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THE pathogenesis of pulmonary arterial hypertensive disease is clearly multifactorial but usually includes increased pressure and flow loads to the pulmonary circulation (Hoffman and Rudolph, 1966; Heath and Edwards, 1958; Rudolph, 1970). Increased flow, as an isolated stress, has varying consequences depending on magnitude, chronicity, velocity gradients, and turbulence patterns, but generally seems to be well tolerated by the pulmonary vascular bed (Wagenvoort, et al. 1967; Fergusson and Varco, 1955; Blank et al., 1961). Most previous studies have used mean pressure and flow measurements that are sensitive primarily to pulmonary vascular perfusing area (arteriolar and capillary recruitment) and intrinsically limit the information obtainable by modeling the vascular bed as a passive complex of recruitable conduits with static pressure-volume relationships perfused by constant flow.

Twelve control dogs were studied and had mean Qp. (pulmonary blood flow) - 2.02 ± 0.15 liters/min, Z0 = 193 ± 20 dyne sec cm"1 and PVR = 416 ± 32 dyne sec cm"'. Ten dogs were studied awake 20 weeks after creation of bilateral arteriovenous fistulae. Five of these shunted dogs, designated group A, developed Qp. = 4-8 liters/min (mean - 5.87 ± 0.16, P < 0.001 different from control group); the other five dogs (group B) developed Qp. = 2-4 liters/min (mean = 3.80 ± 0.09, P < 0.001 different from control group); the other five dogs (group B) developed Qp. = 4-8 liters/min (mean = 3.80 ± 0.09, P < 0.001 different from control group); the other five dogs (group B) developed Qp. = 4-8 liters/min (mean = 3.80 ± 0.09, P < 0.001 different from control group); the other five dogs (group B) developed Qp. = 4-8 liters/min (mean = 3.80 ± 0.09, P < 0.001 different from control group). In group A, Z0 = 90 ± 5 (P < 0.005) and PVR = 126 ± 14 (P < 0.001). The total input power (potential and kinetic) was 125% above the controls for group A (P < 0.001) and 264% for group B (P < 0.001), but the mean energy components increased significantly more than did the pulsatile components. These data demonstrate a lower impedance to pulsatile flow during chronically elevated total flow which effects a reduction in both the work load of the right ventricle and the transmission of energy to the precapillary bed. Analysis of the alterations in characteristic impedance suggests a distinct proximal pulmonary vascular mechanism of decreased vessel stiffness (decreased elastic moduli) for adaptation to chronically elevated flow loads which is in addition to the two geometric alterations of proximal arterial dilation and distal vascular channel recruitment.

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The dynamic transmission characteristics of the proximal vessels are determined by both viscoelastic properties and geometry (Patel et al., 1960). These characteristics govern the amount of energy transferred to the precapillary bed and contribute to the control of regional pulmonary blood flow patterns (Maloney et al., 1968; Reuben et al., 1970). Alterations in vascular “tone” and the physiological mechanisms matching these mechanical properties to the pumping characteristics of the heart can be described only by a careful analysis of pulsatile phenomena (McDonald, 1974; Bergel and Milnor, 1965).

Pulmonary vascular impedance measurements summarize the quantitative relationships between pulsatile pressure and flow and allow calculation of ventricular power output specifically associated with the mean and pulsatile components. Impedance is frequency dependent and modulated by the vessel dimensions, the viscoelastic properties of the vessels, and wave reflections. The characteristic impedance ($Z_c$) is the impedance in the absence of reflected waves and, therefore, in blood vessels, is determined only by dimensions and elastic properties of the walls (McDonald, 1974).

This study was designed to investigate with the methods of impedance analysis the pulmonary vascular adaptation to chronically elevated blood flow achieved with obligatory systemic arteriovenous shunting and the energy consequences of the dynamically altered afterloads. The hemodynamic parameters were also assessed after closure of the shunts. A complete analysis using impedance measurements of the chronically flow-stressed pulmonary circulation in the awake dog previously has not been accomplished.

Methods

Experimental Preparation

Fifteen healthy mongrel dogs certified free of *Dirofilaria immitis* and weighing 22–25 kg were anesthetized with sodium pentobarbital (20 mg/kg, iv) and bilateral 6-cm femoral arteriovenous fistulae were created with side-to-side anastomoses. After recovery, the dogs were placed in a chronic care facility and exercised daily. Eighteen weeks later, they were returned to the laboratory for placement of chronic instrumentation. Using pentobarbital (20 mg/kg) anesthesia and ventilation supported with a Bennett MA-1 respirator, a thoracotomy was performed aseptically in the left 4th intercostal space. The main pulmonary artery was minimally dissected from the aorta and an electromagnetic flow probe (Howell Instruments, Camarillo, Calif.) placed about the pulmonary artery with careful matching of size to ensure good electrical contact and to minimize stenosis.

A Silastic introducer catheter (Dow Corning no. 601-325, 0.104 inch i.d.) was inserted into the right ventricle infundibulum. A bipolar pacing electrode was sutured to the right ventricle. Polyvinyl chloride (14-gauge, Apha Wire Corp.) catheters were filled with heparinized saline and placed in the right atrium, left atrium, and aorta via the left subclavian artery. Another Silastic introducer was placed in the pleural space adjacent to the pulmonary artery. The lead wires and catheters exited through the chest wall and were placed in subcutaneous pouches. The thoracotomy was then repaired and the dogs were allowed to recover for 10–14 days. Intramuscular procaine penicillin G (6 $\times$ 10$^6$ U), dihydrostreptomycin (0.75 g), and oral digoxin (0.25 mg) were administered for 5 days postoperatively and the dogs were returned to the laboratory periodically and trained to lie quietly on their right side. Five dogs died in the postoperative period. Three of these had congestive heart failure with tachypnea and ascites. The shunted dogs were divided into two groups for analysis. Group A dogs were those in which pulmonary blood flows were elevated 1.5–2.0 times normal, whereas group B dogs developed pulmonary blood flows greater than twice normal with a maximum of a quadrupling of flow. Twelve additional control dogs underwent the instrumentation procedure without prior fistulae creation and did not require digoxin perioperatively. None of the dogs was studied while receiving digoxin.

On the day of study the dogs were given morphine sulfate (0.25 mg/kg, im). Under local xylocaine anesthesia, the pockets were opened and the leads and catheters exteriorized. With fluoroscopic visualization, a 7-French high-fidelity micromanometer catheter (PC-470, Millar Instruments) was passed through the introducer catheter and the sensor positioned just distal to the flow probe in the main pulmonary artery. There were no pressure gradients across the flow probe site in the dogs studied. A 5-French micromanometer catheter (PC-350 A, Millar Instruments) was passed through the introducer into the pleural space adjacent to the pulmonary artery. The left atrial catheter was connected to the Statham P23-Gb pressure transducer zeroed to the dog’s thoracic spine. The flow probe was driven by a gated sine wave flowmeter (M4001, Statham Instruments). All data were recorded on paper and stored on magnetic tape for computer processing (Ampex FR 1300A recorder).

Pressure transducers were warmed for 24 hours prior to use and calibrated statically before, during, and after each experiment with a water manometer in a constant temperature bath held at 38°C. Dynamic testing of the micromanometer was performed using a sinusoidal oscillating pressure wave at varying frequencies with responses consistently flat to beyond 200 Hz. Flow probes were calibrated in a constant flow device containing saline before implantation and after the dogs had been killed; if flow calibrations deviated by 5% or more, the ex-
periment was discarded. Dynamic electronic calibration of the flowmeter revealed an amplitude response of 100% to 9 Hz, falling linearly to 40% at 50 Hz (Goodman, 1966). Phase lag was 45° at 10 Hz and linear to 50 Hz. The system phase shift between the pressure and flow waveforms was found to be negligible by a computer cross-covariance technique, and thus no phase correction was required.

Pulsatile pulmonary artery flow \(Q_{pa}\), pulmonary artery pressure, pleural pressure, and left atrial pressure were recorded after the dogs had adjusted to laboratory conditions 2 hours after the exteriorization procedure (Fig. 1).

At the completion of the study, the dogs again were anesthetized and all four limbs of the fistulae ligated. Two weeks after obliteration of the systemic left-to-right shunts, the dogs were restudied by the same protocol.

Data Analysis

Data were recorded on magnetic tape and digitized at 5-msec intervals using an IBM System 7 analog-to-digital converter (sampling rate = 200 Hz/channel) and stored in an IBM 1130 digital computer data file. Seven to 19 cardiac cycles were selected from each intervention for analysis. Systolic and diastolic intervals were identified from the pulmonary flow record. Diastolic flow was assumed to be zero (Bergel and Milnor, 1965).

The computations of impedance and hydraulic power were based on Fourier analysis of the pulmonary artery pressure and flow waveforms (Bergel and Milnor, 1965; Attinger, 1963; Milnor et al., 1966). Ten harmonics were routinely calculated for all data. Total pulmonary flow is expressed:

\[
Q_{t0} = Q_m + \sum_{n=1}^{10} Q_n \sin(n\omega t + \theta_n)
\]

where \(Q_m\) = mean flow, \(Q_n\) = amplitude of the \(n^{th}\) harmonic, \(\omega\) = the fundamental angular frequency, \(t\) = the length of the sequence, and \(\theta_n\) = phase angle of the \(n^{th}\) harmonic. Terms of the equation with flow moduli less than 6.0 ml/sec were eliminated from subsequent analysis as this approached the noise level of the system.

Pressure waves are expressed similarly:

\[
P_{t0} = P_m + \sum_{n=1}^{10} P_n \sin(n\omega t + \beta_n)
\]

where \(P_m\) = mean pressure, \(P_n\) = amplitude of the \(n^{th}\) harmonic, and \(\beta_n\) = the phase angle of the \(n^{th}\) harmonic. Terms of the equation with pressure moduli less than 0.75 mm Hg were eliminated.

Division of the mean terms \(P_m/Q_m\) yielded the input impedance to mean flow \((Z_m)\). Similarly, the division of each of the sinusoidal terms \(P_n/Q_n\) gave the input impedance \((Z_n)\) for the \(n^{th}\) harmonic. The corresponding phase angle \(\phi_n\) was derived from subtraction of the flow phase from the pressure phase \((\beta_n - \theta_n)\). The first harmonic term was the frequency of the heart rate. Characteristic impedance \((Z_0)\) was defined as the average impedance modulus between 7 and 11 Hz.

Impedance data obtained from all cardiac cycles at a particular pacing rate were averaged, and a single impedance spectrum from each dog at that pacing rate was used in the subsequent analysis. This averaging process was carried out separately for each pacing rate employed in the study. Data from all dogs were combined by averaging the impedance values at 1 Hz frequency intervals to
generate the pooled spectra. Differences between group means were assessed by unpaired two-tailed Student's t-test (Zar, 1974).

Pulmonary arterial input power was calculated as described in the classic paper by Milnor and associates (1966) for the mean and oscillatory terms of potential and kinetic power (milliwatts) which can be converted to the units of minute work (ergs) and normalized for total flow (ergs/ml).

**Results**

**Standard Hemodynamics**

Two groups of five dogs each were defined on the basis of the elevated pulmonary blood flows (Qp) achieved by the chronic effects of the systemic arteriovenous fistulae and were compared to the 12 control dogs. Group A dogs developed Qp = 3.0 to 4.0 liters/min (mean 3.80 ± 0.09, P < 0.001 different from controls), whereas group B dogs are those which developed pulmonary artery flows in the range of 4.1 to 8.0 liters/min (mean 5.87 ± 0.16, P < 0.001). The values for standard hemodynamic variables are reported in Table 1. The pulmonary artery pressures were elevated with increasing flows, although the transpulmonary vascular pressure gradients were not dramatically different. Pulmonary vascular resistances (PVR) were lower with the higher flows, indicating recruitment of cross-sectional pulmonary vascular area available for perfusion.

Three weeks after closure of the fistulae, the group A dogs returned to normal mean hemodynamics except for mild residual elevation of left atrial pressure associated with a normal PVR. However, group B dogs had elevations of all pulmonary artery pressures, depression of Qp, and elevated PVR. Histological light microscopic studies revealed no anatomic differences in the pulmonary vasculature of the three groups at the time the dogs were killed.

**Pulsatile Hemodynamics**

The impedance modulus and phase frequency spectra (Fig. 2) are similar in morphology in these experiments to others reported for dogs and man (McDonald, 1974; Bergel and Milnor, 1965; Milnor et al., 1966; Milnor et al. 1969). The highest modulus is for Zm or impedance to mean flow. The moduli reach a first minimum between 2 and 4 Hz and then oscillate about the value of the characteristic impedance (Zo).

The impedance moduli were lower with increased flows and this resulted in lower input impedances at each frequency (Fig. 2). Most importantly, the characteristic impedances (Zo) were lower than the control value. Zo for group A = 143 ± 8 (P < 0.05, different from control). Zo for group B = 90 ± 5 which was less than 50% of controls (P < 0.005).

As chronic pulmonary blood flows increased (Fig. 2), Zo decreased analogously to PVR. This indicates a recruitment of perfusing area.

Three weeks after obliteration of the fistulae, impedances of group A dogs returned essentially to normal while group B dogs evidenced elevated impedances (Fig. 3).

**Table 1 Standard Hemodynamic Measurements**

<table>
<thead>
<tr>
<th></th>
<th>PAS (mm Hg)</th>
<th>PAD (mm Hg)</th>
<th>PAP (mm Hg)</th>
<th>LAP (mm Hg)</th>
<th>HR (beats/min)</th>
<th>Qp (liters/min)</th>
<th>PVR (dynes sec cm⁻²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>25.5 ± 0.6</td>
<td>10.5 ± 0.5</td>
<td>15.1 ± 0.6</td>
<td>4.4 ± 0.4</td>
<td>87 ± 15</td>
<td>2.02 ± 0.15</td>
<td>416 ± 32</td>
</tr>
<tr>
<td>A. Fistulae</td>
<td>30.4 ± 0.6*</td>
<td>16.7 ± 0.6*</td>
<td>22.1 ± 0.7*</td>
<td>9.7 ± 0.3*</td>
<td>97 ± 4</td>
<td>3.80 ± 0.09*</td>
<td>249 ± 6*</td>
</tr>
<tr>
<td>B. Fistulae</td>
<td>30.6 ± 0.6*</td>
<td>20.3 ± 0.7*</td>
<td>25.0 ± 0.7*</td>
<td>15.7 ± 0.3*</td>
<td>126 ± 10*</td>
<td>5.87 ± 16*</td>
<td>126 ± 14*</td>
</tr>
<tr>
<td>A. Shunt closed</td>
<td>24.5 ± 0.5</td>
<td>12.6 ± 0.6</td>
<td>16.5 ± 0.5</td>
<td>6.7 ± 0.3*</td>
<td>84 ± 6</td>
<td>2.12 ± 0.08</td>
<td>336 ± 10</td>
</tr>
<tr>
<td>B. Shunt closed</td>
<td>26.5 ± 0.6</td>
<td>14.0 ± 0.2*</td>
<td>17.9 ± 0.3*</td>
<td>6.0 ± 0.3*</td>
<td>99 ± 8</td>
<td>1.52 ± 0.06*</td>
<td>624 ± 14*</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SEM. Abbreviations: PAS = mean pulmonary artery pressure; PAD = pulmonary artery diastolic pressure; PAP = systolic pulmonary artery pressure; LAP = mean left atrial pressure; HR = heart rate; Qp = cardiac output measured at the pulmonary artery; PVR = pulmonary vascular resistance (PAP - LAP/Qp).

* Different from control, P < 0.05; unpaired two-tailed t-test.
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Hydraulic Power

The potential and kinetic energy measurements as oscillatory (pulsatile) and mean terms are listed in Table 2. Obviously, the total power increases as flow increases. The percentage of total output power in the oscillatory terms (osc%) was 44.9 ± 1.4% in the control dogs, 35.1 ± 0.5% for group A (P < 0.05), and 31.6 ± 0.9% for group B (P < 0.05), indicating a major source of underestimation of right ventricular work requirements if only mean flow and pressure are considered.

Total minute work (Table 3) was 138% (group A) and 386% (group B) above control. However, mean work was higher by 180% (A) and 391% (B), whereas oscillatory work was elevated only 86% (A) and 154% (B).

This blunted increase in oscillatory work is demonstrated further by the observation that, for oscillatory work normalized to flow (ergs/ml), there is no change as the flow load increases (Fig. 4). The kinetic energy components, although small, increased relatively and absolutely as a consequence of increased pulmonary blood flow.

Discussion

Resistance and Impedance

Although elevated blood flow frequently has been incriminated as a significant pathogenic factor in the development of pulmonary vascular obstructive disease, it has not been precisely clear why and at what point the pulmonary vascular bed fails to handle this stress. This difficulty may be a result of the limitations of traditional resistance measurements.

Pulmonary vascular resistance represents a mean pressure-flow relationship with primary dependence on the cross-sectional area perfused as defined by the Poiseuille relationship. Thus, as pulmonary blood flow increases, the PVR and \( Z_m \) typically fall, representing the more distal (small vessel) mechanism for adaptation to changing flow: recruitment of pulmonary vascular channels (Maseri et al., 1972). It is well accepted that significant vasomotor activity exists in small precapillary resistance ves-

### Table 2 Hydraulic Input Power (milliwatts)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Oscillatory</th>
<th>Total</th>
<th>Mean</th>
<th>Oscillatory</th>
<th>Total</th>
<th>Total</th>
<th>Total</th>
<th>Total</th>
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<tr>
<td></td>
<td>potential</td>
<td>potential</td>
<td></td>
<td>kinetic</td>
<td>kinetic</td>
<td></td>
<td></td>
<td></td>
<td>power</td>
</tr>
<tr>
<td>Controls</td>
<td>82.73</td>
<td>49.51</td>
<td>132.05</td>
<td>0.46</td>
<td>4.98</td>
<td>5.45</td>
<td>83.20</td>
<td>54.49</td>
<td>137.0</td>
</tr>
<tr>
<td>±4.96</td>
<td>±1.65</td>
<td>±5.78</td>
<td>±0.04</td>
<td>±0.25</td>
<td>±0.28</td>
<td>±0.51</td>
<td>±1.51</td>
<td>±1.51</td>
<td></td>
</tr>
<tr>
<td>A. Fistulae</td>
<td>198.52</td>
<td>86.71</td>
<td>285.26</td>
<td>2.69</td>
<td>21.13</td>
<td>23.83</td>
<td>201.16</td>
<td>107.86</td>
<td>309.0</td>
</tr>
<tr>
<td>±9.49</td>
<td>±5.65</td>
<td>±11.46*</td>
<td>±0.20*</td>
<td>±1.11*</td>
<td>±1.23*</td>
<td>±3.97*</td>
<td>±5.67*</td>
<td>±1.20*</td>
<td></td>
</tr>
<tr>
<td>B. Fistulae</td>
<td>342.80</td>
<td>88.08</td>
<td>430.88</td>
<td>9.81</td>
<td>59.42</td>
<td>69.20</td>
<td>352.60</td>
<td>147.31</td>
<td>500.0</td>
</tr>
<tr>
<td>±17.97*</td>
<td>±1.54*</td>
<td>±18.52*</td>
<td>±0.92*</td>
<td>±4.79*</td>
<td>±5.68*</td>
<td>±18.82*</td>
<td>±22.22*</td>
<td>±24.0*</td>
<td></td>
</tr>
<tr>
<td>A. Shunt closed</td>
<td>92.04</td>
<td>46.74</td>
<td>138.76</td>
<td>0.70</td>
<td>7.17</td>
<td>7.87</td>
<td>92.77</td>
<td>53.88</td>
<td>147.0</td>
</tr>
<tr>
<td>±6.59</td>
<td>±4.08</td>
<td>±8.61</td>
<td>±0.08*</td>
<td>±0.65*</td>
<td>±0.72*</td>
<td>±6.67*</td>
<td>±4.55</td>
<td>±9.0</td>
<td></td>
</tr>
<tr>
<td>B. Shunt closed</td>
<td>62.05</td>
<td>38.39</td>
<td>100.44</td>
<td>0.15</td>
<td>2.11</td>
<td>2.26</td>
<td>62.21</td>
<td>40.49</td>
<td>102.6</td>
</tr>
<tr>
<td>±2.59*</td>
<td>±2.05*</td>
<td>±3.74*</td>
<td>±0.91*</td>
<td>±0.91*</td>
<td>±1.30*</td>
<td>±2.15*</td>
<td>±2.58*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SEM.

* P < 0.001 different from control.
sels; however, there also is evidence of changes in mechanical properties of the larger pulmonary arteries under physiological stress and adrenergic stimulation (Ingram et al., 1968). Patel et al. (1962) showed that the main pulmonary artery has huge volume distensibility. It has been demonstrated that the dynamic transmission characteristics of the proximal vessels have a contributory role in the control of regional pulmonary flow patterns (Maloney et al., 1968). Others have found in dogs a constancy of pulsatile flow transmission from the main pulmonary artery to the lung capillaries under various acute vasoconstrictor stimuli (e.g., hypoxia, serotonin) and noted that the input impedance pattern changed relating the proximal mechanical properties and the capillary perfusion density (Reuben et al., 1970). Thus, the occurrence of alterations in proximal pulmonary vascular physical properties has been established, but its importance has not been recognized universally because of the difficulties encountered in its measurement. Impedance analysis provides a method for assessing these changes and for quantifying the amount of energy delivered to the pulmonary circulation.

Pulmonary vascular impedance is the major portion of the right ventricular afterload and thus represents a significant factor in determining the power requirements of the pumping heart (Milnor, 1976). Stiffening of the pulmonary arteries may not necessarily change mean pressure but will alter the pressure-flow relationship in phase and magnitude and therefore may increase the opposition to pulsatile flow. It has been shown that autonomic nervous control of resistance and impedance are dissociated (Pace, 1971; Pace et al., 1972).

The percentage of total power that is contained in the pulsatile terms falls with increasing heart rate. This inverse relationship between power and heart rate is a function of the steep negative slope of the input impedance spectrum in the range of physiological heart rates (1–3 Hz) and the harmonic redistribution as a consequence of changing wave morphology to a more sinusoidal form (i.e., fewer harmonics necessary to represent the wave) (Milnor et al., 1966). In the present study, this relationship is maintained in the high-flow animals but is shifted to even lower values as a result of the depressed impedance spectra. Thus, the power-sparing mechanism inherent in the heart rate response is augmented in the chronically flow-stressed dogs.

In contrast to the chronic situation, Hammon et al. studied acute increases in pulmonary blood flow in the awake dog with isoproterenol infusions and found impedance spectra indistinguishable from controls despite elevations in heart rate, flow, and pressure (Hammon et al. unpublished observations). Thus, chronic flow stress induces alterations in the physical properties of the pulmonary vascular system that are not seen in acute elevations of flow.

**Determinants of Reduced Impedance**

The present study shows that in the intact awake canine model the input and characteristic impedances fall during the first few months in response to chronically elevated flow loads, thus reducing increases in ventricular work. This must result from either a true decrease in stiffness or an increase in the diameter of the proximal vessels sufficient to overcome any stiffness increase. Without dynamic diameter measurements, we need to examine the determinants of impedance to understand what must be occurring.

Womersley has defined the relationship between wave velocity ($C_w$), characteristic impedance ($Z_0$) and vessel radius ($R$) of a strongly tethered elastic tube (Womersley, 1957a, 1957b).

$$Z_0 = \frac{\rho C_w}{\pi R^2 \sqrt{1 - \sigma^2}} \cdot \frac{1}{M_{10}} \cdot e^{-\alpha^2/2}$$

where $\rho$ = density of blood = 1.055 g/ml, $\sigma$ = Poisson’s ratio = 0.5, and $j = \sqrt{-1}$. $M_{10}$ and $\epsilon$ are functions of Womersley’s nondimensional parameter $\alpha$:

$$\alpha = R \sqrt{\frac{\omega \rho}{\mu}}$$

where $\mu$ = fluid viscosity = 0.04 Poise. Bargainer (1967) has validated the application of Womersley’s equations to the canine pulmonary vessels.

Thus, $C_w = 325 \pm 94$ cm/sec can be calculated for the normal dogs ($Z_0 = 193 \pm$ dyne sec cm$^{-5}$) assuming pulmonary artery area = 2.25 cm$^2$ (correcting for $h_{2R} = 0.03$ at a frequency of 2 Hz (heart rate = 120/min). This value is consistent with other reports and other methods of measurement (Bergel and Milnor, 1965; Gow and Taylor, 1968; Jarmakani

![Figure 4: Input minute work normalized for total blood flow demonstrating no change in the normalized oscillatory work. The energy cost is significantly higher for each milliliter of blood moved axially as chronic pulmonary blood flow increases ($P < 0.02$), but the right ventricular power required for radial arterial pulsations remains the same.](image-url)
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et al., 1971). Using the Moens-Korteweg equation for wave velocity,

\[ C_0 = \sqrt{\frac{Eh}{\rho 2R}} \]

the relationship of \( Z_0 \) to Young's elastic modulus (E) can then be defined by substitution. With these equations, the calculation of the corresponding Young’s modulus at 2 Hz for the control dogs (assuming \( h/2R = 0.03 \)) is \( E = 3.713 \pm 0.040 \times 10^6 \) dyne cm\(^{-2} \). If the average radius did not change, then the observed \( Z_0 \) differences would be due entirely to viscoelastic changes and hence a dramatic decrease in stiffness in response to chronic high flow. There certainly is a diameter change during high-flow loads. This mean diameter increase could be as high as 40% as seen in some atrial septal defect (ASD) patients (Jarmakani et al., 1971). Pulmonary artery diameters of the high-flow animals averaged 10% larger than the controls when assessed by circumference measurements during instrumentation. Utilizing a 10% increase in radius and assuming no change in the \( h/2R \) ratio, calculations of Young’s elastic modulus for A reveals \( E = 3.117 \pm 0.010 \times 10^6 \) dyne cm\(^{-2} \) (\( P < 0.05 \)). A 40% increase in diameter for group B would only return \( E \) to the normal range (Fig. 5). It is a fundamental passive wall material property of blood vessels for the elastic modulus to increase as the strain increases (McDonald, 1974). Thus, even if dilation were the predominant cause of decreased \( Z_0 \), vessel stiffness does not increase and in fact must decrease relative to passive effects of increased pulmonary arterial pressure and diameter. This is analogous to moving a stress-strain curve to the right and downward.

Energy Consequences of Reduced Impedance

As flow increases, vascular channels are recruited, reducing resistance and, therefore, reducing the increased work associated with the elevated mean flow. Since mean work normalized to flow increases, this mechanism is not perfect. In contrast, the pulsatile work for each milliliter of blood flow is the same in all of the preparations studied. Decreased stiffness and dilation can progressively reduce impedance to pulsatile flow. If the mechanisms decreasing impedance did not function as the flow loads increased, then the potential energy (Wo) used in creating pulsations also would have increased. To demonstrate the magnitude of this effect, we can recalculate Wo for groups A and B but substitute the impedance relationships of the control (i.e., no adaptation) which results in hypothetical pulsatile potential energy requirements of A = 173 mW and B = 569 mW compared to the measured A = 87 mW and B = 88 mW (control Wo = 49.5 mW). Thus, the reduced \( Z_0 \) and \( Z_0 \) effect a power savings for the pulsatile terms of 172% in group A and 962% in group B. It can be concluded therefore that this mechanism is of major significance in terms of reducing the transfer of energy from the right ventricle to the pulmonary vascular bed.

Pulmonary Hypertension and Chronic High-Flow Stress

Increased wall stiffness in established pulmonary hypertension has been reported by several authors (Milnor et al., 1969; Patel et al., 1962; Elkins et al., 1974; Caro and Harrison, 1962). Milnor et al. (1969) reported impedance data on seven patients with mitral valve disease and pulmonary hypertension showing higher \( Z_0 \) and \( C_0 \) with progressive elevations of pulmonary artery pressures; all of these patients had elevated left atrial pressures and normal or decreased blood flows. While noting a large hydraulic capacitance and essentially normal elastic moduli in four ASD patients with normal pulmonary artery pressures, Greenfield and Griggs reported three hypertensive ASD patients with mark-
edly elevated pressure-strain elastic moduli (Greenfield and Griggs, 1963). Jarmakani et al. (1971) found in children that the effects of flow and pressure were independent and additive; despite larger pulmonary artery radii, normotensive ASD patients had normal elastic moduli, but the patients with pulmonary hypertension (e.g., high pressure ventricular septal defect) had increased stiffness. Another laboratory found increased elastance in the main pulmonary arteries of normotensive ASD patients (Boughner and Roach, 1971). Thus, while the viscoelastic properties appear to be primarily dependent on pulmonary artery pressures, a spectrum of adaptation to flow seems to exist in the clinical studies available.

Chronically increased flow alone has long been known to be well tolerated from the standpoint of histological alterations of pulmonary vascular obstructive disease. Traditionally, this has been attributed to the decreased resistance effected by parallel channel recruitment. This certainly occurs (particularly in acute situations) and functions to minimize mean pressure elevations with increasing flows. However, in this study, we have also demonstrated decreased impedance to pulsatile flow in a chronically elevated pulmonary blood flow model. This lower impedance is a consequence of both proximal vessel dilation and altered vessel wall viscoelastic characteristics. This impedance alteration reduces the ultimate work load of the right ventricle and the transmission of energy to the precapillary bed. We hypothesize that this impedance adaptation by the pulmonary arteries is an important component of the remarkable tolerance of the pulmonary vascular bed to chronically elevated blood flow.

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Pulmonary vascular impedance analysis of adaptation to chronically elevated blood flow in the awake dog.

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