Compressibility of the Arterial Wall

By Thomas E. Carew, M.S.E., Ramesh N. Vaishnav, Ph.D.,
and Dali J. Patel, M.D., Ph.D.

ABSTRACT

The assumption of incompressibility has often been applied to the analysis of arterial-wall elasticity; however, the supporting evidence has been incomplete. The present study was designed to explore this problem in greater depth by accurately measuring the changes in tissue volume associated with large, induced strains on 11 thoracic aorta segments excised from dogs. The radial, circumferential, and longitudinal stresses were measured as the artery was subjected to an internal pressure and longitudinal stretch greater than those in vivo. From these data it was possible to calculate the hydrostatic stress. The associated changes in volume of the aortic wall tissue were measured with a specially designed apparatus. The greatest volumetric strain ($\Delta V/V$) was 0.00165. The bulk moduli obtained by dividing the hydrostatic stresses by the corresponding volume strains averaged $4.44 \times 10^8$ g/cm$^2$. Similar studies were also carried out on the abdominal aorta and the carotid, iliac, and pulmonary arteries. The volumetric strains observed were of the same magnitude. It is concluded that for most practical purposes arteries may be considered incompressible.

ADDITIONAL KEY WORDS hydrostatic stress hydrostatic strain deviator stress deviator strain bulk modulus shear modulus volumetric strain

The material properties of the arterial wall have been intensively studied for a number of years (1-6). In investigating these properties many workers have made the assumption that the arterial wall behaves as an incompressible material (1, 3, 5, 7). This assumption considerably simplifies both the experimental and analytical approaches to the problem. The experimental approach is simplified because the wall thicknesses may be calculated for various lengths and diameters from a single measurement of the volume of the segment and the analytical approach because fewer material constants (or functions) are necessary to characterize an incompressible material.

Although the assumption of incompressibility has often been made, the experimental evidence for it is both conflicting and non-definitive. In support of this assumption, Lawton (2) found that excised aortic strips were isovolumic under varying degrees of stretch. Similarly, Dobrin and Rovick (8) found that canine carotid arteries were incompressible when subjected to internal pressurization at a fixed length. Neither of the two investigations presents any details of the nature and level of the stresses and strains involved. On the other hand, Tickner and Sacks (9) reported changes in volume as much as 20 to 40% in walls of excised arteries inflated with air from 0 to 326 cm H$_2$O. Their x-ray technique for measuring wall thickness coupled with the possibility of dehydration due to the air inflation makes their findings questionable.

To carry out meaningful experiments and to interpret the results properly, it is necessary...
to understand the nature of the assumption of incompressibility. A perfectly incompressible material undergoes no strain (i.e., no relative change in distance between material particles) under a hydrostatic state of stress. 1

Thus all the strain of a deformed incompressible body results from the nonhydrostatic (deviatoric) part of the stress. 2 Conversely, it is clear that knowledge of the strain in an incompressible body can be used to determine only the nonhydrostatic part of the stress. The hydrostatic part of the stress remains undetermined and some additional knowledge, such as boundary values of stress, is required to determine the stress fully. From the molecular viewpoint, all real materials must exhibit some degree of compressibility. However, since materials have the property of compressibility to varying degrees, it is quite possible that the mechanical response of some materials may be approximated very closely by the response of an ideally incompressible material under certain circumstances. Whereas the latter is characterized by an absolute insensitivity to hydrostatic stress, a nearly incompressible material would be characterized by a relative insensitivity to hydrostatic stress in comparison with its response to a deviatoric (or deforming) stress. For such materials the assumption of incompressibility would result in a negligible error if the state of stress is not predominantly hydrostatic. Lawton (2) as well as Dobrin and Rovick (8) found small volume strains in arteries, but failed to answer the question whether the assumption of incompressibility may be used in connection with the arterial wall because, by not showing the presence of a significant amount of hydrostatic stress, they did not establish whether their results were of general validity. In other words, it is possible to have a deformation of a compressible body with little or no change in volume simply because of the absence of hydrostatic stress. Thus, the application of the assumption of incompressibility hinges on whether the arterial wall undergoes volumetric strains that are negligible with respect to other strains in response to states of stress wherein the hydrostatic part is not small.

In practice the relative insensitivity in response to hydrostatic stress can best be measured by a high value (relative to unity) of the ratio of the bulk modulus to the shear modulus; the bulk modulus (k) being the ratio of hydrostatic stress to the volumetric strain and the shear modulus (G) being the ratio of deviatoric stress to deviatoric strain. 4

In passing it may be pointed out that a knowledge of the value of the bulk modulus alone is insufficient to determine the validity of the assumption of incompressibility. For example, even though water is considered to be incompressible in its flow behavior, its bulk modulus (2.18 × 10 10 dynes/cm 2) is lower than that of steel (12.8 × 10 11 dynes/cm 2) which is considered a compressible material in structural applications. The reason is that the shear modulus of water is approximately zero but that of steel is 8.11 × 10 11 dynes/cm 2. Hence, although water has a very large value of k/G, steel has a value of k/G of approximately 1.5.

The following is a study which attempts, in the light of the above rationale, to determine the reliability of the assumption of incompressibility for the canine thoracic aorta over the range of stress states of physiologic interest. In addition, certain semiquantitative results concerning the compressibility of other canine arterial segments are discussed.

Method and Results

Seventeen mongrel dogs ranging in weight from 27.7 to 34.3 kg were anesthetized with

---

1 A hydrostatic state of stress implies that the stress (force/unit area) inside a body is equal in all directions. In linear elasticity, the hydrostatic portion of any stress state is uniquely related to the volume change that the body undergoes.

2 A general state of stress may be divided into a hydrostatic part and a deviatoric part. The deviatoric part is responsible for the change in shape of the body. For a more complete description see, for example, reference 6, p. 50.

4 Change in volume divided by initial volume.

*That strain that is not volumetric; it is a measure of the relative change in shape of an element of a body.
COMPRESSIBILITY OF THE ARTERIAL WALL

63

Dimensions of the Arterial Segments

<table>
<thead>
<tr>
<th>Segment</th>
<th>No. of segments</th>
<th>Drug weight (mg/kg)</th>
<th>Mean arterial pressure (cm H2O)</th>
<th>Length (cm)</th>
<th>Radius (cm)</th>
<th>Wall volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UDTA 5</td>
<td>32 ± 0.7</td>
<td>151 ± 6.8</td>
<td>7.5 ± 0.0</td>
<td>5.8 ± 0.08</td>
<td>0.48 ± 0.01</td>
<td>2.03 ± 0.18</td>
</tr>
<tr>
<td>LDTA 6</td>
<td>30.4 ± 0.8</td>
<td>171 ± 11.3</td>
<td>7.4 ± 0.14</td>
<td>5.7 ± 0.1</td>
<td>0.44 ± 0.01</td>
<td>2.17 ± 0.070</td>
</tr>
<tr>
<td>AbA 5</td>
<td>29.6 ± 1.1</td>
<td>171 ± 8.7</td>
<td>6.3 ± 0.2</td>
<td>4.6 ± 0.2</td>
<td>0.34 ± 0.015</td>
<td>1.545 ± 0.000</td>
</tr>
<tr>
<td>IA 5</td>
<td>29.8 ± 1.2</td>
<td>173 ± 9.0</td>
<td>5.1 ± 0.2</td>
<td>3.7 ± 0.2</td>
<td>0.24 ± 0.01</td>
<td>0.469 ± 0.033</td>
</tr>
<tr>
<td>CA 5</td>
<td>29.8 ± 1.1</td>
<td>133 ± 16.0</td>
<td>7.2 ± 0.12</td>
<td>5.0 ± 0.2</td>
<td>0.17 ± 0.005</td>
<td>0.450 ± 0.039</td>
</tr>
<tr>
<td>PA 5</td>
<td>30.0 ± 1.0</td>
<td>164 ± 3.0</td>
<td>7.6 ± 0.3</td>
<td>3.8 ± 0.7</td>
<td></td>
<td>2.364 ± 0.227</td>
</tr>
</tbody>
</table>

UDTA = upper descending thoracic aorta; LDTA = lower descending thoracic aorta; AbA = lower abdominal aorta; PA = pulmonary artery; IA = external iliac artery; CA = common carotid artery. Average values ± SEM are given.

To calculate the bulk modulus, the hydrostatic stress must first be calculated. This requires the measurement of the three orthogonal stresses listed above. These were obtained in the following manner. Two cylindrical plugs, 3 inch long and selected to approximate the in vivo diameter of the segment, were inserted into either end of the excised arterial segment and secured by two ligatures. The artery was then fixed between the legs of a force gauge at a length from 3 to 10% greater than the in vivo length, and inflated with pressures greater than those in vivo (range 220 to 275 cm H2O). At this time measurements of pressure, outer diameter, and the longitudinal force necessary to maintain the segment at that length were obtained.

To calculate the various stresses from these measurements, the membrane stress approximations were made. The formulas for calculating the stresses are:

\[ T_r = -P/2 \] (radial stress),

\[ T_L = -P \] (longitudinal stress),

\[ T_c = 0 \] (circumferential stress),

where \( T_r \) is the hydrostatic stress, \( \Delta V \) is the change in tissue volume. The hydrostatic stress is the average normal stress (i.e. stress perpendicular to the surface) on an element of a body, and is equal to one-third of the sum of the radial, circumferential, and longitudinal stresses.

Circulation Research, Vol. XXIII, July 1968
Diagram of experimental set-up. P.T. = pressure transducer. During an experiment the capillary tube shown at the top of the figure was directed horizontally so that changes in fluid level in the tube would not change the static pressure level. Note from the directional arrows that the end of the artery moves to the right without twisting as the crank is advanced.

\[ T_r = \frac{PR}{H}, \]  
(3) \[ T_z = \frac{(F + P_0 R^2) + 2 \pi RH}{2 \pi R H}, \]  
(4) \[ T_h = -\frac{2}{3} (T_r + T_z + T_h), \]  
(5)

where \( P \) is the internal pressure, \( F \) is the force registered on the force gauge, \( R \) is the radius of the middle surface of the cylindrical segment, and \( H \) is the wall thickness. Since the radial stress varies from \(-P\) at the inner surface to zero at the outer surface of the artery, the stress on the middle surface of the segment in the radial direction was approximated as \(-P/2\). Equations 3 and 4 follow from simple equilibrium considerations (4, 10).

The second factor involved in computing the bulk modulus (see equation 1) is the volumetric strain \( \Delta V/V_0 \). The change in wall volume, \( \Delta V \), was measured with the artery mounted in a sealed glass flask which had a capillary-tube side arm as shown in Figure 3. The flask was designed to allow a variable longitudinal extension and a variable internal pressurization to be imposed on the segment. The flask and side arm were carefully filled with normal saline which had been heated prior to filling to minimize air bubbles. The segment was extended longitudinally and pressurized internally to the same degree as that obtained while the segment was mounted in the force gauge; the artery was completely filled with saline. Then the high-pressure intraluminal fluid was allowed to equilibrate with the extraluminal fluid in the flask which was at atmospheric pressure. Concomitantly, the length of the segment was reduced to the excised length. Assuming for the moment that saline is incompressible, it can be seen that the change in wall volume of the arterial segment when going from a state of high hydrostatic stress to zero hydrostatic stress will be reflected as a change in height of the fluid column in the side arm. The resultant volume change, \( \Delta V \), was then divided by the previously obtained value of the unstretched volume to obtain the volumetric strain.

Table 2 lists the results of these studies on 11 segments of thoracic aorta. Note that the average value of the volumetric strain, \( \Delta V/V_0 \), was 0.059 ± 0.013%, the hydrostatic stress, \( T_h \), was 1798 ± 109 g/cm², and the bulk modulus, \( k \), was 4.44 ± 0.92 × 10⁶ g/cm².

In contrast to the segments of thoracic aorta that were studied in detail, semiquantitative results were obtained for the other arterial sites. Using the method described...
Results from the Descending Thoracic Aorta

<table>
<thead>
<tr>
<th></th>
<th>( \Delta L/L_o ) (%)</th>
<th>( \Delta R/R_o ) (%)</th>
<th>( P ) (cm H-O)</th>
<th>( T_r ) (g/cm²)</th>
<th>( T_c ) (g/cm²)</th>
<th>( T_l ) (g/cm²)</th>
<th>( \Delta V/V_o ) (%)</th>
<th>( k ) (g/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper descending thoracic aorta</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>77</td>
<td>334</td>
<td>-117</td>
<td>2643</td>
<td>1335</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>41</td>
<td>77</td>
<td>334</td>
<td>-117</td>
<td>2634</td>
<td>1326</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>46</td>
<td>65</td>
<td>242</td>
<td>-121</td>
<td>2412</td>
<td>1537</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>37</td>
<td>74</td>
<td>256</td>
<td>-128</td>
<td>2566</td>
<td>1596</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>Lower descending thoracic aorta</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>52</td>
<td>258</td>
<td>-114</td>
<td>3455</td>
<td>2274</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>35</td>
<td>70</td>
<td>246</td>
<td>-123</td>
<td>2741</td>
<td>1710</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>40</td>
<td>75</td>
<td>268</td>
<td>-124</td>
<td>3435</td>
<td>2096</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>42</td>
<td>77</td>
<td>244</td>
<td>-122</td>
<td>3086</td>
<td>2333</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>37</td>
<td>55</td>
<td>254</td>
<td>-127</td>
<td>2714</td>
<td>2012</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
<tr>
<td>40</td>
<td>75</td>
<td>248</td>
<td>-124</td>
<td>2894</td>
<td>1909</td>
<td>1004</td>
<td>0.0587</td>
<td>7.05 ± 10²</td>
</tr>
</tbody>
</table>

**Average values ± SEM** are given for all 11 segments. \( P \) = intraluminal pressure; \( T_r \) = radial stress; \( T_c \) = circumferential stress; \( T_l \) = longitudinal stress; \( Th \) = hydrostatic stress; \( \Delta V/V_o \) = volumetric strain of the wall material; and \( k \) = the bulk modulus. The values of the longitudinal strain, \( \Delta L/L_o \), and circumferential strain, \( \Delta R/R_o \), are included for purposes of comparison.
above, changes in volume were measured in five segments of each artery as the segments were subjected to a longitudinal stretch of 47 ± 3.4%. The volumetric strains observed were 0.02% for the pulmonary artery, 0.07% for the common carotid artery, 0.06% for the iliac artery, and 0.05% for the lower abdominal aorta. In each type of systemic artery one or more segments were also subjected to an internal pressure of approximately 250 cm H₂O and the same longitudinal stretch as before; in this case volumetric strains of the wall were slightly larger, averaging 0.14 ± 0.03%. Similarly, three specimens of pulmonary artery were inflated to a pressure of 40 cm H₂O and extended longitudinally 40%; the volumetric strain was less than 0.05%.

**Discussion**

**Physiologic Considerations**

There is a possibility that the method described will not record changes in wall volume if they are induced by a change in water content of the arterial wall as it is stretched. The question here is actually central to the study of the mechanics of the vascular wall. The wall consists of solid or semisolid fibrillar structures imbedded in a gelatinous matrix. There is some question whether one may treat such a multiphase system as a homogeneous substance. If significant amounts of water shift out of the wall as the wall is mechanically deformed, it would be difficult to apply, even approximately, the laws of continuum mechanics. Therefore, an attempt was made to determine roughly whether there was any phase separation of the wall material upon mechanical deformation of the segment. For this purpose, 12 descending thoracic aortas were excised from dogs after measuring the length in situ. The aortas were then cut longitudinally into two approximately equal segments. The fresh-tissue weight of both segments was obtained, and then one segment served as a control and the other was extended 66%, which was 18% in excess of the in vivo length. Both segments were then pinned to a cork board, and after a two-minute equilibration, the stretched segment and the control segment were blotted uniformly with dry gauze sponges. The segments were then reweighed, and the percent weight loss for each segment was calculated. Three repeat runs were made with each segment, each run reversing the roles of the experimental and control segments. The average weight loss of the stretched segments exceeded the average loss of the control segments by 0.13%. The test for significance gave a value of $P = 0.35$.

It should be noted that there probably was a small degree of systematic error in favor of obtaining larger losses in the stretched specimens, because there was a greater surface area-to-volume ratio and hence a greater potential loss due to evaporation. In addition, the stretched specimen presented a larger and more uniform surface to be blotted, which again raises the likelihood of a systematic error in favor of the stretched segments. In view of the above, it would seem unlikely that this 0.13% difference in the average values represents a significant loss of fluid from the vessel due to stretching. Certainly, this amount of fluid transfer could not account for the discrepancy between the volume changes in the present study and the large negative values of volumetric strain reported by Tickner and Sacks (9).

**Method Error**

There are two possible limitations in the accuracy of the data as a result of the method employed. The first is the degree of accuracy with which small changes in volume could be measured. It was estimated that the height of the column of fluid in the capillary side arm could be measured to an accuracy equivalent to volumetric changes of approximately ± 0.14 X 10⁻⁸ ml. This figure is approximately one-tenth of the average change in volume observed. A second factor concerns artifactual changes in volume due to "leaks" (i.e., evaporation losses around the large glass flange and other fittings in the system, decompression of the intraluminal saline, and the compliance of the manometer and connecting tubings). The magnitude of the observed leak for the duration of an
COMPRESSIBILITY OF THE ARTERIAL WALL

experiment averaged about 10 to 15% of the total volume change. The error here is an additive one, i.e., the volume changes were overestimated by the amount of the leak. The volume change due to decompression of the intraluminal fluid and the compliance of the membrane of the pressure transducer were calculated and found to be within the range of error in reading volume changes (<0.1 µ liter).

VALIDITY OF THE INCOMPRESSIBILITY ASSUMPTION

In the case of small deformations of an isotropic, elastic body, the hydrostatic stress is linearly related to the volumetric strain and likewise the deviator stress to the deviator strain, the constants of proportionality in the two cases being the bulk modulus, k, and the shear modulus, G, respectively. The former is related to the Young modulus E and the Poisson ratio σ by the relation \( k = \frac{E}{3(1-2\sigma)} \), and the latter through the relation \( G = \frac{E}{2(1+\sigma)} \). As discussed in the introduction, an ideally incompressible material, by definition, is one which suffers no volumetric strain under any state of stress. Such a material is characterized by an infinite value of bulk modulus or, equivalently, a value of one-half for the Poisson ratio. In situations such as in a blood vessel under physiologic loading where the hydrostatic and deviatoric components of stress are comparable in magnitude (see below), a large value of the ratio \( k/G \) (\( k/G > 1 \)) indicates that the material is relatively incompressible, and theories based on the assumption of incompressibility may be expected to give valid results. The results of such theories, however, should not be extrapolated to cases in which the hydrostatic stress predominates, as even for high \( k/G \) ratios, significant volumetric strains can exist. It should be noted that in the realm of finite elastic deformation, as in arteries, the picture is not so clear-cut. Even in the second order theory of elasticity, there are additional squared terms which arise in the equation relating hydrostatic stress to deformation (11). However, in a qualitative sense, it is still possible to use the type of rationale developed in the small deformation theory to see if the assumption of incompressibility is valid for a given state of stress.

Let us examine a blood vessel to assess the validity of the assumption of incompressibility. Typically, values of the principal stresses at a mean pressure of 140 cm H2O and at the in vivo length in the descending thoracic aorta of dogs are \( T_r = -70 \text{ g/cm}^2 \), \( T_a = 2388 \text{ g/cm}^2 \), and \( T_s = 2000 \text{ g/cm}^2 \) (Patel and Fry, unpublished observations). This yields a hydrostatic stress \( T_h = 1439 \text{ g/cm}^2 \). The magnitude of the deviator stress, given by

\[
T_d = \sqrt{(T_r - T_h)^2 + (T_a - T_h)^2 + (T_s - T_h)^2},
\]

is 1869 g/cm². Since \( T_h \) and \( T_d \) are comparable in magnitude, the ratio \( k/E \) would determine the validity of the assumption of incompressibility. In the present case, taking the value of \( k \) as about \( 4 \times 10^8 \text{ g/cm}^2 \) and a typical value of the Young modulus for the thoracic aorta as approximately \( 4.4 \times 10^3 \text{ g/cm}^2 \) on the basis of Bergel’s results (1), it is seen that \( k \) is three orders of magnitude larger than \( E \). It is this large ratio that justifies the assumption of incompressibility. Qualitatively, at least, the same result should hold true for the other arteries studied as the volumetric strains observed were quite small even under very large extensions.

A further measure of the adequacy of the assumption of incompressibility could be obtained by examining the error introduced by assuming that the Poisson ratio of such a material is equal to one-half. (This value of the Poisson ratio \( \sigma \) is valid for an incompressible isotropically elastic material undergoing small deformations.) At the same time, it is possible to determine the error incurred in assuming incompressibility in the experimental determination of the Young modulus from a situation wherein arterial segments are inflated at a constant length. From the small strain theory it can be shown that

\[
\text{Circulation Research, Vol. XXIII, July 1968}
\]
\[
\sigma = \frac{3k - E}{6k}
\]

where \( E \) is the Young modulus and \( k \) the bulk modulus \((12)\). For segments inflated at a constant length the formula for calculating the Young modulus is

\[
E = (1 - \sigma^2) \left( \frac{\Delta P}{\Delta R} \frac{2R_i R_o}{(R_o^2 - R_i^2)} \right)
\]

where \( \Delta P \) is the pressure change, \( \Delta R \) is the change in outer radius, \( R_i \) the inner radius, and \( R_o \) the outer radius \((1)\). Since Bergel's value of 4390 g/cm\(^2\) for the Young modulus \( E \) at a mean pressure of 100 mm Hg was calculated, assuming \( \sigma \) to be equal to 0.5 \((1)\), we may evaluate the expression in square brackets in equation 8 for this mean pressure. Substitution of equation 8 into equation 7 yields a quadratic equation in \( \sigma \) with known coefficients which involve only experimentally measured quantities, i.e., \( k \) and the term in square brackets from equation 8. Solving for \( \sigma \) and discarding the physically impossible root of the quadratic, one obtains \( \sigma = 0.4998 \), which represents 0.04% deviation from \( \sigma = 0.5 \). A corrected Young modulus \( E \) calculated from equation 8 using \( \sigma = 0.4998 \) differs by only 0.03% from Bergel's value.

As mentioned in the introduction, the experimental and theoretical tasks of characterizing the elastic properties of the arterial wall are enormously simplified if the assumption of incompressibility can be made. From the preceding it is concluded that under physiologic conditions such an assumption is indeed justified.

Acknowledgment

We are indebted to Dr. D. L. Fry for his help and criticisms and to Mr. Fred Plowman for his technical assistance.

References

Compressibility of the Arterial Wall
THOMAS E. CAREW, RAMESH N. VAISHNAV and DALI J. PATEL

Circ Res. 1968;23:61-68
doi: 10.1161/01.RES.23.1.61
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1968 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org//subscriptions/