ANTIDOTES IN DEPTH

Antivenom (Crotaline and Elapid)

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For decades, Wyeth Laboratories (Marietta, PA) has manufactured a crotaline antivenom for treatment of snakebites in the United States. It is a whole immunoglobulin product derived from horse serum. Wyeth temporarily stopped production of this antivenom but has resumed manufacturing the product; however, supplies are available on a limited basis. In October 2000, the US Food and Drug Administration approved the use of another crotaline antivenom. It is a refined crotaline antivenom (crotalidae polyvalent immune Fab (ovine), Protherics, Savage Laboratories), derived from sheep serum and formulated more specifically for the crotalines found in the United States. Crotalidae polyvalent immune Fab (ovine) is an effective and less allergenic alternative to the horse serum products.[7,11,19] Thus, crotalidae polyvalent immune Fab (ovine) has become the most practical antivenom option currently available, and the most widely used snake antivenom in the United States. A comparison of available crotaline antivenoms is given in Table A33–1.

Wyeth also produces a coral snake antivenom effective against the eastern and Texas coral snakes. Numerous other antivenoms exist for bites from exotic or foreign snakes, but they are of limited availability, are difficult to obtain, and are rarely used. Poison control centers or local zoos may have information regarding access to these antivenoms.

Crotaline antivenom is given to ameliorate the effects of local and systemic envenomation by pit vipers, and it is considered lifesaving by some clinicians.[10] Animal studies document decreased mortality when antivenom is given immediately after envenomation.[8] A delay in treatment of even a few hours lessens the beneficial effects of antivenom in animal models.[12] Case reports, anecdotal evidence, and now prospective studies support the concept that antivenom will halt the progression of local tissue swelling and at least temporarily reverse systemic effects, including most coagulation and platelet defects.[4,9,10,15]

When indicated, antivenom should be given as soon as possible to neutralize circulating venom. However, it is impossible to define the exact benefit at any specific time, and the value of late administration is impossible to quantify. Delay of antivenom administration for a few hours likely will not significantly change morbidity or mortality in the majority of cases. However, crotaline antivenom should not be given "prophylactically" to patients with minimal symptoms, or those with no evidence of envenomation. Envenomation following a rattlesnake bite often progresses such that antivenom is required, whereas envenomation following a copperhead bite is less likely to require antivenom administration. The severity of envenomation by water moccasins is somewhere between that of the relatively benign copperhead and the more tissue-destructive rattlesnake. In contrast, coral snake antivenom should be administered in cases where a coral snake bite is assumed or proven, even in the absence of symptoms.

Indications for crotaline antivenom treatment must be individualized for each patient's condition. Because antivenoms can cause life-threatening allergic reactions and delayed serum sickness, the risks and benefits must be weighed prior to treatment initiation. The major indications for crotaline antivenom therapy are (1) rapid progression of swelling, (2) significant coagulopathy or thrombocytopenia, (3) neuromuscular toxicity, or (4) hemodynamic compromise. Patients with previous life-threatening reactions to specific antivenoms still can receive those antivenoms in the absence of an effective alternative antivenom, but only if the envenomation is suspected to result in severe morbidity or mortality. Precautions must be taken to prevent and treat anaphylaxis prior to initiating antivenom therapy. Patients who are sensitized or have a known allergy to horse-derived antivenoms should receive the newer ovine-derived antivenom for crotaline envenomation.

Patients with only mild local tissue swelling following crotaline envenomation should not be given antivenom. There is no justification for infusions of 1 or 2 vials in minor cases. Standard doses for each antivenom are described. No dosing adjustment is required for children or small adults because the amount of venom requiring neutralization is not dependent upon the patient's weight. The initial dose of antivenom should be given as soon as possible but administered cautiously to limit anaphylactoid reactions from rapid infusion. Anecdotally, antivenom may reverse some of the venom-induced coagulopathy even if the antivenom is given more than 24 hours after the bite. Once symptoms begin to progress rapidly, they usually continue and antivenom is warranted. Early treatment likely will be more effective than late administration. All patients who receive antivenom should be hospitalized for at least 24 hours.

Both the equine- and ovine-derived antivenoms can cause anaphylactic and anaphylactoid reactions, as well as serum sickness.[1] Even though the refined crotaline antivenom is a purified immune Fab product, allergic reactions are reported. The true incidence of these allergic reactions is unknown, but premarketing and postmarketing data report rates much lower than for the equine-derived whole immunoglobulin products.[9,19] Because of the potential for life-threatening reactions, antivenom should be administered only in areas where resuscitation efforts can occur. Epinephrine infusion, H_1 and H_2 antihistamine receptor blockers, and corticosteroids should be available at the patient's bedside before therapy is initiated.

Discharged patients should have telephone followup for 3 weeks after antivenom treatment to permit evaluation for signs of serum sickness. Although the incidence of serum sickness is much lower for the Fab product than for the equine-derived antivenoms, serum sickness from all snake antivenoms is reported.

In addition to evaluation for serum sickness after Fab treatment, repeat outpatient laboratory studies are necessary, following hospital discharge. Crotalidae polyvalent immune Fab (ovine) use has led to the creation of a new term in antivenom treatment called *recurrence.* After crotalidae polyvalent immune Fab (ovine) stops the progression of tissue swelling and reverses coagulopathy and thrombocytopenia, a significant number of patients demonstrate recurrence of either local tissue edema and/or hematologic abnormalities. Several theories have been suggested, but the likely explanation for this phenomenon is an apparent mismatch between effective duration of

TABLE A33–1. Comparison of Available Crotaline Antivenom

	Crotaline Polyvalent Immune Fab Antivenom (Savage Laboratories)	Antivenom Crotalidae Polyvalent (Wyeth Laboratories)
Animal source	Sheep	Horse
Venom component	*Crotalus atrox* *Crotalus adamanteus* *Crotalus scutulatus* *Agkistrodon piscivorus*	*Crotalus atrox* *Crotalus adamanteus* *Crotalus durissus terrificus* *Bothrops atrox*
Immunoglobulin	IgG Fab	IgG (whole)
Hypersensitivity reactions		
Acute	14.3%	23–56%
Delayed	16%	75–86%
Recurrence[a]	Common	Rare
Dose	4–6 vials repeated as needed for control,[b] then 2 vials every 6 hours for 3 doses	10 vials repeated as needed for control[b]

[a]Recurrence of local tissue swelling or hematologic abnormality anytime after completion of treatment.
[b]Control = arrest of local tissue manifestations and clear improvement in coagulopathy and thrombocytopenia.

Fab antivenom and venom-induced local and systemic pathology.[19] Patients who initially have significant coagulopathy or thrombocytopenia appear to be at greater risk for recurrence of these venom effects, although the significance of these findings, or the need for treatment, is unknown. The appropriate management of recurrence is still debated.

CROTALINE POLYVALENT IMMUNE Fab ANTIVENOM (OVINE ORIGIN)

Polyvalent ovine-derived antivenom is obtained by inoculating sheep with the venom of the eastern diamondback rattlesnake (*Crotalus adamanteus*), western diamondback rattlesnake (*Crotalus atrox*), cottonmouth (*Agkistrodon piscivorus*), and Mojave rattlesnake (*Crotalus scutulatus*). This process results in an antivenom that is more specific to snakes found in the United States than the traditional Wyeth product. One report anecdotally suggests that the Fab antivenom has superior activity against the neurotoxicity of the Mojave rattlesnake.[7] The manufacturing process includes papain digestion of isolated IgG antibodies to eliminate the Fc portion of the immunoglobulin and to isolate specific antibody fragments (Fab and $F(ab)_2$), as well as affinity purification and lyophilization. The Fab fragments have a smaller molecular weight, are less immunogenic, and may have increased tissue penetration compared to whole IgG. In preliminary studies, the number of severe acute and chronic hypersensitivity reactions associated with the Fab use was significantly reduced compared with horse serum products, but clinical experience is limited.[9] Few clinical trials have evaluated the safety of antivenom, but a study reported a 14.3% incidence of acute and 16% incidence of delayed hypersensitivity reactions.[10] Despite the uncertainty, antivenom has been safely administered to children as young as 14 months.[17] Urticaria, rash, bronchospasm, pruritus, angioedema, delayed serum sickness, and anaphylaxis all are associated with use of this product.[9,19] The same cautions that have been used with whole immunoglobulin antivenoms should be practiced with the Fab product.

The pharmacokinetics and pharmacodynamics of Fab antivenom differ from those of other antivenoms, and there is an apparent mismatch between effective duration of Fab antivenom and venom-induced local and systemic pathology.[19] The duration of action of the Fab antivenom appears to be less than that of traditional equine-derived polyvalent antivenom. The elimination half-life of 12–23 hours is less than that of the venom itself, so periodic or repeat dosing of Fab antivenom is required to prevent or treat recurrent symptoms.[4]

Prospective data on patients who have been treated with Fab antivenom have generated important information on the clinical utility of antivenom. The use of a clinical severity-of-illness scale has demonstrated that antivenom will correct coagulopathies and thrombocytopenia associated with envenomation from snakes native to the United States.[10] In an animal lethality model, the new ovine-derived antivenom was 5 times more potent than traditional equine-derived antivenom against 14 different crotaline snake venoms.[8] However, the progression of local tissue injury was ameliorated but not significantly reversed, suggesting that once ecchymosis, edema, and local cell injury secondary to crotaline venom develop, they are essentially irreversible. Initial experience with the Fab antivenom has been promising, and the antivenom appears to be effective in halting progression of many aspects of crotaline envenomation while minimizing allergic reactions.

Technique of Administration

A thorough history regarding asthma, atopy, concurrent use of β-adrenergic antagonists, allergy to papaya or papain, and previous use of antivenoms should be obtained. According to the manufacturer, the only absolute contraindication to the Fab antivenom use is allergy to papaya or papain, which is a contaminant left after the Fab portion of the immunoglobulin is cleaved from the Fc portion. A history of asthma, atopy, or use of β-adrenergic antagonists should be carefully considered when weighing the risks and benefits of antivenom for a particular patient. These conditions should not exclude the use of antivenom if the patient is suffering from moderate-to-severe envenomation. In cases of mild envenomation, the risk of allergic reaction to antivenom or inability to effectively treat an allergic reaction in a patient receiving β-adrenergic antagonists might outweigh any benefit in this patient population. Because the Fab antivenom is ovine derived, reactions from previous use of equine-derived antivenoms should not preclude use of this product.

Our practice has been to prepare for administration of the Fab antivenom in the same manner as for administration of the whole immunoglobulin antivenoms. Prior to drug infusion, an intravenous epinephrine infusion (250 mL D_5W mixed with 1 mg epinephrine), 1–2 mg/kg methylprednisolone, 0.5–1 mg/kg diphenhydramine, and an H_2 antihistamine receptor blocker are placed at the patient's bedside. Antivenom is always administered in a monitored unit where resuscitation can be performed and airway supplies can be quickly accessed.

Each vial of the Fab antivenom must be reconstituted in 10 mL sterile 0.9% sodium chloride solution prior to use. A continuous gentle swirl or rolling method is used to expedite the reconstitution. To prevent foaming, shaking and other vigorous methods should not be used. Four to 6 vials of the reconstituted antivenom are mixed in 250 mL 0.9% sodium chloride solution and administered over 1 hour. The exact concentration of antivenom is not critical. For children, the total volume of fluid in which the antivenom is diluted can be decreased when necessary. The antivenom is infused at an initial rate of 10 mL/h while the patient is observed for evidence

of hypersensitivity reactions. The rate is doubled every few minutes as tolerated by the patient. If no adverse reactions are witnessed, the remaining dose can be given over 1 hour. If the patient tolerates the initial dose without adverse effects, subsequent doses can be given over 1 hour without slowly increasing the rate.

When antivenom is administered too rapidly, mast cells release histamine and produce nonimmunogenically mediated anaphylactoid reactions. In general, patients appear to tolerate 4–6 vials per hour without developing anaphylactoid reactions. If the patient requires rapid administration of antivenom because of the severity of the envenomation, H_1 and H_2 antihistamine receptor blockers may be needed in addition to an epinephrine infusion. Clinically differentiating between anaphylactoid and anaphylactic reactions may be difficult, especially when antivenom is administered rapidly.

For acute anaphylactic reactions (which often occur shortly following initiation of even low doses of antivenom), the antivenom should be stopped, and intravenous steroids, H_1 and H_2 antihistamine receptor blockers, and epinephrine given. Epinephrine 2–4 μg/min (0.03–0.06 μg/kg/min for children) can be initiated and then titrated to effect. After the symptoms of hypersensitivity resolve, the antivenom should be restarted only in patients at high risk for significant morbidity or mortality from snake envenomation. In such cases, the antivenom infusion is restarted at 1–2 mL/h, while the epinephrine infusion is continued. The antivenom infusion rate can be slowly increased as the patient tolerates. If anaphylaxis recurs, the antivenom should be stopped and the epinephrine infusion increased until symptoms resolve. Antivenom then can be restarted while epinephrine is continued at the higher rate. With constant monitoring of patients at the bedside and titrating epinephrine and antivenom infusions, patients with life-threatening envenomation should tolerate the full antivenom dose. Patients have safely received subsequent doses of crotalidae polyvalent immune Fab (ovine) after an acute life-threatening reaction.[6]

After two preclinical trials studied crotalidae polyvalent immune Fab (ovine), the therapeutic regimen was empirically determined to include repeat doses of 4–6 vials until "control" is obtained, followed by regularly scheduled maintenance infusions. The manufacturer defines *control* as arrest of local tissue manifestations and return of coagulation parameters, platelet counts, and systemic signs to normal. However, select patients develop coagulopathy and thrombocytopenia that is resistant to antivenom treatment.[19] Some authors advocate control to mean clear improvement in hematologic parameters rather than complete normalization.[19] This definition may be more realistic for the subset of patients with difficult-to-treat coagulopathy and thrombocytopenia. After each dose of 4–6 vials, prothrombin time, fibrinogen, and platelet counts are determined, and the patient's local injury is reexamined. Multiple doses may be required to achieve control. The optimal dose has not yet been determined. After achieving control, a maintenance dose of 2 vials every 6 hours is given, for a total of 3 doses. Again, the 2 vials are added to 250 mL 0.9% sodium chloride solution and administered over 1 hour. Because the duration of action of antivenom is not as prolonged as that of the venom, the maintenance doses are an attempt to prevent recurrence of local manifestations, thrombocytopenia, and coagulopathy. An algorithm for crotalidae polyvalent immune Fab (ovine) antivenom administration for treatment of significant crotaline envenomation is shown in Figure A33–1.

At the time of discharge, the patient should be informed of the possibility of recurrence and told to refrain from activities associated with high risk for trauma and to avoid any surgical procedures for 3 weeks. The patient should receive instructions to watch for signs of bleeding, which may be associated with coagulopathy or thrombocytopenia. Followup prothrombin time, fibrinogen level, and platelet count should be obtained within 3–5 days of antivenom completion in all patients. In most patients who develop recurrence, the decrease in platelets or increase in prothrombin time usually is evident within 3 days of last antivenom therapy. Recurrence occurs in approximately 25–50% of patients with rattlesnake envenomation who receive crotalidae polyvalent immune Fab (ovine).[3,19] Early administration of antivenom may have masked the findings in patients who initially did not demonstrate

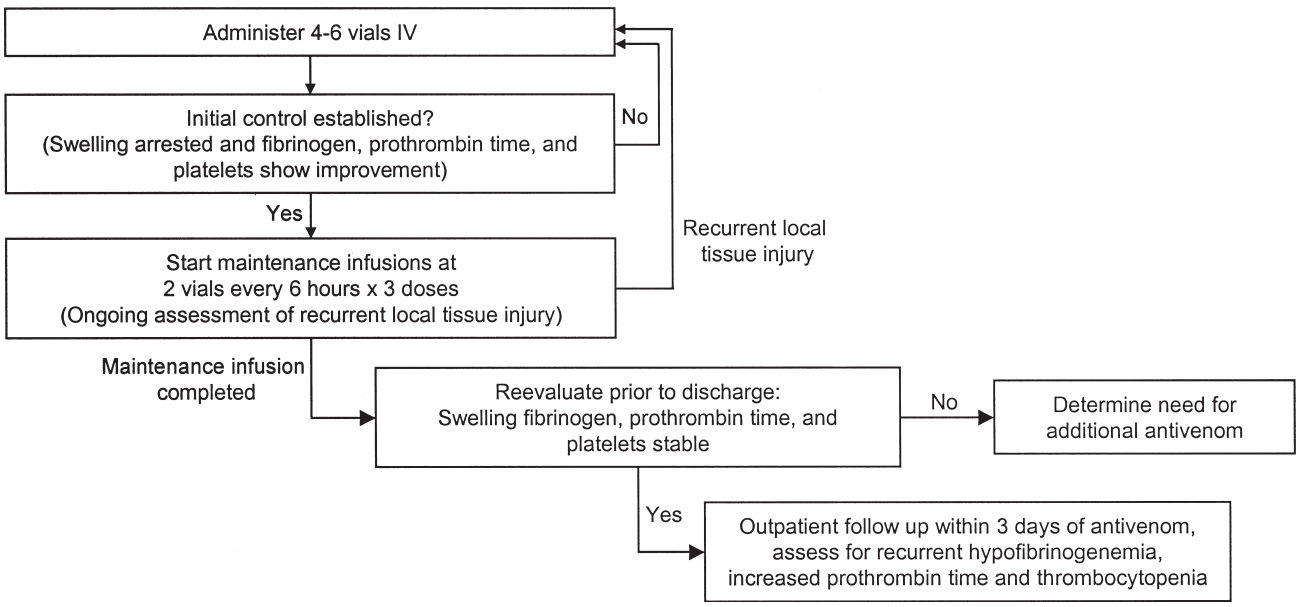

Figure A33–1. Algorithm for crotaline polyvalent immune Fab antivenom administration for treatment of significant crotaline envenomation.

coagulopathy or thrombocytopenia, and these patients still may develop these effects within days of completing antivenom treatment. Treatment recommendations for recurrence of venom effects vary. Clinical experience demonstrates that recurrence may be resistant to additional antivenom,[19] so the benefits of re-treatment in the absence of active bleeding are unclear. No specific dosing regimen for re-treatment is known at this time. In our practice, where we frequently encounter recurrence, our approach is to re-treat patients who develop (1) isolated thrombocytopenia with platelet count $<$10,000–20,000/mm^3, (2) platelet count $<$30,000/mm^3 and prothrombin time $>$20 seconds or fibrinogen $<$150 mg/dL, or (3) active bleeding. A more conservative approach can be used for patients with additional risk factors for bleeding, such as high risk for trauma or use of warfarin (Coumadin). Other patients with less severe recurrence, or isolated coagulopathy without thrombocytopenia, usually can be managed at home with close followup and repeat laboratory tests every few days. Increased local tissue swelling at the time of followup usually is not an indication for redosing antivenom and most often is the result of dependent edema from inadequate extremity elevation. In the absence of any recurrence phenomenon, patients should have regular telephone followup for 3 weeks to check for signs of serum sickness.

Mild cases of serum sickness consist of urticaria, pruritus, and mild systemic symptoms, such as malaise. Occasionally arthralgias, lymphadenopathy, and fever develop. Immune-complex glomerulonephritis, neuritis, vasculitis, and myocarditis occur rarely. The syndrome of serum sickness after antivenom use has not been well characterized or studied, but usually it is neither serious nor associated with chronic sequelae.[13] Most patients respond favorably to antihistamines and systemic corticosteroids. Immediately after onset of symptoms, 2 mg/kg prednisone divided into twice daily dosing are given for 1 week. Oral antihistamines can be used for symptomatic treatment as well. After 1 week of corticosteroid therapy, the dose is slowly tapered over the following week. If symptoms recur during the taper, the dose is increased for 3 days before the taper is reinstated. The vast majority of patients can be managed as outpatients.

As experience with the Fab antivenom expands, alternate dosing regimens may reduce the number of patients who develop recurrence. In the meantime, all patients should be considered at risk for delayed coagulopathy or thrombocytopenia. Furthermore, acute and delayed allergic reactions are less common than those reported with use of whole immunoglobulin antivenoms, but do occur. The same precautions used when administering other antivenoms should be used with the Fab antivenom.

CROTALINE POLYVALENT ANTIVENOM (EQUINE ORIGIN)

Crotaline polyvalent antivenom (Antivenin Crotalidae Polyvalent, Wyeth-Ayerst) is active against the venom of rattlesnakes (*Crotalus*, *Sistrurus*), water moccasins, copperheads (*Agkistrodon*), some South American pit vipers, and some Asian snakes. It is not effective for bites of exotic snakes, such as cobras and other Elapidae. This antivenom is a refined and concentrated preparation of equine serum immunoglobulins (IgG) formulated into a freeze-dried powder that is reconstituted before use. It is a suspension of various venom-neutralizing antibodies prepared from the serum of horses that are gradually hyperimmunized against the venom of a specific cadre of pit vipers found in the western hemisphere: eastern diamondback rattlesnake (*C. adamanteus*), western diamondback rattlesnake (*C. atrox*), tropical rattlesnake (*C. durrisus terrificus*), and fer-de-lance (*Bothrops atrox*). These crotalines share many of the common antigens found in pit viper venom throughout the world, so the polyvalent antivenom is presumed effective against a number of species, including all pit vipers found in the United States. Even though the polyvalent antivenom is not derived from copperheads or other crotalines, such as the Mojave rattlesnake, Pacific rattlesnake, and timber rattlesnake, it is commonly administered following severe envenomation from these species.[2] The antivenom may be less effective against these snakes, and the neurotoxicity from the Mojave rattlesnake has been suggested to be resistant to crotaline polyvalent antivenom.[5]

Because this antivenom is a whole immunoglobulin product, its use entails a significant incidence of immediate and delayed hypersensitivity reactions,[13] including minor cutaneous hypersensitivity (urticaria), anaphylaxis, anaphylactoid reactions, and serum sickness. As the dose or rapidity of administration of antivenom is increased, the incidence of immediate and delayed hypersensitivity reactions also increases. Because the ammonium sulfate precipitation process currently used to prepare this antivenom is inefficient, the serum contains unwanted contaminants in the form of extraneous heterologous proteins such as albumin, α- and β-globulins, and IgM, in addition to the venom-specific IgG. These contaminants are largely responsible for the allergic properties of the antivenom.

Anaphylactic reactions result from the presence of circulating IgE antibodies to horse protein in the recipient's blood leading to degranulation and histamine release from mast cells or basophils. Serum sickness is caused by delayed production of antibodies by the recipient following infusion of a relatively large dose of foreign protein (antigen excess reaction). Serum sickness develops a few days to weeks after administration of horse serum-derived antivenom in the majority of patients who receive this therapy. Fortunately, serum sickness generally is mild, easily treated, and not associated with significant chronic sequelae, although rarely immune-complex vasculitis, myocarditis, neuritis, and glomerulonephritis are noted. Few data on the exact incidence of allergic reactions are available, but some form of acute hypersensitivity reportedly occurs in nearly 25% and delayed serum sickness in 50% of patients receiving antivenom.[14] Moreover, more than 80% of patients develop serum sickness if more than 8 vials of antivenom are administered.[14] The majority of patients given antivenom experience urticaria as the only acute adverse reaction.

Technique of Administration

Before antivenom is administered, the patient should be asked about a history of asthma, atopy, current use of β-adrenergic antagonists, and previous horse serum-derived antivenom exposure. If any of these conditions are present, efforts should be made to obtain crotaline polyvalent immune Fab antivenom. Use of skin testing for sensitivity to horse serum is controversial, and we do not recommend its use before antivenom administration. Skin testing is an unreliable predictor of either immediate or delayed hypersensitivity reactions. Both false-positive (~50%) and false-negative (~20%) skin tests are encountered. A 1-mL vial of horse serum is included in the Wyeth Crotalidae antivenom kit with instructions for skin testing use. In life-threatening situations, and if the Fab antivenom is not available, administration of antivenom to patients with a positive skin test or known allergy to horse serum is warranted.[16,18] Antivenom administration can be continued in selected

cases of serious envenomation even in the presence of an allergic reaction. In such cases, where the skin test is positive or a reaction develops during administration of antivenom, prophylactic or concomitant use of corticosteroids, epinephrine, and antihistamines has alleviated most of the allergic symptoms. Treatment should entail use of both H_1 and H_2 antihistamine receptor blockers. In a study, the cutaneous and systemic signs and symptoms of immediate hypersensitivity were all effectively treated with antihistamines and epinephrine, with no adverse sequelae.[14] Slowing the rate of infusion of antivenom or increasing the dilution frequently lessens the severity of the allergic reaction (Chap. 117). There is no practical way to desensitize patients to horse serum. However, the Fab antivenom is a safe alternative available for horse-serum allergic patients.

The same procedure used in reconstitution of the Fab antivenom can be used for the equine product. A diluent is included in the Wyeth antivenom kit, but the diluent offers no benefit to sterile 0.9% sodium chloride solution and actually may prolong reconstitution because the diluent volume is inadequate to completely fill each antivenom vial. The same technique is described for administration of both products. It is essential that intravenous corticosteroids, H_1 and H_2 antihistamine receptor blockers, and intravenous epinephrine infusion (1 mg epinephrine mixed in 250 mL D_5W) be available at the patient's bedside. Antivenom treatment should never be initiated without close access to resuscitation equipment. Dosing differs for these two products. Ten to 20 vials are given as an initial dose, and no maintenance doses are used. After the initial dose, prothrombin time, fibrinogen level, and platelet counts are drawn, and the patient's local injury is reexamined. Repeat antivenom doses of 10 vials are given as needed to control coagulopathy, thrombocytopenia, and worsening tissue injury. On average, 30 vials are often required for adequate treatment of rattlesnake envenomation.

Followup care for patients receiving equine antivenom usually does not require repeat hematologic studies, unless patients develop signs of bleeding, because recurrence is rarely reported. Although recurrence of coagulopathy and thrombocytopenia is less frequent than with the Fab antivenom patients can have delayed bleeding, if they are not closely monitored. Long-term followup is important following administration of the equine antivenom. There is an approximately 80% chance of developing serum sickness within 3–20 days of antivenom administration, especially if more than 8 vials are administered.[14] The frequency of serum sickness is directly related to the number of vials of antivenom administered. The full description of serum sickness treatment is discussed in the Technique of Administration for the Fab antivenom.

ELAPID ANTIVENOM (EQUINE ORIGIN)

Antivenom of equine origin is available in limited supplies from Wyeth for treatment of envenomation by the eastern coral snake (*Micrurus fulvius fulvius*) and Texas coral snake (*Micrurus fulvius tenere*). Toxicity requiring treatment with antivenom has not been reported following bites from the less virulent Arizona (Sonoran, *Micruroides euryoxanthus*) coral snake. The coral snake antivenom does not treat envenomation from coral snakes found in Mexico, Central America, or South America. In contrast to the recommendation to withhold crotaline polyvalent antivenom unless signs of significant envenomation are evident, prophylactic use of coral snake antivenom is recommended in any asymptomatic cases where a coral snake bit is assumed or proven.[15] Limited supplies of this antivenom may make adherence to this recommendation difficult. For a number of hours following the bite of a coral snake, little objective evidence suggests envenomation, but systemic symptoms can develop insidiously. Therefore, at least 3–5 vials of coral snake antivenom are given initially and repeated on the basis of the clinical condition. The caveats for administration of crotaline antivenom (skin testing, rate of infusion, treatment of reactions) apply to coral snake antivenom, except less antivenom usually is required for coral snakes. Up to 10 vials can be administered, but dosing recommendations are vague.

CONCLUSION

In the past, equine crotaline polyvalent antivenom was the only antivenom available for treatment of crotaline envenomation. It is an effective therapy, but carries a significant risk of life-threatening immediate and delayed hypersensitivity reactions. Some hospital pharmacies still maintain supplies of the antivenom, and Wyeth will provide it on an "as needed" basis. In recent years, ovine crotaline polyvalent immune Fab antivenom (CroFab) has become the more commonly available treatment for crotaline envenomation. Although treatment with the Fab antivenom requires maintenance doses and often leads to recurrence of envenomation effects, it is clearly a safer alternative to the equine product. One aspect of crotaline therapy that has not yet been fully evaluated is a cost-to-benefit analysis comparing the two antivenoms. As experience with the Fab antivenom grows, the cost of drug administration, followup care with repeated laboratory examinations, and possible rehospitalization for recurrence may become more evident. Regardless, most physicians are restricted to the Fab antivenom use merely because supplies are more easily secured, thus making any cost-to-benefit analysis less meaningful.

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