

# A COMPARISON OF THE DIRECT FICK AND THE GROLLMAN METHODS FOR DETERMINATION OF THE CARDIAC OUTPUT IN MAN

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The introduction of the cardiac catheter by Forssman (1) and its later development as a useful physiological instrument by Cournand (2, 3) have made possible the determination of the cardiac output by the direct Fick principle in man (4). Using this method, a number of investigators have reported values of 5.5 to 6.5 liters per minute for the basal cardiac output, which correspond to 3.1 to 3.8 liters per minute per square meter of body surface area (3, 5-8). These values are higher than those obtained earlier with the Grollman acetylene inhalation method or the Krogh-Lindhard nitrogen oxide method (3.9 liters per minute) (9-12). The arteriovenous oxygen difference, determined according to the Fick method, has been found to be 40 to 45 cc. per liter of blood, as compared with 60 cc. per liter of blood using the acetylene method. This discrepancy has been discussed at length. It has been suggested by those working with the gas inhalation methods, that the heart catheterization procedure so disturbs the subject, that basal values cannot be secured. Different investigators using the catheter technique have obtained the same values in similar series, without an increase in oxygen consumption, heart rate or blood pressure (3), and have pointed out that these values have all varied consistently from those obtained by the Grollman technique.

The purpose of the work described in this study was to determine the cardiac output simultaneously by both methods and to account for any differences noted.

## MATERIAL AND METHOD

Medical students, nurses or patients with minor cardiovascular diseases were used as subjects.

The subjects were trained for the Grollman technique the day before the study. The heart catheterization was done according to earlier descriptions (3, 8). The sample of mixed venous blood was always taken from the

pulmonary artery and the arterial blood from the brachial artery. The first cardiac output was determined according to the Fick principle after the heart catheter and the arterial needle had been in place for at least 30 minutes.

Immediately after the first Fick determination, the acetylene rebreathing was performed. The first sample of alveolar air was taken 17 to 18 seconds and the second 26 to 27 seconds after the start of rebreathing acetylene (10, 11, 13, 14). Twenty to 30 minutes later the same procedure was repeated. Twenty to 30 minutes later a third Grollman determination was done.

Twenty minutes later a single blood sample was drawn from the pulmonary artery. Immediately afterward a rebreathing according to Grollman but without acetylene was performed. Another blood sample from the pulmonary artery was drawn between 17 and 27 seconds after the start of rebreathing. These samples were analyzed for oxygen content on the Van Slyke apparatus in order to establish the influence of the rebreathing procedure on the mixed venous blood and the arteriovenous oxygen difference.

In three subjects the effect of recirculation was studied. Blood was drawn in five second periods from the pulmonary artery, during the rebreathing of acetylene. The blood was analyzed for acetylene content of the Van Slyke volumetric apparatus. In each subject two to three experiments were done. It was usually possible to obtain blood during two five second periods at each experiment, for example, between five to 10 and between 15 to 20 seconds after the start of acetylene breathing.

## RESULTS

In Table I the age of the subject, diagnosis, oxygen consumption, and the arteriovenous oxygen difference obtained with the two methods are tabulated. The values for arteriovenous oxygen difference using the acetylene method were always larger than those obtained according to the direct Fick method. The difference varied between 5 and 49 cc. per liter with a mean of  $26.5 \pm 2.79$  and was not proportional to the value given by the Fick method. The third determination of arteriovenous oxygen difference in each subject was done after allowing a 20 minute interval between the two methods. If these are excluded, the dif-

TABLE I

Patient Age Sex	Diagnosis	O <sub>2</sub> -consumption	B.M.R.	Arteriovenous O <sub>2</sub> -difference		
				Catheter method	Grollman method	Difference Grollman- Catheter
1. 52 years M	Ess. hypertension	<i>cc./min.</i>	<i>per cent</i>	<i>cc./liter</i>	<i>cc./liter</i>	
		277	+27	37	50	13
		277	+27	36	74	38
2. 24 years M	Normal	234	-- 10	36	52	16
		250	-- 4	38	61	23
				39	75	36
3. 23 years M	Normal	235	-10	38	78	40
		277	+ 6	39	47	8
				43	76	33
4. 24 years M	Normal	301	+15	43	73	30
		277	-13	42	69	27
				45	73	28
5. 26 years M	Ess. hypertension	291	+10	26	54	28
		331	+25	27	60	33
				28	44	16
6. 31 years F	Pregnancy mens V	207	+12	32	43	11
		179	- 3	33	44	11
7. 33 years F	Normal	255	+40	35	40	5
		233	+28	21	66	45
				24	71	47
8. 29 years F	Normal	243	+13	31	80	49
		240	+12	40	71	31
				37	53	16
Mean:				35.0	61.5	26.5 ± 2.79 N = 22

ference will be the same, or  $26.5 \pm 3.51$  cc. per liter. This value is significant. The determination of arteriovenous oxygen difference according to the direct Fick principle thus gives values about 45 per cent lower than with the acetylene method.

In order to analyze the experimental errors involved, the following procedure was adopted:

The experimental error was defined as the variability of a single determination ( $\delta_x$ ) and calculated in two different ways:

The differences between determination 2 and 1, or 3 and 2, were computed for each method separately.

The differences 2 to 1 and 3 to 2 were of the same order of magnitude; thus all differences constituted a single group of data.

As the mean differences were not significant, the variability of a single determination may be calculated ac-

cording to the following formula:

$$\delta_x = \frac{1}{\sqrt{2}} \cdot \delta_d \quad (15)$$

where

$\delta_x$  = variability of single determination

$\delta_d$  = standard deviation of difference

The results are given in Table II. The greatest differences between the determinations of the catheter method were -14 and +9, corresponding to an experimental error of 9.9 per cent (Table II). The value of -14 was found in patient No. 7, with basal metabolic rate of +40 per cent. This value falls outside the normal range of variation. If it is excluded the experimental error (Table II) will decrease to 5.6 per cent.

The experimental error was then calculated by a combination of analysis of variance (16), using Snedecor F-ratio as test of significance (17), dif-

TABLE II  
*Experimental error of the catheter and Grollman method  
(calculated per differences)*  
(a) Catheter method

No. of diff.	Mean	Mean differences $D \pm \epsilon_D$	Stand. deviation of diff. ( $\delta_d$ )	Exp. error ( $\delta_x$ )	
1	2	3	4	5	6
			ml.	ml.	per cent of mean
15	35.0	$0.67 \pm 1.26$	4.88	3.46	9.9
14	35.6	$1.70 \pm 0.75$	2.81	1.99	5.6

(b) Grollman method

1	2	3	4	5	6
15	61.5	$3.53 \pm 4.39$	17.0	12.1	21.3

ferentiating between the variation between individuals ( $\delta_i$ ) and within individual ( $\delta_x$ ) the latter corresponding to the experimental error, and "classical analysis."

The results are given in Table III.

TABLE III  
*Experimental error of the catheter and the Grollman method  
(calculated by analysis variance)*

	No. of indiv.	No. of determ.	Variability			
			Between individuals ( $\delta_i$ )		Within individuals exp. error ( $\delta_x$ )	
			ml.	per cent of mean	ml.	per cent of mean
Catheter	8	23	10.3	29.7	3.53	10.2
Grollman	8	23	15.3	24.4	13.3	21.2

The agreement between the two methods of calculation was excellent.

The catheter method was thus found to have a coefficient of variation for a single determination of 10 per cent (5.6 per cent), whereas the acetylene method, applied on the same patients under the same conditions during the simultaneous catheterization had a coefficient of variation of 21 per cent, which is significantly higher. The variability between the patients was found to be about the same for both methods (30, or 24 per cent).

There was no difference in oxygen content of the blood in the pulmonary artery sampled before, or 17 to 27 seconds after, the start of rebreathing. In eight cases the maximal difference between

the samples was 0.2 volumes per cent, the oxygen content being higher in some cases and lower in others during rebreathing.

The test for recirculation of acetylene showed that between five and 10 seconds after the start of acetylene breathing there was no acetylene in the pulmonary artery blood. However, in 10 to 15 seconds acetylene was present in the pulmonary artery blood, in amounts corresponding to an acetylene content in the alveolar air of 0.4 to 0.5 volumes per cent. In 15 to 20 seconds, this amount corresponded to approximately 1.5 volumes per cent.

## DISCUSSION

In almost simultaneous determinations there was a statistically significant difference in arteriovenous difference and cardiac output of 45 per cent between values obtained with the direct Fick and the acetylene methods. This confirms earlier work in which separate determinations were done using these two methods. Bauman and Grollman have previously reported values with the acetylene method and the direct Fick that agreed fairly well (18). The mixed venous blood in their cases was sampled after puncture of the heart and the sampling done immediately after the rebreathing of acetylene, both factors making the results uncertain. The belief that the discrepancy between values for cardiac output obtained with heart catheterization and with the acetylene technique is due to apprehension produced by the catheterization is disproved by the result of this study. Instead, the difference must be due to some systematic error in the acetylene method.

Gladstone believed that the rebreathing technique augmented the circulation and thus gave rise to errors (9). The present study conclusively shows that there is no difference in oxygen content in the mixed venous blood during the short time of rebreathing as compared to that before rebreathing.

Hamilton, Spradlin and Saam, working with dogs, have shown (19) that the recirculation of acetylene is too rapid to permit waiting 25 seconds before the second air sample is taken. Rapid recirculation was confirmed by Starr and Collins, who used the dye injection technique in dogs (20).

Grollman and Bauman, on the contrary, after heart puncture in man, found that significant amounts of acetylene did not appear in the blood in the right ventricle until 25 seconds after the start of acetylene breathing (18). Hohwü Christensen was able to demonstrate that the acetylene content in the peripheral venous blood was very low and rose slowly, due to the diffusion of acetylene from the blood to the tissues (21, 22).

The present study shows that significant amounts of acetylene appear in the pulmonary artery blood between 10 and 15 seconds after the start of acetylene breathing. Since it is impossible to get full mixing and equalization of the acetylene within this time, it may be assumed that these factors are inherent sources of error in all methods using inhalation of foreign gas. This error becomes greater the longer the time elapsing before the second sample is taken. That recirculation is the main source of error is also shown by the fact that, in patients with slow circulation, *e.g.*, cardiac failure, gas inhalation methods give values for arteriovenous oxygen difference that equal those obtained with the direct Fick principle, 90 to 100 cc. per liter of blood (3, 13, 23). The results of dye injection experiments in man with the dye injected in the pulmonary artery and the right auricle also show that there is a significant recirculation within 10 seconds (24).

#### SUMMARY AND CONCLUSIONS

1. Almost simultaneous determinations of cardiac output according to the direct Fick (after heart catheterization) and the acetylene methods were made in eight subjects. A total of 22 sets of determinations were made.

2. There was a statistically significant discrepancy in the values obtained by the two methods for the AV oxygen difference. The mean difference averaged  $26.5 \pm 2.79$  cc. per liter; the Fick method giving values about 45 per cent lower than the Grollman.

3. The experimental error for the Fick method was 5.6 per cent and for the acetylene method, 21 per cent.

4. The rebreathing procedure did not change the oxygen content in the pulmonary artery blood during the 27 seconds that the rebreathing lasted.

5. Tests for recirculation showed that within 10 to 15 seconds after the start of acetylene breathing

significant amounts of acetylene were found in the pulmonary artery blood.

6. Any method using inhalation of foreign gas will give values for arteriovenous oxygen difference which are too large, if the gas sampling is not completed before 10 to 15 seconds after the start of rebreathing. This error is not constant but, due to the speed of the circulation, is small or absent with slow circulation and is large with rapid circulation.

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