"Afterload," defined as the external factors that oppose the shortening of muscle fibers, is as important a determinant of myocardial performance in the intact heart (1-3) as it is in the papillary muscle preparation (4). Many investigators are searching for an "index" of contractile state that will be independent of all external forces, but until there is more general agreement on such an index than is now the case afterload must be measured and taken into account in any evaluation of ventricular performance. An operational definition of afterload appropriate to the intact ventricle is more difficult to formulate, however, than one might at first suppose.

In an isotonic experiment on a papillary muscle, the load is simply the weight the muscle is required to lift. Weight has the same dimensions as force, and, if inertial effects are neglected, both are equal to the mass of the object suspended from the muscle multiplied by the gravitational acceleration constant. The force is exerted on a cross section of muscle, and afterload is often expressed as force per unit area or stress. In this kind of experiment, the suspended weight is directly responsible for the muscular stress, and it makes no difference which is regarded as the "load." In the intact ventricle, however, the assumption that load and stress are synonymous terms leads to confusion. Stress in the ventricular wall is related to the external constraints on ventricular ejection, but the relationship is complicated by the globular shape of the contracting chamber and by the physical properties of the artery into which it ejects blood.

The shape of the ventricle is significant because the pressure imparted to the blood by the myocardium is related to, but not the same as, tangential stress in the ventricular wall. The relationship between them would be relatively simple mathematically if the ventricle were of some regular geometric shape. For this reason, much effort has been devoted to discovering whether the ventricle can be represented adequately by a spheroidal or ellipsoidal model or by some other geometric solid whose volume can be determined by measurement of a few critical dimensions (5, 6). Attempts to calculate mural force from intraventricular pressure are made more difficult by the nonuniform thickness of the ventricular wall and the uneven distribution of forces from endocardium to epicardium (7). A completely satisfactory solution of these problems has not yet been found, but realistic models of ventricular geometry and mechanics and reliable techniques for measuring ventricular dimensions continuously in vivo (6) can now be used to estimate ventricular wall stress.

If, however, afterload means the external opposition to ventricular outflow, then wall stress itself is not an adequate measure of afterload. The nature of the opposition to muscle shortening in the ventricle is quite different from that in the isolated papillary muscle. The ventricle is not called on to lift a weight but to move a viscous fluid into a viscoelastic arterial system, and this role has several important consequences. First, the inertial and viscous elements of the system ensure that the more rapidly the ventricle tries to eject blood, the higher the pressure and wall stress. Given the force-velocity relationships that are characteristic of the myocardium (1-4), this situation creates a kind of "feedback," and, if afterload were defined as wall stress, it would be necessary to conclude that the ventricle plays a part in determining its own afterload. Second, stress varies with time during ejection, even though the physical properties of blood and the aorta are constant. Third, the pressure generated by the ventricle acts to distend the compliant aorta as well as to move blood forward, producing a phase shift between pressure and flow at the ventricular outlet. All of these factors make it difficult to translate ventricular pressure or any of the other standard hemodynamic...
variables into a quantitative description of the ventricular load. Stress unquestionably exerts a crucial influence on the contractile mechanisms by affecting sarcomere length (8) and the overlap of intracellular filaments (9), but when the ventricle is considered as a functioning unit it would be desirable to have some rigorous way of describing the external conditions (the properties of the arterial system) that contribute to the stress. The effects on the heart of changes in aortic and arterial properties have been studied in some detail, and the results illustrate the problems involved in finding a suitable way of expressing the load.

**EFFECTS OF CHANGING AFTERLOAD**

Experimental manipulations of ventricular afterload can take a number of different forms, the most common being modifications of the resistance or compliance of the arterial system. In general, an increase in peripheral resistance raises ventricular pressure and reduces ventricular outflow, and a decrease in arterial compliance has the same effects (10–15). Changes in arterial resistance or compliance produce an immediate change in ventricular performance, but under normal conditions in vivo this acute change is followed by gradual alterations of end-diastolic volume (preload) and by reflex or other responses that change the contractile state of the myocardium. Useful information can be obtained by studying both kinds of response (16, 17), but experiments must be designed so as to distinguish between them. One effective method of studying the influence of afterload per se is to change the afterload suddenly during a diastolic period and then to compare the next cardiac cycle with the one immediately preceding the intervention (10, 11). Similarity of end-diastolic and isovolumic contraction pressures in the two beats serves to confirm that they are comparable in preload and contractile state.

There is general agreement on the acute ventricular response to certain kinds of intervention. An increase in arterial resistance raises the peak ventricular and aortic pressures and decreases the peak flow and stroke volume (10, 11, 13, 15). The force-velocity curve, which expresses the relationship between ventricular stress and contractile element velocity, is displaced during ejection in the direction of higher force for a given velocity (3, 18). The effects of resistance changes on external hydraulic work, on the other hand, depend on the initial resistance. The external work performed by the ventricle is apparently maximum at normal levels of resistance and falls when resistance is either increased or decreased from this level (11, 18). Decreasing the compliance of the aorta (or its mechanical analogue) produces essentially the same effects and also increases aortic pulse pressure (12, 15).

In the one series of experiments in which demonstrably pure changes in resistance and compliance could be compared (15), a difference in mean pressure and flow responses was observed. Decreased compliance lowered both mean flow and mean pressure in the aorta, although their ratio (the resistance) was kept constant. Raising the resistance reduced mean flow but increased mean pressure. Quantitative comparison of the two kinds of change in afterload indicates that peak ventricular pressure is more sensitive to increased resistance than it is to decreased compliance. Peak flow is about equally sensitive to the two kinds of intervention, as is stroke volume (15). Decreased compliance also produces a characteristic change in the time course of pressure in the ventricle and aorta, peak pressure being displaced toward the latter third of the ejection period (11, 13, 15). Instantaneous flow amplitudes are reduced throughout ejection under these conditions, and there are small alterations in the shape of the flow pulse (15).

A considerable amount of information about the relationship between ventricular performance and afterload is thus available, but it is largely descriptive. The qualitative description of afterload in most studies is attributable in part to the lack of an accepted quantitative expression. No measure of "mean afterload" will suffice, for it would omit all information about time and frequency dependence. Mean ejection pressure, for example, which is at present the variable most widely used to represent afterload, provides no way of distinguishing between resistive and capacitive changes. The time-varying pressure and the stress in the ventricular wall can be measured, but they are results of the afterload and cannot in any useful sense be said to be equal to the afterload. What is needed is a measure of afterload that expresses all of the external factors that oppose ventricular ejection of blood. By definition, the arterial input impedance (19) meets this requirement.

**VASCULAR IMPEDANCE**

The ratio of pressure to flow in blood vessels is determined by the physical properties of blood and the vascular wall, including the viscosity and density of blood, the viscoelasticity of the wall, and the diameter of the vessel (19). The relationship is complicated, however, by the fact that it must be expressed in terms of sinusoidal waves. Normal
arterial impedance as ventricular afterload

pressure and flow pulses are not simple sinusoidal functions, of course, but for purposes of analysis they can be treated as the sum of a series of such waves superimposed on the mean pressure or flow. By appropriate mathematical techniques an experimentally recorded pressure or flow can be analyzed to identify the particular set of sinusoidal waves, or "harmonics," that is equivalent to the observed pulsation. Each harmonic is complex, in the mathematical sense, and is described by its modulus (amplitude), phase angle (timing in relation to other harmonics), and frequency. The ratio of a pressure harmonic to the flow harmonic at the same frequency is called the impedance at that frequency. (Impedance cannot be computed from the instantaneous ratio of pressure to flow in vivo [13], because the pulsations are composites of different frequencies.)

Vascular impedance is thus analogous to vascular resistance, the former expressing pulsatile and the latter "steady-flow" relationships. Resistance, however, can be expressed by a single number, while impedance must be expressed as a spectrum of moduli and phases versus frequency. The vascular impedance spectrum depends on two factors. (1) The physical properties of the artery being considered (viscoelasticity, dimensions, etc.) determine the "characteristic" impedance. (2) The reflected pressure and flow waves generated in more distal parts of the tree produce frequency-dependent oscillations of the "input" or "local" impedance around the characteristic value. Aortic and pulmonary arterial impedance have been measured in man and experimental animals (19). Both can change significantly under the influence of physiological stimuli (20, 21), pharmacologic agents (12, 19, 22), and disease (23).

The input impedance spectrum of the arterial system in the dog, calculated by frequency analysis of simultaneous measurements of pressure and flow in the ascending aorta, normally resembles that shown by the solid line in Figure 1A. Impedance moduli fall steeply from relatively high values at low frequencies to reach a minimum between 2 and 4 Hz, followed by a maximum and a variable number of additional small oscillations. Normal pressure and flow waves consistent with this impedance spectrum are shown in Figure 1B.

For comparison, the abnormal impedance spectrum that has been observed when the aorta is stiffer than usual (12, 15, 24) is also shown in Figure 1A (broken line). The abnormal stiffness increases characteristic impedance, raising all of the impedance moduli to higher levels, and at the same time increases wave velocity, moving the impedance minimum and the "zero-crossing" of the impedance phase angle to higher frequencies. The relationship between ventricular function and aortic input impedance can be illustrated by considering the changes in pulsatile pressure and flow that might come about if aortic properties were altered experimentally so that aortic input impedance shifted from the normal to the abnormal pattern in Figure 1A. The new pressure-flow harmonic ratios would of necessity be consistent with the new (abnormal) impedance spectrum, but many different wave forms could meet that requirement; ventricular function would determine the particular combination of pressure and flow pulsations that would appear. For example, each of the three pairs of pressure and flow waves in Figure 2 is consistent with the abnormal impedance spectrum. If the behavior of the ventricle were such that it continued to produce exactly the same flow pulse as that with the normal impedance, then the waves would have the form shown in Figure 2A. Alternatively, if the ventricle produced a flow of the same shape as before but of lower amplitude, the waves of Figure 2B would be observed. In most experiments, however, the ventricle adopts neither of these two theoretical options but instead alters

FIGURE 1

A: Spectra of vascular input impedance in the ascending aorta of a dog under two different conditions. Impedance moduli are shown at the top and phase angles at the bottom. A negative phase angle denotes that pressure lags behind flow. Solid line = typical impedance in a conscious dog at rest, and broken line = abnormal impedance similar to that produced by stiffening of the aortic wall, increased wave velocity, and increased reflections from the periphery (12, 19, 23).

B: Typical pulsations of pressure (top) and flow (bottom) in the canine ascending aorta. Heart rate 90/min, mean flow 40 ml/sec, mean pressure 100 mm Hg. The flow pulse was synthesized from products of flow harmonics and corresponding impedances (A, solid line).
Three different pairs of pressure and flow pulses consistent with the abnormal impedance spectrum (broken line) in Figure 1A, i.e., consistent with harmonic pressure-flow ratios implied by that spectrum. Flow pulses were chosen arbitrarily to illustrate some of the possibilities, and their first ten harmonics were then used in conjunction with the abnormal impedance spectrum to compute the pressure pulsations. The input resistance (mean pressure/mean flow) was assumed to be same as it is in Figure 1B in all cases (3,335 dyne sec/cm²). A: Flow pulsations are the same as those in Figure 1B; mean flow 40 ml/sec, mean pressure 100 mm Hg. B: Flow pulse is smaller than that in Figure 1B but of the same shape; mean flow 22 ml/sec, mean pressure 55 mm Hg. C: Flow pulse differs from that in Figure 1B in both amplitude and shape; mean flow 31 ml/sec, mean pressure 78 mm Hg.

Both the amplitude and the shape of its pressure and flow output, as in Figure 2C.

In other words, the physical properties of the aorta and the arterial system restrict left ventricular outflow and pressure pulses by determining the ratio of pressure to flow harmonics that must exist in the aortic root, and the aortic impedance spectrum expresses these ratios quantitatively. As far as the aorta is concerned, the ventricle is free to produce any pulsations that satisfy these ratio requirements, and the particular waves it chooses to generate when it is facing a given aortic impedance tells us something fundamental about ventricular function, if only we knew how to interpret it.

**Impedance as Afterload**

Since the input impedance spectrum of the ascending aorta describes the hemodynamic properties of the system into which the left ventricle ejects blood, and thus the opposition to ventricular outflow, this spectrum constitutes an appropriate definition of the external load imposed on the ventricle. Defining afterload by the impedance spectrum rather than by instantaneous pressure or ventricular wall stress has at least two advantages. First, it accounts for the changing pressures during ejection without assuming that the load is continuously changing. If arterial properties, and hence the impedance spectrum, are constant, then afterload is constant, and the changes in pressure and flow during the cardiac cycle are manifestations of interaction between ventricular function and afterload. Second, the impedance spectrum provides a quantitative description of afterload that is difficult to achieve in any other way. The difference between the normal and the stiffened aorta shown by the impedance spectra in Figure 1A, for example, cannot be described adequately by saying that stiffening "increases aortic impedance." The shift of the first minimum modulus and the impedance phase angles toward the right on the frequency scale with stiffening is as important as the increased impedance moduli. Indeed, the phase shift accounts for the prominent change in the pressure pulse, namely the delay in peak pressure (see Fig. 2). No matter what the inotropic state of the ventricle, a similar phase lag between flow and pressure peaks would be inevitable if the ventricle were working against this kind of aortic impedance.

Although many papers concerned with the influence of afterload on the heart refer to experimental changes of impedance, very few (12, 15) report actual measurements of impedance. Without such measurements, it is impossible to know just how the load imposed on the ventricle has been altered. Resistance and compliance are usually modified experimentally by mechanical devices (air chambers, rigid inserts, bypass circuits, occluders), and hemodynamic theory allows only an approximate prediction of the final arterial input impedance when such structures are in place. In addition, most experimental alterations of aortic compliance are made distal to the aortic arch for practical reasons, although the compliance of the first few centimeters of the ascending aorta is, in theory, the most critical. Measurements of input impedance under these conditions serve to define the experimental conditions exactly. They also identify the particular kind of afterload presented to the heart, because changes in resistance, compliance, and reflected waves differ to some extent in their effects on the impedance spectrum (12, 15, 19, 25). Partial occlusion of the descending thoracic aorta, for example, involves all three factors (25, and Walker and Milnor, unpublished data).

Calculations of arterial impedance also throw light on the connection between heart rate and ventricular afterload, a relationship that comes about in two different ways. First, since impedance is frequency dependent, the opposition to ventricular outflow depends to some extent on the funda-
mental frequency of ejection, which is the heart rate. At frequencies below 3 Hz, aortic impedance tends to increase as frequency falls (12, 19, 22). Second, if cardiac output and other factors remain constant, the slower the heart rate, the larger the pulsations of pressure and flow and the more the afterload depends on aortic compliance. This same relationship can be expressed in terms of external ventricular work per unit time or hydraulic power (24). In the resting state, the power expended by the left ventricle in producing normal pulses (excluding kinetic energy) is 5–20% greater than it would be if the ventricle somehow produced a constant, nonpulsatile outflow, and this proportion varies with heart rate (12).

The choice between aortic impedance and some measure of force (or pressure) as a definition of ventricular load is not merely one of terminology. Aortic impedance expresses what might be called the external (or at least extracardiac) load on the left ventricle. Instantaneous ejection pressure and wall stress depend on this external factor plus a host of other factors, including the shape, dimensions, and velocity of shortening of the chamber, the myocardial viscoelasticity, etc. For some purposes, an investigator concerned with basic mechanisms of contraction may wish to concentrate on the total force that resists the shortening of contractile elements, regardless of the factors involved in producing that force. In that case, he may understandably insist on calling instantaneous force per unit area the load on the muscle fiber, accepting the corollaries that this load varies with time in the normally functioning ventricle and that muscle performance plays a part in determining the load so defined. Aortic impedance measurements simply offer a way of identifying separately the external factors that contribute to instantaneous pressure and flow; for many purposes this information is useful.

**DESCRIPTIONS OF CONTRACTILE STATE**

Adopting arterial impedance as the operational definition of afterload may solve one problem, but it leaves another crucial question unanswered. How can we put afterload and inotropic state into commensurate terms? What is required is an expression of afterload that can be correlated with some description of contractile state; such an expression has not yet been developed. The arterial impedance spectrum and a complete record of instantaneous wall stress and motion contain all of the information needed, but no way of reducing this information to a manageable form has yet been devised. The nature of the difficulty can be appreciated by trying to visualize a force-length-velocity graph in which force varies with time in accordance with impedance moduli and phases that are frequency dependent. A seven-dimensional matrix would be required to express any one contractile state. Unfortunately, the mathematical techniques that are valid for analyzing aortic pressure, flow, and impedance as functions of frequency are not, strictly speaking, applicable to the analysis of ventricular performance. Efforts have been made in this direction (26), but nonlinearity and the discontinuity introduced by the aortic valve make it difficult to interpret the results.

Some investigators have attacked the problem by seeking new ways of describing myocardial function. One approach is to treat the ventricle as a generator (27); in this case, one must decide just what it is that the ventricle generates. A "flow-generator," for example, would produce a certain flow, predetermined by the contractile state, regardless of the pressure required to do so. By this kind of definition, the normal ventricle is obviously neither a flow nor a pressure generator. A case can be made, however, for its resemblance to a power generator, provided both internal and external work are taken into account (18, 25). If ventricular power output and arterial input impedance are known, pulsatile pressure and flow can be calculated. Others have proposed that ventricular status be characterized by a specific "hydromotive pressure" (28) in series with a "source impedance" (15, 26, 28), both of which are functions of the inotropic state. In this analysis, hydromotive pressure is essentially the pressure developed by an isovolumic beat. Again, these two variables and the arterial impedance uniquely determine pressure and flow. Whether these new approaches will enlarge our understanding of myocardial function or lead to better diagnostic and prognostic standards remains to be seen. In any case, they eliminate one source of confusion by treating arterial impedance as the afterload, and they state explicitly the relationships among afterload, contractile state, force-length-velocity curves, and ventricular work.

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