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Effect of cardiac output on pulmonary hemodynamics

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Abstract. The purpose of this study was to test the hypothesis that there is a direct relation between pulmonary arterial input resistance and compliance in seven anesthetized cats. Cardiac output was altered by varying the direction and flow through an arteriovenous fistula with a roller pump. Pulmonary arterial input impedance was calculated from the Fourier analysis of the pressure and flow waveforms. Input resistance, pulmonary arterial compliance and characteristic impedance were estimated from the impedance spectra with a lumped parameter model. We found that pulmonary arterial compliance increased with cardiac output ($P < 0.002$) but characteristic impedance was independent of flow. The observed response has the effect of reducing the hydraulic power lost by the pulmonary vasculature due to wave reflection. In three additional cats we measured the diameter of the main pulmonary artery by sonomicrometry. We found a linear relation between mean pulmonary arterial pressure and pulmonary arterial diameter during alterations of cardiac output. This result suggests that the increase of pulmonary arterial compliance with cardiac output is due to geometric factors rather than changes in vascular elastic properties.

Cat; Elasticity; Impedance; Pressure–diameter relation; Pulmonary arterial compliance; Wave reflection

There are differing hypotheses about the response of compliance to changes in resistance in the pulmonary circulation. On one hand, Piene and Sund (1982) suggested that there should be a direct relation between pulmonary arterial compliance and pulmonary input resistance to maintain right ventricular hydraulic power output at an optimal value. They suggested that under resting conditions the input resistance of the pulmonary vasculature is matched to the apparent source resistance of the right ventricle so that the right ventricle operates at an optimal hydraulic power output (Piene and Sund, 1982). A change of input resistance would disturb this relation, but the pulmonary vasculature may compensate by altering pulmonary arterial compliance in the same direction. Thus, pulmonary arterial compliance should decrease to compensate for a decrease in input resistance. On the other hand, Reuben *et al.* (1970) suggested that there is an inverse

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relation between pulmonary arterial compliance and pulmonary arterial resistance so that the product of these two variables is constant. This product is the time constant of the Windkessel. They argued that the pulsatile properties of the pulmonary microcirculation would be maintained if this product is held constant. Control of the pulsatile properties of the pulmonary vasculature may be of importance because they have been shown to influence lung water balance (Hauge and Nicolaysen, 1979) and the magnitude of the hypoxic pulmonary vascular response (Ellsworth *et al.*, 1983). If there was regulation of the pulsatile properties of the proximal pulmonary arteries as has been proposed for the pulmonary microcirculation, one would anticipate an inverse relation between pulmonary arterial compliance and pulmonary arterial input resistance.

The purpose of this report is to describe two series of experiments. The first series was designed to determine whether there is an inverse or direct relation between pulmonary arterial compliance and input resistance in response to alterations of cardiac output. The second series of experiments was performed to determine the mechanisms responsible for the changes in pulmonary arterial compliance.

Methods

Experimental preparation. Anesthesia was induced in ten cats (average body weight 3.6 kg, range 2.6–6.5 kg) with ketamine (Parke-Davis) 20 mg/kg intramuscularly and maintained with 0.67 ml/kg alpha chloralose (Sigma) solution intravenously. A midline thoracotomy was performed, the pericardium was opened and the main pulmonary artery was dissected free of surrounding tissue. Pancuronium bromide (Organon) 0.1 mg/kg intravenously was used for muscular paralysis. The animals were ventilated through a trachea cannula at approximately 12 breaths per minute with a tidal volume sufficient to maintain an end-tidal F_{CO_2} of 5°. The animals were ventilated with 100% oxygen through a Harvard ventilator (Model 618) to which was attached a microswitch producing a 5 volt pulse to signal end expiration. In seven animals, pulmonary arterial blood flow was measured with an electromagnetic flow probe (Statham SP7515) around the main pulmonary artery. The flow probe was coupled to a Statham 2202 flowmeter which uses a 100 Hz lowpass filter. This system has a 1.8 degree/Hz phase shift with no appreciable effect on amplitude. In the other three animals, we sutured 3 mm piezoelectric crystals on the adventitia of the main pulmonary artery to measure pulmonary arterial diameter. Signals from the ultrasonic crystals were processed with a sonomicrometer (Pagani *et al.*, 1978). The sonomicrometer (Tritron Technology, San Diego, CA) has a resolution of 0.004 cm and uses a transitional filter (– 3 db at 67 Hz; 24 db/octave rolloff and phase lag of 1.9 degrees/Hz). Pulmonary arterial pressure and right ventricular pressure were measured separately with catheter tipped micromanometers which have a flat frequency response up to 2000 Hz (Millar model PC-330). Systemic arterial blood pressure was measured through a fluid-filled catheter in the right carotid artery with a pressure transducer (Gould P23ID). An abdominal incision was made and catheters were placed in the inferior vena cava with its tip close to the right

atrium and in the abdominal aorta with its tip close to the renal arteries. Heparin (200 units/kg) was given intravenously to prevent clotting. The catheters were used to form an arteriovenous fistula by joining the free ends to a roller pump (model 7523-00, Masterflex Barrington, Illinois) which was used to control flow through the fistula.

Protocol. Cardiac output was altered by varying both the direction and the amount of flow through the arteriovenous fistula. After allowing the animal to stabilize following surgical instrumentation, resting cardiac output was determined with the electromagnetic flow probe. The digital display on a roller pump was used to assess flow through the fistula. A left to right shunt was produced by varying flow through the roller pump from zero to 25, 50, 75 and 100% of resting cardiac output and then back to zero in a stepwise manner. Flow through the shunt was then reversed to produce a right to left shunt of 25% of resting cardiac output and then returned to zero. At each level, fistula flow was maintained until pulmonary and systemic arterial pressures had stabilized prior to each period of data collection. If the cardiac output at zero shunt flow was not within $\pm 20\%$ of its initial value, it and subsequent data were excluded from further analysis.

A similar protocol was used in three experiments designed to measure changes of pulmonary arterial diameter except that flow through the arteriovenous shunt was altered in increments of 50 $ml \cdot min^{-1}$ as judged from the digital display on the roller pump. This approach was used because there was insufficient space on the main pulmonary artery to place an electromagnetic flow probe as well as the ultrasonic crystals, therefore resting cardiac output was not measured.

Calculation of results. Pulmonary arterial pressure, flow, right ventricular pressure, systemic blood pressure, the QRS indicator from the EKG signal and the end-expiration indicator from the microswitch on the ventilator were digitized (Data Translation, DT2801A) at a 500 Hz sampling rate for ten breaths. The QRS indicator was used to determine the beginning and end of each heart cycle and to determine end-diastole. Single cardiac cycles were obtained at end-expiration from ten successive breaths and the digitized data stored for data analysis off-line. We determined mean pulmonary arterial pressure and flow, mean right ventricular pressure, mean systemic arterial pressure and maximal value of the first derivative of right ventricular pressure (dP/dt_{max}) from these data. The pulsatility index (PI) was calculated as the ratio of pulmonary arterial systolic pressure to mean pressure which is analogous to the index used by Reuben *et al.* (1970).

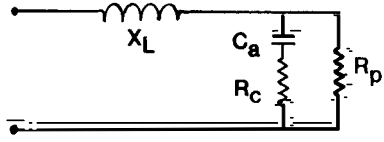

Fig. 1. Electrical representation of the lumped parameter model. Diagram shows the relation between the inductor (X_L), the capacitor (C_a) and the two resistors R_c and R_p.

Pulmonary arterial input impedance was calculated by direct Fourier analysis as described elsewhere (Grant and Paradowski, 1987). In brief, input resistance was calculated as mean pulmonary arterial pressure divided by mean flow. Characteristic impedance and pulmonary arterial compliance were estimated with a four element lumped parameter model (fig. 1) which consists of an inductance (X_L) two resistors (R_c and R_p) and a capacitance (C_a). C_a, R_c and R_p were used to represent pulmonary arterial compliance, characteristic impedance and input resistance respectively.

Westerhof *et al.* (1978) developed equations which enable the measured pressure and flow waves to be resolved into their forward and reflected wave components in the time domain. We used the recovered value for characteristic impedance and the measured pressure and flow waves to calculate the forward pressure and flow waves.

$$P_f(t) = 0.5[(P(t) + Z_c\dot{Q}(t)] \quad (1)$$

$$\dot{Q}_f(t) = Z_c/P_f(t) \quad (2)$$

where $P(t)$ and $\dot{Q}(t)$ are the measured values of pressure and flow at an instant in time, $P_f(t)$ and $\dot{Q}_f(t)$ are the corresponding values for the forward wave, and Z_c is characteristic impedance. $P_f(t)$ and $\dot{Q}_f(t)$ are the corresponding values of pressure and flow for the forward wave. Hydraulic powder was calculated for both the forward and the measured pressure and flow waves by summing the rates of pressure energy and kinetic energy as follows:

$$\dot{W}_m = (1/N)\sum_{n=1}^{n=N} P(t)\dot{Q}(t) + \rho(2N\pi^2R^4)^{-1}\sum_{n=1}^{n=N}(\dot{Q}(t))^3 \quad (3)$$

where $\dot{W}_m$ is the total hydraulic power of the measured wave, N is the total number of data points in the heart cycle measured at 0.002 msec increments ($\triangle t$), and R is the radius of the main pulmonary artery which was assumed to be half the inner diameter of the perivascular flow probe. The same equation was used to calculate the hydraulic power in the forward wave ($\dot{W}_f$) by using $P_f(t)$ and $\dot{Q}_f(t)$ in place of $P(t)$ and $\dot{Q}(t)$, respectively. The term $\dot{W}_m/\dot{W}_f$ is known as the energy transmission ratio (Fung, 1984) and is a measure of the proportion of the hydraulic power in the forward wave to be transmitted into the main pulmonary artery.

The relation between pressure and diameter at different frequencies was analyzed in a manner similar to that used for pressure and flow; the Fourier series for the pressure and diameter waves were obtained from single cardiac cycles selected at end expiration from ten successive breaths. Diameter was corrected for the frequency response of the sonomicrometer. The pressure–diameter relation was obtained by dividing the modulus for diameter by the modulus for pressure at each harmonic; the phase relation was defined by subtracting the phase angle for diameter from the phase angle for pressure. Therefore, a positive phase angle indicates that changes in pressure lead changes in diameter.

Statistical methods. The hemodynamic variables were tested to determine if they were related to changes in cardiac output by analysis of covariance (Snedecor and Cochran,

1980). The changes in cardiac output were expressed as percent changes from the initial cardiac output measured under conditions of zero shunt flow at the beginning of each experimental preparation. This approach avoids introducing bias related to differing initial cardiac outputs due to differences in animal size. Changes in hemodynamic variables from baseline values were used in absolute units with the exception of characteristic impedance and pulmonary arterial compliance which were analyzed with a log normal transformation because the plots of the residuals indicated that its standard deviation was proportional to the predicted mean. Statistical significance was accepted at the 5% level.

Results

Effect of altering cardiac output on input impedance. The changes of cardiac output induced by altering flow through the arteriovenous shunt are shown in fig. 2. The effects of altering cardiac output on pulmonary hemodynamics are shown in table 1. Each hemodynamic variable was related to cardiac output which was expressed as a fraction of its initial value under control conditions. The coefficient was estimated by analysis of covariance. Figure 3 shows that as cardiac output increased there was a significant decrease of input resistance (mean pulmonary arterial pressure divided by cardiac output). This result is prone to bias because cardiac output appears in both the dependent and independent variables. Nevertheless, when the changes in mean pulmonary arterial pressure are plotted against the changes in cardiac output (fig. 3, lower panel), it is apparent that there was a progressive decrease in input resistance as

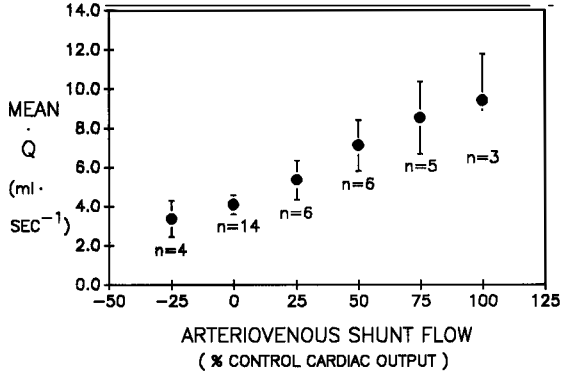

Fig. 2. Effect of arteriovenous shunt flow on cardiac output. This graph plots cardiac output (mean $\dot{Q}$, $ml \cdot sec^{-1}$, ordinate) against flow through the shunt expressed as a percentage of control cardiac output (abscissa). Positive sign indicates arterial to venous shunt flow, negative sign indicates venous to arterial shunt flow. Data are plotted as the mean ± 1 SE. The number of observations were unequal because the protocol was curtailed when difficulties were encountered in withdrawing blood through the shunt which occurred particularly with a right to left shunt at high flows.

TABLE 1

Effect of altering cardiac output on hemodynamic variables.

Variable	Units	Control value	Coefficient (Units/control Q)	*P* value
Z_c	kdyne · cm^{-5} · sec	0.73 $^{+0.84}_{-0.64}$	0	NS
C_a	kdyne^{-1} · cm^5	0.08 $^{+0.10}_{-0.62}$	117%	0.002
PAP	cm H_2O	24.7 ± 1.4	5.41	<0.0001
PI	dimensionless	1.41 ± 0.04	0.039	0.028
RVEDP	cm H_2O	6.8 ± 1.0	1.9	0.008
RVP	cm H_2O	19.6 ± 1.4	5.3	<0.0001
dP/dt_{max}	cm H_2O · sec$^-$	1210 ± 130	820	<0.0001
HR	min^{-1}	227 ± 7	4	0.013
BP	mm Hg	141 ± 11	−16	0.018
$\dot{W}_m$	milliwatts	13.4 ± 1.6	18.6	<0.0001
$\dot{W}_f$	milliwatts	52.9 ± 15.8	68	0.0052
$\dot{W}_m/\dot{W}_f$	%	39.2 ± 6.0	9	<0.01

Control values are the mean ± SE of the seven animals with no flow through the arteriovenous shunt. Coefficient is the slope of the relation between the variable and the fractional change of cardiac output from its control value and was obtained by analysis of covariance (N = 38). Z_c is characteristic impedance, C_a is pulmonary arterial compliance, PAP is mean pulmonary arterial pressure, PI is pulsatility index, RVEDP is right ventricular end-diastolic pressure, RVP is mean right ventricular pressure, dP/dt_{max} is the maximum rate of change of right ventricular pressure during isovolemic contraction, HR is heart rate and BP is systemic arterial blood pressure, $\dot{W}$ is the hydraulic power in the main pulmonary artery in the measured wave (subscript m) and in the forward wave (subscript f), $\dot{W}_m/\dot{W}_f$ is the energy transmission coefficient.

flow increases. Although there was no significant change of characteristic impedance with cardiac output there was an increase in pulmonary arterial compliance (table 1). This increase in compliance with cardiac output occurred in all seven animals. As a result of the opposing effects of cardiac output on input resistance and pulmonary arterial compliance, the arteriovenous shunt did not have any significant effect on the time constant of the Windkessel: the product of input resistance and pulmonary arterial compliance (fig. 4).

Although the product of input resistance and pulmonary arterial compliance was not altered significantly, there was a significant increase in the pulsatility index (pulmonary arterial systolic pressure divided by mean pressure) with cardiac output (table 1). The increase in cardiac output was associated with an increase in right ventricular end diastolic pressure (RVEDP), mean right ventricular pressure (RVP) and an increase in dP/dt_{max}. Most of the increase in cardiac output occurred as the result of an increase in stroke volume because there was only a small increase in heart rate. There was a decrease in the systemic arterial pressure (BP) as cardiac output increased due to the increased withdrawal of blood from the aorta through the arteriovenous shunt.

Although there was a greater increase in hydraulic power in the forward wave ($\dot{W}_f$)

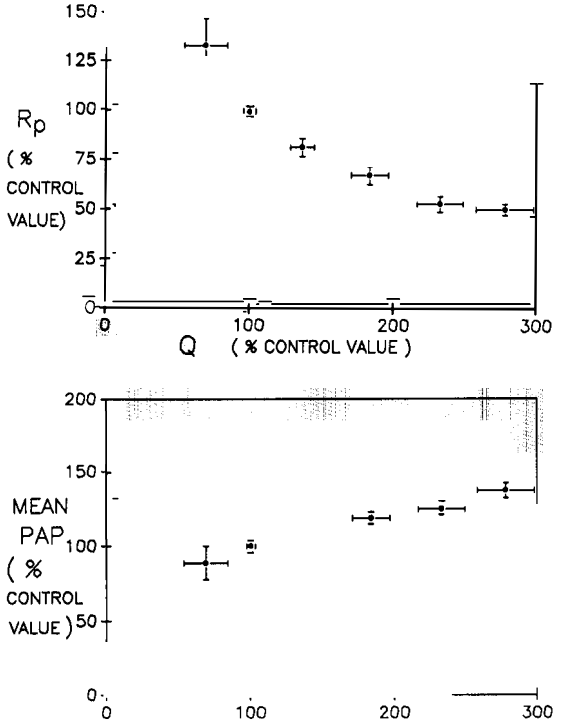

Fig. 3. Upper panel shows the relation between input resistance (R_p) expressed as a percentage of control values (ordinate) against $\dot{Q}$ (abscissa). As $\dot{Q}$ increases, R_p decreases. Data are shown at a level of arteriovenous shunt flow as mean ± 1 SE. Lower panel shows the relation between mean pulmonary arterial pressure (mean PAP) expressed as a percentage of control values (ordinate) and mean cardiac output ($\dot{Q}$) expressed as a percentage of control values (abscissa).

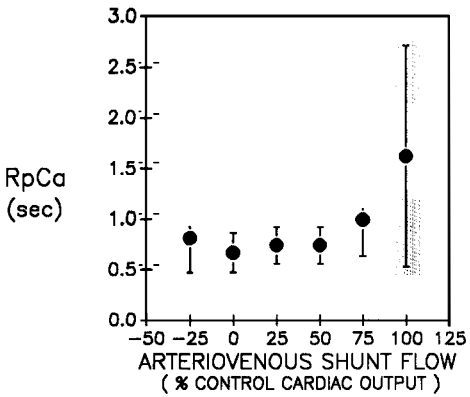

Fig. 4. The effect of arteriovenous shunt flow on the time constant of the Windkessel (R_pC_a). R_pC_a (sec) is plotted on the ordinate. Flow through the shunt expressed as a percentage of control cardiac output on the abscissa. Positive sign indicates arterial to venous shunt, negative sign indicates venous to arterial shunt. Data are shown at each level of flow as mean ± 1 SE. Analysis of variance showed no significant effect of flow on the time constant.

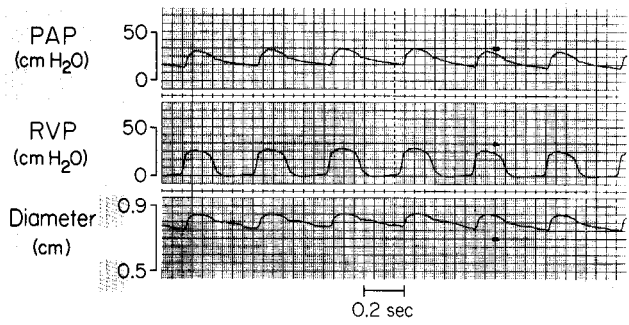

Fig. 5. Chart recording of pulmonary arterial pressure (PAP), right ventricular pressure (RVP) and pulmonary arterial diameter in a cat under control conditions.

than the hydraulic power of the measured waves ($\dot{W}_m$) with cardiac output, the fractional increase of $\dot{W}_f$ from control values was less than the fractional increase of $\dot{W}_m$ from control values. As a result, there was a significant increase in the ratio of $\dot{W}_m/\dot{W}_f$ with increases of cardiac output which occurred in five of the seven animals. The effect of this response is to permit a greater proportion of the hydraulic power in the forward wave to be transmitted into the pulmonary circulation as cardiac output rose.

Effect of altering cardiac output on pressure–diameter relations. An analog record of pulmonary arterial pressure and diameter from a representative animal is shown in fig. 5. We were able to obtain virtually noise free recordings of pulmonary arterial diameter. Figure 6 plots the mean diameter against the mean pulmonary arterial pressure from heart cycles selected at end expiration at different levels of flow through the arteriovenous shunt. In each cat, a linear relation between mean diameter (D) and mean pressure was found (fig. 6); correlation coefficients were 0.98, 0.97 and 0.90. Polynomial expressions did not improve the fit significantly. The fact that the pressure–diameter

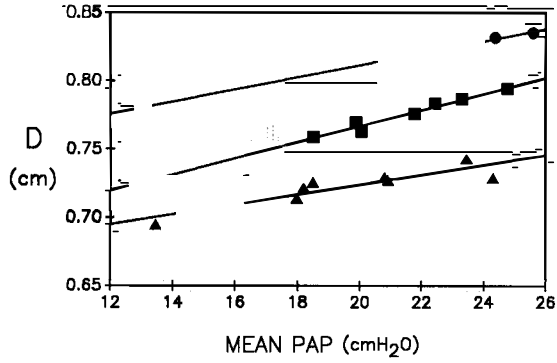

Fig. 6. Relations between mean pulmonary arterial pressure (PAP, cm H_2O) and mean pulmonary arterial diameter (D, cm) in three animals. Individual data points are shown with linear regression lines. The regression lines are D = 0.00589PAP + 0.649, D = 0.00443PAP + 0.723 and D = 0.00364PAP + 0.651.

TABLE 2

Effect of altering pulmonary arterial pressure on dynamic pressure–diameter relations.

Variable	Units	Control value	Coefficient	*P* value
$D(\omega)/P(\omega)$	cm/cm H_2O	0.0065 ± 0.0012	−0.00025	0.0004
Phase angle (ϕ)	radians	0.02 ± 0.05	0	NS
Dynamic pressure-strain modulus	cm H_2O	132 ± 29	8.92	<0.0001
Heart rate	min^{-1}	200 ± 17	0	NS

Coefficient is the slope of the relation between the variable and mean pulmonary arterial pressure obtained by analysis of covariance (N = 19). $D(\omega)/P(\omega)$ is the ratio of the amplitude of the pulmonary arterial diameter oscillations to pressure oscillations at the first harmonic (heart rate); ϕ is the phase angle, where a positive angle indicates that changes of pressure precede changes of diameter. Control values are the mean ± SE of three animals with no flow through the arteriovenous shunt. Dynamic pressure-strain modulus is from the $D\{D(\omega)/P(\omega)\}^{-1} \cos \phi$ (see appendix for details).

relations were linear suggests that the static elastic properties of the main pulmonary artery remain constant since dD/dP is independent of pressure. Diameter changed by 0.76, 0.53 and 0.50% mean diameter · cm H_2O^{-1}.

In contrast, the dynamic elastic properties of the main pulmonary artery appear to change with pulmonary artery pressure (table 2). As pulmonary arterial pressure increases there is a significant decrease in the modulus of the pressure–diameter relation ($D(\omega)/P(\omega)$) at the fundamental frequency (heart rate). This association is not due to alterations of heart rate because there was no significant relation between the changes of pulmonary arterial pressure and heart rate. The dynamic pressure–strain modulus increases with pulmonary arterial pressure because it is calculated from the reciprocal of $D(\omega)/P(\omega)$.

Discussion

We found that an acute increase in cardiac output induced by an arteriovenous shunt caused a decrease of input resistance, an increase of pulmonary arterial compliance, but no significant changes of characteristic impedance. As a result there was an inverse relation between input resistance and pulmonary arterial compliance but no relation between input resistance and characteristic impedance due to alterations of cardiac output. Previous studies have found a relation between input resistance and characteristic impedance with alterations of cardiac output, but not between input resistance and pulmonary arterial compliance. Cardiac output has been increased chronically with arteriovenous shunts for three weeks (Hopkins *et al.*, 1979). They found that the increased flow was associated with a reduction in pulmonary vascular resistance and

a decrease in characteristic impedance. It is not possible from that study to determine the extent to which those changes were related to vascular remodeling. In other studies, mechanical interventions have been made that result in an increase in cardiac output. Elkins and Milnor (1971) increased cardiac output in dogs acutely by exercise and found that input resistance decreased and that there was an increase in characteristic impedance. Dujardin *et al.* (1982) increased cardiac output by volume expansion which resulted in a decrease of input resistance and characteristic impedance. These studies indicate that the effect of altering cardiac output on pulmonary hemodynamics seems to depend on the method by which the change is produced. Pressure–diameter relations during alterations of cardiac output have been measured previously in the dog. Johnson *et al.* (1985) measured diameter in two orthogonal axes of the main pulmonary artery by sonomicrometry. The changes of cardiac output were produced by alterations in blood volume and by pharmacological means. They found that the pressure–diameter relations were linear in both axes. We found a mean value for the static and dynamic changes in diameter with pulmonary arterial pressure to be 0.6 and 0.76% per cm H_2O respectively. This value was less than the 2.7% static change of diameter per cm H_2O found by Zhuang *et al.* (1983) in the largest arteries of the excised feline lung, but are close to the value of 1.0% dynamic change of diameter per cm H_2O (Patel *et al.*, 1959) and 0.6% static change of diameter per cm H_2O (Johnson *et al.*, 1985) in the living dog.

Limitations of methods. We used a lumped parameter model to estimate input resistance, characteristic impedance and pulmonary arterial compliance from the input impedance spectra. There are several limitations associated with this approach.

There is a degree of interdependence between the model parameters. To test its effect, we varied the modulus at zero frequency (input resistance) and found that there was a direct relation between the parameter values for input resistance and pulmonary arterial compliance as opposed to the inverse relation that we found experimentally. Interdependence between model parameters could also cause a spurious inverse relation between input resistance and characteristic impedance, but we found no significant relation between them. The interdependence between input resistance and characteristic impedance could be avoided by using the reciprocal of the sum of $1/R_c$ and $1/R_P$ to represent characteristic impedance. Even when we use this approach, we still find no significant relation between input resistance and characteristic impedance. Therefore, interdependence between lumped parameters had no effect on our conclusions.

The lumped parameter model estimates input resistance rather than pulmonary vascular resistance and neglects the back pressure downstream. During the course of a previous study (Grant and Paradowski, 1987), we found that input impedance of a distributed parameter model of the feline pulmonary circulation is dependent primarily on the dimensions, elasticity and transmural pressure of the first five orders of the pulmonary arterial tree (unpublished data). This result suggests that the pulmonary capillary bed has no direct influence on input impedance. The back pressure only affects input impedance to the extent that it elevates the transmural pressure in the proximal pulmonary arteries.

The measurement of compliance from pressure–diameter relations is limited because we only measured the compliant properties of the main pulmonary artery and not the entire pulmonary arterial tree. Nevertheless, this approach appears to be reasonable because most of pulmonary arterial compliance resides in the proximal pulmonary arteries, as they contain most of the pulmonary arterial blood volume (Singhal et al., 1973). The data of Zhuang *et al.* (1983) and Yen *et al.* (1984) suggest that approximately 21% of pulmonary arterial compliance is located in the main pulmonary artery.

Finally, we measured the diameter of the main pulmonary artery in one axis. There are reports that the main pulmonary artery may be elliptical (Attinger, 1963; Melbin and Noordergraaf, 1971). This eccentricity seems to occur primarily when pulmonary arterial pressures are low: less than 10 cm H_2O. Johnson *et al.* (1985) reported axial differences in the external diameter of the main pulmonary artery in living dogs with two pairs of ultrasonic crystals placed orthogonally on the vessel. The degree of eccentricity of the main pulmonary artery was less than previous studies: the median ratio of minor to major radii was 0.94 (N = 9) with a range of 0.59 to 1.0 (calculated from fig. 5 of their paper). The slope of these relations were the same in both axes which indicates the elastic properties of the vessel are uniform at least in the transverse axis. Therefore our measurements of diameter in a single axis do provide a reasonable assessment of changes in the elastic properties and caliber of the vessel.

Mechanism of the pulmonary vascular response to increased cardiac output. Changes of pulmonary arterial compliance can be separated into two components: changes related to geometry and changes due to alterations of the elastic properties of the vessel wall. In the appendix, we have developed the concept that pulmonary arterial diameter, as it relates to volume of the vessel, represents the geometric factor, and that the change in pulmonary arterial diameter per unit change in mean pulmonary arterial pressure represents elastic properties of the vessel wall. The fact that we found a linear relation between mean pulmonary arterial diameter and pressure suggests that static elastic properties of the vessel wall are unaffected by changes in cardiac output. Therefore, the increase in pulmonary arterial compliance as cardiac output rises seems to be predominantly due to geometric factors. Yen *et al.* (1980) also found a linear relation between pulmonary arterial pressure and diameter in all except the small pulmonary arteries of 100 to 200 microns in excised cat lungs which suggests that the changes we observed can be explained on the passive mechanical properties of the vessel wall.

The fact that characteristic impedance remains unchanged despite an increase in the diameter of the main pulmonary artery is surprising because characteristic impedance is strongly dependent on the vascular compliance. The increase in diameter which would tend to decrease characteristic impedance must have been offset by an increase in pressure–strain modulus (see appendix for further discussion). Indeed that was precisely what was found: as pulmonary arterial pressure increased, the ratio of the amplitude of the diameter oscillations to the amplitude of pressure oscillations ($D(\omega)/P(\omega)$) decreased which caused the pressure–strain modulus to increase ($D\{D(\omega)/P(\omega)\}^{-1}$). Therefore pressure–diameter relations under static conditions

behave differently under dynamic conditions which is consonant with the conclusion that compliance is frequency dependent.

A similar constancy of characteristic impedance with pressure has been reported in the femoral artery by Cox (1975) for acute changes in pressure between 80 and 150 mm Hg. Therefore, the pulmonary and systemic vessels seem to exhibit similar responses in this regard. The pulmonary vascular response to alterations of cardiac output that we have measured in these experiments has been explained entirely on the basis of changes in the passive mechanical properties of the pulmonary vasculature without needing to invoke the presence of active neurohumoral mechanisms. The absence of active mechanisms has not been demonstrated, but merely the pattern of results does not support their presence in this particular experimental preparation.

Relation of the present study to hypotheses concerning right ventricular afterload. It is generally believed that the right ventricle operates at optimal hydraulic power output under normal resting conditions (Piene and Sund, 1982). In the present study, the disturbing input was a change of cardiac output. As cardiac output increases, input resistance decreases, presumably because of distention and recruitment of the pulmonary microcirculation. If we assume that there was no change in the apparent source resistance which is used as a measure of right ventricular contractility, the ratio of input resistance to apparent source resistance will fall. As a result, the right ventricle would no longer be operating at its optimal hydraulic power output. If there is a homeostatic mechanism within the pulmonary circulation that tends to cause the right ventricle to operate at maximal hydraulic power output, then pulmonary arterial compliance should decrease. We observed the opposite response. An increase of cardiac output was associated with an increase of pulmonary arterial compliance.

An alternative explanation of this result is that there was a decrease in apparent source resistance due to a decrease in right ventricular contractility as cardiac output increased so that there was no need for a decrease of pulmonary arterial compliance. This explanation is unlikely for several reasons. First, an increase in cardiac output results in an increase in right ventricular end-diastolic pressure. Previous studies of left ventricular pump function indicate that an increase in end-diastolic pressure does not affect apparent source resistance (Elzinga and Westerhof, 1977). Second, we found that the increased cardiac output was associated with an increase of dP/dt_{max}; this result makes a decrease of apparent source resistance unlikely. Therefore, these experiments tend to refute the optimal hydraulic power output hypothesis (Piene and Sund, 1982). A similar conclusion has been reached for the left ventricle (Van den Horn *et al.*, 1985).

Our results seem to follow the pattern predicted by the constant pulsatility hypothesis insofar that there is an increase of pulmonary arterial compliance as input resistance decreases. As a result, there was no statistically significant change in the "time constant of the Windkessel" ($R_p * C_a$). Nevertheless, the pulsatility of the pulmonary circulation was not held constant as cardiac output increased since there was a significant increase in the pulsatility index.

A major finding of this study is the importance of the pulmonary vascular response

on hydraulic power in the main pulmonary artery. As cardiac output increases, there is a greater increase in the measured wave power than the forward wave power because there is less wave reflection. This result is due to the decrease in input resistance as cardiac output increases; there is no significant change of characteristic impedance, however. It is of interest that Cox (1975) has also reported – in the systemic circulation – a constancy of characteristic impedance despite changes in systemic arterial pressure in the femoral arterial bed. It is uncertain at the present time whether or not the effects of the pulmonary vascular response on wave reflection is applicable to other circulatory disturbances.

In summary, we found that there was an increase in pulmonary arterial compliance when cardiac output was increased by an arteriovenous shunt in two series of experiments in which entirely different methods for assessing pulmonary arterial compliance were used. The increase in cardiac output resulted from changes of geometric factors rather than changes in the elastic properties of the vessel wall. The pattern of our results tends to refute the hypothesis that there are homeostatic mechanisms in the pulmonary circulation that optimize right ventricular power output. Nevertheless, the observed changes have the effect of reducing the changes in pulsatility and the adverse effects of wave reflection.

Appendix

Pulmonary arterial compliance. In this analysis we shall define compliance (C_a) as the change of mean pulmonary arterial volume (V) per unit change of mean pulmonary arterial pressure (P) under static conditions. Total pulmonary arterial compliance is the sum of compliance (C) for each branch of the pulmonary arterial tree.

$$C = dV/dP \tag{A1}$$

As a first approximation, each branch will be considered to be cylindrical in shape. dV/dP can be separated into two components.

$$dV/dP = (\delta V/\delta D_i)(dD_i/dP) + (\delta V/\delta L)(dL/dP) \tag{A2}$$

$$V = L\pi D_i^2/4 \tag{A3}$$

L is length and D_i is the internal diameter of each branch. By differentiation of A2 and substitution into A2, we obtain the following relation:

$$dV/dP = 0.5\ D_i[L\pi dD_i/dP + 0.5\pi D_i dL/dP] \tag{A4}$$

Therefore compliance depends on both geometric factors, the values of D_i and L, and on the elasticity of the vessel as judged by dD_i/dP and dL/dP. We were only able to measure one dimension on these experiments, D_i, a reasonable choice since D_i affects both terms of the above equation. Since the wall thickness of the main pulmonary artery is small, approximately 5% of outer radius (Pollack *et al.*, 1968; Cox, 1975), changes of external diameter (D_o) are reflected closely by changes of D_i.

Characteristic impedance. Characteristic impedance (R_c) can be approximated by the following expression (Cox, 1975):

$$Z_c = 4\rho C_o/(\pi D_i^2) \tag{A5}$$

where ρ is the density of blood (1.06 $g \cdot cm^{-3}$) and C_o is the inviscid wave speed. This expression neglects the viscous resistance of the vessel wall and assumes Womersly's alpha is large (Bergel and Milnor, 1965).

For a vessel with no longitudinal constraints and a Poisson ratio of 0.5 (Cox, 1975):

$$= 2D_i^2(3\rho D_o)^{-1}\,[P(\omega)/D_o(\omega)]\cos\phi \tag{A6}$$

where $P(\omega)$ and $D(\omega)$ are the amplitude of the pressure and diameter oscillations respectively.
By substituting in equation A5 for C_o and ignoring the small difference between D_i and D_o we obtain:

$$Z_c = 1.04\,D_o^{-2}\,[D_o\{D_o(\omega)/P(\omega)\}^{-1}\cos\phi]^{0.5} \tag{A7}$$

Therefore, changes of R_c could occur due to alterations in vascular geometry D_o^{-2} or due to changes in pressure–strain modulus.

$$D_o[D_o(\omega)/P(\omega)]^{-1}\cos\phi$$

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