dative material to induce an increased capillary permeability has been fully restored. When the same procedure is repeated with histamine dihydrochloride in concentrations of 1 :20,000 to 1 :50,000 which, incidentally, according to Bier and Rocha e Silva,[6] are the concentrations of histamine recovered from exudates, the dye usually fails to accumulate homogeneously in the skin as it does in the case of the original exudate or of leukotaxine. Thus, the exact effect on capillary permeability of the exudate is not restored. Histamine has failed to reconstitute the capacity of the exudate when added to the inactive residual exudate fraction obtained after dialysis. This, however, is accomplished perfectly well by leukotaxine or even by the dried diffusate fraction from the dialyzed exudate.[1] The observations are conveniently assembled in Table I.

Conclusions. An inflammatory exudate readily induces an increased capillary permeability as evidenced by the rapid accumulation of trypan blue from the circulation into cutaneous areas treated with the exudative material. Dialysis of the exudate allows the outward diffusion of leukotaxine. The indiffusible residual material remaining after dialysis of the exudate is essentially incapable of increasing capillary permeability with the characteristic homogeneous pattern. The exact original effect of the exudate, however, can be readily reconstituted by merely adding leukotaxine to the indiffusible fraction of the dialyzed exudate. This cannot be obtained by adding histamine in the concentration in which the latter is recovered from exudates. These facts therefore add further support to previous observations that leukotaxine and not histamine is the primary factor concerned in the mechanism of increased capillary permeability in inflammation.

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Effect of Posture on Circulating Blood Volume in a Case of Orthostatic Hypotension and Tachycardia.

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It has been shown[1] that when an individual assumes the erect posture, a decrease in plasma volume follows. This has been explained as due to the augmented hydrostatic pressure in the vascular

bed of the lower part of the body, causing an increased capillary pressure and in turn an increased filtration of fluid from the blood stream. In individuals with orthostatic hypotension and tachycardia, it has been suggested that the abnormal drop of arterial blood pressure and the increase in pulse rate which occur upon standing result from a much greater amount of pooled blood in the lower part of the body as compared to that which occurs in normal subjects.[2] This theory for the most part has been based on experiments in which blood pressure and pulse rate readings were made in patients with orthostatic hypotension and tachycardia in the recumbent and erect positions. Thus, it was demonstrated that when tourniquets were applied to the proximal portion of the thighs and these patients were then placed in the upright position, the arterial blood pressure was maintained at a much higher level than without them.

This explanation has been brought into doubt recently by Stead and Ebert[3] who have shown that patients with orthostatic hypotension do not pool more blood in the lower extremities on standing than do normal subjects under similar conditions and that the fundamental disturbance is the loss of reflex vasoconstriction in response to the fall of blood pressure. Their conclusions were drawn from studies in which the quantities of blood contained in the legs in the recumbent and standing positions were measured in normal subjects and in subjects with orthostatic hypotension.

MacLean and Allen[4] have suggested that the defect in orthostatic hypotension and tachycardia was probably not a fault in the mechanism which produces reflex vasoconstriction of the arterioles but rather a defect in the maintenance of an adequate return of venous blood to the heart as evidenced by the Flack test.[5]

Regardless of the explanation offered, it was thought to be of value to determine in a case of orthostatic hypotension and tachycardia the extent to which the blood volume diminished upon standing and to compare this to similar observations upon normal subjects.

1 (a) Thompson, W. A., Thompson, P. K., and Dailey, M. E., *J. Clin. Invest.*, 1928, **5**, 573; (b) Waterfield, R. L., *J. Physiol.*, 1931, **72**, 110; (c) Keys, A., and Butt, H. R., *Arch. Int. Med.*, 1939, **63**, 165; (d) Turner, A. H., Newton, M. I., and Haynes, F. W., *Am. J. Physiol.*, 1930, **94**, 507.

2 (a) Bradbury, S., and Eggleston, C., *Am. Heart J.*, 1925, **1**, 73; (b) Allen, E. V., and Magee, H. R., *Med. Clin. N. Amer.*, 1934, **18**, 585; (c) Ellis, L. B., and Haynes, F. W., *Arch. Int. Med.*, 1936, **58**, 773.

3 Stead, E. A., Jr., and Ebert, R. V., *Arch. Int. Med.*, 1941, **67**, 546.

4 MacLean, A. R., and Allen, E. V., *J. Am. Med. Assn.*, 1940, **115**, 2162.

5 Flack, Martin, *Brit. Med. J.*, 1923, **2**, 921.

Experiments. Two normal subjects and a subject with orthostatic hypotension and tachycardia were studied. They were kept in the recumbent position overnight and on the following morning while still in the recumbent position, their blood volume, hematocrits, plasma proteins, and hemoglobins were determined. They were then placed in the upright position and kept standing motionless for a period of 10 minutes. The blood studies were then repeated at 5 and 10 minute intervals on standing. The plasma volume was estimated by the Gibson and Evans method[6] as adapted to the Evelyn photoelectric microcolorimeter[7] and the value corrected for the loss of dye from the disappearance curve of the dye from the blood stream. The plasma proteins were estimated by the Barbour and Hamilton method.[8] The hemoglobin concentration in grams per 100 cc was determined with the Evelyn photoelectric colorimeter[9] and the hematocrit percentage was determined with Wintrobe hematocrit tubes.

Results. When 2 normal subjects were placed in the upright position, it will be noted (Table I) that slight hemoconcentration occurs as shown by the increase of hemoglobin, hematocrit, and plasma proteins and that these are in agreement with the decrease of 80 cc of plasma volume which occurred in each case. The plasma volume differences observed in these two normal subjects are small and are reported to show the contrast with the situation found in the pathological subject. These changes, however, are in excellent agreement with those found by Thompson and Thompson,[1a] and Waterfield[1b] in their studies on the effect of upright posture on changes in plasma volume in normal subjects.

When the patient with orthostatic hypotension and tachycardia was placed in the upright posture, a remarkable exaggeration of the normal filtration process was observed (Table II). It should be stated that when this patient was tilted in the upright position, his blood pressure dropped very quickly to 50 mm of Hg. and his pulse rate rose to 150. Although he felt very weak and complained of blurring of vision, there was no loss of mental acuity and he was able to maintain himself in the upright position for 10 minutes without fainting. It will be noted that on standing for 10 minutes there was an absolute decrease of 576 cc (11%) in plasma volume from the resting value and a diminution of 650 cc, or 7½%, of whole blood from the resting value. That this is not due to a mere

[6] Gibson, J. G., and Evans, W. A., Jr., *J. Clin. Invest.*, 1937, **16**, 301.

[7] Gibson, J. G., and Evelyn, K. A., *J. Clin. Invest.*, 1938, **17**, 153.

[8] Barbour and Hamilton, *J. Biol. Chem.*, 1926, **69**, 625.

[9] Evelyn, K. A., *J. Biol. Chem.*, 1936, **115**, 63.

TABLE I.
Effect of Erect Position on Blood Volume, Hematocrit, Plasma Proteins and Hemoglobin in Two Normal Adults.

Position	Blood pressure	Pulse rate	Hemoglobin, g	Hematocrit, %	Plasma proteins, g	Plasma vol., cc	Total blood vol., cc
Case 1							
Recumbent	105/75	72	15.44	51.5	6.63	2,910	6,000
After standing (10 min)	100/75	80	15.89	52.0	7.07	2,830 (diff. 80)	5,900 (diff. 100)
Case 2							
Recumbent	135/79	64	14.57	45.0	8.34	2,480	4,510
After standing (5 min)	110/78	84	15.12	46.2	8.68	2,400 (diff. 80)	4,460 (diff. 50)

pooling of the blood in the vascular bed of the lower part of the body but rather to an augmented filtration into the tissue spaces is supported by the significant rises in the hemoglobin concentration, plasma proteins, and hematocrit readings. In each instance, there is evidence of hemoconcentration; namely, an increase of 0.8 g (5%) in hemoglobin, increase of 6.5% in hematocrit, and an increase of 0.83 g (14%) in plasma proteins. Emphasis is laid upon the fact that in a general way the various measurements, each indicating hemoconcentration, are in agreement with each other.

It may not be amiss to point out that the lower extremities are not necessarily the most important blood reservoirs for a pooling effect but that the splanchnic area is quantitatively very important and may be determining.

Conclusion. Evidence is presented that abnormally great hemoconcentration occurs in the erect posture in a subject with orthostatic hypotension and tachycardia. The magnitude of the effect is great enough to permit the conclusion that abnormal filtration rates aggravate the circulatory embarrassment in this condition.

TABLE II.
Effect of Erect Position on Blood Volume, Hematocrit, Plasma Proteins, and Hemoglobin in Individual with Orthostatic Hypotension and Tachycardia.

Position	Blood pressure	Pulse rate	Hemoglobin, g	Hematocrit, %	Plasma proteins, g	Plasma vol., cc	Total blood vol., cc
Recumbent	104/66	90	15.2	51.5	5.67	4,120	8,490
Standing (10 min)	50/?	150	16.0	54.8	6.5	3,544 (diff. 576)	7,840 (diff. 650)
Two weeks later							
Recumbent	105/70	80		45.		4,280	7,782
Standing (10 min)	52/?	140		48.5		3,690 (diff. 590)	7,235 (diff. 547)