Pulmonary Arterial Pulse Wave Velocity and Impedance in Man

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ABSTRACT

The differential pressure method of Womersley and McDonald was used to measure instantaneous blood flow in the main pulmonary artery in ten human subjects. Three subjects had normal pulmonary arterial pressures and flows, seven had mitral stenosis and pulmonary hypertension. The spectrum of input impedance versus frequency was similar to that previously reported for the dog and rabbit, with the modulus decreasing from relatively high values at zero frequency to a minimum between 2 and 5 cycles/sec. Characteristic impedance and phase velocity were lower in the normal subjects than in those with pulmonary hypertension (averages, 23 dyne sec cm⁻² and 1.68 m/sec in the normals; 46 dyne sec cm⁻² and 4.77 m/sec in the hypertensives). Hydraulic energy dissipated per unit time by pulsations in the pulmonary bed was usually higher in the hypertensive than in the normal cases, because of the greater stiffness of the pulmonary arteries in the subjects with pulmonary hypertension. The elasticity of the pulmonary arterial tree appears to be as important as the state of the arterioles and capillaries in determining the energy required for pulsatile pulmonary blood flow.

ADDITIONAL KEY WORDS differential pressure hydraulic energy vascular elasticity pulmonary hypertension mitral stenosis blood flow

Experimental measurements of the input impedance of a vascular bed not only give a concise expression of pressure-flow relationships at the inlet to the bed, but also provide information about the elasticity and other physical characteristics of the blood vessels involved (1-5). In addition, they permit estimates of the hydraulic energy required to move blood into the bed in a pulsatile fashion.

Pulmonary vascular input impedance in the rabbit and dog is such that the hydraulic energy expended in pulmonary arterial pulsations of pressure and flow accounts for about one-third of the total external energy output of the right ventricle (5, 6). Impedance is highly frequency dependent in these species, so that the energy associated with pulmonary blood flow depends in part on the heart rate (5). Agents that change the elasticity of the
pulmonary arteries alter the pulmonary impedance spectrum significantly (4).

To learn whether the human pulmonary vascular bed shares these characteristics we measured input impedance and apparent phase velocity of the pressure wave in the main pulmonary arteries of ten human subjects who were undergoing cardiac catheterization for purposes of diagnosis or follow-up. Instantaneous velocity of blood flow in the main pulmonary artery was determined from differential pressure by the method of Womersley and McDonald (1, 2).

Methods

Subjects were selected from patients routinely scheduled for cardiac catheterization, and restricted to cases in which mitral stenosis was suspected or had previously been treated by surgery. Measurements were attempted in 16 subjects, and technically satisfactory results were obtained in 10 of these. Three proved to have neither demonstrable obstruction at the mitral valve, nor pulmonary hypertension, and are referred to herein as "normal" subjects (cases 1-3). The others had varying degrees of mitral stenosis and pulmonary hypertension. Pulmonary vascular resistance was less than 200 dyne sec cm⁻² in five cases, and above that level in the other five.

Lateral pressures were measured at two sites in the main pulmonary artery with an 8F double-lumen catheter especially designed for these experiments. The terminal side-holes of the catheter were 28 to 30 mm apart, so that differential pressure could be measured within the relatively short main trunk of the pulmonary artery, and the distal opening was 3 mm from the catheter tip. The catheter was introduced by way of an arm vein into the right ventricle, then advanced until the proximal opening was beyond the pulmonic valve and the distal catheter tip not quite at the bifurcation into right and left pulmonary arteries. The catheter, approximately 1 m long, was connected to a Statham P23H differential pressure gauge, from which three separate signals representing the two pressures and the difference between them were recorded. Tests showed that this particular gauge had a static imbalance of 0.6%, and dynamic imbalance of less than 5% up to a frequency of 15 cycles/sec. The dynamic response of the complete pressure-measuring system (catheter, manometer, and recording instruments), tested immediately after the procedure in 7 subjects, in the average case had a damped natural frequency of 41 cycles/sec (range 18 to 55 cycles/sec) and relative damping of 0.13 (range 0.08 to 0.20). The greatest dynamic imbalance found in the catheter-manometer system after a run was such that the damped natural frequencies of the two sides differed by 7%. The responses were thus within acceptable limits for this application (7), though higher frequency responses and closer balancing would have been desirable.

Left atrial pressures were also recorded in 9 of the 10 cases; catheterization of the left heart was accomplished by the technique of transseptal puncture. The diameter of the pulmonary artery in the frontal plane was measured from angiograms that formed part of the diagnostic procedure, applying suitable correction for parallax.

Pressure data were recorded on magnetic analogue tape at a tape speed of 30 inches/sec, and subsequently converted into digital form on punched cards for analysis on an IBM 7094 digital computer. The computer was programmed to convert the three pressures (proximal, distal, differential) into Fourier series, to correct the observations in accordance with the dynamic responses of the manometer, and to compute at each harmonic frequency: (a) velocity of blood flow, from the differential pressure, by the Womersley equation (2); (b) volume flow, from velocity and pulmonary arterial diameter; (c) pulmonary arterial input impedance (hereafter referred to as simply "impedance"), from the proximal pressure and the computed volume flow; (d) apparent phase velocity of the pressure wave, from the proximal and distal pressures; (e) potential and kinetic hydraulic energy in the main pulmonary artery, from the proximal pressure and computed flow; (f) the steady-flow component of hydraulic energy output of the pulmonary bed, from mean left atrial pressure and mean pulmonary blood flow. The equations on which the calculations of energy were based have been reported elsewhere (5), and the others are given in the Appendix. Calculations were limited to harmonics below 12 cycles/sec because the signal-to-noise ratio approached unity at higher frequencies.

Mean flow was estimated from the computed pulsatile flow by assuming that flow averaged zero during diastole. Cardiac output was measured by the indicator-dilution method 15 to 30 minutes prior to the differential pressure measurements, giving an independent measurement of mean flow. The mean flow computed from differential pressure was within ± 25% of the indicator-dilution determination in each case, and the ratio of mean flow derived from the computed flow curve to that given by the dilution method.
Data from case 1. **Left:** proximal pulmonary arterial pressure, differential pressure per centimeter vessel length, computed flow. The two pressures were resynthesized from first ten harmonics of the Fourier series representing the experimental records, and thus contain no frequency components above 12.5 cycles/sec. **Right:** calculated apparent phase velocity, input impedance modulus and phase. Negative impedance phase denotes that flow leads pressure.

The patients were in the supine position for all measurements, and voluntarily suspended respiration in the mid-position while recordings were made.

**THEORETIC LIMITATIONS**

A fundamental limitation on the validity of our calculated flows and impedances arises from our assumption that conditions in the pulmonary artery in vivo are the same as those assumed in Womersley’s analysis (2). The hydrodynamic theory embodied in his equations for the relation between differential pressure and velocity of flow in longitudinally constrained elastic tubes (2) assumes laminar flow in an infinitely long cylindrical tube, with relatively small radial pulsations. These conditions are never perfectly satisfied in arteries, but the equations have been shown to be valid, or at least very close approximations, in many experimental situations (1, 8-10). Their validity in the human pulmonary artery has not been tested directly, but three kinds of indirect evidence suggest that they are not grossly inapplicable to this vessel.

1. In those instances in which the effects of the known violations of Womersley’s assumptions in the pulmonary artery can be estimated, they are relatively small. It must be added, however, that the theoretic methods of correction are only approximate, and that the data on which they must be based are meager. The elliptical cross section of the artery, for example, assuming a major-minor axis ratio of 1.25 (11), would increase the resistance to flow by 3.5% over that of a comparable cylindrical vessel (12), and the effect on computed flow moduli would presumably be to reduce them by the same order of magnitude. Tapering of the artery, assuming that the cross section decreased peripherally by 5% per
centimeter (a rough estimate from our angiograms), would add 6% in amplitude to the first harmonic of differential pressure, and subtract 0.29 radians from its phase, as compared with a cylindrical vessel. Correction (2) for a pulsatile alteration in the radius of the artery of ± 5% (13) would reduce the amplitude of the first flow harmonic in our average case by approximately 10%, and make its phase more negative by about 0.1 radian. Nonlinearities with respect to pressure and flow in the pulmonary artery, at least in the dog, are too small to detect in experimental measurements of vascular impedance in vivo (4). The net effect of applying these corrections would be to increase the moduli of input impedance given here (Figs. 1-3 and Table 1) by 14% and to make the impedance phases more negative by 0.2 radians, for the first harmonic. While such corrections are not negligible, they do not differ greatly from the experimental errors of measurement.

Unfortunately, the errors introduced by the assumptions that flow is laminar, and that the pulse wave velocity is much greater than the velocity of blood flow (2), cannot be evaluated quantitatively. There is little opportunity in the main pulmonary artery for the development of stable laminar flow because flow is oscillatory, "entrance effects" (1) probably persist throughout the length of the vessel, and Reynolds numbers are often above the critical level. In the present series, Reynolds numbers at peak velocities ranged from 1200 to 3400. Pressure-flow relations in these circumstances are certainly different from those in Womersley's hypothetical vessel, but the nature and magnitude of these differences is difficult to judge in the absence of information about the velocity profiles that actually exist in the human pulmonary artery. In general, instabilities in the flow pattern would lead to falsely high computations of blood velocity.

2. Measurements with an electromagnetic flowmeter of longitudinal impedance in the pulmonary artery of the dog agree fairly well with the Womersley theoretic values in the range...
FIGURE 3

Case 10. Left: Pulmonary arterial pressure (proximal), computed flow, and differential pressure (dp). Right: Apparent gain and phase velocity of pressure, impedance modulus, and phase. Gain is plotted as the ratio of distal to proximal pressure moduli over the distance between the two sites of measurement (not per cm). The second and third harmonics increase in amplitude as they travel down the main pulmonary artery (see text). The heart rhythm was irregular, and the cycle shown on the left was one of six cycles analyzed and averaged to give the data shown on the right and in Table 1.

| Case | Age, Sex | Surface area (m²) | PA area (cm²) | Diagnosis | Rate (per sec) | Mean pressures (mm Hg) | Flow (cm³/sec) | PVR (c m/sec) | $|Z_0|$ (m/sec) |
|------|---------|------------------|--------------|-----------|---------------|------------------------|---------------|--------------|---------------|
| 1    | 21 F    | 1.35             | 5.56         | MS1; MC(1)| 1.25          | 12.1                   | 10            | 59           | 106           |
| 2    | 22 F    | 1.88             | 7.35         | MS1; AI2  | 1.83          | 14.8                   | 120           | 98           | 208           |
| 3    | 54 M    | 1.92             | 8.71         | MS1; MI1  | 1.30*         | 14.8                   | 9             | 58           | 445           |
| 4    | 35 F    | 1.53             | 10.52        | AI1; MC(2)| 1.02          | 15.4                   | 5             | 48           | 270           |
| 5    | 36 F    | 1.62             | 8.04         | MS2       | 2.25          | 34.8                   | 19            | 72           | 337           |
| 6    | 58 F    | 1.79             | 8.35         | MS1       | 1.14*         | 37.0                   | 28            | 77           | 293           |
| 7    | 40 F    | 1.56             | 7.07         | MS3; MC(11)| 1.06         | 42.1                   | 33            | 62           | 564           |
| 8    | 55 F    | 1.68             | 8.04         | MS3       | 1.16          | 42.3                   | 24            | 59           | 281           |
| 9    | 50 F    | 1.54             | 8.71         | MS3; MI1  | 1.64          | 50.6                   | 27            | 90           | 506           |
| 10   | 48 F    | 1.67             | 6.93         | MS3       | 2.13*         | 59.0                   | 33            | 51           | 317           |

*Irregular rate because of atrial fibrillation; value given is average in cycles analyzed.
†PA "wedge" pressure.

Abbreviations: PA = pulmonary artery; LA = left atrium; PVR = pulmonary vascular resistance, in dyne sec cm⁻⁵ (= difference between mean pulmonary arterial and mean left atrial pressures, divided by mean flow); $c$ = characteristic phase velocity; $|Z_0|$ = characteristic input impedance modulus (see text) in dyne sec cm⁻⁵.

Key to diagnosis: M = mitral; A = aortic; S = stenosis; I = insufficiency. The numbers after the valvular lesion indicate the relative severity of the abnormality, judged by hemodynamic criteria: 1 = mild, 2 = moderate, 3 = severe. MC(n) = surgical treatment of mitral stenosis by mitral commissurotomy (n) years prior to this study.

Average impedance modulus observed in this range was 10% greater, and the impedance phase 0.4 radians more
negative, than the Womersley-predicted terms. The discrepancies were much greater at the lower values of \( \alpha \) that represent the first harmonic in the dog (4, 5) and human (15) pulmonary artery. This qualitative evidence is strengthened by the comparison of the computed spectra of input impedance (O'Rourke and Milnor, unpublished data). Similar results in the aorta (4, 5) and human (15) pulmonary artery.

### TECHNICAL LIMITATIONS

Apart from these theoretic considerations, the accuracy of our results depends largely on the accuracy of the differential pressure measurement, and the difficulties inherent in making such measurements over a short distance and through a long catheter are well known. The peak differential pressures were only a few centimeters of water, and the peak signal-to-noise ratio ranged from 20:1 to as low as 4:1. Vibration and axial movement of the catheter with each ventricular contraction was the dominant source of noise, although we made an effort to position the catheter so as to minimize this motion. Lateral pressures would not be distorted by longitudinal motion of the catheter to the extent that "end pressures" would, and acceleration of fluid in both lumens of the moving catheter would not produce artifacts if the system were perfectly balanced, but we cannot estimate the possible error from this source with any accuracy.

Inherent dynamic imbalance in the pressure systems would also distort the differential pressure and the apparent phase velocity. This source of error was limited by the fact that the damped natural frequency of the system was usually more than 4 times the highest frequency analyzed, but this was not true in every case. Owing to the relatively long catheter, and the technical limitations imposed by a procedure designed primarily as a diagnostic catheterization, the frequency response of the differential pressure measuring system in two instances barely met minimum requirements (7). The actual response and imbalance in each case were taken into account in our computations, but it is not certain that the conventional mathematical method of correction applies exactly to differential measurements (1). Quite apart from the accuracy of these pressure measurements, the use in the present work of pressure differences over a finite distance in place of the true spatial differential of pressure required by theory introduces an error into the calculation of blood velocity. Theoretic calculations of this error showed it to be relatively small (less than 2\% of flow modulus and phase) under these conditions.

### TABLE 2

Average Hydraulic Input Power, Pulmonary Artery (Milliwatts)

<table>
<thead>
<tr>
<th>Component</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
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<tr>
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<td></td>
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<td></td>
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<tr>
<td>Steady flow</td>
<td>113.2</td>
<td>236.9</td>
<td>114.4</td>
<td>98.6</td>
<td>334.4</td>
<td>380.0</td>
<td>347.5</td>
<td>332.8</td>
<td>607.5</td>
<td>401.3</td>
</tr>
<tr>
<td>Pulsatile</td>
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<td>102.2</td>
<td>73.3</td>
<td>38.0</td>
<td>142.3</td>
<td>54.6</td>
<td>121.0</td>
<td>31.2</td>
<td>151.6</td>
<td>272.8</td>
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<tr>
<td>Combined</td>
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<td>339.1</td>
<td>187.7</td>
<td>134.6</td>
<td>476.7</td>
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<td>364.0</td>
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<tr>
<td>Steady flow</td>
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<td>1.7</td>
<td>0.1</td>
<td>0.1</td>
<td>0.3</td>
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<td>25.9</td>
<td>6.3</td>
<td>0.8</td>
<td>4.1</td>
<td>1.8</td>
<td>17.7</td>
<td>1.3</td>
<td>9.9</td>
<td>6.1</td>
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<tr>
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<td>27.6</td>
<td>6.4</td>
<td>0.9</td>
<td>4.4</td>
<td>2.1</td>
<td>18.0</td>
<td>1.5</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Steady flow</td>
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<td>238.6</td>
<td>114.5</td>
<td>98.7</td>
<td>334.7</td>
<td>380.3</td>
<td>247.8</td>
<td>332.0</td>
<td>608.0</td>
<td>401.4</td>
</tr>
<tr>
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<td>128.1</td>
<td>79.6</td>
<td>36.8</td>
<td>146.4</td>
<td>56.4</td>
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<td>32.5</td>
<td>161.5</td>
<td>278.9</td>
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<tr>
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<td>366.7</td>
<td>194.1</td>
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<td>481.1</td>
<td>436.7</td>
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<tr>
<td>Kinetic/total</td>
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<tr>
<td>power (%)</td>
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<tr>
<td></td>
<td>6.4</td>
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</tr>
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conditions (Gessner and Milnor, unpublished data).

Finally, the three subjects referred to as “normal” are obviously not a random sample from the normal population, but rather the closest approach to such a group that is available in the routine diagnostic schedule of a cardiac catheterization laboratory. These subjects probably had slight functional and structural abnormalities of the mitral valve (and of the aortic valve in case 2), but there was no evidence to suggest, and no reason to suppose, that these abnormalities had any effect on the pulmonary vessels.

Results

The computed spectra of impedance and apparent phase velocity in each case are shown in Figures 1-3, and other data are summarized in Tables 1 and 2. Cases have been numbered from 1 through 10 in order of increasing mean pulmonary artery pressure.

The contours of the computed flow waves were similar to those that have been recorded in the pulmonary artery of the dog with electromagnetic flowmeters (4, 5, 16), and the average peak-mean flow ratio of approximately 5.8 was similar, though this necessarily varies with cycle length.

In all cases the impedance modulus fell steeply from a relatively high value at zero frequency to a more-or-less well-defined minimum, and showed small oscillations at frequencies above this minimum. These variations in impedance modulus with frequency were repeated in the phase velocity spectrum. Impedance phase was negative (indicating that flow led pressure) at low frequencies, and either rose as frequency increased to cross the zero-phase line somewhere between 3 and 9 cycles/sec (7 cases), or else remained negative at all frequencies observed (3 cases).

Characteristic impedance modulus and phase velocity were higher in the patients with pulmonary hypertension than in the normal subjects, and there was a significant correlation between both of these variables and the mean pulmonary arterial pressure (Fig. 4). Average characteristic impedance modulus was 23 dyne sec cm\(^{-5}\) (range, 20 to 29) in the three normal subjects, and 46 dyne sec cm\(^{-5}\) (range, 25 to 76) in the other subjects; characteristic phase velocity averaged 1.68 m/sec (range, 1.06 to 2.08) in the normals, and 4.77 m/sec (range, 3.15 to 7.11) in the others. These phase velocities agree closely with Caro and Harrison’s measurements in the human pulmonary artery (1.82 m/sec in normals, 4.06 m/sec in subjects with pulmonary hypertension [17]). Comparison of the individual spectra showed that the frequencies at which impedance crossed zero, and at which impedance modulus reached its first minimum, were directly correlated with the degree of pulmonary hypertension, so that in general the spectra “shifted to the right” with increasing pulmonary arterial pressure.

There was no detectable change in the amplitude of the first pressure harmonic as it traveled between the two measuring sites, but the second and third harmonics were larger at the distal than at the proximal site as the example in Figure 3 illustrates. This amplification was greatest at frequencies of 5 to 7 cycles/sec, reaching an average distal-proximal ratio of 1.4 (range 1.07 to 1.77), and diminished at higher frequencies. This increase in the amplitude of some harmonics as they moved downstream, instead of the attenuation that would be expected from viscous effects alone, was presumably due to reflections. Attinger (11) reported similar observations in the right pulmonary artery of the dog. Caro and Harrison (17), on the other hand, found just the opposite effect in the human pulmonary artery, and we cannot account for this difference in observations.

The kinetic and potential (pressure-flow product) energies per unit time, or hydraulic powers, associated with pulmonary arterial blood flow were computed in each case, and are given in Table 2. Two components were calculated separately for each kind of energy, one attributable to the mean pressure and flow alone, the other associated with the pulsations around these means (5). The first, or “steady-flow” term, is the power that would be required to move blood into the pulmonary bed in a steady nonpulsating stream at the observed average flow rate. The second, or “pulsatile,” term represents the energy cost of pulsations per se. Methods of calculating these
components of energy have been published elsewhere (5).

In the three normal subjects, total input power averaged 243 mw, and one-third of this amount was the pulsatile component. This value probably underestimates the total power to be expected in normal subjects, because the cardiac output in two of these patients was relatively low. The value of 367 mw in case 2, who had a normal cardiac output, is probably a better indication of the normal average. Our values are higher than those reported by Prec and his colleagues (18) for power output of the human right ventricle (164 mw), but their figures were based on mean systolic pressure and flow rather than the actual pulsatile values. In the patients with pulmonary hypertension, total input power was usually higher than in the normal cases (greater than 400 mw in five of the seven), and the pulsatile component averaged 24% of the total (range 9 to 41%). Kinetic energy accounted for 6% of the total input power, on the average, in cases 1-3, and somewhat less in the other subjects.

To examine the influence of the pulmonary vascular bed itself (as contrasted with the influence of mitral obstruction or left ventricular dysfunction) on hydraulic power, we also calculated the energy dissipated in the pulmonary vessels (5). Both input and output energies must be known for this calculation, since the difference between them represents energy dissipated. The mean output term could be calculated from our data on mean flow and left atrial pressure, but in the absence of measurements of pulsatile outflow the pulsatile output term was not known. In the dog, we have found that the pulsatile hydraulic power remaining at the end of the pulmonary veins is approximately 6% of the pulsatile input (5). Skalak's calculations (19) and the data of Maloney et al. (20) from perfused lungs suggest that transmission may be even smaller. This led us to assume, as an approximation, that 95% of the pulsatile input power was dissipated in the pulmonary bed. The total energy dissipated. The mean output term could unit time averaged 159 mw (range 83 to 269) in the normal subjects, and 263 mw (103 to 456) in the hypertensives. Since both input and dissipated power depend on the absolute flow, as well as on the state of the vessels, a more useful comparison of the pulmonary beds in different individuals can be made by normalizing the power calculations for a standard inflow (see below).

Discussion

Impedance spectra in the normal subjects were qualitatively similar to those in the pulmonary artery of the dog (4, 5, 16) and rabbit (6), with a relatively high modulus and negative phase at low frequencies, a minimum modulus and zero phase between 2 and 5 cycles/sec, and small oscillations of modulus and phase at higher frequencies. Quantitatively, the characteristic impedance and phase velocity were smaller than those reported in the dog (5, 16, 21), even when allowance was made for the difference in body weight. This may signify a greater distensibility of the pulmonary artery in man, but the direct measurements of distensibility in dogs and man that have been reported show no consistent difference (13, 22-24).

The similarity in shape of the impedance spectra in man and the dog encourages us to believe that conclusions drawn from studies of pulsatile flow in the canine pulmonary artery may also apply to the human pulmonary vessels. The importance of reflections in determining pulmonary pressure-flow relations, and the inverse relation between heart rate and input power (4, 5) are two examples of such conclusions drawn from animal experiments that merit exploration in studies of human pulmonary hemodynamics.

Taylor, in his work on the aorta and systemic circulation, has emphasized the "decoupling" of the heart from the distal part of the circulation that this kind of impedance spectrum implies (3). The oscillations of impedance with frequency that reflections create are much smaller in the aorta and pulmonary artery than in a simple elastic tube, and the input impedances of these vessels are almost constant at frequencies above 5 cycles/sec. Although we agree that
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this decoupling has advantages for the economy of the circulation, the relative constancy of impedance at higher frequencies is surely of less consequence to the heart as a generator, and to the energy dissipated in the pulmonary vessels, than the relatively steep decline of impedance modulus at low frequencies, where most of the energy in physiological pulsations is concentrated. In our present data, as in our earlier experiments on dogs (4, 5), the slope of the impedance at low frequencies makes the modulus at 1 cycle/sec about twice that at 2 cycles/sec. The impedance for the first harmonic is therefore twice as great when the heart rate is 60 beats/min as it is at 120 beats/min. The changes in the impedance spectrum that occur with pulmonary hypertension (Fig. 2) accentuate this difference. The effect of reflections on low-frequency impedance seems, therefore, to be one of the most important factors in pulsatile hemodynamics. In the pulmonary bed, the dominant reflection sites are well out in the arterial tree, extending from vessels perhaps 1 mm in diameter down to the capillaries (4, 6). Alterations in the state of the smallest arteries therefore influence the input impedance spectrum through reflections, while changes in the elasticity of the larger arteries influence it directly.

All of our results indicated that the pulmonary arteries were stiffer than normal in subjects with pulmonary hypertension. The higher characteristic impedances, phase velocities, and pulsatile energy components in the hypertensives all point to this conclusion. The reason for such abnormal stiffness cannot be identified with certainty, but the demonstration by Bergel (25) and others that arteries become stiffer as they are distended immediately comes to mind as a possible explanation. This phenomenon would account to some extent for our results, as Figure 4 illustrates, since there was a direct correlation between characteristic phase velocity, which should be a function of vessel stiffness, and mean pulmonary arterial pressure. This relationship matches that found by Caro and Harrison (17) and is consistent with the measurements of volume distensibility of the pulmonary artery in the dog by Patel et al. (22). Greenfield and Griggs have reported an analogous relationship between mean pressure and pressure-strain elastic modulus in human subjects (23).

One bit of evidence, however, suggests that the elevated phase velocities and impedances in our patients were not entirely due to passive distension of the artery by high transmural pressures. At any given mean pressure, the phase velocity was highest in the subjects with the highest pulmonary vascular resistance (Fig. 4). Increased pulmonary vascular resistance in such patients is almost always the result of diminished caliber or closing of pulmonary arterioles and capillaries (26), which could increase the amount of reflection from peripheral sites, and hence the oscillations of impedance and phase velocity. There is no reason to suppose, however, that it would alter the characteristic input impedance of the bed, or the characteristic phase velocity in the main pulmonary artery, by any mechanism other than raising the pressure in the pulmonary artery. The logical inference is

![Figure 4](http://circres.ahajournals.org/)

Mean pulmonary arterial pressure ($P_{PA}$) and characteristic phase velocity in each of the ten cases. Open circles represent subjects with pulmonary vascular resistances less than 200 dyne sec cm$^{-5}$, closed circles those with pulmonary vascular resistances above that level. Broken line indicates the relationship predicted by the data of Patel et al. (22), extrapolated to pressures higher than were included in their observations.
that the stiffening of larger arteries in the patients with high resistance is greater than that produced by uncomplicated elevation of the distending pressures. If patients with high pulmonary vascular resistance thus have abnormalities in the large arteries as well as in the microcirculation, it is reasonable to suspect that the changes in large vessels, like those in the small vessels, have their origin in a combination of histologic alterations and increased smooth muscle tone in the vascular walls.

Whatever the cause of the increased arterial stiffness, its consequences for the energy required to move blood through the lung in a normal pulsatile fashion are far from negligible. When the energy dissipated per unit time in the pulmonary bed for comparable pulsatile flows was calculated in each of our patients, it was apparent that increased power for pulsations shared proportionately in the great increase of total power dissipated that sometimes occurred (Fig. 5). For purposes of comparison, we computed the total energy that would be dissipated in the pulmonary bed of each patient for a standard inflow, calculating the energy from this flow and the observed impedance spectrum in each individual (5). The standard input was defined as pulses of normal harmonic content, at a rate of 72 pulses/min, of an amplitude that produced a mean flow of 3.5 liters/min per square meter of body surface. The normal harmonic content at this rate was defined by reference to data previously obtained in the dog (5), which was consistent with the harmonic ratios observed in our patients. This procedure for normalization was adopted because mean flows and heart rates among our patients varied by a factor of about two, introducing a variability into the observed hydraulic powers that was attributable to factors other than the state of the pulmonary vessels. Normalizing the power dissipations, as in Figure 5, allowed us to examine the differences between patients that were inherent in the characteristics of the pulmonary vessels themselves, not in the particular output of the heart at the time of our study.

The significance of the values plotted in Figure 5 lies in the fact that the steady-flow terms (below the line), represent energy dissipated predominantly in the arterioles and capillaries, while the pulsatile terms (above the line) depend principally on the elasticity of the larger arteries. The steady-flow term, which is the product of mean pressure and mean flow, necessarily increases with the pulmonary vascular resistance, but the pulsatile term also increases, showing the net effects of the impedance abnormalities in these patients. The largest dissipated power was found in case 10, whose pulsatile and steady-flow terms amounted to more than three times the highest corresponding terms in the normal subjects.

In one of the two instances of pulmonary hypertension with a low pulmonary vascular resistance (case 6), the pulsatile term of dissipated energy was elevated and the steady-flow term was similar to that in the normal subjects. The possibility that such evidence of arterial stiffening without arteriolar narrowing represents a stage in the development of raised pulmonary vascular resistance warrants further investigation.
Our results indicate that control of blood flow through the pulmonary bed in vivo, under normal conditions and in pathological states, is by no means limited to the pulmonary arterioles and capillaries. The elasticity and other physical characteristics of the whole arterial tree are involved in pulsatile pressure-flow relations, and determine to a significant degree the energy that must be supplied to move blood through the lung. Data reported by Ingram and his colleagues (27), as well as unpublished experiments in our own laboratory, show that pulmonary vascular impedance, like pulmonary vascular resistance, is subject to autonomic nervous control. As a consequence, the physiologic adjustment of pulmonary blood flow to normal demands can involve neural modifications of impedance as well as resistance. This may be equally true in pathologic pulmonary hypertension, with abnormalities of vascular tone through the bed superimposed on structural abnormalities.

Appendix

SYMBOLS AND UNITS

$r = \text{radius of pulmonary arterial lumen (cm)}$.

$x = \text{distance between measuring sites (cm)}$.

$\omega = \text{fundamental frequency (radians/sec)}$.

$N = \text{total number of harmonics computed}$; $N = 10$ in the data presented in this paper.

$\eta = \text{blood viscosity, assumed to be 0.035 poise}$.

$\rho = \text{blood density, assumed to be 1.05 g/cm}^3$.

$\alpha_n = \text{Womersley parameter, } r \sqrt{\frac{n \omega \rho}{\eta}}$.

$M_n', \epsilon_n = \text{functions of } \alpha_n, \text{tabulated by Womersley (2)}$.

$c_n' = \text{apparent phase velocity at frequency } = n \omega$.

$D(t) = \text{differential pressure per cm length of vessel, as a function of time, } t$.

$\bar{D} = \text{mean (time average) differential pressure (dyne/cm}^2)$.

$|D|_n = \text{modulus of the } n\text{th harmonic in the Fourier series derived from } D(t).$ (dyne/cm$^2$).

$\Delta_n = \text{phase of the } n\text{th harmonic of differential pressure (radians)}$.

The notation for pulmonary arterial pressures, flow, and impedance is in the same form as that for differential pressure. The symbols for these variables are listed below:

$P_1(t), \bar{P}_1, |P_1|_n, \phi_{1n} = \text{proximal pulmonary arterial pressure}$.

$P_2(t), \bar{P}_2, |P_2|_n, \phi_{2n} = \text{distal pulmonary arterial pressure}$.

$Q(t), \bar{Q}, |Q|_n, \xi_n = \text{computed blood flow}$.

$|Z|_n, \Psi_n = \text{longitudinal impedance per cm of main pulmonary artery, at frequency } = n \omega$.

$|Z|_n, \theta_n = \text{input impedance of main pulmonary artery}$.

EQUATIONS

Longitudinal Impedance

For $n = 1, N$:

$$|Z|_n = \frac{\eta \alpha_n^2}{\pi r^3 M_n}$$

$$\psi_n = (3 \pi - \epsilon_n)$$

For $n = 0$:

$$|Z|_n = \frac{8 \eta \pi}{\pi r^4}$$

$$\psi_{n=0} = 0$$

Volume Flow from Differential Pressure

Fourier analysis of the experimentally determined differential pressure, $D(t)$, gives a harmonic series like that in equation 5 below. Flow as a function of time can be computed by calculating mean flow, calculating each harmonic of flow, and adding them together, as in equations 6-8:

$$D(t) = \bar{D} + \sum_{n=1}^{N} |D|_n \sin (n \omega t + \Delta_n)$$

$$Q(t) = \bar{Q} + \sum_{n=1}^{N} |Q|_n \sin (n \omega t + \epsilon_n)$$

$$\bar{Q} = \bar{D} \frac{\pi r^4}{8 \eta \pi}$$

$$|Q|_n \sin (n \omega t + \epsilon_n) = (|D|_n / |Z|_n) \sin (n \omega t + \Delta_n - \Psi)$$
These equations are the same as those given by Womersley and McDonald (1, 2), except that impedance is expressed here as the ratio of pressure to volume flow, rather than ratio of pressure to flow velocity, and sine rather than cosine expressions are employed.

**Input Impedance**

For $n = 1$, $N$:

$$|Z_n| = \frac{|P_n|}{|Q_n|}$$  \hfill (9)

$$\theta_n = \phi_n - \epsilon_n$$  \hfill (10)

For $n = 0$:

$$|Z|_{n=0} = \frac{P_i}{Q}$$  \hfill (11)

$$\theta_n = \epsilon = 0$$  \hfill (12)

**Apparent Phase Velocity**

$$c_n = \frac{-\omega}{\phi_n - \phi_{n-1}}$$  \hfill (13)

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**References**


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