Measurement of Viscoelastic Properties of Arteries in the Living Dog

By Barry S. Gow, M.D.S., F.A.C.D.S., and Michael G. Taylor, M.D., Ph.D.

ABSTRACT

Dynamic elastic moduli (E\text{dyn}) and viscous moduli (\eta) of the arterial wall were obtained at a number of sites of the systemic vascular tree of living dogs anesthetized with pentobarbital. Constants were calculated using the first harmonics of pressure and diameter obtained from a Fourier analysis of simultaneously recorded pulse waves. The means and standard errors of E\text{dyn}, in dynes cm^{-2} \times 10^6, obtained at mean blood pressures ranging from 87 to 130 mm Hg and pulse frequencies from 1.1 to 2.8 cps were: 3.0 ± 0.33 (9 midthoracic aortas), 9.8 ± 1.2 (7 midabdominal aortas), 11.0 (4 iliac arteries), and 12.3 ± 1.2 (11 femoral arteries). The viscous modulus was approximately 9% of E\text{dyn} in the midthoracic aorta and approximately 12% of E\text{dyn} in the abdominal and femoral arteries. Pulse wave velocities calculated from values of E\text{dyn} and relative wall thickness by the Moens-Korteweg equation agreed with accepted values. A Fourier analysis of pressure and diameter waves was shown to be unsatisfactory for determining the frequency dependence of viscoelastic constants because of anomalous behavior of the viscoelastic parameters. In the midthoracic aorta this behavior may have been partly attributable to artifact; however, there was strong evidence that elsewhere nonlinear pressure and diameter relationships interfered with the accurate determination of the relatively small, higher-order harmonic components.

ADDITIONAL KEY WORDS
relative arterial wall thickness
frequency dependence of viscoelastic parameters
Fourier analysis
dynamic stiffness of arteries
pressure and diameter waves
elastic nonlinearity

Although there have been numerous measurements of arterial elasticity under static conditions, and its importance in the physiology of the arterial system is well appreciated, there have been relatively few measurements of the viscoelastic properties under dynamic conditions. A thorough study of excised arterial specimens was made by Bergel, under both static (1) and dynamic (2) conditions, but, largely because of technical difficulties, only a few reports are available of the viscoelastic properties in vivo. Patel et al. (3) and Peterson et al. (4) have made such measurements, which, when compared with those of Bergel, suggest that living vessels have stiffer walls than excised vessels.

When the viscoelastic properties are expressed as a dynamic elastic modulus, it has been found that the phase angle of this complex quantity lies in the range 3° to 11° (2, 5). In the measurements by Peterson et al. (4), the precision of their method for determining this angle was stated to be ±6°, which is rather too large for accurate studies of the viscoelastic properties, but the recent device of Gow (6) has a precision of better than ±1°, and it is therefore hoped that the present results will represent a useful improvement.

Bergel (2) determined the frequency dependence of the dynamic elastic constant of excised arterial specimens by subjecting them to sinusoidal dilation and measuring the resulting pressure and diameter oscillations, from the amplitude and phase relations between...
these two, the viscoelastic constants of the wall were calculated. Fourier analysis has found wide application in studies of arterial pressure and flow (7, 8), and this technique has been employed in the present problem. We have measured the amplitude and phase relations between the corresponding harmonic components of simultaneously recorded pulsatile pressure and diameter waves in the living animal. As will be shown, however, certain difficulties arose because of the nonlinear elastic properties of the arterial wall, and one of the aims of this paper is to examine the effects of these nonlinearities, and to assess the degree to which they limit the use of harmonic analysis for the measurement of dynamic elastic properties in vivo. With these limitations in mind, however, it has proved possible to make useful measurements of the dynamic elastic constants of the arterial wall at frequencies in the range 1.0 to 2.8 cps at a number of locations in the arterial system of the dog.

Methods

EXPERIMENTAL PREPARATION

Mongrel dogs and greyhounds (approximately 2 to 4 years old) weighing 12.5 to 31 kg (mean 22 kg) were used in this study. Only the mongrels were premedicated with morphine sulfate, 0.7 to 1.4 mg/kg; the greyhounds because of their particularly placid disposition did not require premedication. All dogs were anesthetized with pentobarbital sodium, 20 to 35 mg/kg iv. They were ventilated with a respiratory pump (8 to 12 liters/min) except during brief periods of recording. Pulsatile pressure was measured through a 0.6 mm i.d. nylon catheter 20 to 30 cm long by a Sanborn P267B transducer. Recordings from the thoracic aorta were made by direct puncture of the wall with a 1-cm length of a no. 22 hypodermic needle attached to approximately 20 cm of nylon tubing. Recordings in the abdominal aorta, femoral, iliac, and carotid arteries were made using a catheter with a side hole near the tip. The catheter completely filled the saphenous artery, so recordings were made through an end hole, which was placed immediately distal to the location of the caliper. In all experiments the manometer and attached caliper had a resonant frequency above 75 cps and this was invariably underdamped. The frequency response of the system was determined by the pressure-step or "pop" technique, appropriate corrections being applied during the computations.

Pulsatile diameter changes were recorded using the low-friction calipers previously described (6). These have a frequency response flat to within 5% through 20 cps, without measurable phase lag. The calipers were sewn to the adventitia of the vessel with fine silk on anatraumatic needle. Spasm was occasionally seen in the smaller muscular arteries as a result of manipulation; however, recordings were not made until spasm had disappeared.

Signals from the manometer and caliper were recorded on magnetic tape at 30 inches/sec, and transferred by slow-speed replay to punched paper tape (9). Fourier analyses were carried out on an English Electric KDF9 digital computer. From these analyses, values of the pressure-diameter modulus ratios were obtained for each of 10 harmonics. The difference in phase ($\phi$) between corresponding pressure and diameter harmonics was also computed.

ANALYSES AND COMPUTATIONS

In order that the elastic modulus found in these experiments could be compared with those reported in the literature, they were expressed as pressure-strain moduli ($E_p$), in dynes cm$^{-2}$ x 10$^6$.

$E_p$ is defined to be

$$E_p = \frac{\Delta P}{\Delta D/D_0} \tag{1}$$

where $\Delta P$ and $\Delta D$ are the pressure and diameter changes and $D_0$, the mean outside diameter, respectively. In this study, the analogous quantities, $P$ and $D$, were used, and are the modulus of pressure and diameter for the first harmonic component of the pulse wave.

For purposes of this comparison, the values of the dynamic incremental elastic modulus ($E_{inc}$) given by Bergel (1, 2) were converted to $E_p$ values, using the following relationship:

$$E_{inc} = 1.5E_p (1 - \gamma)^2/[1 - (1 - \gamma)^2], \tag{2}$$

where $\gamma = h/R_0$; $h$ = wall thickness and $R_0$ = external radius; Poisson's ratio for the wall material has been taken to be 0.5. The wall thickness was measured using Archimedes' principle to determine the volume of an excised segment of artery. With this and the value of $E_p$ the elastic modulus $E_{inc}$ was calculated using equation 2.

Knowing the modulus ($E_{inc}$) and the phase ($\phi$) of the complex elastic modulus, the dynamic elastic modulus ($E_{dyn}$) and the viscous modulus ($\zeta$) could also be calculated. Thus, where $\omega$ is the angular frequency, we have:

$$E_{dy} = E_{inc} \cos \phi \tag{3}$$

Correlation Research, Vol. XXIII, July 1968
ARTERIAL VISCOELASTICITY IN VIVO

FIGURE 1
Upper panel: Oscilloscope plot of pressure (y-axis) against diameter (x-axis) for midthoracic aorta, mean blood pressure = 94 mm Hg. Center panel: Oscilloscope plot of pressure (y-axis) against diameter (x-axis) for a femoral artery, mean blood pressure = 120 mm Hg. Lower panel: during vagal stimulation.

Where \( \phi \) is small, \( E_{\text{dyn}} \approx E_{\text{dyn}}^\infty \), the pressure-diameter modulus ratio, \( |P|/|D| \), and the phase lag of the diameter behind the corresponding pressure harmonic (\( \phi \)) can be considered to be parameters of elasticity and viscosity respectively. Hence in this paper, particular attention will be paid to their behavior as a function of frequency.

\[ \eta \omega = E_{\text{dyn}}^\infty \sin \phi. \]  

(4)

Results
The similarity of diameter contour to that of pressure can be readily seen in records previously published (6). However, the diameter...
wave was more rounded at its systolic peak than was the pressure wave. Plots of pressure against diameter on the oscilloscope demonstrated a stable hysteresis loop under conditions of steady heart rate, and in the more peripheral arteries, a small but definite curvature of this loop, convex toward the diameter axis. Loops formed by waves from the thoracic aorta were usually more complex in shape, owing to the presence of greater amounts of higher frequency components; the overall curvature was much less. A plot of a thoracic pressure against diameter can be seen in the upper panel of Figure 1. Although there is no marked curvature of the relationship, there are a number of excursions of the trace lying outside the bounds of the major loop. Such behavior could be interpreted either as a nonlinear pressure-diameter relationship or as the result of artefact. The nonlinear relationship between pressure and diameter waves in the femoral artery is shown in the center panel of the same figure. In the lower panel the nonlinearity is very marked, being obtained over a larger range of pressures.

FOURIER ANALYSIS OF PRESSURE AND DIAMETER WAVES

The frequency dependence of the pressure-diameter modulus ratios is shown in Figure 2 for peripheral arteries (five femoral and one saphenous) and in Figure 3 for the mid-thoracic aorta (five). In all cases the ratio at each harmonic has been normalized by dividing by the value found for the first harmonic.

The results in Figure 2 were obtained from a total of 95 waves, where the fundamental frequencies lay in the range 1 to 2 cycles/sec.
The modulus ratio rose for the first two or three harmonics, but thereafter there was no consistent behavior. The initial increase was generally greater than that found by Bergel (2) or Learoyd and Taylor (5). On the other hand, the modulus ratio for the thoracic aorta (Fig. 3) did not show any consistent rise over the first few harmonics, or indeed any consistent behavior from animal to animal.

The behavior of the phase angle (\( \phi \)) between corresponding harmonics of pressure and diameter in peripheral arteries is shown in Figure 4. For the first two or three harmonics, diameter usually lagged pressure by a small angle (0.1 to 0.2 radians, about 6° to 12°). However, at the higher harmonics the phase angle tended to become smaller and even to change sign so that it indicated diameter leading pressure. In the thoracic aorta (Fig. 5) this unexpected behavior of the phase angle tended to occur at harmonics of relatively lower order than in the peripheral vessels.

**OBSERVATIONS ON NONLINEAR PRESSURE/DIAMETER RELATIONSHIPS**

Because the peculiar behavior of the phase angle \( \phi \) might have been the result of a nonlinear pressure/diameter relationship, calculations were made to examine this possibility. Typical pressure records from the thoracic aorta and the femoral artery (Fig. 6, upper insets) were used to generate artificial diameter waves, by projecting them onto a set of curves having increasing degrees of nonlinearity (Fig. 6, central inset). The waves were then analyzed in the usual way and the modulus and phase relationships determined for ten harmonics.

It is obvious that if the relationship is linear (line A), the modulus ratio will be unity for all harmonics and the phase angle zero. In Figure 6, the normalized modulus ratios and phase differences are shown for four increasing degrees of nonlinearity (B-E). Because of their different harmonic composition, one would not expect identical behavior for the two waveforms; however, the general outcome is clear, and the greater the nonlinearity, the greater the effect on both modulus ratio and phase angle. It is significant that the smallest amount of nonlinearity (curve B), which probably would escape detection if present in a pressure-diameter plot on the oscilloscope face, nonetheless produces quite marked harmonic distortion. There is an increasing phase lag at the fundamental harmonic of both femoral and thoracic waves, while the phase angle of the second harmonic of the femoral wave is relatively little changed. In both, however, the phase angle becomes positive for the higher harmonics, and indeed this is apparent for the second harmonic in the thoracic wave, while it does not become marked until the fourth harmonic of the femoral wave.

**MEASUREMENTS OF VISCOELASTIC CONSTANTS**

To allow comparison of our results with
Effects of nonlinear distortion of pressure wave on $|P|/|D|$ and $\phi$ for the first 10 harmonics. Upper insets show pressure waveforms used, and the relationship between the degree of nonlinearity and the amplitude of the wave. Central inset shows enlarged view of distorting curves.

Those of other studies (2-4), $E_p$, values of $E_p$ calculated using the first harmonics of pressure and diameter, have been plotted on a logarithmic scale against mean blood pressure and the site of measurement (Fig. 7). Pressure and diameter waves were recorded at various sites in the arterial trees of 29 dogs; in all, 682 pairs of waves were analyzed, where between 8 and 25 values of $|P|/|D|$ were computed for each site and used to determine the 57 mean values presented in Figure 7. Fundamental frequencies lay between 0.96 and 3.17 cps, with a mean of 2.2 cps. The mean values for $E_p$ were 0.67, 1.77, 2.78, 3.41, 2.10, and 8.80.

1 The results obtained by Peterson et al. (4) for dogs 4 and 7, a puppy and a very old dog, have been excluded from this and later comparisons.
for 21 thoracic aortas, 8 abdominal aortas, 4 iliac, 21 femoral, 1 carotid, and 2 saphenous arteries, respectively.

**Determination of the Lag of Diameter Behind Pressure**

The phase angles ($\phi$) for the first and second harmonics of waves recorded from various sites in 25 dogs have been plotted against frequency in Figure 8; between 8 and 25 pressure and diameter waves were analyzed to give a mean $\phi$ at any given site. The broken lines represent the range of Bergel's measurements of $\phi$ at 2 cps (2). The upper line is the mean of his combined abdominal and thoracic aorta results, +2 sd, and the lower is the mean of his results for femoral and carotid arteries, −2 sd. With few exceptions the phase angles found in this study lie within these limits.

**Dynamic Elastic and Viscous Moduli**

When measurements of relative wall thickness ($\gamma$) have been made, the dynamic incremental elastic modulus and viscous modulus were calculated using the first harmonics of pressure and diameter. These have been listed in Table 1 with other relevant data. The range of blood pressure over which these determinations were made was 87 to 130 (mean 109) mm Hg and the frequency range was 0.96 to 2.80 (mean 1.87) cps. These viscoelastic constants can therefore readily be compared with Bergel's (2) results for
TABLE 1
Viscoelastic Constants (\(E_{max}\) and \(\nu\)) of the Arterial Wall of Living Dogs

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<tr>
<th>Dog</th>
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Thoracic Aorta

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**Notes:**
- \(D_o\) = mean outside diameter of artery
- \(\nu\) = relative wall thickness
- BP = mean distending blood pressure
- \(c\) = calculated wave velocity

*See text.*

Circulation Research, Vol. XXII, July 1968
Excised vessels obtained at a mean pressure of 100 mm Hg and at a frequency of 2 cps.

In the thoracic aortas of two dogs (6 and 22) an anomalous value of $\phi$ was obtained, indicating that diameter was leading pressure in phase. This precluded the calculation of $\mu$, but as $\phi$ was small (approx. $-0.1$ radians) it was unlikely to have markedly influenced the measurement of $E_{\text{dyn}}$; hence the other information from these dogs has been included. Since the value of $E_{\text{dyn}}$ for the femoral artery of dog S was grossly outside the range of the other measurements for this site, it was not included in the calculation of the mean.

**CALCULATED WAVE VELOCITIES**

Wave velocities calculated using $E_{\text{dyn}}$ values have been listed in Table 1. These velocities agree well with those previously established by other workers who have made direct measurements and thus lend some support to the validity of the elastic constants.

**Discussion**

It has, unfortunately, proved to be impossible to use all the harmonic components of the naturally occurring pressure and diameter waveforms to provide information on the viscoelastic constants over a wide range of frequencies. This is because the modulus ratio and the phase angle between pressure and diameter showed anomalous behavior at the higher frequencies (Figs. 2 to 5); this behavior is considered to be principally due to the nonlinear elastic properties of the arterial wall. Nonlinear distortion of pressure...
waves showed that for these species of waveforms the lower harmonic components were relatively less affected by the presence of non-linearity than were the higher ones. Considering the relative magnitudes of the harmonics of these waveforms, we might expect that the high frequency terms arising from distortion of the large, lower-order components would be sufficient to interfere seriously with the determination of pressure-diameter relationships between the small, higher-order components.

While nonlinearity was a consistent feature in the abdominal aorta and the more peripheral arteries, it was often less marked in the descending thoracic aorta. Hence, some additional explanation is necessary to account for the anomalous behavior of $|P|/|D|$ and $\phi$ at this site. One possible cause is the longitudinal stretch of the aortic wall, which accompanies systolic ejection of blood from the heart, and consequent alteration in stiffness. Patel and Fry (10) have offered a somewhat similar explanation for anomalous results in their experiments. It is also clear from the observations of Barnett et al. (11), as well as from our own, that pressure-diameter relationships in the descending thoracic aorta can be particularly complex. Barnett et al. have shown that small changes in the position of the catheter tip in the thoracic aorta brought about large alterations in the shape of oscilloscope displays of pressure and diameter; under some circumstances they observed that diameter led pressure.

The anomalous behavior of $\phi$, especially, has prevented the complete determination of the frequency behavior of viscoelastic constants within the physiological range. In retrospect one can see that the problem also resides in the smallness of the oscillations of pressure and diameter which correspond to the higher harmonic components. It is now clear that if one intends to study the frequency behavior of the arterial wall at, say, 10 cps, then it is necessary to inject into the circulation artificial oscillations at this frequency. This is at present being investigated.

**MEASUREMENTS OF VISCOELASTIC CONSTANTS**

It is well recognized that the arterial wall is anisotropic and frequency dependent, and has elastic properties dependent on the mean distending pressure and its site in the arterial tree. Hence, there is no single set of viscoelastic constants ($E_{dn}$, $\eta_0$) which expresses its properties. Notwithstanding, a set of viscoelastic constants calculated for a given artery at the frequency of the heart beat at rest and at normal mean blood pressure is useful. The incremental dynamic elastic modulus ($E_{dn}$) is considered to be the best single measurement of wall stiffness, since, unlike the $E_p$ elastic modulus, it takes account of wall thickness, tethering, and Poisson's ratio. However, it is clear from the work of others (1, 4), as well as from our own findings, that the relative wall thickness ratio, $\gamma$, is extremely variable and is also difficult to determine accurately. Hence, although $E_p$ has its limitations, it is still a useful quantity by which we may compare the values obtained here with those of other workers who have used it.

**RELATIVE WALL THICKNESS AND ITS INFLUENCE ON THE CALCULATED VALUES OF $E_{dn}$**

A comparison of the values of relative wall thickness obtained by different investigators reveals large differences, some of which may be due to technique and some possibly due to the various ages, sizes, and breeds of the dogs used. The mean values are, in ascending order: 0.11, Bergel (11); 0.13, this study; 0.15, Peterson et al. (4); 0.15, Hurthle (12); 0.16, McDonald (7). Whereas $\gamma$ was determined indirectly by Bergel (1) and by us, it was measured directly by Peterson et al. (4). Clearly there is a need for a detailed study of relative wall thickness measurement.

The marked influence of variations in $\gamma$ on the calculated $E_{dn}$ value can readily be demonstrated in the femoral artery, for example, using the mean $\gamma$ reported by Bergel (0.115) and that calculated from the data of Peterson et al. (0.199). Substitution of these values into equation 2, assuming all other things to be equal, yields $E_{dn}$ values of 5.41 $\times E_p$ and 2.68 $\times E_p$, respectively, a difference of approximately 100%. As some of the differ-
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ence in the two $y$ values is likely to be the consequence of the technique used, there is some advantage in making comparisons using $E_p$.

ELASTICITY OF THE ARTERIAL WALL

One might conclude from the results of Patel et al. (3) and of Bergel (2) that the arterial wall is less distensible in vivo than following its excision. Even though higher mean distending pressures were recorded in the former study, Bergel (13) did not believe that this fact would explain the discrepancy. However, there is the possibility that such differences in findings could be related to size, age, and breed of dog.

At all sites (Fig. 7) the mean elastic modulus ($E_p$) is lower than that previously reported by Patel et al. Their result for the iliac artery is particularly high, and if substituted into the Moens-Korteweg equation, $c = (E_p \cdot g/2p)^{1/2}$, yields a pulse wave velocity of 21 m/sec, which is about twice that observed by direct measurements.

There are too few data of Peterson et al. (4) to make satisfactory comparisons at most sites. Their mean result for $E_p$ for the femoral artery was higher than that calculated from Bergel's data but similar to that found here. However, because of higher values of $\gamma$, the mean $E_{iy}$ for the femoral artery calculated from their data was lower than either Bergel's or ours.

Comparing Bergel's results with those of this investigation, one finds that there is good agreement for the abdominal aorta and femoral artery. Our results for the descending thoracic aorta are lower than his principally because of differences in the $y$ values of the two studies.

ARTERIAL WALL VISCOSITY

For purposes of comparison, we may use the fact that the viscous modulus $\eta$ is approximately the product of $E_{iy}$ and $\phi$ (where $\phi$ is small). Since the values of $\phi$ (Fig. 8) are similar in magnitude to those of Bergel (2), no better agreement of his $\eta$ values and those presented here can exist than has already been shown for the corresponding $E_{iy}$ values. Furthermore, an increased scatter of $\eta$ occurs because $\phi$ is also variable. Despite this scatter there is, for the mid-thoracic aorta, general agreement with the findings of Bergel that $\eta$ is approximately 8% of $E_{iy}$. This ratio is approximately 12% in the abdominal and femoral artery because of slightly higher values of $\phi$ at this site and agrees favorably with the results of Bergel.

The ratio of spring to dashpot constant ($E/R$) of Peterson et al. (4) is of interest in this context, since it is analogous to the ratio $E_{iy}/\eta$ obtained here. The mean values for $E_{iy}/\eta$ (in sec$^{-1}$) were as follows: Thoracic aorta, 145; abdominal aorta, 113; iliac artery, 67; and femoral artery, 57. These are higher than the $E/R$ ratios of Peterson et al. If one assumes comparable heart rates in the two investigations then their values for wall viscosity will be higher than ours, as will also their values of $\phi$ computed as $\tan^{-1}(\omega R/E)$. Bergel (2) and Learoyd and Taylor (5) have observed relatively small changes in $\phi$ with frequency, hence demonstrating the marked frequency dependence of $\eta$. Values of wall viscosity should always be accompanied by information about the frequency or range of frequencies over which they were determined; the use of single L-R-C model, such as was employed in the analog computation of Peterson et al., is thus obviously of limited value.

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