

potent thrombin might readily mask any antithrombic action. The phospholipid antagonisms, in our experience, are difficult to demonstrate except with limiting dilutions of heparin. The dilution method permits experimentation in the zone of minimal quantities of reagents which we are still unable to isolate and work with in pure chemical form.

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### Reflex Inhibition of the Human Heart: Complete A-V Block and Parasystole.

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Certain phenomena observed in the electrocardiogram have forced the question: May reflex augmentation of inhibitory tone during the systolic rise in arterial pressure produce effects which wax and wane within the time of a single cycle, or are the reflex effects smoothed out so that little change in the degree of inhibition occurs within a single cycle?

The experimental results of Brown and Eccles<sup>1</sup> suggest that the first alternative may be the true one. In their experiments, however, one (or 2) stimuli were applied to the vagus nerve and time was then allowed for full recovery from inhibition before another stimulus was given. If a stimulus be applied every 2 cycles, or less, conditions as they sometimes obtain in the human heart are more closely approximated. A curve illustrating the time course of vagus slowing is shown in Fig. 1. Make-break shocks were applied about every  $650\sigma$  to the peripheral end of the cut right vagus of a dog under urethane anesthesia. The other vagus was also cut. Electrocardiograms were taken. The uninhibited cycle was  $350\sigma$ . Several experiments were carried out with similar results.

The curve shown rests upon a background of inhibition resulting from the frequency of nerve stimulation. The zero point on the ordinates is an arbitrary point of reference. The latency of inhibitory effect is  $170\sigma$ ; the ascending limb of the curve is about  $300\sigma$ .

In several experiments the rate of vagus stimulation was only slightly slower than the inhibited sinus rate. Under these condi-

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<sup>1</sup> Brown, G. L., and Eccles, J. C., *J. Physiol.*, 1934, **82**, 211, 242.

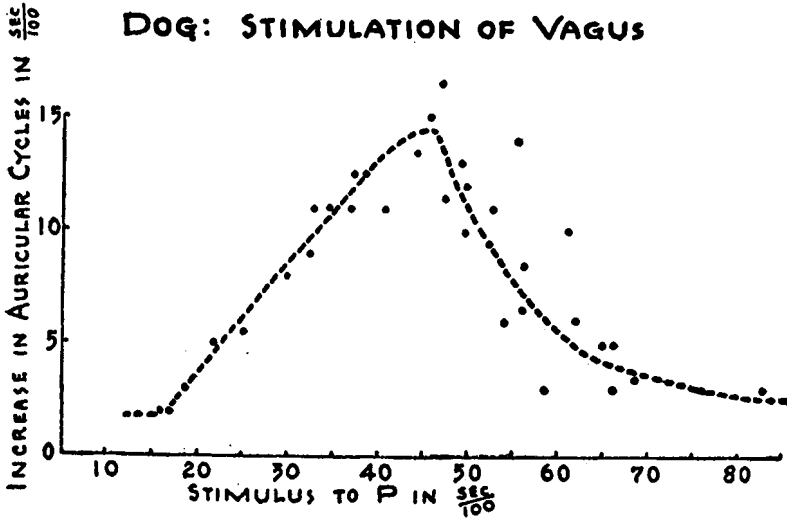


FIG. 1.

tions the heart slowed or accelerated, depending upon the time in the cycle at which the stimuli fell.

Only when the rhythm of the physiological inhibitory reflex pulses differs from the rhythm of the pacemaking structure can a waxing and waning of inhibitory effects be demonstrated in the human heart. This requirement is satisfied in the following examples.

**COMPLETE A-V BLOCK - VENT. CYCLE 1.76 SEC.**

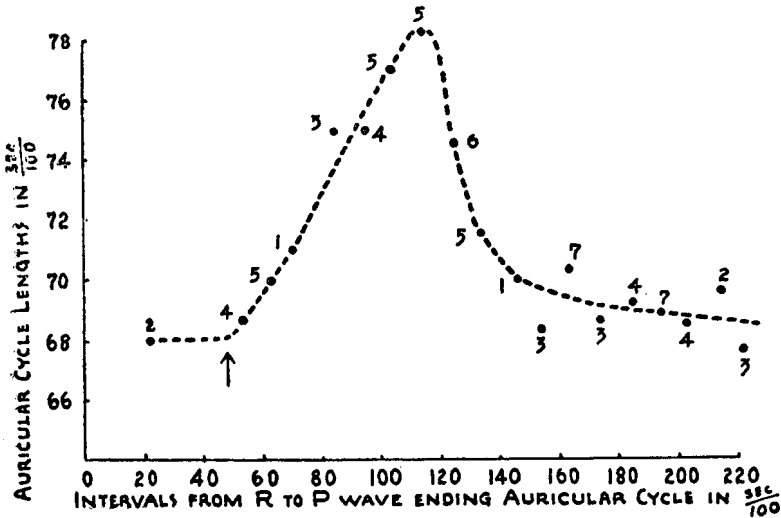


FIG. 2.

Figure 2 is derived from the electrocardiogram of a patient with complete A-V heart-block. Each point is the average of the number of individual measurements shown by the numbers. The reflex latency is  $480\sigma$ . When corrected for the delay between the electrical and mechanical responses, for the presphygmic period, and for transmission of pressure to aortic nerve receptors, this latency becomes about  $370\sigma$ . In experiments upon 2 dogs in which reflex slowing of the heart was brought about by raising the pressure in the carotid sinus, the latency was found to be of this order of magnitude or a little longer. The ascending limb of the curve is  $700\sigma$ . Since the ejection phase lasted about  $500\sigma$ , a gradual cumulation of inhibition can be assumed.

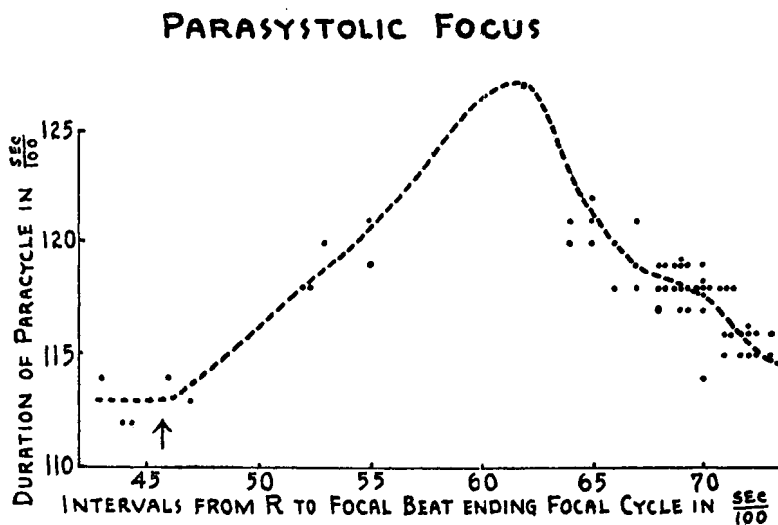


FIG. 3.

Figure 3 is from the case reported in another communication. It illustrates the reflex chronotropic effect upon an ectopic focus of normal systoles interpolated between successive manifest ectopic beats. The latency is  $460\sigma$ ; corrected, about  $360\sigma$ . Here the ascending limb of the curve is only about  $170\sigma$ . Possible reasons for its brevity cannot be discussed here.

These results and observations support the view that reflex inhibition of a pacemaker may wax and wane within the time of a single cardiac cycle.