Measurement of the Second Derivative of Left Ventricular Pressure Using a Fiberoptic Catheter* (32621)

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(Introduced by F. J. Stare)
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The initial stage of ventricular ejection is a crucial one in the study of ventricular function(1). Measurement of the rate of change of pressure and flow at the onset of systolic ejection have been identified as valid indices of the state of myocardial contractility(2,3). Until now, the only measurement of proven sensitivity is the maximum rate of increase of left ventricular pressure, or peak left ventricular dP/dt. This occurs just before the opening of the aortic valve, at the end of the isometric phase of the ventricular contraction. Recently, it has been shown that the measurement of blood flow acceleration at the root of the aorta exhibits a greater sensitivity to changes in myocardial contractility in the intact animal than left ventricular dP/dt(4). However such measurements of flow and its derivatives examine a phase of systole after the isometric contraction period when the aortic valve has opened and ejection has begun.

The present investigation deals with the measurement of acceleration of left ventricular pressure, i.e., the second derivative of the ventricular pressure pulse or left ventricular d^2P/dt^2. This expression of left ventricular function shows maximal changes early in the isometric contraction period, at the very inception of systole. Investigation of this parameter has been made possible by the development of a new high fidelity fiberoptic pressure catheter(5).

Methods. Twelve mongrel dogs were anesthetized with 30 mg/kg of pentobarbital and ventilated with room air using a Harvard respiratory pump. A fiberoptic catheter was passed retrogradely into the left ventricle via a carotid artery. In some instances a 7F Cournand catheter was also passed retrogradely into the left ventricle via a femoral artery to check baseline and gain stability of the fiberoptic catheter. Baseline drift was substantial, but the device showed stable gain characteristics and the measurement of d^2P/dt^2 was therefore valid. A pacing catheter was introduced in the right atrium.

The construction and performance characteristics of the fiberoptic catheter have been previously described(5). In brief, pressure is recorded from changes in intensity of light reflected from a fine membrane attached to the tip of the catheter. Deformation of the membrane by pressure causes changes in intensity of a light beam which is transported to and from the catheter tip by a fiberoptic bundle. This transducer tip catheter has a linear frequency response up to 3000 Hz with a noise level equivalent to 0.5 mm Hg or less. The prototype catheter used in this experiment displayed some nonlinearity, with decreasing gain at higher pressures. This does not however affect measurement of dp/dt and d^2P/dt^2 provided calibrations are corrected for this nonlinearity.

Recordings were made of left ventricular pressure and of its first and second derivatives. The latter were obtained from two analog differentiators in cascade using resistance–capacitance (R–C) networks and operational amplifiers. Spurious phase shift introduced by the differentiators was 0.8 msec. To provide optimal signal to noise ratios, the frequency response was made adjustable, and arbitrary cutoff frequencies of 300, 600, and 1200 Hz were chosen for comparative measurements.

The unit was standardized by performing a static calibration of the fiberoptic transducer, then taking a separately generated linear ramp of appropriate rise time and feeding it

* Supported by Grants HE-0776-04 and 5 T1 HE-5242 from the National Heart Institute; United States Public Health Service PO 1 HE-11306-1; The Life Insurance Medical Research Fund; the John A. Hartford Foundation; and the Fund for Research and Teaching, Department of Nutrition, Harvard School of Public Health.

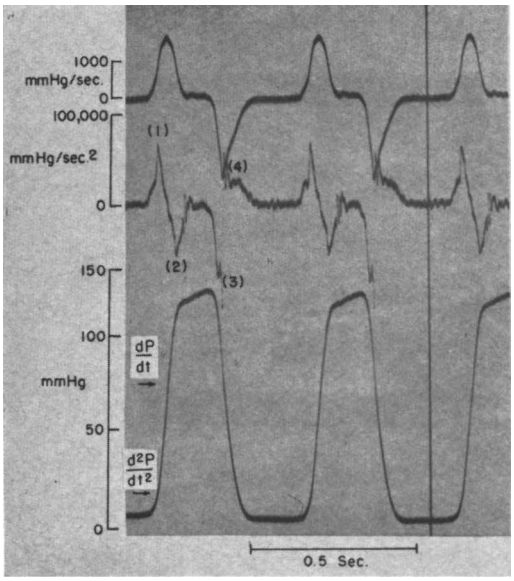

FIG. 1. From top to bottom, dP/dt, d^2P/dt^2, and left ventricular pressure. On the d^2P/dt^2 complex, nos. 1–4 indicate the successive deflections. Only the second complex of d^2P/dt^2 exhibits the small initial hump which is distinct from the main peak. The arrows on the left ventricular tracing indicate the moment at which the derivative peaks occur.

into the input of the first differentiator as a surrogate for the left ventricular pressure. This gives a step response from the first derivative output. The first derivative was then calibrated graphically. The same ramp signal was then used as the input for the second differentiator, and the second derivative was then calibrated using the value of the first derivative as previously determined. Using this technique, calibration of the second derivative is repeatable within 5%. Use of the actual ventricular pressure tracing for graphical calibration may lead to serious errors of 30% or greater in the second derivative.

Results. The second derivative of left ventricular pressure (d^2P/dt^2) is shown in Fig. 1. There are four principle deflections, in order: positive, negative, negative, and positive. Each of these deflections corresponds to a peak of acceleration of left ventricular pressure during the cardiac cycle and indicates the maximum and minimum slopes of each side of the two deflections of the first derivative.

The peak of the first deflection of d^2P/dt^2 indicates the maximum acceleration sustained by the left ventricular pressure during isometric contraction. The contour of this deflection is generally smooth from the baseline to the peak. In one third of the records, however, a smaller initial hump, approximately 50% the height of the main peak, was present. This reflects a "break" in the first derivative tracing (Fig. 1). When changes in myocardial contractility were induced, the initial hump, when present, changed in the same direction and in the same proportion as the main peak. However the initial hump was unstable and sometimes disappeared during the period of observation as shown in Fig. 1.

Relating the main peak of d^2P/dt^2 to the ventricular pressure tracing, it was noted that it corresponds to a point about one fifth or one sixth of the distance from baseline to maximum ventricular pressure. When the initial hump is present it occurs earlier in systole, at the very beginning of the rise of the ventricular pressure curve. Although the initial hump may reflect the earliest events in systole, its inconsistent presence and lability suggest that the main peak offers a more valid index of myocardial contractility. The main peak of the second derivative precedes the peak of the first derivative, which occurs at the end of isometric contraction, just before valve opening (Fig. 1).

The 300 and 600 Hz filters were noted to cause attenuation of the peak of left ventricular d^2P/dt^2 tracing by approximately 40% and 20% respectively, indicating the requirement for wide bandwidth for accurate measurement of this parameter (Fig. 2). Control values of d^2P/dt^2 ranged from 35,000 to 92,000 mm Hg/sec^2 using the 1200 Hz filter.

Increase in heart rate by atrial pacing augmented both dP/dt and d^2P/dt^2. However, the relative increase was two to three times greater for d^2P/dt^2 than for dP/dt. To eliminate the effect of heart rate changes, other procedures were carried out while the heart was paced at a constant rate.

Elevation of the proximal aortic pressure by balloon inflation caused no significant change in dP/dt, but d^2P/dt^2 increased by 20%. Infusion of isoproterenol carried out in 12 animals resulted in increase in both derivatives, but showed a more marked effect on d^2P/dt^2 than on dP/dt (Fig. 3). However, infusion of acetyl strophanthidin in

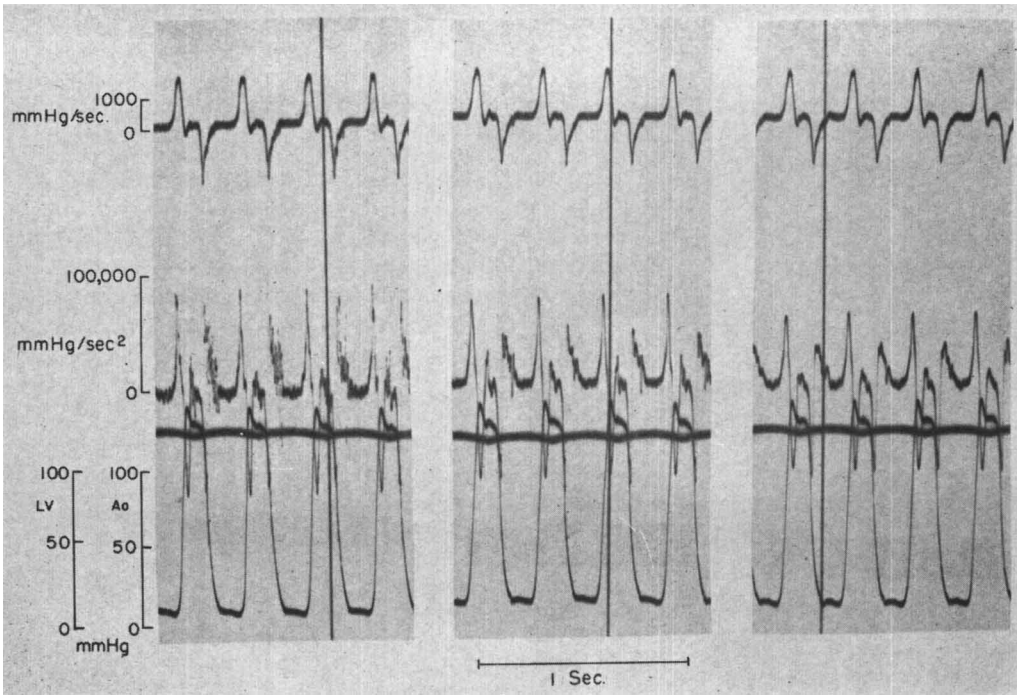

FIG. 2. Recordings of dP/dt, d^2P/dt^2, and left ventricular pressure different filters: left, 1200 Hz; center, 600 Hz; 300 Hz; Mean aortic pressure is recorded with a Cournand catheter. The three samples are recorded on the same dog, under the same conditions, at intervals of a few seconds.

12 animals, while producing an increase in the first derivative, failed to cause a significant increase in the second derivative (Fig. 4).

Discussion. Previous authors have noted the desirability of performing measurements of the second derivative of left ventricular pressure (6). The availability of a high fidelity fiberoptic pressure catheter has made this objective possible.

From the present study, it appears that d^2P/dt^2 offers an index of myocardial contractility, which for most inotropic stimuli provides approximately a twofold amplification of changes noted in the first derivative. However, the results with acetyl strophanthidin emphasize the fact that the peak first and second derivatives are derived from entirely different portions of the upstroke of the ventricular pressure curve, and that they can vary independently. Thus first and second derivatives may have quite different significance with reference to the contractile process. These findings also suggest that the mode of

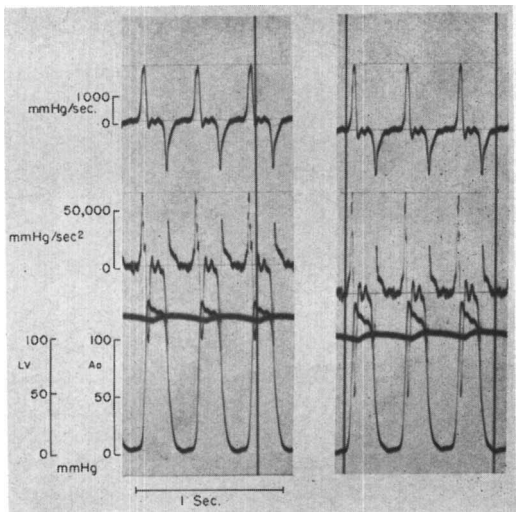

FIG. 3. From top to bottom, dP/dt, d^2P/d^2t, aortic mean pressure, and left ventricular pressure. Left, control; right, during infusion 2.5 μg/min of isoproterenol. In the second panel the zero baseline for both derivatives has shifted downward. The dP/dt increases by 21% and d^2P/dt^2 by 37%. Atrium is paced at a rate of 170.

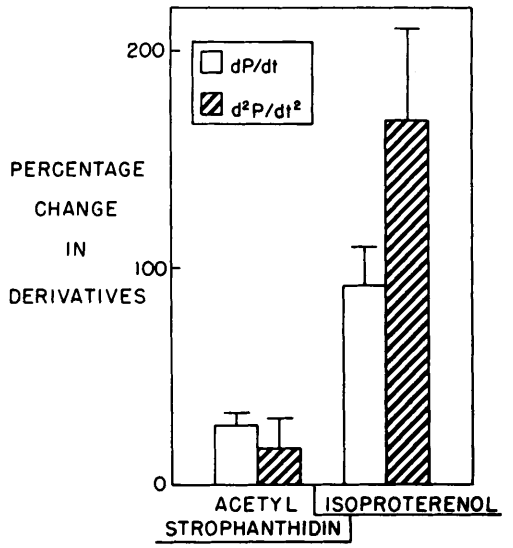

FIG. 4. Percentage change in dP/dt and d^2P/dt^2 with infusion of acetyl strophanthidin and isoproterenol. For acetyl strophanthidin, measurements made at ninth minute of infusion of 100 micrograms/min. For isoproterenol, measurements made at second minute of infusion of 9 micrograms/min. Data presented as mean ± SEM. Both derivatives increased significantly over the control value with isoproterenol infusion; the increase in d^2P/dt^2 was significantly greater than dP/dt ($p < .05$). With acetyl strophanthidin infusion, only dP/dt showed a significant increase over the control value ($p < .05$).

action of digitalis on the myocardial contractile apparatus differs in some fundamental way from that of other inotropic stimuli.

Summary. A new high fidelity fiberoptic pressure catheter has been used to measure the second derivative of left ventricular pressure, which constitutes an index of myocardial contractility. It may provide new information about the early phase of isometric ventricular contraction.

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Received June 12, 1967. P.S.E.B.M., 1968, Vol. 127.

Changes in Carbohydrate Metabolism of Squirrel Monkeys with Chromium Dietary Supplementation* (32622)

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A high prevalence of an impairment of carbohydrate metabolism is found in squirrel monkeys maintained on a standard commercial chow under controlled laboratory conditions (1,2). The animals are asymptomatic of diabetes but exhibit abnormal diagnostic tolbutamide and glucose tolerance tests. Mertz and his co-workers have shown that progressive impairment of glucose tolerance associated with a diminished response of isolated tissues to insulin *in vitro* develops in rats and humans maintained on suboptimal intake of trivalent chromium (3). The metabolic defect was reversed by supplementation of trivalent chromium in drinking water or diet. Analysis (8) of the diet and drinking water of the squirrel monkeys revealed that the total chromium content was relatively low and of unknown valency state. The present investigation was undertaken to determine if the abnormal diagnostic tolbutamide responses characteristic of metabolically impaired squirrel monkeys could be reversed and their glucose tolerance improved with chromium (III) dietary supplementation.

Methods and Materials. The squirrel monkeys from the colony used in these experiments

* This study was supported in part by NIH grants FR-00180-01 and CA-06474.