22. FURTHER OBSERVATIONS ON CORAL SNAKE BITES IN THE UNITED STATES: SYMPTOMS AND THERAPY

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Since our first observations on the bite of a North American coral snake were published (*Journal of the Florida Medical Assoc.*, **49**, 968, 1963), our work has continued along parallel experimental and clinical lines. The snakes used in these experiments are part of a colony of over two hundred animals, primarily of *Micrurus fulvius*, from which venom has been collected for toxicological study.

Histological studies of the venom apparatus of the North American coral snake indicate that the venom gland is a combined serous and mucus secreting organ. The mucus portion of the gland is somewhat more extensive in proportion to the total glandular structure than that which has been described in the pit viper (Gennaro *et al.*, New York Academy of Sciences) and other vipers (Kochva & Gans, American Journal of Anatomy). Since it has been shown that the mucus secreting portion may be responsible for spreading and enhancing the toxicity of the serous secretion, the increase in relative size of the mucus secreting portion of the gland may be responsible, in the coral snake, for the high level of toxicity manifested by the venom.

The lyophilized venom of *Micrurus fulvius* used in the experiments here was titer for lethality in mice and dogs. The $L.D._{50}$ in the albino mouse (20 grams) is 0.23 microgram per gram of mouse or 0.23 milligrams per kilo. The $L.D._{50}$ value in dogs is 0.3 microgram per gram or 0.3 milligrams per kilo. Though these values appear to be similar, it is easy to see that the amount of venom injected in the dog is really much greater than that lethal in a mouse. It is interesting to note that the dog exhibited very little variation in sensitivity to this venom as they commonly do to the venom of the *Crotalus* snakes.

The symptoms most frequently occurring in coral snake envenomation in dogs followed two general patterns.

In sublethal doses the initial aspect (first hour) was characterized by a drowsiness and favoring of the injected leg. The total course of envenomation in the sublethally injected dog proceeded with various body tremors, some respiratory difficulty, and dizziness ,possibly associated with bloody urine.

In lethally injected animals the course of symptoms presenting in the first hour included vomiting and a general parasympathetic-stimulation picture which included salivation and defecation. Death in these animals usually followed paralysis, respiratory difficulty, continued salivation, and repeated vomiting, some impairment of the blink reflex, and fixation of the pupils centrally. No retinal hemorrhage is indicated although hematuria is common and blood can appear from most of the body orifices.

In cases of actual snake bite the character of the bite itself, and its duration, was established to be more painful than has been recorded in the literature and much more quickly occurring. Some pain, favoring, and tenderness always seem to accompany the bite which lasts from four or five seconds to too short a period to measure using a stop watch; all bites of sufficient duration do produce a lethal effect.

In most of the human cases recorded in the literature death occurs within twenty-four hours or not at all. In dogs, the $L.D._{50}$ dose produces survival in the range of 9½ hours. When this dose is increased by five times the survival is shortened but there is considerable variation in the survival period which can be as little as fifty-eight minutes or as long as five and one-half hours at this dose.

The $L.D._{50}$ dose is completely reversible by the administration of antiserum (Butantan anticoral or the rabbit anticoral made in our laboratory). The first effect of the antiserum is to lengthen the survival time. Doses as high as three times the $L.D._{50}$ may be survived if the antiserum is given in a dose sufficient to provide 2½ milliliters for every milligram of venom injected as soon as two hours after the bite (intravenously). The importance of the treatment time is illustrated by the fact that 3.3 milliliters of antiserum per milligram of venom is valueless if the treatment time is delayed until five hours after the bite. On the other hand the $L.D._{50}$ dose may be neutralized and the animal may survive with only 1.4 ml of antiserum per milligram of venom if it is given within the hour after the bite.