XXIII. ON THE THEORY OF THE BARCROFT DIFFERENTIAL BLOOD-GAS APPARATUS.

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DURING the course of a lengthy series of investigations in which the Barcroft differential apparatus has been used for blood-gas measurements a certain number of results were encountered which seemed to suggest that the evolution of a given volume of gas in one of the bottles of the apparatus might give rise to a somewhat smaller difference of level on the clove oil manometer than the absorption of an equal volume of the gas from the same bottle under similar conditions. In other words, it seemed possible that the value of the constant of the apparatus might not be identical for the two cases of evolution and absorption of gas. At first sight there seems to be some *a priori* reason why such a difference should be expected, for in the ordinary method of using the apparatus the air in each bottle is always at atmospheric pressure at the beginning of the experiment; if then the apparatus is closed and an evolution of gas takes place in one bottle the pressure in each bottle will be increased above atmospheric, while in the case where an absorption of gas occurs, the pressure in each bottle will sink below atmospheric. These relationships have been pointed out by Hill [1915], and more recently by Münzer and Neumann [1917]: we mention them here in order to emphasise the circumstance that when an evolution of gas is taking place the conditions in the apparatus are somewhat different from those obtaining during gas absorption. As no data appear to exist in the literature from which it could be determined whether or not this difference of pressure conditions would produce an appreciable effect on the results obtained by the apparatus, and in view of the widespread use of the apparatus, particularly for the determination of the percentage saturation of blood with oxygen by comparing the further amount of oxygen the blood sample is capable of absorbing from the air in the apparatus with the total amount of oxygen subsequently expelled from the fully saturated blood by treatment with potassium ferricyanide, it was decided that the matter was of sufficient importance for an experimental investigation.

While the work was in progress, a paper by Wertheimer [1920] became accessible dealing with the question of the extent to which the volume of gas evolved in one bottle of the apparatus (deduced from the resulting difference

of level on the manometer and the dimensions of the apparatus) should be corrected for the vapour tension of the water with which the gas is saturated. This consideration does not affect the method of treatment here given, as the actual volumes of air added or withdrawn have been measured directly, but it is necessary to call attention to Wertheimer's paper in order to complete the list of the more recent papers on the differential apparatus.

The apparatus used for the purpose was of the newest form described by Barcroft [1914]. In order to simplify the measurements and also to carry out the addition and abstraction of a measured volume of air from the bottle under as nearly similar circumstances as possible, the modification of Hoffmann's [1913] method of calibration described by Münzer and Neumann was chosen in preference to a chemical method. Minute details as to apparatus and procedure are unnecessary as they are contained in the accounts given by these authors. Suffice it to say that in order to imitate the actual conditions under which the differential apparatus is used, 3 cc. of distilled water were placed in each bottle, and the apparatus was hung over the side of a water bath in the usual way. By raising or lowering a reservoir we were able to expel into or abstract from one of the bottles a known volume (measured at the atmospheric pressure and at the temperature of the water bath) of the air collected over water in a graduated 1 cc. pipette, and at the same time to notice the difference of level produced on the clove oil manometer. In the first experiments which were carried out, the measuring pipette was filled completely with air, and by pressing successive quantities of this into the blood-gas bottle a series of readings was obtained in all of which the pressure in the apparatus was above atmospheric. The measuring pipette was then filled with water, and into it were drawn successive measured quantities of air from the bottle in order to obtain a series of readings in which the pressure was less than atmospheric. The results obtained in this way are recorded in Table I, in which a + sign indicates that air was forced into the bottle and a - sign that air was withdrawn from it. The values of the constant of the apparatus are calculated in terms of mm.³ of gas per mm. difference of level of the manometer. It will be seen that the average value of the constant obtained by adding air to the apparatus is almost 4 % higher than the average value obtained in the experiments in which air was withdrawn. But a closer examination of these figures shows that in the experiments carried out at increased pressure a different portion of the air-measuring pipette was in use from that into which air was drawn in the experiments at diminished pressure. As the pipette used had not been specially calibrated it seemed possible that a difference in the accuracy of these two parts of the scale of graduations might partly account for this result. Further, it is evident that the error due to drainage of the water from the internal walls of the pipette will affect differently the readings taken under the two conditions. In all cases the volume of the water adhering to the sides of the pipette will cause an error such that the actual volume of air driven into or removed from the apparatus will be less than the apparent

Table I. *Preliminary experiments. Apparatus L.*

Initial reading of air pipette cc.	Final reading of air pipette cc.	Vol. of air added or abstracted (room temp. and pressure) cc.	Difference of level in clove oil manometer cm.	Constant (cmm. gas per mm. difference of level)	
.353	.254	+ .099	3.16	3.13	
	.212	+ .141	4.51	3.13	
	.146	+ .207	6.59	3.14	
	.092	+ .261	8.31	3.14	
.389	.260	+ .129	4.19	3.08	
	.183	+ .206	6.60	3.12	
	.072	+ .317	10.04	3.13	
Mean value of constant for addition of gas			...	...	3.12
.044	.086	- .042	1.45	2.90	
	.121	- .077	2.60	3.00	
	.158	- .114	3.71	3.07	
	.160	- .116	3.86	3.01	
.002	.058	- .056	1.87	3.00	
	.093	- .091	3.01	3.02	
	.136	- .134	4.33	3.09	
Mean value of constant for abstraction of gas			...	...	3.01

volume read off from the pipette, so that the values obtained for the constant of the apparatus, *i.e.* for the ratio $\frac{\text{volume of air added or withdrawn}}{\text{difference of level produced}}$, will throughout tend to be too large. But in the experiments in which air was added to the bottle, the lower part of the pipette was in use, and this would tend to contain an extra amount of drainage from the upper parts, so that the drainage error would be particularly large in this case. On the other hand, while air was being drawn out of the bottle only the upper portion of the pipette was in use, so that the drainage error would be less in accordance with the diminution in the amount of surface exposed. In view of these considerations, in later experiments, the "positive" and "negative" experiments were carried out alternately and in pairs, and the determinations were so arranged that as nearly as possible the same particular portion of the pipette was used for (say) a "positive" experiment as for the "negative" experiment which immediately succeeded it. In this way, although we were no more certain of the absolute volume of air measured, we ensured that this volume was measured under the same conditions and in the same portion of the pipette in both the "positive" and the "negative" experiment of each pair. Typical results obtained in this way are recorded in Table II from which it will at once be seen that the value of the constant obtained when the apparatus was working at increased pressure is identical, within the range of our measurements, with that observed when the general pressure in the apparatus was diminished.

In order to confirm the assumption that in these later experiments the measurement of the volume of air added to or withdrawn from the apparatus was not affected by an error due to the drainage of the confining liquid, a further series of observations was also carried out in which the measured volume of air was collected over mercury. It was found that the use of mercury

Table II. *Later experiments. "Positive" and "negative" determinations carried out alternately. Apparatus 3 and 4.*

Initial reading of air pipette cc.	Final reading of air pipette cc.	Vol. of air added or abstracted (room temp. and pressure cc.)	Difference of level in clove oil manometer cm.	Constant (cmm. gas per mm. difference of level)
·035	·254	− ·219	6·54	3·35
·253	·023	+ ·230	6·78	3·39
·053	·258	− ·205	6·21	3·30
·257	·057	+ ·200	6·08	3·29
·034	·250	− ·216	6·57	3·29
·254	·036	+ ·218	6·57	3·32
·047	·240	− ·193	5·84	3·31
·234	·047	+ ·187	5·61	3·33
·029	·245	− ·216	6·34	3·41
·244	·033	+ ·211	6·37	3·31
·034	·240	− ·206	6·17	3·34
·231	·040	+ ·191	5·76	3·32
·013	·235	− ·222	6·61	3·36
·224	·016	+ ·208	6·23	3·34
·013	·123	− ·110	3·36	3·27
·124	·014	+ ·110	3·35	3·28
Mean constant for addition of gas		...	...	3·32
Mean constant for abstraction of gas		...	...	3·33

as a confining fluid made the apparatus very convenient to handle, and that, provided due care were taken with the levelling on taking readings of the gas volume, the results were no less consistent than when water was used (Table III).

Table III. *Experiments in which mercury was used as confining fluid. Apparatus 3 and 4.*

Initial reading of air pipette cc.	Final reading of air pipette cc.	Vol. of air added or abstracted (room temp. and pressure) cc.	Difference of level in clove oil manometer cm.	Constant (cmm. gas per mm. difference of level)
·664	·436	+ ·228	6·77	3·37
·446	·667	− ·221	6·60	3·35
·670	·333	+ ·337	10·15	3·32
·340	·680	− ·340	10·18	3·34
·682	·206	+ ·476	14·20	3·35
·211	·686	− ·475	14·16	3·35
Mean constant for addition of gas		...	...	3·35
Mean constant for abstraction of gas		...	...	3·35

The conclusion from the results of these experiments is that under the ordinary conditions of use of the differential apparatus the evolution of a given volume of gas in one bottle produces exactly the same change in level on the clove oil manometer as occurs in the opposite direction when the same volume of gas is absorbed from the same bottle.

It is of interest to compare this experimental result with that to which the mathematical theory of the differential apparatus leads. This was worked out originally by Sir Robert Ball [1908]; Hill [1915] calculates the relation between the actual reading observed and the difference between the amounts of gas

absorbed in each bottle, while Münzer and Neumann [1917] apply a somewhat different method of treatment for the case in which *evolution* of gas takes place in one bottle. But the mathematical comparison by similar methods of the two separate cases of absorption and evolution of gas seems not to have been undertaken. To consider the question, let us assume that we have an apparatus which is of the usual form, and in which, for the sake of a general case, the volumes of the left and right bottles are slightly unequal, namely L and R respectively. Each of these volumes includes the volume of the capillary tube down to the surface of the clove oil when this is standing level in the manometer.

Let A be the area of cross section of the manometer tube (supposed uniform), and P be the atmospheric pressure in mm. of the manometer liquid. The temperature at which the experiment is performed is constant throughout.

In the case of evolution of gas let a volume x of gas (measured at atmospheric pressure and room temperature) be liberated in the left hand bottle, and let the resulting difference of pressure shown by the manometer be 2ϵ mm.

Then by applying Boyle's law it is seen that the pressure in the left hand bottle

$$= \frac{(L+x)P}{L+\epsilon A}$$

while that in the right hand bottle

$$= \frac{RP}{R-\epsilon A}.$$

The difference between these is equal to the difference of level shown by the manometer,

$$\therefore \frac{(L+x)P}{L+\epsilon A} - \frac{RP}{R-\epsilon A} = 2\epsilon \dots\dots\dots(1).$$

On simplification, this expression becomes

$$x = \epsilon \frac{\left[A \left(\frac{L}{R} + 1 \right) + 2 \left(\frac{L}{P} - \frac{\epsilon AL}{PR} + \frac{\epsilon A}{P} - \frac{\epsilon^2 A^2}{PR} \right) \right]}{1 - \frac{\epsilon A}{R}},$$

and, on approximating by the binomial theorem, neglecting all terms of the order $\frac{1}{PR}$ and $\frac{1}{R^2}$, which are obviously small,

$$x = 2\epsilon \left[\frac{L}{P} + \frac{A}{2} \left(\frac{L}{R} + 1 \right) + \frac{\epsilon A}{P} + \frac{\epsilon A^2}{2R} \left(\frac{L}{R} + 1 \right) \right] \dots\dots\dots(2).$$

In the case of absorption of gas let an equal volume x of gas (measured at atmospheric pressure and room temperature) be absorbed from the left hand bottle, and let the resulting difference of pressure shown by the manometer be 2α mm.

Then by applying Boyle's law, as before, it is seen that the pressure in the left hand bottle

$$= \frac{(L-x)P}{L-\alpha A},$$

while that in the right hand bottle

$$= \frac{RP}{R+\alpha A}.$$

The difference between these is equal to the difference of level shown by the manometer,

$$\therefore \frac{RP}{R + \alpha A} - \frac{(L-x)P}{L - \alpha A} = 2\alpha \dots\dots\dots(3).$$

On simplification, this expression becomes

$$x = \alpha \frac{\left[A + \frac{AL}{R} + 2 \left(\frac{L}{P} - \frac{\alpha A}{P} + \frac{\alpha AL}{PR} - \frac{\alpha^2 A^2}{PR} \right) \right]}{1 + \frac{\alpha A}{R}},$$

and, on approximating by the binomial theorem, neglecting all terms of the order $\frac{1}{PR}$ and $\frac{1}{R^2}$, which are obviously small,

$$x = 2\alpha \left[\frac{L}{P} + \frac{A}{2} \left(\frac{L}{R} + 1 \right) - \frac{\alpha A}{P} - \frac{\alpha A^2}{2R} \left(\frac{L}{R} + 1 \right) \right] \dots\dots\dots(4).$$

From the equations (2) and (4) it is evident that, for a given value of x , α will be sensibly equal to ϵ provided that the terms

$$\left\{ \frac{\epsilon A}{P} + \frac{\epsilon A^2}{2R} \left(\frac{L}{R} + 1 \right) \right\} \text{ and } \left\{ \frac{\alpha A}{P} + \frac{\alpha A^2}{2R} \left(\frac{L}{R} + 1 \right) \right\}$$

are of sufficiently small magnitude to be neglected in comparison with

$$\frac{L}{P} + \frac{A}{2} \left(\frac{L}{R} + 1 \right).$$

That this condition is fulfilled in practice may most readily be seen by taking an actual example referring to an apparatus of the usual dimensions. For instance, in an extreme case let the volumes of the bottles L and R be 24 and 25 cc., i.e. 24,000 and 25,000 mm.³ respectively. Let the area of cross section of the bore of the manometer tubing be 1 mm.² and the atmospheric pressure 760 mm. Hg or about 10,000 mm. of the manometer liquid. If so much gas has been liberated or absorbed as to produce a difference of level of 100 mm. then

$$\frac{L}{P} + \frac{A}{2} \left(\frac{L}{R} + 1 \right) = 3.38,$$

while

$$\begin{aligned} & \frac{\epsilon A}{P} + \frac{\epsilon A^2}{2R} \left(\frac{L}{R} + 1 \right) \\ & = .007 \text{ (approximately).} \end{aligned}$$

The neglected terms thus contribute a smaller share to the value of the constant than can be detected experimentally. The conclusion that under practical conditions the constant of the apparatus is the same no matter whether absorption or evolution of gas is taking place is thus supported by the theoretical as well as by the experimental results. In conclusion it might be mentioned that when the small terms in question are omitted from equations (2) and (4) they both reduce to

$$x = \frac{2\alpha L}{P} + \alpha AL \left(\frac{1}{L} + \frac{1}{R} \right)$$

which is seen to be identical with the formula given by Hill [1915], when it is remembered that Hill expressed the volume of gas absorbed in the apparatus as a fraction of the volume of the bottle in which the absorption takes place.

As mentioned above, Münzer and Neumann's method of treatment of the problem differs somewhat from the present one inasmuch as these authors express their results in a form involving a term p which expresses the amount by which the general pressure in the apparatus exceeds the initial atmospheric pressure when evolution of gas takes place. The value of p is given by

$$p = \frac{PV}{V - \epsilon A} - P + \epsilon \dots \dots \dots (5),$$

while the constant of the differential apparatus deduced in terms of this factor for the case of evolution of gas is equal to

$$\left[\frac{V}{P} + A \left(1 + \frac{2p}{P} \right) \right] \dots \dots \dots (6).$$

In both these latter equations V is the volume of each of the bottles which are assumed to be identical in size. In order to show that this method of treatment leads to a formula identical with that given above in equation (2), it is necessary to avoid the approximations introduced by Münzer and Neumann [1917, p. 330].

In this way it is found that the exact form of formula (6) is

$$\frac{\left[\frac{V}{P} + A \left(1 + \frac{2p}{P} + \frac{p^2 - \epsilon^2}{P^2} \right) \right]}{1 + \frac{p}{P} - \frac{\epsilon}{P}},$$

but from (5)

$$1 + \frac{p}{P} - \frac{\epsilon}{P} = \frac{V}{V - \epsilon A} = \frac{1}{1 - \frac{\epsilon A}{V}}$$

so that (7) becomes

$$\left[\frac{V}{P} - \frac{\epsilon A}{P} + A \left(1 - \frac{\epsilon A}{V} \right) \left(1 + \frac{2p}{P} \right) + A \left(1 - \frac{\epsilon A}{V} \right) \left(\frac{p^2 - \epsilon^2}{P^2} \right) \right]$$

and by substituting the value of p from (5) and neglecting terms of the order

$\frac{1}{PV}$ and $\frac{1}{V^2}$ we obtain

$$\left[\frac{V}{P} + A \left(1 + \frac{\epsilon}{P} + \frac{\epsilon A}{V} \right) \right]$$

which is identical with the value of the constant expressed in equation (2) when L and R are both made equal to V .

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