Pulmonary Vascular Response
to Exercise in the Dog

By Ronald C. Elkins and William R. Milnor

ABSTRACT

The effects of exercise on the pulmonary circulation were studied in seven experiments on five dogs. Pulsatile pulmonary arterial flow and pressure and left atrial pressure were measured by chronically implanted transducers; pulmonary vascular input impedance, resistance, and hydraulic power were computed. The average effects of running on a treadmill at 6.5 mph, as compared with the resting state, were an increase in cardiac output from 2.59 liters/min to 5.30 liters/min, a rise in mean pulmonary arterial pressure from 18 mm Hg to 28 mm Hg, and no consistent change in mean left atrial pressure. Pulmonary vascular resistance fell from 482 dyne sec cm$^{-5}$ at rest to 372 dyne sec cm$^{-5}$ during exercise. Characteristic input impedance rose from 147 dyne sec cm$^{-5}$ at rest to 199 dyne sec cm$^{-5}$ during exercise, and the oscillations of the impedance modulus with frequency decreased in magnitude. These changes were consistent with passive distention of the pulmonary vessels, decreasing the compliance of the large arteries and improving the impedance match between proximal and distal vessels.

KEY WORDS

vascular impedance
characteristic impedance

The hemodynamic changes that take place in the pulmonary bed with exercise have never been satisfactorily explained, although there is abundant evidence that some alteration of vascular caliber or configuration does occur (1–7). The relatively small increase in mean pulmonary arterial pressure as cardiac output rises during exercise was one of the earliest observations in human cardiac catheterizations (8), and for a time it was thought that pulmonary blood flow could increase as much as threefold with no elevation of pulmonary arterial pressure. Subsequent work, however, has shown a small but consistent rise in mean pulmonary arterial pressure even with mild degrees of exercise, in both man (1–5) and the dog (6, 7), and a gradual further rise as the level of exercise and cardiac output increase (2, 3, 6, 7). Some investigators have reported a fall in pulmonary vascular resistance (3, 4, 6), whereas others have noted a rise (1, 5), and interpretation of these conflicting results is made still more difficult by the fact that
Simultaneously recording the flowmeter signal and was determined, and correction factors were applied in the calculation of results (13, 16). The wall-to-external radius ratio of 0.1, the luminal area of the artery with the probe in place averaged 1.25 cm². Frequency response of the flowmeter was determined, and the approximate location of the vessels involved (12, 13). Pulmonary vascular impedance is particularly sensitive to alterations in arterial compliance (13, 14), which is to some extent under autonomic nervous control (15), so that one effect of an active vasomotor response is a modification of the relationship between pulsatile pressure and flow. With this in mind, the present experiments were designed to measure the effects of exercise on pulmonary vascular input impedance as well as resistance to describe the response more completely, learn whether large as well as small vessels are affected, and gain information about the mechanisms involved. The hydraulic energy associated with pulmonary blood flow during exercise was also measured, as a way of gauging the net effect of the pulmonary vascular alterations on circulatory function.

Methods

Seven experiments were carried out in five mongrel dogs weighing 10.2–23.1 kg (mean 16.2 kg). In all experiments, pulmonary arterial blood flow was measured, using hinged coreless probes, with Statham K-2000 electromagnetic flowmeter. The diameter of the pulmonary artery before the probe was applied averaged 1.5 cm, and probes were selected that would not constrict the cross-sectional area by more than 15%. Assuming a wall-to-external radius ratio of 0.1, the luminal area of the artery with the probe in place averaged 1.25 cm². Frequency response of the flowmeter was determined, and correction factors were applied in the calculation of results (13, 16). The flowmeter and probes were calibrated in vivo by simultaneously recording the flowmeter signal and an indicator dilution curve for determination of cardiac output. Cardiogreen dye was the indicator used. Pulmonary arterial pressure was measured in three experiments with a Statham SF-1 catheter-tip pressure transducer and in four experiments with a chronically implanted Microsystems model 1017 miniature pressure transducer. Left atrial pressure was measured in six of the seven experiments with a chronically implanted miniature transducer and in one experiment with a polyvinyl catheter filled with heparinized saline and attached to a Statham P23 Db transducer. The dynamic response of the gauges was tested after each experiment. The Statham SF-1 catheter-tip gauge had a natural frequency above 1,000 Hz, with a damping factor of 0.016. The Microsystems pressure transducer had a natural frequency above 1,600 Hz, with a damping factor of 0.23. In vivo calibration of the implanted miniature pressure transducers was performed at the time of insertion of the transducer by simultaneously measuring the output of the transducer and pulmonary artery pressure and left atrial pressure through catheters inserted into the left atrium and pulmonary artery. This was repeated when the animals were killed, as a further check of calibration. A horizontal plane through the middle of the thorax at the level of the heart constituted the hydrostatic reference level for zero pressure. Measurements of pressure and flow were made in the resting expiratory phase of respiration.

Preparation

A left thoracotomy was performed under sterile conditions with pentobarbital anesthesia (20 mg/kg iv), and a flowmeter was placed around the main pulmonary artery. When the Microsystems pressure transducer was used in the pulmonary artery, it was inserted through a small incision in the vessel proximal to the flow probe and sutured in position. When a catheter-tip transducer was used instead, the catheter was not inserted until the day of the experiment, at which time an incision was made over the jugular vein under local anesthesia (lidocaine) and the catheter introduced by that route. Another miniature transducer (or, in one experiment, a polyvinyl catheter) was inserted in the left atrial appendage through a small stab wound for measurement of left atrial pressure. The cables and external plugs (and left atrial catheter, if used) were brought out through the skin on the dorsolateral chest wall. The animals were allowed to recover from the operation and were then trained daily to lie quietly in the laboratory for recording of resting data and to exercise on a horizontal treadmill running at 6.5 mph (10.5 km/hr). Experiments were usually carried out in...
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The third postoperative week, but times ranged from 5 to 62 days after the operation. In each experiment, measurements were made under three conditions: (1) at rest, with the animal quiet and in the prone position, 10–20 minutes before exercise; (2) standing on the treadmill, 30 seconds to 2 minutes before exercise; (3) after running steadily on the treadmill for 1–2 minutes. A steady state in the variables measured was usually reached in 10–30 seconds and maintained for the remainder of the exercise period. The effect of prolonged exercise was not studied in these experiments, although further changes are known to occur in man after 10 minutes or more of constant exertion (2, 3). Unless otherwise specified, the changes in pulmonary hemodynamics with exercise discussed in this paper refer to differences between the resting state (prone) and exercise.

DATA ANALYSIS

Data were recorded in analog form on magnetic tape (Honeywell model 8100). Analog-to-digital conversion was accomplished electronically (Computer of Average Transients model 400-B, Technical Measurements Corp.). Digital data were stored on punched cards and analyzed on an IBM 7094 or CDC 3300 digital computer.

The computation of impedance was based on either harmonic analysis or spectral analysis by cross correlation. The methods for calculation of impedance and hydraulic power using harmonic analysis have been reported previously (13, 14). Components with a frequency greater than 12 Hz were not calculated. The computation of impedance by spectral analysis was adapted from the work of Randall (17) and Taylor (18).

In calculating hydraulic energy per unit time, or power, in the pulmonary artery, the total energy was separated into two components, potential (the product of pressure and volume) and kinetic (half the mass of the blood multiplied by the square of its velocity). These two components were further subdivided into a portion associated with mean pressure and flow (the energies that would exist if there were no oscillations around the means) and the part associated with pulsations. Our methods of calculating these energy components have been described elsewhere (14). The pressure equivalent of kinetic energy, which equals the kinetic energy/ml of blood, was calculated as a function of time from the instantaneous velocities of blood flow by multiplying one-half the density of blood (taken as 1.05 g/ml) by the square of the velocity.

In each experiment, the average of the impedance moduli between 2 and 12 Hz was calculated and designated the characteristic input impedance. This parameter is analogous to the characteristic impedance of a transmission line, which is defined as the impedance in the absence of reflected waves. In a vascular bed, it is determined by the dimensions and elastic properties of the blood vessels (12, 19), predominantly those of the large artery at the input. The magnitude of the frequency-dependent oscillations of impedance modulus around the characteristic input impedance, which are produced by reflections, was expressed as the ratio of the difference between the minimum and maximum value to the characteristic impedance.

The significance of the observed changes in pulmonary vascular resistance and characteristic input impedance was evaluated by comparison with measurements of the reproducibility of these measurements under constant conditions. Duplicate determinations of characteristic impedance in previous experiments in our laboratory (21 pairs of measurements, 1–20 minutes apart, in 13 dogs) show that the second determination can be expected to fall within ± 20% of the first in 95% of cases (mean ratio 0.97). Similar comparison of duplicate measurements of pulmonary vascular resistance (20 pairs in 13 dogs) gave a ratio of second to first determinations of 0.98 with a standard deviation of 0.093. The changes observed in these variables with exercise in the present experiments were compared with these duplicate controls by Student's t-test.

Results

Experimental data are summarized in Table 1 in the form of averages and ranges of observed values in the seven experiments. Figure 1 shows a continuous record of the measurements in one animal. In the control period, while the dogs were at rest in the prone position, the data were similar to those reported previously by many investigators: an average cardiac output of 2.59 liters/min, stroke volume of 25 ml, mean pulmonary arterial pressure of 18 mm Hg (systolic/diastolic pressure 28/12 mm Hg), mean left atrial pressure of 3 mm Hg, and pulmonary vascular resistance of 482 dyne sec cm⁻⁵. Characteristic input impedance of the pulmonary bed averaged 147 dyne sec cm⁻⁵ at rest (2381 dyne sec cm⁻⁵ kg, when adjusted for body weight), and the ratio of oscillations of the modulus to the characteristic value was 0.86. The first minimum of impedance modulus fell between 1.9 and 4.0 Hz (mean 2.8 Hz). Impedance phase was negative (flow leading pressure) at
**TABLE 1**

Summary of Experimental Data from Seven Experiments

<table>
<thead>
<tr>
<th></th>
<th>Rest (prone)</th>
<th>Standing</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>16.2</td>
<td>130</td>
<td>234</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>10.2 - 23.1</td>
<td>94 - 182</td>
<td>143 - 287</td>
</tr>
<tr>
<td>PA Blood flow (ml/sec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>43.1</td>
<td>179</td>
<td>24.9</td>
</tr>
<tr>
<td>Peak</td>
<td>29.4 - 59.0</td>
<td>120 - 226</td>
<td>10.5 - 37.1</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>24.9</td>
<td>182</td>
<td>23.1</td>
</tr>
<tr>
<td>Maximum acceleration (cm/sec²)</td>
<td>2110</td>
<td>1400 - 3130</td>
<td>1900 - 3650</td>
</tr>
<tr>
<td>Pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean PA</td>
<td>18.2</td>
<td>14.7 - 22.9</td>
<td>14.7</td>
</tr>
<tr>
<td>Mean LA</td>
<td>3.4</td>
<td>1.1 - 6.0</td>
<td>14.7</td>
</tr>
<tr>
<td>PA - LA</td>
<td>14.8</td>
<td>10.9 - 17.9</td>
<td>10.7 - 19.2</td>
</tr>
<tr>
<td>Pulmonary vascular resistance (dyne sec cm⁻¹)</td>
<td>482</td>
<td>275 - 809</td>
<td>416 - 621</td>
</tr>
<tr>
<td>Characteristic input impedance (dyne sec cm⁻¹)</td>
<td>147</td>
<td>66 - 312</td>
<td>164 - 370</td>
</tr>
<tr>
<td>Impedance oscillations*a</td>
<td>0.86</td>
<td>0.45 - 1.55</td>
<td>0.73</td>
</tr>
<tr>
<td>Hydraulic power, (mw)</td>
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<td></td>
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<tr>
<td>Potential, oscillatory</td>
<td>39.4</td>
<td>32 - 96</td>
<td>41.9</td>
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<tr>
<td>Potential, total</td>
<td>151.3</td>
<td>105 - 291</td>
<td>172.7</td>
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<tr>
<td>Kinetic, oscillatory</td>
<td>35.6</td>
<td>10 - 71</td>
<td>41.7</td>
</tr>
<tr>
<td>Kinetic, total</td>
<td>39.5</td>
<td>11 - 78</td>
<td>47.4</td>
</tr>
<tr>
<td>Power component ratios</td>
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<tr>
<td>Oscillatory/total</td>
<td>0.40</td>
<td>0.30 - 0.43</td>
<td>0.38</td>
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<tr>
<td>Kinetic/total</td>
<td>0.19</td>
<td>0.08 - 0.28</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Impedances and hydraulic powers refer to pulmonary arterial flow. PA = pulmonary artery; LA = left atrium. *Difference between maximum and minimum modulus divided by characteristic impedance.

**FIGURE 1**

Continuous record in one experiment during the resting control period, standing, and running. Q<sub>PA</sub> = pulmonary arterial blood flow in ml/sec; P<sub>PA</sub> = pulmonary arterial pressure in mm Hg; P<sub>LA</sub> = left atrial pressure in mm Hg.

frequencies below this minimum and generally positive at higher frequencies. All these properties of the input impedance spectrum resembled those previously reported for the
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FIGURE 2

Pulmonary vascular input impedance at rest and during exercise in one experiment. Input impedance modulus is in dyne sec cm\(^{-6}\), and phase is in radians. Negative phase angles denote that flow leads pressure. Pulmonary vascular resistance is plotted at zero on the frequency scale.

When the animal stood quietly on the treadmill, heart rate and cardiac output were higher than at rest (26% and 16%, respectively) with little or no change in stroke volume.

With exercise, the heart rate and cardiac output increased to approximately twice their resting levels, and pulmonary arterial pressure increased by 25–73% (average mean pulmonary arterial pressure 23.0 mm Hg, systolic/diastolic pressure 40/16 mm Hg). There was no consistent change in mean left atrial pressure, which decreased in four and rose in one of the five animals in which it was measured. The mean pressure difference between pulmonary artery and left atrium increased in all experiments, but always to a lesser degree than the cardiac output, so that pulmonary vascular resistance during exercise was lower than at rest (average decrease 18%, range 5% to 34%, \(P < 0.01\)). Peak flow rose by 22–82% with exercise, while changes in stroke volume ranged from −28% to 26%. Peak and mean flow velocities in the pulmonary artery averaged 136 and 35 cm/sec, respectively, at rest and increased to 176 and 71 cm/sec during exercise. Maximum acceleration of blood in the pulmonary artery at rest averaged 2110 cm/sec\(^2\) and rose with exercise to an average of 4800 cm/sec\(^2\).

The changes in impedance associated with exercise were similar to the example shown in Figure 2 in each experiment. The characteristic impedance increased in six experiments (8–142%) and fell in one (−35%), giving an average value during exercise of 199 dyne sec cm\(^{-5}\) (3324 dyne sec cm\(^{-5}\) kg). The average change was an increase of 46% above the resting value \((P < 0.02)\). The oscillations of impedance modulus diminished with exercise, both absolutely and in proportion to the characteristic impedance, in six experiments. The frequency of the minimum modulus increased in four instances (range 0.3 to 1.1 Hz) and decreased in three (range −0.3 to −0.8 Hz). The zero-crossing of the impedance phase spectrum shifted to frequencies 0.2–0.5 Hz higher than at rest in each experiment.

HYDRAULIC POWER

Hydraulic power was computed at rest and during exercise in six of the seven experiments, and the mean values are illustrated in Figure 3. Total input power at rest was 191 mw, of which 19% was kinetic energy per unit time, and the remainder was potential power \((\text{pressure} \times \text{flow})\). Forty percent of the input power was associated with pulsations and 60% with mean, or “steady-flow,” terms. Total input power at rest was somewhat higher than in our earlier series of experiments in conscious dogs (14), presumably because the present animals were larger and had higher cardiac outputs. The velocities of flow were also higher than in the previous report, accounting for the proportionally larger kinetic power term.
With exercise, total power increased by a factor of 3.1, and all components shared in this increase. The ratio of oscillatory to mean-term components decreased with exercise in each experiment, the average ratios being 0.40 at rest and 0.33 during exercise. Total kinetic power increased from 40 mw at rest to 126 mw in exercise and amounted to approximately one-fifth of the total input power in both situations.

**Discussion**

The principal changes in the pulmonary vascular input impedance spectrum with exercise consisted of an increase in the characteristic impedance, a decrease in magnitude of the oscillations of impedance modulus with frequency, and a slight rise in the frequency at which the impedance phase angle changed from negative to positive. All of these changes were consistent with passive distention of the pulmonary vascular bed as the arterial transmural pressure rose, the elevation of pressure in turn being attributable to increased cardiac output. The reasoning behind this interpretation of the results follows.

The characteristic impedance at the input of a vascular bed is determined by the properties of the large arteries just beyond the inlet (12, 19). The main pulmonary arteries become stiffer as they are distended (20), as do other arteries, and this diminished compliance causes an increase in wave velocity and characteristic impedance (12). The rise in impedance observed with exercise could, therefore, be the passive result of distention by the increased pulmonary arterial pressure. The impedance changes in these experiments were quantitatively as well as qualitatively consistent with this explanation. From Patel's data (20) on distensibility, we estimate that a rise in mean pulmonary pressure from 25 to 38 cm H2O (the average change with exercise in our experiments) would decrease the volume distensibility of the artery from 2.25% to 1.4% per cm H2O. The nominal wave velocity and the characteristic impedance of the artery are inversely proportional to the square root of the distensibility, so this would result in a 27% increase in impedance, which is close to the 35% increase we observed.

In evaluating the distensibility changes in the main pulmonary artery, no allowance was made for the loading effect of the flow transducer on the pulmonary artery. The presence of this short segment of nondistensible artery would increase the characteristic impedance, and therefore our estimates of characteristic impedance are higher than the true value by an undetermined amount.

The frequency-dependent oscillations of input impedance modulus around the characteristic value depend on reflections originating distally in the bed. The magnitude of such reflections, and hence of the impedance oscillations, is a function of the changes of impedance at each point of branching in the vascular tree. In general, characteristic impedance increases gradually toward the distal part of the arterial tree (12, 19). Anything that raises the wave velocity in the larger proximal arteries to a level nearer that in the distal bed will tend to improve the impedance match at branch points and thereby reduce reflections. Passive distention of the large arteries would have just this effect, provided the impedance...
of distal vessels did not rise at the same time. Although transmural pressure presumably rises to some extent in the small pulmonary vessels during exercise, as it does in the main pulmonary artery, our results thus indicate that the effects on local vascular impedance are different. The most probable explanation is that in the microcirculation the influence of increased total vascular cross section, which tends to reduce characteristic impedance (12), outweighs any increase in the stiffness and impedance that might be produced by distention. The pulmonary capillary blood volume increases during exercise (10), presumably by the opening of a large number of capillaries that were closed at rest (21) and some degree of actual capillary distention (22). Such an increase in the number of parallel channels would lower the characteristic impedance as well as the resistance of the arterioles and capillary bed. The net effect of such a fall in impedance in the distal part of the bed, combined with a rise of input impedance in the proximal arterial tree, would be an improved matching of impedances and consequently a lowering of the reflection coefficient. An increase in mean pulmonary arterial pressure, in other words, in the absence of any alteration of vasomotor activity in the pulmonary vessels, would lower distal and raise proximal impedances in the arterial tree, leading to a more nearly constant impedance in the successive generations of vessels and thus to a decrease in reflections.

The changes in pulmonary vascular volume that have been observed in exercise are consistent with this interpretation and with the changes in impedance and resistance reported here. The increase in capillary volume with exercise amounts to about 80% (10), and if we assume that this is the result of opening of capillaries previously closed (23), neglecting distention, and that these newly opened vessels are identical in dimensions with those open at rest, the capillary resistance would fall by 56%. If the capillary resistance at rest amounts to one-third of the total pulmonary vascular resistance (24), this opening up of capillaries would reduce the total pulmonary vascular resistance to 81% of the resting value, which is approximately the change we observed.

All of the changes we observed in the pulmonary vascular input impedance spectrum are thus consistent with the effects of passive vascular distention by increased transmural pressure. Alterations in the active tension of pulmonary vascular smooth muscle need not be invoked to explain these results, and indeed the removal of sympathetic impulses to the pulmonary vessels by chronic thoracic sympathectomy has somewhat different effects, lowering both impedance and resistance (Milnor and Elkins, unpublished data). Stimulation of the stellate ganglia, on the other hand, stiffens the large pulmonary arteries and raises their input impedance (15), so that the possibility of an increase in sympathetic impulses to the proximal pulmonary arteries during exercise cannot be ruled out by the data now available.

HYDRAULIC POWER

The calculations of hydraulic power in these experiments demonstrate that during exercise, as at rest, the energy per unit time associated with pulsations of flow (14) is one-third or more of the total input power. The relatively large values of kinetic energy during exercise also suggest that the conversion of kinetic energy to pressure as the diverging arterial tree increases in cross section may have a significant influence on the microcirculation under these conditions. The magnitude of this effect has generally been considered to be negligible on the basis of calculations made from mean flow velocities, but the mean velocity of blood flow can be misleading in this respect, for kinetic energy is a function of the square of the instantaneous velocity and with pulsatile flow the mean kinetic energy cannot be calculated from the mean velocity (14). The instantaneous kinetic energy/ml blood calculated from the pulmonary arterial velocities during exercise was the equivalent of a pulsatile pressure of 10.2 mm Hg (peak-to-peak) with a mean of 3.7 mm Hg. At rest, the corresponding averages were a pulse of 6.0 mm Hg with a mean of 2.0 mm Hg. Since the
blood velocity constantly diminishes as the total arterial cross section becomes greater, reaching very low velocities in the capillaries, almost all of this energy is converted to pressure in the precapillary bed. The conversion takes place gradually, however, at each branching of the system where cross section increases, and the pressures thus generated are partially dissipated by viscous flow en route to the microcirculation. The contribution of kinetic energy to the pressures that finally reach the entrance of the capillaries could be assessed accurately only by a detailed analysis, segment by vascular segment, of transmission in the arterial tree. If, however, we assume as a first approximation that one-half the pulmonary arterial pressure pulse is transmitted to the midcapillary region and that one-half the pulmonary vascular resistance is proximal to that level, then the conversion of the kinetic energy in the pulmonary arterial tree during exercise in these experiments contributed a pulse of about 5.1 mm Hg, with a mean of 1.8 mm Hg, to the intravascular pressure in that region. These are relatively small pressures, but may well be significant in the critically balanced forces that determine the patency of pulmonary capillaries.

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References


**Books Received**

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