Effects of *Chrysaora quinquecirrha* (Sea Nettle) Toxin on the Rat Cardiovascular System (34213)

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(Introduced by Frank H. J. Figge)
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Contact with sea nettle tentacles (*Chrysaora quinquecirrha*) is painful and results in a cutaneous eruption. Many other coelenterate species produce cutaneous lesions in man. The toxin of some of these organisms also adversely affects the cardiovascular system of lower animals (1–5). In the present study, the action of *Chrysaora* toxin on the rat cardiovascular system was investigated to determine whether this agent was capable of injuring tissues other than skin.

Materials and Methods. Fresh nematocyst suspensions (NS) of *C. quinquecirrha* were prepared as described previously and stored at —60° until used (6). On the day of the experiment, NS were diluted in distilled water or in a solution consisting of 2 mercaptoethanol (7.5×10^{-3} *M*) and EDTA (2.5×10^{-6} *M*) in 0.01 *M* phosphate buffer (pH 7.0–7.5). The resulting suspension was ground in a mortar and centrifuged at 100,000*g* for 150 min. In some experiments this supernatant was purified by passage through Sephadex G-200 and DEAE columns. Control solutions (1 mg of bovine serum albumin/ml of the above solvents) were prepared at the same temperature.

Adult albino rats (150 g) were anesthetized with intraperitoneal pentobarbital and supplementary ether. The femoral artery blood pressure and electrocardiogram (Lead I, intradermal electrodes) were recorded continuously[2]. The inocula were injected by two different techniques: continuously at a rate of 1 ml/min with an infusion pump;[3] or manually in 1-ml volumes every 30 sec. Ten sec were required to inject each 1 ml of inocula.

The mouse LD_{50} of the intraperitoneally injected solution was determined as described previously (6). The technique of Waddell was employed for protein analysis on a spectrophotometer[4] (7).

Results. The effects of the toxin on the EKG and blood pressure were not modified either by the fluid used for dilution or by prior passage of the inoculum through Sephadex or DEAE columns.

Slowing of the pulse rate was a consistent observation 2–3 sec after the injection of a large volume of either control or toxin solutions. Except for this phenomenon there was no difference in results between the animals receiving continuous injections and those receiving intermittent injections. No alteration in pulse was seen in control animals, even after injection of 17 ml.

A 30–50 mm Hg elevation of arterial blood pressure was observed within a few seconds after injection in animals receiving solutions containing at least 1 mouse LD_{50} dose/ml. Decrease in blood pressure appeared following arrhythmias or ineffective ventricular beats (Fig. 1c).

Injection of 5–6 ml of control fluids produced flattening of the T waves. Mild ST depression appeared after approximately 7 ml. No other EKG abnormalities were noted with further injections.

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[2] Sanborn 350 hp polygraph, Sanborn Company, Division of Hewlett-Packard Co., Watham, Mass.

[3] Compact infusion pump, model 975, Harvard Apparatus Co., Millis, Mass.

[4] Beckman DU_2 spectrophotometer, Beckman Instruments, Inc., Fullerton, California.

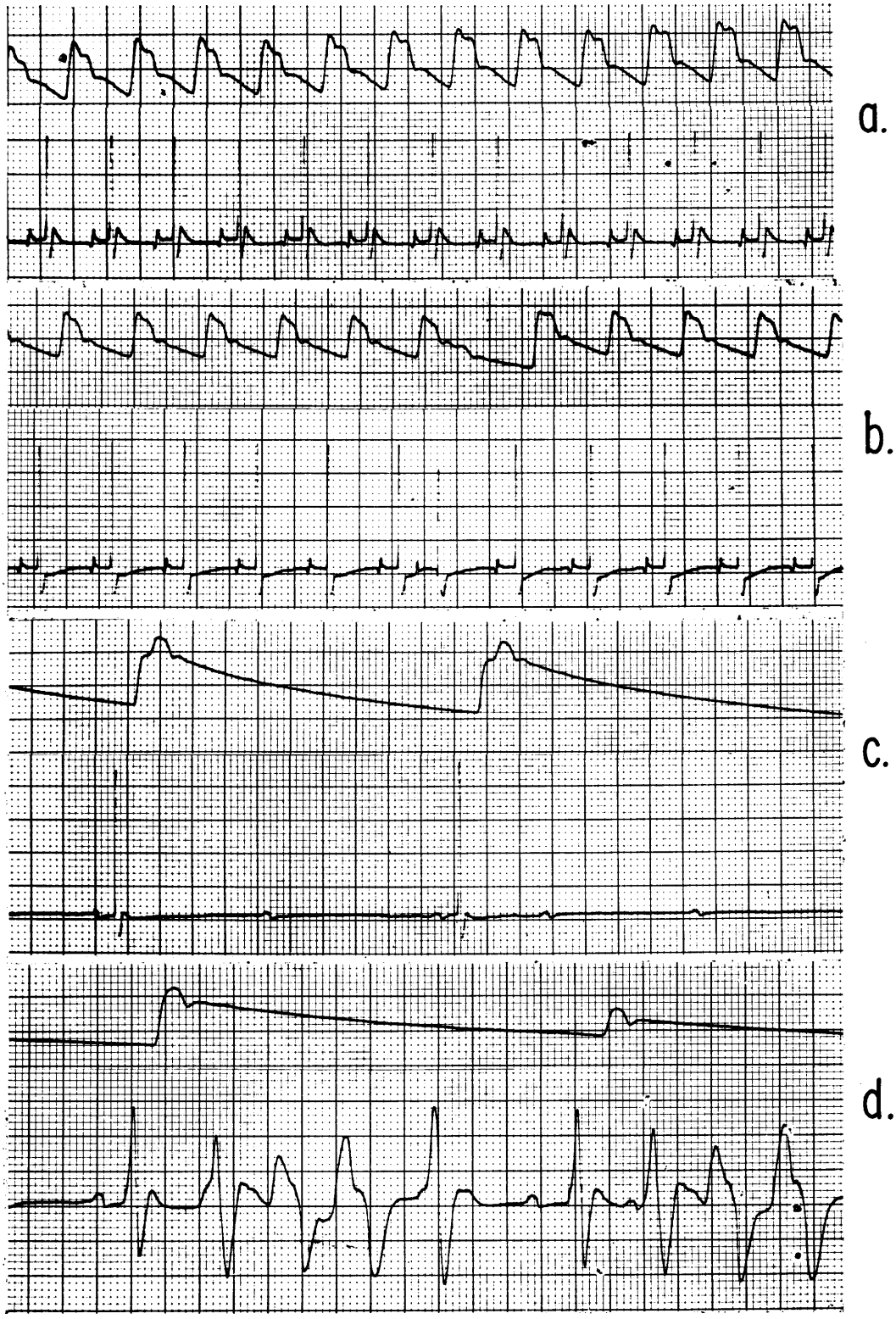
a.
b.
c.
d.

FIG. 1. Effect of toxin: arterial pressure tracing is on top, EKG on bottom. Speed of paper is 50 mm/sec. The inoculum, which contained 1 mouse ip LD_{50} and 0.35 mg of protein/ml was constantly infused. (a) control; BP = 145/105, pulse = 301. (b) Twenty-two sec after start of injection the blood pressure rose to 170/135; the pulse was 295. Note the ST depression and the premature auricular beat accompanied by a decrease in the blood pressure. There was an increase in the amplitude of the R wave. (c) Two min after start of injection; a variable 2:1 and 3:1 block is shown. (d) Three min after start of injection; many abnormal ventricular beats and complete AV block were present. Only a few ventricular beats produced an increase in blood pressure.

Infusion of the toxin solutions produced an increased amplitude of the R wave (Fig. 1b), and ST depression with flat, biphasic or inverted T waves (Fig. 1b). Varying degrees of AV block were subsequently observed (Fig. 1c–d). Deep S waves, bradycardia, AV dissociation, and abberant ventricular complexes appeared shortly before death. (Fig. 1c and d).

The administration of atropine (0.5 mg iv) reversed the heart block and temporarily supported blood pressure for a few minutes. Repeated doses of atropine did not continue to protect the animal.

All animals receiving toxin solutions died whereas all controls appeared to tolerate volumes up to 17 ml.

Discussion. Chrysaora toxin in concentrations greater than 1 mouse LD_{50}/ml, appears to have a vasopressor effect. Control solutions containing higher levels of protein produced no blood pressure alterations.

Some of the ST, T wave changes are apparently due to the large volumes of fluid since they were observed both in animals receiving control and those receiving toxic solutions. The profound ST wave alterations indicating myocardial ischemia usually appeared prior to the onset of arrhythmias (Fig. 1b, c, d). Atropine temporarily reversed some of the conduction abnormalities.

These effects of *Chrysaora* toxin, *i.e.*, systemic blood pressure elevation, myocardial ischemia and cardiac arrhythmias are similar to those attributed to other invertebrate toxins (1–5). In a review of marine animals toxins (1), Lane commented upon the similar biochemical activities of toxins in unrelated animals.

Electrocardiograms recorded from rats injected with toxin from the Portuguese man-of-war (*Physalia physalis*) showed change in the length of PR, QRS, and QT intervals and gross abnormalities in the EKG pattern (2). No pressor effect was detected. Several abnormalities in the P waves were observed.

Physalia toxins injected intravenously into dogs activated ectopic pacemakers resulting eventually in ineffectual ventricular beats and cardiovascular collapse (3). Sublethal doses caused arterial hypertension and increased cardiac output. Some of the conduction abnormalities were reversed by potassium infusions (3).

Intravenous injection of *Chironex fleckeri* (sea wasp) toxin into rats resulted in a rise in the arterial blood pressure. The EKG abnormalities produced by this toxin consist of: an increased amplitude of the R wave, depression or inversion of the T wave, bradycardia, varying degree of AV block, ectopic ventricular beats, a loss of the P wave and finally cardiac arrest (4).

Similar toxicological effects have been produced in cats after inoculation with stingray venom (5). Bradycardia, variable degrees of heart block, and immediate ST-T wave changes indicative of ischemia were seen. High concentrations of toxin produced vasoconstriction, hypertension, and direct cardiac damage.

The cardiovascular effects of *Chrysaora* toxin in the rat are the same as those produced by *Chironex* and they have many similarities with those seen after those experiments using injections of *Physalia* and stingray toxins.

Summary. Sea nettle (*Chrysaora quinquecirrha*) tentacles inflict cutaneous damage on many animals, including man. The cardiovascular action of the nettle toxin was investigated to determine whether this agent was capable of injuring tissues other than skin. Cardiac conduction abnormalities and

ischemic electrocardiographic changes occurred in rats shortly after intravenous injections of the nettle toxin. Large doses of toxin produced a prompt increase in arterial blood pressure. These results support the premise that the nettle's sting, which clinically injures human skin, might affect other tissues if an adequate dosage were administered.

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