Physiologic Mechanisms in Aortic Insufficiency

I. The Effect of Changing Heart Rate on Flow Dynamics
II. Determinants of Austin Flint Murmur

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SUMMARY We studied the dynamic changes in mitral flow patterns and in mitral valve motion before and after producing acute, reversible aortic insufficiency (AI) in nine open-chest dogs. Phasic mitral flow, the mitral valve echocardiogram, the intracardiac phonocardiogram and other hemodynamic variables were measured. During moderate AI (mean regurgitant fraction 52 ± 5%) (± sd), the antegrade filling volume decreased from 31 ± 7 to 24 ± 6 ml (p < 0.01), but the peak protodiastolic mitral flow rate increased from 139 ± 37 to 157 ± 42 ml/sec (p < 0.01), reflecting the shift of a larger fraction of total mitral filling volume to early diastole. In six dogs, atrial pacing was used to examine the hemodynamic effects of tachycardia. Increasing the heart rate from 90 to 120 beats/min increased cardiac output from 2.64 ± 0.56 to 3.3 ± 0.831/min (p < 0.05) and decreased left atrial pressure from 24 ± 8 to 17 ± 7 mm Hg (p < 0.05). Increasing heart rate to 150 beats/min compromised mitral filling, reduced cardiac output and increased left atrial pressure. Moderate tachycardia improves cardiac performance in AI by reducing regurgitant volume, without significantly reducing transmural filling volume. The mitral valve echocardiogram showed only a small decrease in cusp opening amplitude during AI. A low-pitched left ventricular inflow tract murmur was recorded in protodiastole and corresponded in time to the rapidly increasing mitral flow. We conclude that the major determinant of the turbulence responsible for the creation of the Austin Flint murmur is the antegrade mitral flow stream and its mixing with the retrograde aortic flow.

THE PATHOPHYSIOLOGY, clinical recognition and management of aortic insufficiency (AI) have been studied extensively in recent years. Clinical expressions of chronic and acute aortic regurgitation have been well defined,1 and data regarding the natural history of the disease2 3 and the proper selection of patients for medical vs surgical treatment is rapidly accumulating.4 7 However, little is known about the dynamics of aortic ventricular diastolic flow transport and, hence, about the significance of alterations in diastolic left ventricular (LV) filling in AI. To compensate for the immediate decrease in effective flow, AI may rapidly activate other physiologic mechanisms in addition to the Starling mechanism. Tachycardia is of particular benefit to patients with chronic or acute AI,4 although the mechanism by which increased heart rate (HR) specifically favors the hemodynamics of AI is not clear.5 9 12

We undertook the present study to investigate the dynamic changes that occur on the left side of the heart with the onset of acute AI. Using our established technique of simultaneous phasic mitral flow and echocardiographic measurements, we placed particular emphasis on LV filling and mitral valve motion during the different phases of diastole. We concentrated on two aspects of mitral flow: the mechanism by which moderate increases in HR affect mitral and aortic flow to improve LV pump function, and the role of mitral flow in the production of the Austin Flint murmur.

Animal Preparation and Instrumentation

Nine healthy mongrel dogs that weighed 25–30 kg were anesthetized with i.v. pentobarbital, 30 mg/kg, and placed on artificial respiration. The chest was opened by midsternotomy and left thoracotomy, the pericardium was incised, and the heart was suspended in a pericardial cradle. Cardiac instrumentation was carried out as described previously.13 15 Briefly, transmural flow was recorded with an electromagnetic flow probe sutured above the mitral annulus during cardiopulmonary bypass. A second flow probe was positioned around the proximal ascending aorta.

High-fidelity pressure readings were obtained by inserting catheter-tip micromanometers (Millar) into the left ventricle and left atrium. The aortic pressure was measured with a fluid-filled catheter and a Statham gauge. All three pressures were calibrated for equal sensitivity and common zero. The rate of rise of LV pressure (LV dp/dt) and the LV intracardiac phonocardiogram were derived from the high-fidelity LV pressure signal.13 When the phonocardiogram was recorded, the transducer was located at the LV inflow tract. M-mode or two-dimensional echocardiograms of the mitral valve or LV structures were obtained by lightly placing the transducer on the right ventricular surface adjacent to the interventricular septum.14

Reversible AI was induced with a collapsible basket carried at the tip of a catheter. The basket was intro-
duced through the aortic valve through the LV apex or through the carotid artery (fig. 1), and was opened and closed by remote control.\textsuperscript{16, 17} To investigate the effects of increased HR on the hemodynamics of AI, in six dogs the sinoatrial node was crushed and the left atrium was paced at rates of 90, 120 and 150 beats/min. Atrial pacing was also used to achieve a constant HR when regular sinus rhythm was absent.

**Measurements and Calculations**

The hemodynamic data and ECG were recorded on an oscillographic recorder (DR-12, Electronics for Medicine) at 100 mm/sec. M-mode echocardiograms were recorded using a separate echocardiograph (Picker, model 80 C1). To synchronize different events accurately, the aortic flow curves were registered simultaneously by both recorders. Two-dimensional echocardiograms were recorded on a video tape recorder (Sanyo 7100) and events were synchronized by the ECG and audio input.

Aortic stroke volume (SV), aortic regurgitant volume (RV) and LV filling volume (FV) (fig. 2) were calculated by digitizing the respective aortic and mitral flow curves with a sonic digitizer (Science Accessories GP-3) coupled to a digital computer (PDP 11/34). The accuracy of the method has been verified.\textsuperscript{15} Regurgitant fraction (RF) was calculated as RV/SV; cardiac output as (SV − RV) × HR = FV × HR; total ejected volume (TEV) as SV × HR; and total regurgitant volume (TRV) as RV × HR.

The zero level for mitral flow was determined during systole and for aortic flow during diastole before the induction of AI. Occasionally, the opening of the basket apparently shifted the aortic flow curve and a new baseline was established as follows. For each test sequence to be analyzed, the average FV of three control (before AI) cardiac beats was divided by the average of a similar number of aortic SVs. The ratio was defined as a correction factor to the aortic flow calibration. The aortic flow baseline during regurgitation was then determined by setting FV = SV − RV. FV was chosen as the standard because the mitral flow probe is

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**Figure 1.** A frame taken from a two-dimensional echocardiogram showing a longitudinal view of the mitral valve with the basket in an open position in the aortic valve. The mitral flow probe is seen in profile (arrow, right panel). Ao = aorta; LV = left ventricle; LA = left atrium; LVPW = left ventricular posterior wall.

**Figure 2.** Original oscillographic record of hemodynamic data before aortic insufficiency (A) and during steady-state aortic insufficiency (B). (C) Records before and during aortic insufficiency are superposed to illustrate changes in mitral flow (MiF) configuration, left ventricular pressure (LVP) and left atrial diastolic pressure (LAP). During aortic insufficiency, total mitral filling volume (FV) decreased, but FV during the first 100 msec of diastole and maximal MiF velocity both increased. A small amount of mid-diastolic mitral regurgitation is evident during aortic insufficiency (solid black area under mitral flow in panel B). AoF = aortic flow; SV = total aortic stroke volume; RV = regurgitant volume; AoP = aortic pressure. ECG lead II is shown.
**Table 1. Control and Steady-state Hemodynamic Results After Production of Aortic Insufficiency**

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<tr>
<th>Dog</th>
<th>HR (beats/min)</th>
<th>CO (l/min)</th>
<th>RF (%)</th>
<th>AoP (mm Hg)</th>
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All values are mean ± sd. The diastolic period was measured from the duration of mitral flow; the systolic period is the balance of the cycle.

*p < 0.01 vs control (by analysis of variance).

Abbreviations: HR = heart rate; CO = cardiac output; RF = regurgitant fraction; AoP = aortic pressure; LVP = left ventricular pressure; LAP = left atrial pressure measured at onset of filling; FV = filling volume; FV100 = filling volume at 100 ms per beat; MiF = mitral flow; AI = aortic insufficiency; C = control; n = number of runs.

in direct contact with the blood, making it inherently more accurate than the cuff-type aortic flow probe. With the newly adjusted baseline, FV equaled effective SV during the steady state.

The diastolic period was defined as the time between the onset and end of mitral flow. The remainder of the cycle was defined as the systolic period. Time was measured with the resolution of 5 msec (0.5 mm at a paper speed of 100 mm/sec). To compare changes in mitral flow patterns before and during AI, the FV during the first 100 msec of diastole was calculated.

Statistical significance was determined by analysis of variance and t test for grouped data or by paired t test for individual changes during pacing. Differences were considered significant at the p < 0.05 level. Data are mean ± sd.

**Results**

The amount of induced aortic regurgitation varied from physiologically insignificant to 70%. Because a regurgitant fraction less than 35% produced negligible immediate physiologic alterations in atrioventricular flow transport, we analyzed only experimental sequences with regurgitant fractions greater than 35%.

**Hemodynamic Changes**

The steady-state hemodynamic changes (achieved within 10 beats after opening the basket) are summarized in table 1 and illustrated in figures 2–5. The HRs shown in table 1 are all normal sinus rhythm and are either the baseline value for the dog or the result of slowed sinoatrial node activity due to mechanical crushing. The control HR, cardiac output, and pressures were all in the physiologic range. AI produced regurgitant fractions averaging 52%. The ratio of AI to control FV was 77%. The dogs tolerated this level of lesion severity for the duration of each run, which lasted at most approximately 1 minute for the changing HR procedure. Typical steady-state hemodynamic changes after the creation of AI are shown in figure 2.

After severe AI was induced, LV, aortic and left atrial pressures reached similar levels during diastole (fig. 3). LV diastolic and left atrial filling pressures also increased significantly.

Figure 4 is an oscillographic record from an experiment in which the control left atrial pressure was greater than that in figures 2 and 3. During AI, antegrade LV filling was completed before the first half of diastole. During the rest of diastole, the left ventricle was filled solely from retrograde aortic flow.

**Figure**

Table 1 is a summary of the hemodynamic results in nine dogs. In steady-state AI, the left atrial filling pressure was greater than control (92%, p < 0.01), resulting in a greater left atrial–LV pressure gradient in early diastole. The increased gradient caused mitral flow to accelerate more rapidly to a peak that was higher than control (13%, p < 0.01). Thereafter, a sharp decline in the atrioventricular pressure gradient decelerated mitral flow to zero or sometimes a negative level (figs. 2 and 3). The increase in early-phase peak mitral flow during the steady state partially compensated for the immediate decrease in total FV observed in
the beats immediately after the creation of AI (23%, p < 0.01). Figures 2–4 and table 1 demonstrate the temporal shift in diastolic atrioventricular flow transport after AI. A larger fraction of the total transmural FV was shifted to the early phase of diastole. The changes in the temporal distribution of mitral flow and FV, and the relative contribution of the rapid filling phase to the total FV, have been quantified by arbitrarily dividing the total diastolic filling period into two parts—the first 100 msec and the rest of diastole (fig. 2, table 1). Before AI, 39% of the mitral FV entered the left ventricle during the first 100 msec, but during AI, the ratio was reversed to 54% (p < 0.01).

Since a considerable amount of the total mitral filling is shifted to an earlier phase of diastole in AI, one can presume that slow HRs with long diastolic periods will selectively favor the filling of the left ventricle from the aortic (backward) source. In contrast, increasing the HR and shortening diastole should decrease retrograde flow relatively more than antegrade flow, thereby decreasing the regurgitant fraction and increasing the effective cardiac output. This concept

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FIGURE 3. Oscillographic record illustrating the transient (A) and steady-state (B) response to severe acute aortic insufficiency (AI) (regurgitant fraction 67%). With the creation of aortic insufficiency, there was an immediate increase in left ventricular diastolic pressure (LVP) and left atrial pressure (LAP). Early in diastole, LVP, aortic pressure (AoP) and LAP were at a similar level; phasic differences accounted for the variations in flow configurations. Time lines indicate 1 second. AoF = aortic flow; MiF = mitral flow.
was validated by changing the HR in a stepwise manner by atrial pacing during AI in six dogs.

Figure 5 shows the hemodynamic changes in flow patterns and the calculated values of SV, RV and FV in an experiment with HRs of 87, 120, and 150 beats/min. During AI, as HR increased from 87 to 120 beats/min, effective cardiac output increased significantly (2.7 to 3.4 l/min) with a decrease in LV end-diastolic and left atrial pressures; stroke volume decreased (23%), but the total forward minute output increased.
slightly (5.4 to 5.8 l/min) and regurgitant fraction decreased (52% to 44%). Increasing HR to 150 beats/min decreased the length of diastole to a degree where both mitral and regurgitant flow were compromised; total filling and cardiac output decreased and LV end-diastolic pressure increased. Figure 6 shows the effects of increased rate on the hemodynamics in the six dogs subjected to atrial pacing. Increasing the HR from 90 to 120 beats/min increased cardiac output (2.64 ± 0.56 to 3.30 ± 0.83 l/min, p < 0.05), reduced left atrial pressure (24 ± 8 to 17 ± 7 mm Hg, p < 0.05) and increased ejected volume per minute (4.76 ± 1.04 to 5.18 ± 1.15 l/min, p < 0.05), but did not significantly change the RV per minute (2.12 ± 0.66 to 1.90 ± 0.48 l/min) and decreased regurgitant fraction (44 ± 7% to 37 ± 6%, p < 0.05). These results occurred because when HR was increased from 90 to 120 beats/min, the FV decreased by only 8% (29 ± 6 to 27 ± 7 ml, p < 0.05), while RV decreased by 33% (24 ± 7 to 16 ± 4, p < 0.001). Although total RV and regurgitant fraction both decreased at HRs of 150 beats/min, their beneficial effects were offset by the decrease in cardiac output and increase in left atrial filling pressure. In these experiments, optimal hemodynamics in AI were achieved at HRs of about 120 beats/min.

**Echocardiographic Observations**

Two-dimensional echocardiography was used to verify that the basket did not interfere with full opening motion of the mitral valve (figs. 1 and 7). Occasional fine flutter of the septum and mitral valve was observed, and LV chamber dimensions increased after acute AI was produced.

When both cusps could be sufficiently delineated by M-mode echocardiography during AI, distance between the tips of the opened cusps was reduced. The amplitude of opening was reduced 10–20%, and at mid-diastole the cusps came closer to each other (fig. 7). However, the reduction in cusp amplitude was not seen in all the experiments.

Figure 8 shows a tendency for the cusps to move toward premature but incomplete closure of the mitral valve. This was more common in experiments with severe regurgitation, signs of failure, low cardiac output, and high LV end-diastolic pressure. In figure 8, LV depression before induction of AI was due to myocardial ischemia.

**Phonocardiographic Observations**

Figures 9 and 10 show phonocardiograms derived from a high-fidelity transducer located at the inflow.
tract of the left ventricle. In aortic regurgitation, a low-pitched murmur was recorded during the first phase of diastole. The murmur started with the onset of rapid filling when mitral flow was accelerating to its peak, persisted almost to the end of the decelerating phase, and tended to vanish when mitral flow approached zero. The murmur was not recorded when only the aortic regurgitant jet was present.

**Discussion**

The hemodynamic changes we observed after the production of acute AI are consistent with expected physiologic compensations and with the results of other studies in the closed-chest dog.18 SV, LV size and LV filling pressure increased immediately. FV and aortic diastolic pressure decreased, and peak LV pressure remained the same. Because the sinoatrial node was crushed in six dogs, and because central nervous system reflexes were depressed by anesthesia, we could not observe a reflex increase in HR.18 Nevertheless, atrial pacing and the direct measurement of phasic mitral flow and other hemodynamic variables allowed us to define the mechanism by which moderately increased HR benefits patients with AI. By simultaneously recording the intracardiac phonogram and the mitral valve echocardiogram, we have provided greater insight into the genesis of the Austin Flint murmur.

**Changing Pattern of Atrioventricular Flow Transport and the Significance of Increasing Heart Rate**

Whereas the reduction in mitral inflow (and thus cardiac output) is expected in AI, the changes in mitral flow patterns were unexpected and interesting. Within 10 beats after the induction of AI, peak mitral flow increased and almost all transmitral flow occurred during the first half of diastole. The only late diastolic flow was due to the atrial contraction, and it tended to be weak, possibly because the atrium was emptied early in diastole (figs. 2, 4, 8, 9 and 10). Because mitral flow is a direct function of the atrioventricular pressure difference,19 the origin of the changing flow pattern can be found in the phasic left atrial and LV pressures.

The atrial filling pressure (v-wave) increases so that at the moment of mitral valve opening, the developing atrioventricular pressure difference causes mitral flow to accelerate more rapidly and to a slightly greater level than control (figs. 2, 3, 4, 5 and 9). Thus, early in diastole the ventricle fills rapidly from both the atrium and aorta and quickly reaches the portion of its pressure-volume relation where it is relatively stiff. The combination of increasing LV pressure and decreasing left atrial pressure leads either to early-diastolic pressure equilibration or to reversal of the pressure gradient (figs. 3B and 4B). In our experience, an atrioventricular gradient reversal of less than 1 mm Hg will rapidly decelerate mitral flow. When oscillographic records are produced at low gain, such small differences are within the limits of error and resolution of the pressure traces and are not always obvious. When an early pressure crossover occurs, it may produce a small amount of mid-diastolic mitral regurgitation (figs. 2B, 3B and 7B), or late diastolic mitral regurgitation with a long PR interval.19,20 Even though the aortic pressure is decreasing, the momentum of the regurgitant jet serves to maintain the retrograde flow, albeit at a slightly decreasing rate. Thus, moderate increases in HR significantly decrease the RV with only an insignificant intrusion into atrial flow transport.

Although one should use caution in applying the results of acute animal experiments to the hemodynamic behavior of the human heart in chronic AI, the
Observations of this study appear to be directly applicable. In the advanced stages of chronic AI, the left ventricle is stiff and the filling pressure is high.2, 3 Thus, the mitral flow configuration recorded in these experiments may be similar, to that in patients.

Clinicians have long noted that moderate tachycardia is beneficial for patients with AI, but the effect of increased HR on forward and regurgitant flows, i.e., what causes this phenomenon, have been in conflict.9-12 Our results are in agreement with those of Judge et al.,12 who found a significant increase in cardiac output, a decrease in LV end-diastolic pressure and no change in total regurgitant output with moderate increases in HR. Belenkie and Rademaker18 produced AI and found that the increased LV end-diastolic pressure tended to return toward control values primarily in dogs with increased HR. This is consistent with our findings (figs. 5 and 6).

Because we only paced at three rates, we cannot clearly define an optimal HR. The optimal HR will be one at which diastole is shortened without significantly affecting mitral flow. Clinically, the optimal HR will vary from patient to patient or even in the same patient as the effects of the disease change with time.

Relation of Mitral Cusp Motion to Instantaneous Diastolic Flows

The mechanism responsible for the curtailment of the full opening of mitral valve in some of our AI experiments was not completely clear. Maximal opening amplitude of the anterior cusp may have been restrained by interference from the basket located in the aortic valve, or it may have been prevented from full opening by direct impingement of the regurgitant jet. However, the increased mid-diastolic excursion of the anterior cusp toward closure (EF segment) was undoubtedly the result of the changing pattern of mitral flow after AI. We previously demonstrated that anterior cusp motion grossly followed changes in flow, and that mid-diastolic deceleration of mitral flow to zero or less was accompanied by increased closing excursion of the anterior cusp to achieve incomplete valve closure.14, 19 Rapid deceleration of mitral flow, as can be seen in experimental animals,14, 19 can induce premature but incomplete or nonoptimal valve closure even without AI. Such closure not preceded by a ventricular contraction may be associated with a small amount of mitral regurgitation and often accompanies a prolonged PR interval.19, 20 In animals with experimental AI, mitral regurgitation was seen particularly in bradycardia and with prolonged PR interval.20 Premature closure of the mitral valve is also common in patients with severe acute AI.21

The Austin Flint Murmur

The mechanism of production of a mid-diastolic or presystolic apical low-pitched murmur in AI has been debated for years. Proposed mechanisms include incomplete opening or premature closure of the mitral valve, relative mitral stenosis, diastolic mitral regurgitation and fluttering of the cusp.22-28 Fortuin and Craig29 used combined echo-phonocardiographic studies and concluded that the Austin Flint murmur was due to antegrade flow across the mitral valve. This was also suggested by Reddy et al.,30 using intracardiac phonocardiography and high-fidelity pressure recordings. This conclusion was supported by our findings, since the intracardiac murmur, obtained from the high-fidelity micromanometer located at the LV inflow tract, was recorded only when mitral flow advanced antegradely through the valve, and subsided when mitral flow vanished or was greatly diminished (figs. 9 and 10). Using intracardiac phonocardiographic recordings, Reddy et al.30 demonstrated that the typical externally recorded Austin Flint murmur was localized to the inflow of the left ventricular tract. The intracardiac murmur tended to have the characteristics of the externally recorded murmur, but had earlier onset, i.e., during the DE phase of the mitral valve echocardiogram.30 In our previous experiments, the opening phase (DE) of the mitral valve echocardiogram was the time of mitral flow acceleration.14, 19 Indeed, the LV inflow murmur started with the onset of mitral flow (figs. 9 and 10).

Fortuin and Craig29 suggested that the rumbling murmur occurs during rapid closure of the mitral valve and postulated that flow velocity increases, although actual volume flow may decrease. However, Reddy and co-workers30 did not find significant changes in the rate of diastolic mitral valve closure in patients with AI compared with normal subjects.

Although in the present study mitral flow velocity during the rapid filling phase increased in AI compared with control, and valve opening was moderately reduced in mid-diastole, the temporal relationship between motion and flow precluded orifice narrowing as the only mechanism of the murmur. The motion toward closure of the mitral valve, either mid-diastolic or
presystolic, always lagged behind the decelerating flow (figs. 7 and 8). When the mid-diastolic separation between the cusps was the smallest, flow velocity (measured at the level of the mitral ring) was minimal (arrow, fig. 8B), and when flow was increasing, the cusps had already moved to achieve a larger opening. Fortuin and Craigs showed that the Austin Flint murmur had a greater intensity at a time when the two peaks of mitral flow would be predicted from the mitral valve echocardiogram, i.e., the rapid filling wave and the atrial contribution. The echocardiogram between these two peaks showed partial valve closure, and the murmur was of minimal intensity. The externally recorded murmur, which started with the opening of the mitral valve, resembled the intracardiac Austin Flint murmur recorded by Reddy et al. Echo-phonocardiographic records from patients with AI (Criley M: personal communication) confirmed the findings of Fortuin and Craige that the Austin Flint murmur was registered at the time of rapid mitral valve closure. Criley suggested that because the cusps formed a funnel-like conduit with the smaller diameter at the tips, mitral flow velocity was higher at the tips of the cusps compared with the ring. We measured mitral flow velocity at the proximal level of this conduit (i.e., the ring); although a higher velocity near the tips of the cusps could have played a role in the genesis of turbulence in the LV inflow tract, the pressure-flow data do not indicate a significant functional stenosis. If there were a functional stenosis (which we did not observe in the echocardiogram), the 13% increase in peak mitral volume flow after the production of AI (table 1) and the presumed reduction in area would produce a very much increased flow velocity at the cusp tips. Since the energy loss across a stenosis is proportional to the square of the velocity, we would have recorded a large increase in the atriocentric pressure difference. This did not occur (figs. 2, 3, 4, 5, and 9), and we conclude that a significant functional stenosis did not exist in our experiments. Shaefer et al. examined patients with Starr-Edwards mitral prostheses and suggested that the Austin Flint murmur resulted from turbulence generated by the intersection of an expanding turbulent jet flowing retrogradely through the aortic valve and a more slowly moving stream flowing antegradely across the mitral valve. In contrast, we found that the mitral flow was a rapidly rising and decelerating flow. Because their findings were based on observations in patients with prosthetic mitral valves, the relevance to the Austin Flint murmur in the natural valve can be questioned. Since in this study there was no murmur in the absence of a regurgitant jet (fig. 9A) and there was no functional mitral stenosis in early diastole (figs. 7 and 8), we conclude that the combination of an aortic regurgitant jet and a rapidly rising and decelerating antegrade mitral flow is apparently responsible for the turbulence leading to the Austin Flint murmur. The results of this study should be applied with caution to the clinical situation. The characteristics of a murmur recorded at its origin may not be the same as those recorded at the body surface. Furthermore, the chamber and muscle properties of a ventricle subjected to an acute volume load are different from those due to chronic stress. Thus, the timing and characteristics of the murmur recorded in this study may differ from the classic Austin Flint murmur, and may also explain why we could not record the characteristic late diastolic Austin Flint murmur.  

Acknowledgment

This work could not have been done without the skilled technical help of A. Leon, P. Bon and F. Rivera. We thank M. Olivera for typing the manuscript.

References


The Relationship of the First Heart Sound to Mitral Valve Closure in Dogs
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SUMMARY The relationship between the first heart sound (S₁), mitral valve (MV) closure, and left atrial (LA) and left ventricular (LV) hemodynamics was investigated in dogs during right-heart bypass. High-speed cineradiography (~350 frames/sec) of lightweight clips attached to the free edge of the anterior and posterior MV leaflets permitted study of MV motion with high time resolution. LA and LV pressures were recorded, along with simultaneous phono- and echocardiograms, on a multichannel strip-chart recorder. S₁ occurred 25.5 ± 3 msec after LA-LV pressure crossover and coincided with MV closure measured either echocardiographically or cineradiographically. Atrial-ventricular (AS-VS) sequential pacing was performed to vary the interval between atrial and ventricular systole. At AS-VS intervals of 0-50 msec, S₁ and MV closure occurred simultaneously approximately 25 msec after the onset of LV systole as described above. At an AS-VS interval of 100 msec, S₁ and MV closure occurred simultaneously but closer to the onset of ventricular systole. At an AS-VS interval of 150 msec, MV closure occurred before S₁, just preceding the onset of LV systole, and S₁ closely followed the onset of LV systole. At longer AS-VS intervals (200-300 msec), MV closure occurred at progressively earlier points in diastole without a detectable heart sound. Later in diastole, the MV reopened and then closed a second time after the onset of LV systole; S₁ was recorded with this closure. The amplitude of S₁ varied with the degree of separation of the mitral valve leaflets at the onset of LV systole. The results show that the S₁ occurs with MV closure when it follows the onset of LV systole. The timing and amplitude of S₁ are related to the degree of separation of the MV leaflets at the onset of LV systole and to the relative timing of LA and LV systole.

DESPITE 150 years of experimental study, debate about the genesis of the first heart sound (S₁) continues.¹ The two conflicting theories most frequently proposed are based on either a ventricular or a mitral valvular origin of the sound. Laennec attributed S₁ to ventricular systole, specifically vibrations developing in the heart muscle with contraction.² Joseph Rouanet presented evidence for a valvular origin of S₁, based on experiments with a model of the working heart and with membranes similar to valvular tissue.³ ⁴

Dock, in studies beginning in the 1930s, using both intact heart models and strips of cardiac tissue, also argued for the valvular theory.⁵ ⁶ He found that a filled contracting ventricle tied off at the atrioventricular ring produced no sound; strips of ventricular muscle pulled taut under water produced little sound, whereas strips of chordae and cardiac valves pulled taut could be made to produce loud sounds quite easily.

Luisada and co-workers⁷ ⁸ found that the left atrial-left ventricular pressure crossover point — which they assumed represented mitral valve closure — consistently preceded S₁. They concluded that sudden tension development in the closed left ventricular cham-
Physiologic mechanisms in aortic insufficiency. I. The effect of changing heart rate on flow dynamics. II. Determinants of Austin Flint murmur.
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Circulation. 1982;66:226-235
doi: 10.1161/01.CIR.66.1.226

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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