Pulse Wave Velocity in the Main Pulmonary Artery of the Dog

By Jack D. Bargainer, M.D.

ABSTRACT

Apparent phase velocities in the main pulmonary artery were calculated from simultaneous measurements of pressure at two sites in 11 anesthetized, open-chest dogs, at heart rates ranging from 24 to 240 beat/min. The distribution of apparent phase velocity with harmonic frequency was similar to that reported previously for input impedance and frequency. Phase velocity in the absence of reflections, estimated by averaging apparent phase velocities at frequencies from 9 to 23 cycle/sec, averaged 275 cm/sec in the control state and 417 cm/sec during the infusion of 5-hydroxytryptamine (serotonin). The elastic modulus of the pulmonary arterial wall implied by these velocities was calculated to be approximately 1.2 x 10⁶ dyne/cm² in the controls and 2.7 x 10⁶ dyne/cm² during serotonin. These results are consistent with previous observations on normal pulmonary vascular input impedance in the dog under these conditions, and with the relationships predicted by the Womersley equations, and suggest that the effects of serotonin on the input impedance spectrum are due in part to an increase in pulse wave velocity.

ADDITIONAL KEY WORDS phase velocity elastic modulus pressure reflections serotonin characteristic impedance

The speed with which a blood vessel and the blood enclosed within it transmit a pressure pulse is an important element in theories of hemodynamics, since this pulse wave velocity is a function of the geometry of the vascular bed, the rheology of blood, and the elasticity of the vessel walls, and these same factors determine the relationship between oscillatory pressure and flow. The velocity of a pressure pulse and the effects of reflected waves on this velocity can best be determined by subjecting the observed pressure pulses to Fourier analysis and measuring the velocity of propagation, or phase velocity, of the component sinusoidal waves. Several investigators have used this analytic method to simplify description of the behavior of normal pressure and flow pulses, and have presented the theoretic basis for its use (1-5). Strong support for the validity of this approach is provided by experiments which show that the response to mechanically generated sinusoidal waves is the same as that predicted by Fourier analysis of normal pulsations (6, 7).

The velocity of pressure waves in the major branches of the pulmonary arteries has been determined in man (8) and in animals (6, 9), but measurements of pressure pulse wave velocity within the main pulmonary artery itself, with which the present study is concerned, have not been reported previously. In the present experiments, differential pressure was measured by direct needle puncture of the main pulmonary artery in anesthetized, open-chest dogs and phase velocity was determined through Fourier analysis. Heart rate was altered experimentally over a wide range to obtain a complete spectrum of phase velocity versus frequency, and the effects of 5-hydroxytryptamine (serotonin) were examined in some experiments.
WAVE VELOCITY IN THE PULMONARY ARTERY

Methods

Experiments were performed on 11 mongrel dogs weighing from 9.7 to 26.2 kg, with an average of 17.8 kg. The animals were given morphine sulfate 1 mg/kg im and then anesthetized with sodium pentobarbital 20 mg/kg iv. A metal tracheostomy tube was inserted and positive pressure respiration maintained with a Harvard Respirator at a tidal volume of 18 ml/kg of room air, a rate of 14 to 16 cycle/min, and an end-expiratory pressure of 2 to 3 cm of water. The chest was entered through the fourth left intercostal space, the pericardium widely incised, and the main pulmonary artery was dissected free circumferentially. The mean external circumference of the main pulmonary artery, measured with a loop of silk suture, ranged from 4.5 to 7.0 cm, with an average of 5.5 cm. In 3 of the animals, complete atrioventricular (AV) block was produced by the technique of Tauffic, Bashour and Lewis (11) 2 to 3 weeks prior to study. These 3 animals were studied at their slow spontaneous heart rates. The remaining 8 animals were studied at their spontaneous rates also, but in addition, 6 of these were studied at heart rates of 180 to 240 beat/min, which were controlled by pacing the ventricles with a small bipolar electrode sutured to the epicardium.

In the 8 animals without complete AV block, pulmonary artery pressures were measured by direct puncture of the main pulmonary artery at two sites. Two Statham P23Db strain gauges were rigidly mounted on a rack and pinion and connected directly to short, 16-gauge needles. This assembly was lowered over the pulmonary artery and respiration was suspended while the lungs were kept inflated at a transpulmonary pressure of 5 cm of water with 100% oxygen. The vessel was quickly punctured by both needles by lowering the rack. In this manner, both needles entered the vessel perpendicularly to the same depth, with the bevels facing the vessel wall. Ten to twenty pressure pulses were recorded at both spontaneous and driven rates, after which the needles were removed and the respirator started. Total static inflation time was always less than 30 sec. Minimal digital pressure over the puncture sites was sufficient to stop bleeding after removal of the needles. In 5 of the 8 dogs, the procedure was repeated once in the control period, inserting the needles into the vessel through the previous puncture wounds. Following control measurements, 4 of these 8 dogs were given 5-hydroxytryptamine (serotonin) 0.05 mg/kg per min iv with a Harvard Infusion Pump. Infusion speed was 0.2 to 2.0 ml/min and infusion time was 10 to 15 min. Pulmonary artery pressures were again measured during suspended respiration at spontaneous and driven rates with the needles inserted through the previous puncture wounds. The needles were inserted into the vessel of a given dog a maximum of three times.

In the 3 dogs with complete AV block, pulmonary artery pressures were measured with a 15-cm length of Teflon double-lumen catheter inserted through a stab wound in the right ventricular outflow tract. The heart rates of these dogs varied from 24 to 30 beat/min and only 1 was studied during the infusion of serotonin.

The hydrostatic baseline for all pressures was 2.5 cm above the top of the operating table, a position which corresponded to the level of the left atrium. The electrocardiogram and proximal and distal pulmonary artery pressures were recorded simultaneously on an Electronics for Medicine multichannel recorder, at a paper speed of 100 or 200 mm/sec. At the end of each experiment, the pressure measuring systems were calibrated and their natural frequencies were determined by analyzing their response to the square-wave pressure input that resulted from bursting a rubber balloon over the tip of the catheter or needles. In general, the natural frequency was 60 cycle/sec and the relative damping was 0.3 to 0.4. The distance between the lumen of the needles was carefully measured with a vernier caliper, the average distance being 2.23 cm.

The pressure tracings were digitized with a manual scaling device (Data Scaler) at intervals of 0.01 sec. Two to six pulses at both spontaneous and paced rates were analyzed, beginning at the foot of the proximal pressure. These data were then processed on an IBM 7094 computer. The computer program first subtracted zero baselines, converted ordinate measurements into pressure units, and computed mean values for each pressure. Mean pressure was then subtracted from all values and a Fourier analysis was performed on the remaining oscillatory waves. The observed pressure pulsations as a function of time, \( P(t) \), could thereby be expressed as the sum of the mean pressure, \( \overline{P} \), and a series of sinusoidal waves at integral multiples of the fundamental rate:

\[
P(t) = \overline{P} + \sum_{n=1}^{N} P_n \sin (n \omega t + \phi_n)
\]  

(1)

where \( n \) is the harmonic number, \( N \) is the number of the highest harmonic computed, \( \omega \) the fundamental frequency in radians per second, \( t \) is time in seconds, \( P_n \) the modulus or amplitude of the nth harmonic and \( \phi_n \) its phase (3, 10).

Pressure modulus and phase were then corrected for the distortion introduced by the frequency characteristics of the pressure-measuring de-
vices and apparent phase velocity was computed for each harmonic by the equation:

\[ c' = \frac{2\pi f \Delta L}{\Delta \phi} \]  

(2)

where \( c' \) is the apparent phase velocity in centimeters per second, \( f \) is the frequency of the harmonic in cycles per second, \( \Delta L \) is the distance between measuring sites in centimeters, and \( \Delta \phi \) is the phase difference in radians between proximal and distal pressure pulses. This apparent phase velocity, \( c' \), is the experimentally measured propagation velocity of the sinusoidal wave, and is affected by the summation and cancellation of incident and reflected waves. Phase velocity stripped of the effect of reflections, \( c \), was estimated by averaging the apparent phase velocities at frequencies from 9 to 23 cycle/sec. In all cases the apparent phase velocity was computed for 10 harmonics, but values derived from pressure moduli less than 0.1 mm Hg were discarded, as being within the noise level of the pressure measuring and recording system.

Results

Twenty-one experiments on 11 dogs under control conditions were analyzed, giving estimates of apparent phase velocity at frequencies ranging from 0.5 to 23 cycle/sec. The variations in apparent phase velocity with frequency were similar in all animals, and were not consistently altered by changes in heart rate (see Fig. 1). Control measurements of apparent phase velocity from all animals were grouped according to frequency and averaged, using a bandwidth of 1 cycle/sec from 0.5 to 7.5 cycle/sec, 2 cycle/sec from 7.5 to 17.5, and 4 cycle/sec for the highest frequency band. The results, shown in Figure 2, indicated a minimum (292 cm/sec) between 2 and 3 cycle/sec, followed by a maximum (397 cm/sec) at about 5 cycle/sec, with smaller and less regular oscillations thereafter.

At higher frequencies, for which the pathway out to reflecting sites and back is relatively long in terms of wavelength, viscous damping minimizes the effect of reflections at the origin. True phase velocity can, therefore, be estimated by averaging the apparent phase velocities in this frequency region. The phase velocity calculated by averaging apparent phase velocities between 9 and 23 cycle/sec in each experimental animal is shown in Table 1. The average phase velocity in 11 control animals was 275 cm/sec, with a standard error of the mean (SEM) of ±16 cm/sec. Phase velocity was higher during serotonin infusion than in the control period in each of the dogs that received this drug. Mean phase velocity in these 5 animals was 267 cm/sec (SEM, ±22) in the control period, and 417 cm/sec (SEM, ±29) during serotonin.
Experimental estimates of phase velocity obtained in this way are actually the sum of the velocity of the pressure wave and the mean velocity of blood flow (2, 6), and therefore overestimate the pressure pulse wave velocity. The magnitude of this error in these animals cannot be determined exactly in the absence of blood flow measurements, but published data on pulmonary blood flow in the dog suggest that it is not large. If we assume, for example, an average volume blood flow for the controls of 2.2 cm³/sec kg [the average found in dogs similarly prepared in this laboratory (10)], the mean blood flow velocity in these 11 dogs would be 20 cm/sec, indicating that the experimental measurement overestimates pressure phase velocity by about 8%. Subtracting 20 cm/sec from the control experimental average gives 255 cm/sec for the corrected pressure phase velocity. Since serotonin under these conditions produces only a small increase in pulmonary blood flow (10), the analogous correction during serotonin infusion is probably nearly the same as in the controls. In the discussion that follows, as in most published data on phase velocity, the experimental measurements of phase velocity have not been corrected for flow velocity.

**Discussion**

A number of different methods for estimating pulse wave velocity have been applied to the pulmonary arteries in animals and in man (6, 8, 9, 14). Each technique, including the one used in our experiments, has certain inherent sources of inaccuracy and it is not surprising that values ranging from 182 cm/sec (8) to 325 cm/sec (9) have been reported. Attinger, in his detailed study of the transmission of pressure in the pulmonary arterial bed (9), found a phase velocity of 230 cm/sec in lungs inflated at a transpulmonary pressure of 25 cm water, but 325 cm/sec when the inflation pressure was 5 cm water. The latter situation resembles the condition in our experiments and is close to physiological transpulmonary pressures, but Attinger’s data refer to measurements made in part beyond the main pulmonary artery.

Our average control value of 275 cm/sec (without correction for mean flow velocity) is considerably higher than the 182 cm/sec reported by Caro and Harrison (8) for pulmonary arteries in man, although they used a

### TABLE 1

<table>
<thead>
<tr>
<th>Dog number</th>
<th>Controls</th>
<th>Serotonin</th>
</tr>
</thead>
<tbody>
<tr>
<td>c (cm/sec)</td>
<td>P (PA) (mm Hg)</td>
<td>c (cm/sec)</td>
</tr>
<tr>
<td>1*</td>
<td>316</td>
<td>11.1</td>
</tr>
<tr>
<td>2</td>
<td>263</td>
<td>10.6</td>
</tr>
<tr>
<td>3</td>
<td>259</td>
<td>11.6</td>
</tr>
<tr>
<td>4</td>
<td>190</td>
<td>13.5</td>
</tr>
<tr>
<td>5</td>
<td>307</td>
<td>15.4</td>
</tr>
<tr>
<td>Mean (1 to 5), ± SEM</td>
<td>297 ± 22</td>
<td>12.4 ± 0.89</td>
</tr>
<tr>
<td>6*</td>
<td>179</td>
<td>17.8</td>
</tr>
<tr>
<td>7*</td>
<td>292</td>
<td>17.4</td>
</tr>
<tr>
<td>8</td>
<td>319</td>
<td>16.4</td>
</tr>
<tr>
<td>9</td>
<td>330</td>
<td>18.2</td>
</tr>
<tr>
<td>10</td>
<td>329</td>
<td>15.0</td>
</tr>
<tr>
<td>11</td>
<td>242</td>
<td>14.1</td>
</tr>
<tr>
<td>Mean (1 to 11), ± SEM</td>
<td>275 ± 16</td>
<td>14.6 ± 0.82</td>
</tr>
</tbody>
</table>

* = phase velocity, calculated by averaging apparent phase velocities at frequencies from 9 to 23 cycle/sec. P (PA) = mean pulmonary arterial pressure. Mean values for all 11 controls are given at the bottom of the "controls" column.

*Dogs with complete AV block, in which apparent phase velocities were measured with a double-lumen catheter.
double needle-puncture technique similar to that employed in our experiments. Three of the four subjects from whom the value of 182 cm/sec was derived had mean pulmonary arterial pressures less than 9 mm Hg, however, and since they also demonstrated in other cases a direct correlation between pulse wave velocity and mean pulmonary arterial pressure, their estimate may be unduly low.

Fleischner, Romano, and Luisada (14) reported an average pulse wave velocity of 200 cm/sec in human subjects, but their radio-kymographic technique of measuring movements of the pulmonary hilar shadows was doubtless influenced by a number of factors other than pressure changes in the pulmonary arteries, and therefore provided a less accurate method of measuring pulse wave velocity than do direct pressure measurements.

The advantages as well as the disadvantages of the technique used in the present experiments derive from the direct needle-puncture of the pulmonary artery. Large-bore needles inserted through the vessel wall may load the wall significantly and lead to spuriously high values of phase velocity, but the effect of this loading must be small, since the velocities measured by direct puncture were not significantly different from those obtained in the experiments where intravascular catheters were used (see Table 1). In comparison with methods using intravascular catheters, the direct puncture technique has the advantage of measuring lateral pressures without the artifacts introduced by whipping of the catheter.

**PHASE VELOCITY AND ELASTIC MODULUS**

Phase velocity is determined in part by the elasticity of the vessel wall, and the relationship between Young’s modulus of elasticity (E) for a very thin-walled tube and phase velocity in a nonviscous fluid (c₀), is expressed by the Moens-Korteweg equation:

\[ c_0 = \left( \frac{E h}{2 \rho} \right)^{1/2} \]  

where \( c_0 \) is expressed in centimeters per second, \( E \) in dynes per square centimeter, \( h/2r \) is the ratio of wall thickness to vessel diameter, and \( \rho \) is fluid density in grams per cubic centimeter. This formula does not express accurately the relationships in blood vessels, which are filled with a viscous fluid and have an appreciable wall thickness that varies with radius, but a close approximation to the true wave velocity, \( c \), in blood vessels is given by (12, 13-17):

\[ c = \frac{c_0}{\sqrt{1 - \sigma^2}} \]  

where \( \sigma \) is Poisson’s ratio. If \( c \) has been determined experimentally, the elastic modulus can be calculated by combining equations 3 and 4 to give:

\[ E = \frac{2 r \rho}{h} c^2 (1 - \sigma^2). \]
PHASE VELOCITY AND CHARACTERISTIC IMPEDANCE

The theoretic relationship between phase velocity and characteristic impedance in a strongly tethered elastic tube has been defined by Womersley (12) as:

\[ Z_o = \frac{\rho c_o}{\sqrt{1 - \sigma^2}} \cdot \frac{1}{M'} \cdot e^{-\kappa'^2} \]  

(7)

where \( Z_o \) is the characteristic impedance in dyne sec cm\(^{-3} \) (ratio of pressure in dyne/cm\(^2 \) to velocity of blood flow in cm/sec), \( M' \) and \( \epsilon \) are functions of Womersley's nondimensional \( \alpha \) (which in turn is determined by vessel radius, frequency, and the kinematic viscosity of blood), and \( j = V - 1 \) (the other symbols have already been defined). For vessels of relatively large radius, such as the pulmonary artery, \( M' \) approaches unity and \( \epsilon \) approaches zero. Under these conditions, since by equation 4 our experimentally determined phase velocity (275 cm/sec) equals \( c_o/\sqrt{1 - \sigma^2} \), the characteristic impedance predicted by equation 7 is 289 dyne sec cm\(^{-3} \). Measurements of pulmonary vascular input impedance in the dog by Bergel and Milnor (10) indicated an average characteristic impedance of 268 dyne sec cm\(^{-3} \). The reasonably close agreement between these two estimates lends further support for the application of Womersley's equations to the pulmonary vessels.

EFFECTS OF SEROTONIN

Phase velocity increased by about 50% during the infusion of serotonin (Table 1), which implies an increase of the same proportions in characteristic impedance in accordance with equation 7. This contrasts with Bergel and Milnor's data on pulmonary input impedance (10) obtained under comparable conditions, which suggested that serotonin had little or no effect on characteristic impedance, and hence on phase velocity. The reason for this discrepancy is not clear. It may be that averaging input impedances between 8 and 18 cycle/sec to determine characteristic impedance (10) gives a distorted estimate during serotonin infusion because the swings of impedance modulus with frequency are then still prominent in this range (10), yet one would have expected an analogous source of error in estimating phase velocity by averaging apparent phase velocities at these higher frequencies. Whatever the explanation, it seems reasonable to assume that the present direct measurements of phase velocity are more accurate than estimates of velocity derived indirectly from impedance, and that phase velocity is in fact increased by serotonin. If this be the case, the shift of the minima and maxima of impedance modulus toward higher frequencies that Bergel and Milnor (10) observed with serotonin was presumably due in part to an increase in pulse wave velocity. An increase of 50% in wave velocity would account for only about half of this shift, however, and some displacement of the major reflecting sites in an upstream direction must have contributed to the full effect observed.

A 50% increase in wave velocity corresponds to an increase of 125% in elastic modulus, since this modulus varies with the square of the wave velocity. The elastic modulus of the pulmonary arterial wall during serotonin infusion, calculated from the measured phase velocity (417 cm/sec) as outlined above (equation 5), was 2.74 \( \times 10^9 \) dyne/cm\(^2 \).

The mechanism by which serotonin increases phase velocity and calculated elastic modulus of the pulmonary arterial wall cannot be identified with certainty from the data obtained in these experiments. It is well known that systemic arteries become stiffer as they are distended, or in other words, that their elastic modulus increases with increasing radius (15, 16) and Patel has demonstrated this same phenomenon in the pulmonary artery (18). Our calculations from Patel's data (18) indicate that the rise in mean pulmonary arterial pressure that we observed with serotonin (see Table 1) would reduce the volume distensibility from about 2.05%/cm water to perhaps 0.75%/cm water, which would be equivalent (equations 5 and 6) to approximately the same increase in elastic modulus (150%) that we observed during serotonin infusion. This calculation assumes, however, that the volume distensibilities measured by Patel (18) under control conditions
are not altered by serotonin, i.e., that serotonin has no effect on wall elasticity other than the nonspecific effects of changes in distending pressure, which is probably not true.

Somlyo and Somlyo (22) showed that serotonin causes contraction of helically cut strips of the main pulmonary artery, indicating a direct effect of serotonin quite apart from changes in distending pressure, presumably through stimulation of smooth muscle in the vascular wall. This would tend to reduce volume distensibility and increase elastic modulus over the control values at any given radius, and might lead to little or no change in pulmonary arterial radius as pressure rises during serotonin infusion, or even to a decreased radius, as norepinephrine (13). Since the concentration of serotonin in the blood in our experiments exceeded the threshold values of Somlyo and Somlyo (22) 50- to 100-fold, however, it is by no means certain that their results may be applied to this situation.

What part of the serotonin effects in the present experiments was due to passive distention of the pulmonary artery and what part to activation of vascular smooth muscle in its walls, therefore, remains uncertain, but it is probable that both are involved.

**APPARENT PHASE VELOCITY AND REFLECTIONS**

The oscillations of apparent phase velocity with harmonic frequency (Fig. 2) form a pattern very similar to those of pulmonary vascular input impedance with frequency (6, 10), and like them are generally considered to be the results of waves reflected back from more distal parts of the vascular bed (2-4). The rather wide scatter of our observations is indicated by the magnitude of the standard errors shown in Figure 2, but the trend toward a minimum just below 3 cycle/sec, followed by a maximum at approximately 5 cycle/sec and smaller oscillations at higher frequencies, is evident. This behavior of the vascular bed has been likened to that of an electrical transmission line leading to a single reflecting site (4, 6, 10), and in such a model the distance out to the reflecting site can be calculated from the phase velocity and the frequencies at which minima and maxima occur. The first minimum would occur at that frequency for which this distance is one-quarter of a wavelength; if the phase velocity, c, were 275 cm/sec, and the minimum occurred at 2.5 cycle/sec (as in Fig. 2), a quarter wavelength at this frequency would be 27.5 cm and this would equal the distance from the site of measurement in the main pulmonary artery out to the reflecting site. The measurements reported by Attinger (9), or for that matter, even superficial measurements of the external dimensions of the canine lung, show that the vascular pathway out to the most remote pulmonary capillary is not this long. Since the geometric and physical characteristics of the bed make it unlikely that the principal sites of reflection are postcapillary, we conclude that the simple transmission line, while useful as a model of a single vessel, is inadequate as a model of the pulmonary vascular bed. More complex models that take into account the variations in branching, path lengths, and elasticity in a vascular bed (23) may prove to be more helpful in the interpretation of these phenomena.

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JACK D. BARGAINER

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