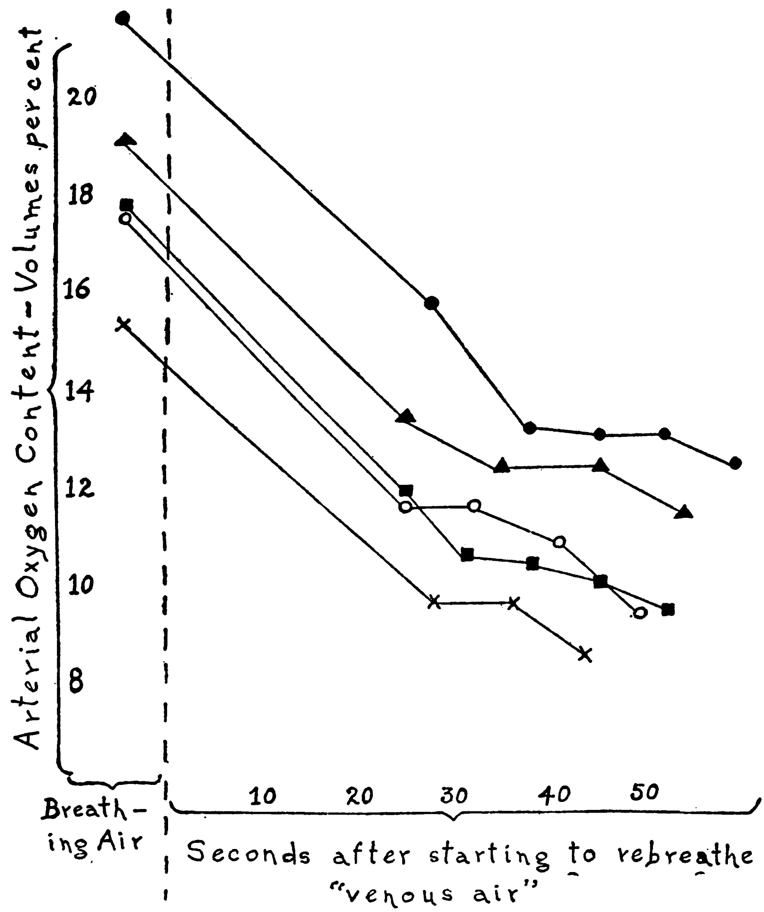


FIG. 5. THE OXYGEN CONTENT OF ARTERIAL BLOOD BEFORE AND DURING THE REBREATHING OF "VENOUS AIR"

The plateau in the curve is believed, for reasons mentioned in the text, to represent the oxygen content of mixed venous blood.

rebreathings gas samples were taken from the bag, in order to determine whether the oxygen and carbon dioxide tensions had become constant. The top of the apparatus was then removed and blood was drawn from the right ventricle by puncture of the chest wall. The top was then replaced and a final rebreathing was done, during which repeated blood samples were drawn from a cannula in the carotid artery.

Examples of six such experiments are shown in Figure 6. In three of them no plateau occurred in the blood oxygen curve, but in the other three instances a plateau was found and in each of them it corresponded accurately with the oxygen content of the blood obtained from the right ventricle. These observations appear to justify the assumptions that a similar relationship exists in man and that the procedure described enables one to obtain mixed venous blood from a peripheral artery.

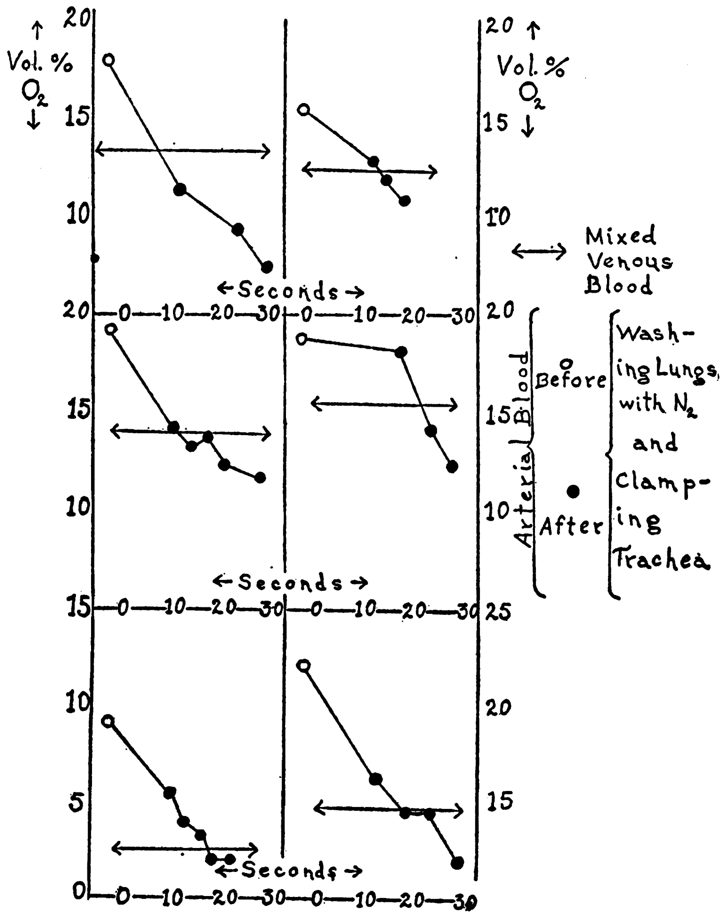


FIG. 6. "VENOUS AIR" OBTAINED IN DOGS BY REPEATED REBREATHINGS

In three animals a plateau was found and in each instance it corresponded accurately with the oxygen content of the mixed venous blood drawn directly from the heart by puncture of the chest wall.

APPLICATION OF THE METHOD TO PERSONS WITH CARDIAC DISEASE

The respiratory procedure causes well marked dyspnea in normal persons and even greater distress in patients with cardiac disease. It is therefore inapplicable in persons with advanced congestive failure. Neurotic subjects are also unsuitable. The rather severe arterial anoxemia might precipitate an attack of angina pectoris in persons with either coronary arteriosclerosis or syphilitic aortic insufficiency. In such cases the procedure should not be applied.

Experiments have been made in an attempt to determine whether edema of the lung bases renders the method inaccurate. Two hundred cubic centimeters of fluid were introduced into the lungs of dogs *via* the trachea. The respiratory procedure was then carried out as described above. In Table I

TABLE I

*A comparison in dogs of the venous plateau and direct Fick methods for determining the cardiac output*

| Animal number | Conditions | Arterial oxygen saturation | Cardiac output | | | |
|---|---|---|---|---|---|---|
| | | | By oxygen | | By carbon dioxide | |
| | | | Direct Fick method | Venous plateau method | Direct Fick method | Venous plateau method |
| | | *per cent* | *liters* | *liters* | *liters* | *liters* |
| $D_1$ | Normal | | 1.85 | 2.06 | 2.09 | 2.44 |
| $D_2$ | Normal | 93.8 | 1.81 | 2.00 | 1.94 | 1.88 |
| $D_3$ | Normal | 92.4 | 1.21 | 1.04 | 1.19 | 1.18 |
| $D_4$ | 100 cc. saline solution in lungs | 74.8 | 1.41 | 1.40 | 1.58 | 1.52 |
| $D_5$ | 100 cc. saline solution in lungs | 82.8 | 2.00 | 2.06 | 2.05 | 2.05 |
| $D_6$ | 200 cc. saline solution in lungs | 77.4 | 2.18 | No plateau | 2.50 | 2.31 |

are shown the results of such experiments in which the cardiac output was determined by the direct Fick method and by the venous plateau method. When a plateau was obtained in the blood gas curves, it corresponded satisfactorily with the gas contents of the blood obtained from the right ventricle. The experiments indicate that "edema" of the lungs of sufficient severity to reduce the arterial oxygen saturation to eighty per cent or less does not invalidate the method.

A more detailed consideration of the applicability of the method in persons with cardiac disease has been given in another study of this series (2).

## THE DETERMINATION OF THE CARBON DIOXIDE CONTENT OF THE MIXED VENOUS BLOOD

Thus far our discussion has been concerned chiefly with the venous oxygen. The same procedure allows one to determine the carbon dioxide content of the mixed venous blood, and the values so obtained are in anesthetized dogs in close agreement with those found by analysis of the blood from the right side of the heart (Table I). In our earlier experiments the cardiac output was measured both by oxygen absorption and by carbon dioxide elimination. In some subjects good agreement was obtained between the internal respiratory quotient—as determined by blood analysis—and the external respiratory quotient as determined by analysis of the expired air. Often however, the agreement was very poor, the discrepancy being dependent on the lability of the carbon dioxide excretion and of the arterial carbon dioxide content, both of these functions being readily affected by changes in the respiration. Consequently, the carbon dioxide method was abandoned.

The following protocol illustrates the procedure for determining the cardiac output by the venous plateau method.

R. F., the subject, was a white male aged 28, with a mediastinal tumor causing partial venous obstruction. Under basal conditions oxygen consumption was measured by means of a Tissot spirometer and gas analysis, and found to be 253 cubic centimeters per minute. The subject then rebreathed a gas mixture for the determination of the arteriovenous difference by the acetylene method. Following a rest period of fifteen minutes the lungs were "washed" with 5.8 liters of the nitrogen-carbon dioxide mixture from a spirometer. This required five seconds. During the subsequent 22 seconds he rebreathed nine liters of an oxygen-poor, carbon dioxide-rich gas mixture from the bag. After nine repetitions of the "washing" and rebreathing procedures, gas samples for analysis were taken from the bag and were introduced into an evacuated seven hundred cubic centimeter tonometer to equilibrate with blood at 37° C. for the determination of the venous oxygen by the method of Burwell and Robinson.

The femoral artery was then punctured while the subject breathed air through the mouthpiece. After twenty cubic centimeters of blood had been obtained the syringe was detached from the needle which remained in the artery. The lungs were then "washed" in the usual way and the final rebreathing was begun, and continued for sixty seconds, samples of lung-bag air being taken into evacuated sampling tubes at 15 seconds, 40 seconds, and at the end of the procedure. From the twenty-fifth to the seventy-fifth second, seven samples of blood were taken from the femoral artery.

The results of the analysis of the gas samples are shown in Table II and the values for the blood oxygen are indicated in Table III. A summary of the cardiac output values as determined by the acetylene, Burwell and Robinson, and venous plateau methods is given in Table IV.

## DISCUSSION

The data which have been presented indicate that the gases of the mixed venous blood and the cardiac output can be determined with considerable accuracy by the method described. It has been demonstrated that the presence of fluid in the pulmonary alveoli does not invalidate the procedure, which is applicable to patients with mild congestive heart failure as well as to normal persons. The method appears to be the nearest approach which has yet been devised to the direct Fick procedure.

TABLE II

*Results of gas analyses: Subject R. F.*

| Sample | Carbon dioxide *per cent* | Oxygen *per cent* |
|---|---|---|
| Wash mixture | 7.11 | 0.93 |
| Bag before rebreathing | 6.54 | 4.62 |
| Bag after eighth rebreathing | 6.10 | 3.93 |
| Bag after ninth rebreathing | 6.10 | 3.86 |
| Lung-bag air after 15 seconds final rebreathing | 6.32 | 4.37 |
| Lung-bag air after 40 seconds final rebreathing | 6.16 | 3.94 |
| Bag at end of final rebreathing | 6.45 | 3.58 |
| Tonometer gas after equilibration with blood | 5.81 | 3.87 |

TABLE III

*Results of arterial blood analyses: Subject R. F.*

| Conditions | Time of blood sample *seconds* | Oxygen content *volumes per cent* |
|---|---|---|
| Breathing air | Before final rebreathing | 21.70 |
| During final rebreathing of "venous" air | 26–34 | 13.90 |
| | 35–41 | 13.14 |
| | 42–47 | 13.02 |
| | 48–55 | 13.02 |
| | 56–62 | 12.60 |
| | 63–73 | 15.31 |
| | 73–75 | Bright red—not analysed |
| Equilibrated with "venous" air at 37° C. for 30 minutes | | 13.20 |

TABLE IV

*Cardiac output: Subject R. F.*

<table>
<tr><th></th><th>Acetylene method</th><th>Burwell-Robinson method</th><th>Venous plateau method</th></tr>
<tr><td>Oxygen consumption per minute, cc</td><td></td><td>253</td><td></td></tr>
<tr><td>Arterial oxygen content per liter, cc</td><td></td><td colspan="2">217.0</td></tr>
<tr><td>Venous oxygen content per liter, cc</td><td></td><td>132.0</td><td>130.2</td></tr>
<tr><td>Arteriovenous $O_2$ difference per liter, cc</td><td>84.8</td><td>85.0</td><td>86.8</td></tr>
<tr><td>Cardiac output per minute, liters</td><td>2.98</td><td>2.97</td><td>2.91</td></tr>
</table>

On the other hand the venous plateau method has serious disadvantages. It causes severe dyspnea to the subject and at the same time requires his active cooperation. It is possibly dangerous in cases with disturbance of coronary blood flow. Moreover, it is very tedious for the operators, requiring many analyses of blood and air. Aside from technical difficulties there are many pitfalls which may lead to inaccurate results unless the greatest care is taken.

Furthermore, the cardiac output can be determined accurately in many persons with cardiac failure by a simpler, easier method, which has been described in another study of this series by Grollman, et al. (2). The latter procedure which involves a modification of the original acetylene method causes practically no discomfort to the subject and does not necessitate arterial puncture. When the two methods are properly applied they yield similar results. The venous plateau method has been described in detail in the present paper because we believe that its agreement with the modified acetylene procedure furnished additional evidence for the validity of the latter, which is based on an entirely different principle. In the study of the cardiac output in cardiac disease such safeguards are necessary. Their neglect has already led to questionable conclusions based on methods of doubtful validity.

## SUMMARY

A modification of the method of Burwell and Robinson for determining the gas contents of " mixed " venous blood has been described. The procedure depends on obtaining blood from a peripheral artery while the subject breathes a gas mixture which has been equilibrated with his venous blood by previous repeated rebreathings.

The several procedures involved in the method have been checked by various experiments.

Application of the method to dogs has demonstrated that the values found for the blood gases by this indirect method are in close agreement with the gas contents of blood obtained by puncture of the right ventricle. The presence in the lungs of sufficient fluid to produce well marked arterial anoxemia does not invalidate the results.

The method is difficult to employ and involves considerable discomfort to the subject. Its agreement with the modified acetylene procedure constitutes additional evidence as to the validity of the latter in subjects with cardiac disease.

## BIBLIOGRAPHY

1. Burwell, C. S., and Robinson, G. C., A method for the determination of the amount of oxygen and carbon dioxide in the mixed venous blood of man. J. Clin. Invest., 1924, **1**, 47.
2. Grollman, A., Friedman, B., Clark, G., and Harrison, T. R., Studies in congestive heart failure. XXIII. A critical study of methods for determining the cardiac output of patients with cardiac disease. J. Clin. Invest., 1933, **12**, 751.