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Experimental studies of the pharmacology of quinidin.

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It has recently been shown that in certain patients suffering from fibrillation of the auricles, the normal cardiac mechanism may be restored by the oral administration of quinidin sulphate. Knowledge concerning the pharmacological action of this drug is desirable for the clinic and is important insofar as it may furnish information concerning the nature of the fibrillatory process.

Experiments were done on 12 dogs. Anesthesia was accomplished by intratracheal etherization. The thorax was opened in the median line. A myocardiograph of the Roy and Adami type was sewed into the tip and base of the ventricles and connected with a system of Marey tambours. Changes in the degree of cardiac contraction obtained by this method may be taken to represent alterations in volume output. The blood pressure was recorded from the right femoral artery; injections of the drug were made into the left femoral vein. In eight experiments the threshold for the production of transient auricular fibrillation was determined by faradization of the right auricle. Electrocardiograms were made at frequent intervals.

The results may be summarized as follows:

1. *Rate.*—No constant effect was noted. There was acceleration 4 times, slowing 4 times and fluctuation in the remainder of the animals.

2. *P-R (conduction) Time.*—The changes were slight and relatively insignificant. There was prolongation four times and shortening once.

3. *T-wave.*—A change in this portion of the electrocardiogram occurred eight times. This consisted either of reversal in the direction of the deflection, or of increase in the voltage of the original wave.

4. *Blood Pressure.*—In all of the animals a striking fall in blood pressure was observed, the extent of the fall depending in a measure on the amount of the drug injected. There was partial, but never complete return to the former pressure level.

5. *Degree of Contraction.*—There was always an increase in the height of the stroke recorded by the lever, the increase ranging from 16 to 162 per cent. A point was always reached after which further introduction of the drug caused diminution in volume output. The increase in cardiac contraction occurred simultaneously with the fall in blood pressure, but persisted and often continued after partial restoration of the blood pressure level. Unlike the augmentation accompanying the fall in pressure induced by histamine or hemorrhage, the increase produced by quinidin is usually due to greater muscle shortening, not to diastolic relaxation. The persistence of effect likewise indicates a direct stimulating action on the heart muscle. The relation of the fall of pressure to the height of contraction is, however, not finally determined by these experiments.

6. *Threshold for the Production of Auricular Fibrillation by Faradization.*—In four experiments this was slightly raised; in four others, there was no demonstrable change.

7. *Effect on Premature Contractions.*—In one animal frequent spontaneous ventricular premature contractions were noted. These disappeared after the injection of quinidin.

8. *Mode of Death.*—Only one animal died with ventricular fibrillation. In the others, there was progressive slowing of the heart, sometimes with the occurrence of sino-auricular block. The auricles, as a rule, ceased before the ventricles. In the final curves were seen isolated, orderly ventricular beats.

9. *Lethal Dose.*—The lethal dose (mg. per kg.) was extremely variable. In general, the greater the fractionation of dosage, the greater was the amount of drug necessary to cause death.

Experiments dealing with the effect of quinidin on the rate of conduction of the excitation wave through heart muscle are in progress.