The Splitting of the Second Heart Sound in Normal Subjects and in Patients with Congenital Heart Disease

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ROUANET, in 1832, demonstrated that the second heart sound results from closure of the semilunar valves. In 1865, on the basis of clinical observations, Potain indicated that the second heart sound may be split into two components and that the degree of this splitting may vary with respiration. More recently the studies of Leatham and collaborators have focused considerable attention on the splitting of the second heart sound and, at the present time, precise characterization of this sound is of prime importance in auscultation of the heart. A physiologic basis for the interpretation of this auscultatory finding was first provided by Katz, in a study in which the timing of the dynamic events of the cardiac cycle in the two sides of the heart was determined, and slight asynchrony in the closure of the semilunar valves was noted. These observations were subsequently extended to human subjects with normal cardiovascular systems, in whom it was observed that pulmonic valve closure followed aortic valve closure by 0.028 ± 0.010 second.

It is now well established that in normal subjects as well as in patients with many forms of heart disease, the time interval between the sounds of aortic and pulmonary valve closure increases with inspiration. It has been reported that in patients with atrial septal defects (ASD) this time interval is longer than in normal subjects during expiration and shows relatively little change during the respiratory cycle. The mechanisms responsible for these abnormalities are still under debate. The purpose of the present report is (1) to supply measurements of the effects of respiration and of the Valsalva maneuver on the second heart sound in normal subjects, in a large series of patients proved to have ASD, as well as in patients with other forms of congenital heart disease, (2) to provide hemodynamic-phonocardiographic correlations in these patients, (3) to demonstrate the effects of successful surgical closure of ASD on the splitting of the second heart sound, and (4) to present observations that provide an explanation for the mechanism of splitting of the second heart sound in normal subjects and in patients with ASD.

Clinical Material

This study is based on an analysis of the phonocardiograms obtained from 350 patients studied at the National Heart Institute between 1958 and 1961. The diagnosis was considered to be firmly established in every instance by means of detailed clinical examination and specialized studies. Right heart catheterization was performed on all patients with functional heart murmurs and congenital heart disease. In these patients the presence of a left-to-right shunt was detected by either the nitrous oxide or the inhaled Kr test. In addition, all patients had dye-dilution curves further to characterize their circulatory shunts. The patients with aortic stenosis were all studied by left heart catheterization, which was generally carried out by the transbronchial, transseptal, or anterior percutaneous technique. The diagnosis was confirmed at operation in 194 of the 350 patients. The age range for each group of patients reported is presented in Table 1.

As indicated above, particular attention was directed to the effects of operation on the behavior of the second heart sound of patients with ASD. Preoperative and postoperative phonocardiograms were available for analysis in 31 patients, all of whom were operated upon with the aid of extracorporeal circulation; 29 had the ostium secundum or sinus venosus type of defect, while two had ostium primum defects, i.e., a low atrial septal defect with a cleft in the mitral valve. The postoperative phonocardiographic and cardiac catheterization studies were carried out 3 to 12 months after the operation.

All phonocardiograms were taken on a Sanborn-Twin beam photographic recorder at a paper speed of 75 mm. per second utilizing a logarithmic amplifying system. The recordings were obtained from the four valvular areas, and the tracing in which the second heart sound was most clearly defined

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Effects of inspiration on the duration of left ventricular systole (Q-A2) plotted along the abscissa, and on the duration of right ventricular systole (Q-P2) plotted along the ordinate. The diagonal lines demonstrate the effects of inspiration on the width of splitting of the second heart sound. The broken diagonal line separates most of the normal subjects from patients with ASD. The solid triangles represent those patients with ASD who had pulmonary artery mean pressures in excess of 50 mm. Hg or pulmonary/systemic flow ratios less than 1.5/1.0, or both.

was employed in the analysis. An electrocardiographic lead and indirect carotid pressure pulse were utilized for timing reference. Recordings were obtained during continuous spontaneous respiration and in many patients during and immediately after the Valsalva maneuver. In determining the time intervals between aortic and pulmonic valve closure, the longest interval recorded during inspiration and the shortest interval recorded during expiration in a single respiratory cycle.
Relationship between the preceding R-R interval and Q-P2, Q-A2, and A2-P2 in a patient with ASD and atrial fibrillation.

were utilized for analysis. All measurements were made from the onset of the QRS and of each component of the second sound. The error of measurement was considered to be below 0.005 second.

In the performance of the Valsalva maneuver the subject was asked to expire against a closed glottis with the chest in the mid-respiratory position for a period of several seconds, and then to relax without inspiring. The phonocardiographic observations were carried out during and immediately after the Valsalva maneuver for a total of 8 to 10 cardiac cycles.

Results

Effect of Respiration on Q-A2, Q-P2 and A2-P2

In the 51 normal subjects the changes in the duration of the interval from the onset of ventricular depolarization to the aortic valve closure sound (Q-A2) during inspiration ranged from -20 msec. to +10 msec. and the average change was -5.2 msec. (fig. 1). Q-P2 increased during inspiration in all but one of these subjects. The maximum increase was 50 msec. while the average increase was 32.6 msec. The time interval between aortic and pulmonic valve closure (A2-P2) increased in all of the normal subjects, these increases ranging from 10 to 60 msec., with an average increase of 37.8 msec.

In the patients with ASD a pattern different from the normal was observed. The inspiratory increase of Q-P2 averaged only 4.6 msec. for the entire group, with an increase less than 20 msec. in 112 patients. Q-A2 showed no change during respiration in eight of the 118 patients, and in the remainder it increased or decreased up to 20 msec. The change in A2-P2 was much less during respiration than in the normal subjects. In 87 patients there was no change, and in 28 there was an increase of only 10 msec. In three patients the increase of A2-P2 equaled 40 msec., and they had either pulmonary hypertension (pulmonary artery mean pressure greater than 50 mm. Hg) or small left-to-right shunts, with pulmonary to systemic flow ratios less than 1.5/1.0 (fig. 1).

Although Q-P2 and A2-P2 showed little change with respiration in patients with ASD, alterations in the duration of the preceding R-R interval resulted in significant changes in these time intervals. Phonocardiograms were recorded at a constant respiratory position in four patients with ASD in whom atrial arrhythmias resulted in marked beat-to-beat variations in the R-R intervals. A representative result is plotted in figure 2 in which it is evident that as the preceding R-R interval lengthened, Q-P2 increased more than Q-A2 and, therefore, A2-P2 increased.

Relationship between Heart Rate and the Duration of Systole

The relationship between heart rate and the

<table>
<thead>
<tr>
<th>Diagnosis and Age Distribution of Patients Studied</th>
<th>Number studied</th>
<th>Ages (years)</th>
<th>Average</th>
<th>Number operated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>51</td>
<td>4-49</td>
<td>14.2</td>
<td>0</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>118</td>
<td>3-65</td>
<td>27.1</td>
<td>80</td>
</tr>
<tr>
<td>Pulmonic stenosis</td>
<td>30</td>
<td>1-36</td>
<td>14.1</td>
<td>20</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>69</td>
<td>2-40</td>
<td>11.9</td>
<td>40</td>
</tr>
<tr>
<td>Ventricular septal defect with pulmonic stenosis</td>
<td>10</td>
<td>2-23</td>
<td>12.0</td>
<td>5</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>16</td>
<td>3-9</td>
<td>5.8</td>
<td>6</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>44</td>
<td>4-32</td>
<td>13.7</td>
<td>30</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>13</td>
<td>2-41</td>
<td>12.8</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>350</td>
<td></td>
<td></td>
<td>194</td>
</tr>
</tbody>
</table>
time interval from the onset of ventricular depolarization to the pulmonic valve closure sound (Q-P₂) in normal subjects and in patients with ASD during expiration is shown in figure 3. It is clear that there is an inverse relationship between heart rate and Q-P₂ in both groups of patients. The broken line outlines the highest values for Q-P₂ encountered in the normal subjects. Although at any given heart rate there was considerable overlap between the values for Q-P₂ in the normal subjects and in the patients with ASD, 62 of the 118 patients with this malformation had values of Q-P₂ which exceeded the highest values observed in normal subjects at similar heart rates. Similarly, 16 of the 30 patients with pure pulmonic stenosis (PS), 12 of the 67 patients with ventricular septal defect (VSD) and eight of the 10 patients with combined VSD and PS also had prolongation of Q-P₂ above the greatest normal values. The other patients with the malformations listed above had values in the normal range. The Q-P₂ and Q-A₂ intervals in patients with congenital aortic stenosis (CAS) and patent ductus arteriosus (PDA) also tended to be related inversely to the heart rate but showed no consistent deviation from the normal.

**Effect of Valsalva Maneuver on Q-A₂, Q-P₂, and A₂-P₂**

In general, release of the Valsalva maneuver exaggerated the effects of inspiration in normal subjects (fig. 4) but had relatively little effect on Q-P₂, Q-A₂, and A₂-P₂ in patients with ASD (fig. 5). In the normal subjects release of Valsalva increased Q-P₂ by 15 to 75 msec. (av. = 40.7 msec.) ; Q-A₂ changed by -30 to +10 msec. (av. = -9 msec.); A₂-P₂ increased by 20 to 80 msec. (av. = 49.7 msec.). In contrast, in the 42 patients with ASD studied, the change of Q-A₂ after release of the Valsalva maneuver ranged from -20 to +20 msec. (av. = +1.4 msec.) ; the change of Q-P₂ ranged from -10 to 50 (av. = +4.7 msec.) and A₂-P₂ increased by an average of only 3.3 msec. (fig. 6). Thus, it is evident that analysis of changes in Q-A₂ and Q-P₂ following release of Valsalva permits separation of

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*Figure 3*

*Relationship between heart rate and Q-P₂, recorded during expiration in normal subjects and patients with ASD.*
normal subjects from patients with ASD. Again the patients with this malformation whose values were similar to those encountered in normal subjects had severe pulmonary hypertension or a very small left-to-right shunt.

**A2-P2 during the Respiratory Cycle**

**Normal Subjects**

During expiration in normal subjects A2-P2 ranged from 0 to 40 msec., with an average of 10.6 msec. (fig. 7). As already indicated, this time interval increased during inspiration in all these subjects. In general there was an inverse correlation between A2-P2 during expiration and the augmentation of this interval during inspiration (fig. 7).

**ASD, Preoperative**

In patients with ASD the expiratory A2-P2 tended to be greater than in the normal subjects and averaged 50.2 msec. The inspiratory augmentation of this interval was less than in normal subjects. One hundred and thirteen of the 118 patients with ASD had expiratory A2-P2 intervals of at least 30 msec. and an inspiratory augmentation of less than 20 msec. but only one normal subject had an A2-P2 interval that fell within these limits. Of the five patients with ASD who did not fall into these
limits, three had severe pulmonary hypertension or only a small left-to-right shunt, or both, as defined above (fig. 7).

The average values for $A_2$-$P_2$ during normal respiration, and immediately after release of the Valsalva maneuver in the normal subjects...
and in the patients with ASD are summarized in figures 8 and 9.

ASD, Effect of Operation

At the time of the postoperative catheterizations it was observed that the left-to-right shunts had been completely abolished in 29 of the 31 patients with ASD. In the other two patients the magnitude of the shunt was reduced from the preoperative level but it had not been completely eliminated. There was a distinct tendency for \( A_2-P_2 \) to return to normal limits following successful surgical clo-

**Figure 6**

*Effects of release of the Valsalva maneuver on \( Q-A_2, Q-P_2, \) and \( A_2-P_2 \). For explanation see legend of figure 1.*
A decrease in A₂-P₂ during expiration occurred in 29 of the 31 patients; one of the two exceptions had pulmonary hypertension and normal splitting of the second heart sound prior to operation. Following complete closure of the defect the inspiratory increase of A₂-P₂ exceeded 10 msec. in 26 of the 29 patients. The two patients with residual left-to-right shunts exhibited a decrease in the expiratory A₂-P₂ interval from that observed preoperatively, but showed an augmentation of only 0 and 10 msec. respectively during inspiration (fig. 10). Thus, in the postoperative period both of these patients exhibited splitting of the second heart sound, which was indistinguishable from that observed in patients with unoperated ASD (fig. 7) but which could be differentiated from the pattern of splitting observed in those patients whose defects had been successfully closed.

**Pulmonic Stenosis**

The expiratory A₂-P₂ interval and its augmentation during inspiration in the normal subjects and in the patients with pulmonic stenosis (PS) is plotted in figure 12. During expiration A₂-P₂ was less than 40 msec. in 46 of the 51 normal subjects and in all six of the patients with PS whose peak systolic pressure gradients between the right ventricle and pulmonary artery were less than 20 mm. Hg. In contrast A₂-P₂ during expiration equaled 40 msec. or more in all 24 patients with PS whose pressure gradients exceeded 20 mm. Hg. During inspiration the augmentation of A₂-P₂ was within normal limits in these patients (fig. 13).

**Aortic Stenosis, Patent Ductus Arteriosus**

During expiration A₂ and P₂ were fused and occurred synchronously in 38 of the 44 patients with congenital aortic stenosis (AS). In the other six patients A₂ followed P₂ by
20 to 40 msec., i.e., the A₂-P₂ interval was negative (fig. 14). In 21 patients with AS there was no inspiratory increase of A₂-P₂. In the others this increase ranged from 10 to 60 msec., as in the normal subjects. When the combination of A₂-P₂ during expiration and the change of this interval during inspiration are considered, it was observed that 29 of the 44 patients with congenital AS fell outside the range encountered in the normal subjects (fig. 14). In 12 of the 15 patients with AS in whom A₂-P₂ fell into the normal range, the peak systolic pressure gradients between the left ventricle and brachial artery measured at left heart catheterization was less than 75 mm. Hg.

The behavior of the second heart sound in patients with PDA resembled that observed in patients with congenital AS. During expiration A₂ and P₂ were fused in eight patients, negative in four, and positive in only one patient. When the combination of the expiratory A₂-P₂ and its change during inspiration was considered, seven of the 13 patients with PDA fell outside the range encountered in the normal subjects (fig. 14).

Other Malformations

In patients with ventricular septal defect (VSD), the relationship between the two components of the second heart sound was observed to fall into the normal range with only an occasional exception. There was a lower incidence of a single second heart sound during expiration in the patients with VSD and large left-to-right shunts than in the normal subjects.

In 16 patients with PS, VSD, and a right-to-left shunt (tetralogy of Fallot) only one component of the second heart sound could be recorded; simultaneous carotid pulse tracings indicated that this was the sound of aortic valve closure (A₂).

Effect of Respiration on Pulmonary Arterial Oxygen Saturation in Patients with ASD

In order to elucidate the mechanism responsible for the relative constancy of A₂-P₂ during respiration in patients with ASD, blood samples were withdrawn from the pulmonary artery first during inspiration and then during expiration. Several respiratory cycles were required to obtain each sample, and the oxygen saturations were determined by the manometric method of Van Slyke and Neill. In each of the eight patients studied, the pulmonary arterial oxygen saturation during expiration exceeded the saturation during inspiration (table 2); the average difference in saturation was 3.6 per cent. The oxygen saturation of mixed venous blood proximal to the entry of the left-to-right shunt was calculated from the arterial oxygen saturation and

Table 2
Systemic and Pulmonary Arterial Oxygen Saturation in Patients with ASD

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age (years)</th>
<th>Arterial O₂ sat.</th>
<th>P.A. O₂ sat. during insp.</th>
<th>P.A. O₂ sat. during exp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>G.G.</td>
<td>13</td>
<td>94.6</td>
<td>85.0</td>
<td>91.4</td>
</tr>
<tr>
<td>F.D.</td>
<td>7</td>
<td>93.2</td>
<td>77.2</td>
<td>82.7</td>
</tr>
<tr>
<td>P.S.</td>
<td>39</td>
<td>93.0</td>
<td>83.0</td>
<td>85.9</td>
</tr>
<tr>
<td>H.J.</td>
<td>22</td>
<td>99.0</td>
<td>90.0</td>
<td>91.5</td>
</tr>
<tr>
<td>K.E.</td>
<td>19</td>
<td>97.0</td>
<td>85.8</td>
<td>88.8</td>
</tr>
<tr>
<td>M.M.</td>
<td>8</td>
<td>92.9</td>
<td>88.8</td>
<td>90.0</td>
</tr>
<tr>
<td>M.A.</td>
<td>12</td>
<td>96.0</td>
<td>88.0</td>
<td>92.0</td>
</tr>
<tr>
<td>L.B.</td>
<td>9</td>
<td>94.0</td>
<td>84.0</td>
<td>88.0</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>95.0</td>
<td>85.2</td>
<td>88.8</td>
</tr>
</tbody>
</table>

ASD, atrial septal defect; Insp., inspiration; Exp., expiration.

Average values for A₂-P₂ during respiration in normal subjects and patients with ASD.

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the pulmonary/systemic flow ratio determined by the Kr²⁶ test. Assuming the durations of inspiration and expiration to have been equal, it was then possible to calculate the shunt/systemic flow ratio during both phases of the respiratory cycle. In each of the patients this ratio was greater during expiration (av. = 1.80/1.00) than during inspiration (av. = 0.64/1.00).

Discussion

In the present study the onset of ventricular depolarization (the Q wave of the electrocardiogram) was chosen as the reference point for all measurements, since this point can be easily recognized on all tracings. The time interval between the onset of ventricular depolarization and of closure of either of the semilunar valves (Q-A₂ and Q-P₂) actually represents the sum of three periods: (1) the interval between the onset of ventricular depolarization and the onset of ventricular contraction, (2) the duration of isometric ventricular contraction, and (3) the duration of ventricular ejection. The first two of these periods remain virtually constant under a wide variety of conditions and constitute only a small fraction of the total interval between the Q wave and the second heart sound. It is considered that in the absence of gross abnormalities of intraventricular conduction, changes in Q-P₂ and Q-A₂ represent changes in the duration of right and left ventricular ejection respectively.

Consideration of the well-established fact that the duration of ventricular ejection varies directly with the stroke volume₁⁵ permits explanation of the observed effects of respiration and of the Valsalva maneuver on the splitting of the second heart sound in normal individuals. Inspiration augments the inflow,₂⁶ the effective filling pressure,₁⁷ the end-diastolic volume,₁⁸ and the stroke output₁⁹ of the right ventricle and has an opposite but smaller effect on the left ventricle.₁⁹ This explains the prolongation of Q-P₂ and the simultaneous shortening of Q-A₂ during inspiration, resulting in an increase in A₂-P₂. It has been suggested by Boyer and Chisholm₂⁰ and more recently by Shafter₂¹ that in normal individuals the inspiratory abbreviation of left ventricular systole is approximately equal to the prolongation of right ventricular systole. The observations on normal subjects presented in figure 1 are not consonant with these views. Of the average inspiratory increase of A₂-P₂ of 37.8 msec., 32.6 msec. or 86 per cent was contributed by prolongation of right ventricular systole and only 5.2 msec., or 14 per cent, by shortening of left ventricular systole. In only seven of the 51 subjects did the shortening of left ventricular systole during inspiration equal or exceed the prolongation of right ventricular systole. The observation that during respiration the duration of left ventricular systole is altered far less than the duration of right ventricular systole is also consistent with the experimental observations that the respiratory variations in the filling and stroke volume of the right ventricle exceed those of the left.₁⁹

The abnormally wide splitting of the second heart sound in patients with ASD is a well-known clinical sign.₈,₉,₂² It was suggested that the alterations in the pattern of right ventricular depolarization commonly observed in patients with this anomaly may account for
the delay in pulmonic valve closure. However, hemodynamic studies in patients with ASD and so-called "incomplete right bundle-branch block" have clearly established that there is no prolongation of the time interval between the onset of ventricular depolarization and of right ventricular contraction. In addition, the observations of Leatham and of Perloff and Harvey, have shown that following surgical closure of ASD the splitting of the second heart sound often demonstrates a normal pattern while the electrocardiographic changes characteristic of this malformation persist.

As shown in figure 3, at any given heart rate, right ventricular systole tends to be longer in patients with ASD than in normal subjects. In patients with this malformation the stroke volume of the right ventricle is abnormally large and exceeds that of the left ventricle. All these considerations suggest that prolongation of right ventricular ejection is responsible for the abnormally wide splitting of the second heart sound in these patients.

Another important characteristic of the second heart sound in patients with ASD is that the wide splitting tends to show little variation during the respiratory cycle. Leatham and Gray observed no measurable change in the time interval between the two components of the second heart sound in 21 of 30 patients with ASD, whereas Shafter found that among 16 patients the maximum change with respiration was 29 msec. In the present series of patients with ASD it was observed that in 87 there was no measurable change in A2-P2, and that in 30 there was an increase of 5 to 10 msec. The three patients with larger changes had severe pulmonary hypertension and only small left-to-right shunts (figs. 1 and 7).

The mechanism for this tendency of the splitting of the second heart sound to show little, if any, variation during the respiratory cycle is not clear. Leatham and Gray consid-
erated the inequality of right and left ventricular outputs to be the responsible factor. It has also been suggested that in these patients the "overfilled" right ventricle cannot further augment its filling during inspiration and therefore does not increase its stroke volume. If this hypothesis were correct, however, it would be anticipated that the duration of right ventricular ejection would be shortened when the systemic venous return is impeded by prolonged expiration or by the Valsalva maneuver.

It has been shown by Perloff and Harvey as well as in figure 2, that the duration of right ventricular systole in patients with ASD does not always remain constant. In the presence of changes in the duration of diastole due to atrial arrhythmias, Q-P₂ and A₂-P₂ were found to increase with the R-R interval. In the same patients no variation in A₂-P₂ was observed throughout the respiratory cycle. Thus, it is apparent that when changes in right ventricular filling do occur in patients with ASD the duration of right ventricular ejection and the degree of splitting of the second heart sound may be altered.

An alternative explanation for the tendency to fixation of splitting of the second heart sound in patients with ASD is that during the respiratory cycle the two venous systems (systemic and pulmonary) that contribute blood to the right ventricle vary the magnitude of their contributions reciprocally. As already mentioned, in normal subjects the in-
flow of blood into the right heart from the systemic venous bed is augmented during inspiration and a decline in filling of the left side of the heart takes place simultaneously. It is suggested that this sequence of events is not disturbed in patients with ASD. If one considers that in these patients the two atria form a common reservoir for the filling of the ventricles, then the effect of inspiration on the stroke volume of the ventricles would be determined by the net effect of inspirations on the inflow into this common atrial reservoir. When the inspiratory augmentation of the systemic venous return is balanced by an equal decrease in pulmonary venous return, no significant inspiratory change of inflow into the atrial reservoir, of ventricular filling and discharge and, therefore, of Q-P₂, Q-A₂, and A₂-P₂ would be expected. Indeed, no change in these intervals was observed in 63 of the patients with ASD studied. However, if there is a net augmentation of inflow into the atrial reservoir during inspiration, an increase of the filling and discharge of the ventricles and a prolongation of both Q-A₂ and Q-P₂ would be expected; in 25 of the patients with ASD there was an inspiratory increase of both Q-P₂ and Q-A₂. If the inspiratory decline in pulmonary venous filling exceeds the simultaneous augmentation of right ventricular filling, then a shortening of the duration of ventricular ejection would be expected; this occurred in only two patients. Under all circumstances, the exact distribution of blood between the two ventricles depends on the relative compliance of these chambers during diastole.²⁵

If, as described above, respiratory variations in the magnitude of the inflow of blood from the systemic and pulmonary venous beds into the atria takes place, it would be anticipated that variations in the magnitude of the left-to-right shunt would also occur. Suggestive evidence that the left-to-right shunt actua-

Figure 12

A₂-P₂ during expiration and increase of this interval during inspiration in normal subjects and patients with PS. The broken vertical line separates the majority of these patients.
SPLITTING SECOND HEART SOUND

A representative phonocardiogram recorded from a patient with PS. Although there is significant splitting of the second sound during expiration, \( A_2P_2 \) increases further during inspiration.

ally diminishes during inspiration and becomes augmented during expiration was provided by the observation that in patients with ASD the oxygen saturation of blood withdrawn from the pulmonary artery during expiration exceeds the saturation of blood withdrawn during inspiration (table 2). In conclusion, these considerations would suggest that the relative constancy of the splitting of the second heart sound in patients with ASD is not due to an inability of the right ventricle to augment its stroke output during inspiration, but it is postulated that the constancy of splitting is due to reciprocal changes in the magnitude of the left-to-right shunt and the systemic venous inflow into the right ventricle during respiration.

Regardless of the exact mechanism underlying the variations in the splitting of the second heart sound, precise auscultatory and phonocardiographic analyses of the effects of normal respiration and of the Valsalva maneuver on this sound are of great clinical value. In addition to indicating the time of closure of the pulmonic and aortic valves, the relative intensities of the two components of the second heart sound provide some information regarding the relative levels of pressure in the pulmonary artery and aorta. The width of splitting during expiration and the mag-
Figure 14

A2-P2 interval during expiration, and the increase of this interval during inspiration in normal subjects and in patients with AS and PDA. When A2 followed P2 the A2-P2 interval was considered to be negative. All values to the left and below the broken line were outside of the normal range.

Magnitude of the changes in this time interval during inspiration can generally be appreciated by careful auscultation, but phonocardiographic tracings are necessary for precise measurements. In the vast majority of patients with ASD the inspiratory increase of A2-P2 is 10 msec. or less. An increase of 10 msec. was found in only two of 51 normal subjects, and it would seem appropriate to designate a change of A2-P2 up to 10 msec. during normal respiration as "fixed splitting" of the second heart sound. It is of interest that the three patients with ASD who did not demonstrate fixed splitting did not have the hemodynamic features that are typical for ASD; all three had very small left-to-right shunts and one also had severe pulmonary hypertension.

In normal subjects the Valsalva maneuver tends to exaggerate the changes in Q-P2, Q-A2, and A2-P2 observed during quiet respiration (figs. 4, 6, and 9), but this maneuver does not abolish the "fixed splitting" of the second sound in patients with ASD (fig. 5). In the normal subjects the mean increase of A2-P2 during inspiration equaled 37.8 msec.; this time interval increased to an average of 49.7 msec. following the Valsalva maneuver. In contrast, A2-P2 increased by a mean value of only 3.3 msec. both during inspiration and following the Valsalva maneuver in patients with ASD. During auscultation this maneuver has been found to be helpful in distinguishing patients with ASD from those subjects who on clinical examination tend to show little variation in A2-P2 during normal respiration. We have encountered five patients without ASD, including two subjects without cardiovascular disease, who demonstrated "fixed splitting" of the second heart sound during normal respiration phonocardiographically and in whom greater changes in A2-P2 were
observed following the Valsalva maneuver. Exaggeration of the change in splitting of the second heart sound by this maneuver has also been of considerable aid during cardiac auscultation of patients with unusually wide splitting of this sound during expiration. In such patients any given change in $A_2-P_2$ is far more difficult to appreciate by auscultation than a similar change in patients with shorter $A_2-P_2$ intervals.

In the immediate postoperative period following repair of an ASD some patients show little, if any, change of $A_2-P_2$ during normal respiration. These patients also showed a normal increase of $A_2-P_2$ following the Valsalva maneuver. When studied 3 to 12 months following operation the second heart sound tended to exhibit a normal pattern during quiet respiration in those patients in whom the defects were closed. In two patients with residual shunts, however, distinctly abnormal splitting persisted. Thus, phonocardiographic study in the postoperative period is a useful technic in the clinical assessment of patients with ASD (fig. 10).

In the patients with moderate or severe PS and an intact ventricular septum, $A_2-P_2$ during expiration tended to be prolonged and in the same range as observed in patients with ASD. The patients with PS showed a greater increase in this interval during inspiration, however, than did those with ASD. In both patients with PS and fixed splitting of the second heart sound, illustrated in figure 12, a normal increase of $A_2-P_2$ occurred following the Valsalva maneuver. These results are in agreement with those of Leatham and Weitzman28 and of other investigators.27-29 As in patients with ASD with a small shunt, mild degrees of PS generally result in normal splitting of the second heart sound. The increased resistance to right ventricular ejection in these patients is apparently the cause of the prolongation of $Q-P_2$ and the abnormally wide splitting of the second heart sound. When a VSD is associated with obstruction to right ventricular outflow, there is only a tendency to abnormal prolongation of $A_2-P_2$ during expiration in those patients with a large left-to-right shunt. When the obstruction to right ventricular ejection is severe and there is a large right-to-left shunt (tetralogy of Fallot) the pulmonary closure sound cannot usually be recorded.

Figure 15

A representative phonocardiogram recorded from a patient with severe AS. There is paradoxical splitting of the second heart sound, which is single during inspiration but split during expiration. The carotid pulse (lower tracing) shows that $A_2$ follows $P_2$. 
In patients with obstruction to left ventricular outflow, there is a tendency to prolongation of left ventricular ejection, and this is reflected either in reversal of the normal sequence of semilunar valve closure or simultaneous valve closure during expiration (figs. 14 and 15). In those patients in whom the sequence is reversed, prolongation of Q-P₂ and abbreviation of Q-A₂ occur during inspiration, resulting in narrowing of the P₂-A₂ interval. This abnormality has been termed "paradoxical" splitting of the second heart sound, and it is also evident in some patients with patent ductus arteriosus (fig. 14) in whom the prolongation of left ventricular ejection is presumably related to the increased stroke volume of the left ventricle.

Summary
The characteristics of the second heart sound were analyzed in 350 phonocardiograms recorded from patients in all of whom the diagnosis was proved either at operation or by detailed catheterization studies. A₂-P₂ during expiration averaged 10.6 msec. in normal subjects. Q-A₂ changed little during inspiration, with an average decrease of only 5.2 msec., while Q-P₂ increased by an average of 32.6 msec. The average increase of A₂-P₂ during inspiration was therefore 37.8 msec. In patients with ASD, A₂-P₂ during expiration averaged 50.2 msec. and the inspiratory change in Q-P₂ averaged only 4.6 msec. In 115 of 118 patients with ASD the inspiratory increase of A₂-P₂ ranged from 0 to 10 msec. Following successful surgical closure 29 patients with ASD developed the normal inspiratory augmentation of A₂-P₂; in the two patients in whom the defect was not completely closed the relatively constant A₂-P₂ noted preoperatively persisted.

Release of the Valsalva maneuver exaggerated the inspiratory increase of A₂-P₂ observed in normal subjects but did not modify this interval in patients with ASD. Analysis of the effect of release of the Valsalva maneuver on A₂-P₂ was helpful in separating patients with ASD from normal subjects. Evidence was presented that the relative constancy of the splitting of the second heart sound in patients with ASD is due to reciprocal changes in the magnitude of the left-to-right shunt and the systemic venous inflow into the right ventricle during respiration.

In patients with moderate or severe pulmonary stenosis, A₂-P₂ during expiration was longer than in normal subjects and in the same range as in patients with ASD. However, patients with PS showed a normal augmentation of A₂-P₂ during expiration. In patients with congenital AS, and those with PDA, left ventricular ejection tended to be prolonged with reversal of the normal sequence of semilunar valve closure or simultaneous closure of these valves during expiration.

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References

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The Early History of Instrumental Precision in Medicine

The true rate of advance in medicine is, however, not to be tested by the work of single men, but by the practical capacity of the mass. The truer test of national medical progress is what the country doctor is. How useful, how simple, it seemed to count the pulse and respiration, or to put a thermometer under the tongue, and yet it took in the one case a century, and in another far more, before the mass of the profession learned to profit by the wisdom of the few.—S. Weir Mitchell, M.D., Transactions of the Congress of American Physicians and Surgeons held at Washington, D.C., 1891.

The Splitting of the Second Heart Sound in Normal Subjects and in Patients with Congenital Heart Disease

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