6756

A Method for the Study of the Rhythmic Property of the Human Heart.

M. H. NATHANSON.

From the Department of Medicine, University of Minnesota, Medical Service, General Hospital.

In the normal heart several centers of rhythm formation are potentially active, but the sinus node, which generates the impulse most rapidly, sets the pace of the heart. Observations on experimental animals indicate that there is considerable variation in the rhythmic efficiency of other portions of the heart. Cohn, Kessel and Mason,[1] after removing the sinus node in dogs, found a transitory quiescence of the heart varying from 4 seconds to 3 minutes, the interval being less than 30 seconds in most instances. The period of the quiescence was interpreted as representing the time required for some other portion of the heart to take on the pacemaking function. Rothberger and Winterberg[2] demonstrated in dogs that depression of the sinus node by stimulation of the right vagus nerve usually resulted in cardiac standstill. After eliminating the sinus node by vagus stimulation these observers studied the influence of various procedures in inducing new centers of impulse initiation. Thus they found that upon stimulation of the left sympathetic nerve, cardiac standstill was prevented by the development of new rhythmic centers in the ventricles. The addition of barium chloride or calcium chloride further increased the automaticity of the ventricles.

The purpose of this report is to point out that the above experiments may be reproduced in man, permitting a study of the rhythmic property of the human heart and also a direct method for the investigation of the action of drugs on this function. Utilizing the carotid sinus reflex of Hering,[3] pressure over the right carotid artery in the neck induces a reflex stimulation of the vagus nerve. In most individuals the degree of vagal stimulation is such that only a moderate slowing of the heart occurs. In some subjects, most frequently in elderly individuals, a very active vagus effect is obtained and the

[1] Cohn, A. E., Kessel, L., and Mason, H. H., *Heart*, 1912, **2**, 311.

[2] Rothberger, C. J., and Winterberg, H., *Arch. f. d. ges. Physiol.*, 1911, **142**, 461.

[3] Hering, H. E., *Die Karotissinus reflexe auf Herz and Gefasse.* Dresden and Leipzig, 1927, T. Steinkopff.

function of the sinus node may be entirely eliminated for a comparatively long period.[4]

In a series of electrocardiographic observations applying this reflex, an exaggerated reaction was obtained in 34 cases in which the heart was deprived of its normal pacemaker for intervals varying from 5 to 15 seconds. In 6 cases the elimination of the normal pacemaker was followed promptly, or within a few seconds, by an ectopic rhythm of ventricular origin. (Fig. 1.) In 25 instances the

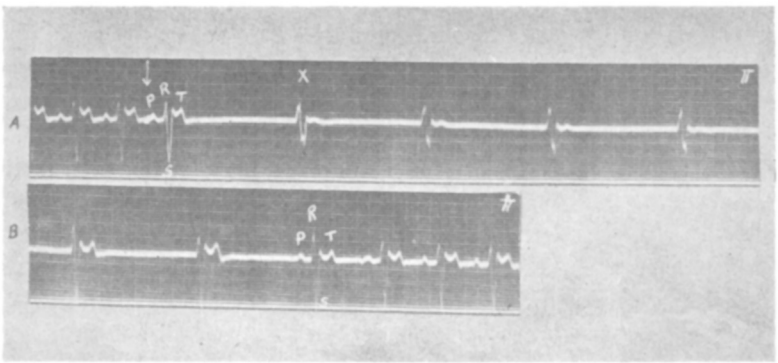

FIG. 1.

A and B form a continuous strip. Ventricular rhythm starting at "x" following pressure on right carotid sinus (arrow). P–P interval (inactivity of sinus node) is 14 seconds.

carotid sinus stimulation induced a prolonged standstill of the heart, as there was no spontaneous tendency for the ventricles to take on the pacemaking function. (Fig. 2-a.) The cardiac activity was resumed only when the sinus node again became active. In many cases the reflex was carried out repeatedly over a long period with a consistent response. In 3 instances the reaction was variable, resulting in cardiac standstill on one occasion and in a ventricular rhythm on repetition of the experiment. These observations indicate in most instances a relatively low efficiency of the secondary rhythmic centers of the human heart.

The subjects who show no tendency for a spontaneous formation of ectopic rhythmic centers permit a direct and objective study of the action of drugs on the rhythmic function of the human heart. The method consists of a control electrocardiogram recording the effect of the right carotid sinus pressure. (Fig. 2-a.) The drug is then administered and after suitable intervals, records are taken again, observing the response to stimulation of the carotid sinus.

[4] Nathanson, M. H., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1037.

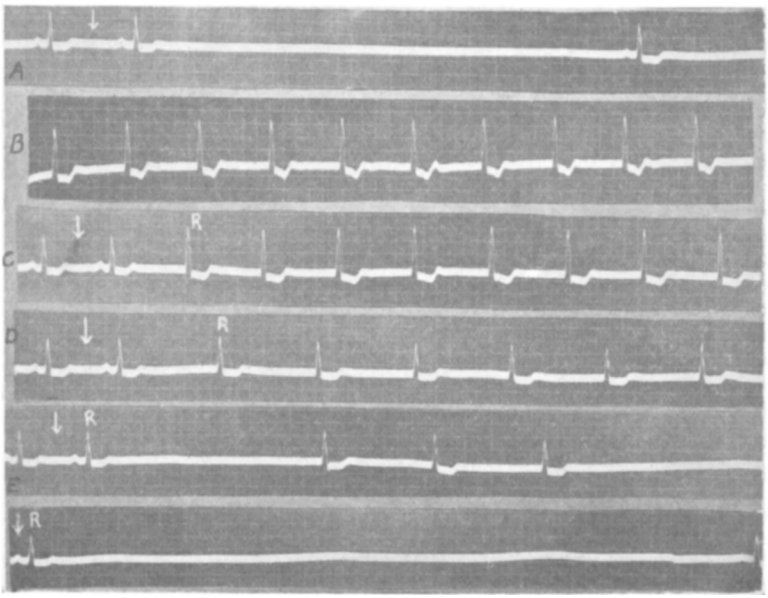

FIG. 2.

Strip A shows standstill of 7.6 seconds on stimulation of the right carotid sinus (arrow). Lower strips taken at intervals following 1/20 mg. epinephrin intravenously. Standstill abolished by development of an idioventricular rhythm. Lowest strip shows disappearance of epinephrin effect, 15 minutes after injection.

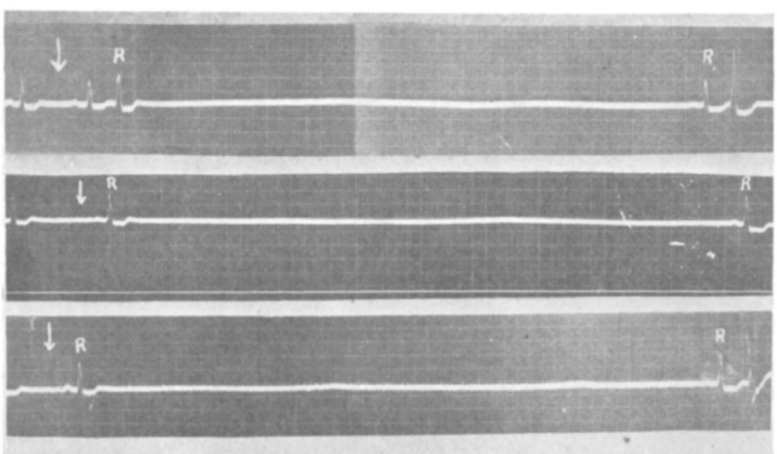

FIG. 3.

Effect of 50 mg. of ephedrine sulphate intravenously. Upper strip before and lower strips 5 and 15 minutes after the injection. No effect in stimulating secondary rhythmic centers.

The indication that a drug effectively increases the rhythmic function of the heart is the abolition of the cardiac standstill by the formation of new rhythmic centers. Figures 2 and 3 illustrate the effect of 2 chemically related substances, epinephrin and ephedrin. Epinephrin actively increases the impulse-initiating property of the ventricle as evidenced by the formation of a secondary rhythmic center near the auriculo-ventricular node. Ephedrin is entirely ineffective. The effect of epinephrin was studied in 8 subjects and the drug abolished the cardiac standstill in all cases by inducing a ventricular rhythm. It is possible by this method to study accurately the time of onset, duration and intensity of the effect. It was also apparent from the results of varying doses of epinephrin that the rate and site of the ectopic pacemaker may be utilized for quantitative studies. Observations with a large series of drugs are in progress and will be reported in detail.

6757

Improved Single Injection Method for Rapid Diagnosis of Early Pregnancy from Urine.

FREDERICK EBERSON.

From the Medical Laboratory, University of California Medical School, and the Geo. Williams Hooper Foundation for Medical Research, San Francisco.

A modification of the Ascheim-Zondek method was reported for the rapid diagnosis of early pregnancy.[1] The luteinizing hormone was concentrated in samples of urine and injected in 2 doses into immature female rats which were autopsied within 36 hours. A total of 265 specimens collected up to that time was diagnosed without error.

During the past 2 years I have attempted to shorten the time required for diagnosis and to use immature female mice as well as rats in performing the test. Notwithstanding the preference expressed in certain quarters for the rabbit as a test animal in the diagnosis of pregnancy by the Friedman[2] technic, this method does not appear to offer any special advantages. If greater accuracy can be obtained by another method and the time required for diag-

[1] Eberson, F., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 407; *J. Am. Med. Assn.*, 1931, **96**, 2176.

[2] Friedman, M. H., and Lapham, M. E., *Am. J. Obst. and Gynec.*, 1931, **21**, 405.