THE DETERMINATION OF THE TOTAL OXYGEN CAPACITY AND BLOOD VOLUME AT DIFFERENT ALTITUDES BY THE CARBON MONOXIDE METHOD.

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THE precise changes which are undergone by the hæmoglobin of the blood as a reaction to changes of altitude have been a matter of controversy for a considerable time[1], and it cannot be yet said with certainty whether at high altitudes the hæmoglobin shows a real increase in total amount or whether the increase in the percentage value of the hæmoglobin in the blood which is so frequently observed is due to a mere concentration of the blood, or whether both factors come into play.

When one looks through the literature it is evident that much of the uncertainty is due to differences of the interpretation of single results obtained on individual animals, some of which have been kept at the low and others at the high altitude, for the method of estimating the total amount of hæmoglobin and blood in the animal has hitherto been Welcker's or some modification of that method, each estimation necessitating the death of the animal examined. To solve the problem some *intra vitam* method of making the required observations, and one which does no harm to the subject, is therefore necessary. For this purpose Haldane and Lorrain Smith's carbonic oxide method[2] for determining the total oxygen capacity and blood volume of man was employed during a recent expedition to the Peak of Teneriffe which has been described in greater detail in the preceding paper.

In order to render the necessary apparatus easier to transport a modification of the original method of administering the carbonic oxide was adopted. Hill's oxygen bag[3] in which the gas is produced

[1] Cf. Abderhalden. *Zschr. f. Biol.* XLIII. p. 125. 1902. *Ibid.* p. 443. *Pflüger's Arch.* XCII. p. 1. Zuntz and others. *Höhenklima*, Berlin, p. 172. 1906.

[2] Haldane and Lorrain Smith. This *Journal*, XXV. p. 331. 1900.

[3] Leonard Hill. *Brit. Med. Journ.* p. 1522. 1909.

by the action of water on oxylith was substituted for the older respiration apparatus with its weighty oxygen cylinder. A great advantage of this method is that no special means for absorbing the carbonic acid of the expired air is essential, as the caustic soda formed in the reaction remains in the bag and serves for this purpose. An additional rubber tube was inserted into the upper part of the bag to serve as a means of entrance for the carbonic oxide which was run in under water pressure from a 500 c.c. measuring cylinder. The whole apparatus is shown in the accompanying figure.

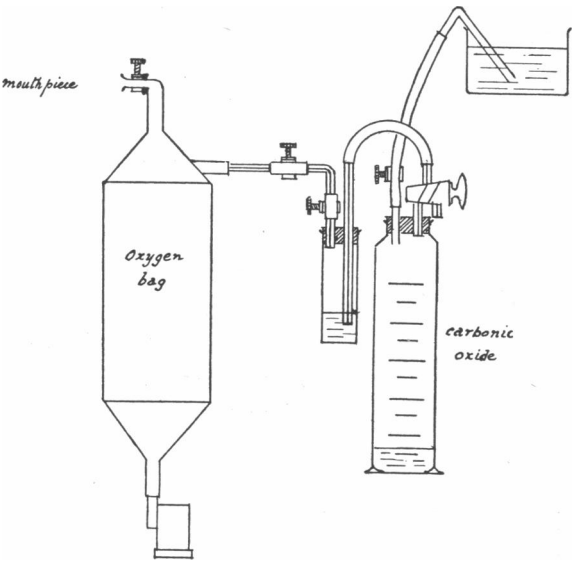

Fig. 1.

The oxygen generated from one lump (50 gms.) of oxylith was found to be quite sufficient for an experiment. The whole of the required quantity of carbonic oxide was admitted at once into the bag and this was then disconnected from the rest of the apparatus, as this permits of the subject breathing into it with greater convenience. At first breathing into the bag was continued until it was almost empty at the end of an inspiration (12 to 15 minutes) before taking the blood sample for determining the percentage saturation with carbonic oxide, but later on a routine period of 10 mins. was chosen as analysis showed that there was but a negligible quantity of carbonic oxide left in the bag by that time, and this shorter period obviated the somewhat violent hyperpnœa

which is apt to occur when there is only a small quantity of gas in the bag owing to the insufficient rapidity of absorption of carbonic acid by the caustic soda. The apparatus described proved extremely convenient throughout, though finally the caustic soda worked its way through the fabric of the bags and brought the experiments to a close.

It may be said at once that so far as the effects of altitude on the blood volume and hæmoglobin were concerned no positive information was obtained. Presumably the altitude, which was only moderate (7000 feet), or the length of time spent at that altitude, was insufficient in the case of each of the two subjects examined to produce any marked change. The percentage value of the hæmoglobin in the blood showed a slight rise but even this was by no means marked. The total hæmoglobin remained, so far as can be judged, at the sea-level value; this was quite certain in the case of J. B. Dr Boycott was kind enough to examine some blood films taken from C. G. D. while on the Peak but was unable to find any evidence pointing to the regeneration of red cells.

It is curious that C. G. D. gave four consistent values at sea level in Teneriffe for the total oxygen capacity which were 10 % above the mean values found in England. It is true that three of these determinations in England gave values which were nearly as high but these were not sustained by other experiments made about the same time and were probably due to experimental error. Whether the week's sea voyage to Teneriffe had anything to do with this increase of hæmoglobin must remain uncertain. There is another possible explanation for these high figures, that is that the solution of blood in which the percentage saturation with carbonic oxide was being determined may have been dissociated to an abnormal extent owing to the intensity of the light in Teneriffe, the apparent saturation being therefore too low. An attempt was made to combat this possible source of fallacy by making the estimations early in the morning (8 to 9 a.m.) and excluding from the room all the light save that from the north-west. Judging from the consistent results obtained in all the experiments on J. B. one would say that this effort had been successful.

Though then the main purpose for which the experiments were undertaken remains unfulfilled some interesting facts which bear on the carbonic oxide method in its application to man may be derived from the figures obtained.

In the first place the results obtained at sea level for C. G. D. show the sort of variation which is found when estimations are made on the same individual at frequent intervals over a considerable interval of time, in

	Date	% of hæmoglobin [Haldane scale]	% O_2 capacity in c.c.	Total O_2 capacity in c.c.	Volume of blood in c.c.
Subject C. G. D. weight 65 kilos.	Jan. 20	96	17·7	783	4420
	21	95	17·6	817	4640
	Feb. 3	96	17·7	812	4600
	9	100	18·5	808	4370
	10	98	18·1	870	4810
	14	94	17·4	849	4880
Oxford	16	94	17·4	775	4460
	18	93·5	17·3	894	5170
	22	92	17·0	891	5240
	26	100	18·5	806	4360
	March 1	100	18·5	831	4500
	5	100	18·5	880	4760
	8	94	17·4	765	4400
	11	96	17·8	816	4590
Mean for Oxford		96	17·8	828 =1·27 c.c. per 100 gms. body weight	4657 =7·17 c.c. per 100 gms. body weight
	21	96	17·8	945	5310
	22	100	18·5	890	4310
Orotava, sea level	23	97	17·9	905	5060
	24	96·5	17·8	920	5170
	25	97	17·9	—	—
Mean for Orotava		97	17·9	915	4963
	27	95·5	17·7	—	—
	28	102·5	19·0	—	—
	29	103	19·1	929	4860
Observatory.	30	107·5	19·9	—	—
Las Cañadas,	31	101	18·7	1070	5720
7000 feet.	April 1	96	17·8	—	—
	2	103	19·0	869	4570
	3	105·5	19·5	979	5020
	4	107·5	19·9	838	4210
Alta Vista.	6	106·5	19·7	—	—
10,700 feet.	8	107	19·8	—	—
	9	107	19·8	—	—
Observatory.	10	108·5	20·1	1030	5120
	11	107	19·8	985	4970
Orotava.	14	97	17·9		
	16	103	19·1		
Subject J. B. weight 70 kilos.	Feb. 5	100	18·5	1017	5500
	6	100	18·5	1053	5700
	21	100	18·5	1025	5550
Mean for Cambridge		100	18·5	1032 =1·47 c.c. per 100 gms. body weight	5583 =7·98 c.c. per 100 gms. body weight
	March 21	103	19·1	995	5220
Orotava.	23	105	19·4	—	—
	25	113·5	21·0	1000	4770
				998	4995
	29	108	20·0	—	—
	April 2	108	20·0	950	4750
Observatory.	4	—	—	1075	—
	11	111	20·5	940	4580

this instance three months, during which time the course of life was quite uniform. The figures for the total oxygen capacity vary up to $\pm 8\%$ of the mean value, a variation of the same order as that found by the same method in the case of rabbits[1]. This variation probably expresses the experimental error of the method and affords no indication that the hæmoglobin in the body was really varying during the period of observation.

All the colorimetric determinations for ascertaining the percentage saturation of the blood with carbonic oxide in the case of myself were made by me soon after inhaling the gas, at a time that is when my blood was still perhaps 20 % saturation with carbonic oxide, for as a rule the saturation reached during the course of the experiment was in the neighbourhood of 25 %. On several occasions Dr Haldane was good enough to make the titrations in duplicate with me and the two analyses always agreed closely, so it appears that in this series of experiments partial saturation with carbonic oxide had little effect upon the accuracy with which I was able to do the colorimetric titration. At the same time it appeared to me that under these circumstances I was not able to estimate the differences of colour with such facility as when I was completely free from carbonic oxide.

The normal values of the total oxygen capacity and blood volume were much larger in both C. G. D. and J. B. than the average values obtained by Haldane and Lorrain Smith in the original series of 14 men as well as the more recent results of Oerum and Plesch[2]. Haldane and Lorrain Smith give per 100 gms. body weight 0·98 c.c. of oxygen capacity and 4·78 c.c. of blood, Plesch 1·12 c.c. of oxygen capacity and 5·64 c.c. of blood and Oerum 5·2 c.c. of blood. Cases have been described previously of apparently normal people who have what one would consider an excessive quantity of hæmoglobin and blood judged in the light of the first series of determinations made by the *intra vitam* method[3], but agreeing with the two cases under discussion here.

There is however a possible source of fallacy in Haldane and Lorrain Smith's determinations. Dr Haldane and I have made two determinations on myself in the middle of June of this year,

[1] Boycott and Douglas. *Journal of Path. and Bact.* XIII. p. 256. 1909.

[2] Oerum. *Deutsch. Arch. f. klin. Med.* XCIII. p. 357. 1908. Plesch. *Zschr. f. exp. Path. und Ther.* VI. p. 380. 1909.

[3] Boycott and Douglas. *Guy's Hospital Reports*, LXII. p. 163. 1908. Plesch. *loc. cit.*

employing the original apparatus (breathing through soda lime into a small closed space into which the oxygen and carbonic oxide were admitted) in order to administer the carbonic oxide. In the first instance 209 c.c. of carbonic oxide were given in 6½ minutes, and after this I continued to breathe into the apparatus for 21½ minutes. The saturation of the blood with carbonic oxide determined in a sample taken from the finger 3½ minutes after the whole of the carbonic oxide had been given was 28·6 %, and from this point the saturation gradually fell till it became constant at 22·6 % after the lapse of a further 13 minutes. In the second instance 300 c.c. of carbonic oxide were given in 26½ minutes, and breathing into the apparatus was continued for another 35 minutes. The first sample of blood taken 1 minute after all the carbonic oxide had been given gave a saturation of 39 %, but a constant value of 35·2 % was reached 5 minutes later. My total oxygen capacity in these two experiments calculated from the saturation when this became constant was 925 c.c. and 852 c.c.

It would seem probable therefore that the time allowed in the experiments of Haldane and Lorrain Smith for complete mixture of the blood after giving the carbonic oxide was insufficient. The apparatus described in this paper helps to get over this difficulty, presumably owing to the accumulation of a fair amount of carbonic acid in the bag and a consequent acceleration of the circulation, for I cannot satisfy myself that there is any definite relation between the duration of the experiment and the values found for the total oxygen capacity.

To what extent Haldane and Lorrain Smith's or other observers' results are affected by this error it is of course impossible to say, but we are at present investigating the matter. The limits of the hæmoglobin and blood volume which are to be considered normal for man must no doubt be extended. Haldane for instance has now about 900 c.c. of oxygen capacity, whereas his original determination gave a value of 660 c.c.

It will be noticed that the values for the total oxygen capacity in the case of C. G. D. showed a very great irregularity at the higher altitude of the Meteorological Observatory. Taking the figures as they stand it cannot be said that there is any distinct indication that the total oxygen capacity was any different from what it was at sea level, even though the period spent at or above the altitude of 7000 feet lasted for 16 days. It appears only that the experimental error was vastly greater than at the lower altitude. J. B. on the other hand gave values throughout

which were perfectly consistent with one another and showed no alteration at the higher altitude. The probable explanation of the difference in the two cases is this. The actual determinations, including the colorimetric titration, were all made by C.G.D. The experiments on J.B. were in all cases made first when C. G. D. was entirely free from carbonic oxide. In the experiments on C.G.D. the colorimetric titration was done at a time when the observer was still considerably saturated with carbonic oxide, the average saturation reached in the course of the experiment being as before 25 %. It appears therefore that the want of oxygen induced by partial saturation with carbonic oxide plus the lowered atmospheric tension of oxygen rendered the power of colour discrimination far less exact than under normal circumstances. The light by which the titrations were made was not to blame, for it was particularly good. Dr Haldane has informed me that he has found it extremely difficult to do the titration when saturated to 40 % with carbonic oxide at sea level. The two cases are not however parallel for in the last instance the oxygen tension in the blood was probably higher than in the first.

There are some who find difficulty in making accurate determinations of the total oxygen capacity on themselves even at normal barometric pressures by the method of Haldane and Lorrain Smith though they can obtain perfectly reliable and consistent results on other subjects, and it would seem that their colour discriminating power is dulled even by the comparatively low saturation with carbonic oxide which is necessary for the determination.

The figures obtained for the blood volumes are not discussed here because by Haldane and Lorrain Smith's method they are obtained by calculation from the percentage and total oxygen capacity and therefore reflect the experimental errors of each of these two determinations. They are therefore the least reliable of the results, though in the case of J.B. they point to a slight concentration of the blood. The concentration in this case cannot however be ascribed to the high altitude for it was quite evident at sea level in Teneriffe, and may have been due to the fact that J.B. did not drink much fluid.

I am greatly indebted to Mr Barcroft for his assistance in this work, as he served willingly as one of the subjects of investigation in the midst of the pressure of other work.

SUMMARY.

1. In a series of determinations on the same individual of the total oxygen capacity by the carbonic oxide method variations up to $\pm$ 8% of the mean value were found. This probably gives a measure of the experimental error of the method when applied to man.

2. Evidence is given that partial saturation of the observer with carbonic oxide, especially if the atmospheric oxygen tension is lowered as at high altitudes, may seriously interfere with his capacity for performing the colorimetric titration necessary for determining the percentage saturation of the blood with carbonic oxide by Haldane and Lorrain Smith's method.

3. The limits of the total oxygen capacity and blood volume of normal men are probably more extensive than would be supposed from the mean values derived from recent *intra vitam* determinations. The two individuals in the present instance had each about 1·4 c.c. oxygen capacity and 7·5 c.c. blood per 100 gms. body weight.

4. In employing Haldane and Lorrain Smith's original method of administering the carbonic oxide a source of fallacy is liable to arise owing to the experiment not lasting a sufficient time for thorough mixture of all the blood in the body to take place before taking the necessary blood sample.

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