Electrocardiographic Patterns Evoked by Venom of the Stingray.*† (23560)

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(Introduced by C. H. Thienes)
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Parenteral administration of stingray venom produces profound changes in the mammalian cardiovascular system. Low concentrations of the venom give rise to simple peripheral vasodilatation or vasoconstriction. High concentrations cause marked vasoconstriction of the large arteries and veins as well as of the arterioles. Much more serious is the direct effect on the heart muscle producing changes in the rate and amplitude of systole. The venom may cause complete, often irreversible, cardiac standstill. It is apparent that the venom affects the normal pace-maker. The new rhythm evoked following cardiac standstill is often irregular and appears to be elaborated outside the sino-auricular node(1). These effects may be potentiated by concomitant changes in the respiratory, urinary and central nervous systems(2).‡ The present experiments were initiated to determine the ECG patterns elicited by the intravenous administration of stingray venom.

Methods and materials. The venom of the round stingray *Urolophus halleri,* was used in all experiments. The venom was prepared by scraping the integumentary sheath(3) free of the animal's sting or caudal spine and macerating it with Ringer's solution in a cooled tissue homogenizer. Fresh stings were used in 12 preparations. Stings which had been immediately refrigerated at −20°C after being severed from the live animal were used in 14 preparations. Preliminary studies indicated that extracts of the venom from stings refrigerated for one week at −20°C were as lethal, or non-lethal, as extracts from freshly severed stings. The crude extract was centrifuged at 3000 rpm for 10 minutes. Each ml of the supernatant represented the venom from one, 4 cm sting. Electrocardiograms were made on 25 adult, pentobarbital anesthetized cats. Conventional limb, unipolar extremity and precordial leads were recorded on the electrocardiograms. In 10 cats, the systemic arterial pressure was recorded from the femoral artery. In 9 of the cats, intermittent artificial respiration was carried out by positive pressure breathing through a tracheal cannula. The remaining animals were allowed to breath normally. The venom extract was administered through the jugular vein.

Results. Abnormal electrocardiograms, prior to the injection of the venom, were obtained in 3 cats; these are not included in the data presented. There was no significant difference in the electrocardiograms of animals receiving the fresh extract as opposed to those receiving the extract from the refrigerated stings. The animals which received intermittent positive pressure respiratory stimulation tolerated the venom with fewer deleterious changes than those animals receiving no artificial respiratory stimulation. One ml of the extract provoked respiratory standstill of less than one minute duration in several of the uncannulated animals. The immediate ensuing respiration was slower, often irregular, and occasionally gasping in nature. Regular respiratory movements returned in 3 to 7 minutes following the injection of this amount of the venom. These appeared to be of lesser amplitude though adequate for survival. The anoxia was possibly reflected in the ECG pattern though similar patterns were elicited in the animals receiving artificial respiration. With larger doses of the venom the interruption of the respiratory cycle was longer. In 2 of the 3 cats receiving 3 to 4 ml, complete cessation of respiration occurred.

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Two distinct effects on the heart were noted in the electrocardiograms: disturbances in rhythm and ischemic injury patterns. On injection of 1 ml of the venom the usual initial and immediate response was bradycardia with no apparent increase in the PR interval. Following this, and usually before the injection was completed, a prolongation of the PR interval was noted with characteristic patterns of first degree, second degree, and in some cases, third degree auriculo-ventricular block. Sinus arrest often followed the second degree block. Nodal, and less frequently, ventricular escape beats were recorded, usually with reversal to a normal sinus rhythm 20 to 30 seconds following the end of the injection period. In 3 of the cats receiving 1 ml of the extract and in 8 receiving 2 ml, there was an almost immediate ST, T wave change indicating an ischemic-type pattern. These changes persisted for 1 to 10 minutes then reverted to normal. On several occasions marked ST, T segment elevations were observed.

Where larger amounts of the venom were injected the patterns were abnormal and unpredictable. Seen frequently were all degrees of AV block, sinus arrest, interventricular block, decreased amplitude of QRS complex and patterns of various degrees of ischemia and injury. The rapid alteration of auriculo-ventricular conduction suggests strong vagal action, or more probably, direct toxic action on the auricles. The almost immediate ST, T wave changes indicate a direct toxic action on the ventricles. The late effects were too variable for interpretation. They were often influenced by the severe drop in systemic arterial pressure and anoxia.

Summary. Intravenous injection of stingray venom produced various changes in the ECG patterns of cats. The extent of the change depends, for the most part, on the amount of venom injected. Small amounts of the venom produce bradycardia with an increase in the PR interval giving a first, second or third degree auriculo-ventricular block. The second degree block is usually followed by sinus arrest. Reversal of the small dose effects occurs within 30 seconds following the end of the injection. Cats receiving larger amounts of the venom show, in addition to the PR interval change, almost immediate ST, T wave change indicative of ischemia and in some animals true muscle injury. These changes often persist for 10 minutes before reverting to normal. When fatal amounts of the venom are injected the pattern is abnormal and unpredictable. All degrees of auriculo-ventricular block, sinus arrest, interventricular block, decreased amplitude of QRS complex, and various degrees of ischemia and injury are seen. The rapid alteration of auriculo-ventricular conduction suggests that the venom has a direct effect on the auricles. The alteration in the ST, T wave suggests that the venom also has a direct effect on the ventricles. These experiments support previous observations(1).

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