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Venous Distensibility in Patients with Varicose Veins

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Forearm veins were studied to determine whether patients with primary varicosity of the saphenous veins had a generalized abnormality of the venous system. Distensibility of the superficial forearm and hand veins was measured in 25 patients with varicosity of the saphenous veins, and in 25 control subjects. Patients with saphenous varicosity had a significantly greater distensibility of the undistorted forearm veins than control subjects. Hysteresis of distensibility curves was more pronounced in patients with varicosity than in control subjects; mean hysteresis index was 0.65 ± 0.06 *versus* 0.28 ± 0.02 in controls. These investigations suggest that an increased distensibility of the venous system is the predisposing factor in the development of varicose veins.

On a étudié les veines de l'avant-bras pour établir si des malades souffrant de varicosité primaire des veines saphènes présentaient une anomalie généralisée du système veineux. On a donc mesuré la distensibilité des veines superficielles de l'avant-bras et de la main chez 25 sujets souffrant de varices da la saphène et chez 25 sujets-témoins. On a constaté que les malades souffrant de varicosités de la saphène possédaient une plus grande distensibilité des veines non contournées de l'avant-bras que les témoins. L'hystérésis des courbes de distensibilité était plus prononcée chez les variqueux que chez les témoins: l'indice moyen de l'hystérésis était de 0.65 ± 0.06 contre 0.28 ± 0.02 chez les témoins. Ces expériences permettent de croire qu'une distensibilité augmentée du système veineux est le facteur prédisposant de la maladie variqueuse.

PRIMARY varicosity of the leg veins is a very common disease of middle age. The etiology and pathogenesis of these varicosities, however, are far from clear. A variety of causes have been suggested, such as obesity, endocrine disorders, infections, alcoholism and incompetence of venous valves.[1-3] This latter abnormality seems to be a consequence rather than a cause of varicosity.[4] Inherent abnormality of the venous wall has long been held responsible for the development of this disease but the nature of this abnormality has never been specified. We believed, therefore, that it would be of interest to study whether such an abnormality, predisposing to varicosities, could be demonstrated in patients with primary varicosities. Since it seemed unlikely to us that such an alteration would be localized only in the veins of the legs but would be detectable also in the veins of the upper extremities, this study consists of an investigation of the forearm veins, in which deformity and tortuosity were not present.

Because we believed that varicosities might develop as a result of an increased distensibility of the vascular wall, we decided to study the distensibility of the uninvolved veins, in order to detect whether a generalized abnormality of the venous wall exists in patients with primary varicosity. Data on *in vivo* measurements of venous distensibility (i.e. △ volume/△ pressure) are relatively few. One of the reasons for the scarcity of information is the lack of appropriate methods for its measurement. Methods measuring volume changes in an extremity by plethysmography and pressure in one vein assume that all of the volume change produced by venous congestion is accounted for by volume changes in the veins.[5-8] One rather important shortcoming of these methods is that at venous pressures above 40 mm. Hg increased capillary filtration renders volume measurements invalid. Consequently, we decided to study venous distensibility with a more direct method.

Method

Twenty-five subjects with varicosities and 25 control subjects were studied. The first group included patients with varicosities of varying severity in the saphenous veins, in none of whom was the disease secondary to thrombophlebitis. The control

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subjects were patients convalescing from various diseases, but none had congestive heart failure, hepatic cirrhosis or diabetes.

The subjects were studied recumbent with the arm resting on a sidetable, the height of which was set at the level of the back. Before venipuncture the veins were carefully examined, both with and without a tourniquet on the arm, to find a 3-cm. long segment without any tributaries or valves. The approximate outside diameter of these veins at heart level was 2-4 mm. After a suitable segment of a superficial vein on the volar or radial surface of the forearm or on the dorsal surface of the hand was chosen for the test, a needle (No. 23) bent at a right angle was inserted. The needle was connected to a Statham P 23D transducer, to a micrometer syringe* with 0.002-ml. divisions and to a Sanborn infusion pump, as shown in Fig. 1.

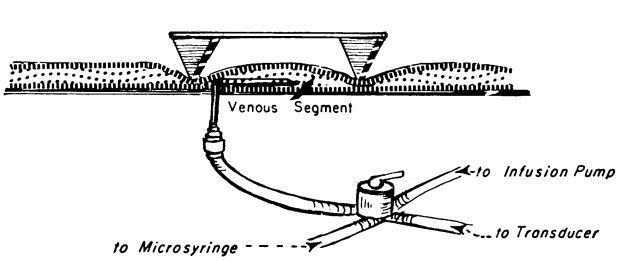


Fig. 1.—A No. 23 G needle in the venous segment is connected to the transducer, the micrometer syringe and the infusion pump through a four-way stopcock.

Saline, containing about 1 mg. heparin/ml., was slowly infused into the vein before and between the tests (i.e. when the venous segment was not isolated). Pressure in the vein was recorded via the transducer on a Sanborn Twin Viso direct writing recorder. The venous segment was isolated from the rest of the vessel from outside by two rubber wedges 3 cm. apart, applying a forceful occluding pressure on the vein. The rubber wedges were fixed in this position by a clamp. Pressure was continuously recorded in the venous segment, while heparinized saline was injected and withdrawn into the segment. In most cases eight injections were given at 0.02-ml. increments, followed by withdrawal of saline at the same rate. The interval between the injections and withdrawals of saline was approximately 10 seconds. When all the saline was withdrawn, pressure was further recorded every 30 seconds until it returned to approximately the original level. The same test was then repeated either with the wedges remaining in place or allowing several minutes' rest with the wedges removed. In several subjects two different veins were studied.

The distensibility curve (i.e. $\triangle$ pressure/$\triangle$ volume) was plotted from each satisfactory test, the pressure changes represented on the abscissa and the volume changes on the ordinate, as in Fig. 2a and 2b. The pressure in the venous segment before the first injection of saline was taken as zero pressure.

Prior to the experiments, the microsyringe transducer connection system was tested in each case to assure that it was completely leakproof. A pressure of 150 mm. Hg or higher was applied for 10 seconds and the system was accepted as ready for measurements only if the pressure decline was not more than 2 mm. Hg during this period.

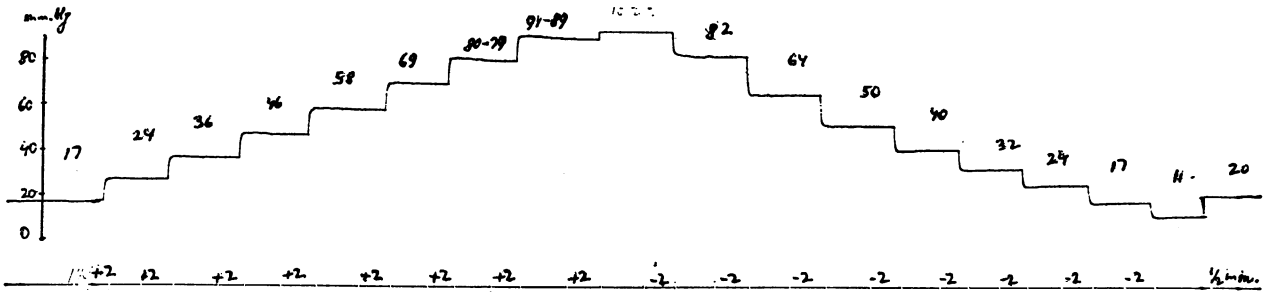
The method has the advantage of simplicity, but in order that accurate data may be obtained several requirements must be met. The system has to be absolutely leakproof; otherwise the minute volume increases will not produce appropriate pressure changes. Specially made stopcocks were necessary to provide completely leakproof connections.* Any damage caused by the needle in the vein, such as a minute leak from the vessel, would destroy the validity of the results. The complete isolation of the venous segment studied is obviously important. When the isolation of such a segment is incomplete, the injected saline may escape as the intraluminar pressure rises. When the pressure after withdrawal of the injected saline returned to the original level, either immediately or in one to three minutes, this was accepted as an indication that the venous segment under study was well separated from adjacent parts of the vessel. Only tests fulfilling these criteria were accepted.

When these criteria were fulfilled, the pressure increments and decrements produced by the same amount of saline were similar in the same segment of vein on successive occasions. In one patient no variation was observed when the test was repeated after an interval of one day.

In some experiments saline was injected more rapidly, at intervals of four seconds, and in others more slowly, at intervals of 30 seconds. Although distensibility tended to be somewhat greater in the latter cases, no major difference was evident between the results. Pressure increments were nearly identical in the same segments whether the volume changes were produced by smaller or larger increments. While this method, in contrast to methods using plethysmography, allows measurements of distensibility at pressures well above 40 mm. Hg, some leakage of injected saline from the segment at pressures over 100 mm. Hg cannot be completely excluded, and this might explain the observation that the pressure increment produced by the last injection of saline was usually less than by the earlier ones. Removal of blood from the isolated vascular segment was not attempted; consequently the injections of saline might produce some disruption of red blood cells with consequent release of vasoactive substances (adenosine triphosphate, etc.). The possibility that these materials affected venous distensibility cannot be excluded, but this does not deny the validity of

*Cole Palmer Instruments & Equipment Co.

*Obtained through X-ray & Radium Ltd.



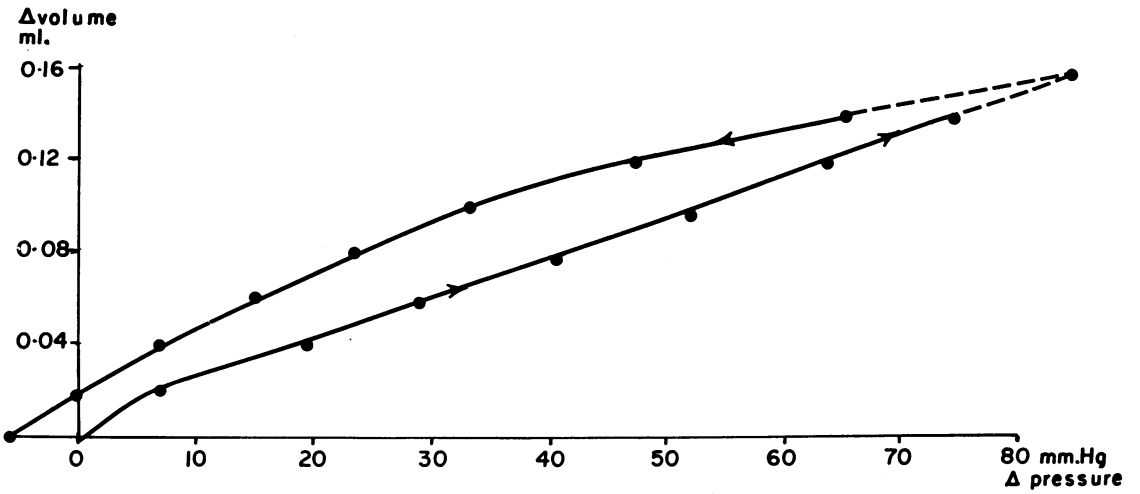
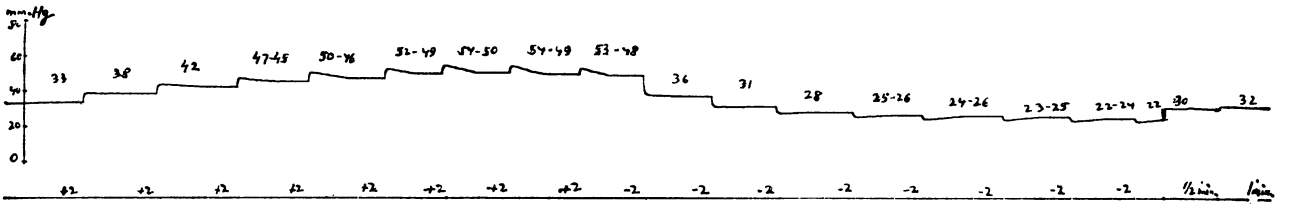


Fig. 2a.—Control subject, 23-year-old man.



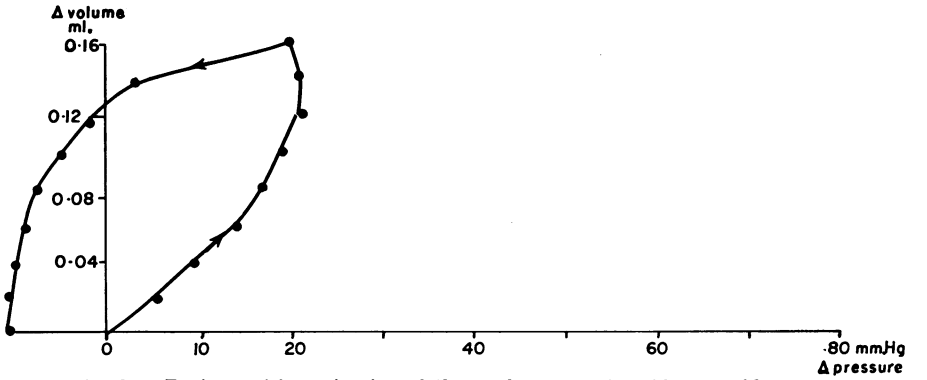


Fig. 2b.—Patient with varicosity of the saphenous veins, 50-year-old man.

The upper parts of the figures show pressure records in the venous segment in the volar surface of the forearm during injection and withdrawal of saline. The +2 means injection of 0.02 ml. and −2 withdrawal of 0.02 ml. saline. The lower parts demonstrate distensibility curves plotted from the above records. The initial pressure in venous segment was taken as 0 mm. Hg.

comparing the results obtained in control and varicose subjects.

RESULTS

The initial pressure in the isolated venous segments varied over a wide range (8-44 mm. Hg). This pressure was independent from that in the non-occluded vein, which was always less than 10 mm. Hg. There was no significant difference in the initial pressure of isolated venous segments between controls (average: 31.9 mm. Hg) and the varicose subjects (average: 25.1 mm. Hg). The upper parts of Figs. 2a and 2b show the pressure record from a control and from a varicose patient respectively. The pressure increase produced by each injection of saline is usually diminished by a

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TABLE I.—PRESSURE INCREMENTS AND DECREMENTS IN ISOLATED VENOUS SEGMENTS, PRODUCED BY INJECTION AND WITHDRAWAL OF SALINE (MEAN PRESSURE CHANGES IN MM. HG)

		△ Volume in ml.											
		Increments of volume					Decrements of volume						
	No. of veins	0.00→ 0.025	0.025→ 0.05	0.05→ 0.075	0.075→ 0.10	0.10→ 0.125	0.125→ 0.15	0.15→ 0.125	0.125→ 0.10	0.10→ 0.075	0.075→ 0.05	0.05→ 0.025	0.025→ 0.00
Control subjects.....	31	15.5	17.3	18.7	18.8	19.6	14.1	37.7	28.2	22.6	12.4	8.1	6.5
S.E.....		1.24	1.36	1.64	2.06	2.24	1.80	4.71	3.39	2.40	1.29	0.92	0.75
Patients with varicosities..	31	11.5	10.4	8.6	5.5	2.6	1.9	16.1	10.2	8.7	6.0	4.2	2.7
S.E.....		1.09	1.27	1.23	1.31	0.86	1.18	2.64	1.84	1.65	0.77	0.69	0.36
P.....		< 0.05	≪ 0.01	≪ 0.01	≪ 0.01	≪ 0.01	≪ 0.01	≪0.01	≪ 0.01	≪ 0.01	≪ 0.01	<0.01	≪0.01

S.E.—Standard error.

few mm. Hg in the first few seconds. On withdrawal of saline the opposite of this phenomenon could be observed, namely, the pressure rose in the first few seconds after withdrawal. No consistent difference was observed in this respect between control and varicose subjects. The lower parts of Figs. 2a and 2b represent the distensibility curves plotted from the pressure records in the upper parts.

The curves in the control subjects, similar to the one in Fig. 2a, show a nearly linear relationship between volume and pressure increase. On withdrawal of the same volume of saline, pressure declined following an asymptotic curve. Hysteresis was consistently present in all experiments, i.e. pressure was always lower at the same volume levels on withdrawal than on injection. When all the injected volume was withdrawn, the pressure in the segment was below the initial level in nearly all cases but it returned in one to three minutes to the initial level or slightly above.

The results obtained from arm veins in patients with varicosities of the saphenous veins were clearly different from those obtained in control subjects. Table I compares pressure increments and decrements produced by injection and withdrawal of saline in control and varicose patients. The table records pressure changes at every 0.25-ml. volume increase and decrease taken from the individual distensibility curves. P values were calculated using the *t* test. The injection of the same amount of saline produced significantly less pressure increase in varicose patients at all levels examined. The difference from control subjects was particularly pronounced at higher volume levels, when there was virtually no pressure increase in the segment; indeed, some decrease was occasionally observed.

The withdrawal of saline in varicose patients also produced an asymptotic decline in pressure and a marked hysteresis. The amount of hysteresis or hysteresis index was estimated in the following way. The area between the ascending and descending curve was measured by planimetry and divided by the product of pressure x volume, where pressure was the maximal pressure obtained and volume the corresponding value. In this way an arbitrary index was calculated for each distensibility curve. In the 25 control subjects a mean value of 0.28 ± 0.02 was obtained, while in 25 varicose subjects the mean was 0.65 ± 0.06. Using the *t* test the difference between these "hysteresis indices" was highly significant (P « 0.01).

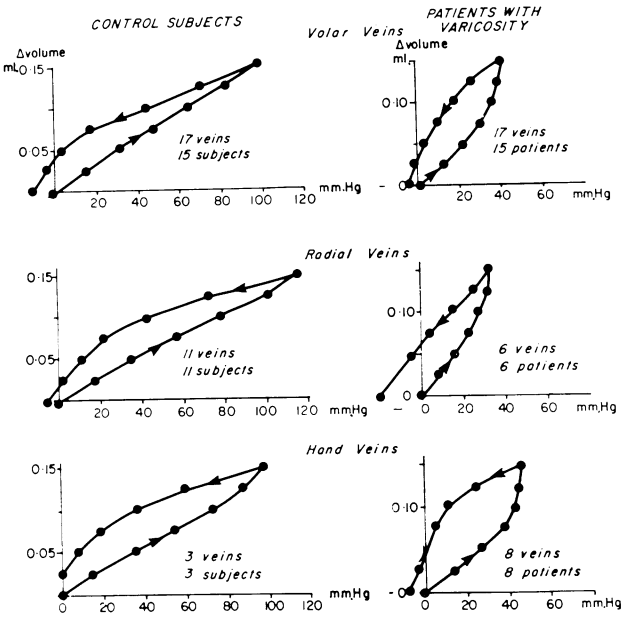

Fig. 3.—Distensibility curves plotted from mean values, separately represented for volar, radial and hand veins. △ pressure values, control subjects *versus* patients with varicosity, with the *t* test gave the following results: P was < 0.01 for all pressure increments and decrements in volar veins, except the first injection; P was < 0.01 for all pressure increments and at withdrawals from 0.15 → 0.10 ml. in radial veins; P was < 0.01 at 0.075 → 0.15 ml. volume increments in hand veins; no significant difference at other levels.

Distensibility curves in control subjects were quite similar whether veins of the volar or radial surface of the forearm or of the hand were examined, as shown by the curves created from the mean values (Fig. 3). The same figure demonstrates that the results obtained in varicose patients were also similar in the three types of veins examined, but different from those in control subjects.

DISCUSSION

Since the method used in the experiments reported here differs from those previously used for measuring venous distensibility *in vivo*, direct comparison of our data with those of others is not possible. Tension of the venous wall (radius x

pressure) was not calculated, because the diameter of the vessels through the skin cannot be adequately measured and because during the injections of saline the segment examined does not have a truly cylindrical form. Nevertheless, the shape of the distensibility curve found in our control subjects corresponds closely to those obtained by other methods.[5]

Our results indicate an abnormally increased distensibility and hyteresis in superficial forearm and hand veins in most patients having primary varicosity of leg veins when compared to the values observed in control subjects. The highly significant difference between the two groups could not be explained by differences in age, sex, by the size and type of vein examined, or by the initial blood volume in the isolated segment. The average age of control subjects was 48.9 years (range: 19-72 years) and of varicose subjects was 57.3 years (range: 30-78 years). Fifteen of the control and 13 of the varicose subjects were male. Abnormal distensibility curves in the arm veins were found as often in younger as in older subjects and as often in female as in male subjects with leg varicosities. As might be expected, injection of the same volume of saline into a venous segment with a smaller diameter, in the same individual, caused a greater pressure increase than into a vein with a larger diameter. There was, however, no difference in the diameter of the examined veins between control and varicose subjects.

We found that after several injections of saline in varicose patients there was practically no increase in pressure, as their veins would yield to the volume increase without measurable resistance. These results might be explained by a functional abnormality of the venous wall or by an abnormally low interstitial pressure. *In vitro* experiments on extirpated saphenous veins are being carried out to answer the question whether the latter possibility could be a factor. If the greatly increased distensibility of veins in varicose patients is due to abnormality of the venous wall, it is interesting to speculate whether this abnormality is in the collagen, elastic or muscular elements of the vessel. While this study was being undertaken, Svejcar *et al.*[9] reported decreased collagen content in saphenous veins of varicose patients, even in segments without varicosity. If such a decrease in the collagen elements were to exist in the forearm veins, which have a histological composition rather similar to that of saphenous veins,[10, 11] this might explain the increased distensibility found in our experiments.

The pressures produced in isolated venous segments by saline injection in this study were high, but not unphysiologically high. Venous pressure in the leg in the standing position has been measured at approximately 80 mm. Hg.[12, 13] Consequently, if the abnormal distensibility found in the forearm veins were present in the saphenous veins which are exposed to a higher pressure in the erect position, this could well explain the development of varicosity in these patients.

SUMMARY

Distensibility of superficial forearm and hand veins was studied in 25 patients with primary varicosity of the saphenous veins and in 25 control subjects. Saline was injected into and withdrawn from a 3-cm. long venous segment, isolated by rubber wedges from the rest of the vessel, while pressure was recorded.

The results indicate a significantly greater distensibility of the undistorted forearm veins in patients with varicosity in the leg than in control subjects.

On the basis of these investigations an increased distensibility of the venous system is proposed as the predisposing factor to the development of varicose veins.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

THE "LIGHT OF NATURE" ALONE

The Faculty of Medicine of Dalhousie University at a recent meeting sanctioned the inauguration of a course of lectures on Medical Ethics and Etiquette. The lectures, which were open to students of the final year only, were three in number as follows: (1) The relations of the practitioner to the patient, by Professor D. Fraser Harris, M.D., D.Sc.; (2) The relations of the practitioner to his brother practitioners, by Professor W. H. Hattie, M.D., C.M.; (3) The relations of the practitioner to the public, by J. J. Macdougall, Esq., M.D., C.M.

The Faculty was of the opinion that there was much need for such instruction, that unfortunately in some cases the "light of Nature" alone was not sufficient to illuminate all the dark places of medical relationships. Some years ago at the University of Birmingham, in England, Professor Robert Saundly, at that time in the Chair of Medicine, delivered during two summer sessions a short course of lectures on Medical Ethics which were later published in book form. In Paris a course of lectures called "Medical Deontology" has been delivered for the past few years: but with the exception of these two courses, this important branch of medicine does not seem to have been studied at any seat of learning. Dalhousie University is, therefore, to be congratulated on having been the pioneer in dealing with this valuable addition to the medical curriculum.—News, *Canad. Med. Ass. J.*, 6: 462, 1916.