Atriogenic Mitral Valve Reflux: Diastolic Mitral Incompetence Following Isolated Atrial Systoles

By John C. P. Williams, T. Paul B. O'Donovan, Russell A. Vandenberg, Ralph E. Sturm, and Earl H. Wood

ABSTRACT

Cardiac and aortic pressures were recorded after stellate ganglionectomy and vagotomy. Acute heart block was produced by injecting the atrioventricular node, and atrial and ventricular systoles were controlled electronically to occur independently or in any desired relationship. Angiocardiograms recorded on video tape after injections of 4 ml 69% Renovist into the left ventricle were analyzed with a videodensitometer able to detect small refluxes of contrast medium into the left atrium and correlate them with phases of the cardiac cycle. When ventricular driving was temporarily suspended but atrial driving continued, pressure records indicated mitral valve closure after each atrial systole, but reflux of contrast medium into the atrium occurred after each systole not followed by a normally sequenced ventricular systole. Driving with a 2:1 atrioventricular stimulation resulted in reflux, with the alternate atrial contraction dissociated from ventricular systole. Thus, the mitral valve was not effectively closed by atrial systoles that were not followed by normally sequenced ventricular systoles.

ADDITIONAL KEY WORDS  mitral valve closure  atrial contraction  heart block  ventricular asystole  mitral incompetence  videodensitometry  extrasystoles  dogs

The classic observations by Dean (1) on presystolic movements of the mitral valve cusps and the demonstration by Henderson and Johnson (2), and later by Little (3), of reversal of the atrioventricular pressure gradient after atrial systole gave grounds to assign to atrial systole the dominant role in closure of the atrioventricular valves. Further supporting evidence was provided by Sarnoff and associates (4), Skinner and associates (5), Brockman (6), and Grant and associates (7). The functional importance of presystolic closure of the atrioventricular valves was further emphasized when data obtained by these and other workers seemed to indicate that significant regurgitation occurs if the mitral valve is closed by ventricular systole alone, unaided by the effects of preceding atrial contraction and relaxation (8, 9).

However, observations by Conn and associates (10), and by Williams and associates (11), designed for direct measurement of retrograde movement of labeled blood from the left ventricle to the atrium, during cardiac rhythms which excluded a possible contribution to valve closure from atrial contraction, indicated that the ventricle closed the mitral valve with little or no incompetence. Not only did these investigations indicate that atrial systole was unnecessary for effective valve closure, but Hawthorne's investigation (12) suggested that atrially induced valve closure might itself be associated with regurgitation of blood into the atria. In dogs with acute heart block he noted that the increase...
in ventricular circumference after atrial contraction was not sustained.

With the use of an indicator-dilution upstream sampling technique in which regurgitation of contrast medium injected into the left ventricle was detected by densitometric analysis of videotape angiograms (13), direct evidence of atrially induced mitral valve regurgitation has now been obtained. The results of this study indicate that reevaluation of the role of ventricular systole in mitral valve closure seems necessary.

**Method**

Cardiac rate and rhythm were controlled in dogs by electronic stimulation via unipolar electrode catheters in the right atrium close to the sinus node and the right ventricular outflow tract. Spontaneous sinus rate was regulated, when necessary, by bilateral stimulation of the distal ends of the sectioned cervical vagi. Acute heart block was produced by a percutaneous technique. Vascular and cardiac pressures were monitored. A spray-tip, blind-end Rodriguez catheter (no. 5F) advanced retrogradely into the left ventricle was used for injection of 69% of a compound of sodium and methylglucamine diatrizoate (Renovist). This contrast medium (4 to 6 ml) was delivered to the proximal end of the catheter at 75 to 150 psi by a syringe activated by compressed air and triggered by the R wave of the electrocardiogram. The duration of the injections was adjusted to extend over two to three cardiac cycles. The dogs were placed supine in a half-body molded fiber-glass cast and tilted on the fluoroscopy table into a modified right anterior oblique position so that the plane of the mitral valve was parallel to the x-ray beam. Respiration, at other times sustained by a Bird respirator, was suspended during the recording of selective left ventricular angiograms on video tape for subsequent densitometric analysis (13).

Three types of experiments were undertaken to separate the effects of atrial contraction and relaxation on mitral valve closure from the effect of associated ventricular systoles. In one series of experiments in seven dogs, the atria and ventricles were driven regularly with an atrioventricular stimulus interval adjusted to produce optimal cardiac output at the selected heart rate. Left ventricular angiograms were then recorded while, at the time of the injection of contrast medium, cardiac driving was temporarily suspended. Spontaneous atrial systoles would frequently occur soon after cessation of driving but, since the dogs had atrioventricular block, the ventricles remained in asystole until stimulated or excitation from a ventricular focus occurred. In two additional dogs, cardiac driving was suspended in a similar manner, but immediately thereafter (and before the onset of spontaneous atrial systoles) an electronically controlled ventricular extrasystole was produced. Assessment by videodensitometry of

![Diagram](http://circres.ahajournals.org/)

**FIGURE 1**

Demonstration using roentgen video densitometry of diastolic reflux across the mitral valve after atrial contraction and relaxation during a period of ventricular asystole in a dog with acute heart block. Slow-speed (2.5 cm/sec) video densograms showing changes in left ventricular density just downstream and in left atrial density just upstream to mitral valve. In both left and right panels, regular 2:1 atrioventricular driving was temporarily stopped immediately after the injection of 4 ml of 69% Renovist. On cessation of driving, there was in the right panel a period of total asystole, but in the left panel, a spontaneous atrial systole (F) interrupted the period of asystole. Both left ventricular densograms show marked reduction in x-ray transmission, commencing with the injection of contrast medium; only the atrial densogram on the left shows a marked downward deflection.

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1 Courtesy of David Clark Co.
the competency of mitral valve reflux at this time enabled the relative effects of isolated ventricular and atrial contractions on valve closure to be compared. In a third series of experiments in six dogs, angiocardiograms were recorded during cardiac driving with 2:1 atrioventricular dissociation. The rate and timing of atrial and ventricular stimulation were adjusted so that an atrial systole occurred relatively isolated during ventricular diastole.

**Results**

In the first series of experiments in 7 dogs, in which a relatively isolated atrial beat occurred during a period of ventricular asystole, atrial relaxation was always associated with reflux of contrast medium across the mitral valve. This was readily seen with the naked eye on viewing the video-tape angiograms. When video densograms recorded over the left atrium were compared with simultaneous vascular pressure changes (Figs. 1 and 2), the reflux of contrast medium was always found to begin during the period of reversal of the normal diastolic atrial-to-ventricular pressure gradient which followed each isolated spontaneous atrial systole. If no spontaneous atrial contraction occurred, there was no diastolic reflux of blood tagged with contrast medium during the short periods of asystole used in this experiment, and, furthermore, the subsequent ventricular systole with its associated high ventricular-to-atrial pressure gradient also did not produce regurgitation.

When angiograms were recorded during cardiac driving with 2:1 atrioventricular dissociation, mitral reflux was displayed during each cardiac cycle (Figs. 3 and 4). Analysis of the relation between left atrial video densograms and simultaneous vascular pressures showed that repetitive increments in atrial opacification coincided with each alternate period of atrial relaxation, those not associated with a ventricular systole; that is, as in the
Video densograms demonstrating atriovenous reflux across mitral valve in a dog during 2:1 atrioventricular driving. Slow-speed recordings obtained with densitometer sampling opacity of left ventricle after injection of 4 ml of 69% Renovist mounted above simultaneous left atrial densogram recorded with densitometer sampling at the same sensitivity just upstream to the mitral valve. Note sharp deflection in left atrial densogram during period of left ventricular opacification (dog—17.2 kg, morphine-pentobarbital anesthesia).

The same left atrial densogram as in Fig. 3 rerecorded at fast paper speed, with cardiac pressures during period of injection of contrast. Vertical dashed lines indicate simultaneous events in Figs. 3 and 4. Note that the deflections, in the left atrial densogram, indicating reflux of contrast medium to the left atrium, began after the atrial systolic pressure waves (A) were transmitted into the ventricle (A') when a reversal of the normal diastolic atrioventricular pressure gradient occurred. 

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other experiments, diastolic mitral reflux occurred when the normal diastolic atrial-to-ventricular pressure gradient was reversed by an isolated atrial systole.

Angiograms recorded while repetitive atrial contractions occurred during prolonged periods of ventricular asystole showed progressive opacification of the left atrium after each atrial contraction in all dogs. In some cases, as in Figure 5, the successive to-and-fro movement of blood through the mitral valve occurring with atrial contraction and relaxation finally produced quite complete atrial-ventricular mixing. On view of replays of these angiograms, the left atrium was seen to become, to the naked eye, almost as opaque as the left ventricle. Although progressive atrial opacification also occurred in all 7 dogs, the reflux after each successive contraction was less severe. It has not yet been established whether this variability was related to differences in diastolic compliance of the ventricles.

Figures 6 and 7 illustrate the findings in experiments designed to compare the effect on the competence of closure of the mitral valve by isolated atrial contraction and relaxation with the effect of single ventricular extrasystoles. The initial ventricular extrasystole produced little change in atrial opacity, but...

Video densitometer-dilution curves demonstrating reflux through the mitral valve caused by repetitive atrial contractions during ventricular asystole in a dog with complete heart block. Spontaneous atrial rate was 160 beats/minute, and ventricles were electronically driven at 125 beats/minute. Immediately after injection of contrast medium in the left ventricle, ventricular driving was temporarily suspended. Note large deflection in left atrial densogram, thus indicating that blood containing contrast medium refluxed freely until left atrial opacification approached left ventricular opacification. Vertical lines demonstrate that successive downward steps in left atrial densograms can be related to spontaneous atrial contractions (A) during the period of ventricular asystole. Note that progressive opacification of the atrium was interrupted as soon as a ventricular systole occurred, indicating the much greater efficacy of ventriculogenic as compared to atriogenic closure of the mitral valve. (Dog—19.5 kg, morphone-pentobarbital anesthesia.)
The effects on mitral valve competency of "isolated" ventricular and isolated atrial systoles in two dogs. Synchronized left ventricular and atrial densagrams recorded at slow paper speed on replay of left ventricular videotape angiograms recorded after injection of 4.5 ml of 69% Renovist. Panel 1, Regular atrioventricular driving at heart rate of 114 beats/minute, with atrioventricular stimulus delay of 0.9 second. Panel 2, Same dog, isolated ventricular systole \( V_g \) stimulated electronically while atrioventricular driving was temporarily suspended. Panel 3, Same dog, isolated ventricular extrasystole followed by repetitive atrial stimulation. Panel 4, Repeat of panel 3 in another dog.

The succeeding atrial systole in these 10 dogs was always followed by clearly discernible reflux of contrast medium.

Comment

These experiments utilize new indicator-dilution recording and sampling techniques (13) which have features particularly suited to the study of the efficacy of mitral valve closure. Atrial catheterization is unnecessary, and the sites of sampling upstream and downstream to the mitral valve are visualized and can be adjusted accurately on the monitoring television screen during as many replays of the video tape as desired so as to be juxtaposed but not to impinge on the

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mitral valve. It is, therefore, certain that contrast medium—the indicator—is presented directly to the downstream face of the valve and that the upstream site covers the upstream face of the valve, directly in the path of regurgitation, should this occur. Recordings of dilution curves from any individual videotape angiogram can be repeated as many times as desired with variations in the sampling sites to assure that assessment of valve competency was not invalidated by positioning sampling sites within either ventricle or atrium. Moreover, the smoothing or "slurring" that occurs in conventional dye-dilution curves, due to the effects of passage of the dyed blood through the catheter system, is avoided. The video densitometer records the time course of density fluctuation integrated over the area of the cardiac silhouette selected for sampling at the repetition rate of the television system, which is 60 times per second. The dynamic response of the system is therefore fast enough for accurate correlation of changes in opacity of cardiac chambers with hemodynamic events within a cardiac cycle.

The pressure data and angiograms recorded in the experiments described in this article support the common view that during atrial relaxation, the cusps of the mitral valve move toward the position of closure. However, atrial contraction had to be followed closely by a ventricular systole to ensure competency of the valve. When, under experimental conditions, the valve is closed by an atrial mechanism alone, it fails to close effectively.

On the other hand, the finding that incompetence was not produced by isolated ventricular extrasystoles adds further weight to indicator-dilution studies establishing efficacy of ventricle-induced mitral valve closure during atrial fibrillation as reported by Conn and co-workers (10) (using radioisotopes) and by Wood and associates (using indocyanine green and also densitometer analysis of video-tape angiograms in dogs [11, 13]), and the confirmation of these findings by Braunwald (14) from analysis of angiograms in humans. In contrast to this mechanism of valve closure, conveniently referred to as ventriculogenic, it is clear that valve closure produced by reversal of the atrioventricular pressure gradient during atrial relaxation (or atrogenic closure), if not followed by a normally timed ventricular systole, usually causes marked reflux of left ventricular blood to the atrium. This concept has been confirmed recently with the use of selective thermal dilution curves in patients who have heart block (15).

The demonstration of diastolic reflux after isolated atrial beats is of considerable physiologic interest in defining the effects of atrial and ventricular contractions and relaxation on movements of the mitral valve cusps, and their interrelated roles in normal and abnormal valve closure. It is true that the hemodynamic significance of atrogenic diastolic reflux, considered in terms of its effect on forward flow, is probably small. Unlike the immediate deficit in stroke volume caused by systolic mitral regurgitation, cardiac output would not be directly impaired by recurrent diastolic ebb and flow across the mitral valve. Of course, if no reflux occurred, ventricular diastolic filling and pressure would be incremented and would remain elevated after each atrial systole. Then when the ventricle finally contracted, it might eject a larger stroke volume than it would if part of each atrial systolic moiety refluxed. However, it could be argued that reflux after each atrial systole is desirable during heart block in order to avoid the ventricular overdistention which might develop if successive atrial systoles progressively incremented ventricular filling during the long diastolic pauses associated with slow idioventricular rates or periods of ventricular asystole.

In one circumstance, diastolic reflux may affect stroke volume more directly. Reflux has been shown to occur during abnormally long P-R intervals, and although the effect of such reflux is not yet quantitated, it probably contributes to the fall in stroke volume found when the P-R interval lengthens beyond an optimal period.
Atriogenic diastolic reflux is a likely basis for the observations that ventricular extrasystoles, during diagnostic left ventricular angiograms, are frequently associated with reflux of contrast medium into the atrium. It would usually be difficult in such procedures to distinguish regurgitation occurring during a ventricular extrasystole from reflux through the valve during the diastolic pause immediately following the extrasystole when the occurrence of isolated atrial systoles would not be uncommon. Since atriogenic mitral valve reflux can be demonstrated in the presence of a normal valve, its occurrence under such circumstances is not indicative of anatomic pathology of the valve.

It is also of interest that the atrial-ventricular mixing of blood associated with atriogenic reflux would be expected to produce abnormalities in the contour of indicator-dilution curves (for example, prolonged disappearance slope) which would be difficult to distinguish from the dilution curves frequently associated with true systolic mitral incompetence.

It is clear from these studies that closure of the valve by a moderate ventricular-to-atrial pressure gradient generated by an atrial systole is not complete unless this pressure gradient-induced closure is followed immediately by a normally sequenced ventricular systole. This implies that ventricular systole must alter the geometry of the valve ring, its leaflets, their manner of support, or some combination of these and possible other factors so that it is changed from a badly leaking to a fully competent valve in spite of, or perhaps in part because of, the much higher ventricular-to-atrial pressure gradient generated by the ventricular systole.

Ventriculogenic valve closure has been likened to the closing of a door by wind (16) so that before the valve is swung shut by a pressure gradient, some regurgitation must occur. This analogy has not been applied to atriogenic closure, but it can be so applied. It is curious that the ventricle, which quickly generates a high-pressure gradient, has been considered to produce incompetence by this mechanism, whereas a much smaller atriogenic ventricular-atrial pressure gradient has been considered to close the valve effectively. The "door in the wind" analogy is, however, certainly inexact, and more detailed knowledge of valve leaflet and ring movements (1, 16-19) in systole and diastole seems necessary before the role of the atria and ventricles in valve closure can be described completely. The relationships between the area of the valve cusps, their contours under varied degrees of tension (20), the lack of activation of the muscular elements in the valve cusps (21), and the diastolic area of the mitral valve ring may critically influence the amount of atrially induced reflux. Physiologic and pathologic variations in ventricular diastolic volume, therefore, could affect the competency of atriogenic closure. Whether ventricular contraction closely following an atrial contraction makes the mitral valve leaflets oppose more effectively by (1) generating a higher atrioventricular pressure gradient, (2) narrowing the atrioventricular ring, (3) activating intracusp muscular elements, (4) contracting papillary muscle, or (5) a combination of these is a question on which there is, as yet, only meager data and some of it at variance (22).

The recent demonstration by Cooper and co-workers (21, 23) of the presence of both muscular and neural elements in the mitral valve cusps suggests that these leaflet structures may participate actively in the process of valve closure. Furthermore, electrograms recorded from the leaflets indicate that these valvular structures are activated in synchrony with ventricular action potentials and not from the atria.

Clearly the contribution of the process of ventricular systole to effective atrioventricular valve closure is of major importance. Its contribution has tended to be ignored, and emphasis has been placed on the role of presystolic atriogenic closure. In normal circumstances, ventricular systole and possibly active valve elements associated with ventricular contraction seal and sustain the valve closure initiated by the atrium. During atrial arrhythmias such as atrial fibrillation or nodal
rhythm, that is, when there is no or only an ill-timed atrial contraction, ventricular systole would still seem to be capable of closing the mitral valve efficiently (11). However, if the vigor of ventricular contraction is impaired, ventriculogenic valve closure may be incompetent, and this incompetence may then cease or be greatly relieved if an associated and suitably timed atrial systole is introduced (13).

Therefore, the evidence points to a mechanism of mitral valve closure which combines contributions from both atrial and ventricular systole so that, over a fairly wide range of variation in physiologic and pathologic conditions, there is no incompetence or only minimal incompetence.

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References

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