ABSTRACT

Ten normal and four transplanted canine jugular vein segments and four human saphenous vein segments were studied to determine the in vitro static elastic properties of venous tissue and their modification by transplantation into the arterial system. Both the intraluminal pressure and the longitudinal force were varied, and the resulting dimensions were recorded photographically. Venous segments manifested a hysteresis response but showed minimum tendency to creep. The pressure-strain relationships were curvilinear with an initial, highly compliant phase over the physiological venous pressure range followed by a relatively noncompliant phase. This transition occurred at lower pressures for jugular segments than it did for saphenous segments. In contrast, comparable-sized canine carotid artery segments did not show this essentially noncompliant phase over the pressure range studied (0 to 200 cm H₂O). At comparable pressures and strains, the jugular vein segments were stiffer than the saphenous vein segments in both the circumferential and the longitudinal directions. At comparable strains, the saphenous vein moduli were similar to those in the carotid artery segments. Jugular segments transplanted into arterial circuits became virtually noncompliant and markedly inhomogeneous, with wall thickening and a histologic picture of intimal proliferation. They showed no tendency to "arterialize," that is, they failed to assume either the elastic or the histologic characteristics of arterial tissue.

The application of venous tissue to the problem of femoral-popliteal arterial reconstruction by Kunlin in 1951 (1) and its subsequent utilization in the aortocoronary saphenous vein bypass procedure by Favaloro in 1968 (2) have focused attention recently on the mechanical properties of venous tissue. Transplantation imposes many new stresses: (a) the venous tissue is forced to bear a pressure load which is ten- to twentyfold greater than that which is experienced normally, (b) it loses its medial and adventitial nutrient supply, since it is stripped of its vasa vasorum, and (c) frequently it is no longer surrounded by supportive, tethering tissues. The ability of the graft to adapt to these stresses may have a marked effect on its functional capability and survival. The intimal fibrotic lesions that several authors (3-5) have described in postmortem saphenous vein graft specimens may well represent a failure to compensate adequately for these stresses.

Surprisingly, examinations of the mechanical properties of venous tissue to date have largely excluded the medium-sized veins utilized in vascular reconstruction. A review of the literature reveals that the early studies of MacWilliam (6) in 1902 and Clark (7) in 1933 are the most thorough analyses of the elastic properties of vessels of this caliber. Caro and Saffman (8) have described extensibility values for pulmonary veins that are smaller than those for pulmonary arteries of similar size, and they have shown a decrease in venous extensibility with increasing vessel diameter. Bocking and Roach (9, 10) have examined the effects of prolonged periods of elevated hydrostatic pressure on feline jugular and human saphenous veins in an attempt to define the biophysical determinants of venous varicosities. They have shown a progressive increase in radius and a progressive decrease in distensibility as increased hydrostatic pressure is maintained. In addition, Bergel (11) has described observations on several
venous segments, but he did not perform an extensive study of venous elasticity. A number of investigators have examined the properties of venous caval segments (12). The mechanical properties of vein segments which have been transplanted into the arterial circulation have not been studied to date.

The experiments detailed in this paper were designed to examine the elastic properties of normal canine jugular and human saphenous veins in detail. The stresses on vessel segments were varied by altering the intraluminal pressure, the longitudinal force, or both while the resulting strains were monitored. In addition, similar data were obtained on several veins which had been transplanted chronically into the arterial circulation.

**Methods**

**EXPERIMENTAL MATERIAL**

Ten canine venous segments were obtained by careful dissection of the external jugular vein in normal mongrel dogs anesthetized with morphine sulfate (1 mg/kg, iv) and alpha-chloralose (80 mg/kg, iv). The jugular vein was chosen because of the similarity between its caliber and the caliber of the human saphenous vein. A 5- to 10-cm segment of vein was dissected from the perivascular tissues, and its branches were ligated. Ligatures were placed at both ends of the segment. The segment was then occluded, and its length and diameter were measured in vivo. This portion of the vein was then removed, and the dog was killed with a lethal dose of sodium pentobarbital. A small transverse incision was made central to each of the ligatures, and special supporting plugs (Fig. 1) were inserted into the lumen. The superior plug contained an 18-gauge needle to allow subsequent connection to a pressure source. After insertion of this plug, the vein segment was flushed with normal saline to remove any remaining blood, and all valves were rendered incompetent. The solid inferior plug then was inserted, and both plugs were secured by ligatures.

Four human saphenous vein segments were obtained at necropsy within 12 hours of death and were prepared utilizing the same techniques. Patients with evidence of venous insufficiency were excluded. The average age at death was 33 years.

The elastic properties of veins which had been transplanted chronically into the arterial circulation were studied also. Jugular vein segments from four dogs were removed, reversed, and transplanted into autologous arterial circuits. These segments were not studied prior to transplantation, but the contralateral veins provided a control segment. Two segments were anastomosed into the carotid arteries on the same side after removal of an arterial segment of similar size. Static elastic experiments were performed on these carotid arterial segments to provide both a check on the methodology and a comparison of venous and arterial elastic moduli. Care was taken to ensure that the transplanted length was within 20% of the original vein segment length, thus minimizing tension on the graft. The other two jugular venous segments were placed in an aortomammary position. A proximal end-to-side anastomosis to the aorta was created, and the distal end was anastomosed end-to-side to the left internal mammary artery. Afteligation of the mammary artery proximal to the anastomosis, flows in the two transplanted segments measured with an electromagnetic flowmeter were 62 and 5 ml/min. The dogs were maintained on a normal diet and normal activity for at least 10 months. At the time of death, each of the venous segments was patent. These segments were dissected free and prepared for study as described previously.

**EXPERIMENTAL METHODS**

The prepared vein segments were suspended vertically from their superior plugs, which were then connected to a pressure reservoir (Fig. 1). The reservoir and the connecting tubing were filled with either the dogs' heparinized blood or with 5% dextrose in normal saline. Pressure in the reservoir could be varied by altering the air pressure over the reservoir fluid via an intake valve and a variable outlet resistance. A Statham P23Db pressure transducer monitored with a Hewlett-Packard direct-writing amplifier oscillograph system, provided a linear measurement of the pressure in the system. The reference for zero pressure was set at the midpoint of the vein segment, and the meniscus of the reservoir was kept at that level.

After suspension of the vein segment and establishment of the zero pressure, a static elasticity experiment was performed. The vein segment was restored to approximately its in vivo length by suspension of a small weight (generally 5 g) from the lower plug. Because biologic materials exhibit marked hysteresis when the area is initially stressed, two hysteresis cycles were carried out on each segment by gradually raising the reservoir pressure in increments of 25 cm H2O and allowing 2- minutes for equilibration before the next pressure increase. In each instance, the final level of pressure....
achieved during the hysteresis cycles was 10% greater than the largest pressure which was studied during the actual static experiment. There was no evidence that this approach resulted in damage to the wall material. Pressure-radius-length data were obtained in three of the canine and two of the human veins to characterize the hysteresis responses of these tissues.

After the hysteresis cycles had been completed, several pressure-force runs were recorded by suspending weights from the lower plug and incrementally varying the pressure over a range of 0 to 200 cm H₂O. Small pressure ranges (0 to 20, 0 to 50, and 0 to 100 cm H₂O) were studied in a number of veins to preclude the possibility of irreversible damage to venous tissue at high pressures. The total time of pressure application was minimized to preclude the possibility of irreversible alterations in elastic properties of the type shown by Bocking and Roach (9, 10). After several pressure series at one longitudinal force, the weight (force) was increased, and additional pressure series were run over the same range. In all, pressures ranging from 0 to 200 cm H₂O and longitudinal forces ranging from 0 to 20 g were studied. Above these levels, the tissue lost its elastic properties, as will be discussed later in this paper. At the conclusion of an experiment, the vein segment was removed from its plugs and opened longitudinally; the length and the width of the resulting rectangle were then measured. These values were taken to represent the undeformed length, L₀, and width, W₀, respectively. Undeformed midwall radius, R₀, was determined by dividing W₀ by 2π. The weight of the tissue provided values for the undeformed wall volume, V₀ (assuming a density of 1.06) (13), and the undeformed wall thickness, h₀, using the relationship

\[ h₀ = \frac{V₀}{W₀L₀} - \frac{V₀}{2\pi R₀L₀} = \frac{\text{weight}}{2.12\pi R₀L₀} \]  (1)

Changes in external diameter and segment length at each stress were monitored via a photographic method. Either a 35-mm format Nikon F or a Nikkormat FTN camera equipped with a 55-mm Micro-Nikkor lens was attached to a stand at a film-to-subject distance of 20–30 cm. This distance was chosen so that the vein segment nearly filled the 35-mm format of the negative. Hence, an image magnification of 0.3–0.7 was obtained. Illumination was provided by a Bauer F110 electronic flash mounted 50 cm from the vein segment at a 45° angle to a line drawn from the camera to the segment. All exposures were made at 1/16 and 1/60 seconds on Kodak Panatomic-X film. Each frame also included a metric ruler for subsequent calibration and an identifying number. Measurements of external radius and length were obtained from 8 × 10-inch prints using engineering calipers accurate to 0.001 inches and were taken in triplicate. Measurements taken from uniform cylinders and grids photographed under conditions identical to those used for the vein segments revealed a random measurement error that was consistently less than 0.1%.

When they are subjected to a constant stress level, biologic materials may creep, i.e., gradually alter their dimensions with time. This characteristic is particularly prominent in arterial tissue and is primarily a property of the smooth muscle (14). The degree of creep in venous tissues has not been examined previously. Since it is of considerable importance in any analysis of the results of these experiments, the following studies were done. Three of the jugular vein segments were prepared as previously described. After two inflation-deflation cycles to remove the hysteresis effects, the segments were restored to their in vivo lengths at zero intraluminal pressure and subjected to sudden increases of pressure to 10, 50, or 150 cm H₂O; thereafter, they were held at that pressure for 3 hours. Dimensions of the segments were followed optically at intervals up to 3 hours after the application of these pressures. It was found that at 60 seconds after a change in pressure the radius and the length reached steady values (within 2% of the values reached at 3 hours). Consequently, in all studies, each pressure increase was followed by at least a 2-minute delay prior to taking measurements to allow for the creep to occur.

THEORETICAL CONSIDERATIONS

The analysis of the stresses and strains in venous segments used in this study involves a number of assumptions. The vessel segment is assumed to be a thin-walled, circular cylinder with a homogeneous, incompressible wall (15). Although all vessels are eccentric structures to some degree, preliminary studies using measurements in orthogonal directions did not produce qualitatively different results. The material of the wall is assumed to be anisotropic, i.e., to exhibit different material properties in the circumferential, longitudinal, and radial directions. Specifically, the segment is assumed to be curvilinearly orthotropic, i.e., to possess a symmetry which allows the shearing strains to be ignored when the segment is subjected to only an internal pressure and a longitudinal force (16). Finally, the function which relates the finite deformation to the applied stress is assumed to be nonlinear. These assumptions, which have been verified in detail in arterial tissue, are an extension of the formulation employed in current studies of arterial elastic properties (17, 18). Although they have not been specifically verified for venous tissues, the basic structural similarities between arterial and venous walls should permit this extrapolation.

In a homogeneous, thin-walled, cylindrical vessel segment, the stresses resulting from application of an intraluminal pressure, P, and a longitudinal force, F, can, for many purposes, be taken to be uniform throughout the thickness, h, of the wall, and throughout the segment length, L, and can be determined from the following equations (17, 19).

\[ S_r = \frac{P}{2h} \left( \frac{R}{h} - 1 \right) + \frac{F}{2\pi Rh}, \]  (2)

\[ S_\lambda = \frac{-P}{2}, \]  (3)

\[ S_\theta = \frac{P}{2h} \left( \frac{R}{h} - 1 \right), \]  (4)

where \( S_r, S_\lambda, \) and \( S_\theta \) represent the stresses in the circumferential, longitudinal, and radial directions, respectively, and \( R \) is the midwall radius.

The stretches or the extension ratios, \( \lambda \), corresponding to these stresses may be represented as:

\[ \lambda = \frac{R}{R_0}, \]  (5)
\[ \lambda_r = \frac{L}{L_0}, \quad \lambda_h = \frac{h}{h_0}. \]

These dimensionless ratios relate the dimensions, \( R, L, \) and \( h, \) in the deformed state to the dimensions in the undeformed state, \( R_0, L_0, \) and \( h_0, \) obtained from each unstressed vessel segment. The assumption of incompressibility leads directly to the constraint

\[ \lambda_r \lambda_t \lambda_l = 1. \]

Hence, determination of any two of the stretches allows calculation of the third.

The relationship between the applied stresses and the resulting strains can be expressed through elastic moduli, which provide an index of the "stiffness" of the material. To describe the relationship between a uniaxial stress and the corresponding strain in a classical Hookean material only one modulus is required, since the strain in such a material is strictly proportional to the applied stress. In general, biologic materials do not exhibit the linear elasticity of a Hookean material but instead deform in a nonlinear fashion. However, it is meaningful to look at small segments of the nonlinear stress-strain relationships in the physiological range and to define incremental moduli as ratios of small changes in stress to the corresponding changes in strain. These moduli, however, will be different for different levels of large strain. Thus, comparisons of moduli must be made at similar levels of large strains. Consequently, elastic moduli for venous tissues were obtained at several strains. In addition, since the material was assumed to be anisotropic, moduli were calculated for both the circumferential and the longitudinal directions.

A rough index of elasticity, \( E_h, \) is provided by computing an "apparent stiffness" value as follows:

\[ E_{\text{app}} = \frac{\Delta P \Delta R}{h}, \quad E_h = \frac{\Delta P \Delta L}{h}. \]

This index provides a "feel" for the interaction of pressure and vessel dimensions but is not a true modulus in that it is not a ratio of the change in stress required to produce a given change in strain. As can be seen from Eqs. 2 and 3, the stresses in the circumferential and longitudinal directions do not consist simply of the intraluminal pressure but incorporate the wall thickness and the longitudinal force as well.

A true incremental tensile or Young's modulus, \( E, \) can be obtained as follows:

\[ E = (1 - \sigma)^\frac{dS}{d\lambda}, \quad E = 0.75(1 - \sigma)^\frac{dS}{d\lambda} \text{ if } \sigma = 0.5. \]

This modulus may be calculated in both the circumferential and longitudinal directions by using the appropriate values for the Poisson ratio, \( \sigma, \) stress, and strain. The Poisson ratios are assumed to be 0.5 in this paper. More precise evaluation of these ratios demands their prediction from an approximation of the data by an anisotropic elastic model. Note further that, for values of \( E \) given by Eq. 11a or 11b to be true moduli, and moduli must be obtained at a constant level of stress in the other direction, i.e., \( E_r \) must be obtained at a constant \( \lambda_r, \) and vice versa. The use of multiple values of both longitudinal force and pressure provided ample points to determine these moduli.

Additionally, the incremental moduli of Bergel, \( E_{\text{inc}} \) (11), was determined at several extensions:

\[ E_{\text{inc}} = (1 - \sigma)^\frac{\Delta P \Delta R}{h}, \quad E_{\text{inc}} = 0.75(1 - \sigma)^\frac{\Delta P \Delta L}{h} \text{ if } \sigma = 0.5. \]

All numerical data analysis was performed on an IBM 1130 digital computer. Each experimental data point, consisting of simultaneous values for pressure, force, radius, and length, was entered into Eqs. 2-7 to determine the corresponding stresses \((S_r, S_t, \) and \( S_l))\) and stretches \((\lambda_r, \lambda_t, \) and \( \lambda_l)).\) These data were graphed to obtain the stress-strain curves, whose slopes were then used to obtain the elastic moduli.

The computer was used to perform stepwise polynomial regressions on all stress-strain data. It was found that an equation of the second order adequately described all of the data. In all cases, in the regions of low and medium values of stress, strain was a parabolic function of stress, with the parabola oriented concave toward the stress axis; for higher values of stress, the strain remained essentially constant beyond the apex of the parabola. Therefore, the stress-strain curves were assumed to be parabolic to the apex only; thereafter, a constant level of strain was assumed. Thus, in all figures showing regression results, the data past the apex of the parabola are shown as a line parallel to the abscissa. This finding accurately reflects the actual data, which indeed did show a plateau at arterial pressure levels. Elastic moduli were compared using Student's t-test on an unpaired model, assuming unequal sample sizes and unequal sample variances where applicable (20).

Results

NORMAL VENOUS SEGMENTS

As is characteristic of biologic materials, the normal veins exhibited hysteresis when they were subjected to several inflation-deflation cycles immediately after isolation of the segment. Representative canine jugular pressure-volume curves are shown in Figure 2 for both a low and a high range of pressures. Results for the human saphenous vein were similar. In each instance the return to zero pressure after the first cycle was accompanied by a marked residual strain which appeared not to vary significantly with time. Subsequent cycles returned to essentially the same volume after deflation. In contrast, the second and third cycles were similar to each other and did not exhibit this difference between inflation and deflation. In all cases they resembled the deflation curve.
ELASTICITY OF VEINS

Representative hysteresis responses during two cycles in canine jugular segments for both a low range (0 to 20 cm H$_2$O) and a high range (0 to 200 cm H$_2$O) of pressure are shown. Veins of different initial volumes were chosen to avoid overlap of results for this display. The second cycle for the low-range vessel was not different from the deflation portion of its first cycle and hence is omitted. Behavior of human saphenous vein segments were similar.

Data for the low pressure range (0 to 50 cm H$_2$O) were obtained from seven of the jugular vessel segments and those for the high pressure range (0 to 200 cm H$_2$O) from three of the jugular and all of the saphenous vein segments. The pressures used were still below the level at which irreversible damage to the tissue might occur: two segments were pressurized to 300 cm H$_2$O for periods up to 1 minute without apparent irreversible effects such as yielding, aneurysmal dilation, or rupture.

The relationships between pressure and the resulting radius and length are presented in Figure 3 for a typical jugular vein segment. Results from the regression analysis of this data on all veins are presented in Figures 4–6 and in Table 1. Results for both types of normal vein are depicted at several values of longitudinal force and are presented with data from a carotid artery for comparison. Data are presented in terms of the extension ratios, $\lambda_0$ and $\lambda_z$ (Figs. 4 and 5) rather than as absolute dimensions to reduce the variability between animals. The variance of vessel volume with pressure is shown in Figure 6. Results for the third extension ratio, $\lambda_r$ (change in wall thickness), are not graphically presented but may be obtained from the incompressibility constraint.

All pressure-strain curves (Figs. 4–6) were curvilinear and could be adequately described using a second-order regression equation (Table 1). The experimental curves appeared to consist of two phases: a rapidly rising phase over the physiological venous pressure range (0 to 25 cm H$_2$O) followed by a transition to a curve of much smaller slope over the arterial range of pressures. This pattern was quite pronounced for jugular segments and less so for saphenous segments.

The transition point was independent of longitudinal force over the physiological range of forces employed, but venous segments became noncompliant as the weight was increased to 15 g and did not alter their dimensions over the range of pressures studied. Consequently, data for weights greater than 10 g are not presented. Arterial segments did not show a sharp transition and continued to show a gradual increase in dimensions over the range studied.

The circumferential and longitudinal stretches, $\lambda_0$ and $\lambda_z$, computed using Eqs. 5 and 6, were plotted against the corresponding stresses computed from Eqs. 2 and 3. The resulting stress-strain curves were used to calculate the elastic moduli (Table 2). The nonlinearity apparent in the pressure-strain curves was likewise manifested in the calculated elastic moduli.

The apparent stiffness in the circumferential direction of jugular segments was larger at each level of pressure than that for saphenous segments.
Figure 4
Circumferential extension ratios, $\lambda_\theta$, for canine jugular vein (jv) and human saphenous vein (sv) segments. Data from a segment of canine carotid artery (ca) are shown for comparison. Data shown are plots of second-order polynomial regression results for the pooled data from all studies (see Table 1). $F$ represents the weight in grams of the longitudinal force. Average undeformed radius, $R_0$, was $0.302 \pm 0.011$ (SE) cm for the jugular vein, $0.151 \pm 0.024$ cm for the saphenous vein, and $0.174 \pm 0.023$ cm for the carotid artery.

Figure 5
Polynomial regression results for longitudinal extension ratios, $\lambda_z$, for canine jugular vein (jv) and human saphenous vein (sv) segments at several longitudinal forces. Data from a segment of carotid artery (ca) are shown for comparison. The average undeformed length, $L_0$, was $4.724 \pm 0.335$ (SE) cm for the jugular vein, $4.472 \pm 0.113$ cm for the saphenous vein, and $4.966 \pm 0.48$ cm for the carotid artery.

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FIGURE 6

Polynomial regression results for the variation of volume with pressure for canine jugular vein (jv) and human saphenous vein (sv) segments at several longitudinal forces. Data from a segment of carotid artery (ca) are shown for comparison. The average undeformed volume, \( V_0 \), was 1.536 ± 0.131 (SE) cm for the jugular vein, 0.342 ± 0.102 cm for the saphenous vein, and 0.472 ± 0.119 cm for the carotid artery.

Typically, this modulus was twice as large for jugular segments. The longitudinal stiffness, while starting at comparable levels for both vein types, rose more rapidly at high pressure in the jugular segments, so that at pressures greater than 100 cm H2O the values for the jugular segments were significantly greater. In addition, both types of vein were considerably stiffer in the circumferential direction than they were in the longitudinal direction by at least an order of magnitude.

The true incremental elastic moduli in the circumferential direction, \( E_\theta \), were likewise larger for jugular segments than they were for saphenous segments by roughly an order of magnitude at each point. The values for the carotid artery were intermediate and similar to those for the saphenous vein.

### TABLE 1

Second-Order Regression Results of Pressure (P) vs. Extension Ratio (λ)

<table>
<thead>
<tr>
<th>Force (g)</th>
<th>N</th>
<th>Circumferential extension ratio, ( \lambda_\theta ) equation</th>
<th>SEE</th>
<th>( r )</th>
<th>Longitudinal extension ratio, ( \lambda_z ) equation</th>
<th>SEE</th>
<th>( r )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Canine Jugular Vein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.3</td>
<td>37</td>
<td>( \lambda_\theta = 1.466 + 0.308 \times 10^{-3} (P) )</td>
<td>± 0.011</td>
<td>0.73</td>
<td>( \lambda_z = 1.348 + 0.503 \times 10^{-2} (P) )</td>
<td>± 0.049</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(- 0.103 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
<td>(- 0.490 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>117</td>
<td>( \lambda_\theta = 1.452 + 0.490 \times 10^{-3} (P) )</td>
<td>± 0.018</td>
<td>0.75</td>
<td>( \lambda_z = 1.444 + 0.382 \times 10^{-2} (P) )</td>
<td>± 0.060</td>
<td>0.77</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(- 0.187 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
<td>(- 0.151 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>71</td>
<td>( \lambda_\theta = 1.496 + 0.780 \times 10^{-3} (P) )</td>
<td>± 0.021</td>
<td>0.77</td>
<td>( \lambda_z = 1.552 + 0.248 \times 10^{-2} (P) )</td>
<td>± 0.066</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(- 0.321 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
<td>(- 0.104 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Human Saphenous Vein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>( \lambda_\theta = 1.313 + 0.458 \times 10^{-3} (P) )</td>
<td>± 0.079</td>
<td>0.71</td>
<td>( \lambda_z = 1.144 + 0.264 \times 10^{-2} (P) )</td>
<td>± 0.058</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(- 0.170 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
<td>(- 0.381 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>62</td>
<td>( \lambda_\theta = 1.220 + 0.400 \times 10^{-3} (P) )</td>
<td>± 0.101</td>
<td>0.67</td>
<td>( \lambda_z = 1.204 + 0.314 \times 10^{-2} (P) )</td>
<td>± 0.061</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(- 0.143 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
<td>(- 0.968 \times 10^{-4} (P)^2 )</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results of the regression analysis using a second-order model for the pooled data from all seven jugular vein and all four saphenous vein studies. \( F \) = force. \( N \) = number of points included in the analysis. \( \text{SEE} \) = standard error of the estimate about this equation. \( \text{SEE} \) did not vary systematically with pressure. \( r \) = multiple correlation coefficient. All results differed significantly from linearity (\( P < 0.001 \)).

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level of pressure (Table 2). The longitudinal moduli, $E_L$, were likewise larger for jugular segments than they were for their saphenous counterpart at pressures of 25 cm H$_2$O or more. Again, the circumferential moduli for jugular segments were larger than the longitudinal values at most levels of pressure. Saphenous vein segments, however, started with a circumferential modulus which was larger by an order of magnitude for jugular segments than it was for saphenous segments at all pressures greater than 50 cm H$_2$O.

The incremental modulus of Bergel, $E_{inc}$, was larger by an order of magnitude for jugular segments than it was for saphenous segments at all pressures greater than 10 cm H$_2$O (Table 2).

As noted previously, any discussion of incremental elastic moduli of a nonlinear material must, of necessity, state the corresponding level of large strain, and, for comparison of tissue properties, comparisons of moduli should be made only at comparable levels of strain. The moduli in Table 2 are listed as a function of pressure, but it can be readily seen from Figures 4 and 5 that the two types of vein exhibited different levels of strain at comparable pressures. Thus, the values of moduli as a function of pressure, although of interest for the physiologist, do not allow a comparison between vein types. However, at 40 cm H$_2$O pressure, the circumferential stretches in the jugular and saphenous veins were the same ($X_0 = 1.465$). By interpolation from Table 2, we find, for this value of $X_0$, that the true incremental modulus of Bergel ($E_{inc}$) was 5 times as large for the jugular segments as it was for the saphenous segments ($72 \pm 4 \times 10^4$ vs. $1.39 \pm 0.18 \times 10^4$ dynes/cm$^2$, $P < 0.001$) and the Berge modulus was 43 times as large for the jugular segments as it was for the saphenous segments (1.99 ± 0.26 x 10$^6$ dynes/cm$^2$, $P < 0.001$). Similar comparisons were not possible at other strains or in the longitudinal direction because comparable strains did not exist.

Comparison of the true incremental moduli of the veins with those of a canine carotid artery

### Table 2

<table>
<thead>
<tr>
<th>Pressure (cm H$_2$O)</th>
<th>Apparent stiffness (cm H$_2$O/cm)</th>
<th>Circumferential modulus ($E_c$, dynes/cm$^2 \times 10^4$)</th>
<th>Longitudinal modulus ($E_L$, dynes/cm$^2 \times 10^4$)</th>
<th>$R^2/h$ (cm)</th>
<th>$E_{inc}$ (dynes/cm$^2 \times 10^4$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Canine Jugular Vein</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>49 ± 7</td>
<td>15 ± 3</td>
<td>1.2 ± 0.18</td>
<td>11.41 ± 0.37</td>
<td>32 ± 14</td>
</tr>
<tr>
<td>25</td>
<td>62 ± 7f</td>
<td>41 ± 6f</td>
<td>4.4 ± 0.35*</td>
<td>12.24 ± 0.42</td>
<td>44 ± 11f</td>
</tr>
<tr>
<td>50</td>
<td>98 ± 7f</td>
<td>88 ± 7f</td>
<td>11.8 ± 2.1f</td>
<td>13.51 ± 0.7</td>
<td>115 ± 28f</td>
</tr>
<tr>
<td>75</td>
<td>139 ± 15</td>
<td>98 ± 7f</td>
<td>46 ± 15*</td>
<td>13.96 ± 1.28</td>
<td>158 ± 48f</td>
</tr>
<tr>
<td>100</td>
<td>201 ± 7f</td>
<td>117 ± 10f</td>
<td>67 ± 25*</td>
<td>14.45 ± 1.48</td>
<td>196 ± 24f</td>
</tr>
<tr>
<td>125</td>
<td>463 ± 77f</td>
<td>134 ± 24f</td>
<td>89 ± 32*</td>
<td>14.73 ± 1.65</td>
<td>252 ± 40f</td>
</tr>
<tr>
<td>150</td>
<td>670 ± 62f</td>
<td>171 ± 9f</td>
<td>113 ± 13f</td>
<td>15.93 ± 1.98</td>
<td>281 ± 32f</td>
</tr>
<tr>
<td><strong>Human Saphenous Vein</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4</td>
<td>87 ± 16</td>
<td>0.27 ± 0.12f</td>
<td>1.61 ± 0.32</td>
<td>0.800 ± 0.27</td>
<td>1.18 ± 0.18</td>
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<tr>
<td>25</td>
<td>91 ± 5</td>
<td>0.65 ± 0.13f</td>
<td>2.03 ± 0.39</td>
<td>0.909 ± 0.27</td>
<td>1.52 ± 0.22</td>
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<tr>
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<td>108 ± 9</td>
<td>1.89 ± 0.41f</td>
<td>2.75 ± 0.78</td>
<td>1.090 ± 0.29</td>
<td>2.31 ± 0.31</td>
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<tr>
<td>75</td>
<td>123 ± 8</td>
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<td>3.18 ± 0.76</td>
<td>1.616 ± 0.06</td>
<td>3.54 ± 0.59</td>
</tr>
<tr>
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<td>142 ± 12</td>
<td>15.0 ± 2.65f</td>
<td>3.56 ± 0.58</td>
<td>1.871 ± 0.06</td>
<td>5.69 ± 0.48</td>
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<tr>
<td>125</td>
<td>169 ± 10</td>
<td>20.4 ± 1.65f</td>
<td>3.98 ± 0.96</td>
<td>2.100 ± 0.19</td>
<td>10.50 ± 1.40</td>
</tr>
<tr>
<td>150</td>
<td>206 ± 17</td>
<td>25.1 ± 7.5f</td>
<td>4.75 ± 1.2</td>
<td>2.508 ± 0.40</td>
<td>21.60 ± 1.57</td>
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</tbody>
</table>
ELASTICITY OF VEINS

could be made at all levels of large strain (Table 3). Carotid moduli were predicted by applying the nonlinear anisotropic elastic theory of Vaishnav et al. (18) to four carotid segments. This approach expresses the strain-energy density in a blood vessel segment as a third-degree polynomial and obtains the circumferential and longitudinal stresses as polynomial functions of the circumferential and longitudinal strains. This procedure results in seven constitutive constants for each vessel which adequately described their elastic properties. The resulting constants were then used to predict an elastic modulus at the desired state of strain. The usefulness of this approach is that it allows the prediction of an elastic modulus at any level of large strain (over the elastic range of the material). The carotid artery moduli predicted from the present data agreed within ± 1 SE with those reported by Patel and Janicki (21). The comparison of elastic moduli showed that the jugular segments were stiffer than the carotid artery in the circumferential direction over the whole range of pressures studied. Jugular vein moduli were typically an order of magnitude larger at arterial pressures. In the longitudinal direction, the jugular modulus was smaller than the carotid modulus at physiological venous pressures but was larger than the carotid modulus over the arterial range of pressures. This observation is consistent with the view that the longitudinal modulus of the jugular vein starts at a smaller value but rises more rapidly than does the arterial modulus, exceeding the latter over the arterial pressure range.

The saphenous moduli in the circumferential direction were considerably smaller initially (Table 3) but were similar to the carotid values at pressures of 75 and 100 cm H$_2$O. The incremental

<table>
<thead>
<tr>
<th>Pressure (cm H$_2$O)</th>
<th>Carotid artery Incremental modulus</th>
<th>Canine Jugular Vein Incremental modulus</th>
<th>Human Saphenous Vein Incremental modulus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$E_g$ (dynes/cm$^2 \times 10^6$)</td>
<td>$E_e$ (dynes/cm$^2 \times 10^6$)</td>
<td>$E_g$ (dynes/cm$^2 \times 10^6$)</td>
</tr>
<tr>
<td>10</td>
<td>15 ± 3*</td>
<td>1.2 ± 0.18†</td>
<td>7.62</td>
</tr>
<tr>
<td>25</td>
<td>47 ± 6†</td>
<td>4.4 ± 0.35†</td>
<td>8.39</td>
</tr>
<tr>
<td>50</td>
<td>88 ± 7†</td>
<td>11.8 ± 2.1†</td>
<td>9.51</td>
</tr>
<tr>
<td>75</td>
<td>98 ± 7†</td>
<td>46 ± 13*</td>
<td>10.37</td>
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<td>100</td>
<td>117 ± 10†</td>
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<td>10.92</td>
</tr>
<tr>
<td>125</td>
<td>134 ± 24†</td>
<td>89 ± 32</td>
<td>11.16</td>
</tr>
<tr>
<td>150</td>
<td>171 ± 9†</td>
<td>113 ± 13†</td>
<td>11.16</td>
</tr>
</tbody>
</table>

Comparison between the elastic moduli for venous segments (as defined in Table 2) and those predicted for the canine carotid artery; the regression equations in Table 1 were utilized to determine the average strain at each level of pressure. The resulting strains were used to predict an elastic modulus for the carotid artery at similar extension ratios, utilizing the nonlinear anisotropic model of Vaishnav et al. (18) and the elastic constants derived from the experimental data for the four carotid segments. Note that carotid moduli are quoted as a function of vessel strain, not as a function of pressure. They differ at a given level of pressure for the two types of vein as a result of the difference in coexistent strains (see columns 2 and 3). All comparisons were made in the common direction only and were performed under the hypothesis that the mean venous modulus was identical to the carotid modulus. Since the variance about the carotid modulus could not be determined, it was assumed to be a "correct" value, not a mean, and its variance was therefore not taken into consideration (14).

* $P < 0.05$ for the comparison between the venous and carotid moduli.
† $P < 0.01$ for the comparison between the venous and carotid moduli.
circumferential modulus for saphenous vein segments exceeded the comparable carotid artery modulus at 125 cm H₂O but was not statistically different at 150 cm H₂O. The longitudinal saphenous vein moduli were likewise larger than the carotid moduli at pressures of 10 and 25 cm H₂O but were not different from the carotid moduli thereafter.

TRANSPLANTED VENOUS SEGMENTS

Two jugular vein segments transplanted into the carotid artery and two segments transplanted into an aortomammary position were studied. In each case, the vessel in vivo appeared grossly rigid and fairly inhomogeneous. These characteristics were confirmed when these vessels were studied in vitro (Fig. 7). All of the segments were virtually nondistensible and remained at extension ratios of 1.0-1.3 throughout the pressure range (0 to 200 cm H₂O). Two segments also showed a tendency to kink. Furthermore, the segments could not be described as cylinders; they exhibited several areas of marked wall thickening in all cases. Subsequent cross sections of various sites proved that the wall was extremely thickened, up to 2 mm, in several locations. Such thickening represents a tenfold increase over the normal wall thickness and invalidates the assumption of thinness for these transplanted segments. Histologic examination showed that this thickening consisted primarily of intimal proliferation and adventitial scarring in a pattern similar to that observed in postmortem human saphenous vein segments (3-5). No organized thrombotic lesions were found. Because these segments violated the assumptions of uniformity and thinness, calculation of elastic moduli was not appropriate. The transplanted segments were virtually inextensible in both directions, however, implying moduli significantly larger than those observed for the normal segments.

Discussion

Although the elastic properties of arterial tissues have been examined in detail for segments throughout the arterial tree (11, 17), venous properties have previously been largely ignored. Roy (22) demonstrated the nonlinear elasticity of arterial segments in 1880 and showed that these tissues were more extensible than conventional engineering materials (e.g., steel) and also non-Hookean, i.e., they tended to decrease in compliance with stretch rather than to deform strictly proportionally to the applied stress. These observations were extended to venous tissue by MacWilliam (6), who demonstrated the nonlinear elasticity of these tissues. His report does not include quantitative data or calculations of elastic moduli. Using a plethysmographic technique, Clark (7) provided the first estimates of venous elastic moduli (a distensibility modulus) as a function of pressure. Subsequently, Bergel (11) presented data for the incremental elastic modulus as a function of pressure for a segment of a canine jugular vein. We have confirmed the nonlinearity of elastic properties for both vein types studied. The stress-strain data obtained could be adequately described using a second-order regression equation. Our work also confirms the observations of Caro and Saffman (8) and Bergel (11) that veins are typically less compliant than are arteries of comparable size, yet the two vein types studied exhibited surprisingly large differences in elastic moduli. At all pressures, the circumferential jugular vein moduli were an order of magnitude larger than the corresponding saphenous vein moduli. In addition, the jugular vein was stiffer in the longitudinal direction than the saphenous segments were, and its incremental moduli were an order of magnitude larger. Moreover, when compared with the carotid artery at comparable strains (Table 3), jugular segments were considerably stiffer in both directions, but saphenous segments had moduli similar to those of the carotid artery. Thus, there appear to be large differences in stiffness within the venous system, differences larger than those exhibited throughout the arterial tree. The possibility that this difference in modul is a consequence of size alone, as might be inferred from the work of Caro and Saffman (8), is intriguing but awaits further experimental verification.
ELASTICITY OF VEINS

To what degree species differences play a role is not known at this time. Moreover, the influence of posture, gravitational factors (9, 10), and tethering cannot be determined from the present data. A more systematic examination of venous elasticity within and across species is needed to assess the relative importance of the various determinants of venous wall structure and its resultant elastic properties.

HISTOLOGIC CONSIDERATIONS

In 1957, Roach and Burton (23) introduced the concept that elastin fibers are responsible for the distensibility characteristics at low pressures, whereas at high pressures the less distensible medial and adventitial collagen predominates. This concept of arterial elasticity led to the analysis of collagen-elastin ratios in vessel segments, with the view that a high ratio should predict an inextensible vessel. Comparable moduli, however, have been obtained for the aorta and the carotid artery, which have approximately reciprocal collagen/elastin ratios (despite similar values for the total content of these polymers) (11). Hence, it appears as though the coupling of the two fiber types, not their preponderance, is the determinant of wall elasticity. Indeed, the human saphenous vein reportedly has three to five times as much collagen as elastin compared with a ratio of only two for most arterial segments (11, 24). Despite this preponderance of collagen, this vessel is not noticeably stiffer. Thus, the determination of these ratios provides little predictive information.

Given this concept of wall structure, it appears as though jugular segments possess a wall structure which "transfers" strain to collagen fibers at lower pressures than do the wall structures of the saphenous vein and arterial segments. The pronounced transition of the stress-strain curves at a pressure of 40 cm H$_2$O probably reflects the relatively inextensible collagen fibers coming into play. A similar transition does not occur in arterial segments until pressures exceed 300 mm Hg (14), and saphenous segments undergo the transition at approximately 120 cm H$_2$O.

Although they were subjected to arterial pressures for at least 10 months, none of the transplanted veins acquired the histologic or elastic characteristics of their host artery. In fact, all of the transplanted segments showed marked wall thickening and a histologic picture of intimal proliferation and medial and adventitial scarring. In short, these segments could best be described as rigid tubes.

IMPLICATIONS FOR VASCULAR SURGERY

From a first glance at the data presented in this paper, it might appear that saphenous veins should be a reasonably good grafting material for the arterial system. However, they become stiff at the usual arterial pressures and are unable to pulsate. It is likely that such a state of affairs is quite detrimental to the long-term integrity of the graft. Fry (25) has postulated that disturbed flow patterns can lead to fibromuscular hyperplasia. The altered geometry and distensibility seen in these grafts may lead to disturbed flow patterns which may be the cause of the intimal growth seen in aortocoronary grafts (3-5). Although grafts which have been in place for less than 1 week show minimal changes, intimal fibrosis becomes increasingly more prominent with longer periods of implantation. The entire wall thickens, primarily due to intimal proliferation, and may even occlude the lumen. Vlodaver and Edwards (3) have noted that "the intimal proliferative lesion appears to be a natural consequence of subjecting a vein to arterial pressure. Similar lesions are present in veins associated with arteriovenous fistulae." We would add that this process may be a direct consequence of the wall properties of venous tissue, in that they are relatively inextensible at arterial pressure. In addition, Kern et al. (4) have described lipid inclusions in smooth muscle cells and lipid-filled macrophages within the intima. A study of the incidence of these lesions in a large series of autopsy cases is presently not available, but the early results are worrisome. Although the grafts do not rupture or dilate aneurysmally, they do constrict and may occlude on that basis or by a supervening thrombus. In addition, it is not known at present what percent will develop atherosclerotic lesions in an otherwise functional graft.

Our data show that jugular venous segments are considerably less extensible than their arterial counterparts at arterial pressures and that they do not acquire the characteristics of arterial tissue when they are used as graft material. Rather, they respond as damaged tissue, with the reparative pattern known as intimal proliferation. Although the saphenous vein possesses wall characteristics which are more analogous to those of arteries, there are significant differences. It seems reasonable to conclude that these grafts do not develop the characteristics of arteries but probably respond in a manner similar to the jugular segments in this study. The implications of these physical characteristics and their possible dependence on the source of vein graft material suggest that this
information may be highly applicable to vascular procedures in use today.

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