THE EFFECT OF POSTURE (STANDING) ON THE SERUM PROTEIN CONCENTRATION AND COLLOID OSMOTIC PRESSURE OF BLOOD FROM THE FOOT IN RELATION TO THE FORMATION OF EDEMA

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These studies were made to determine the effect of the erect posture on the colloid osmotic pressure and the concentration of the serum proteins of the blood of the foot with particular reference to the occurrence of edema in persons with slightly lowered serum proteins (1, 4). Studies by others (2, 9, 10, 11) have shown that standing causes a general concentration of blood in the body, but determinations of the serum protein concentration and osmotic pressure of blood from the local dependent parts have not been reported.

EXPERIMENTAL

The subjects included normal persons, five patients with nutritional edema and one patient with nephrosis. Four of the cases of nutritional edema were of the simple, endemic type described previously (1, 4); in one case the nutritional edema was associated with a carcinoma of the stomach. In some of the patients the edema was slight.

The following procedure was employed. One or two hours after a light breakfast the subject reclined for an hour or more. At the end of this time the venous pressure in the arm was determined by the direct method and a sample of blood was drawn for the determination of the serum protein concentration, colloid osmotic pressure and in some experiments, the relative cell volume (hematocrit). The volume of the leg while standing was then roughly determined by measuring the amount of water it displaced from a rigid metal boot which reached to approximately the mid-thigh. The subject now stood, moving as little as possible, at an angle of 75 degrees [1] against an inclined table. A supporting belt under the arms and across the knees, so arranged as to avoid constriction, proved a necessary precaution. At the end of an hour or more the pressure in a

[1] According to Turner, Newton and Haynes (Am. J. Physiol., 1930, **94**, 507) this position is equivalent to the vertical in respect to hydrostatic and vascular changes.

vein of the foot, on the dorsum or at the level of the internal malleolus, was measured and a sample of blood was drawn from the same vein for the determinations listed above. In several experiments a sample of blood was also drawn from the arm for comparison with that from the foot. As soon as possible after the "standing" specimens were obtained the volume of the leg was measured again. In one experiment the order was reversed and the subject first stood and then reclined. Various technical difficulties and, in some instances, fainting on the part of the subject, made it impossible to carry out these procedures in strictly uniform time. In some experiments fainting made it necessary for the subject to recline for a short time after the standing period before blood could be obtained from the arm or the leg volume measured. These variations may have caused some irregularities in the results. Most of the experiments were purposely carried out during hot weather. The serum protein concentration was determined by the method of Howe (3) as described elsewhere (4). The colloid osmotic pressure was measured by Krogh's method (5) as modified by Wells (6). Hematocrit determinations were carried out in duplicate, using tubes with an inside diameter of 1 mm. and a length of 10 cm. The filled tubes were rotated at a speed of 3000 r.p.m. for 30 minutes. Heparin was used as the anticoagulant.

RESULTS

The principal data are shown in the accompanying tables and charts. All but two of the normal subjects fainted during or at the end of the standing period and those two nearly lost consciousness. In most instances fainting seemed to be precipitated by the venipuncture in the foot but pallor of the face, yawning and giddiness before the venipuncture were indicative of an increasing cerebral anemia. One normal subject became nauseated and vomited. None of the *patients* lost consciousness but two became faint and giddy. Two of the patients voided large amounts of urine, 800 and 720 cc., respectively, at the end of the period of reclining, though the bladder had been emptied shortly before lying down. This fluid was partly replaced by drinking water.

The data show very clearly that standing for approximately one hour causes a large increase in the concentration of serum proteins and a great rise in the osmotic pressure of blood in the feet and legs of normal subjects.[2] (Table I.) Thus, in Subject 1, who stood for 62 minutes with a

[2] It is assumed that blood in the foot at the end of the reclining period had the same concentration of protein and the same colloid osmotic pressure as blood from the arm. With the subject in the reclining position it is very difficult and many times impossible to obtain a sufficiently large sample of blood from the foot without using stasis. In a special study practically identical values were found in blood from these two regions after the subjects had reclined an hour or more. The correspondence is probably not as close in patients with edema due to a slower and irregular resorption of fluid from the tissues of the feet and legs.

TABLE I

Experimental data

Subject		Serum protein									Colloid osmotic pressure			Venous pressure	Hematocrit cell volume		Increase in leg volume		Standing time	Pitting edema (legs)
		Total			Albumin			Globulin												
			Difference	Increase		Difference	Increase		Difference	Increase		Difference	Increase			Difference				
Normals		*grams per cent*	*grams per cent*	*per cent*	*grams per cent*	*grams per cent*	*per cent*	*grams per cent*	*grams per cent*	*per cent*	*cm. water*	*cm. water*	*per cent*	*cm. water*	*per cent*	*per cent*	*cc.*	*cc. per 100 cc. leg*	*minutes*	
1	R*	7.14			4.79			2.35			37.1			9.7	40.0					
	S	9.05	1.91	26.7	6.08	1.29	26.9	2.97	0.62	26.3	51.9	14.8	39.8	92.7	46.0	6.0	260	4.28	62	0
2	R	6.87			4.72			2.15			34.7			7.5	37.0					
	S	9.64	2.77	40.3	6.62	1.90	40.2	3.02	0.87	40.4	57.1	22.4	64.5	109.3	49.0	12.0	270	4.63	63	0
3†	R	6.69			4.57			2.12			32.9			7.4	39.5					
	S	8.66	1.97	29.4	5.93	1.36	29.7	2.73	0.61	28.8	48.7	15.8	48.0	103.7	45.0	5.5	290	4.87	43	0
4	R	7.03			4.87			2.25			34.5			11.8	37.0					
	S	8.30	1.27	18.0	5.60	0.73	17.1	2.70	0.45	20.0	45.5	11.0	31.9	96.6	37.0 (clotted)		225	3.11	66	0
5	R	6.33			4.13			2.20			29.8			5.7	45.0					
	S	7.70	1.37	21.6	5.02	0.89	21.5	2.86	0.48	21.8	38.5	8.6	29.2	120.0	60.0	15.0	300	3.61	90	+
Average				27.2			27.1			27.5			42.7				272	4.10	66	

TABLE I (*continued*)

Subject		Serum protein									Colloid osmotic pressure			Venous pressure	Hematocrit cell volume		Increase in leg volume		Standing time	Pitting edema (legs)
		Total			Albumin			Globulin												
			Difference	Increase		Difference	Increase		Difference	Increase		Difference	Increase			Difference				
Patients		*grams per cent*	*grams per cent*	*per cent*	*grams per cent*	*grams per cent*	*per cent*	*grams per cent*	*grams per cent*	*per cent*	*cm. water*	*cm. water*	*per cent*	*cm. water*	*per cent*	*per cent*	*cc.*	*cc. per 100 cc. leg*	*minutes*	
6	R	6.47			4.36			2.11			31.5			4.5	29.3					+
	S	7.92	1.45	22.4	5.45	1.09	25.0	2.47	0.36	17.1	43.7	12.2	38.7	105.7	38.0	8.7	410	7.45	88	++
7	R	6.58			3.62			2.96			28.8			5.2	34.0					++
	S	7.54	0.96	14.6	4.22	0.60	16.5	3.32	0.36	12.2	37.1	8.3	28.8	98.6	38.0	4.0	250	4.29	75	+++
8	R	6.67			4.27			2.40			31.8			10.7						+
	S	8.54	1.87	28.0	5.49	1.22	28.5	3.05	0.65	27.0	46.7	14.9	46.8	99.5			253	3.07	110	++
9‡	R	4.88			3.11			1.77			19.9			1.1						++
	S	6.27	1.39	28.5	3.94	0.83	26.7	2.33	0.56	31.6	27.3	7.4	37.1	88.4					85	++++
10	R	6.53			4.63			1.90			33.4			7.4						+
	S	8.68	2.15	32.9	6.14	1.51	32.6	2.54	0.64	33.6	49.4	16.0	47.9				410	7.20	90	++
11§	R	4.16			2.41			1.75			14.4			7.9	34.0					++++
	S	4.09	−.07	−1.7‖	2.28	−.13	−5.7‖	1.81	0.06	4.0	15.8	1.4	7.9	65.7	35.5	1.5	330	3.79	85	+++++
Average				25.3			25.9			24.3			40.1				330	5.16	88	

* R = Reclining; S = Standing—Analyses of the edema fluid from Subjects 9 and 11 showed a protein content of 0.37 and 0.27 gram per cent respectively.

† Could not stand continuously.

‡ Reverse order.

§ Sat in chair.

‖ Apparent decrease.

venous pressure in the foot of 92.7 cm. of water, the total proteins increased from 7.14 to 9.05 grams per 100 cc. or 26.7 per cent, albumin from 4.79 to 6.08 or 26.9 per cent and globulin from 2.35 to 2.97 or 26.3 per cent. The colloid osmotic pressure rose from 37.1 to 51.9 cm. of water, an increase of 39.8 per cent and the volume of the leg increased 260 cc. or 4.28 cc. per 100 cc. of leg.

Among the normal subjects, venous pressures while standing varied between 92.7 and 120 cm. of water. Standing time was from 43 to 90 minutes. The increase in total protein ranged from 18 to 40 per cent, albumin from 17 to 40 per cent and globulin from 20 to 40 per cent. The average increase in these three values was 27.2, 26.6, and 27.6 per cent respectively. Accompanying the increased concentration of proteins there was a rise in the colloid osmotic pressure of the blood serum ranging from 8.6 to 22.4 cm. of water, an increase of from 29.2 to 64.5 per cent. The average increase was 42.7 per cent. The rise in osmotic pressure was proportionately greater than the increase in the concentration of proteins because of an increase in specific osmotic pressure, i.e., pressure per gram of protein, which becomes greater as the concentration of protein increases (Table II). In one sub-

TABLE II

Increase in specific osmotic pressure (Pressure per gram per cent of protein) with increased concentration of serum proteins

Subject	Reclining	Standing	Difference	Increase
Normals	*cm. water*	*cm. water*	*cm. water*	*per cent*
1	5.2	5.7	0.5	9.6
2	5.1	5.9	0.8	15.7
3	4.9	5.6	0.7	14.2
4	4.9	5.5	0.6	12.2
5	4.7	5.0	0.3	6.4
Average	5.0	5.5	0.5	8.9
Patients				
6	4.9	5.5	0.6	12.2
7	4.4	4.9	0.5	11.3
8	4.8	5.5	0.7	14.6
9	4.1	4.4	0.3	7.3
10	5.1	5.7	0.6	11.8
11	3.5	3.9	0.9	11.5
Average	4.5	5.0	0.5	11.5

ject this increase in specific colloid osmotic pressure amounted to as much as 16 per cent.

With the loss of fluid from the blood there was a corresponding increase in leg volume ranging from 225 to 300 cc. Calculated on a comparable basis of the increase per 100 cc. of leg, the increase ranged from

3.11 to 4.87 cc. None of the strictly normal subjects developed pitting edema. Subject 5, though included in the group of normals, was found to have a serum protein concentration slightly below the lower normal limit and developed slight pitting edema of the legs. Although she stood longer than the other normal subjects pitting edema was already present at the end of 60 minutes.

The concentration of blood was greater in the feet and legs than in the upper part of the body (arms) where the average increase in total protein was only 13.2 per cent, and in osmotic pressure 23.1 per cent, compared with 27.2 and 42.7 per cent respectively in the foot (Table III).

TABLE III

Comparison of the increase in the concentration of serum proteins and in the colloid osmotic pressure of blood in the arm and in the foot after standing

Subject	Total serum protein				Colloid osmotic pressure			
	Reclining	Standing	Difference	Increase	Reclining	Standing	Difference	Increase
	grams per cent	*grams per cent*	*grams per cent*	*per cent*	*cm. water*	*cm. water*	*cm. water*	*per cent*
1 Arm	7.14	7.82	0.68	9.5	37.1	42.4	5.3	14.2
Leg*	7.14	9.05	1.91	26.7	37.1	51.9	14.8	39.8
2 Arm	6.87	7.96	1.09	15.8	34.7	43.0	8.3	23.9
Leg	6.87	9.64	2.77	40.3	34.7	57.1	22.4	64.5
3 Arm	6.69	7.55	0.86	12.8	32.9	40.0	7.1	21.5
Leg	6.69	8.66	1.97	29.4	32.9	48.7	15.8	48.0
4 Arm	7.03	7.72	0.65	9.2	34.5	44.7	10.2	29.6
Leg	7.03	8.30	1.27	18.1	34.5	45.5	11.0	31.9
5 Arm	6.33	7.50	1.17	18.5	29.8	37.6	7.8	26.2
Leg	6.33	7.70	1.37	21.6	29.8	38.5	8.7	29.2
Average								
Arm				13.2				23.1
Leg				27.2				42.7

* The concentration of protein and the colloid osmotic pressure of the blood in the foot is assumed to be the same as in the blood from the arm while the subject was reclining. See footnote 2.

Some of the subjects with edema showed a concentration of serum proteins and a rise of colloid osmotic pressure equal to that observed in some of the normal subjects but the average for the group was somewhat less (Table I). In the case of Subject 7, the increase was less than in any of the normal subjects. Subject 11, with nephrosis, who was unable to stand and sat in a chair with a venous pressure in the foot of 65.7 cm. of water, showed slight apparent decreases in the concentration of total proteins

and albumin which are probably within the range of experimental error. Excluding this latter experiment the increase in total proteins in the subjects with edema ranged from 14.6 to 32.9 per cent, albumin from 16.5 to 32.6 per cent and globulin from 12.2 to 33.6 per cent, an average of 25.3, 25.9 and 24.3 per cent respectively. Colloid osmotic pressure increased from 28.8 to 47.9 per cent. Specific colloid osmotic pressure increased as in the normal subjects and to about the same degree (Table II). The average increase in leg volume, 330 cc., was somewhat greater than in the normal subjects. The increase per 100 cc. of leg ranged from 3.07 to 7.45 cc. with an average of 5.68. The average standing time, however, was considerably longer in the case of the patients. All of the patients had more or less pitting edema which became demonstrably greater on standing.

In those experiments in which hematocrit determinations were made the increase in cell volume after standing indicates that a true concentration of the blood had occurred (Table I). The lack of agreement in the degree of concentration as expressed by the hematocrit readings and the protein content respectively is not due to errors in analysis but to the fact, as Landis and his associates have pointed out (7), that changes in cell and plasma volume are calculated on the basis of whole blood while protein concentration is expressed on the basis of grams per 100 cc. of plasma or serum.

DISCUSSION

There is little doubt that the great concentration of the blood observed in these experiments was due to the filtration of fluid from the blood into the tissues of the dependent parts, as evidenced by the increase in leg volume. In our experiments, however, none of the strictly normal subjects developed pitting edema in spite of filtering pressures which should, unopposed, cause enough fluid to be filtered in the time the subjects stood to induce such an edema. Landis and Gibbon (8) have shown that filtration of fluid from the vessels (arm) begins at a venous pressure of about 15 cm. of water and increases at the rate of around 0.0033 cc. per minute per 100 cc. of tissue (arm) for every 1 cm. rise in pressure In our normal subjects venous pressures in the foot of 96.6 to 120 cm. of water were recorded. Undoubtedly, as Krogh and his associates (9) have shown, the rising colloid osmotic pressure, itself due to the loss of fluid from the blood, automatically diminishes filtration. This is, however, insufficient to stop filtration short of edema and will oppose only a part of the effective filtering pressure. Other mechanisms must operate to limit filtration, the most important of which appears to be an increasing tissue pressure which rises with the accumulation of extravascular fluid. Attempts at direct measurement of tissue pressure proved unsatisfactory but Landis and Gibbon (8) have found that the accumulation of 1 cc. of fluid per 100 cc. of tissue (arm) will raise the tissue pressure sufficiently to slow filtration .033 cc. per minute per 100 cc. of tissue, corresponding to a reduction in venous

pressure of 10 cm. of water. Five cc. of extravascular fluid per 100 cc. of tissue slows filtration 1.10 cc. per minute and is equal to a reduction of 35 cm. of water in venous pressure. On the basis of these results we have calculated the assumed tissue pressures at the end of the standing period (Table IV). The method is as follows: The calculations of the tissue pressure and of the effective filtering and antifiltering pressures are based on the observations of Krogh, Landis and Turner (9) and Landis and Gibbon (8). It has been necessary to assume (1) that these authors' constants of filtration and retardation of filtration for the arm are applicable to the leg of the standing individual; (2) that the colloid osmotic pressure of venous blood from the foot is, on the average, the same as that of capillary blood of the leg; that the increase of mean capillary pressure of the leg is two-thirds the venous pressure as measured at the level of the foot and represents the average hydrostatic pressure of that part of the leg whose volume was measured. The level representing the average venous pressure in the part of the leg whose volume was measured was taken to be the mid-point of the boot. This was roughly one-third the distance from the point at which venous pressure was measured to the xiphoid; (3) that the value of the mean venous pressure above which filtration of fluid occurs is $3/7\ \pi_1$ when π_1 is the initial colloid osmotic pressure and π_2 the final colloid osmotic pressure. (The average normal colloid osmotic pressure while reclining is taken to be 35.0 cm. Filtration begins at a venous pressure of approximately 15 cm. of H_2O (Krogh, Landis and Turner) which is 3/7 of the osmotic pressure); (4) that the increase in colloid osmotic pressure plus the other changes (tissue pressure) have produced a balance at the end of the observation so that equilibrium exists. Then, where V is the venous pressure at the foot, $(2/3\ V - 3/7\ \pi_1)$ should be equal to $(\pi_2 - \pi_1) +$ increase in tissue pressure. The increase in tissue pressure is approximately 10 cc. of water for each 1 cc. of fluid per 100 cc. of leg. Hence $2/3\ V - 3/7\ \pi_1$ (filtering pressure) should equal $\pi_2 - \pi_1 + 10\ F$ (antifiltering pressure) where F equals in cc. the increased fluid per 100 cc. of leg at the end of the experiment. If the above is not approximately true then (1) equilibrium has not been established, (2) some other factor must come in to balance the equation, (3) any or all the above assumptions are wrong. Attention is directed to the large part which tissue pressure apparently plays in limiting the escape of fluid from the vessels. In most of the subjects this pressure was at least twice as great as the effective colloid osmotic pressure. In Subject 11, with nephrosis and a severe grade of edema, it was twenty-seven times greater and in the "normal" subject who developed pitting edema (Subject 5) more than four times greater.

If the rising colloid osmotic pressure of the blood and the increasing tissue pressure are the primary factors restricting filtration, then, at the point of equilibrium, their combined pressures should equal or slightly exceed the filtering pressure. In Table IV, we have compared the effective

TABLE IV

Comparison of the effective filtering pressure and the combined effective osmotic and tissue (antifiltering) pressures at the end of the experiment *

Subject	Effective osmotic pressure	Effective tissue pressure	Combined effective osmotic and tissue (antifiltering) pressures	Filtering pressure	Standing time
Normals	*cc. water*	*cc. water*	*cc. water*	*cc. water*	*minutes*
1	14.8	42.8	57.6	45.8	62
2	22.4	46.3	68.7	58.0	63
3†	15.8	48.7	64.5	55.0	43
4	11.0	31.1	42.1	49.7	66
5	8.6	36.1	44.7	67.0	90
Patients					
7	8.3	42.9	51.2	53.2	75
8	14.9	30.7	45.6	52.7	110
11‡	1.4	37.9	39.3	37.5	85

* The method of calculating these pressures is given in the body of the paper.
† Could not stand continuously.
‡ Sat in chair.

filtering pressure with the antifiltering pressure (combined effective colloid osmotic and tissue pressure) at the end of the experiment in those experiments in which the data are available. In three of the five normal subjects the forces opposed to filtration were, at the end of the experimental period, larger than the filtering pressure by a greater or less amount. In two the filtering pressure was the greater and it is probable that filtration had not ceased. Whether in Subject 4, further standing would have resulted in an equilibrium with the production of a pitting edema cannot be determined. From simple inspection and palpation she seemed close to such a state. Subject 5 did show a definite though slight pitting edema at this stage even though equilibrium had apparently not been reached. One of the patients showed an excess of pressure opposed to filtration suggesting that filtration had been stopped at the level of pitting edema existing at the end of the experiment. In the others filtration may still have been occurring.

It may be doubted whether these calculations are justified or the results significant in view of the relatively inaccurate method of measuring leg volume and the number of assumptions which were necessary. Nevertheless, we believe that the magnitude of the changes are sufficient to allow for a considerable error without seriously impairing the significance of the results. Even though there may be large errors in the tissue pressures and in the filtering pressures as we have calculated them, the magnitude of the colloid osmotic pressures, which are much more accurately determined, indicates that some other factor, presumably tissue pressure, was of much

greater importance in limiting filtration than was the increase in colloid osmotic pressure.

According to Thompson et al. (10), equilibrium in the standing position is reached after about 30 minutes. While this may in general be true our results suggest that individual variations occur and that individuals who have lower serum colloid osmotic pressures or whose tissues are relaxed and less well filled with extravascular fluid may require a longer time to reach equilibrium. In persons with serum colloid osmotic pressures close to, or slightly below, the lower normal limits equilibrium might not be reached until sufficient fluid had accumulated in the tissues to cause pitting edema. For example, Subject 5, with a serum protein concentration and colloid osmotic pressure just below normal values, did actually develop slight pitting edema and had apparently not reached equilibrium after 90 minutes. On the other hand individuals with more than the usual amount of fluid in the tissues or with unusually high osmotic pressures might establish equilibrium in a shorter time than 30 minutes. It should be emphasized that equilibrium as referred to here is to be understood as existing for a limited time only. With continued high filtering pressures (standing) it is probable that the tissues would stretch, permitting further filtration.

It will be observed (Table I) that in the normal subjects the percentage increases in the concentration of total protein, albumin and globulin respectively were very nearly the same. This might be taken as evidence that the vessels in those subjects were impermeable to plasma proteins on the assumption that had they been permeable they would have been more permeable to the smaller albumin molecule. This should have resulted in a relatively greater concentration of globulin than albumin had there occurred any significant leak of proteins through the capillary wall. The assumption that the capillaries are practically impermeable to the proteins under conditions similar to those in our experiments has been made by Thompson, Thompson and Dailey (10) and by Krogh, Landis and Turner (9). Waterfield (11) found, however, that standing caused not only a loss of fluid from the blood but considerable amounts of protein as well, while Drinker and his associates (12) believed that the capillaries are quite permeable to the proteins even at venous pressures much lower than obtained in our experiments. More recently Landis and his associates (7), using the arm and artificially raised venous pressures, have shown that while the capillaries under normal conditions are nearly impermeable to protein up to venous pressures of 60 mm. of mercury (71.6 cm. H_2O), above that pressure significant losses occur. At venous pressures of 80 mm. of mercury losses as high as 2.8 grams per 100 cc. of filtrate were found. No difference in permeability of the protein fractions as shown by consistent differences in their percentage increase in concentration in the blood was observed in their experiments or in those of Plass and Rourke

(13) and Rowe (14). In our experiments venous pressures considerably exceeded 60 mm. of mercury and it is probable that there was some loss of protein through the vessel wall. It is possible, however, that the capillaries of the leg are less permeable than those of the arm.

Analysis of the protein content of the filtrate was impossible in the normal subjects because the amount of extravascular fluid was too small to permit obtaining a sample uncontaminated with blood. In Subjects 11 and 9, analysis of the edema fluid showed a protein content of 0.37 and 0.27 grams per cent respectively. However, edema fluid in cases of chronic edema is probably not representative of the capillary filtrate from which it was formed, nor in the present instance was it representative of the filtrate which was produced under the conditions of the experiment.

If significant amounts of protein were lost with the filtrate it is obvious that it would affect the relations between the filtering and antifiltering forces and also the calculations made above with reference to the equilibrium between these forces. It is impossible to calculate the effect of this factor and one would not be justified in simply subtracting the calculated colloid osmotic pressure of the escaped protein, assuming the amount was known, from the colloid osmotic pressure of the protein remaining in the blood. It is believed, however, that whatever the effect might be it would but emphasize the part played by tissue pressure in limiting the loss of fluid from the blood.

Although a rising colloid osmotic pressure of the blood and an increasing tissue pressure appear to be the ultimate mechanisms which limit the filtration of fluid from the blood in the erect posture, both are affected by secondary factors such as circulatory stasis, temperature and tissue tone. Stasis, by causing a greater local concentration of blood probably limits the total loss of fluid from the blood. The importance of this mechanism may be indicated by the fact that stasis occurred in our experiments with environmental temperature as high as 32.8° C. Nevertheless, environmental temperature modifies blood flow greatly and affects the rate of filtration of water from the blood, especially at high venous pressures (8, 15). The influence of higher temperatures may explain, in part, the greater frequency of edema in warmer weather in our patients with nutritional edema and the occurrence of "heat edemas," described by Castellani (16). The effect of tissue tone on the development of edema is obvious.

So far in this discussion no allowance has been made for the effect of the removal of the extravascular fluid. According to Krogh, Landis and Turner (9), small amounts of fluid in the arm are removed principally by resorption, larger amounts by some other mechanism, presumably lymph drainage. In our experiments, as long as the subject stood, any removal of fluid, by either absorption or lymph drainage must have been carried out against a large hydrostatic pressure and it is difficult to believe that much

fluid was removed under the circumstances. The influence of muscular contractions was, of course, inoperative.

The unexpected finding that patients with a relatively constant amount of chronic edema behaved essentially as normal subjects in spite of lower osmotic pressures and an excess of extravascular fluid may be explained by an adjustment to the edema (stretching) which resulted in tissue pressures similar to the normal. Under these conditions the changes in concentration of the blood with changes in posture would be relatively the same unless the amount of edema was rapidly changing, either increasing or decreasing.

In spite of high filtering pressures it is probable that standing for approximately one hour will not cause pitting edema in the legs or feet of most normal persons. However, persons with slightly lowered serum proteins, as Subject 5, might well develop edema under these conditions. Although the experimental conditions are severe, if the factor of time is considered our results suggest that normal ambulatory activity might produce pitting edema in the legs of such individuals. In this case the loss of fluid from the blood might, at certain times, raise an initial serum protein concentration from slightly below normal to within normal limits.

SUMMARY

Standing at an angle of 75 degrees for approximately one hour caused an increase of 18 to 40 per cent in the concentration of serum protein and an increase of 29 to 65 per cent in the colloid osmotic pressure of the blood in the foot of normal subjects. The percentile increase in the total protein concentration and that of the two protein fractions were practically identical. The increase in the concentration of protein and in the osmotic pressure was approximately twice as great as occurred in the blood in the arm. The volume of the leg increased from 3.11 to 4.87 cc. per 100 cc. of leg but pitting edema did not occur in any of the strictly normal subjects.

Patients with chronic (nutritional) edema showed essentially similar changes with a demonstrable increase in the pitting edema. Calculations based on the data obtained suggest that an increase in tissue pressure was three to five times as important in limiting the loss of fluid from the blood as was the increase in colloid osmotic pressure.

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