Mechanism of Normal Splitting of the Second Heart Sound

By Edward I. Curtiss, M.D., Robert G. Matthews, M.D., and James A. Shaver, M.D.

SUMMARY

The mode of inspiratory augmentation (IA) of the A2-P2 interval was investigated in seven normal volunteers (group 1) and six patients with pulmonary hypertension of diverse etiology (group 2) using catheter-tip micromanometers. In group 1 subjects, inspiratory widening of this interval was found to average 27.2 msec, of which 7.6 ± 2.7 msec (1 SD) or 27 ± 7% was due to a decrease in the Q-A2 interval. The major contribution of Q-P2 interval prolongation was divided into two components: a) Q-O was measured from the onset of the QRS to the onset of the rapid descent of the right ventricular (RV) negative dp/dt, which was felt to reflect the duration of RV electromechanical systole, b) O-P2 or Q-P2 = Q-O. Increase in the O-P2 interval accounted for only 7.7 ± 5.0 msec or 28 ± 12% of the total IA. The major single component of IA was the increase in O-P2 which averaged 11.9 ± 3.0 msec. Five of six group 2 patients demonstrated significant respiratory change in Q-P2 intervals. In contrast to group 1 subjects, however, this was accomplished primarily via increases in the duration of RV electromechanical systole. The O-P2 interval is felt to primarily reflect the impedance characteristics of the pulmonary vascular bed. It is concluded that physiologic splitting of the second heart sound in normal subjects is most probably due to an inspiratory decrease in impedance of the pulmonary bed rather than the traditional explanation of prolongation of RV systole secondary to an increase in venous return. When the normal impedance characteristics of this bed are lost, as in pulmonary hypertension, IA must occur primarily via increases in the duration of RV systole. The inspiratory delay from the conclusion of RV systole to the occurrence of P2 is attributed to the inerterance of the RV stroke mass.

Additional Indexing Words:

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ALTHOUGH INSPIRATORY SPLITTING of the second heart sound was first recognized by Pottain in 1866, its usefulness in the diagnosis of clinical heart disease was not fully appreciated until the reports of Leatham and Towers in the early 1950s. Several studies 4-5 since then have further defined the mechanism responsible for this event, all concluding that the majority of inspiratory augmentation (IA) of A2-P2 is due to delayed pulmonic closure. This delay is attributed to the increased venous return during inspiration which selectively prolongs right ventricular (RV) systole. 6 However, in our laboratory, recent observations of the sound-pressure correlates found in various disease states, which alter splitting of the second sound have suggested that the hydraulic capacitance of the pulmonary vascular bed might be a dynamic variable with respect to respiration and could be an important factor in normal physiologic splitting. 8 Accordingly, the present investigation was undertaken to characterize the interval alterations responsible for normal inspiratory widening of the A2-P2 interval.

Methods

Group 1

Six normal male volunteers between ages 21 and 26 years and an 18-year-old male with a functional systolic murmur were studied in the basal unpremedicated state in the resting supine position. Fully informed written consent was obtained from all participants in the study following project clearance by an expert committee. From a superficial antecubital vein, a Dallons-Telco* catheter-tip micromanometer was placed in an arrhythmia-free position at the apex of the right ventricle. The following traces were ob-

*Carolina Medical Electronics.
tained simultaneously on an oscillographic recorder* at paper speeds of 100–200 mm/sec and 20 msec lines: a) right ventricular pressure and b) its first derivative dp/dt, c) surface electrocardiogram, and d) a phonocardiogram with the microphone placed on the chest wall at the point of maximal intensity of the aortic and pulmonic components of the second heart sound. Respiratory phase was identified by a nasal thermistor. Recordings were made during spontaneous respirations with no effort made to control depth or frequency. Figure 1 is a typical record and illustrates the method for obtaining the measurements described in the preceding paragraphs.

At least six respiratory cycles were analyzed for each subject. For each cycle, the following measurements were made during the widest inspiratory split of the second sound and the narrowest expiratory split.

1. The Q-A3 interval — measured from the onset of the electrocardiographic QRS to the first high frequency component of A3.

2. The Q-P2 interval — measured from the onset of QRS to a consistent major deflection of P2 which could be consistently identified despite partial merger with A3. The Q-P2 interval was divided into a measured and a derived component.

3. The Q-O interval — this was felt to reflect the duration of true RV systole which, according to Wiggers,2 terminates at the point of sharp downward deflection of the ventricular pressure trace. This point was identified as O by differentiating the RV pressure and marking the onset of the rapid descent of negative dp/dt. The Q-O interval was measured from the onset of QRS to the onset of rapid descent of negative dp/dt. While the point designated as O might not truly define the end of RV mechanical systole, we were primarily interested in the relative change in systole from expiration to inspiration and were not concerned with its absolute duration. We assumed that changes in RV mechanical systole would be reflected by changes in Q-O which, in turn, would quantitatively change in the same direction. The following intervals were then derived:

   a) O-P2, or protodiastolic interval, in keeping with Wiggers’ terminology, was obtained by subtracting Q-O from Q-P2.

   b) A2-P2 = Q-P2 − Q-A3.

   c) Inspiratory augmentation of A2-P2 = A2-P2 (insp) − A2-P2 (exp). Intervals were measured to the nearest 2 msec.

For each subject the total IA of A2-P2 was obtained in msec. The contribution to this augmentation of the following three components was then expressed in milliseconds and as a percentage of the total augmentation preceded by the appropriate sign: Δ Q-A3, Δ Q-O, and Δ O-P2. For each subject, the change in each interval from expiration to inspiration was analyzed for statistical significance using the Student’s t-test for paired differences. All deviations from the mean are given as one standard deviation. For any individual there were no significant differences in heart rate from expiration to inspiration; therefore, this factor was ignored.

Group 2

A second group of six patients with mild to severe pulmonary hypertension was studied for comparison. Data were obtained in two patients (E. L. and M. S.) similar to the normal group. In four other patients, right ventricular dp/dt was not obtained. Instead, simultaneous tracings of RV and pulmonary artery pressure were recorded from equisensitive catheter-tipped micromanometers according to methods previously described.4 The remaining traces were identical to those alluded to above. For these four subjects, the separation in milliseconds between the dicrotic notch of the pulmonary artery trace and the RV trace at the same pressure level was measured. This interval has been termed “hangout” by Shaver et al.5 It was subtracted from Q-P2 to obtain an interval, RV electromechanical systole (QRV), which was felt to reflect the true duration of RV systole. The measured hangout interval was handled analogously to the derived O-P2 interval in the normals. The remaining data were analyzed as described above. QRV and hangout intervals were also determined for E. L. and M. S. and revealed no significant differences from the analysis of Q-O and O-P2 intervals.

Results

Group 1 — Normal Subjects

During inspiration the A2-P2 interval increased from 31.3 ± 8.2 msec to 55.5 ± 10 msec, i.e., an IA totaling 2.2 ± 1.2 sec.

Curtiss, Matthews, Shaver

Figure 1

Record from a typical study illustrating the method for obtaining Q-O and O-P2 intervals.

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*Electronics for Medicine DR-12.
27.2 ± 7.8 msec. The relatively wide expiratory split is due to utilization of a major high frequency component of P₂ rather than the onset of this sound. Figure 2 demonstrates that in each subject the majority of this increase could be accounted for by Q-P₂ prolongation with a lesser contribution afforded by a decrease in Q-A₂. The IA of 27 msec was divided into three components. Component changes for individual subjects in milliseconds are illustrated in Figure 3, while the component change as a percentage of the total IA is shown in Figure 4.

Change in Q-A₂

A decrease in the Q-A₂ interval was found uniformly. It varied from 4-11 msec and averaged 7.6 ± 2.7 msec. Similar to the findings of other investigators, this decrease accounted for 27 ± 7% of the total IA.² ³ ⁴

Change in Q-O

Inspiratory augmentation of the Q-P₂ interval averaged 19.6 ± 6.2 msec; 7.7 ± 5.0 msec of this increase was due to prolongation of Q-O which averaged 28 ± 12% of the total augmentation and 37 ± 14% of Q-P₂ prolongation. The Q-O interval showed the widest variation of the three analyzed. Although it was found to increase in all subjects, it was statistically insignificant in subjects D. S. and T. H. Despite the fact that the average increase in Q-O was essentially identical to the average decrease in Q-A₂, this quantitative relation did not appear to be present in any given subject (correlation coefficient = 0.04).

Change in O-P₂ or Protodiastolic Interval

The average increase of 11.9 ± 3.0 msec in this interval was the largest of the three components, accounting for 45 ± 7% of the total IA and 63 ± 14% of the increase in Q-P₂. The percentage increase in O-P₂ demonstrated the least variability from subject to subject.
showed some significant movement of Q-P₂ from expiration to inspiration and in all it was due to changes in RV electromechanical systole. Thus, in five out of six patients, changes in protodiastolic or hangout intervals were insignificant or attenuated.

M. S., who is representative of the group, had an IA of +8 msec which was due entirely to prolongation of the Q-O interval. No significant change occurred in the O-P₂ interval. As seen in figure 5, simultaneous RV and pulmonary artery pressure tracings also showed no significant change in hangout interval.

**Discussion**

The inspiratory prolongation of the Q-P₂ interval, which accounts for the majority of A₂-P₂ interval augmentation, cannot be ascribed to increased duration of the RV pre-ejection period. During this respiratory phase isometric contraction time shortens, primarily due to a fall in pulmonary artery end-diastolic pressure, and thus the pre-ejection period decreases in duration. The mechanism for Q-P₂ interval augmentation must be sought in an explanation of ejection period prolongation. While this might solely be due to increased duration of ventricular mechanical systole, the uniform occurrence of P₂ near the nadir of the RV pressure pulse suggests that factors other than mechanical systole are responsible for the temporal location of P₂.

Recent work in our laboratory has been concerned with the sound pressure correlates of the second heart sound in normal and various disease states. Figure 6 contrasts the sound-pressure relationships found in the normal systemic and pulmonary circulations. A₂ and P₂ are coincident with the incisurae in their respective arterial pressure traces. Figure 6A demonstrates the aortic incisura to be separated from the left ventricular pressure trace by a narrow interval of 10 msec, denoted as hangout. However, in figure 6B, the pulmonary artery incisura is seen to be separated by a much greater hangout interval, 65 msec. Figures 7A and 7B contrast the effect on the right-sided hangout interval of marked isolated dilatation of the pulmonary artery and severe pulmonary hypertension, respectively. The wide hangout interval in the first case is a reflection of increased capacitance of the pulmonary artery, while the narrow hangout interval in the second case is due to the decreased capacitance and increased resistance known to be associated with severe pulmonary hypertension.11, 12

Determination of opposition to forward flow in a pulsatile, distensible system requires consideration not only of the conventional resistance term but also of other factors which include inertance and compliance. The interaction of these multiple factors can
be described by the term impedance. The low impedance of the pulmonary vascular bed is responsible for the relatively wide hangout interval encountered in this circulation. Impedance appears to be a primary determinant of the hangout interval and shows considerable change when altered by various disease states. In the light of these findings, we felt that the impedance of the pulmonary bed might be altered by respiratory phase, which would account for a significant proportion of inspiratory prolongation of the Q-P2 interval.

We attempted to employ a marker that would reflect alterations in RV electromechanical systole and be relatively independent of changes in the
pulmonary vascular bed. Because it was a consistent and easily measurable point, the onset of rapid descent of RV negative dp/dt was the marker chosen to represent the conclusion of systole. No attempt was made to justify this point as the actual end of mechanical systole since, as mentioned above, we were trying to determine relative changes rather than absolute interval durations.

In young normal individuals, the Q-0 interval was found to variably increase during inspiration contrasting with a consistent increase in Q-P2. The reasons for this variability were not specifically investigated, but could be due to differences in depth of respiration which were uncontrolled in our study. Changes in respiratory depth would affect what is probably the primary determinant of inspiratory prolongation of the Q-O interval, i.e., the increase in venous return during this phase. An alternative explanation of Q-O interval variability is that the maximal increase in duration of RV systole, as reflected in Q-O, does not always occur simultaneously with changes maximally augmenting Q-P2 interval. This was the case in five of the seven normal subjects in whom interval measurements were made during successive cardiac cycles.

Although the mean increase in Q-O closely paralleled the mean decrease in Q-A2, no significant correlation was found for these intervals. This is not surprising since there is a variable time lag in the transfer of augmented RV stroke volume to the left side, and the cardiac cycles chosen for measurement frequently did not demonstrate the maximum increase in Q-O interval.

The remaining interval, O-P2 or protodiastolic interval, was felt to include the period which would be affected by the status of the pulmonary vascular bed. The striking finding of this study was the consistent inspiratory increase in O-P2 accounting for the majority of both A2-P2 and Q-P2 interval augmentation. It demonstrated the least variability from subject to subject. The specific events accounting for O-P2 interval prolongation were not elucidated by this study. Among the factors which might influence the alterations in this interval are 1) the structural character of the pulmonic valve, 2) pulmonary vascular resistance and compliance, 3) stroke volume, and 4) the transvalvular pressure gradient.

While the structure or compliance of the semilunar valve would affect the absolute duration of the O-P2 interval, and may vary from subject to subject, in any individual it is likely to be a constant factor from expiration to inspiration. Thus, its character would not

Figure 7

A) Equisensitive micromanometer pressure tracings in the right ventricle and pulmonary artery in a patient with idiopathic dilatation of the pulmonary artery. Note the wide hangout interval of 100 msec. B) Similar record as in A in a patient with severe pulmonary hypertension. Note the narrow hangout interval comparable to that seen in the systemic circulation.
be important in determining respiratory variation of the interval.

In 12 patients with normal calculated pulmonary vascular resistance, Shaver et al. found no significant correlation between the value for this parameter and the right-sided hangout interval. When pulmonary vascular resistance is significantly elevated, however, hangout interval is nearly always narrow. This may not be cause and effect since pulmonary vascular compliance is usually also reduced when resistance rises. When clinically evident enlargement of the pulmonary artery is present in the absence of increased pulmonary vascular resistance, the hangout interval is widened. On the basis of static studies in dog lungs, Roos et al. suggest that during spontaneous inspiration, there would be a small increase in pulmonary resistance accompanied by a considerable increase in flow. An inspiratory decrease in impedance to flow might be accounted for by an increase in pulmonary vascular capacitance taking place in the larger rather than smaller pulmonary vessels. The appropriate volume changes have been demonstrated by Howell et al. It is likely that compliance or capacitance plays a more important role than resistance in determining normal alterations in O-P₂ intervals.

The greater IA of O-P₂ than Q-O interval implies a dissociation between the cessation of RV mechanical systole and the continuation of forward flow past the pulmonic valve. The dissociation between these two events can be explained by considering that forward flow in a large elastic vessel, such as the pulmonary artery, is governed primarily by inertance or that property of mass which resists change in velocity. The positive pressure gradient from right ventricle to pulmonary artery seen in figure 6B represents acceleration of blood flow. Following reversal of this gradient, the impedance of the pulmonary vascular bed is decelerating the RV stroke output while flow is being maintained in a forward direction. Since deceleratory forces are determined in the pulmonary vascular bed, it is possible that inertance maintains forward flow beyond the point at which RV relaxation begins. Analogously, the recent study of Laniado et al. has shown forward flow to persist across the mitral valve for 20–40 msec after the onset of isometric left ventricular contraction and left ventricular-left atrial pressure crossover.

During inspiration, augmented venous return increases the RV end-diastolic volume, thereby increasing both the force of RV contraction and RV stroke volume via the Frank Starling mechanism. Right ventricular stroke mass as well as its peak ejection velocity may be significantly increased, increasing the momentum of forward flow. An inspiratory increase in stroke mass would increase the inertial term even if unaccompanied by a rise in acceleration. Theoretically, even if the impedance characteristics of the pulmonary circulation were unchanged, one could postulate that a longer deceleration period might be necessary, thereby increasing the O-P₂ interval. With our data, it is impossible to determine the role of these theoretical considerations due to the complex interplay of physiologic events occurring during the O-P₂ interval.

However, if the components of normal pulmonary vascular impedance were significantly altered, then it is conceivable that IA would have to occur primarily via increases or decreases in the durations of right or left ventricular systole respectively. The change in the pulmonary vascular bed encountered in pulmonary hypertension would fulfill this condition. Since the hangout interval appears to reflect changes in the pulmonary bed in the same way we have employed the Q-O interval to reflect changes in ventricular events, it was utilized as a direct measurement in four patients with pulmonary hypertension to derive an estimate of the duration of RV systole. Five of six patients with pulmonary hypertension had significant respiratory movement of Q-P₂. In marked contrast to the normal group, four of five demonstrated no significant change in hangout or O-P₂ intervals from expiration to inspiration. Respiratory changes in A₂-P₂ were due to alterations in duration of ventricular mechanical systole.

The rate of pulmonic valve closure between the normal and pulmonary hypertensive groups might seemingly be influenced by the significant differences in absolute pressures. However, when scale changes are accounted for, the transvalvular pressure gradients, following mid-systolic pressure crossover as seen in figure 6B (normal) and figure 7B (pulmonary hypertension), are not significantly different.

The contrast in the mode of IA of the A₂-P₂ interval between the normal and pulmonary hypertensive groups is thus compatible with the hypothesis that normal pulmonary vascular impedance, as reflected in O-P₂ or hangout intervals, plays an important role in producing physiologic splitting of the second heart sound.

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E I Curtiss, R G Matthews and J A Shaver

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