

22. THE DIAGNOSIS, SYMPTOMS, TREATMENT AND SEQUELLA OF ENVENOMATION BY *CROTALUS ADAMANTEUS* AND GENUS *AGKISTRODON*

NEWTON C. McCOLLOUGH and JOSEPH G. GENNARO

(U.S.A.)

For the past ten years the authors have had an intense interest in the effect of the *Crotalus adamanteus* and the *Agkistrodon piscivorus* venom on the soft tissues of the extremities of patients bitten in Florida. Dr. Gennaro carried out a large amount of experimental work and I, interested in the clinical portion of the study, took careful case histories of all patients who were involved in loss of major tissue in either amputation or slough. Dr. Gennaro's studies, largely through the tagging of venom and antivenom, came to some conclusions long before I did in the clinical study. The clinical and laboratory findings were parallel to a rather remarkable degree. This involved not only the envenomation and the symptomatology but also the results of treatment. The number of amputations in the clinical series amounted to 39 and the serious sloughs which led to severe disability amounted to 20 additional cases. By far the majority of the bites treated were those of *Crotalus adamanteus* and only a few of the *Agkistrodon piscivorus* were seen.

Epidemiology of the situation in Florida was taken up very seriously January 1st, 1962, by the Department of Health and a Venomous Snake Bite Committee appointed by the Florida Medical Association. The Department then began a Registry of Venomous Bites by snakes and these have been tabulated statistically each year. At the present time, in Florida, we have registered annually approximately 270 to 300 snake bites, all of which have not been definitely identified as to the snake; but the large majority of them were definitely venomous according to fang mark description and sequelae. The number of deaths has averaged about three a year. We have been fortunate insofar as a number of treating physicians took colored photographs of the patient consecutively until either the extremity was lost or recovery of partial function occurred.

We have concluded of course that the character of the venom, i.e. L.D.₅₀ or the amount of the venom injected into the patient by the bite of either one of these snakes can only be estimated by analyzing the gravity of the clinical picture. Then, and only then, can the proper treatment be carried out. For instance, the bite of a snake which delivers a relatively small amount of venom in a small child may be an extremely serious matter when in an adult it would not. So, the weight of the victim has a great deal to do with the therapeutic considerations as does the number of fang marks. The most important, however, are those signs derived from the clinical picture of the patient and the rapidity in the sequence of symptoms which leads one to evaluate the amount of the envenomation. Wood, Hoback, & Green began a classification of envenomation in their original article: Grade I encompassing only local symptoms. Grade II, local symptoms plus some

mild systemic symptoms. Grade III, severe local symptoms with moderate systemic symptoms. These gradations were drawn from their observation of bites of *Crotalus horridus* of the eastern and northeastern United States.

Dr. H. M. Parrish, who has done a great deal of work with this subject, added a very important classification, namely Grade 0, in which the patient has the fang marks but exhibits no local or systemic symptoms of envenomation. This simply is applied to the patient bitten by a venomous snake which has fixed his fangs in the soft tissue but has not delivered any venom. We have found this in our statewide studies to be a not uncommon situation. The accuracy of the snake, as far as injecting the venom at the moment of fang penetration, is often questionable. Dr. Gennaro and this author, in consideration of the severe local symptoms and systemic collapse of individuals bitten by *Crotalus adamanteus* enlarged this classification to include Class IV. We felt this necessary insofar as the *Crotalus horridus* which Wood, Hoback & Green were studying does not, by any stretch of the imagination, except in very rare cases, provide the severe clinical picture which appears in the slides we will show you today of *Crotalus adamanteus* bites in man.

From the clinical standpoint there is a curious variation in the venoms of *Crotalus adamanteus* bites from individual to individual. Whether this is the reaction of the patient to the venom, or whether the venom of the snake varies in these regards, we do not understand. We have seen the hemorrhagic features develop to the point that they resulted in death from bowel, bladder, subcutaneous, intraperitoneal and intrathoracic hemorrhage and yet, in others, the neurotoxic features are dominant: i.e. fasciculation, immediate severe weakness which is usually generalized and marked painful muscular cramping. In these particular patients who exhibit these neurotoxic symptoms, there may be very little evidence of the hemolytic picture and even the local swelling may not be as marked. These are some of the characteristics of the *Crotalus adamanteus* which seem to be akin to those found in the *terrificus* and to a lesser extent in the *Crotalus durissus*. From reading case reports from the western part of the United States, and studying the number of amputees which have been reported in these areas, it is our feeling that there may be a tendency in the *Crotalus atrox* and others in the western and south western states for the neurotoxic factors to be more prominent than the hemolytic and proteolytic factors. The typical bite of the *Crotalus adamanteus* has a mixture of both, the locally destructive predominating. The onset is immediate and progression rapid. I will not attempt to discuss the fact that the secondary tissue products of the hemolytic and proteolytic factors magnify and add to both the systemic and local clinical situations.

In treatment of Grade III and IV bites, I will point out to you in the very beginning, that the intravenous route utilizing the polyvalent antivenin is the only way that antivenin should be administered. The four hours or more required for intramuscular absorption is a waste of time. Both experimentally and clinically we agree with Jackson, who did the original work, in 1926, that incision and suction for 30 minutes is beneficial if properly carried out. The use of a complete tourniquet we have never been able to prove is of any value unless you are intent on saving the patient at the risk of damaging the extremity. The incisions should be very small, one to two millimeters in length, and can be cruciate or single incisions across the orifice of the fang mark. They merely slightly enlarge the fang puncture, should only go through the skin itself, and can be classified as

percutaneous. They open the orifice of the fang mark to the point that suction is more effective. A larger or deeper incision will make suction less effective because of bleeding and may result in deeper spread of the venom.

If the local swelling is classified as a Grade I bite, there is a question as to whether antivenin is necessary at all. If no sensitivity is demonstrable, the local and systemic evidence of envenomation of Grades III and IV are best abolished by intravenous injection of antivenin in 250 to 500 c.c. of saline. If an anaphylactic reaction occurs it will be as prompt and severe as if serum is administered intramuscularly. In fact, if such a reaction occurs after one cubic centimeter is given by vein, it can be stopped and proper therapy administered by the same vein. To the contrary 10-15 c.c. buried in muscle cannot be retrieved and the treatment of anaphylactic shock rendered more difficult.

We have collected a series of cases, which does not exceed more than four or five, in which the intramuscular or local injection of antivenin apparently had no effect on the precipitous downward course in both the bitten extremity and the vital signs of the patient. When large amounts of antivenin are given intravenously, and we have used up twelve to sixteen ampules in a single instance over a period of two hours, with a total of twenty, the change in the patient is noted in a matter of two or three hours. The pulse settles to a reasonable level, the blood pressure rises, and the patient becomes alert and cooperative. No patients treated in this manner have failed to respond. We are firmly convinced that the amount of antivenin administered should be in excess of that needed to precipitate the venom injected by the snake and one can never estimate this until he recognizes the improvement previously mentioned. At this time there can be a reasonable waiting period before further antivenin is given. We have always administered rather massive doses of antivenin when confronted with what we considered to be a critical situation and we, apparently in all of the cases, have covered the venom injected to the point that there was never any sign of reversal of the clinical picture, i.e. dominance of the venom over the antivenin injected.

You will note the type of incision that we have recommended for the relief of tension which is blocking circulation to the distal portions of the extremity. These leave intact most of the skin and the subcutaneous fatty layer of fascia with its network of blood vessels, and permit it to act as a dressing over the deep longitudinal fascial incisions which release the inner tension of the muscles. It is the deep fascia which is the harmful constrictive agent in these instances, not the skin. If longitudinal incisions of the skin correspond anatomically to the longitudinal incisions of the deep fascia, the muscle would burst through the wound in a massive herniation and more tissue would be lost. There is some gentle compression which results from the skin as it holds back the herniation of the muscle in the method described. This is really beneficial control of edema and can't be controversial. We have also noted that there is an escape through these small transverse incisions, in the skin and subcutaneous fascia, after deep fascial release, of a profuse amount of serosanguinous fluid from the extremity, which certainly plays a major part also in diminishing the internal tension which is blocking the efferent circulation to the hand or foot digits. Supportive therapy i.e. blood etc. is understood.

In conclusion, I would like to report that the epidemiological studies by the Snake Bite Committee of the Florida Medical Association, and the Florida Public Health Department, have reported annually in the past three years 250 to 300 bites per year. Two-hundred of these bites have been due to venomous snakes.

By far the majority are due to the *Crotalus* snakes. About one per cent of these bites have proven fatal. There are usually eight to ten coral snake bites per year and the remainder of the venomous snake bites are due to the *Agkistrodon piscivorus* and *contortrix*. We had one death last year from *Agkistrodon piscivorus* envenomation. The reports which have accompanied the bites of this snake show rather marked hemolysis and marked fibrinolysis with the clotting mechanism of the blood almost reduced to zero in severe cases. Fewer and fewer doctors in Florida are using cryotherapy and more are using intravenous polyvalent antivenin, with rather astonishing success. There have been no cases of anaphylaxis reported. Last year an AK (above knee) and then later a hip disarticulation was done on one patient who was treated with cryotherapy for eighteen successive days due a bite of a *Crotalus adamanteus* in the lower extremity. It is our mutual conclusion that cooling or icing has no place in treatment. Six coral snake bites were treated with the antivenin from the Instituto Butantan with success. In each instance the antiserum was used intravenously. The reports of the program initiated by the Snake Bite Committee serves as a guidepost to the treatment and is also a source available to the practicing in management. Most of the bites in the past year reached hospital care within one-half hour of the time of the bite.

It has been my pleasure and a great honor to bring you this small bit of information from Florida and the southern part of the United States; but I must say that 98% of our statistics and case collections have originated within the State of Florida.

DISCUSSION

A. Delgado: "Please, I would like to know which should be the precise indications and advantages for making transversal incisions in the arm or leg bitten, (if even doing so the patient will probably lose the member according to the evolution shown by the slides)."

N. C. McCollough: "The transverse skin incisions through which longitudinal deep fascial releases can be easily accomplished may readily save all or a large part of the limb. This is really vascular surgery in so far as it opens collapsed arteries."

H. Bicher: "Did the speaker observe cardiovascular failure in his patients? And if so, did the transversal section help to this situation?"

N. C. McCollough: "I did not understand this question fully, but stated we felt there was a definite cardiotoxin."

F. Kornalik: "Have you any evidence about the blood-coagulation changes in patients bitten by *Agkistrodon contortrix* or *A. piscivorus*."

N. C. McCollough: "Yes, in one or two cases the coagulations properties of the blood in patients bitten by this snake were markedly reduced."

P. J. Deoras: "It is necessary to make an incision at the site of bite when this kind of measure may not be useful as a first aid?"

N. C. McCollough: "Yes, we feel it increases the efficiency of suction. As described, it is not harmful."

A. do Amaral: "In your opinion (or Dr. Gennaro's) which is the maximum (record) amount of venom secured from a full-grown specimen of *C. adamanteus*?"

N. C. McCollough: "About 600 mg dried weight."

A. do Amaral: "Has Dr. Gennaro ever used enzymic medication (hyaluronidase) against the oedema producing effect of the venom hyaluronic acid, when used in connection with specific antivenin."

N. C. McCollough: "Not that I know of."