

of the skin. A few typical protocols of such experiments on rabbits are given in Table I.

In the course of repeated experiments on the same animals, some rabbits apparently became refractory after the insulin had been applied to the skin of the abdomen 3 or 4 times. It was found, however, that such animals were not refractory if the hair was shaved off the back or the thigh and the insulin applied on this fresh area.

The above observations on normal rabbits indicate that under the proper conditions insulin may be absorbed through the skin and produce a definite and marked fall in blood sugar.

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Capillary Fragility and Vitamin C.

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It has recently been suggested that tests of capillary resistance may be used as an index of the presence of mild states of vitamin C deficiency or subclinical scurvy.¹⁻⁴ Attempts to correlate the capillary resistance with other laboratory and clinical manifestations of scurvy have resulted in conflicting opinions.⁵⁻¹³

Two methods, fundamentally different in principle, have been used to determine capillary strength. Both depend on the produc-

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¹ Göthlin, Gustaf F., *Skand. Arch. f. Physiol.*, 1931, **61**, 225.

² Göthlin, Gustaf F., *J. Lab. and Clin. Med.*, 1933, **18**, 484.

³ Dalldorf, Gilbert, *Am. J. Dis. Child.*, 1933, **46**, 797.

⁴ Stocking, Ruth E., *Arch. Ped.*, 1933, **50**, 823.

⁵ Hess, Alfred, *J. A. M. A.*, 1932, **98**, 1429.

⁶ Greene, David, *J. A. M. A.*, 1934, **103**, 4.

⁷ Perry, C. B., *Lancet*, 1935, **2**, 426.

⁸ Schultzer, P., and Grüs, O., *Acta Med. Scand.*, 1935, **85**, 563.

⁹ Abt, A. F., Farmer, C. J., and Epstein, I. M., *J. Ped.*, 1936, **8**, 1.

¹⁰ Wright, I. S., *Proc. Soc. Exp. Biol. and Med.*, 1934, **32**, 475.

¹¹ Rinehart, James F., *Ann. Int. Med.*, 1935, **9**, 671.

¹² Harris, L. J., and Ray, S. N., *Lancet*, 1935, **1**, 71.

¹³ Molitsch, M., *J. Lab. and Clin. Med.*, 1935, **21**, 43.

tion of skin hemorrhages, presumably due to rupture of capillary walls. The Rumpel-Leede test, which has been placed on a quantitative basis by the modifications of Göthlin,¹ depends on increasing the intracapillary pressure to the point where petechiae appear in the skin. The "suction" or "negative pressure" test, on the other hand, measures the amount of partial vacuum, applied to the skin, necessary to produce petechiae. The latter procedure has the advantages of being less time-consuming than the Göthlin method and in permitting repeated observations in the same skin area at frequent intervals. The original apparatus of Hecht has been modified by da Silva-Mello,¹⁴ by Dalldorf,³ and by Cutter and Johnson.¹⁵ Difficulties in the interpretation of the literature arise from the fact that the results of the two methods are not comparable, and may lead to different impressions of the capillary strength.^{16, 17}

The purpose of this study was to determine the range and degree of variation of the capillary resistance in normal individuals and to observe its relation to the intake and urinary excretion of ascorbic acid in normal subjects, and the correlation, if any, between capillary strength and specific disease conditions. It should be emphasized that our observations and conclusions relate only to capillary resistance as measured by the suction method. The apparatus used (designed by Dr. S. W. Clausen) consisted of a mercury manometer to which was connected a suction cup and a syringe, by means of which a partial vacuum could be produced, maintained and measured to within one cm. of mercury. The suction cup had an opening one cm. in diameter, with a flange 8 mm. in width, by which the cup could be sealed to the skin with vaseline. The capillary resistance was taken as the least amount of negative pressure (vacuum) in cm. of Hg. applied to the skin for one minute, necessary to produce macroscopic intracutaneous bleeding. In taking the readings, successive, adjacent areas of the skin were taken at intervals of one cm. of Hg., until the lowest level was found at which a single petechial hemorrhage, large enough to be identified by the naked eye, appeared. All readings were made under artificial light—a desk lamp.

A group of 100 normal individuals (75 men, 25 women) between the ages of 15 and 50 were tested. Subjects were, for the most part, physicians, medical students, nurses and other members of the

¹⁴ da Silva-Mello, *München Med. Wchnsch.*, 1929, **41**, 1717.

¹⁵ Cutter, I. S., and Johnson, C. A., *J. A. M. A.*, 1935, **105**, 505.

¹⁶ Weimer, P., *Z. f. d. ges. exp. med.*, 1931, **78**, 229.

¹⁷ Anderson, G. K., unpublished observations.

hospital staff. All were in good health. In each instance, inquiry as to the intake of antiscorbutic foods was made and recorded and the capillary resistance determined. Repeated readings at intervals of several days to several months were made in many of the subjects. It has been shown by Weimer,¹⁶ and confirmed by us, that readings obtained by the suction method vary widely in different areas of the skin surface. The majority of our observations have been made on the inner surface of the upper arm, as this area was found to exhibit the most constant results. In a number of instances, readings were taken on the outer surface of the upper arm as well in order that our observations might be compared with those of others who have used this area.

TABLE I.
Capillary Resistance of Normal Men and Women.

	No. individuals	No. observations	Mean Capillary Resistance mm. Hg.	Standard Deviation	Coefficient of variation
Inner Arm	100	338	13.18 ± 0.141	$\pm 3.83 \pm 0.0994$	29.2%
Outer Arm	66	245	19.82 ± 0.256	$\pm 5.97 \pm 0.165$	30.2%

Table I presents the results of a statistical analysis of the observations in normal men and women. Frequency distribution curves of determinations made on the inner and outer surfaces of the upper arm are shown in Fig. 1. A high degree of variation is apparent in both groups. The coefficient of variation of approximately 30% is higher than the majority of anatomic and physiologic characteristics.¹⁸ Further analysis of the results showed no significant effect of age, sex, coloring (blond or brunette), or of season (fall and spring). Although the mean values for the outer arm were significantly higher than those for the inner arm, the spread between the readings taken in both areas at the same time was quite variable. In a number of instances, the capillary resistance determined on the outer arm was only a centimeter or two greater than that determined on the inner arm at the same time. On a few occasions the capillary resistance was lower on the outer arm than on the inner arm.

A second study was made. One hundred patients in the hospital wards were picked at random. Here, again, the values obtained were without significance either individually or when grouped according to disease condition—the range was similar to the normal series.

¹⁸ Pearl, R., *Medical Biometry and Statistics*, 1923, W. B. Saunders & Co., p. 276.

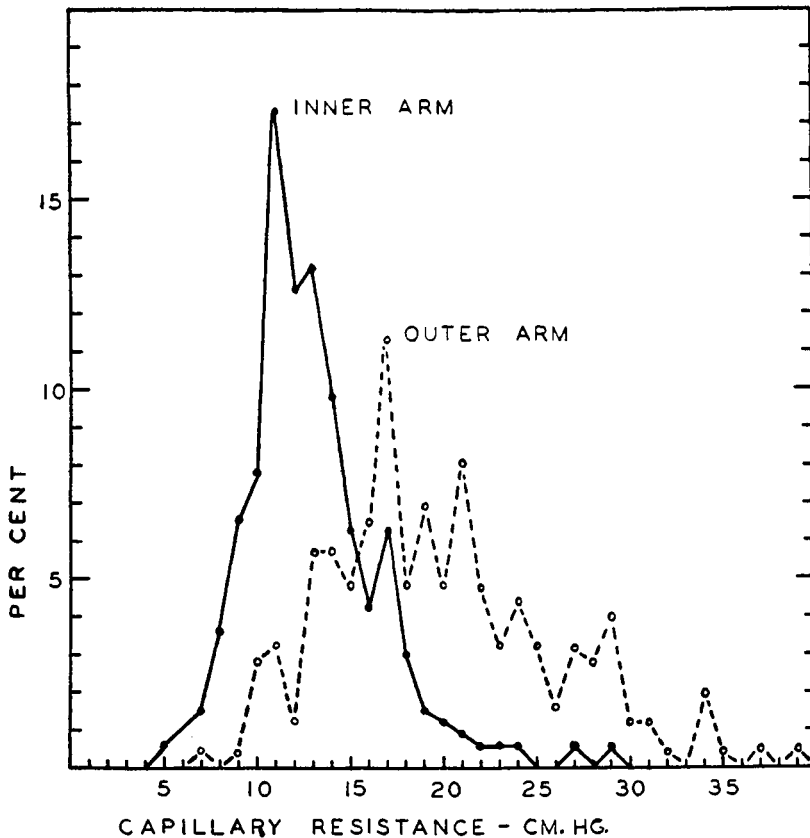


FIG. 1.

Frequency distribution curves of capillary resistance in normal individuals.

Daily observations of the capillary resistance were made in the normal individuals in whom the urinary excretion of ascorbic acid was determined during varying levels of vitamin C intake. The details of this experiment in relation to vitamin C excretion have been reported elsewhere.¹⁷ During a preliminary period of 6 days a diet low in vitamin C was administered. This was followed by the administration of large amounts of vitamin C in the form of 400 cc. of orange juice daily. A delay of from 2 to 9 days in the excretion of the test dose was interpreted as evidence that a mild degree of vitamin C depletion had been induced in each of the 12 subjects. The average values of capillary resistance, summarized in Table II, showed a slight decrease during the period of low vitamin C intake, due to marked changes in a few individuals. The significance of this observation is minimized by the failure of the capillary resistance to increase when large amounts of orange juice were

given and evidences of vitamin C saturation appeared. The individual curves of capillary resistance, in some of which there were marked variations, showed no relation to the intake or excretion of vitamin C.

TABLE II.
The Effect of Variations in Vitamin C Intake on the Average Values of Capillary Resistance and Urinary Excretion of Ascorbic Acid in 12 Subjects.

Days	Orange Juice, cc.	Urinary Excretion Ascorbic Acid, mg. per 24 hours	Capillary Resistance, cm. Hg.
1	—	17	17.2
2	—	15	16.0
3	—	16	14.3
4	—	17	13.6
5	—	18	14.2
6	—	12	13.8
7	400	14	12.8
8	400	22	11.0
9	400	69	12.2
10	400	104	13.8
11	400	113	13.6
12	400	120	10.6
13	400	126	12.0
14	400	148	13.8
15	400	133	11.6
16	200	93	11.4
17	200	89	11.6
18	200	83	12.6
19	200	58	12.6
20	200	47	13.4
21	200	49	14.0
22	200	73	14.6
23	200	67	14.0

It is of interest that in an independent, as yet unpublished, study of capillary resistance determined by a method similar to that here described, the threshold level and the range of variation agreed closely with the values observed by us.²⁰

Summary. 1. Determinations of capillary resistance to negative pressure were made in 100 normal individuals. 2. Attention is called to the high degree of variation in values for the capillary resistance in normal subjects. 3. Variations in the vitamin C intake of normal individuals, under the conditions of these experiments, had no significant effect on the capillary resistance.

¹⁹ Hawley, E. E., Stephens, D. J., and Anderson, G. K., *J. Nutrition*, 1936, **11**, 135.

²⁰ Hauck, Hazel, personal communication, Cornell University, Ithaca, New York.