case of death, the blood from the heart was cultured. In mice treated with sulfapyridine, the blood was positive throughout 5 days of examination. Pneumococci were present in the blood of mice after 24 hours' treatment with sulfanilamide; after 48 hours mice were dead, and the heart culture proved positive for pneumococci. Mice receiving sodium sulfapyridine, however, showed a number of negative results for pneumococci during 5 days of observation. (Table III.)

Conclusions. 1. Sulfapyridine administered orally to rabbits is slightly less toxic than sulfanilamide. 2. Sodium sulfapyridine given intravenously is considerably more toxic than sodium sulfanilamide. 3. While the protective effect of sulfapyridine in pneumococcal bacteremia types I, II, and III is small, 20 to 30% of mice surviving on the 4th day and less than 10% on the 7th day, it is somewhat higher than that afforded by sulfanilamide, which results in an average survival of 2 to 3 days. Sulfapyridine prolongs life of infected mice only for an additional period of 2 to 4 days. The protective effect of sodium sulfapyridine is of the same order as that of sulfapyridine.

10784

Monophasic Action Currents from the Uninjured Turtle Ventricle.

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Monophasic action currents obtained by derivation from 2 uninjured points on heart muscle have often been mentioned in the literature. Samojloff,[1] for example, produced a block by transverse cutting or compression of the frog heart and recorded monophasic action currents by derivation from uninjured base and apex. In this experiment, however, the apical muscle constitutes an extension of the lead to the injured surface. DeBoer[2] has recently stressed his observation that, employing base-apex leads in the frog, the weak beat in alternation may be associated with monophasic action currents. Although no injury was produced in these experiments by mechanical means, the blocking of the impulse must have been due

1 Samojloff, A., *Arch. f. d. exp. Physiol.*, 1914, **155**, 471.

2 De Boer, S., *Cardiologia*, 1938, **2**, 292.

to the presence of muscle in an abnormal physiological state. Gilson[3] has recorded monophasic action currents following injury, but at a time when the demarcation current had shrunk practically to zero.

In our observations, which are incidental to a study of the action currents of the turtle heart, monophasic action currents were produced as follows. The whole heart was excised. A thread was tied to the frenum, care being taken not to injure the apex. Threads were attached to the great arteries, which were cut near the ventricle, and to the apex of each auricular appendage. Each of the 3 threads, excluding that at the frenum, was tied to a very thin strip of rubber elastic by which the heart was suspended from a rod. The heart was partly lowered into a small beaker. The apical thread was then passed under a hook attached to the floor of the beaker by cardboard and paraffin, and fixed outside the beaker. Thus, on contraction, the base of the heart was drawn down, and the apex was relatively immobile. Fine wires from an inductorium were inserted into an auricle. Ringer's solution at room temperature was then poured into the beaker until the apex was slightly immersed. Galvanometer contacts consisted of wicks of absorbent cotton, connected to Zn-$ZnSO_4$ "boot" electrodes, one dipping into the Ringer's, the other resting on the ventricular base. Electrograms were then recorded, of both sinus and premature beats, the latter being induced by auricular stimulation. The diastolic base line was also recorded. No compensating current was used. Each curve was standardized in 3 millivolt steps. The Ringer's solution was then siphoned off and replaced by Ringer's, cooled to nearly 0°C. In one experiment, with typical results, the Ringer's solution was not cooled to below 5°C.

In the 5 hearts used with this procedure, monophasic action currents were recorded. These were wholly unassociated with any consistent change in the diastolic line of zero potential difference. The observed changes, indicating either slight positivity or slight negativity of the resting apex, were almost negligible in comparison with the recorded action potentials. The QRS complex, in the uncooled heart, consisted of an upright "R" wave, sometimes followed by a small "S" wave. Except in one experiment (F in the figure), after slight, inadvertent injury of the extreme apex, the RS-T segment was within 2 millivolts of the base line. The T wave was sometimes inverted, sometimes upright.

On cooling the apex, the T, if inverted before, became much deeper and wider. If originally upright, it became inverted and deep. In one experiment, slightly impure monophasic action currents,

[3] Gilson, A. S., Jr., personal communication.

in a direction indicating apical positivity, were obtained in association with spontaneous premature beats. Later, from this same heart, slightly impure monophasic action currents appeared with every

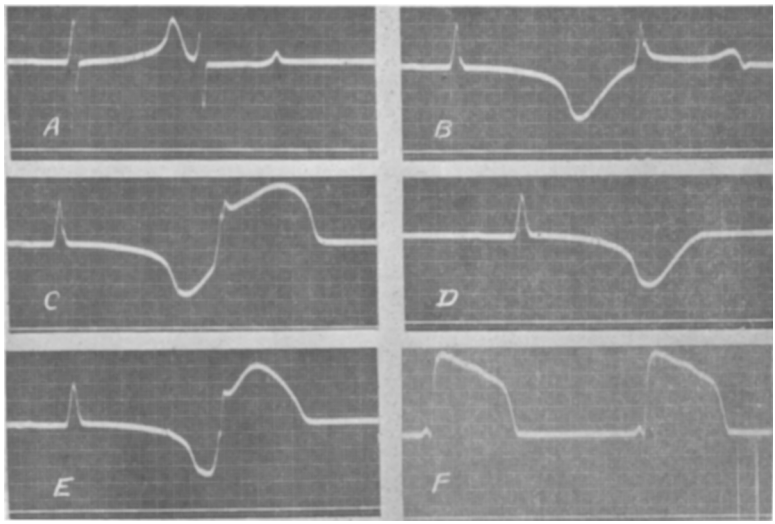

FIG. 1.

Records A to E, inclusive, for experiment of May 13, 1939. F, from experiment of May 6, 1939.

A, control. Apex in Ringer's solution at room temperature. A very small, upright P wave is seen, followed after 0.45 sec. by the initial ventricular complex. The RS-T segment lies practically on the isoelectric level. The artefacts on the early T upstroke are make-break shocks applied to an auricle to induce the premature response of the ventricle which begins late on the T downstroke.

B to E, inclusive, taken while apex is cold, and soon after A. In B the line of resting potential difference has descended just 1 mm., corresponding to 1.875 millivolts relative negativity of the apex. Later (D and E) this returns to the original level. The "S" wave of the initial deflections has disappeared. The T wave, previously upright, is now a large, downward deflection. The signal of auricular stimulation appears on the upstroke of this T in B. The premature response of the ventricle is essentially diphasic, because the wave of excitation has activated most of the apical muscle. In C, the premature response begins earlier. The electrogram is nearly, but not purely, monophasic. This electrogram is longer than the diphasic curve in A, partly because the base of the ventricle has rested longer; partly because the base may be slightly cooled. In D, a few beats after C was recorded, a diphasic response is recorded for comparison with E. Time, between D and E strips, 1.8 sec. In E, the premature response of the ventricle begins at almost the trough of the T wave. This curve is almost, but not quite, purely monophasic. The shoulder after the slight spike, is chiefly due to the superposition of the curve on the end of the T wave of the previous beat. The amplitude of this curve corresponds to 37.5 mvt.

F shows practically pure monophasic curves, from a more rapidly beating heart, which developed after the apex was cooled. The resting level shows 2 mvt. relative negativity of the apex. The diphasic form was restored when the apex was again brought to room temperature.

Standardizations: A to E, 1 cm = 18.75 mvt. F, 1 cm. = 20 mvt.

Time in 0.2 sec and 0.04 sec intervals.

The white line at the bottom of the curve gives a fixed reference level. No compensating current was employed in either experiment.

second sinus beat, a two-to-one block presumably having developed between base and apex because of the prolonged refractory period of the latter. In another experiment, practically pure monophasic action currents were associated with every beat for a time. In the other experiments, the beats of sinus origin were typically diphasic, but premature beats, induced between the trough and end of the T wave, were monophasic. (Fig. 1.) In no instance was any pure or nearly pure monophasic curve followed by a T wave. The duration of the monophasic curves was much less than the duration of the diphasic curves from the cooled heart, but they were slightly longer than the prematurely induced diphasic curves recorded before cooling. This prolongation may quite safely be attributed to the fact that there was always some cooling of the whole heart. Except for a greater or less rounding of the crest of the upstroke, the monophasic form was exactly similar to that induced by injury, and of the same order of magnitude. Typical diphasic curves were restored when the apex was returned to room temperature.

Although we were unable to prove that the occurrence of these monophasic action currents was associated with failure of response of the cooled surface, this interpretation seems to be almost certain, in view of the known blocking effect of cooling and from other considerations. It would be a simple matter to repeat the experiment with muscle strips, cooled at one end, but the necessary injury involved in cutting a strip complicates the interpretation.

These experiments demonstrate, we believe, that the only essential condition for the recording of monophasic action currents is the presence of a non-responding membrane (or surface). We have evidence to show that such a membrane, feebly polarized, appears, or is formed, at an injured surface. Its presence sufficiently accounts for the positive phase of the "injury action potential."[4] With cooling, there is no current of injury. The whole monophasic deflection is positive. Failure of response may be induced by injury, by cooling, by anesthetics, by KCl. The effects are essentially the same in all cases. This fact is difficult to reconcile with the conception that the monophasic action current is a specific effect of an injury, or of local depolarization of the resting muscle.

[4] Eyster, J. A. E., Meek, Walter J., Goldberg, H., and Gilson, W. E., *Am. J. Physiol.*, 1938, **124**, 717.