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The "Iterative" Nature of the Vagus Nerve Fibers to the Heart.

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If the right vagus nerve of a turtle be stimulated electrically, the degree of inhibition produced in the heart depends upon a number of factors. If we consider only those introduced by changing the nature of the stimulation used, the inhibitory effect will depend upon (1) the shape of the time-voltage curve of the shock used, (2) the strength of the individual shocks used, (3) the number of stimuli applied to the nerve, and (4) the frequency of stimulation. Since such variables must act through changes in the nerve fiber responses and since such responses follow the all-or-none law of fiber response, the following argument must hold. The strength of stimulus applied must, of course, be great enough to reach the threshold of one or more vagus inhibitory fibers before any cardiac inhibitory effects will appear. As the shock strength is increased above this threshold strength, there will be a resultant increase in the number of nerve fibers stimulated. There will also be an increased inhibitory effect upon the heart. The inhibition may attain a certain maximum which is probably achieved in consequence of the stimulation of all of the cardiac inhibitory fibers in the nerve. The effect of an increasing number of stimuli in producing an increased inhibitory effect can be thought of only as an increase in peripheral effect. The effect of changing the stimulus frequency is such that increasing the frequency of stimulation up to a certain amount (between 10 and 40 stimuli per second in most cases) causes an increased inhibitory effect upon the heart. With increasing rates of stimulation the inhibitory effects become no greater but rather become less. The decrease in effect with an increase in rate is probably related to a Wedensky type of inhibition which develops in the nerve (or the end mechanism) with too rapid stimulation.

The summating effect of repeated stimulation of the vagus and certain other nerves led Lapicque[1] to the expression of the theory of *iterative nerves.* In iterative nerves, the chronaxie values of the nerves are presumably much less than the chronaxies of the respective end organ mechanisms. A series of several nerve impulses are supposed to be necessary for building up, by the phenomenon of *latent addition,* an excitation process in the end organ sufficient

[1] Lapicque, L., *C. R. de l'Acad. des Sci.*, Paris, 1912, **155**, 70.

for a threshold response. The vagus nerve as inhibitor to the heart is considered to be typical of this group of nerves.[2] The criterion of threshold effect which is adopted in this case by Lapicque and Meyerson is the complete stoppage of the heart.

We find that in many preparations, it is possible to stop completely the entire heart of a turtle by a single shock applied to the right vagus nerve. It can be demonstrated by means of a recording instrument such as the cathode ray oscillograph that the stimulus produces but one single response volley in the nerve. The assumption of the necessity of repetitive stimulation of the nerve to produce stopping of the heart is therefore without support in fact, even if we were to accept the stopping of the heart as being a threshold effect. That peripheral summation is of importance may be recognized from any group of records such as those of Figure 1.

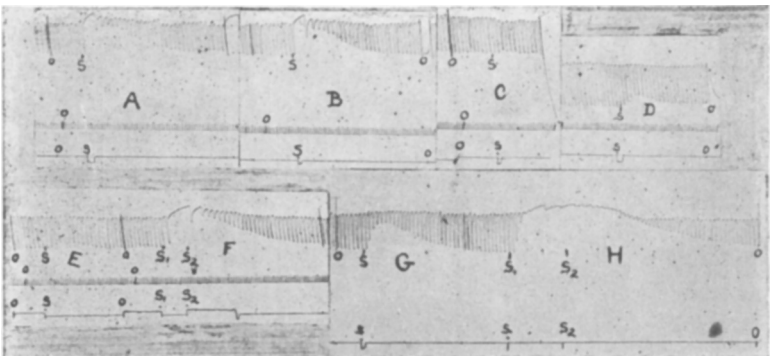

FIG. 1.

Records obtained with lever attached to one atrium of turtle *(P. elegans)*, 3/10/31.
A. 1.0 mfd., 22 volts, right atrium, right vagus, single shock.
B. 1.0 mfd., 6 " " " " " " "
C. 1.0 mfd., 3 " " " " " " "
D. 0.25 mfd., 6 " " " " " " "
E. 0.01 mfd., 45 " " " " " " "
F. 0.01 mfd., 45 " " " " " 3 per second between S_1 and S_2.
G. 0.25 mfd., 22 " left atrium, left vagus, single shock.
H. 0.25 mfd., 22 " " " " " 3 stimuli per sec. between S_1 and S_2.
Time intervals, 1.0 second.
Condenser in series with 10,000 ohms. Nerve on silver wire electrodes, 5 mm. separation.

The inhibitory effects upon the heart as a result of stimulation of the vagus by electrical shocks of various forms, strength, frequency, and number have been studied in our own records and those published by previous workers in this field. The results obtained appear to be entirely consistent with the view that the amount of cardiac inhibition produced is dependent upon the number of

[2] Lapicque and Meyerson, *C. R. de la Soc. Biol.*, Paris, 1912, **72**, 63.

vagus inhibitory fiber impulses delivered in a given period of time. If stopping of the heart be taken as an example, we may say that n vagus fiber impulses are necessary to produce this effect. Considering only shocks, each one of which produces a single vagus response volley as determined by the cathode ray oscillograph, a long lasting shock of sufficient intensity will, in certain preparations, stop the heart, *i. e.*, stimulate n vagus fibers. If the shock duration be made shorter, or the intensity be made less, so that each shock stimulates only n/a fibers, *at least* a shocks must be delivered to the nerve before the heart is stopped. Since the effect of a single vagus volley does not last indefinitely, the condition of repeated stimulation may require that more than a shocks be used, this number being dependent upon the frequency of stimulation. It seems probable that a similar argument can be applied to the other so-called iterative nerves.

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Serum Sickness in Rabbits.*

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It is well known that serum sickness appears in a very large proportion of individuals injected for the first time with normal horse serum or with various antisera. For the experimental study of this reaction it is of value to be able to reproduce in laboratory animals a condition analogous to serum sickness in man. We believe that the results reported below are the first ones concerning the occurrence of serum sickness in rabbits.

When a single injection of horse serum is given to rabbits in sufficient quantities either intravenously, intramuscularly, subcutaneously or into the subscapular tissues, there appears, from 3 to 7 days after the injection, a reaction characterized by erythema and edema. This reaction is evident on the rabbit's ears; there is noted a generalized flush which may involve the entire lower three-quarters of the ear, and which may be diffuse, confluent and of even

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