Atriogenic Diastolic Reflux in Patients with Atrioventricular Block

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Several concepts of atrioventricular (A-V) valvular closure have been suggested in the past. From experiments in dogs with open chests, some authors have proposed that atrial contraction per se is able to close completely the A-V valves. Certainly, repositioning of mitral and tricuspid valves in a position of preclosure occurs during atrial contraction. Recently, however, Williams and associates have shown that regurgitation due to improperly timed atrial contraction may occur in anesthetized dogs with A-V block studied without thoracotomy.

The present report gives evidence that diastolic reflux from the ventricle to the atrium occurs when atrial systoles are not followed by correctly timed ventricular contractions in intact conscious man with A-V block and indicates that only ventricular systole is capable of closing tricuspid and mitral valves efficiently.

Methods

Five patients with complete A-V block were studied by thermodilution method during cardiac catheterization. Except for 10 mg of Librium in the first and the fifth patient no premedication was given. Procaine in 2% solution was used as a local anesthetic.

The first patient (K.H., a woman, 22 years old, 168 cm tall, weighing 53 kg, with a surface area [SA] of 1.59 m²) presented a probably congenital, complete A-V block and moderate scoliosis of the thoracic spine. Apart from the A-V block, there were no clinical signs of cardiac disease and catheterization gave no evidence of shunt or organic valvular incompetence.

The second patient (A.W., a man, 26 years old, 174 cm tall, weighing 72 kg, with SA of 1.86 m²) presented an endocardial cushion defect with complete A-V block probably of congenital type. The vectorcardiogram was consistent with this abnormality. During catheterization an atrial septal defect situated caudad in the atrium could be passed, and mitral incompetence was proved by left ventricular angiocardiography. No ventricular septal defect could be detected with this procedure.

The third patient (E.G., a man, 72 years old, 175 cm tall, weighing 77 kg, with SA of 1.93 m²) had an acquired complete A-V block, probably of arteriosclerotic etiology. No signs of valvular abnormality or shunt were present.

The fourth patient (I.C., a man, 62 years old, 171 cm tall, weighing 79 kg, with SA of 1.92 m²) presented acquired complete A-V block, probably of arteriosclerotic origin. Dye curves after injection of Evans blue into a brachial vein and recording of concentration at the ear showed a right-to-left shunt of about 2% of body flow without any detectable left-to-right shunt. Arterial oxygen saturation at the ear decreased quickly for some seconds after the Valsalva maneuver. An open foramen ovale could be catheterized. No valvular abnormality was present.

The fifth patient (M.O., a man, 43 years old, 170 cm tall, weighing 72 kg, with SA of 1.83 m²) presented an acquired complete A-V block of unknown etiology and no other valvular abnormalities.

In all patients 10 to 25 ml of cold saline at 15 to 12°C were repeatedly infused manually during a period of 2 to 5 seconds through a spray tip, 10F catheter (I.D., 2.2 mm; length, 80 cm, with six side openings within 1.5 cm from the tip) advanced from the left axillary vein into the right ventricle. Previous withdrawal of an end-hole catheter while monitoring pressure served to localize tricuspid valve level. On advancing the 10F catheter toward the apex and the left wall of the right ventricle, care was taken that all the spray holes were within the right ventricle (fig. 1A). Temperature within the right atrium was sensed with a Philips thermistor mounted on a 7F Courand catheter also introduced from the axillary vein.

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*7-Chlor-2-methylamino-3-phenyl-3H-I, 4-benzodiazepin-4-oxyl hydrochloride. Hoffman-La Roche, Basle, Switzerland.
Chest x-rays showing position of catheters to detect atriogenic reflux in patients with complete A-V block. (A) First patient. Infusion catheter in the right ventricle, thermistor catheter in the right atrium (corresponds to figure 2). (B) Fourth patient. Infusion catheter (I) in the left ventricle by retrograde insertion. Two thermistor catheters (T₁ and T₂) were placed by transseptal route in the left atrium (corresponds to figure 3).

In the first, fourth, and fifth patients, a thermistor mounted on a ureteric catheter (O.D., 1.0 mm; length, 90 cm) was placed in the left atrium by advancing it through an 8 F Brockenbrough catheter* until the thermistor protruded 2 mm. The Brockenbrough catheter had been placed previously from the right femoral vein by transseptal catheterization¹¹ into the left atrium. From 10 to 25 ml of saline at about 18 to 15 °C was infused repeatedly over a period of 2 to 5 seconds into the left ventricle via a yellow Oedmann-Ledin catheter (length 90 cm) with end- and multiple sideholes inserted percutaneously from the left femoral artery. In the fourth patient furthermore a 7 F thermistor catheter was advanced from the left axillary vein through a foramen ovale, allowing simultaneous temperature measurements at two points in the left atrium of which one was nearer and the other further upstream from the mitral valve. The position of the catheters of the fourth patient is visible in figure 1B.

Three-tenths volt was applied to the thermistors and the changes in resistance (27 Ω/°C and 35 Ω/°C, respectively) were sensed by a Wheatstone-bridge, amplified and recorded with an Electronics for Medicine recorder.‡ The dynamic response of the thermistors was 90% of total deflection in 0.36 and 0.34 second, respectively, when tested in unstirred water.

In the second, third, and fifth patients pressure in the right ventricle was measured by a Telecatheter tip manometer§,¹² also inserted from one of the left axillary veins. Using P 23 Db Statham manometers, simultaneous pressures were measured in the right atrium (7 F Cournand catheter; length, 125 cm) and the right ventricle in the third and the fifth patient and simultaneous pressures in the left atrium and left ventricle were recorded in the fourth and fifth patients. In the fifth patient, furthermore, the heart was stimulated with a 6 F Goetz bipolar electrode-catheter* from the right ventricular outflow tract at a rate of 75 per minute and atriogenic reflux was studied during and after sudden stop of pacing, when the ventricular frequency was very low. Aortic pressure in this patient was monitored continuously with a percutaneously inserted red

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Oedmann-Ledin catheter (length, 100 cm) and intracardiac phonocardiograms were recorded with a Telco manometer from the right ventricle. Furthermore, changes in left ventricular volume were estimated by sudden injection of 5 ml of cold saline into the left ventricle and recording of temperature in the ascending aorta with a thermistor introduced from the left femoral artery.

**Results**

Atrial systoles unaccompanied by properly timed ventricular systoles caused diastolic reflux through the A-V valves in all five patients studied. Figures 2 to 7 show this phenomenon. The marker indicates the time during which the cold saline was infused into the ventricle. The drop of the temperature in the atrium occurring after P waves not followed in a normal sequence by QRS complexes indicates atrogenic reflux. A-V intervals as short as 0.3 second caused presystolic reflux (fig. 2). Depending upon whether the thermistor catheter was nearer or further away from the A-V valves, time elapsing between the beginning of the P waves and the temperature drop at the point of registration in the atrium varied usually between 0.25 and 0.7 second. In the upper part of the atrium the retardation could even reach 1.0 second. When the thermistor catheter was replaced nearer to the tricuspid or mitral valves, decrease in temperature was generally earlier and more marked. Simultaneous measurements of temperature at two different points in the left atrium as made in the fourth patient show that the temperature drop during ventricular infusion of cold saline was earlier and more intense near the valves (fig. 3).

Atrial systoles occurring in a normal temporal relationship to a QRS complex did not cause reflux. Also atrial systoles in the early part of ventricular diastole did not always cause reflux. In a patient with a 2:1 A-V block, in whom one P wave began 0.18 second before the QRS complex and the other P wave

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**Figure 2**

Detection of atrogenic reflux in the first patient with complete A-V block, corresponding to figure 1A. (Upper tracing) Temperature in the right atrium. (Middle tracing) Marking of the time during which 20 ml of cold saline was infused into the right ventricle. (Lowest tracing) ECG. After late diastolic P waves that are not followed by QRS complexes in normal sequence reflux occurs. Atrial contractions during or immediately after ventricular contractions do not cause regurgitation.

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Simultaneous measurements of temperature in the fourth patient at two points in the left atrium during infusion of cold saline into the left ventricle, corresponding to figure 1B. The upper tracing in each panel is the temperature sensed with thermistor T1 placed through a Brockenbrough catheter by transseptal catheterization into the upper part of the left atrium (T1 in Fig. 1B). The lower tracing is from thermistor T2, manipulated from the left axillary vein through a foramen ovale approximately into the middle of the left atrium (T2 in Fig. 1B). Note (1) the temperature decrease is less marked and occurs later in the upper than in the lower tracing; (2) ectopic beats with different sequence of contraction do not cause increased regurgitation.
began very early in diastole, no atriogenic reflux could be detected.

Lowering of atrial temperature after atrial systoles unaccompanied by properly timed ventricular systoles was present not only during infusion of cold saline but also after infusion had been stopped (figs. 3 to 5); this indicates that reflux did not take place only because of volume overload by the infusion.

When the heart was driven electrically at a frequency of 75 per minute in the fifth patient, left ventricular end-diastolic volume, as measured by thermodilution, decreased to 65% of the volume measured during its own slow ventricular rhythm of about 32 per minute. Atriogenic reflux could still be detected during pacing when diastolic P waves were followed with a delay of 0.3 second or longer by a ventricular excitation (fig. 6). However, atriogenic reflux was probably smaller and under these circumstances could not be demonstrated as clearly as in the same patient on his own slow ventricular rhythm. Maximal atriogenic reflux occurred when fast electrical driving of the ventricle suddenly was stopped (fig. 7). Since the ventricle took over at a very low frequency with several seconds of diastole between ventricular beats, multiple P waves occurred, each being followed by a temperature drop in the left atrium. Because the ventricle is more distended under these circumstances, one could conclude that heart size may play a dominant role in the amount of atriogenic regurgitation. On the other hand, temperature measurement at a certain point in the atrium is not representative of mean atrial temperature. Therefore, conclusions from the temperature drop at the thermistor on the amount of reflux have to be drawn with caution and a quantitation of the amount of regurgitated blood was not attempted.

In contrast to retrograde flow of indicator-tagged blood after isolated atrial systoles, ventricular contractions not preceded by an atrial systole as well as isolated ventricular extrasystoles during infusion of cold saline into the ventricle were not accompanied by a significant drop of temperature in the atrium (fig. 3). Ventricular extrasystoles, therefore, seem to close the valves nearly as effectively as normal beats although the ventricular contraction is altered. Thus, a properly timed atrial contraction is not absolutely
necessary for closure of the A-V value without significant regurgitation.

Simultaneous measurements of pressure in the atria and ventricles did not contribute much to an understanding of the atrio-genic reflux phenomenon. Atrial contraction generally produced an increase in ventricular pressure and beginning with atrial relaxation a sharp decrease in atrial pressure. Therefore, a ventricular-to-atrial pressure gradient after atrial relaxation was present. As seen in figure 8, this reversed pressure gradient was very small or even absent after a waves which occurred in the earliest part of diastole, but was progressively more marked, the later in ventricular diastole atrial contraction occurred. After a waves in the late diastolic phase the pressure gradient attained 3 to 4 mm Hg. This pressure gradient, maximal after atrial relaxation, tends to decrease with time mostly because of an increase in atrial pressure probably due to venous return. Sometimes, however, ventricular pressure also showed a slight tendency to decrease instead of a real plateau after each a wave, compatible with retrograde flow through the A-V valves. The reversed pressure gradient indicates at least partial closure of the A-V valves. The fact that with intracardiac phonocardiography a sound could be detected at the

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**Figure 5**

*Detection of atrio-genic reflux in the left heart of the fifth patient with complete A-V block, corresponding to pressure relationship in figure 8 (lower panel). In both panels the upper tracing is the temperature within the left atrium; the middle tracing is the aortic pressure and the zero-pressure line is used to mark the time during which 10 ml of cold saline was infused into the left ventricle. Note that after completion of the injection, since there is still indicator in the residual volume, temperature in the left atrium decreases after a P wave not followed in normal sequence by a ventricular contraction (arrows).*
Figure 6

Detection of atriogenic reflux in the fifth patient with A-V block. The ventricle is paced at a rate of 75 per minute by an electrode catheter in the right ventricle. The upper tracings in each panel show the temperature within the left atrium. Aortic pressure is recorded in the middle tracings. The infusion of 20 ml of cold saline into the left ventricle is indicated. Note that the P waves indicated by arrows caused significant reflux in the left atrium.

Figure 7

Detection of atriogenic reflux during periods of ventricular standstill induced by sudden stop of fast ventricular pacing in the fifth patient with A-V block. During and after left ventricular infusion of 15 ml of cold saline each of the series of P waves induced a more or less progressive fall of temperature in the left atrium, even after the infusion was stopped.

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Simultaneous measurements of pressure in the right atrium and ventricle (upper panel) and in the left atrium and ventricle (lower panel) in the fifth patient with complete A-V block. Zero and calibration scale of the pressure records were the same for all four heart chambers. Note that, after P waves occurring during the earliest part of diastole, no reversed diastolic gradient was present. However, after P waves occurring later in diastole, a distinct reversed pressure gradient is present, the pressure in the ventricle being 3 to 4 mm higher than in the atrium after atrial relaxation. The gradient tends to decrease mainly because of an increase in atrial pressure. Pressure within the right ventricle was sensed with a Telco catheter tip manometer, and an intracardiac phonocardiogram is recorded below the zero-pressure line in the upper panel. Note that a distinct sound is present 0.27 second after beginning of the P wave probably occurring from a stretching of the A-V valves brought in apposition. The first derivative dp/dt of ventricular pressure is recorded on top of each panel.

Discussion

The factors contributing to efficient closure of the mitral and tricuspid valves have not been clearly and completely delineated. Saroff and associates in 1965 stated that "the mitral valve can be closed solely as a result of atrial contraction and relaxation independently of the onset of ventricular systole." They based this conclusion on the maintained level of ventricular segment-length after each atrial systole and on pressure measurements in an open-chest dog with A-V block. The same authors also concluded from a set of pressure measurements "that some regurgitation was taking place when ventricular systole
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was not preceded by a properly placed atrial systole.” Bushmer’s book stated also: “The occurrence of such regurgitation is widely acknowledged when A-V valves are closed by ventricular systole which is not preceded by an atrial contraction, i.e. premature ventricular contraction.”

Our observations in conscious man are in contradiction to these statements. However, they are in agreement with the reports by Williams and associates and Vandenberg and associates studying anesthetized dogs with A-V block by retrograde injection of contrast medium into the left ventricle without thoracotomy and detecting the regurgitation into the left atrium by roentgen videodensitometry, a technique developed by Wood and associates.

Congenital or acquired A-V block in man or in dog without thoracotomy is an adequate model to study separately the contribution of atrium and ventricle to closure of the mitral and the tricuspid valves. Certainly the ventricles are more distended toward the end of long diastolic periods in complete A-V block than in normal hearts. Since the ventricular volume may be of crucial importance in the mechanism of closure of the A-V valves, decrease of ventricular volume by electrical stimulation at higher frequency was attempted in the fifth patient. It was possible to detect atriogenic reflux at normal heart rates, even though its amount was probably smaller than that during long diastolic intervals. In contrast, the heart in a dog exposed by thoracotomy probably functions at abnormally small dimensions, and the A-V valve mechanics may be different under these conditions. The discrepancy may also arise because Sarnoff’s statements are derived from the indirect evidence of segment-length and pressure observations while the indicator-dilution method is the adequate way to detect movement of tagged blood from the ventricle to the atrium. Both videodensitometry and thermodilution are sensitive methods for detecting small changes in indicator concentration. While by videodensitometry the indicator can be measured as integrated sample over most of the atrium, the thermodilution and dye-dilution method measure indicator concentration only at a point or a circumscribed small area.

Our material shows that pressure measurements do not give clear-cut information regarding valve closure. As Grant and coworkers have shown for A-V block of the right heart, we found also in the left heart a small reversed pressure gradient (ventricular pressure exceeding atrial pressure) after a waves occurring during ventricular diastole. In two patients showing this phenomenon, atriogenic reflux could be detected repeatedly and under varying conditions so that the conclusion that the A-V valves are completely closed based on a small reversed pressure gradient must be wrong.

In the wake of the jet produced by atrial systole and eddy currents behind the valves, apposition of the valve cusps may occur. Intracardiac phonocardiograms showed a distinct sound with atrial relaxation (fig. 8 upper panel). However, as indicated by the reflux phenomenon, no firm sealing of the A-V valves as a consequence of the small pressure gradient due to atrial contraction and relaxation results. Only ventricular contraction, which leads quickly to a considerable systolic pressure gradient over the A-V valves, seals the cusps firmly. It must be assumed that after relaxation of the atrium retrograde flow from the distended ventricle into the atrium takes place if the valves are not shut after the normal delay by the rapid rise of ventricular pressure and papillary muscle contraction.

To explain the delay between the P wave and the beginning of the temperature drop in the atrium, we have to consider that there is probably no quick jetlike retrograde flow through the A-V valves and rapid mixing with all the blood in the atria but rather a slow streamline movement which may reach certain points of the atria where the thermistors lie after a considerable delay.

The continuous infusion of indicator even when the ventricle has been physiologically filled would favor some reflux in the later part of ventricular diastole. However, after discontinuation of infusion, since there was

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still indicator in the residual volume, P waves not followed by ventricular complexes in normal sequence still caused diastolic reflux indicating that the infused volume of indicator was not the cause of diastolic reflux.

The infusion of cold saline sometimes caused ectopic ventricular beats. Regurgitation, however, did not occur or was not increased after such extrasystoles. Recently Braunwald and associates\textsuperscript{17} have shown from a review of angiocardiograms that effective closure of the mitral valve is possible without atrial systole. Our measurements after normal or extrasystolic beats or after ventricular arrhythmia during which we were not able to detect reflux in the atria are in accord with these observations. Important differences between isolated atrial and isolated ventricular contractions regarding A-V valve closure result not only from the magnitude of the pressure gradient induced over the A-V valve, but also from the contraction of the papillary muscles drawing the valve edges together and from the diminution of the valve ring which would tend to seal better the A-V valves during ventricular contraction.

Librium used as premedication in two patients is known to decrease emotional tension, anxiety, and fear and to have some relaxing effects on striated muscles. However, blood pressure and flow do not change in the small dosage used. It seems unlikely that the mechanism of A-V valve closure is changed by Librium.

During measurements of temperature in the right atrium the infusion catheter was lying through the tricuspid valve. The same catheter during infusion of saline in hearts with normal A-V sequence did not cause regurgitation and, therefore, probably did not impede valvular function seriously. The effects of atrial and ventricular contraction in the left heart as studied in the first, fourth, and fifth patients when no catheter passed through the mitral valve were similar.

Our findings in conscious man, therefore, agree with the observations of the Mayo Clinic group\textsuperscript{2, 13} based on their studies in intact dogs that only ventricular contraction, whether normal or extrasystolic, produces efficient closure of the A-V valves. An isolated atrial contraction, also capable of partially closing the valves, as indicated by the ventricular to atrial-pressure gradient, does not efficiently seal the mitral and tricuspid valves since atrioenergetic reflux can be demonstrated.

**Summary**

In five patients with total A-V block studied by thermodilution, infusion of 10 to 25 ml of cold saline into the right ventricle over a period of several seconds resulted in lowering right atrial temperature usually 0.25 to 0.7 second after P waves not followed in normal temporal sequence by QRS complexes. In three of these patients, in whom left heart catheterization was performed, the same phenomenon could be detected during and after infusion of cold saline into the left ventricle while temperature was measured by a thermistor introduced by transseptal route into the left atrium. Isolated atrial contractions, although capable of partially closing the A-V valves as indicated by the higher ventricular than atrial pressure, lead to atrioenergetic reflux from the ventricle. Ventricular contraction, however, whether normal or extrasystolic, produced efficient closure of the A-V valves.

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**References**


A Philosopher’s Comment on Angina

My anguish pain has increased during the past year, tho’ nitro-glycerin stops it like magic. I go to Paris to consult one Dr. Montier, whose high frequency currents have performed a wonder kur on a neighbor of mine (reducing his arterial tension from 230 to 150 in four applications) with a relief of all his formidable symptoms, that has now been complete for six months! I know of two cases of similar relief by him, tho’ I am unacquainted with the details. It sounds impossible, and I hear that M. is regarded as a quack by medical opinion. Nevertheless I don’t wish to leave that stone unturned, since my own trouble (in which I gladly acknowledge an element of nervous hyperesthesia) seems progressive. I will let you know the results!—Letter of William James to William Osler, May 3, 1910—(James died August 26, 1910, age 68).—Ludwig Edelstein: William Osler’s Philosophy. Bull Hist Med 20: 293, 1946.
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