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BLOOD VOLUME AND HAEMOGLOBIN CONCENTRATION AT ALTITUDES ABOVE 18,000 ft. (5500 m)

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The haemoglobin levels of climbers ascending to great altitudes in the Himalaya or the Karakoram do not as a rule reach the high values ($22{\cdot}9 \pm 2{\cdot}6$ g/100 ml.) reported on South American miners living at 17,500 ft. (5340 m; Dill, Talbott & Consolazio, 1937). Observations on sixty subjects on eight mountaineering expeditions (including the present one) showed a final mean haemoglobin value of 20·19 g/100 ml. (Table 1). On Mount Cho Oyu (1952) and Mount Everest (1953) mean haemoglobin values were similar to each other, although the time spent at high altitude was longer and the altitudes greater on the later expedition. Pace, Meyer & Vaughan (1956) found that haemoglobin values reached a steady level in about 50 days, and the same was true on Mount Cho Oyu (1952; Pugh, unpublished). These results (as well as the small variation between expeditions) suggest that $20 \pm 1{\cdot}5$ g/100 ml. is a physiological limit for plainsmen living at heights above 18,000 ft. (5500 m). However, rather large variations have been observed occasionally in small groups after final assaults on high peaks. For example, Luft (1941) reported a mean value of 24 g/100 ml. on four subjects, while Somervell (1925) and Brendel (1956) noted falls in haemoglobin. The Himalayan Scientific and Mountaineering expedition of 1960/61 made a further contribution to the subject by measuring blood volume and haemotocrit changes as well as haemoglobin. This expedition spent $8\frac{1}{2}$ months above 15,000 ft. (4570 m), including 5 months at 19,000 ft. (5800 m), and was therefore in the field much longer than previous expeditions, most of which have lasted 3 months and none longer than 6 months.

METHODS

Blood volumes were estimated by a carbon monoxide method twice before leaving England and three times in the Himalaya. The procedure was as follows:

The subjects rebreathed a gas mixture containing a known quantity of carbon monoxide. Venous blood samples were drawn without stasis before and after 10 min of rebreathing. The rebreathing system consisted of a mouthpiece, soda-lime container and 2-l. anaesthetic bag, to which oxygen could be added from another bag via a three-way tap. The other arm of the tap was connected to a calibrated chamber of either 150 or 250 ml. capacity, according to the altitude. This was similar to the absorption chamber of a Van Slyke manometric apparatus, and was fitted with a water jacket. Carbon monoxide of measured purity was drawn into this chamber over mercury and stored at known temperature,

TABLE 1. Haemoglobin values and red cell counts on mountaineering expeditions in the Himalaya and Karakoram

Region	Year	Number of subjects	Mean Hb (g/100 ml.)	R.B.C. (10^6/mm^3)	Method	Author
1. Mt. Everest, 29,028 ft. (8848 m)	1924	5	20·6	—	Acid haematin	Somervell (1925)
2. Mt. Nanga Parbat, 26,660 ft. (8125 m)	1938	5	20·0	7·0	Acid haematin	Luft (1941)
3. Mt. Cho Oyu, 26,750 ft. (8153 m)	1952	8	20·3	—	Oxyhaemoglobin	Pugh (1954)
4. Mt. Everest, 29,028 ft. (8848 m)	1953	12	20·9	—	Fe analysis	Pugh (1954)
5. Mt. Kanchenjunga, 28,146 ft. (8580 m)	1954	6	20·3	—	Fe analysis	Matthews *et al.* (1955)
6. Mt. Makalu, 27,750 ft. (8458 m)	1954	10	19·0	6·29	Fe analysis	Pace *et al.* (1956)
7. Chomo Lungma glacier, Karakoram	1955	6	21·1	—	Reflecting spectrophotometer	Brendel (1956)
8. Mingbo glacier, 19,000 ft. (5800 m)	1960/61	8	19·6	5·72	Oxygen capacity	Pugh (1962)
Weighted mean and S.D.			$20·19 \pm 0·69$	6·25		

pressure and humidity. The capacity of the system with the rebreathing bag empty was approximately 0·5 l. Rebreathing was started at the end of a normal inspiration and with the rebreathing bag empty. The carbon monoxide was introduced during 1 min, 150 ml. being used at sea level and 250 ml. at altitude; small amounts of oxygen were admitted at intervals. Infra-red analysis of the gas left in the bag at the end of 10 min rebreathing yielded carbon monoxide concentrations varying from 0·015 to 0·03 %, and it was calculated that all but 0·5–1·0 ml. of the carbon monoxide was absorbed.

The blood samples were analysed immediately by Scholander & Roughton's (1943) special method for small quantities of carbon monoxide, using a pipette delivering 76·0 mm^3 of blood and a syringe having 50 divisions on the capillary. The same calibrated syringe and pipette were used in all experiments. The haematocrit of both blood samples was read after 30 min rotation at 3000 rev/min and 10 cm mean radius. Haemoglobin was estimated from COHb capacity (Scholander & Roughton, 1943) using pipettes calibrated to deliver 39·30 mm^3 of blood at sea level and 19·65 mm^3 at altitude respectively.

The blood volume measurements carried out in the Himalaya were all done at the Mingbo base camp situated at 15,300 ft. (4650 m), and subjects who had been living at the laboratory at 19,000 ft. came down specially to have this done. The subjects were engaged in ordinary light activities when the estimations were carried out, and were thoroughly warm, with distended hand veins.

In the final series of experiments, carried out in March 1961, the centrifuge could not be used and haematocrit and haemoglobin data from other experiments conducted some days later at 19,000 ft. were used in calculating cell volume and plasma volume.

RESULTS

The results are set out in Table 2.

TABLE 2. Results obtained on six subjects at

Subject and age (yr)	Date	Place	Time above sea-level (weeks)	Body weight (kg)	Blood volume (total) ml.	Change (%)	ml./kg body wt.	Change (%)	Haematocrit (%)
JBW 32	18.viii.60	London	—	73·9	6050	—	81·9	—	43·2
	1. ix.60	London	—	—	6092	—	—	—	—
	22. i.61	Mingbo	8	69·4	6040	− 0·2	87·0	+ 6·2	54·0
	24. iii.61	Mingbo	17	64·0	6760	+11·7	105·6	+28·9	58·5
MPW 35	18.viii.60	London	—	72·5	5690	—	78·5	—	42·5
	2. ix.60	London	—	—	5580	—	—	—	—
	22. i.61	Mingbo	8	70·8	5781	+ 1·6	81·7	+ 4·1	59·0
	25. iii.61	Mingbo	17	66·7	6811	+19·7	102·1	+30·1	65·5
MBG 23	10.viii.60	London	—	73·9	5320	—	72·0	—	42·0
	6.viii.60	London	—	—	5300	—	—	—	—
	14. xii.60	Mingbo	14	69·9	4870	− 8·5	69·7	− 3·2	52·0
	10. i.61	Mingbo	18	69·9	5350	+ 0·6	76·5	+ 6·3	52·0
	25. iii.61	Mingbo	28	67·6	6231	+17·1	92·2	+28·1	57·2
JSM 30	10.viii.60	London	—	72·5	5275	—	72·8	—	42·0
	11.viii.60	London	—	—	5290	—	—	—	—
	11. xii.60	Mingbo	14	64·4	4457	−15·5	69·2	− 4·9	58·0
	12. i.61	Mingbo	18	63·5	5176	− 1·9	81·5	+12·0	59·2
	24. iii.61	Mingbo	28	60·8	5190	− 1·6	85·4	+17·3	54·0
LGP 51	18.viii.60	London	—	75·0	6313	—	84·2	—	40·0
	29. xii.60	Mingbo	15	73·0	5815	− 7·9	79·7	− 5·3	52·0
	25. i.61	Mingbo	19	73·0	5743	− 9·0	78·7	− 6·5	53·6
	25. iii.61	Mingbo	27	68·2	6291	− 0·3	92·2	+ 9·5	50·2
TON 31	4. vii.60	London	—	68·0	5290	—	77·8	—	48·0
	19. xii.60	Mingbo	15	62·0?	5166	− 2·3	83·3	+ 8·2	57·0
	1. i.61	Mingbo	17	—	5070	− 4·2	—	—	—

Blood volume. The largest difference between blood volume determinations on different days on a given subject at sea level was 135 ml., which coincided with the onset of cold weather; but including this result the mean difference between days was only 70 ml. and the standard deviation of a single measurement was ± 31 ml.

Blood volume measurements at altitude were started in December as soon as the Mingbo laboratory was ready, and determinations were done on subjects MBG, JSM, LGP and TON, who had been above sea level since early September, and had been living for varying periods between 13,000 ft. (4000 m) and 19,000 ft. TON had been approximately 4 weeks longer at 19,000 ft. than the others and showed only a minor change in blood volume, while the others showed falls of −7·9 to −15·5 %. One month later MBG and JSM, who had been continuously at 19,000 ft. showed restoration of blood volume to sea-level value, but the value for LGP, who had remained at 15,300 ft. was still significantly reduced. Meanwhile, TON had left the expedition, suffering from tropical sprue (Pugh, 1962).

At this stage the first altitude measurements were made on JBW and MPW, who had joined the expedition at Mingbo on 17 December (3 weeks after leaving sea level) and gone straight up to 19,000 ft. They were thus

sea level and after varying periods at 19,000 ft

Red cell volume				Plasma volume				Haemoglobin concentration	
ml.	Change (%)	ml./kg body wt.	Change (%)	ml.	Change (%)	ml./kg body wt.	Change (%)	(g/100 ml.)	Change (%)
2614	—	35·4	—	3436	—	46·5	—	14·7	—
—	—	—	—	—	—	—	—	—	—
3262	+24·8	47·0	+32·8	2778	−19·2	40·0	−14·0	18·6	+26·5
3955	+51·3	61·8	+74·6	2805	−18·4	43·8	− 5·8	20·0	+36·1
2418	—	33·4	—	3272	—	45·1	—	14·0	—
—	—	—	—	—	—	—	—	—	—
3411	+41·1	48·2	+44·3	2370	−27·6	33·5	−25·7	19·7	+40·7
4461	+84·5	66·9	+100·3	2350	−28·2	35·2	−22·0	21·3	+52·1
2234	—	30·2	—	3086	—	41·8	—	14·1	—
—	—	—	—	—	—	—	—	—	—
2532	+13·3	36·2	+19·9	2338	−24·2	33·5	−19·9	17·4	+23·4
2782	+24·5	39·8	+31·8	2568	−16·8	36·7	−12·2	17·6	+24·8
3564	+59·5	52·7	+74·5	2667	−13·6	39·5	− 5·5	19·2	+36·2
2216	—	30·6	—	3059	—	42·2		13·5	—
—	—	—	—	—	—	—	—	—	—
2585	+16·7	40·1	+31·0	1872	−38·8	29·1	−31·0	19·2	+42·2
3064	+38·3	48·3	+57·8	2112	−31·0	33·2	−21·3	19·3	+43·0
2803	+26·5	46·1	+50·7	2387	−22·0	39·3	− 6·9	17·8	+31·9
2525	—	33·7	—	3788	—	50·5	—	12·3	—
3024	+19·8	41·4	+22·8	2791	−26·3	38·3	−24·2	16·3	+32·5
3078	+21·9	42·2	+25·2	2665	−29·6	36·5	−27·7	17·4	+41·5
3158	+25·1	46·3	+37·4	3133	−17·3	45·9	− 9·1	17·0	+38·2
2539	—	37·3	—	2751	—	40·5	—	15·7	—
2945	+16·0	47·5	+27·3	2221	−19·3	35·8	−11·5	19·4	+23·6
—	—	—	—	—	—	—	—	—	—

subjected to severe altitude stimulation comparatively soon after leaving sea level, and their blood volume levels did not show the preliminary fall seen in the other subjects, but were comparable with their sea-level values.

The final series of measurements were made after a further period of 2 months, which all subjects spent mainly at 19,000 ft. MPW and MBG, however, spent the last 3 weeks climbing Mount Ama Dablam (22,500 ft. = 6860 m) and were subject to greater altitude stress as well as mountaineering stresses. Their blood volumes were now 20 and 17 % higher than at sea level. JBW, who had remained continuously at 19,000 ft., also showed a considerable increase (13·5 %). But the blood volumes of the other two subjects (JSM and LGP) were still at sea-level value. JSM, late in the 2 months period, had spent 10 days at 13,000 ft. LGP was less tolerant of altitude than other subjects and had had to go down for a few days' rest at 15,300 ft. every month; he was also 51 years of age, while the other subjects were all under 37.

Red cell volume. In contrast with the fluctuation of blood volume, red cell volume increased progressively in all subjects throughout the expedition. The largest changes (+60 % and +85 %) were seen in the two subjects who climbed Ama Dablam. JSM and LGP, whose final blood volumes were similar to their sea-level values, showed increases of approximately 25 %, while JBW was intermediate.

Plasma volume. Plasma volume decreased drastically in all subjects, but recovered to some extent with the passage of time. The values after 2–4½ months at altitude were 18–39 % lower than at sea level, and the final values 11–27 % lower than at sea level.

Haemoglobin. The principal changes in haemoglobin concentration took place in the first half of the expedition. Between January and April the mean value for the five subjects on whom blood volume determinations were done rose only from 18·5 to 19·1 g/100 ml., although there was considerable individual variation. The largest increases of 2·1 and 1·6 g/100 ml. were found in the subjects climbing Mount Ama Dablam (MPW and MBG). LGP and JSM showed slight reductions.

Mean corpuscular haemoglobin concentration (*M.C.H.C.*). There was satisfactory agreement between the haematocrit readings and the haemoglobin determinations. The average mean corpuscular haemoglobin concentration (M.C.H.C.) was 33·2 %, which may be compared with a figure of 33·6 % from the data of Dill *et al.* (1937). The standard deviation of difference between haemoglobin as measured and haemoglobin predicted from haematocrit (i.e. Hc × 33·2) was ± 0·5 g/100 ml. for sixteen pairs of observations, excluding the data on subject LGP. This subject's M.C.H.C., which was initially 30·8 %, rose progressively during the expedition, the final value in April 1963 being 33·9 %. There were no significant changes in M.C.H.C. in other members of the party.

Total haemoglobin (THb). Since M.C.H.C. was constant and independent of altitude, percentage changes in total haemoglobin (THb) were the same as the percentage changes in cell volume shown in Tables 2 and 3.

Relation to body weight. All members of the scientific party lost weight during the expedition, especially while they were at 19,000 ft. When this is taken into account, the apparent increase in blood volume and red cell volume in each individual is considerably magnified and the change in plasma volume reduced. The final values for red cell volume/kg body weight in JBW and MPW were 74–100 % greater than the corresponding values at sea level in JBW, MBG and MPW, and 37–51 % greater in JSM and LGP. The final values for plasma volume/kg body weight were close to the sea-level values, with one exception (MPW), the largest difference being −9 %.

Table 3 summarizes the above results for all subjects. The mean values

TABLE 3. Percentage changes in blood after (I) 18 weeks at altitudes between 13,000 ft. (4000 m) and 19,000 ft. (5800 m); (II) 3–6 weeks at 19,000 ft.; and (III) 9–14 weeks at or above 19,000 ft.: figures in brackets are percentage changes/kg body wt. Four subjects (MBG, JSM, LGP and TON) in Phase I; five subjects (MBG, JSM, LGP, JBW and MPW) in Phases II and III.

	Percentage change from sea level		
	I	II	III
Blood volume	− 8·6 (− 1·3)	− 1·8 (+ 4·42)	+ 9·3 (+22·8)
Red cell volume and total haemoglobin	+16·5 (+25·3)	+30·1 (+38·4)	+49·4 (+67·5)
Plasma volume	−27·2 (+21·7)	−24·8 (−20·4)	−19·9 (− 9·9)
Haemoglobin concentration	+30·4	+35·4	+38·9

show (1) a small initial reduction in blood volume in Phase I, return to sea-level value by Phase II, and a moderate increase after a longer period at or above 19,000 ft. (Phase III); (2) major reduction of plasma volume in Phase I, with partial recovery in Phases II and III; (3) progressive increase in red cell volume (and total haemoglobin) throughout the expedition; and (4) major increase in haemoglobin in Phase I, a small further increase by Phase II and a minimal change by Phase III.

DISCUSSION

The reproducibility of the blood volume measurements was satisfactory as judged by the sea-level data, and there is no reason to suppose that the accuracy suffered at altitude. The accepted correction factors, by which observed haematocrit should be multiplied in order to correct for trapped plasma (0·96) and for the difference between venous and body haematocrit (0·91) (Gregersen & Rawson, 1959), have not been applied in calculating blood volume, cell volume and plasma volume, since we were interested in changes rather than absolute values (see Appendix, p. 353).

On Mount Everest (1953) there was no correlation between haemoglobin concentration and climbing performance, and Somervell had made a somewhat similar observation on the 1924 Everest expedition. On the present expedition, Sherpa porters wintering at 19,000 ft. had greater endurance and work capacity than members of the scientific party, but they had similar or lower haemoglobin values, as was also the case on Mount Everest (Pugh, 1954).

The highest blood volumes and red cell volumes were observed in JBW and MPW. The former, on the one hand, had the highest aerobic capacity among the scientific party at 19,000 ft. and performed well at 24,400 ft. (7440 m). The latter had a lower aerobic capacity than JBW at both these altitudes, and at 19,000 ft. his aerobic capacity was only average; but his red cell volume, haemoglobin concentration and haematocrit were significantly higher than anyone else's. This was associated with a low arterial oxygen saturation and lower ventilation than in other subjects.

That hypoxia was the dominant influence determining red cell volume and haemoglobin concentration is shown by the increases in all subjects on ascending from 15,300 to 19,000 ft. and by the further increase shown by subjects taking part in the ascent of Mount Ama Dablam. As well as the greater mean altitude while climbing the mountain, the subjects would have been more hypoxic for 5–7 hr/day while they were climbing, because of the reduction in arterial oxygen saturation during physical work (West, Lahiri, Gill, Milledge, Pugh & Ward, 1962). Nevertheless, as far as haemoglobin concentration is concerned, their values were still within the normal range for Himalayan parties.

The present results are qualitatively similar to the findings of Reynafarje and his colleagues (1957) on five subjects who spent a year at Morococha (14,900 ft., 4470 m). Like us, they observed major reductions in plasma volume during the first 2–4 months at altitude. Earlier observations by Asmussen & Consolazio (1941) on Mount Evans had suggested that plasma volume reduction is an early response to altitude and causes an increase in haemoglobin concentration of 10–15 % during the first few days at altitude, the continued rise in subsequent weeks being due to increased erythropoiesis.

Reynafarje found that red cell volume went on increasing for 10–12 months, which is consistent with our results during a shorter stay at 19,000 ft. In later months he observed a rise in blood volume and partial recovery of plasma volume, which is also similar to our findings. Like us, he observed reduction of blood volume and plasma volume during the first 2–4 months, and increase of blood volume above the sea-level control values during subsequent months, but only partial recovery of plasma volume. Red cell volume rose progressively throughout their stay.

The fact that in both investigations haemoglobin concentration stayed constant or rose only very slowly after the first few months, while red cell volume rose continuously, shows clearly that plasma volume changes play an important part in the regulation of haemoglobin concentration at altitude. Changes in plasma volume would also explain rapid fluctuations in haemoglobin concentration which have been noted in members of Himalayan assault parties. Hitherto increases have been attributed to extreme erythropoietic stimulation and reductions to inhibition of erythropoiesis and/or increased haemolysis.

Another source of variation in haemoglobin concentration on Himalayan expeditions is the fact that the haemoglobin estimations have been made on finger blood. In our experience, variations of 1–2 g/100 ml. can occur under Himalayan conditions, unless great care is taken to see that the subjects are thoroughly warm and a free flow of blood is obtained A large number of haemoglobin estimations were done on the present expedition with finger blood and the Medical Research Council colorimeter. The calibration was checked against oxygen capacity by means of venous samples, and was satisfactory. Mean values on finger blood were approximately 0·5 g/100 ml. higher than the results on arterialized venous samples. The day-to-day individual fluctuation was of the order of $\pm$ 1·5 g. Inclusion of these data in calculating absolute values for erythrocytes accounts for the rather high M.C.H.C. of 35 % given in a preliminary report on the expedition's findings (Pugh, 1962).

The lack of correlation between physical performance and haemoglobin concentration at altitude has suggested to some investigators that elevation of haemoglobin plays a relatively minor role in adjustment to altitude, and Houston & Riley (1947) pointed out that it has little effect on the mean capillary oxygen tension, on account of the shape of the HbO_2 dissociation curve. However, according to measurements of cardiac output (Pugh, 1964), the cardiac output for a given work load at 19,000 ft. was the same as at sea level, and it was shown this would be impossible without elevation of haemoglobin. The superior work capacity of the only Sherpa studied depended on greater cardiac output and superior lung diffusion and not on difference in haemoglobin level.

SUMMARY

1. Blood volume, haematocrit and haemoglobin concentration were followed in six subjects during prolonged acclimatization at varying altitudes up to 19,000 ft. (5800 m).

2. After 18 weeks at heights ranging from 13,000 ft. (4000 m) to 19,000 ft., blood volume was lower than at sea level in four out of six subjects, the mean reduction being 9 %. During further periods of 3–6

weeks, and 9–14 weeks, at (or above) 19,000 ft., blood volume rose slowly, the final mean value being 9 % above the sea-level control value.

3. The fall in blood volume was associated with a reduction in plasma volume which amounted to 27 %. Plasma volume subsequently rose slowly, but the final mean value was still 19 % below sea-level control value.

4. Red cell volume and total haemoglobin rose progressively, reaching mean values 49 % above the sea-level control values.

5. Haemoglobin concentration rose by 30 % in the first 18 weeks, and 8 % during the following 9–14 weeks.

6. According to data collected on eight expeditions to the Himalaya and Karakoram, haemoglobin concentrations in plainsmen living at 18,000 ft. (5500 m) and above do not reach the values (22·9 g/100 ml.) reported in Andean natives living at 17,500 ft. (5340 m). The mean value for eight parties was 20·19 g/100 ml. (S.D. ± 0·69). It was concluded that change of plasma volume is a major factor in the regulation of haemoglobin concentration under these conditions.

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APPENDIX

Blood volume (BV), red cell volume (CV) and plasma volume (PV) were computed from (i) volume of CO absorbed (V_{CO}), (ii) the difference between the initial and final blood CO concentration (F_{CO}), and (iii) the venous haematocrit (Hct), as follows:

$$BV = \frac{V_{CO}}{F_{CO}}, \quad CV = BV \times Hct, \quad PV = BV - CV.$$

For comparison with data which have been corrected for plasma trapping and difference between body and venous haematocrit, the following corrections may be applied (Gregersen & Rawson, 1959):

Correction factor for trapped plasma	0·96,
Correction factor for body/venous haematocrit	0·91.

In the blood volume estimation F_{CO} is a function of haemoglobin concentration (Hb), and therefore of haematocrit, for Hct = M.C.H.C. × Hb; and M.C.H.C. was constant and independent of altitude. The correction for difference between body and venous haematocrit should therefore be applied, but the correction for plasma trapping is not required because it applies equally to F_{CO} body and F_{CO} venous. Thus

$$\frac{F_{CO\ body}}{F_{CO\ venous}} = \frac{f(\text{Hb body})}{f(\text{Hb venous})} = \frac{f(\text{Hct body}) \times 0{\cdot}96}{f(\text{Hct venous}) \times 0{\cdot}96} = 0{\cdot}91$$

and F_{CO} body = F_{CO} venous × 0·91. Therefore

$$\text{corrected BV} = \frac{V_{CO}}{F_{CO} \times 0{\cdot}91} = BV \times 1{\cdot}1.$$

In the CV and PV estimation the corrections for trapped plasma and difference between body and venous haematocrit produce the following results:

$$\begin{aligned} \text{corrected CV} &= \frac{V_{CO}}{F_{CO} \times 0{\cdot}91} \times Hct \times 0{\cdot}91 \times 0{\cdot}96 \\ &= BV \times Hct \times 0{\cdot}96, \\ \text{and corrected PV} &= (BV \times 1{\cdot}1) - (BV \times Hct \times 0{\cdot}96) \\ &= BV\ (1{\cdot}1 - 0{\cdot}96\ Hct). \end{aligned}$$

Courtice & Gunton (1949), however, using a CO method similar to ours, found no significant difference between simultaneous PV determinations by the CO method and the dye method in healthy young men. They point out that in investigations designed to compare venous and body haematocrit it has not been ascertained that the dye method employed gives a true

unequivocal value for plasma volume. The only correction they applied was the correction for trapped plasma (0·96).

Extravascular CO. Root, Roughton & Gregersen (1946) have fully discussed the CO method for blood volume and the disappearance of CO from the blood. Their arguments apply to our work and need not be repeated. From their results, as well as those of Courtice & Gunton (1949), a slow diffusion of CO from the blood is apparent, but it is impossible to say dogmatically whether or not there is a large uptake of CO by the myoglobin in the first 5 min. However, since the resting cardiac output is approximately equal to the blood volume and since about only one-fifth of the cardiac output goes to the resting muscles, it seems unlikely that any large fraction of CO diffuses into the myoglobin in the first few minutes, especially as the affinity of myoglobin for CO compared with O_2 is only a twentieth of that of blood haemoglobin. If this is true, then any change in the myoglobin content of the muscles during acclimatization to altitude would have a negligible effect on the blood volume estimation.

Sjöstrand, using a somewhat different CO method (Sjöstrand, 1953), has adduced evidence that a 5% correction for extravascular CO is adequate, and according to Roughton & Root (1945) only half of this is accounted for by respiratory pigments. Hence, if myoglobin shows the same increase with acclimatization as the blood haemoglobin, then the effect on the estimate of blood volume would be less than 1%.

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