Studies on Mitral Valve Function. Effect of Acute Hypervolemia, Premature Beats and Other Arrhythmias

By Ben Friedman, M.D., William M. Daily, M.D. and Russell H. Wilson, M.D.

A direct method for studying valvular competence is described based on changes in impedance in the blood induced by injections of concentrated saline. It does not require withdrawal of blood samples and may be repeated at frequent intervals in the same animal. It detected mitral insufficiency in the absence of significant changes in atrial pressure tracings. Mitral insufficiency was observed frequently in association with ventricular arrhythmias, occasionally with atrial arrhythmias and in half of the dogs made acutely hypervolemic.

PREVIOUSLY, valvular regurgitation was measured indirectly through phasic changes in pressure or volume in the heart chambers. The present report describes a method for detecting valvular insufficiency by blood impedance changes, and its application to study the effect of certain arrhythmias and hypervolemia on the competence of the mitral valve. In principle the method employed consists of injecting a foreign substance into the left ventricle and detecting its presence in the left atrium within one or two heart beats following injection and before recirculation. The test substance employed was five per cent sodium chloride. The technique of detection is an adaptation of the method of H. L. White which, in turn, is based on the conductivity cell device introduced by G. N. Stewart fifty years earlier.

METHODS

The apparatus for detecting impedance changes consists of five major units: (fig. 1) a conductivity cell, a power supply, an oscillator, a Wheatstone bridge, and an amplifier. The arrangement is similar to the one employed by White except for full wave rectification of the output, and elimination of the oscilloscope. The output was attached to an electrocardiographic recorder of a Sanborn Polyviso. A 0.5 microfarad capacitor was added to the ECG recorder circuit to eliminate high frequency variations in impedance and to minimize deflections induced by heart beats. The conductivity cell was of the concentric needle type described by White. The Wheatstone bridge was balanced by adjusting the resistor and capacitor elements of the detector apparatus to give the lowest possible position of the recorder stylus.

Using mongrel dogs anesthetized with sodium pentobarbital, the heart was exposed by left thoracotomy. The lungs were ventilated under positive pressure with 100 per cent oxygen.

The placement of the conductivity cell in the left atrium proved to be critical. If the tip of this unit touched the atrial wall, as it was apt to do because of cardiac and respiratory movements, a large change in impedance occurred. If the tip slipped out of the main stream of blood, the unit failed to detect salt at all. A satisfactory placement was one which gave less than 5 mm. deflections of the recording stylus, but a deflection of at least 40 mm., in response to 1 ml. of 5 per cent saline injected into the external jugular vein. Determinations showing no regurgitation were regarded as valid only if immediate check revealed normal sensitivity of the cell. The conductivity cell, being a hollow needle, served also for recording atrial pressures.

Intraventricular pressures were recorded and 5 per cent saline injected through a polyethylene catheter which was inserted into the left ventricle either through the carotid artery or the anterolateral wall near the apex.

Atrial arrhythmias were produced by application of aconitine or by electric stimulation, ventricular arrhythmias by direct mechanical, electrical, or chemical stimulation using 1 per cent sodium citrate or oxalate. Mitral insufficiency due to direct injury was
produced by cutting one or more of the chordae tendinae with a sharp hook-like instrument described by MacCollum and McClure.4

This method of detecting valvular insufficiency is qualitatively exquisitely sensitive. Evidence of regurgitation by impedance changes was frequently encountered with entirely normal atrial pressure levels and contours. In vitro, the amplitude of the deflection varies quantitatively with the concentration of salt. In the animal a rough quantitative relationship between the concentration of saline injected and the amplitude of deflection or the area under impedance curve was seen. However, the concentration of the salt that flows past the tip of the conductivity cell depends upon the volume and concentration of salt injected into the ventricle, the degree of mixing in the ventricle, the volume of blood and salt regurgitated, the extent of dilution within the atrium, and the position of the needle within the main axis of the regurgitated stream. Thus, a quantitative relation between impedance change and volume of blood regurgitated cannot be achieved in vivo except in a general sense. The method may be applied to study regurgitation across any valve and permits repeated tests in a single animal.

Results

Following the injection of 1 ml. of 5 per cent saline into the ventricle, mitral insufficiency was detected by a sharp upward deflection of the atrial impedance curve. This evidence of regurgitation usually coincided with systole or early diastole of the first beat following injection. Figure 2 shows a record before (A) and after (B) cutting one of the chordae tendinae. This change in impedance was not a result of mechanical displacement of the valves since it did not occur when blood was substituted for saline in the intraventricular injection, and since there was usually a latent period up to one cardiac cycle length between injection and electrical change. When saline was introduced directly into the atrium, the latent period between injection and electrical impedance change was less than 0.02 seconds.

![Figure 1. Apparatus for detecting impedance changes in circulating blood. Description in text.](http://circres.ahajournals.org/)

![Figure 2. Records of left atrial pressure, ECG and conductivity changes in left atrium. Solid line at bottom denotes injection of 5 per cent saline.](http://circres.ahajournals.org/)
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Records showing mitral regurgitation with premature ventricular contraction (B) but not with sinus tachycardia (A and C). Horizontal lines above letters indicate points of injection.

Mitrail insufficiency was noted initially in 8 of 41 dogs, prior to induction of arrhythmias or hypervolemia. This finding, in general, was met in technically good preparations in which placement of the conductivity cell and balancing of the bridge was such that the apparatus was maximally sensitive.

Atrial Tachycardia Flutter and Fibrillation: Atrial tachycardia was produced in 6 dogs, the ventricular rates varying between 160 and 330 per minute. Mitrail regurgitation was noted in only one of the 6 animals. It was slight and inconstant, becoming more pronounced when in the presence of induced hypoxia.

Atrial flutter with 2:1 ventricular response was noted in two dogs, the ventricular rates being 150 and 215 per minute respectively. Mitrail valve competence appeared intact in both instances. Atrial fibrillation occurred in two animals. In one, at a ventricular rate of 390 per minute, mitral insufficiency was absent. In the other mitral regurgitation was recorded at a ventricular rate of 300 but not at a rate of 210 per minute.

Ventricular Premature Contractions: Repeatedly in 10 dogs, premature ventricular contraction occurred at the moment of injection of saline into the ventricle. With the premature beats mitral insufficiency was present in 9 of the 10 animals and in more than 80 per cent of the separate trials. In 4 dogs it was observed in every trial. A typical record is depicted in figure 3.

Ventricular Tachycardia: Mitrail valve function was studied in 13 dogs with ventricular tachycardia. Mitrail regurgitation was absent in 8, consistently present in 4 and inconstant in 3 dogs. In the last group the mitral valve was competent at rates of stimulation of 180 to 240 per minute, but was insufficient when the ventricular rate was stepped up to 290 and 300 per minute. In several animals in which the rate of stimulation was kept constant the mitral valve became insufficient after several minutes of continuous stimulation, the development of regurgitation usually coinciding with a decided decline in intraventricular pressure. In three instances stimulation at rates in excess of 300 per minute failed to produce mitral regurgitation.

Ventricular Flutter and Fibrillation: Ventricular flutter and fibrillation was recorded in seven dogs and was invariably accompanied by mitral regurgitation. In all instances, valvular function was intact immediately preceding development of fibrillation and in two cases following successful defibrillation and restoration of normal sinus rhythm.

Acute Hypervolemia: Acute hypervolemia was infused 1800 cc.

FIG. 3. Records showing mitral regurgitation with premature ventricular contraction (B) but not with sinus tachycardia (A and C). Horizontal lines above letters indicate points of injection.

FIG. 4. Records as in figure 1. A, mitral valves competent in control state; C, mitral valves insufficient after 1800 cc. was infused. This reversed to a normal pattern similar to A following phlebotomy of 800 cc.
was produced in six dogs by rapid infusion of large volumes of unmatched blood or of dextran. Mitral valve regurgitation was recorded in three of these animals after infusions of 375, 400 and 1800 ml., respectively (fig. 4). The valvular insufficiency pattern seemed to appear in conjunction with development of congestive failure as evidenced by a rise in end-diastolic intraventricular pressure. Partial or complete reversal of regurgitation was accomplished in 2 of these 3 dogs by bleeding. In three instances no abnormality of mitral valve function was discernible after infusions of 650, 1000 and 1300 ml. respectively.

**Discussion**

The finding of mitral valve regurgitation in approximately 1 out of 5 dogs in the control state was unexpected and without explanation. Berglund and his co-workers recently emphasized the role of an intact pericardium in preventing ventriculo-auricular regurgitation. It is possible that the minor hemorrhage incidental to operation, the open pericardium and the undetected hypoxia attending an open chest may have resulted in functional mitral valve insufficiency. It is also possible that we may be detecting the minute degree of physiologic regurgitation which has been hypothesized by some workers to occur at the onset of ventricular systole.

The mechanism, whereby a premature ventricular contraction results in mitral insufficiency, is probably related first to mitral valve position at the onset of ventricular systole in the absence of antecedent atrial systole as demonstrated by Henderson and Johnson and by Little, second to the altered dynamics of ventricular contraction. Wiggers and Feil reported that with a given injury to the mitral valve, the volume regurgitated is determined in part by the velocity of tension developed during isometric contraction and by the vigor of systolic ejection, regurgitation being greater with slow than with rapidly rising ejection curves. The steepness in the gradient of ejection in rapidly beating hearts may explain the observation that mitral insufficiency occurred less often with ventricular tachycardia than with isolated ventricular premature beats.

Another mechanism to explain mitral regurgitation with ventricular premature beats may be postulated on the basis of delayed excitation and contraction of the ring of muscle surrounding the mitral valve. Hurwitt has demonstrated the importance of this sphincter-like contraction in partially narrowing the mitral orifice.

The observations, here recorded, suggest that one of the mechanisms whereby ectopic rhythms precipitate or aggravate congestive heart failure may reside in the atrioventricular valve regurgitation which may accompany them.

**Summary**

Impedance changes in the blood induced by injections of concentrated saline may be utilized to obtain direct evidence of valvular insufficiency.

Mitral regurgitation was detected in dogs in the absence of significant changes in atrial pressure tracings.

Mitral insufficiency was observed regularly in association with ventricular flutter and fibrillation, frequently with ventricular premature beats and less often with ventricular tachycardia.

Acute hypervolemic states and ectopic rhythms of atrial origin produced mitral insufficiency only under conditions of severe ventricular muscle strain or failure.

**Acknowledgment**

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**Summario in Interlingua**

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ventricular, frequentemente con pulsos prematur ventricular, e minus frequentemente con tachycardia ventricular.

Acute stastos hypervolemic e rhythmos ectopic de origine atrial produceva insufficiencia mitral solmente sub conditiones de sever efforio muscular ventricular o de disfallimento.

REFERENCES


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Pharmacology of Protoveratrine

Following Bezold and Hirt’s demonstration that the cardiac slowing and hypotension produced by veratrine (a mixture of veratum viride alkaloids) is abolished by vagotomy it has been generally accepted that it acts through the “von Bezold reflex.” Receptors causing these circulatory effects have been located around the coronary vessels and in the lungs. However, many other observers using pure veratum alkaloids have concluded that reflexes from chest receptors are not solely concerned.

Recent reinvestigation of the pharmacology of protoveratrine in the J. F. Heymans Institute of Pharmacology seems to confirm previous observations that in dogs under morphine-chloralose anesthesia (1) hypotension without bradycardia can occur in vagotomized or atropinized animals; (2) this is not due to direct depression of the vasmotor center but (3) is provoked mainly through stimulation of carotid sinus baroreceptors. Applied locally to the carotid sinus areas, protoveratrine decreased or suppressed the carotid vasopressor reflexes.

The conclusion is also reached that the reflex hypotension provoked by protoveratrine is only due in small part to cardiac slowing and stimulation of heart receptors.

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BEN FRIEDMAN, WILLIAM M. DAILY and RUSSELL H. WILSON

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