Influence of the Cardiac Sympathetics on Synchrony of Ventricular Contraction.* (28826)

WALTER C. RANDALL AND DONALD V. PRIOLA
Stritch School of Medicine and the Graduate School, Loyola University, Chicago, Ill.

It is generally accepted that excitation of the sympathetic innervation of the heart significantly alters myocardial excitability, conductivity and contractility. Actual experimental demonstration of each of these properties has occurred only within relatively recent years although the influence of the catecholamines has been known. Marked alterations in the rate of rise of ventricular systolic pressure and the rate of fall of diastolic pressure have led to the deduction that sympathetic excitation exerts an important influence on the synchrony of myocardial contraction(1,2). While recording pressure simultaneously from both ventricles, it became obvious to us that the pressure elevations in the ventricles early in systole were asynchronous. During stellate stimulation, however, these pressure elevations became more nearly simultaneous. The present report describes this synchronization of contraction of the two ventricles as a result of stellate stimulation.

Methods. Pressures were recorded simultaneously from the 2 heart chambers of the dog as previously described(1). An Offner Type R Dynograph was employed as the recording instrument. Through the widely opened chest, cannulae were introduced into each of the ventricular chambers and the Statham transducers adjusted to chamber level to insure accurate zero recordings. The animals were anesthetized with Sernylan† (2 mg/kg) followed by i.v. chloralose (80 mg/kg). Both stellate ganglia were prepared for stimulation by means of bipolar electrodes and a Grass model S 5 stimulator set to deliver square-wave pulses at 5 msec., 10/sec. and 4-5 volts. Stimulation pulses were monitored by an oscilloscope across the stimulating electrodes. Records were made at 2.5, 25 and 250 mm/sec., the latter being employed in precise measurement of time intervals. Positive pressure respiration was maintained by means of a Harvard respirator. Standard limb leads of the ECG were recorded and stellate ganglion stimulation repeated several times from each side, both before and after bilateral vagotomy.

Results. Fig. 1 shows simultaneously recorded pressure pulses from both the right and left ventricles together with the ECG, before (A), immediately after cessation of electrical excitation of the left stellate ganglion (B) and following 2 minutes recovery time (C). Brief segments of the traces recorded at 25 mm/sec are followed by pulses recorded at 250 mm/sec in each instance. Although small presystolic pressure waves were associated with the a-wave of atrial contraction in each of the ventricles, the point of *initial* rise in intraventricular pressure is clear. It is evident that pressure

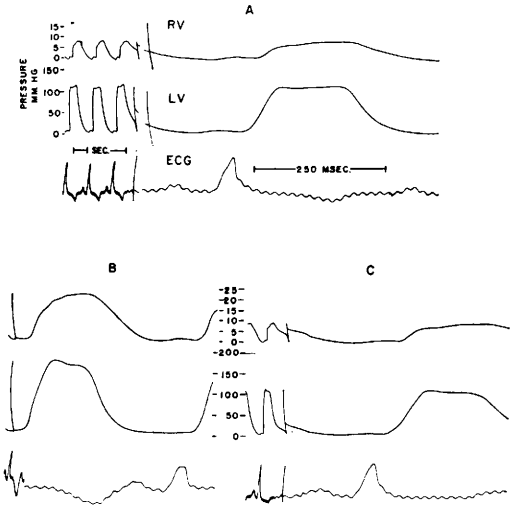

FIG. 1. Simultaneously recorded intraventricular pressure curves in the open chest dog. ECG was recorded from standard limb lead I. Panel A represents control, B—pulses 5 sec after cessation of left stellate stimulation (5 msec, 10 per sec, 5 volts), C—2 min after cessation of stimulation. ECG traces are shown both at 25 and 250 mm/sec.

* Supported by a grant from NIH.

† The Sernylan was generously furnished by Parke, Davis and Co.

began to rise in the left ventricle (LV) significantly earlier than in the right (RV); careful measurement reveals this interval to be 24 msec. The duration of the P-R and QRS intervals during the same cardiac cycle measured 100 msec each. Comparable measurements on pulses recorded during stellate stimulation revealed remarkable reduction in the interval between the onset of pressure rise in left and right ventricles, but since ECG was not recorded during the actual stimulation (due to electrical interference), similar pulses are shown 5 seconds following cessation of stimulation. At this point both timing of events and pressure alterations remained essentially unchanged from those observed during the stimulation. Heart rate had accelerated from a control rate of 136 to 180 beats per minute, and intraventricular systolic pressures had increased from 115 to 177 mm Hg in LV and from 9 to 22 mm Hg in RV. The interval between the initial rise in left ventricular pressure and that in the right ventricle was scarcely 6 msec., while the P-R and QRS intervals measured 84 and 70 msec, respectively. Although the T-wave was inverted during the control period, it became more deeply inverted during stimulation. A remarkable increase in the slope of the rise in pressure in both of the intraventricular pressure curves occurred with stellate ganglion stimulation. The rate of pressure rise in LV was 2.08 mm Hg/msec in the control and 5.36 mm Hg/msec in the stimulation pulse. Comparable data for the RV traces were 0.16 mm Hg/msec in the control and 0.58 mm Hg/msec as a result of stimulation. Although total cycle time was shortened, it is evident that the duration of systole in both ventricles was decreased relatively more than the duration of diastole.

The third set of pulses were recorded approximately 2 minutes following cessation of stimulation. Heart rate, systolic pressures, P-R and QRS intervals returned essentially to normal values. The interval between the onset of pressure rise in LV and RV measured precisely 26 msec. Similar measurements in a series of 12 separate experiments thoroughly confirm these observations. Thus, it is clear that under the influence of stellate ganglion stimulation the left and right ventricles contract more nearly simultaneously.

Discussion. There is excellent evidence indicating that during normal contraction of the heart not all of the myocardial units attain the contracted state simultaneously. A certain period is required to activate the entire atrium and each of the individual ventricles. Wiggers suggested that the activating process may be considered as a recruiting mechanism which progressively and quickly incorporates more and more fibers(3). Asynchronous myocardial activation is represented in the intraventricular pressure curve by a relatively slow increase in pressure at the beginning of the isometric contraction phase. Wiggers called this the "entrant phase." When all of the fractions have been excited the pressure trace shows a much steeper ascent. The more nearly simultaneously the individual fractions are excited, the more rapid will be the rise in intraventricular pressure. The present study sheds no light on time of shortening of individual segments of the ventricles, but the marked alteration in rate of rise in ventricular pressure may be interpreted to indicate that such recruitment occurs during stellate ganglion stimulation. A preliminary report strongly suggests that individual segments of the ventricular myocardium shorten more synchronously during stellate stimulation(4).

Careful measurements of the sequence of ventricular excitation have been made from epicardial electrodes(5,6) and more recently from multipolar electrodes plunged into the walls of the ventricles and conductile tissues (7). Electrical activity begins in the proximal terminations of the bundle branches, spreads rapidly along endocardial surfaces, transmurally from endocardial to epicardial surfaces in the middle and apical free walls, and finally toward the base of the walls and septum. A plot of ventricular epicardial potentials (monkey) reveals the earliest appearance in the center of the trabecular region on the anterior surface of the right ventricle (7). The coupling time between electrical excitation and mechanical shortening within a small muscle unit of myocardium remains essentially unknown. The spread of excita-

tion through the large mass of contractile units is certainly not instantaneous and is apparently quite variable in different portions of the heart. In spite of the early appearance of epicardial potentials on the anterior wall of the right ventricle, and despite the relatively smaller muscle mass to be excited in the right ventricle, the initial ventricular pressure rise was invariably observed in the left ventricle under control conditions of these experiments. This consistency in the earlier pressure rise in LV contrasts with that reported by Samet *et al*(8) and Di Bartolo *et al*(9) who observed the initial rise in pressure to occur simultaneously or either in right or left ventricle. In both reports, however, illustrative traces and speed of recording would seem to make precise measurements difficult.

The remarkable decrease in the interval between onset of intraventricular pressure rise in the 2 ventricles resulting from stellate ganglion stimulation is a measure of the greater degree of synchronicity of contraction in the 2 ventricles. We have no data to describe the altered velocity of conduction within the musculature of the 2 chambers, but it must be concluded that spread of excitation through the right ventricle is relatively faster than through the left, since LV invariably preceded RV during controls but both chambers contracted more nearly simultaneously during sympathetic stimulation.

The modest decrease in duration of the P wave and P-R interval elicited by stellate ganglion stimulation suggests more rapid conduction over atrial muscle, as well as across the A-V nodal junction. These results have been more specifically demonstrated by Wallace(10) who employed the bipolar electrode method of Hoffman *et al*(11,12). Wallace concluded that stellate ganglion stimulation enhances conduction through the A-V node and ventricular muscle, but it affects the specialized purkinje system only slightly. The variable, but generally less marked shortening of the QRS interval in the present experiments, tends to confirm these data.

Alterations in heart rate, such as that observed in Fig. 1, may be expected to be accompanied by many of the changes attributed here to stellate ganglion stimulation. However, even in experiments in which left stellate ganglion stimulation elicited marked augmentation in force of contraction with little or no alteration in heart rate, the interval between the onset of intraventricular pressure rise in the two ventricles was shortened. Again, this implies a relatively greater alteration in conduction time in the right heart than in the left during sympathetic stimulation. This may be associated with the relative density of post ganglionic axon endings in these different portions of the heart.

Summary. In the open chest animal, contraction of the left ventricle precedes that of the right by 5 to 35 msec. During electrical excitation of the stellate ganglion this interval decreases markedly, and in some instances, the initial elevations in intraventricular pressures occur simultaneously or nearly so. The P-R and QRS intervals generally shorten during stimulation. These observations confirm the inference that sympathetic excitation significantly alters the synchronicity of excitation and contraction of the heart chambers.

1. Ulmer, R. H., Randall, W. C., *Am. J. Physiol.,* 1961, v201, 134.

2. Sarnoff, S. J., *The Control of the Function of the Heart,* Chap. 15, Sec. 2, Vol. 1, *Handbook of Physiology, Am. Physiol. Soc.,* 1962.

3. Wiggers, C. J., *Am. J. Physiol.,* 1927, v80, 12.

4. Osadjan, C. E., Randall, W. C., *Fed. Proc.,* 1963, v22, 578.

5. Lewis, T., Rothschild, M. A., *Phil. Trans. Roy. Soc. B.,* 1915, v206, 181.

6. Harris, A. S., *Am. J. Physiol.,* 1941, v134, 319.

7. Scher, A. M., *Excitation of the Heart,* Chap. 12, Sec. 2, Vol. 1, *Handbook of Physiology, Am. Physiol. Soc.,* 1962.

8. Samet, P., Bernstein, W. H., Litwak, R. S., *Circ. Research,* 1959, v7, 228.

9. Di Bartolo, G., Nunez-Dey, D., Muiesan, G., McCannon, D. M., Luisada, A. A., *Am. J. Physiol.,* 1961, v201, 888.

10. Wallace, A. G., *Fed. Proc.,* 1963, v22, 578.

11. Hoffman, B. F., Cranefield, P. F., Stuckey, J. H., Amer, N. S., Cappelletti, R., Domingo, R. T., PROC. SOC. EXP. BIOL. AND MED., 1959, v102, 55.

12. Stuckey, J. H., Hoffman, B. F., Begdonas, A. A., Venerose, R. S., *ibid.,* 1961, v106, 90.

Received July 11, 1963. P.S.E.B.M., 1964, v115.