

STATE TOXINOLOGY SERVICES

Toxinology Dept., Women's & Children's Hospital, North Adelaide SA 5006 AUSTRALIA

SNAKEBITE MANAGEMENT OVERVIEW DOCUMENT

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Family	Scientific name combined
Viperidae	<i>Crotalus atrox</i>
Common name	
Western Diamond Rattlesnake	

Global region in which snake is found

North America + Central America

CLINICAL OVERVIEW

Crotalus atrox is amongst the most dangerous of all North American rattlesnakes, with a high probability of causing envenoming, either local, or local and systemic. Bites cause local swelling, which may be severe, pain, bruising, blistering and sometimes necrosis. In cases with severe swelling, fluid shifts into the bitten limb can cause secondary shock and its sequelae. In addition to local effects, systemic effects are can occur, though are not commonly severe, though both non-specific symptoms and coagulopathy, bleeding and paralytic features are possible. Neurotoxic envenoming is usually minor and is uncommon to rare, but major paralysis, including respiratory paralysis is possible, though is exceptionally rare. Coagulopathy is more common, however, as is persistent thrombocytopenia. In all except minor cases, antivenom therapy is the mainstay of treatment. CroFab is the current preferred product. Antivipmyn remains unproven in clinical practice, though holds promise.



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Crotalus atrox

First aid

1. After ensuring the patient and onlookers have moved out of range of further strikes by the snake, the bitten person should be reassured and persuaded to lie down and remain still. Many will be terrified, fearing sudden death and, in this mood, they may behave irrationally or even hysterically. The basis for reassurance is the fact that many venomous bites do not result in envenoming, the relatively slow progression to severe envenoming (hours following elapid bites, days following viper bites) and the effectiveness of modern medical treatment.
2. The bite wound should not be tampered with in any way. Wiping it once with a damp cloth to remove surface venom is unlikely to do much harm (or good) but the wound must not be massaged.
3. All rings or other jewellery on the bitten limb, especially on fingers, should be removed, as they may act as tourniquets if oedema develops.
4. The bitten limb should be immobilised as effectively as possible using an extemporised splint or sling; if available, crepe bandaging of the splinted limb is an effective form of immobilisation.
5. If there is any impairment of vital functions, such as problems with respiration, airway, circulation, heart function, these must be supported as a priority. In particular, for bites causing flaccid paralysis, including respiratory paralysis, both airway and respiration may be impaired, requiring urgent and prolonged treatment, which may include the mouth to mask (mouth to mouth) technique of expired air transfer. Seek urgent medical attention.
6. Do not use Tourniquets, cut, suck or scarify the wound or apply chemicals or electric shock.
7. Avoid peroral intake, absolutely no alcohol. No sedatives outside hospital. If there will be considerable delay before reaching medical aid, measured in several hours to days, then give clear fluids by mouth to prevent dehydration.
8. If the offending snake has been killed it should be brought with the patient for identification (only relevant in areas where there are more than one naturally occurring venomous snake species), but be careful to avoid touching the head, as even a dead snake can envenom. No attempt should be made to pursue the snake into the undergrowth as this will risk further bites.
9. The snakebite victim should be transported as quickly and as passively as possible to the nearest place where they can be seen by a medically-trained person (health station, dispensary, clinic or hospital). The bitten limb must not be exercised as muscular contraction will promote systemic absorption of venom. If no motor vehicle or boat is available, the patient can be carried on a stretcher or hurdle, on the pillion or crossbar of a bicycle or on someone's back.
10. Most traditional, and many of the more recently fashionable, first aid measures are useless and potentially dangerous. These include local cauterization, incision, excision, amputation, suction by mouth, vacuum pump or syringe, combined incision and suction ("venom-ex" apparatus), injection or instillation of compounds such as potassium permanganate, phenol (carbolic soap) and trypsin, application of electric shocks or ice (cryotherapy), use of traditional herbal, folk and other remedies including the ingestion of emetic plant products and parts of the snake, multiple incisions, tattooing and so on.

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Crotalus atrox

Clinical summary

With the exception of the neurotoxic specimens of *Crotalus scutulatus*, Mojave rattlesnake, envenoming by all North American rattlesnakes is similar in overall effects, but with differences in likely severity, depending on size, and other, often subtle differences between species. These latter are often not well documented. *Crotalus atrox* is a large snake and one of the more common causes of both bites and severe envenoming.

In general rattlesnake bites cause both local and systemic effects. The bite is usually associated with local pain, which can be severe, but may also be trivial, at least for some species. The fangs are generally at least moderate sized and bite marks are almost always obvious, as double or single punctures. Occasionally other non-fang teeth may make contact, resulting in more complex bite marks. The same may occur if there have been multiple bites. A concentric half-ring of teeth marks is more suggestive of a python bite, while parallel sets of teeth marks without clear fang marks at the anterior extent might indicate a colubrid bite.

In addition to local pain, swelling may develop. In almost all cases with envenoming there will be at least some swelling present, usually within 15-30 minutes post bite, certainly within 1 hour. The complete absence of local swelling (and any other local or systemic effects) at 2hrs post bite is strongly suggestive of a dry bite, EXCEPT if the bite might have been caused by a Mojave rattlesnake (which has a limited geographic range).

The extent of swelling may be restricted, but can also be severe and extensive, sometimes involving all of the bitten limb and beyond. The rapidity of swelling is closely related to the severity of the bite. In addition to swelling, there may be local blistering (bleb formation) which may be restricted to the bite area, or far more widespread on the bitten limb, the latter indicating a severe bite in most cases, as does bloody content of blisters. Blisters often take several hours to become evident, usually 8-36hrs post bite. They may not develop at all in cases given antivenom early. Local necrosis can develop at the bite site or more widely. Necrosis is more likely in tight areas, such as fingers or toes, but even quite severe local haemorrhagic blisters of fingers are not always associated with ultimate necrosis of the finger. At least one expert believes that early antivenom therapy, in sufficient doses, may greatly reduce the chance of necrosis developing. There may be major fluid shifts into the bitten limb, potentially causing hypovolaemic shock. Bruising can develop in the bite area or whole limb and can be associated with active bleeding. Massive swelling can cause temporary nerve dysfunction. True compartment syndrome, though it does occur, is uncommon to rare and muscle necrosis is as likely to be due to direct venom toxicity as to compartment syndrome. If compartment syndrome is suspected on clinical grounds, then it should be confirmed by intracompartment pressure measurement, before considering fasciotomy.

Systemic effects of rattlesnake bites include both general and specific effects. General symptoms include nausea, vomiting, abdominal pain, metallic taste in the mouth, fasciculations of muscles (especially of face), dizziness, weakness (not true flaccid paralysis), fever, chills, collapse, rarely convulsions. A metallic taste in the mouth is particularly a feature of envenoming by *Crotalus viridis* and *Crotalus adamanteus* and is thought to be absent after envenoming by *Crotalus ruber* and *Crotalus scutulatus* according to one expert, who suggests this may help distinguish between bites by these snakes. Similarly, fasciculations are a feature of rattlesnake bites, but not *Agkistrodon* (copperhead, cottonmouth) or *Sistrurus* (massasauga, pygmy rattlesnake) bites.

Specific systemic effects are principally those associated with coagulopathy. Most rattlesnake venoms contain toxins affecting haemostasis, including procoagulants, fibrinogenases, haemorrhagins and platelet-active toxins. Thus there may be abnormalities of coagulation blood tests, including prolonged PT and aPTT, decreased fibrinogen, increased FDP/d-dimer and thrombocytopenia. Active bleeding can occur, especially from blisters on the bitten limb, and other spontaneous bleeding may manifest as bleeding gums, haematemesis, haematuria, melena, but major bleeding, though it can occur, is uncommon and limited to severe cases of envenoming. Severe coagulopathy is not a feature of *Agkistrodon* or *Sistrurus* envenoming.

Rattlesnakes are generally considered to be non-neurotoxic, so true paralysis is often considered very unlikely. However, it appears that in addition to the Mojave rattlesnake, *Crotalus scutulatus*, some (but not all) specimens of which can cause flaccid paralysis, often without the severe local and coagulopathic effects of other rattlesnakes, quite a number of "non-neurotoxic" species can, on occasion, cause at least some paralytic effects. These vary from very local effects, usually involving cranial nerves (ptosis, facial weakness etc), to major generalised paralysis, though the latter is rare. It is most likely after bites by *Crotalus adamanteus* (in addition to *Crotalus scutulatus*), but should be considered an exceptional feature.

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Crotalus atrox

Treatment summary

North American rattlesnake bites are generally managed as a group, without specific differences between species, except for *Crotalus scutulatus* bites (potential for significant neurotoxicity). While this approach will be listed here, it should be noted that each species of rattlesnake is likely to have individual characteristics of envenoming, which, where known and well documented, might justify subtle adjustments in management approach. The often poor documentation of such species specific information makes it currently impractical to list such subtleties here.

Around 20% of all rattlesnake bites will be dry bites, without significant local or systemic effects. If no local or systemic effects have developed by 12 hrs (some would suggest 6hrs as sufficient), then the bite is almost certainly a dry bite, UNLESS it is or just might be by a neurotoxic species/specimen (principally some specimens of the Mojave rattlesnake, *Crotalus scutulatus*). If the latter can be excluded, then these non-envenomed cases can usually be allowed to go home, providing there is a responsible adult available to observe them until the following day. Such an approach should be carefully discussed with the patient/relatives, before proceeding.

For cases showing clear evidence of local effects, ± systemic symptoms, insert an IV line and give an initial IV fluid load. If there is evidence of major local swelling, with the potential for fluid shifts and shock, monitor BP closely and consider giving further IV fluids to maintain adequate BP and renal perfusion. In such cases, beware later resolution of the swelling resulting in circulatory overload and pulmonary oedema, especially in children.

Both local necrosis and compartment syndrome are a potential risk, but the latter is uncommon to rare, and can be confused with direct venom-induced muscle necrosis. If clinically it appears there may be a developing compartment syndrome, confirm this with pressure measurement before considering fasciotomy, otherwise unnecessary long term limb dysfunction and deformity may well result. Fasciotomy is rarely justified for snakebite. Unless the compartment syndrome is severe and well established, it is usually advisable to first try adequate antivenom therapy before proceeding to fasciotomy. Risks versus benefits must be carefully weighed for each individual case before deciding whether to first give antivenom, or proceed directly to fasciotomy.

In all cases with significant local or systemic effects, consider antivenom therapy. Not all cases of envenoming by *Crotalus* species will require antivenom therapy.

In North America it is common practice to grade the degree of envenoming and use this to determine the need for intervention (antivenom etc). While this process is not accepted by all, it does form a basis of common care guidelines and therefore its use should be considered, at least by those working in the USA. The grading is based on experience with rattlesnake (*Crotalus*) bites and any grading should be subject to reassessment, in a dynamic fashion, reflecting the dynamic nature of envenoming. It should be emphasised that this grading is for North American rattlesnake bites (excluding neurotoxic *Crotalus scutulatus* bites).

Grade 0: Non-envenoming (a dry bite); there may be fang puncture marks, but no other local effects or systemic effects.

Grade 1: Mild envenoming; local effects (pain, swelling) limited to bite area, no systemic effects or blood test abnormalities.

Grade 2: Moderate envenoming; local effects extend beyond the bitten area, but not the whole bitten limb, systemic effects present (such as nausea, vomiting, abdominal pain, metallic taste in mouth, fasciculations of isolated muscle groups, especially the face), blood tests abnormal (may include thrombocytopenia, hypofibrinogenaemia, prolonged prothrombin time, elevated CK).

Grade 3: Severe envenoming; rapidly evolving swelling, blistering or ecchymosis or swelling extending to involve the whole bitten limb or beyond, potential for compartment syndrome, major systemic effects (including those seen in moderate envenoming, plus some or all of shock, widespread or severe bleeding, renal failure, respiratory problems, altered conscious state) and blood test abnormalities (severe thrombocytopenia, abnormal coagulation tests, myolysis with grossly elevated CK, myoglobinuria/anaemia, renal failure).

Antivenom would not be required or appropriate for Grade 0 cases, would not necessarily be required for Grade 1 cases, but if used would be at a low dose, while all Grade 2 & 3 cases require antivenom. Grade 3 cases will require a higher initial dose, and often require larger subsequent doses of infusions.

At least in North America (USA) the only approved antivenom for *Crotalus* species envenoming is the new ovine F(ab)' "Crofab", as the Wyeth Polyvalent Crotalidae antivenom is now either unavailable for restocking or out of production. It is unclear if this older product will again become available. Crofab is a safe, expensive, but effective antivenom which has only a short half life, owing to the small molecular size, compared to IgG antivenoms (eg Wyeth), so repeat doses or infusions are often required. The initial dose is usually suggested as 4-6 vials, followed by a further 6+ vials, either stat or, preferably, as ar

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infusion. The common regime suggested is 4-6 vials (each vial is reconstituted with 10mls sterile water) diluted in normal saline (250mls), given IV, initially at a slow rate (20-60ml/min) until it is clear no adverse reaction is occurring, then increase the rate to around 250ml/hr, until the whole initial dose is given. A slower rate or less volume might be required in small children, but still the same dose of antivenom. On completion, reassess to determine if antivenom has been effective. If there is still significant envenoming (eg advancing swelling, major systemic symptoms etc), consider further antivenom, at a similar dose and rate. Thereafter, it is often advisable to maintain antivenom levels by a continuous infusion, at a rate of 2 vials every 6hrs, up to 18+hrs, longer if major envenoming present. Higher doses may be justified in severe cases. Always have epinephrine & resuscitation equipment readily available prior to commencing antivenom therapy, in case of adverse reactions. In the past in the USA it was common practice to perform a skin sensitivity test prior to starting antivenom. This dangerous and ineffective procedure is not appropriate and is not advocated by the producer of Crofab; **DO NOT USE SKIN SENSITIVITY TESTING!**

The Mexican antivenom, Antivipmyn, is F(ab)₂, not Fab', so is expected to have a longer half life and will not require such frequent doses to maintain levels. However, a higher initial dose is likely to be required, at least 10-12 vials (producer, Bioclon, suggests 5-16 vials initially in adults, depending on severity, with double this dose in children), and further doses may be needed to neutralise all circulating venom. The indication for further doses is unclear, but consider worsening local swelling or effects, or worsening or developing systemic effects, especially coagulopathy or thrombocytopenia (uncertain if this antivenom will affect the latter). Note that while this antivenom has been recommended for use in North American snakebite, it has only rarely been used in this role and does not yet have US FDA approval; the immunising snake species are central-south American, not North American.

In general, if there is a major coagulopathy or bleeding, antivenom will be the most effective treatment and should always be tried first, before considering blood product replacement therapy, except if there is life-threatening bleeding. If antivenom in adequate amounts fails to reverse coagulopathy sufficiently, over a reasonable period of time (allow several hours for such an effect, not minutes), then replacement therapy may be considered. Depending on the nature of the clinical problem or lab test abnormality, FFP, cryoprecipitate, platelet concentrate or whole blood might all be considered.

All patients receiving antivenom or suffering any significant local or systemic effects should be followed up after discharge, particularly looking for delayed reactions to the antivenom (serum sickness) and functional problems affecting the bitten limb, as a result of venom-induced tissue injury. It should be stressed that even with the best treatment possible, full pre-injury function and appearance of the bitten limb cannot be guaranteed. Therefore, any such defect is not automatically an indication of malpractice, nor should it occasion legal action by the patient. It is best to advise patients/relatives from the outset that snakebite is a potentially severe injury, with a potential for adverse outcomes beyond the control of modern medical practice. Honest early discussion of the potential short and long term risks of both the bite and its treatment (ie anaphylactoid or serum sickness reactions to antivenom) are in the interests of both the patient and those offering treatment and may reduce the chance of later dissatisfaction or litigation.

Few doctors see snakebite cases frequently. Unless the treating doctors see many cases and feel justifiably confident in treating envenoming, they should consider early discussion with colleagues expert in this area of medicine. Such expert advice may be available through the regional poisons centre, who will likely have a list of on-call experts. Early consultation may well avoid unpleasant problems developing later.

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Available antivenoms

Antivipmyn
Instituto Bioclon
Calzada de Tlalpan No. 4687
Toriello Guerra
C.P. 14050
Mexico, D.F.,
Mexico
Phone: ++525-488-3716
Fax: ++525-688-2074
Email:
Website:

Polyvalent crotalid antivenom (CroFab), Ovine, Fab
Protherics Inc. (US)
1207 17th Avenue South
Suite 103, Nashville
Tennessee 37212
U.S.A.
Phone: ++1-615-327-1027
Fax: ++1-615-320-1212
Email: info@protherics.com
Website: www.protherics.com

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Management Flowchart

