Rattlesnake Bites in Southern California and Rationale for Recommended Treatment

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Rattlesnake bite is most common in young men who often are intoxicated and have purposely handled a venomous snake. The incidence of bites is highest in the spring and early summer months, and they most often occur in the afternoon. The hands and feet only are involved in 95% of all bites. First-aid therapy should be limited to splinting the extremity and transporting the victim to a medical facility. Definitive therapy is administering antivenin (Crotalidae) polyvalent intravenously in adequate initial doses and repeating every two hours until the venom is completely neutralized. Serum sickness usually follows all doses of more than five vials but is readily controlled by giving corticosteroids. Bites are avoided by protecting the hands and feet, not handling venomous snakes, and using utmost caution while in the snakes' habitat.

(Wingert WA, Chan L: Rattlesnake bites in southern California and rationale for recommended treatment. West J Med 1988 Jan; 148:37-44)

In the United States, 8,000 people a year are estimated to be bitten by venomous snakes, an incidence of 3.74 bites per 100,000 population, with 14 to 20 deaths resulting.[1,2] This estimate was made more than two decades ago. With the rapid encroachment of humans into the natural habitat of rattlesnakes, particularly in the western deserts and mountains, it is likely that the incidence of snakebites has increased appreciably. The problem is compounded by the legal or illegal importing of venomous exotic snakes into the United States, some of which are sold in pet stores.[3]

In 1975 Russell and co-workers reported the experience of the Los Angeles County-University of Southern California Medical Center with 550 cases of snake venom poisoning.[4] In this report we review the cases of envenomation treated at the same center during the ensuing 11 years (January 1975 to January 1986), with recommendations for therapy based both on the experience of handling these cases and on recent developments in the field.

Patients and Methods

At this medical center, all patients with snakebite, regardless of age, are examined in the Communicable Disease Section of the Department of Pediatrics. The cases of 282 patients either seen as outpatients or admitted to the hospital were identified by a computer search of medical records. Most of these patients were seen in consultation with either Findlay E. Russell, MD, or one of us (W.A.W.). A protocol for treatment was available for the house staff if a consultant was not immediately accessible.

The following demographic variables were considered significant in assessing the degree of envenomation and the therapy required:

- Size and species of the offending reptile. Whereas rattlesnakes are venomous at birth and the venom of young snakes is more potent than that of older rattlesnakes,[5] mature snakes have a larger amount of venom stored in their venom glands. Hence, the bite of a large snake may be more dangerous. The lethality of venom varies widely among the various species of crotalids.[6(p139)] *Crotalus scutulatus,* the Mojave rattlesnake, possesses an extremely potent neurotoxic venom, indeed, one of the most lethal venoms among the world's reptiles. *Crotalus cerastes* (sidewinder), with the same distribution, has far less toxic venom. The venom of *Crotalus viridis helleri* (Pacific rattlesnake)—the only species native to the Los Angeles basin—is intermediate.
- Circumstances related to the bite: drug or alcohol abuse and accidental versus nonaccidental occurrence. A nonaccidental envenomation is defined as that occurring when a victim purposely handled the snake.
- The month and time of day the bite occurred. The optimal temperature range for maximal activity of rattlesnakes is 27°C to 32°C (80°F to 90°F),[7(p77)] which occurs during the day in the spring months and in the summer evening hours in southern California.
- The number of bites inflicted and the body area bitten.
- The first-aid methods used, because many such procedures are not done aseptically.
- The transport time required. In general, definitive therapy is more effective if administered as early as possible.
- Relationship of laboratory results to the envenomation. Venoms are complex compounds whose components vary with the species of snake. Venom affects every body organ and perhaps every cell. The major deleterious effects are directed toward the vascular system, the muscle and subcutaneous tissues, the blood, and the nervous system. The blood chemistry, urine analysis, and blood cell count and morphology reflect much of the damage.

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ABBREVIATIONS USED IN TEXT

Ig = immunoglobulin
LD_{50} = lethal dose for 50% survival of group

Assessment and Treatment

The severity of the envenomation was graded (see "Hospital Therapy") and related to the amount of antivenin required to neutralize its effects. The relationship of the skin test results and of the amount of antivenin administered to both serum sickness and side effects of the horse-serum antidote were compared.

Statistical Analysis

A total of 66 data elements were included in the study. One of us (W.A.W.) abstracted data from the medical records onto predesigned data forms, which information was later logged into a computer for analysis. The Statistical Analysis System was used for the statistical analysis.

TABLE 1.—*Characteristics of Rattlesnake Envenomation by Degree of Severity*

Characteristics	Grade of Envenomation					
	None	Minimal	Moderate	Severe	Total	P Value*
Patients, No.	3	61	138	25	227	...
Age, years						
Median (range)	26 (16-26)	21 (8-83)	22 (1-82)	23 (14-48)	22 (1-83)	...
Sex						
Male, No.	3	56	126	25	210 (93)†	...
Female, No.	0	5	12	0	17 (7)†	...
Month of incident						
January-March	0	6	15	5	26 (11)†	...
April-June	3	31	60	14	108 (48)†	...
July-September	0	13	38	6	57 (25)†	...
October-December	0	11	25	0	36 (16)†	...
Time of incident‡						
6 AM-10 AM	0	0	6	1	7 (3)†	...
10 AM- 2 PM	0	11	28	5	44 (20)†	...
2 PM- 6 PM	0	28	56	10	94 (43)†	...
6 PM-10 PM	3	13	32	6	54 (25)†	...
10 PM- 6 AM	0	7	5	3	18 (9)†	...
Related factors of incident						
Accidental, %	0	33	48	44	43‡	...
Alcoholic, %	33	25	26	44	28‡	...
Area of bite§						
Finger	2	48	95	11	156 (70)†	...
Hand	0	4	22	9	35 (15)†	...
Arm	1	0	3	0	4 (2)†	...
Torso	0	2	0	0	2 (1)†	...
Leg or foot	0	6	16	5	27 (12)†	...
Snake species, when determined						
Crotalus viridis helleri	1	47	119	22	189 (87)†	...
Crotalus scutulatus	2	1	5	2	10 (5)†	...
Crotalus cerastes	0	6	1	0	7 (3)†	...
Crotalus atrox	0	3	3	0	6 (3)†	...
Foreign	0	1	3	1	5 (2)†	...
Estimated size of snakes, cm						
Median		30	35	75	35	.05
Range		20-270	20-150	30-180	20-270	...
Number of bites						
One, No.	0	54	109	21	184 (81)†	...
Two, No.	2	6	27	4	39 (17)†	...
Three or more, No.	1	1	2	0	4 (2)†	...
First aid applied†‖						
Tourniquet	1	26 (29)	54 (61)	8 (9)	89 (39)	...
Incision	0	22 (28)	49 (62)	8 (10)	79 (35)	...
Suction	0	32 (32)	59 (58)	10 (10)	101 (44)	...
Splint	0	0	4	0	4 (2)	...
Cryotherapy	0	3	5	2	10 (4)	...
Hours from bite to treatment						
Median (range)	3 (1½-3½)	1 (1-27)	1 (½-12)	1 (1-24)	1 (½-27)	...

*Significant at $P = .05$ by the median test for medians or the Kruskal-Wallis test for means or the Mantel-Haenszel test for proportions: Comparison of differences of variable among the four grades of severity.
†The numbers in parentheses represent percentages.
‡These figures represent the median percentages of "Accidental" and "Alcoholic" causes of envenomations.
§Data are not available for some patients.
‖Some patients had more than one type of first-aid treatment applied.

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The data were analyzed to determine the differences of the severity of envenomation with respect to demographic and environmental factors, characteristics of bites, symptoms, treatment modality, laboratory findings, and the course and outcome of therapy. For each factor that was recorded as a categoric variable, the Mantel-Haenszel χ^2 test was used to test the significance of its association with the four severity groups. For each factor recorded as a continuous variable, the Kruskal-Wallis test was used. The nonparametric test was used because of the sample sizes in two of the four severity groups.

The Mantel-Haenszel χ^2 test was also used to determine the statistical significance of the relationship of the skin test results and of the amount of antivenin administered to both the occurrence of serum sickness and side effects of the horse-serum antidote.

Results

A total of 282 patients had a diagnosis of snakebite during the ten-year period, but 55 records were not available. Laboratory data were not complete in many of the 227 records reviewed, as many envenomations were mild and did not warrant extensive laboratory study. The histories were not always reliable because of the intoxicated state of a patient or a lack of careful observation of the circumstances by excited or by very young patients.

Demographic Characteristics of Bites

Our findings are summarized in Table 1, which also lists variables relating to the severity of envenomation. Male victims outnumbered females 9:1. Two thirds of the bites occurred during the months of April, May, June, and July. In all, 43% of the bites occurred in the afternoon (2 to 6 PM) and the next most frequent time periods were 10 AM to 2 PM (20%) and 6 to 10 PM (25%). Only 44% of the injuries were accidental; 57% of the victims had been handling a venomous snake, and 28% of the patients appeared intoxicated. The patients ranged in age from 1 to 83 years, the median age being 22 years and the average age 24. Of all the bites, 55% were in the age group of 17 to 27 years. Most of the injuries involved the fingers and hands (85%). Of the remaining bites, 13% were on the lower extremity, rarely above the ankle, and only 2% were elsewhere.

C viridis helleri accounted for 87% of the injuries, *C scutulatus* for 5%, *C cerastes* for 3%, *Crotalus atrox* for 3%, and other species for 2%. Bites by reptiles other than *C viridis helleri* occurred in patients referred from the Mojave Desert region or in persons who kept venomous or exotic snakes as pets. The size of the snake usually could be judged only by a patient's observation and therefore can be considered only an estimate. The size of the offending snakes varied from 20 to 270 cm. Most of the injuries were restricted to a single bite as manifested by one or two fang marks. Four patients had two or more bites, sustained when persistently handling the reptile even after the initial bite.

Treatment of the Bites

First-aid treatment was given to two thirds of the victims. In 35%, the bite area had been incised, rarely by equipment from commercial snakebite kits, but usually by any handy sharp instrument. Several patients bit their wounds. Suction was administered to 45%, usually orally. Suction sometimes was applied to the fang marks without incision. A tourniquet was applied to 40% of the bites and outmoded cryotherapy

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TABLE 1.—*Characteristics of Rattlesnake Envenomation by Degree of Severity*

Characteristics	Grade of Envenomation					
	None	Minimal	Moderate	Severe	Total	P Value*
Laboratory Tests						
Leukocyte count (median)/μl	8,500	8,800	9,050	10,700	9,100	...
Immature leukocytes (mean)/μl	...	3.3	4.1	5.8	4.1	...
Hemoglobin (mean), grams/dl	15.6	15.0	14.8	15.1	14.9	...
Hematocrit (mean), %	44.5	43.9	42.8	44.6	43.3	...
Creatine kinase (median), units/liter	91	202	192	312	205	.05
Fibrinogen level, % abnormal	0	38	29	57	35	...
Platelet count, % abnormal	0	0	4	8	3	...
Urinalysis						
Proteinemia, % patients	...	4	7	60	9	.05
Hematuria, % patients	...	0	8	50	9	.05
Patients with systemic reactions, %						
Paresthesia	0	55	80	92	73	.05
Ecchymosis	0	32	26	28	27	.05
Fasciculation	0	2	20	60	20	.05
Bullae	0	2	6	16	6	.05
Antivenin treatment						
Initial dose in vials						
Median (range)	...	5 (1- 7)	5 (1-17)	10 (2-25)	5 (1-17)	.05
Total dose in vials						
Median (range)	...	5 (1-12)	10 (1-26)	22 (10-43)	10 (1-43)	.05
Recovery time in days						
Median (range)	1 (1)	1 (0- 8)	1 (0- 8)	2 (1-13)	1 (1-13)	.05
Patients with tissue loss, %	0	5	4	4	4	...

*Significant at $P=.05$ by the median test for medians or the Kruskal-Wallis test for means or the Mantel-Haenszel test for proportions: Comparison of differences of variable among the four grades of severity.

was used in 4%, sometimes by an attending physician. Only 2% received splinting. Patients arrived promptly at medical facilities, the median time being one hour, but most obtained assistance within 30 minutes after the accident. The longest delay was 27 hours. Three victims were bitten without any reaction, a "dry bite." Reactions in 61 cases were considered mild, in 138 cases moderate, and in 25 severe. Demographic characteristics and the nature of the incident were not found to differ among the groups. The estimated size of the snake, however, and the physiologic reaction to the bite were positively correlated with increased severity: paresthesia, fasciculation, and the formation of bullae increased significantly with severity ($P = .05$).

The results of laboratory tests were of only minor assistance in assessing the severity of envenomation. The creatine kinase levels were significantly increased in patients with severe envenomation ($P = .05$), and the prothrombin times, fibrinogen levels, and platelet counts were altered substantially. No other laboratory test results showed notable abnormalities. Urine analyses, although infrequently done, tended to show proteinuria and hematuria more often in severe cases. Overt hemorrhage did not occur in any rattlesnake-envenomated patients. One patient, bitten by the rear-fanged imported *Rhabdophis subminatus,* experienced a severe coagulopathy requiring transfusion of 16 units of packed red cells over seven days.[3]

Of 227 patients, 211 received antivenin (Crotalidae) polyvalent and 16 were observed and treated symptomatically. Of those treated with antivenin, 82 (39%) received secondary doses. The initial antivenin doses, often administered in a referring medical facility, varied from 1 to 17 vials, with a median of 5 vials. The secondary doses, usually administered at our facility, ranged from 1 to 35 vials, with a median of 5 vials. The total dose ranged from 1 to 43 vials, with a median of 10. The total amount of antivenin, however, was related to the severity of the poisoning: patients with mild cases received a total median dose of 5 vials, moderately envenomated patients, 10 vials, and patients with severe envenomations, 22 vials. Recovery time also lengthened with increased severity.

Serum sickness was correlated positively with the total dose of antivenin. The median dose for the group with no serum sickness was 5.5 vials, the median for mild sickness was 10 vials, and for the most severe group, 15. No patient had severe serum sickness requiring either admission to hospital or prolonged treatment.

The skin test was an unreliable predictor of immediate systemic reactions (Table 2). Of eight patients with positive skin tests, urticaria and pruritus developed in only four, one of whom had a systemic reaction consisting of hypotension and bradycardia. Of 199 patients with negative tests, urticaria developed in 26 (13%), itching developed in 16 (8%), and edema developed in 5 (3%). Thus, a false-positive reaction occurred in 50% and a false-negative in about 8% of all tests. The intradermal skin test result also did not predict serum sickness.

Of the 94 patients who were observed in follow-up, serum sickness developed in 10. Of these, only two had a positive skin test before treatment. Of the 84 who were asymptomatic, 55 had negative skin tests ($P = .004$), actually a reverse result.

Several differences were noted between bites occurring in the daytime (10 AM to 6 PM) and those occurring at night. A significantly higher proportion of alcohol-related cases occurred at night (36% night, 23% day, $P = .04$). The night cases had a significantly higher proportion of injuries from species other than *C viridis helleri* (24% versus 6% $P = .008$), and the estimated size of the snake was found to be larger among the night injuries, an average of 60 cm versus 46 cm in the day cases.

TABLE 2.—*Relationship of Skin Test Reaction and Allergic Reaction to Antivenin*

Reactions	Negative Skin Test Group (N=199), %	Positive Skin Test Group (N=8), %	P Value*
Urticaria	13	50	.017
Itching	8	50	.004
Hypotension	6	13	.385
Bradycardia	1	13	.076
Apnea	1	0	.961

*By Fisher's exact test.

Therapy was limited to the use of antivenin. No fasciotomies were done, although the severely envenomated patients had massive edema of the bitten extremities. This edema invariably subsided without sequelae in five to ten days. Blebs, present in ten cases, were debrided on the fourth hospital day. Antibiotics were administered to 44 patients who either had severe envenomation or had received vigorous first aid.

The outcome of therapy was favorable. One death occurred in an 80-year-old man who suffered a myocardial infarction within 30 minutes of arriving at our center and before therapy was started. No amputations were done, and tissue loss was superficial except in a single case in which a child lost about 50% of the soft tissue from the distal phalanx of a severely bitten index finger. This required a reconstructive operation. Of those patients who required admission to hospital, half were discharged the following day, and 80% were dismissed within 48 hours. Only 10% remained more than three days, and these were seriously envenomated patients.

Discussion and Recommendations for Treatment

To understand the rationale of treatment for rattlesnake envenomation, a knowledge of the pharmacologic action of snake venom is helpful. *Crotalus* venom is a complex poison consisting chemically of 90% water, 5 to 15 enzymes, 3 to 12 nonenzymatic proteins and peptides, and at least 6 as-yet-unidentified substances. Basically, crotalid venom consists of two major pharmacologic components: The lethal factors responsible for the immediate death of prey are low-molecular-weight peptides and polypeptides consisting of 20 to 82 amino acid chains with molecular weights varying from 4,800 to 100,000.[8] These small proteins transiently damage the endothelial cells of vascular walls. On electron microscopy, there is blebbing of the endothelium, dilatation of the perinuclear spaces, and lysis of the plasma membrane.[9] The result is a microangiopathic vascular permeability to plasma, plasma proteins, and erythrocytes that "leak" into the surrounding tissues. This loss of fluid into the "third space" finally results in hemoconcentration, lactic acidosis, and hypovolemic shock. The same action on the pulmonary blood vessels results in pulmonary edema and hemorrhage, compounded by pooling of blood in the vasculature of the lung. This is a consistent autopsy finding.

The second function of venom relates to digestion.[6] Rat-

tlesnakes do not tear or shred food by mastication, but swallow their prey whole. Thus it is advantageous for the snake to introduce digestive enzymes into the bloodstream of an immobilized but still living prey, permitting distribution of the digestive enzymes throughout the tissues.[10] The enzymes important in changing human tissues include proteolytic enzymes or proteases that cause necrosis of muscle and subcutaneous tissues by a trypsinlike action[11]; L-amino acid oxidase catalyzes the oxidation of amino acids, causing tissue destruction; and phospholipase A_2, a general esterolytic enzyme, catalyzes the hydrolysis of the ester bond at the C2 position on lecithin, releasing a molecule of fatty acid and producing lysolecithin. Because erythrocyte membranes contain lecithin, the permeability of the cell wall may be altered, allowing water to enter the cell, and resulting in hemolysis and the precipitation of hemoglobin and ghosts of erythrocytes in renal tubules. Phospholipase A_2 also damages the plasma membrane of muscle cells, disrupts intracellular organelles, and causes an influx of calcium and an efflux of creatine and the muscle cell enzyme creatine kinase.[12,13] Necrosis of muscle fibers results. Serine esterase and other thrombinlike enzymes split fibrinogen molecules but remove only fibrinopeptide A from the molecule and do not activate factor XIII. An unstable fibrin clot results with the consumption of platelets and fibrinogen (disseminated intravascular coagulation). These clots are readily lysed by plasmin and by proteolytic enzymes in the venom. Afibrinogenemia, thrombocytopenia,[14] and profuse hemorrhage follow.

Current medical treatment generally is not based on that recommended for more than 2½ millenia. First aid for snakebite is an exception. Some time between 1000 BC and 600 BC, a Hindu physician, Sushruta, described and illustrated in the medical literature, the *Ayurveda,* the application of a tourniquet above the bitten area and incision and suction of the fang marks, followed by cauterizing the wound.[15] Only the cautery component of recommended treatment has failed to survive into the 20th century.

Early experiments in animals indicated that suction removed more than 50% of radioisotope-labeled venom injected subcutaneously into dogs, if the suction was instituted within three minutes.[16] These data have not been verified in humans, and not even a significant improvement in survival of experimentally envenomated animals has been shown with the use of this technique.[17] In our experience, incision and suction did not mitigate the severity of envenomation (Table 3), and they were frequently done by an excited nonphysician using an unsterile technique, resulting in a secondary infection that sometimes required plastic surgery or orthopedic repair. The use of constriction bands and tourniquets is based on impeding lymphatic return from a bitten extremity and presumably restricting venom to the wound site. The distribution of venom to body organs, however, certainly must occur through capillary, not lymphatic drainage, thus requiring the use of a tourniquet that completely occludes venous return. This would produce even more disastrous results than the bite itself. Because the swelling in the extremity appears to be plasma spreading through subcutaneous tissues, there would appear to be no benefit and even some disadvantage in restricting the edema to a limited area. Therefore, we recommend only the following measures, regardless of whether a patient has immediate access to medical care or is in a remote area where treatment will be delayed:

- Avoid excessive activity. Retreat out of the snake's accurate range, which is usually less than the length of the snake. Studies on experimental animals indicate that the median lethal dose (LD_{50}) of venom increases substantially by increasing the animal's activity.[18] Case studies, admittedly subjective, show a more severe hospital course in patients extremely active after envenomation compared with patients immobilized early.[19]

TABLE 3.—*Relation of First-Aid Treatment to Severity of Envenomation*

Use of First Aid*	None	Minimal	Moderate	Severe	Total
Yes	1	40	90	16	147
No	2	20	47	9	78
Total	3	60	137	25	225
Patients receiving first-aid, %†		67	66	64	65

*First-aid treatment includes incision, suction, tourniquet, cryotherapy, or any combination thereof.
†χ^2 Test for association, $P=.7$, no relationship of severity to using first-aid.

- Observe the approximate size of the snake. In our experience, larger snakes cause more severe envenomation.
- Immobilize the bitten extremity by splinting as if for a fracture.
- Mark the level of swelling with a pen, and write on the skin the time the mark was made. Repeat this procedure every 15 minutes during transport. The rapidity with which the swelling appears and progresses is an important factor in assessing severity.
- Transport the victim at a safe speed to the nearest medical facility that is equipped and staffed to care for envenomation—that is, one that has an adequate supply of antivenin available and a knowledgeable professional staff.

Hospital Therapy

Snakebites usually occur in young men in their third decade of life who have a blood alcohol concentration of more than 0.1%. Often they have been handling or attempting to feed a pet rattlesnake and have sustained a bite on the index finger. Although in other series a high incidence of bites is reported in children (50%),[20] only 19% of our patients were younger than 16 years.

The definitive therapy for rattlesnake envenomation is administering a specific antidote to the poison: antivenin in adequate amounts given intravenously and as early as possible. Secondary treatment consists of support of the various organ systems affected by the venom and avoiding modalities and drugs that are not effective and that may actually complicate the problem. Treatment in an emergency department may be carried out in the following ten steps, the sequence depending on the condition of the patient:

STEP 1. *Establish a physiologic baseline.* First, determine whether the patient was bitten by a poisonous snake. Signs of a bite of a venomous snake are fang marks, typically with ragged edges; local edema, usually limited to subcutaneous tissues because fangs usually penetrate only 1 to 8 mm[6]; ecchymoses around the bite site; variable pain; muscle fasciculations; paresthesias of scalp, face, and extremities; and a metallic taste in the mouth, especially in bites by the Pacific, diamondback *(C atrox),* and timber *(Crotalus horridus)* rattlesnakes.

The venom of *C scutulatus* may cause minimal local reac-

tion but produce neuromuscular blockade, shown early by cranial nerve palsies, and leading to respiratory paralysis.

Second, rapidly evaluate presenting signs and symptoms. Inquire specifically regarding the approximate time of the bite, first-aid methods, previous episodes of bites and the treatment used, known allergies, especially to horse serum and antibiotics, and the date of last tetanus immunization.

Next, take a blood specimen for a complete blood count and hematocrit determination. Request that the blood smear be examined carefully. Severe envenomation causes morphologic changes in erythrocytes, including spherocytosis and "burring" or pyknocytosis.[21] The hematocrit is a rough estimate of hemoconcentration.

The important coagulation studies are fibrinogen levels, fibrin-split products, and the platelet count. If the envenomation is severe, the following should be measured: blood urea nitrogen level, electrolytes, serum protein levels, blood gas tensions, and pH. These studies are not helpful in cases of moderate envenomation. An electrocardiogram is indicated for patients older than 50 years or those with a history of heart disease. A urinalysis should be done, with particular attention paid to the presence of protein and blood.

Measure and record (including time) the circumference of the injured extremity at the leading point of edema and 10 cm (4 in) proximal to this level. A mark on the skin with a felt pen is helpful in monitoring edema.

STEP 2. *Determine the severity of envenomation.* Severity depends on three factors: The size of the patient, the toxicity of the venom, which is species-related, and the quantity of venom injected—most rattlesnakes discharging between 25% and 75% of their venom in a single strike.[6,22] Therefore, knowing the size of the snake is important because the larger the snake, the greater the quantity of venom in their glands. Other important factors are the length of time the fangs remain embedded, allowing a greater discharge of venom; the number of bites sustained; interference by clothing, gloves, or boots; and the activity of the victim following the bite.

We use a grading system based on local and systemic reactions, the size and species of the snake involved, and the historical factors noted above. Reactions are graded as follows:

- No envenomation: Fang marks present but no local swelling or hemorrhage and no paresthesias (depending on species).
- Minimal envenomation: Fang marks, with local swelling limited to hand or foot and not progressing, and no systemic reactions.
- Moderate envenomation: Swelling progressing rapidly beyond the site of the bite, such as to the elbow or knee, systemic reactions, laboratory changes such as a fall in the platelet count or fibrinogen levels, a large offending snake, and more than one bite.
- Severe envenomation: Pronounced and rapidly progressive swelling, ecchymoses, severe generalized symptoms such as hypotension, and laboratory study abnormalities. A report of a large snake or a highly toxic species, such as *C atrox,* or multiple bites indicate a severe case of envenomation.

It should be emphasized that the grade of estimated severity when the patient is examined initially may *not* be the final picture. A mild case of envenomation that is inadequately treated may progress to a severe grade within hours.

STEP 3. *Do a skin test to determine sensitivity to horse serum.* For medicolegal purposes, follow precisely the instructions in the brochure enclosed in the package. Our study indicates that the skin test is not infallible and the results should be used only as a precautionary guide to further therapy. No systemic reactions to the skin test have occurred in more than 850 patients at this center.

STEP 4. *Start intravenous infusions in two extremities.* One line is for administering the antivenin. The second line is primarily for cardiovascular support, giving epinephrine and antihistamines or fluids, electrolytes, or colloid solution.

STEP 5. *Administer an adequate amount of antivenin (Crotalidae) polyvalent intravenously.* The following amounts diluted 1:4 with 0.5N saline solution should be administered for the first dose:

- No envenomation—no antivenin and no skin test.
- Minimal—5 vials (50 ml).
- Moderate—10 vials (100 ml).
- Severe—15 vials (150 ml).

Exceptions: Children and small persons (< 45 kg [100 lb]) should receive a *larger* dose by about 50%. Patients known to be bitten by *C scutulatus* should receive ten vials initially, then carefully monitored for delayed neurologic symptoms. To avoid allergic reactions, the infusion should be started at a very slow rate—such as 15 drops per minute—while observing the patient closely. If no reaction occurs in 15 minutes, the rate may be increased so that the solution is infused over two hours.

The initial dose of antivenin should be repeated every two hours until the progression of swelling has stopped and all paresthesias and muscle fasciculations cease. There is no maximal dose; the total dose is the amount required to neutralize the poison as measured by the clinical response.

Experiments in mice and rabbits have shown that venom labeled with iodine 131 can be detected in the circulation as long as 72 hours after injection (W.A. Wingert, MD, T.R. Pattabhiraman, PhD, and F.E. Russell, MD, unpublished data, January to June 1978). If this finding can be extrapolated to humans, antivenin should be of some value in symptomatic patients for at least 60 hours after envenomation.

Two types of anaphylactic reactions occur with horse serum: A type 1 allergic anaphylactic reaction caused by circulating immunoglobulin (Ig) E antihorse protein antibodies and an anaphylactoid reaction that may be due to direct degranulation of mast cells by the horse proteins with release of histamine or to activation of complement by either pathway with formation of the mediators prostaglandin G_2 and leukotriene. Either reaction usually is heralded by urticaria and pruritus and may be followed by severe laryngospasm and bronchospasm, hypotension, bradycardia, loss of consciousness, and possibly death. Anaphylactoid reactions may be avoided by premedicating patients with an antihistamine—that is, diphenhydramine hydrochloride, 50 mg (children, 1 mg per kg of body weight) given intravenously 15 minutes before giving the antivenin—then administering diluted antivenin at a slow rate initially. A positive skin test indicates the presence of IgE antibodies. The physician then must decide whether the patient will survive and not suffer substantial tissue loss without using antivenin. If the patient is seriously envenomated, however, antivenin may be successfully administered by diluting at 1:10, decreasing the rate of adminis-

tration, premedicating the patient with diphenhydramine, and titrating the patient's response by giving either epinephrine, 0.01 ml per kg, or more diphenhydramine intravenously.[23] A consultation through one of the Regional Poison Control Centers is suggested if this procedure is required.

Although the components of the venoms of each species of Crotalidae differ somewhat as indicated by the varying LD_{50}, they, fortunately, share enough components—phospholipase A_2 is common to all species—that the polyvalent antivenin neutralizes at least a portion of each species' venom. Unfortunately, the serum is processed by ammonium sulfate precipitation, which destroys as much as 50% of the neutralizing IgG, leaving most of the other proteins, α_1 and α_2 and β_1 and β_2, intact.[24] Physicians should not be deluded that this is a highly potent antidote, especially for bites of Crotalidae species, other than those species used in its production. An improved equine-derived antivenom is being developed by the procedure of polyacrylamide gel affinity chromatography, isolating the IgG fraction from the other proteins.[25] It is about five times as effective in neutralizing venom in human tissue culture and has not produced anaphylaxis in animals sensitive to horse serum. Further research has indicated that the Fab fragment of IgG (mole weight to 50,000) is as effective as the whole molecule (mole weight 150,000), is distributed more rapidly and more widely in body tissues, and is cleared renally in only nine hours.[26] These antivenoms must undergo extensive human trials before release by the Food and Drug Administration, however, and may not be available before 1989.

STEP 6. *Prevent secondary infection by administering an appropriate broad-spectrum antibiotic,* especially if unsterile first-aid measures were used. Pathogenic bacteria, predominantly gram-negative, occur in the snake's mouth (but not in the venom).[27]

STEP 7. *Prevent tetanus.* Tetanus rarely occurs following rattlesnake bite,[6] and snakes' mouths do not harbor *Clostridium tetani.*[27] It is prudent, however, to treat fang puncture wounds by adequately immunizing a patient, using a tetanus toxoid booster or hyperimmune tetanus globulin as indicated.

STEP 8. *Monitor and support the circulatory, respiratory, and hematologic systems.* Schaeffer and associates have repeatedly shown that crystalloid solutions do not correct shock in envenomated animals, and colloidal solutions are required.[28,29] Therefore, shock in humans should be treated with a plasma expander rather than a saline solution. Vasopressor drugs should not be used unless the intravascular volume has been restored.

We do not monitor for increased compartment pressure and have not encountered any adverse effects, even in massively swollen arms and legs. The edema fluid is reabsorbed in seven to ten days without sequelae. We do not recommend a fasciotomy. In a series of well-controlled experiments, Garfin and colleagues have shown that muscle necrosis is the direct result of proteolytic venom enzymes rather than intracompartmental pressure per se and that a fasciotomy done *before* injecting venom into a muscle did not alter the degree of necrosis resulting.[30]

Blebs and bullae forming in the edematous area should be debrided surgically between the third and fifth day after the danger of extensive bleeding is past. The area then is treated as a second-degree burn.

STEP 9. *Prepare to treat serum sickness during the following 21 days.* Corticosteroids are the drug of choice for treating serum sickness and should be administered at the first signs, usually urticaria and itching. If urticaria is treated with an antihistamine, the disease usually progresses in severity and is prolonged until steroids are used. The patient should be spared this complication. The steroids should be administered until all signs and symptoms have subsided for 24 hours and then the dose tapered over 72 hours. Our drug of choice is prednisone, 10 mg given four times a day for adults, or 1 mg per kg per day in children.

STEP 10. *Report all illegally possessed reptiles to the police or to the appropriate Fish and Game Agency.* Possessing a dangerous venomous snake without a permit is illegal in most states. The patient has broken the law and the snake may bite another victim, placing the physician at risk medicolegally for not reporting the initial incident.

A helpful large wall chart for hospitals and emergency departments detailing snake identification and medical treatment is available from the Arizona Poison Information Center, the University of Arizona, 1501 North Campbell Avenue, Tucson, AZ 85724.

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Medical Practice Opinion

EDITOR'S NOTE: *From time to time medical practice questions from organizations with a legitimate interest in the information are referred to the Scientific Board by the Quality Care Review Commission of the California Medical Association. The opinions offered are based on training, experience and literature reviewed by specialists. These opinions are, however, informational only and should not be interpreted as directives, instructions or policy statements.*

Radial Keratotomy

QUESTION:

Is radial keratotomy considered acceptable medical treatment for correction of myopia?

OPINION:

In the opinion of the Scientific Advisory Panel on Ophthalmology, it appears that radial keratotomy does have value for selected patients in reducing both myopia and dependence on the use of spectacles or contact lenses to correct that condition. However, the techniques of the procedure and its appropriate indications and contraindications are still evolving. Further, although often successful, the procedure is not uniformly predictable, and, though small, there is some risk of permanent damage to the eye. Long-term results are unknown. The risks and complications should be detailed for all patients undergoing the procedure, particularly those whose motivation is purely cosmetic.

All patients should be advised that a significant minority of patients have expressed dissatisfaction with the results of the procedure. Until the questions of long-term safety and effectiveness have been answered, this advisory panel thinks that radial keratotomy should be used with caution and with fully informed consent.

Approved: January 1981
Revised: May 1987

This opinion has been prepared by the CMA Scientific Advisory Panel on Ophthalmology based on available information. It is only an advisory opinion and should not be construed as binding on any individual or as expressing an absolute standard of medical practice. Medical opinion may vary regarding the appropriateness of a particular treatment or service in a given situation. Differences in an individual case should be reviewed by physician medical advisors. Differences of opinion between a medical advisor and attending physician should be referred to the county medical society where the physician practices.