that propagation of poliomyelitis virus did not occur in the absence of viable testicular cells and that an extraneous virus was not inadvertently acquired during the course of these studies. It is plain that the results of the present investigation substantiate the observations of other workers that poliomyelitis virus can propagate in extraneural tissues. From these findings it is apparent that the assumption of an obligate neurotrophism for poliomyelitis virus no longer is tenable. This observation and the demonstration regularly of the natural occurrence in poliomyelitis of virus in the oro-intestinal tract emphasize the need for a renewal of investigative studies of the factors that make possible invasion of the central nervous system to result in the overt and residual manifestations of poliomyelitis.

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Further Studies on Experimental Parasystole and Extrasystoles in Groups.* (18666)

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In parasystole a center in one chamber of the heart forms rhythmic stimuli, undisturbed by the basic cardiac rhythm or by any other stimulus spreading over the heart. This leads to a regular interference of the basic and the ectopic rhythm. An experimental study of this interesting arrhythmia, which is not too rare in man, was impossible because no method was available to provoke it regularly.

Recently, we reported that the subepicardial application of veratrine alkaloids regularly leads to the appearance of parasystole, lasting for a few minutes, and showing all its characteristic features(1). In this paper another method will be reported for eliciting parasystole with ease. It consists of applying mechanical or electrical stimuli to the ventricles of the dog's heart after the intravenous administration of acetylcholine and complete atropinization.

Method. All 18 experiments were performed on dogs with the same technic as reported in previous investigations of the senior author in this journal. The electrocardiograms were taken in lead 2. A fresh solution of acetylcholine chloride "Roche" was used in all experiments. The amount of 0.05 g of acetylcholine was injected intravenously in 3-4 divided doses within 10 minutes and 0.2 mg per kg of atropine sulfate was given intravenously shortly afterwards. When acetylcholine was administered without atropinization, mechanical or electrical stimulation of the ventricles initiated ventricular fibrillation(2).

Results. Following the injection of acetylcholine and atropine, the mechanical stimulation of the ventricles by a stroke with a blunt instrument or the application of a few induction shocks provoke a heteropic ventricular tachycardia originating in the stimulated area. In 15 out of 18 experiments a parasystole was observed; in 3 experiments a regular ectopic tachycardia appeared, which persisted for 45 to 160 seconds and then reverted to regular sinus rhythm.

Fig. 1 shows a representative electrocardiogram exhibiting parasystole. A short part of the tracing between Fig. 1a and Fig. 1b is omitted. Fig. 1b and Fig. 1c are continuous. The dog had received acetylcholine and atropine in the doses mentioned above. The stormy changes caused by the acetylcholine, with the primary inhibition of the heart and the secondary increase of rate and motility had subsided. At the beginning of Fig. 1a a regular sinus tachycardia exists with a rate of

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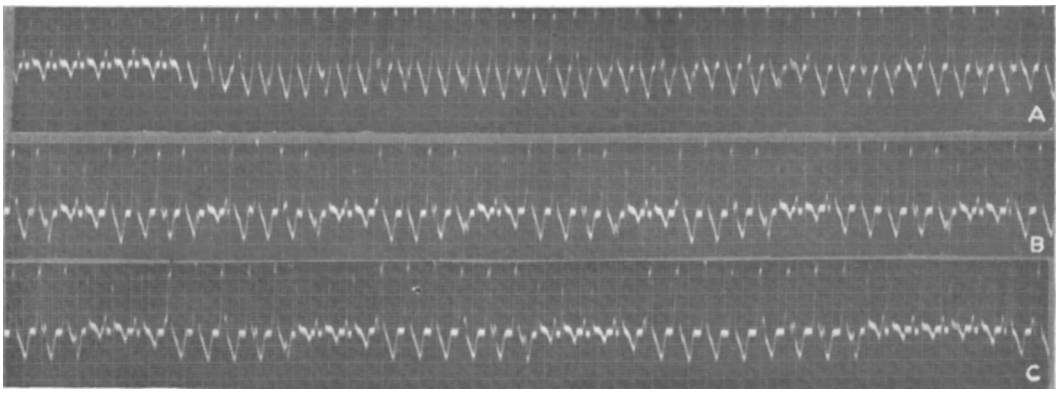

FIG. 1.
Parasystole following administration of acetylcholine and atropine with stimulation of the ventricle.

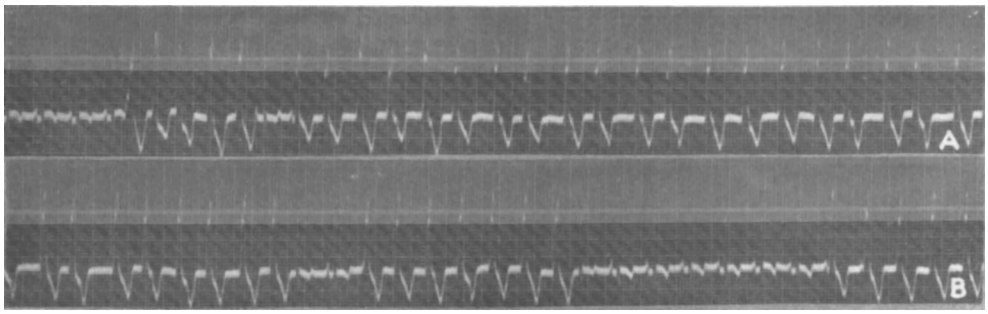

FIG. 2.
Parasystole with group formation of the ectopic beats.

188 beats per minute. Mechanical stimulation of the right ventricle elicited 2 ventricular extrasystoles followed by a chain of spontaneous ectopic beats with a rate of 200. This tachycardia gradually slowed down and occasionally (the second, the seventh, the twelfth, and the sixteenth beat counted from the end of the tracing in Fig. 1a) a sinus beat succeeds in activating a greater or lesser part of the ventricles, so that combination beats appear. When the ectopic stimulus formation slowed down, more sinus beats reached the ventricle and a typical interference of both rhythms appeared. In Fig. 1b, one or 2 sinus beats appeared in succession between groups of 4 ectopic beats. The length of one period of the ectopic rhythm measured 0.28 second. The duration of the pauses between ectopic beats, filled with sinus beats, is 0.56 second when only one sinus beat appears, and 0.85 second when 2 sinus beats follow each other. In Fig. 1c the length of an ectopic period in the beginning of the tracing measured 0.28 second and at the end it is 0.32 second. In 4 instances 3 to 4 sinus beats or combination beats are seen between the groups of ectopic beats. The length of these pauses between the groups of ectopic beats measure: 1.13 (28 x 4), 1.19, 1.19 (29.7 x 4), 1.84 (30.6 x 6). Accordingly, we are dealing with a center which is protected, the rhythmic stimulus formation proceeding without disturbance by the sinus beats.

The appearance of combination beats and the longer pauses between ectopic beats having the length of a multiple of a single ectopic period, were noted in all experiments in which parasystole could be elicited.

Fig. 2 shows a tracing obtained after stimulation of the right ventricle by a few induction shocks. Previously acetylcholine and atropine had been given in the same amount as in the experiment discussed earlier. Three extrasystoles resulting from the inductian shocks (Fig.

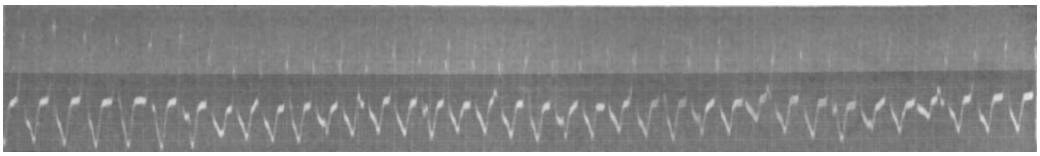

FIG. 3.
Increase of rate of the ectopic tachycardia on warming the focus of origin.

2a), are followed by 2 spontaneous ectopic beats which succeed each other at a distance of 0.32 second. Then a sinus beat caused a period lasting 0.64 second free of ectopic beats. Parasystole is present, because the sinus beat does not disturb the rhythm of the ectopic center. A few seconds later successive ectopic beats show distinct group formation, a short interval of 0.33 second being followed by one of 0.44 second. In Fig. 2b (Fig. 2a and Fig. 2b are continuous) the successive ectopic beats again appear regularly (period: 0.38-0.34 second). At one place the chain of ectopic beats is interrupted by 2 successive sinus beats. The period free of ectopic beats measures 1.06 (0.35 x 3) second and later another pause filled by 7 sinus beats measures 3.12 (0.346 x 9) second.

To prove that these ectopic beats actually originated in the area to which stimuli had been applied and also prove that they are due to stimulus formation in a center and not to a re-entry mechanism, we warmed the point which had been stimulated. This invariably increased the rate.

Fig. 3 shows an ectopic rhythm obtained after the intravenous injection of acetylcholine and electrical stimulation of the conus of the right ventricle with a few rapid stimuli from an electrodyne stimulator. Ectopic beats appeared with a rate of 150-166 (periods of 0.40, 0.36, 0.36, 0.37 second). Warming the stimulated area increased the rate to 200. At the end of Fig. 3, on 2 occasions, sinus beats reach the ventricle without disturbance of the ectopic center. The two pauses free of ectopic beats measure 0.62 second; consequently they represent a simple multiple of an ectopic period.

Discussion. Abnormal ectopic stimulus formation occurs under the influence of acetylcholine. It is more pronounced in the auricles, where fibrillation is a common event(2).

The experiments just discussed show that in the atropinized heart under the influence of acetylcholine, typical parasystole is induced by electrical or mechanical stimulation, with all characteristic signs, namely, changes of the length of coupling, protection of the ectopic center and combination beats. Of importance is the fact that in these experiments extrasystoles with fixed coupling were not observed. Fixed coupling appeared readily after topical application of barium, sodium chloride, digitalis, or strophanthin as previous experiments have shown(3,4). One may conclude therefore that in parasystole a special type of stimulus formation occurs and that the heart exhibiting a parasystolic stimulus formation need not show an extrasystolic one.

Of interest is the appearance of ectopic beats in groups, with alternation in length of diastole, during parasystole (Fig. 2), as described before by one of us(5). This demonstrates conclusively that stimulus formation in the heart, like the spontaneous firing of impulses in nerve and muscle(6,7) may occur in groups of "multiple responses" and still originate in a focus.

Conclusions. Short mechanical or electrical stimulation of the dog's ventricle, following the administration of acetylcholine and atropine, leads to the temporary appearance of parasystolic arrhythmias. The ectopic parasystolic center may form stimuli in groups.

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