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BLOOD VOLUMES OF ESKIMOS AND WHITE MEN BEFORE AND DURING ACUTE COLD STRESS

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Several investigators have shown that average blood and plasma volumes of Eskimos are greater than are those found in white subjects living in a temperate climate. This evidence has recently been reviewed by Bass & Henschel (1956). Other reports have shown that in Eskimos the blood flow through the hand and forearm was greater than in a control group of medical students at rest in a room at 20° C (Brown & Page, 1952; Brown, Hatcher & Page, 1953) and it has also been noted that during a test exposure to cold a greater reduction of blood flow through the hand and forearm occurred in the Eskimos than in the white controls.

This report will present the results of more recent studies that have been made of the blood volume changes which occur in the two groups during a test cold exposure.

METHODS

The Eskimo subjects were six adult males found free of disease on a thorough medical examination and known from inquiry to be making their living by hunting and trapping in the traditional Eskimo fashion. The observations on the Eskimos were made at Coral Harbour, Southampton Island, N.W.T., during July and August 1954 when the mean daily maximum temperature was about 12° C and the mean daily minimum about 3.5° C. The white men were medical students and internes at Queen's University, and the observations on them were made in September and October 1954 at Kingston, Ontario. The temperature of the rooms used for the experiments was $20 \pm 1^\circ \text{C}$ and the relative humidity 47-57%. Air movement was kept constant by an electric fan 8 ft. from the feet of the subject. Each subject was dressed in the same flannel drawers, trousers, shirt and socks and lay supine in bed with head and thorax raised to an angle of 45°. The age, height and weight of each subject are given in Table 1.

Two series of determinations of plasma volume were made on the Eskimos using the methods of Allen & Semple (1951) and Allen (1953). In the first (preliminary) series all six subjects were used and six blood samples obtained from each subject at 15 min intervals after the injection of T-1824. These observations showed that for 90 min after injection the relation between time and plasma concentration of dye was linear (Fig. 1A). The second series consisted of seven experiments on five of the subjects used in the first series and blood samples were secured every 15 min for

1 hr after dye injection, to redetermine control volumes. Then the right arm was immersed to a level just above the elbow in a water-bath at $5 \pm 0.5^\circ$ C. The exposure to cold was continued for 1 hr and during this period blood samples were secured at 20 min intervals. Two more blood samples were secured at 20 min intervals during the recovery period. Dye concentrations were determined in the control samples and in the samples secured 20 min after the start of the immersion. Any change in plasma volume during the 20 min of cold exposure was determined from the concentration of dye. If no change in plasma volume occurred, the dye concentration in the plasma could be expected to decrease at the same rate as in the control period, and it was assumed that deviation from the expected disappearance rate indicated a change in plasma volume (Fig. 1 B).

TABLE 1. Measured and predicted plasma volumes of Eskimo and white subjects

Subject	Expt. no.	Age (yr)	Height (m)	Weight (kg)	Plasma volumes			M/P (%)
					Measured, M		Predicted*, P	
					(l.)	(ml./kg)		
Eskimos								
Okalik	1	34	1.64	68.0	3.46	50.9	2.80	123.6
	2			68.3	3.45	50.5	2.81	122.8
	3			68.0	3.65	53.7	2.80	130.4
Evalayuk	4	31	1.66	61.7	2.95	47.8	2.67	110.5
	5			59.7	2.94	49.2	2.63	111.8
	6			60.0	3.03	50.5	2.63	115.2
Akat	7	23	1.61	64.9	2.85	43.9	2.66	107.1
	8			63.5	3.00	47.2	2.63	114.1
Pootolik	9	20	1.63	61.8	3.54	57.3	2.62	135.1
	10			62.0	3.53	56.9	2.63	134.2
Tatti	11	28	1.87	77.4	4.62	59.7	3.55	130.1
	12			75.3	4.60	61.1	3.50	131.4
Napyuk	13	29	1.66	65.4	3.22	49.2	2.77	116.2
				Means	3.45	52.1	2.82	121.7
Whites								
A. S.	I	34	1.74	68.0	2.86	42.1	3.01	95.0
D. M.	II	35	1.79	76.6	3.26	42.6	3.34	97.6
H. H.	III	35	1.74	66.3	3.07	46.3	2.96	103.7
S. B.	IV	31	1.86	73.7	3.39	46.0	3.43	98.8
M. M.	V	22	1.83	63.5	2.92	46.0	3.09	94.5
C. W.	VI	22	1.85	79.8	3.92	49.1	3.56	110.1
				Means	3.24	45.4	3.23	100.0

* Predicted plasma volumes were calculated by multiplying the predicted blood volumes (see Table 2) by 0.575, which is the reciprocal of the average human male haematocrit reading.

Wintrobe tubes were used to measure the haematocrit values of all blood samples, and the cell percentages so obtained were multiplied by the factor 0.96 to correct for trapped plasma and by the factor 0.91 to correct for unequal cell distribution in the blood stream (Chaplin, Mollison & Vetter, 1953). Haematocrits were also corrected for cells removed in previous blood samples (Allen & Semple, 1951). Each plasma sample was frozen as soon as the dye concentration had been determined, and on return to Kingston the protein concentrations were determined by measuring the total nitrogen and the non-protein nitrogen by micro-Kjeldahl methods.

A single control determination of plasma volume was made on each white subject during the 40 min that preceded immersion of the arm, and during this time blood samples were secured at 10 min intervals. In all other respects experiments on the white subjects were identical to those described for the Eskimos.

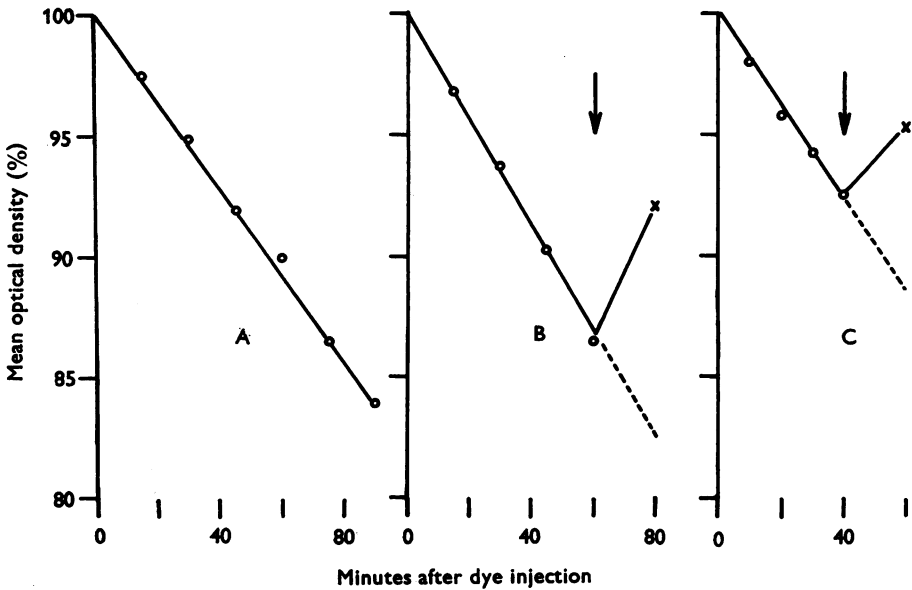


Fig. 1. Mean optical densities (expressed as percentages of optical densities at zero time) of serial plasma samples after injection of T-1824 at zero time. Each percentage plotted represents a mean value (at given time) for all experiments. A, six experiments on six Eskimo subjects, no cold immersion; B, seven experiments on five of the subjects in A, ↓ indicates time of arm immersion in 5° C water-bath; C, six experiments on six white men, arm immersion as in B.

RESULTS

Control measurements. Table 1 shows that Eskimo plasma volumes were significantly greater ($P < 0.01$) than those of the white men when expressed in terms of body weight. In terms of surface area the plasma volumes of the six Eskimos ranged from 1.75 to 2.28 l./m² (mean 1.98) as compared with the range in white men of 1.58–1.92 l./m² (mean 1.70) ($P < 0.05$). The Eskimo haematocrit values (Fig. 2 and Table 2) were lower than those of the white men and the difference was roughly proportional to the difference between the plasma volumes. There was, therefore, no significant difference between the Eskimos and white men with respect to total red cell volume, but the greater plasma volume of the Eskimos resulted in this group having a larger total blood volume.

Protein concentrations (Fig. 2) of Eskimo plasma under control conditions ranged from 6.97 to 8.48 g/100 ml. (mean 7.45) which were significantly higher ($P < 0.02$) than the concentrations in the plasma samples obtained from the white men, which ranged from 5.98 to 7.21 g/100 ml. plasma (mean 6.62).

Post-immersion measurements. After 20 min of immersion of the arm in cold water the mean dye concentration in the plasma was increased (Fig. 1 B and 1 C) in all experiments. The mean reduction in plasma volume, thus indicated, was slightly greater in the five Eskimos than in the six white men but the difference was not significant (Table 3).

TABLE 2. Blood and cell volumes of Eskimo and white subjects

Expt. no.	Haematocrit (%)	Blood volumes				Cell volumes			
		Measured, M		Predicted, P*	M/P (%)	Measured, M		Predicted, P†	M/P (%)
		(l.)	(ml./kg)	(l.)		(l.)	(ml./kg)	(l.)	
Eskimos									
1	43.7	6.15	90.4	4.87	126.3	2.69	39.6	2.07	130.0
2	41.6	5.91	86.5	4.88	121.1	2.46	36.0	2.07	118.8
3	36.0	5.70	83.8	4.87	117.0	2.05	30.1	2.07	99.0
4	39.9	4.91	79.6	4.65	105.6	1.96	31.8	1.98	99.0
5	36.0	4.59	76.9	4.57	100.4	1.65	27.6	1.94	85.1
6	34.9	4.65	77.5	4.58	101.5	1.62	27.0	1.95	83.0
7	42.3	4.94	76.1	4.63	106.7	2.09	32.2	1.97	106.1
8	39.6	4.97	78.3	4.57	108.8	1.97	31.0	1.94	101.5
9	37.7	5.68	91.9	4.56	124.6	2.14	34.6	1.94	110.3
10	36.0	5.52	89.0	4.57	120.8	1.99	32.1	1.94	102.6
11	36.1	7.23	93.4	6.18	117.0	2.61	33.7	2.63	99.2
12	36.7	7.27	96.5	6.09	119.4	2.67	35.3	2.59	103.1
13	39.6	5.33	81.5	4.82	110.6	2.11	32.3	2.05	102.9
Mean	38.5	5.60	84.7	4.91	113.8	2.16	32.6	2.09	103.1
Whites									
I	42.5	4.97	73.1	5.23	95.0	2.11	31.0	2.22	95.0
II	37.2	5.19	67.7	5.81	89.3	1.93	25.2	2.47	78.1
III	42.2	5.31	80.1	5.15	103.1	2.24	33.8	2.19	97.7
IV	43.5	6.00	81.4	5.97	100.5	2.61	35.4	2.54	97.2
V	43.7	5.19	81.7	5.38	96.5	2.27	35.7	2.29	99.1
VI	37.5	6.27	78.6	6.20	101.1	2.35	29.4	2.64	89.0
Mean	41.1	5.49	77.1	5.62	97.6	2.25	31.8	2.39	94.4

* Calculated from the equation: $BV_1 = (0.417 \times \text{height}_{\text{m}}^3) + (0.045 \times \text{weight}_{\text{kg}}) - 0.03$ (Allen *et al.* 1956).

† Calculated from the equation: $CV_1 = (\text{predicted blood volume}) \times 0.425$ (average human male haematocrit.)

The haematocrit values of blood samples drawn 20 min after immersion varied considerably, but were on the average slightly higher than in the control period in both Eskimos and white men; but again the difference was not significant. At the end of the exposure to cold the haematocrit values were significantly increased in both groups (Fig. 2). During the recovery period the haematocrit values of the Eskimos immediately began to decrease but did not, on the average, reach control values (Fig. 2). Those of the white men, on the other hand, tended to rise further and remained significantly elevated at the end of the 40 min recovery period. Fig. 2 shows that the test exposure to cold resulted in no significant changes in the protein concentration of plasma of either group, although in the Kingston subjects there was a slight rise during the recovery period.

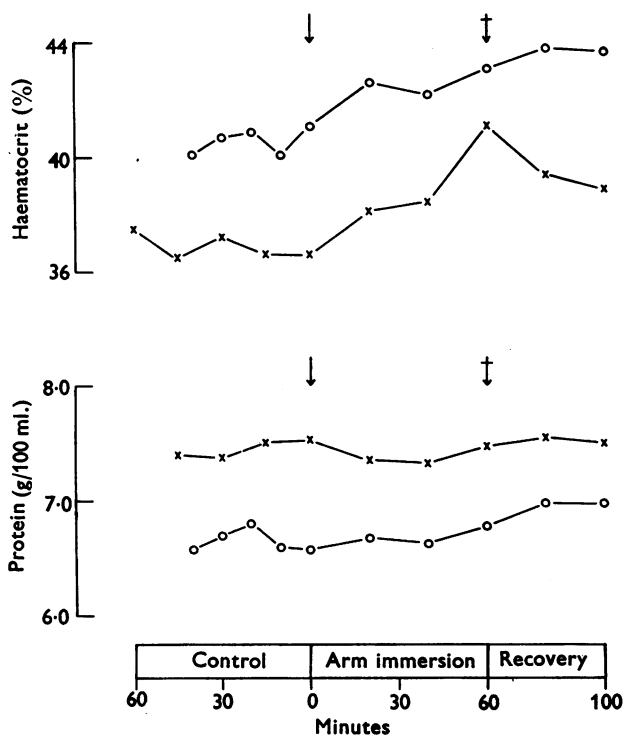


Fig. 2. Changes in mean haematocrit percentages and in mean protein concentrations in plasma during control, immersion and recovery periods. Each point plotted represents the mean (at given time) for seven experiments on Eskimos (x) or for six experiments on white men (o). ↓, start of arm immersion in 5° C water-bath; ↓̄, end of immersion.

TABLE 3. Changes in plasma and red cell volumes that resulted from the immersion of one arm in a 5° C water-bath for 20 min. Volumes are expressed as percentages of control volumes

Expt. no.	Eskimos. Changes in		Expt. no.	Whites. Changes in	
	Plasma volume (%)	Cell volume (%)		Plasma volume (%)	Cell volume (%)
2	-6.2	+7.3	I	-5.5	-1.4
3	-0.5	-11.7	II	-13.7	-9.1
5	-12.2	-6.0	III	-5.6	+1.4
6	-17.3	-13.6	IV	-5.9	-0.4
8	-7.7	-2.5	V	-5.5	-5.8
10	-9.8	+8.0	VI	-6.1	+2.3
12	-15.0	-10.5			
Means (7 Expts.)	-9.8	-4.1	Means	-7.1	-2.2
Means (5 Eskimos)	-10.1	-3.4			

DISCUSSION

The present results confirm earlier observations (Brown, Bird, Boag, Delahaye, Green, Hatcher & Page, 1954*a*; Brown, Bird, Boag, Boag, Delahaye, Green, Hatcher and Page, 1954*b*; Meehan, 1954) that Eskimos who still hunt and trap and thereby incur considerable exposure to cold have a greater plasma volume than do Caucasians, when volumes are referred either to body weight or surface area. However, it has long been understood that correlations between blood and plasma volumes and body type or, more specifically, lean body mass, are better than are correlations between these volumes and either weight or surface area. A formula for the ready estimation of body fat, and hence of lean body mass, has recently been worked out by Allen, Peng, Chen, Huang, Chang & Fang (1956) and they have shown that blood volume predictions based on their formula are appreciably more reliable than are predictions based on either weight or surface area. Plasma volumes for both the Eskimos and the white men in the present series of experiments were calculated using the formula proposed by Allen *et al.* (1956) and these volumes are included in Table 1. There is very good agreement between measured and predicted volumes in the white men but the average measured plasma volume of the Eskimo is very significantly greater ($P < 0.01$) than the predicted volume. Thus the Eskimos have significantly more plasma than either the control group of white men used in these experiments or the very much larger and more representative group of adult males used by Allen *et al.* (1956) to establish the prediction formula. In an investigation in 1950 by two of the present authors and others (Brown *et al.* 1954*a, b*) the average plasma volume in nineteen adult male Eskimos was found to be 3.69 l. and when the Allen formula was applied to the average height and weight of this group the predicted plasma volume was 2.75 l. In the present group the total red cell volumes are not significantly different from the red cell volumes of the white men or from predicted red cell volumes. This result is apparently not in agreement with earlier observations, in which increased red cell volumes were noted (Brown *et al.* 1954*a, b*). The haematocrit values in the earlier work were not, however, corrected for either 'trapped' plasma or for unequal cell distribution. When the data are appropriately corrected the average cell volume is appreciably less than first reported, but is still 2.43 l. as compared with a predicted volume of 2.03 l. (+21.2%). It may be that the Eskimos of the group studied in 1948 were better acclimatized to cold than those of the present group. The Eskimos of Southampton Island are gradually acquiring more of the white man's habits and many of them are leading a more sheltered existence than formerly. To-day many of the group live at the trading post, whereas in 1948 most of them came to the post by water after the break-up of the ice, which occurs early in July, and left for isolated parts of the island well before freeze-up,

which can occur as early as mid September. For the present experiments it was difficult to get subjects who had employed themselves during the previous winter entirely at hunting and trapping.

The elevated blood and plasma volumes of the Eskimos are considered by us to be a physiological adjustment to repeated and severe exposure to cold. Bass & Henschel (1956) criticized this conclusion as being largely speculative, and suggested that factors other than acclimatization, such as diet and genetics, may be the cause of the Eskimo high blood volume. There is little evidence that diet *per se* affects blood volume, and indeed there is good evidence that it does not. Thus Lippman (1948) showed that in rats a large increase in protein consumption produced no significant changes in plasma or blood volumes. Davis (1942) reported the blood volumes of eleven normal men living on British war-time rations, a diet relatively rich in carbohydrate and poor in fat and protein, and they were similar to those reported in comparable American studies (Stewart & Rourke, 1941; Noble & Gregerson, 1946), where the subjects lived on a diet much richer in protein and fat. Other large experimental groups existing on very low protein-high carbohydrate diets in Formosa (Allen *et al.* 1956) and Nanking (Gregerson, Lu & Wang, 1949) showed blood volumes that were essentially the same as those from the control group of Kingston students observed in this study. Eskimos in the Canadian Eastern Arctic have a high intake of vitamin A, but the maintenance of a similarly high vitamin A intake for one month in Caucasians has been found by us to have no effect on blood volume (Bird, Brown, Morley & Semple, unpublished). There is also little evidence to suggest that genetics plays a role in Eskimo high blood volume. These people are related to the folk of Asia who, as noted above, have the same relative blood volumes as Caucasians (Gregerson *et al.* 1949; Allen *et al.* 1956). Among the Eskimos themselves those of mixed racial origin showed the same high blood and plasma volumes as the men of pure Eskimo stock. An example in the present series is the Eskimo subject Tatti, 1.87 m (Tables 1 and 2), and other examples have been reported (Brown *et al.* 1954*b*). In our opinion it is the suggestion that either diet or genetics plays a role in this phenomenon which is speculative.

Bass & Henschel (1956) also questioned the assumption that Eskimos are actually cold-acclimatized. There is some cause for such criticism if reports by Stefansson (1921) and Rodahl (1953) are uncritically accepted. The truth is that the summer conditions near Great Bear Lake as described by Stefansson (1921) are quite different from those prevailing in the central and eastern Canadian Arctic. Stefansson (1921) writes '...for six weeks the temperature rose to 90° in the shade nearly every day...the sun does not set and there is no respite through the cooling darkness' (90° = 32.2°C.). The conditions actually encountered at Coral Harbour have been given in the earlier section of this report. Similarly, Rodahl (1953) states that Eskimos spend most of the day

in temperatures higher than those found in the white man's house. These reports led Bass & Henschel (1956) to conclude that the Eskimo lives largely in a tropical or subtropical microclimate. In winter the group of Eskimos on whom the present report is based lived outdoors for weeks on end while at work on their trap-lines. For periods in the day they could be described as keeping part of their bodies in a tropical microclimate, but for other periods circumstances do not permit such ideal conditions and there is in fact a good deal of exposure to cold. The temperatures of their living quarters are interesting. Morning temperatures in two igloos in the month of April were between -8.5° and 0° C and in two typical shacks they were between -2.5° and 11° C. Wisely chosen clothing can do much to compensate for a low ambient temperature, but for an Eskimo still living the traditional native life completely to avoid exposure to cold is an impossibility. To be an Eskimo is not necessarily to be acclimatized to cold, but it is our conclusion, for the reasons given, that our selected Eskimo subjects were so acclimatized.

The acute effects of cold stress have been noted by several investigators and are quite different from the acclimatization changes that result from repeated or prolonged exposure. In general a decrease in blood volume has been reported (Conley & Nickerson, 1945; Stein, Elliott & Bader, 1948; Rodbard, Saiki, Malin & Young, 1951; D'Amato & Hegnauer, 1953). Conley & Nickerson (1945) found the decrease was temporary and the volumes tended to return to normal in a few days. When the exposure to cold has been somewhat longer and more severe, there has been evidence that plasma volume possibly increased. LeBlanc, Stewart, Marier & Whillans (1954) exposed men dressed in shorts, socks and shoes to $15.0 \pm 0.5^{\circ}$ C for 16 days and found the haematocrit values decreased during the exposure. Barlow (1954) made haematocrit readings on soldiers before and after a 23-day winter exercise and reported a 2% decrease. It may also be noted here that Deb & Hart (1956) reported that the blood volume of rats exposed for 5 weeks to 6° C was 22% greater than the blood volume of rats kept at 30° C. The localized acute cold stress used in the present series of experiments resulted, as expected, in decreases in blood volumes of both Eskimos and whites. Table 3 shows that the decrease came about chiefly as a result of decreased plasma volumes, although there was some evidence of lowered red cell volume in most individuals. The adjustments made by the Eskimos were greater and occurred more quickly than those made by the white group, although the differences are not statistically significant. The changes in haematocrit values, which were observed throughout the entire period of exposure to cold, suggested continuing decreases in Eskimo plasma volume; decreases that were more rapid and of greater magnitude than the changes in the plasma volumes of the Kingston group. During the recovery period the return to control levels was also more rapid in the Eskimo group.

Indeed, Fig. 2 shows that haematocrit levels suggested no trend back to control plasma volumes in the Kingston subjects during the 40 min period of observation that followed immersion.

It is interesting that there occurred no significant changes in plasma protein concentrations throughout these experiments (Fig. 2). Rodbard *et al.* (1951) and D'Amato & Hegnauer (1953) have also reported that hypothermia resulted in no change in the total protein concentration of the plasma but a reduction in the volume available for the distribution of T-1824. They concluded that part of the circulation was closed off as a result of this stress and thus plasma (D'Amato & Hegnauer, 1953) or blood (Rodbard *et al.* 1951) was locked away. This explanation would account for their evidence, inasmuch as they used successive injections of the dye; the first was a control and subsequent injections were given during cold stress. In our case the disappearance of a single dye injection was observed and the 'shutting off' of a part of the circulatory system would not account for the changes observed in the rate of disappearance of the dye that occurred after cold immersion. It might be argued that in the case of the work cited above (Rodbard *et al.* 1951; D'Amato & Hegnauer, 1953) that changes in the endogenous optical properties of plasma were responsible for the observed increase in dye density. However, such an argument does not hold when the dye concentration has been ascertained by quantitative extraction as in our experiments. To explain the failure of the proteins to reflect, by increased concentration, egress of fluid, we offer two possible explanations. There may be, as a temporary result of the increased metabolic rate accompanying cold stress (Bird, Brown, Lennox & Semple, unpublished), a change in the quality of the circulating protein. Wasserman & Mayerson (1951, 1952) have shown that in normal dogs the globulin fractions are metabolized at about twice the rate of the albumin fraction. It is thus possible that on cold immersion there would occur a preferential reduction in the globulin fraction. Semple (1955) has reported that after haemorrhage and dextran infusion there is at first preferential reduction in the globulin and fibrinogen fractions of dog plasma. In the case of fibrinogen there is evidence of a specific reaction with the dextran (Ricketts, 1952) but there is no such evidence for globulins. It is true that stress is usually followed by an increase in globulin fractions (Selye, 1950) but this does not preclude the possibility that there occurs with cold a temporary and preferential increase in globulin catabolism, a marked decrease in the rate of return of protein to the circulation, and a significant fluid loss to the interstitial spaces. An alternative possibility is that the dye-labelled albumin has a different metabolic behaviour from albumin not so labelled. The results of a number of investigations indicate that the *in vivo* activity of the albumin molecule is affected by either chemical or radioactive 'labels'. Sear, Allen & Gregersen (1953) have shown that in dogs the disappearance rate of T-1824 from plasma is very much

greater than is the disappearance rate of ^{131}I . Similarly, Masouredis & Beeckmans (1955) found that albumin labelled with ^{131}I leaves the plasma at more than twice the rate of ^{14}C -labelled albumin, and Margen & Tarver (1956) report large differences between the metabolic activities of ^{131}I and ^{35}S -labelled albumins. In cold stress experiments, then, the possibility that the dye-tagged albumin did not share proportionately in the increased metabolism cannot be excluded. If this were the case, the artificial protein fraction has reflected the loss of vascular fluid, whereas the unlabelled albumin and the other protein fractions have not. The mechanisms behind the failure of the total protein concentration of plasma to reflect the fluid loss that accompanies acute cold stress are in need of further study.

SUMMARY

1. Plasma volumes, haematocrit values and plasma proteins were measured under control conditions in a group of adult male Eskimos and in a group of medical students in Kingston, Ontario. Changes in these parameters that resulted from immersion of one arm in a water-bath at 5°C for one hour were then observed, and final observations were made during the forty minutes that followed the end of arm immersion.

2. The Eskimo plasma volumes were significantly greater relative to body weight, surface area and body fat content than those of the Kingston group, and resulted in high blood volumes. The authors believe the high blood and plasma volumes of Eskimos to be a feature of cold acclimatization. Eskimo haematocrit values were lower than those of the Kingston group, but there was no significant difference between the two groups in respect to red cell volumes. Protein concentrations in Eskimo plasma were significantly higher than those of the Kingston group.

3. Immersion resulted in decreased plasma volumes and increased haematocrit values. These changes were somewhat greater and occurred more rapidly in the Eskimo group, but the differences between the two groups in these respects were not significant. Immersion resulted in no significant changes in total red cell volumes.

4. After the end of the immersion the haematocrit values returned more quickly to control levels in the Eskimo group than in the white group.

5. Plasma protein concentrations remained essentially constant in spite of the reductions in vascular fluid that were indicated by changes in T-1824 concentrations and increases in haematocrit readings during immersion. These observations are discussed.

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