Static Anisotropic Elastic Properties of the Aorta in Living Dogs

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ABSTRACT

Static anisotropic elasticity was studied in the middle descending thoracic aorta of 14 living dogs. Special transducers were used to measure radius and longitudinal stress at several pressures in situ in an isolated vessel segment. From these data, moduli describing elastic properties of the vessel wall were calculated. Results indicate that (1) at a physiologic pressure of 154 cm H₂O (extension ratio of 1.52 circumferentially) the mean values for the incremental elastic moduli in the radial, circumferential, and longitudinal directions were 5480, 7510, and 10,100 g/cm², respectively; (2) these moduli increased with an increase in intravascular pressure; and (3) the longitudinal modulus decreased when the vessel was studied in vitro (from the removal of longitudinal tethering).

ADDITIONAL KEY WORDS

static elastic properties
incremental anisotropic elasticity

The elastic properties of blood vessels have been of interest to the pathologist, physiologist, and clinician for many years. The physician Thomas Young was the first to describe a relation between vessel elasticity and circulatory hemodynamics. He suggested that pulse wave mechanics could be studied by using an acoustic analogy in which the blood vessel was considered to be an "equivalent elastic fluid" (1). This simplified picture of blood vessel rheology has not changed significantly over the ensuing 150 years and still represents a useful first approximation to the true state of affairs.

In more recent years, however, questions that have arisen in a number of areas require a more detailed and realistic picture of vascular rheology. For example, the intelligent design of vascular prostheses or artificial organs must include detailed considerations of vascular architecture and rheology. Any meaningful approach to the analysis of pulse contours or other circulatory variables for diagnostic or therapeutic purposes requires accurate knowledge of the principal rheologic parameters of the blood vessel. Moreover, vascular rheology is intimately related to degenerative vascular diseases. It is well recognized that the elastic properties of the arterial tree change significantly with the aging process; the artery becomes dilated, nonuniform, less compliant, and elongated, occasionally to the extent that it may assume a kinked and tortuous course. Finally, recent evidence indicates that the permeability and the integrity of the endothelial surface is sensitive to adjacent hydrodynamic events (2). If the drag of the adjacent flow produces a shearing stress on the endothelial cells in excess of about 400 dynes/cm², the surface rapidly degenerates and erodes. The high frequency components of turbulence also can produce rapid deterioration of the endothelial surface. Increased normal stress has been shown to increase the permeability of the endothelium to large molecules such as albumin. These observations led Fry (2) to conclude that the underlying cause of vessel damage in the examples cited...
above is the increase in strain energy density. The magnitude of the strain energy density will be determined among other things by the geometry and rheology of the vessel wall.

It thus becomes necessary to reexamine the older data and concepts of vascular rheology in light of these modern needs. These needs will require new data obtained from in-vivo measurements. It is the purpose of the present study to obtain such data in order to examine in detail the static elastic properties of the blood vessel. However, prior to describing these experiments, it will be necessary first to discuss certain concepts and definitions germane to understanding the logic and methods to be presented.

**Theoretical Consideration**

Unfortunately, rheologic study of a blood vessel in vivo presents a host of considerations which are a blend of practical and conceptual problems. A comprehensive discussion of these would exceed the scope of the present communication, and therefore only a brief presentation of the salient features pertinent to the logic of the present studies can be given.

Two classes of problems must be considered. The first deals with how one infers the states of stress and strain at a point in the wall of a blood vessel from externally measurable quantities such as intravascular pressure, longitudinal force, and radial displacement. The second deals with how one establishes unique and meaningful relations (constitutive relations) between the state of stress and the resulting state of strain.

**STRESS AND STRAIN**

There is general agreement that a segment of a large blood vessel such as the aorta may be assumed to be a thin-walled cylinder. If a cylindrical coordinate system is imagined in this vessel segment such that the z coordinate corresponds to the centerline of the lumen, the r coordinate to a vessel radius and the θ coordinate to the vessel circumference, then the state of stress due to intraluminal pressure and an evenly applied longitudinal stress (physiologic loading) can be shown to consist of purely normal (tensile or compressional) stresses along each of the coordinate axes. Formulas (3) relating the intravascular pressure, and the longitudinal force to the stresses (S) in the r, θ, and z direction are given by

\[
S_r = -p/2, \quad (1a) \\
S_θ = pR/h, \quad (1b) \\
S_z = f/2πRh, \quad (1c)
\]

wherein the subscripts indicate the direction of the normal stress, R is the radius of the middle surface of the vessel wall, h is the wall thickness, f is the net longitudinal force tending to elongate the cylinder, and p is the intravascular pressure. The formulas assume that R >> h, that Sr varies linearly across the wall, and that the extramural pressure is zero. Therefore, it is possible to estimate the average stress acting in the three coordinate directions from the measurement of intraluminal pressure, longitudinal force on the segment, vessel radius, and wall thickness.

The corresponding elongating (or contracting) strains could be estimated by following the radial, circumferential, and longitudinal dimensions from the unstressed condition to any desired degree of pressurization and longitudinal stress. Formulas (3) relating various dimensions to the strains are given by

\[
γ_r = \frac{h - h_0}{h_0} = λ_r - 1, \quad (2a) \\
γ_θ = \frac{R - R_0}{R_0} = λ_θ - 1, \quad (2b) \\
γ_z = \frac{L - L_0}{L_0} = λ_z - 1, \quad (2c)
\]

where γr, γθ, and γz are the elongating (or contracting) strains in the specified directions; h0, R0 and L0 are the unstressed values of thickness, radius and length, and L is the length at a given intravascular pressure and longitudinal stress. Thus γr, γθ, and γz define the average strain of the blood vessel segment measured from the unstressed state. Equivalently, as is often convenient in the theory of large deformations, the average state of strain can also be defined by the extension.
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ratios (stretches) \( \lambda_r, \lambda_\theta, \) and \( \lambda_z \) which are merely the ratios
\[
\frac{h}{h_0}, \quad \frac{R}{R_0}, \quad \text{and} \quad \frac{L}{L_0}
\]
respectively.

In a previous study (4) from this laboratory it was shown that the shearing strains which develop in a vessel segment under physiologic loading could be neglected. The values of shearing strains in the middle descending thoracic aorta varied from 0.003 to 0.115 over the pressure range of 3 to 270 cm H\(_2\)O, and were much smaller than the corresponding elongating strains (0.6 to 0.83). This observation greatly simplified the problem of strain measurement, since only orthogonal elongating strains need to be considered. Moreover, this fact also has important implications in establishing the constitutive relations between stress and strain in vascular tissues.

In a second study (6) it was shown that all three of the aforementioned elongating strains were not independent since vascular tissue remained virtually isovolumic under 40% longitudinal strain and 0 to 240 cm H\(_2\)O pressure. This simplifies the problem still further. As will be seen, these observations also have important implications with respect to both experimental measurements and the form of the constitutive relations.

From the foregoing, we arrive at three important conclusions: First, the only stresses that are normally developed in a blood vessel segment are orthogonal tensile or compressional stresses, acting in the direction of the cylindrical coordinate axes of the vessel. Second, the elastic properties of the vessel wall are such that the vessel responds to these stresses by simple elongation or contraction along these same coordinates, and no significant shearing strains occur, i.e., the vessel exhibits elastic symmetry about the planes perpendicular to \( r, \theta, \) and \( z \) axes. Third, although only two of these elongating strains can be measured accurately by present techniques, the third will always be related to the other two through the incompressibility condition, i.e., tissue volume must always remain constant.

CONSTITUTIVE RELATIONS

Constitutive relations relate a given state of stress to the corresponding state of strain for a purely elastic body, or to the corresponding strain and rates of strain for a viscoelastic body. The simplest examples of these are the equations of linear isotropic elasticity, which contain the well-known Young's modulus and Poisson's ratio. More general elastic materials, e.g. orthotropic materials, require more than two moduli for their characterization even in a linear region. Since the present study is concerned primarily with the elastic properties of blood vessels it is useful to consider in more detail to what extent simple moduli, similar to the Young's modulus and Poisson's ratio, can be used meaningfully to relate vessel wall stress to its corresponding strain. The use of such moduli would ordinarily require two conditions to be met. The first is that the substance be truly elastic, i.e., when a deforming stress is removed, it returns to its original shape. The second is that only small strains around the unstressed state be considered. Blood vessels satisfy neither of these two conditions exactly.

Let us consider the first condition. In general, a blood vessel responds to large stresses in a manner which is both amplitude (nonlinear) and frequency (viscoelastic) dependent. However, in its normal physiologic state, a blood vessel appears to respond to the cyclic stress of the pressure pulse in a predominantly elastic manner. If the amplitude or the average value of the pressure pulse is changed rapidly to some new value, a transient period of readjustment occurs, during which time the relation between stress and strain changes to a new set of values. This is related to several factors. For example, the elastic elements of the blood vessel are embedded in a gelatinous matrix and are surrounded by numerous smooth muscle cells. These substances have viscous properties as well as elastic properties, which depend very much on previous strain history, rate of strain,  

\footnote{Similar results were obtained by Lee et al. in the carotid artery (5).}
neurohumoral control, and ionic milieu. Although the latter two factors can, in principle, be controlled by proper experimental design the former must be incorporated into any complete rheologic description. However, in most practical circumstances interest is centered around the steady-state behavior of the blood vessel over restricted ranges of stress, for example, over the range of pulse pressure. As noted above, a blood vessel responds like a typical elastic body in these restricted circumstances.

The second condition, namely, small strains around an unstressed state poses a somewhat more difficult problem. A blood vessel normally operates around an initially stressed state such that the average strain in the wall may be as much as 70%. The oscillations of strain around this value, however, are small, typically only about 3 or 4%. This suggests a simplified approach to the problem of large strains which has proved useful, both in engineering as well as in previous considerations of vessel rheology (7, 8). In this simplified approach one considers the incremental stress-strain relation at some initially stressed state. This approach is necessary for in-vivo measurements and is satisfactory for most applications. The major disadvantage is that in applications wherein wide ranges of stress and strain must be considered it is necessary to define elastic behavior around a number of average strains to cover the range of interest. Moreover, if one wishes to compare these incremental elastic moduli obtained under different experimental conditions or obtained from other animals, one must be sure that their values are measured around identical states of average strains.

Thus, we conclude that it is possible to consider a blood vessel to be a linear elastic body over restricted ranges of strain. Furthermore, that by using the concepts of incremental stress and strain, it is possible to apply certain equations of linear elasticity to calculate corresponding incremental elastic moduli which will describe the stress-strain behavior of the blood vessel around selected average values of strain. For a more complete theoretical justification of this approach one is referred to Biot (7).

Classical linear elasticity theory assumes that stress is proportional to strain and that the principle of superposition applies such that a strain along a given coordinate is the sum of a number of strains, one of which is related to the stress acting along that coordinate and the rest of which are related to the interactions of the stresses acting along the other coordinates. These considerations also apply to the incremental elasticity theory provided the fluctuations in strain around the average value are kept small. For example, let us consider the incremental elongating strain, $e_z$, acting along the $z$ direction. As discussed earlier, in a blood vessel under physiologic loading, we need consider only the three incremental tensile (or compressional) stresses, $P_r, P_\theta, P_z$. Thus we may write the following linear relation between the incremental strain and the incremental stresses:

$$e_z = C_{zz}P_z - C_{z\theta}P_\theta - C_{z\phi}P_\phi$$  \hspace{1cm} (3a)

wherein the $C_{ij}$ $(i,j = r, \theta, z)$ are proportionality constants that relate the component of strain along the $z$ direction to the corresponding stresses in all three directions. Thus, if we applied only the stress $P_z$ we would obtain a strain in the $z$ direction equal to the first term on the right of equation 3a. If then we superimposed a stress in the $\theta$ direction, $P_\theta$, we would get an added increment of strain in the $z$ direction equal to the second term; finally, if we impose another stress $P_r$ in the $r$ direction we would superimpose a third increment of strain in the $z$ direction equal to the last term. Writing down similar expressions for the incremental strains in the other two directions we obtain three simultaneous equations:

$$e_\theta = C_{\theta\theta}P_\theta - C_{\theta\phi}P_\phi - C_{\theta r}P_r$$  \hspace{1cm} (3b)

$$e_r = C_{rr}P_r - C_{r\theta}P_\theta - C_{r\phi}P_\phi$$  \hspace{1cm} (3c)

wherein there appear nine elasticity coeffi-
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As will be seen all of the incremental stresses are measurable quantities and two of the incremental strains, $e_z$ and $e_{th}$, are measurable. Therefore, we have three equations with ten unknown quantities, $e_r$ plus the nine elasticity coefficients. All of the elasticity coefficients, however, are not independent. For instance in the classical linear elasticity theory the following relations hold:

\begin{align}
C_{rr} &= C_{rr}, \quad (4a) \\
C_{sth} &= C_{th}, \quad (4b) \\
C_{sth} &= C_{sr}. \quad (4c)
\end{align}

$C_{rr}$, $C_{sth}$, and $C_{z}$:

\begin{align}
e_0 &= C_{rr} \left[ -\frac{P_r + P_z}{2} \right] + C_{sth} \left[ -\frac{P_r + 2P_z - P_z}{2} \right] + C_{z} \left[ \frac{P_z - P_z}{2} \right], \quad (7a) \\
e_z &= C_{rr} \left[ -\frac{P_z + P_z}{2} \right] + C_{sth} \left[ \frac{P_r - P_z}{2} \right] + C_{z} \left[ -\frac{P_r - P_z + 2P_z}{2} \right]. \quad (7b)
\end{align}

A particularly lucid thermodynamic proof of the foregoing for a simple two-dimensional case is given by Katchalsky and Curran (9). Further it can be shown that these relations also apply to the incremental elasticity theory if the material is incompressible (7). Since the vascular tissue has been shown to be incompressible, equations 4 apply (6). Moreover, the incompressibility of the vascular tissue permits the use of the relation

\begin{equation}
e_r + e_0 + e_z = 0, \quad (5)
\end{equation}

which states that the incremental volumetric strain should be zero. Substituting equations 3 and 4 into equation 5, it is possible to derive (10) the following three independent relations among the elasticity coefficients:

\begin{align}
C_{z} &= \frac{1}{3} \left[ -C_{rr} + C_{sth} + C_{z} \right], \quad (6a) \\
C_{z} &= \frac{1}{3} \left[ C_{rr} - C_{sth} + C_{z} \right], \quad (6b) \\
C_{z} &= \frac{1}{3} \left[ C_{rr} + C_{sth} - C_{z} \right]. \quad (6c)
\end{align}

Thus, equations 3 through 6 give us nine independent equations that must be satisfied simultaneously. The algebra of this system of equations may be simplified by substituting equations 4 into equations 3 and in turn equation 6 into the result to obtain the following two equations in the three unknowns,

\begin{align}
&\text{Since there are three unknowns and only two equations (7a and 7b), we must find one more independent relation before this system is completely determined. This can be accomplished by creating a new state of stress so that the incremental stresses and strains in equations 3 assume new values. In accordance with the earlier discussion regarding the concept of incremental moduli, however, one must be careful in doing this to maintain the same average values of stress. As will be discussed in greater detail later, it is possible to manipulate experimentally the values of these stresses such that $P_r$ and $P_{th}$ remain virtually zero while $P_z$ varies. In this particular circumstance the second two terms on the right of equation 3a can be considered zero. Therefore, we may rewrite equation 3a to be}
\end{align}

\begin{equation}
e^* = C_{rr} P_z^*, \quad (8)
\end{equation}

\begin{align}
&\text{wherein the asterisks indicate that these values of stress and strain obtain only for the condition that $P_{th}$ and $P_r$ are zero. Equation 8 may be used for the third independent relation. Thus equations 7 and 8 constitute a set of three independent relationships in three}
\end{align}

\begin{align}
&\text{Constitutive relations of this kind are typical of a linear orthotropically elastic material. Such equations are also the proper form of incremental constitutive relations for an orthotropic material subject to an initial stress (7). There are, in general, three additional equations relating shearing stresses to the corresponding shearing strains with associated independent elastic moduli. Since these stresses and strains are considered negligible in a blood vessel segment (4), these equations are neglected.}
\end{align}

\begin{align}
&\text{The incompressibility condition reduces equations 3 to only two independent equations (10).}
\end{align}

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unknowns. Therefore, if $e_9$, $e_z$, $P_r$, $P_\theta$, $P_z$, $P^*$ and $e^*$ are measured experimentally and equations 7 and 8 solved simultaneously, the numerical values of $C_{rr}$, $C_{\theta\theta}$, and $C_{zz}$ are obtained. Values of all other elastic moduli can be calculated from these.

The relations between $C_{rr}$, $C_{\theta\theta}$ and $C_{zz}$ and other incremental moduli similar to the familiar Young's moduli ($E$) in the $r$, $\theta$, and $z$ directions are given by the following relations:

$$C_{rr} = \frac{1}{E_r},$$

$$C_{\theta\theta} = \frac{1}{E_\theta},$$

$$C_{zz} = \frac{1}{E_z}.$$  (9c)

If the values of $C_{rr}$, $C_{\theta\theta}$, and $C_{zz}$ are substituted into equation 6, values for $C_{r\theta}$, $C_{rz}$ and $C_{z\theta}$ can be obtained. These latter moduli are related to the corresponding incremental Poisson's ratios ($\sigma_{ij}$) by the following:

$$C_{r\theta} = \frac{\sigma_{r\theta}}{E_\theta} = \frac{\sigma_{\theta r}}{E_r},$$

$$C_{rz} = \frac{\sigma_{rz}}{E_r} = \frac{\sigma_{rz}}{E_z},$$

$$C_{z\theta} = \frac{\sigma_{z\theta}}{E_\theta} = \frac{\sigma_{z\theta}}{E_r}.$$  (10c)

wherein the $\sigma_{ij}$ represent the ratios of the contractile strain in the $i$th direction due to an elongating strain in the $j$th direction. The experimental methods for obtaining these data will now be presented.

**Methods**

As discussed in the previous section, the calculations of the elastic moduli requires knowledge of the following variables: $e_9$, $e_z$, $P_r$, $P_\theta$, $P_z$, $P^*$ and $e^*$. The experimental design, instrumentation, and computational procedures for determining these variables in the living dog will be presented below.

**EXPERIMENTAL DESIGN**

Fourteen dogs weighing 23.4 to 37.8 kg (average weight 28.6 kg) were studied under chloralose and urethane anesthesia (about 76 and 760 mg/kg, respectively). The dog's chest was opened and adequate ventilation was maintained with a positive pressure respirato-

The experimental setup is shown in Figure 1. The thoracic aorta was exposed and the external radii were measured with vernier calipers. A relatively uniform segment of the aorta was chosen. A 7.5-cm length, $L$, was marked on this segment, and the mean aortic pressure noted. The segment was isolated and bypassed from the main systemic circulation ($E$ positions in Fig. 1). An assembly consisting of two plastic cylindrical plugs connected by a hollow metal rod (step 1, Fig. 1) was then fitted snugly to the segment. The plug assembly was inserted from the proximal end. The segment was then restored to length $L$. Small tunnels were made under the vessel and the segment was tied snugly around the coupling grooves of the plugs. Dissection of periaortic tissue was kept to a minimum. The proximal end of the rod was connected to a reservoir, D, filled with oxygenated blood, the height of which maintained selected constant pressures in the vessel segment. Pressure was measured through a cannulated intercostal artery in the midportion of the segment. The remaining intercostal arteries were ligated about 1 cm away from the segment. The segment pressure was adjusted to the same mean value at which the segment length was initially marked. A displacement sensing device (R), for continuous measurement of radius, was then sutured to the segment. A force gauge (F), for continuous measurement of longitudinal force, was attached to the plugs and a base line (zero force) was recorded. The threaded rod of the plug assembly was unscrewed, withdrawn, and reengaged to the proximal plug (step 2, Fig. 1). The force required to maintain the vessel

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4This length was considered adequate ($L > 10R$) to avoid "end effects" and was short enough to trap a reasonably uniform aortic segment, minimizing taper.
A Typical Experiment.—The objective of the experiment was twofold: (1) to minimize hysteresis effects in order to obtain reproducible results for elastic properties, and (2) to collect data for computation of various elasticity coefficients.

Bergel and Remington (8, 11) have shown that the pressure-radius curve in an aorta that is under static distension does not follow the same path over an inflation and deflation cycle and a hysteresis loop is obtained. This implies that the energy put into the system during inflation is not fully recovered during deflation. We modified the standard technique used by various workers (3, 8, 12) to minimize hysteresis effects. Prior to an experiment to determine elastic coefficients, we inflated and deflated the vessel for three cycles over the physiologic range of pressure (from 110 to 190 cm H$_2$O). This was in contrast to the pressure range of 0 to 270 or 400 cm H$_2$O used by others. Hysteresis was quantified by comparing the width of the hysteresis loop measured as change in radius ($\delta R$) at mid-pressure, to the change in radius ($\Delta R$) over the range of pressure used. The average value of the ratio $\delta R / \Delta R$ in 14 dogs, was 0.045 ± 0.008 se.

The experimental design to obtain data for computation of elastic constants consisted of the pressure, radius and longitudinal force measurements at three segment lengths, $L$, $L^+$ and $L^-$. The data were always collected from the ascending limb of the pressure-radius curve as the pressure was raised to cover the physiologic range. The pressure was raised in steps of 20 cm H$_2$O, and the data collected at least 1 minute after the step was imposed; this time period appeared to be optimum for minimizing the effect of creep, since waiting longer than 1 minute produced a very small
additional change in radius (<0.3%). In 14 dogs the vessel segment was studied around three mean pressures (i.e. at 3 values of \( \lambda \)). In nine dogs the experiment was then repeated around one of the mean pressures to test reproducibility. In four dogs the entire experiment was repeated in vitro after completion of the in-vivo study.

**Physiologic Status of the Preparation.**—Besides receiving blood from the reservoir, the segment received blood from the main circulation through the vasa vasorum. India ink injected into the main circulation of one dog was detected histologically in the outer one-third of the vessel segment wall. Furthermore, when 2 ml of levarterenol (Levophed, Winthrop) was injected into the main circulation of two dogs, the average longitudinal force of the vessel segment increased 27% and the average external radius decreased 0.5%.

An attempt was made to maintain blood \( \text{PO}_2 \), \( \text{pH} \), and \( \text{PCO}_2 \) within physiologic limits, and these were determined periodically from blood obtained both from the segment and the main circulation. The segment: oxygen saturation 98% (± 1 SE), \( \text{pH} \) 7.37 (±0.004 SE), and \( \text{PCO}_2 \) 28 mm Hg (± 8 SE). Main circulation: oxygen saturation 86% (±3 SE), \( \text{pH} \) 7.21 (± 0.03 SE), and \( \text{PCO}_2 \) 49 mm Hg (± 5 SE). The vessel segment was kept moist during the experiment. The temperature of the blood in the segment remained around 26 or 27°C.

**INSTRUMENTATION**

**Pressure.**—All pressures were measured with a Statham P23 Db transducer (P in Fig. 1) coupled to the vessel lumen through polyethylene catheters (PE-100).

**Radius.**—The external radius of the vessel segment was measured by an electric caliper, (R in Fig. 1), the details of which have been described previously (13). The instrument consists of two foil strain gauges bonded to a very thin piece of shim stock suspended between the hinged legs of a caliper. Displacement of one leg of the caliper with respect to the other results in a proportional change in electrical resistance of the strain gauge.

Although it has been reported (13) that the recording accuracy of the device is adequate in practice, it has been found that errors related to the coupling of the device to the vessel wall can occur. Therefore a technique for in-vivo calibration was devised which was essentially free of errors related to coupling. As shown in Figure 1, a syringe was used to inject a known volume of blood (≈ 0.7 ml) into the segment. This superimposed a pressure change of approximately 20 cm H\(_2\)O onto a given mean pressure. This was repeated over the entire mean pressure range of the study. As the volume was being changed, the caliper output signal was recorded. From each

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This was determined in a separate unpublished x-ray study on vessel segments filled with contrast medium.
increment of volume we calculated the change in internal cross-sectional area of the vessel segment with the length of the segment fixed. This calibration procedure was carried out immediately before and after the experiment. To attach an absolute value to this area, we made a Geltrate cast (L. D. Caulk Co., Milford, Delaware) of the vessel segment after the last calibration, with the caliper still attached to the segment. The average cross-sectional area of this cast was then used in calibrating the caliper output signal obtained when the cast was made. From these data we plotted a curve of inner cross-sectional area vs. caliper output. A quadratic function was found to fit this curve by the least squares technique. By dividing the cross-sectional area by π and taking the square root, we obtained an expression relating inner radius of the vessel to caliper output (Fig. 2). The calibration curves obtained before and after the experiment were almost identical.

**Force.** The longitudinal force was measured with a specially designed gauge (14), which is shown as F in Figure 1. It consists of a stiff, adjustable metal arch coupled to intraluminal plugs by two circumferential screw clamps. The difference in longitudinal force on the two plugs is transmitted to the sensing elements of the gauge through the two vertical legs. Conventional foil strain gauges convert the minute strain produced by the force to a proportional electric signal. The gauge was calibrated against known increments of force. The calibration curve representing force vs. signal output was linear (±1%) and exhibited no measurable hysteresis or creep. The force displacement coefficient for the system was 45,000 g/cm. Thus, for the incremental longitudinal force encountered in this study, the internal displacement of the force gauge was very small (≈0.001 cm).

All data were recorded simultaneously on an FM tape system (Ampex FR 100) and on a direct-writing recorder (Sanborn Model 350) for observation and analysis.

**Computation Procedures**

Values of the variables $e_z$, $e_\theta$, $P_z$, $P_\theta$, and $P_r$ were calculated from the pressure-radius-longitudinal force relations obtained at constant length, $L$. The value of $e_z$ under these circumstances was zero.

The incremental circumferential strain, $e_\theta$, was calculated from

$$e_\theta = \frac{\Delta R}{R}$$

where $\Delta R$ is the change in mid-wall radius corresponding to the increase in pressure, $\Delta p$, imposed on the vessel segment of length $L$. $R$ refers to the radius at the middle of the vessel wall and is calculated by using the measured value of internal radius, $R_i$, and wall thickness, $h$, in the relation

$$R = R_i + \frac{h}{2}.$$  

The wall volume, $V$, was determined for each specimen by measuring its loss of weight when excised and suspended in distilled water. Since the material is incompressible, $V$ remains constant and $h$ can be calculated for different values of $R_i$ and $L$ from

$$h = R_i + \frac{\sqrt{R_i^2 + \frac{V}{\pi L}}}{2}.$$  

The incremental longitudinal stress is

$$P_z = [S_z]_2 - [S_z]_1,$$  

where 1 and 2 refer to the evaluation of the total stress, $S_z$, at the initial and final values of the pressure, respectively. $S_z$ may be calculated from equation 1c, remembering that the net longitudinal force, $f$, is given by

$$f = F + \pi R^2 p,$$

where $F$ is the force measured by the force gauge and $\pi R^2 p$ is the force due to the intravascular pressure acting on the closed ends of the vessel segment.

The incremental circumferential stress is given by

$$P_\theta = [S_\theta]_2 - [S_\theta]_1.$$  

$S_\theta$ may be calculated from equation 1b.

Finally, the incremental radial stress is

$$P_r = -\frac{\Delta p}{2}.$$
This is an approximation, since the exact value of \( P_r \) would require a knowledge of the stress distribution across the vessel wall. However, for present purposes this is adequate since \( P_r \) is very small compared to \( P_z \) and \( P_e \).

Values of the variables \( P_z^* \) and \( e_z^* \) were calculated in the following manner. The value of \( P_z^* \) was obtained by measuring the longitudinal force due to a change in length of the vessel segment, holding the circumferential stress, \( S_e \), constant and the radial stress, \( S_r \), approximately constant. Under these circumstances the value of the incremental stresses \( P_e \) will be zero and \( P_r \) will be negligibly small (<1% of \( P_z^* \)). This was accomplished by measuring the pressure-radius-longitudinal force relations at the three segment lengths \( L \), \( L^+ \) and \( L^- \). The circumferential stress, \( S_e \), was then plotted vs. pressure for the two lengths \( L^+ \) and \( L^- \) as shown in Figure 3A. The value of \( S_e \) at 150 cm H\(_2\)O pressure (mean pressure used in this experiment) for length \( L \) was plotted as point 1 on the graph. A line parallel to the abscissa passing through this point was drawn. The values of pressure where this line intersects the \( L^+ \) and \( L^- \) lines (points 2 and 3) were noted. The corresponding longitudinal forces for these pressures were obtained from Figure 3B at points 2 and 3, in which the longitudinal force vs. pressure is plotted for the two lengths \( L^+ \) and \( L^- \).

The incremental stress, \( P_z^* \), can now be calculated using the above data in the equation

\[
P_z^* = \left[ \frac{F}{2\pi R h} \right]_{t} - \left[ \frac{F}{2\pi R h} \right]_{t'}.
\]

Note that this equation is a special case of equation 14.

The value of the incremental longitudinal strain \( (e_z^*) \) was calculated from

\[
e_z^* = \frac{(L^+)}{L} - \frac{(L^-)}{L} = \frac{\Delta L}{L}.
\]

Thus, we have obtained all the variables necessary to solve equations 7 and 8 for the three unknowns, \( C_{rr} \), \( C_{io} \), and \( C_{cz} \). From these we could obtain the remaining incremental elastic moduli using equations 9 and 10.

Stability of Equations.—It was important to test the stability of equations 7a and 7b. For this purpose two lines satisfying these linear equations were plotted using data from one dog. The intersection of these two lines would represent the simultaneous solution of the two equations. If the lines were nearly parallel and the angle of intersection small, then the solution would be very sensitive to small experimental errors and the equations would be unstable or ill conditioned (15). However, the angle of intersection was found to be 80°, indicating that the system of equations was stable.

Independent Validation of the Method.—As an overall check of the methods and instrumentation, a study was carried out on an isotropic rubber (polyurethane) tube and the results compared to those obtained in an independent manner. The independent experiment was performed by measuring lengths and diameters from photographic transparencies of a vertically mounted tube subjected to a series of internal pressures and longitudinal weights.\(^6\) The elastic constants at equivalent

\(^6\)We are indebted to Dr. V. J. Parks and the staff of the Stress Analysis Laboratory, Catholic University of America, for the use of their laboratory and for casting the polyurethane tube.
TABLE 1

Summary of Experimental Data

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (λe from 1.29 to 1.45)</th>
<th>Group 2 (λe from 1.46 to 1.55)</th>
<th>Group 3 (λe from 1.56 to 1.72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. dogs</td>
<td>6</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>No. experimental points</td>
<td>18</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Wt (kg)</td>
<td>29.2 ± .8</td>
<td>27.4 ± .7</td>
<td>26.7 ± .7</td>
</tr>
<tr>
<td>p (cm H₂)</td>
<td>145 ± 4</td>
<td>154 ± 3</td>
<td>162 ± 3</td>
</tr>
<tr>
<td>R (cm)</td>
<td>0.62 ± .02</td>
<td>0.60 ± .01</td>
<td>0.63 ± .01</td>
</tr>
<tr>
<td>R/h</td>
<td>8.1 ± .17</td>
<td>9.8 ± .50</td>
<td>10.0 ± .42</td>
</tr>
<tr>
<td>αe × 100</td>
<td>4.2 ± 21</td>
<td>4.5 ± 22</td>
<td>3.8 ± .16</td>
</tr>
<tr>
<td>e₂* × 100</td>
<td>2.8 ± .01</td>
<td>2.7 ± .01</td>
<td>2.7 ± .01</td>
</tr>
<tr>
<td>P₁ (g/cm²)</td>
<td>260 ± 4</td>
<td>330 ± 17</td>
<td>323 ± 13</td>
</tr>
<tr>
<td>P₉ (g/cm²)</td>
<td>69 ± 3</td>
<td>80 ± 6</td>
<td>81 ± 6</td>
</tr>
<tr>
<td>P₆ (g/cm²)</td>
<td>188 ± 16</td>
<td>281 ± 23</td>
<td>305 ± 17</td>
</tr>
<tr>
<td>S₁ (g/cm²)</td>
<td>1170 ± 28</td>
<td>1510 ± 87</td>
<td>1630 ± 83</td>
</tr>
<tr>
<td>S₂ (g/cm²)</td>
<td>1060 ± 50</td>
<td>1170 ± 77</td>
<td>1210 ± 84</td>
</tr>
</tbody>
</table>

Average values ± SE of various parameters (as explained in the text) are shown for each group. The numerical values of Sₙ, for each group, can be obtained by using equation 1a. The value of P₁ = -10 g/cm² in each case.

Results and Discussion

IN-VIVO STUDIES

The results are summarized in Table 1 and Figure 4. In Table 1 data are grouped according to the range of extension ratio, λₑ. As expected, the mean pressure, p, for each group increased with higher λₑ; however, the mean value of midwall radius, R, did not increase monotonically, because relatively larger dogs contributed to group 1. The average value of R/h varied from 8.1 to 10 and was considered adequate to permit calculation of wall stresses based on thin-wall theory (16). Values of similar ratios in the literature (8, 12) are reported as h/Rₑ, where Rₑ is the external radius of the artery and, after appropriate correction, these results agree with ours.

The incremental stresses and strains (Pₑ, Pₑ, Pₑ, eₑ, eₑ, eₑ) were small compared to the average stresses and strains (Sₑ, Sₑ, yₑ, yₑ). The local stresses and strains were purposely kept small to permit linear incremental elasticity theory to apply around a given initial state of strain.

The values of incremental Poisson’s ratios (σᵦₑ) were always positive and averaged to 0.5 in a given experiment because of the incompressibility constraint.

In Figure 4, the incremental elastic moduli are plotted against the mean values of three groups of λₑ (upper panels) and against the mean values of three groups of λₑ (lower panels). Two features of these plots are noteworthy: (1) The average value of the elastic moduli in the third group were always

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Incremental elastic moduli and extension ratios. $E_\theta =$ circumferential modulus; $E_z =$ longitudinal modulus; $E_r =$ radial modulus; $\lambda_\theta =$ circumferential extension ratio; $\lambda_z =$ longitudinal extension ratio. Horizontal and vertical bars indicate the standard error of the mean for each of the groups. In the upper panels the moduli are plotted vs. the mean $\lambda_\theta$ for each of three groups; the corresponding values of $\lambda_\theta$ (from left to right) are $1.45 \pm .04$ SE, $1.56 \pm .02$, and $1.51 \pm .02$. In the lower panels the moduli are plotted vs. $\lambda_z$; the corresponding values of $\lambda_z$ for each of these groups (left to right) are $1.46 \pm .02$, $1.58 \pm .02$, and $1.48 \pm .02$.

significantly higher ($P < 0.01$) than in the first group. Thus the modulus increased with an increase in extension ratio which indicated that the vessel has nonlinear elastic properties.

(2) In general, $E_z > E_\theta > E_r$ for in-vivo studies at physiologic pressures. These results indicated that the vessel wall is anisotropic, at least locally around a given state of strain. It is possible to observe this behavior even in isotropic materials with large deformations when different amounts of initial stresses are imposed in $z$, $\theta$, and $r$ directions. In that case, one is looking at different parts of the nonlinear stress-strain curves for each direction and therefore one finds different values of incremental moduli (17). Thus, irrespective of whether the elastic properties of a blood vessel are initially isotropic or anisotropic, one is likely to find anisotropic behavior locally when the stress-strain relations are studied around a given mean pressure. In this situation one wonders how meaningful it is to calculate the isotropic incremental elastic modulus\(^7\) as an index of material property of the arterial wall.

In nine dogs, the experiment was repeated\(^7\)It should be mentioned that, in general, the incremental isotropic Young's modulus often used in the physiologic literature (8, 12) is not a simple average of the three anisotropic moduli, $E_r$, $E_\theta$ and $E_z$. This was also confirmed experimentally.

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around one of the mean pressures. The elastic properties were then compared at the same values of $\Delta p$ and $\Delta A$. $E_r$ and $E_z$ were found to be reproducible within 2% and $E_z$ within 16%. Therefore, it can be concluded that the preparation was reasonably stable over the 2-hour period of study.

**IN-VIVO VERSUS IN-VITRO STUDIES**

In four dogs the experiment was repeated in vitro. The vessel segment was removed from the thorax with all the instruments in place, stripped of surrounding tissue up to adventitia and then studied. The temperature of the blood in the segment was 2°C lower than that in vivo. In general, the values of all the elastic moduli decreased when compared to their in-vivo values at corresponding stretches; $E_r$ decreased by 32% ($P<.01$), $E_z$ by 20% ($0.2<P<.05$), and $E_z$ by 9% ($0.05 < P < .1$). The above temperature difference was too small to account for this decrease (18). However, the loss of normal tethering of the blood vessel in situ can account for the decrease. Using data from a previous study (19) it was possible to calculate the contribution of vascular tethering to the in-vivo longitudinal modulus, $E_z$. This was found to be 40%. Thus, we conclude that the 32% decrease in the value of $E_z$ noted in vitro can be explained by removal of longitudinal tethering of the vessel segment.

**COMPARISON WITH OTHER STUDIES IN THE LITERATURE**

To our knowledge, the anisotropic elastic properties of a blood vessel have not been previously studied in a living animal. However, Tickner and Sacks (3) have reported similar in-vitro studies on segments from the thoracic aorta of two dogs. These authors considered the vessel compressible and anisotropic and evaluated various incremental elastic moduli in the $r$, $\theta$, and $z$ directions. In general, our results are similar in three respects: (1) The vessel wall was anisotropic. (2) At comparable extension ratios, their values of $E_r$ and $E_z$ were of the same order of magnitude as ours and tended to increase with increased stretch. (3) The value of $E_z$ was greater than that of $E_r$, especially at higher stretches as in our in-vitro studies. Their results differed from ours in two respects: (1) Their values of $E_r$ were much lower than ours, almost an order of magnitude lower in one dog. (The values of $E_r$ reported in our study are similar to those obtained directly on a test stand [20].) (2) They reported negative values of Poisson's ratios. In some instances, all six Poisson's ratios were negative simultaneously. This is difficult to visualize physically since it would mean that if the substance were stretched in one direction it would expand in all directions.

No direct comparison can be made between the incremental orthotropic moduli in our study and the moduli reported in various other vessel elasticity studies in the literature (8, 12, 21-23) since the other studies assume the vessel wall to have isotropic properties and do not include the unstressed dimensions. However, we believe that a comparison of the raw data used in deriving the elastic moduli, namely, the incremental pressure-radius ($\Delta p/\Delta R$) relation, can and should be made. For this purpose, a derived parameter, $C_\alpha$, assumed to represent the associated pulse wave velocity, can be calculated for all studies. The formula (12) commonly used for this purpose is

$$C_\alpha = \left[ \frac{\Delta p}{\Delta R_0} \frac{(1-\gamma)^2}{(2-\gamma)} \frac{G}{\rho} \right]$$  (20)

where $\Delta R_0$ is the change in outside radius of the blood vessel, $\gamma$ is the ratio of $h$ to $R_0$, $\rho$ is the density of blood, and $G$ is the acceleration due to gravity. The parameter $C_\alpha$ in this equation depends both on the material properties of the wall as well as the geometry (or dimensions) of the tube. From a theoretical viewpoint the wave velocity in an orthotropic initially stressed tube is a complicated function of the elastic moduli and the initial stresses as pointed out by Atabek (24). Strictly interpreted then, our use of equation 20 is merely a convenient means of comparing the basic data common to all studies. Despite the theoretical shortcomings, however, as will be shown below, the simple formula does predict pulse wave velocity surprisingly well.
TABLE 2
Computed and Measured Wave Velocities

<table>
<thead>
<tr>
<th>Dog wt (kg)</th>
<th>Computed velocity from static elastic measurements (cm/sec)</th>
<th>Measured foot-to-foot velocity (cm/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25.8</td>
<td>527</td>
<td>579</td>
</tr>
<tr>
<td>24.8</td>
<td>587</td>
<td>507</td>
</tr>
<tr>
<td>26.4</td>
<td>540</td>
<td>567</td>
</tr>
<tr>
<td>34.4</td>
<td>520</td>
<td>548</td>
</tr>
<tr>
<td>26.5</td>
<td>565</td>
<td>537</td>
</tr>
<tr>
<td><strong>MEAN ± se</strong></td>
<td><strong>27.6 ± 1.9</strong></td>
<td><strong>548 ± 13</strong></td>
</tr>
</tbody>
</table>

Reported values (23) of measured foot-to-foot velocity in the thoracic aorta of dogs vary from 450 to 700 cm/sec.

TABLE 3
Computed Wave Velocity (C_o) in Descending Thoracic Aorta

<table>
<thead>
<tr>
<th>Type of data</th>
<th>Present study</th>
<th>Bergel (8, 23)</th>
<th>Gow &amp; Taylor (12)</th>
<th>Peterson et al. (22)</th>
<th>Patel et al. (21)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Static in vivo from isolated vessel segment</td>
<td>Static in vitro from isolated vessel segment</td>
<td>Dynamic in vivo from intact aorta</td>
<td>Dynamic in vivo from intact aorta</td>
<td>Dynamic in vivo from intact aorta</td>
</tr>
<tr>
<td>C_o (cm/sec)</td>
<td>525</td>
<td>506</td>
<td>503</td>
<td>490</td>
<td>743</td>
</tr>
<tr>
<td>p (cm H_2O)</td>
<td>153</td>
<td>136</td>
<td>136</td>
<td>143</td>
<td>142</td>
</tr>
<tr>
<td>No. dogs</td>
<td>14</td>
<td>12</td>
<td>10</td>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>

*Since that thickness was not measured in this study, we used R_0/h ratio from Bergel’s study (8) to estimate C_o.

In order to compare the computed wave velocity, C_o, with the measured pulse wave velocity, we measured foot-to-foot velocity directly in the intact thoracic aorta of five dogs, before the vessel segment was isolated. C_o was also calculated from the static elastic measurements carried out subsequently in the isolated vessel segment of these dogs. It can be seen in Table 2 that the values of measured foot-to-foot velocity were close to the calculated values of C_o.

In Table 3 the calculated average value of C_o from the present study is compared to similar values of others (8, 12, 21-23). The value of C_o from the present study agrees with those of Bergel, and Gow and Taylor, but is much lower than those reported by Peterson et al. and Patel et al. Several factors may be responsible for the differences: (1) possible systematic errors (as explained in the methods section) in the measurement of radius in Patel’s study, and (2) normal variations in C_o due to aortic size and local chemical milieu.

In conclusion, we have studied rheology of the thoracic aorta within the physiologic range of pressures. The incremental static anisotropic elastic properties are evaluated around an average state of strain. The initial dimensions are included so that one could locate precisely the point where the incremental properties were evaluated on the large, nonlinear, stress-strain curve. This is important for comparison

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of data from various sources. In this framework the incremental elastic constants represent the true material properties at a given state of strain.

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Doli J. Patel, Joseph S. Janicki and Thomas E. Carew

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