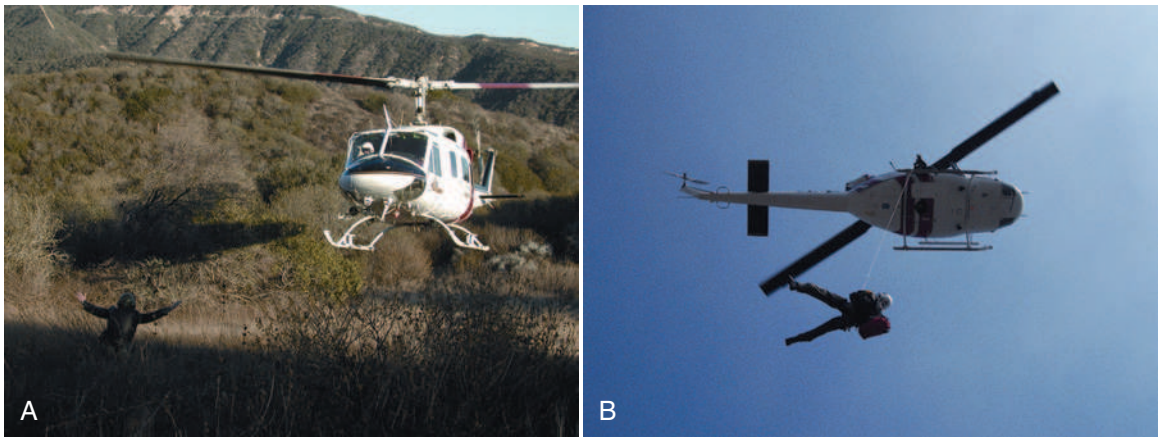


FIGURE 35-29 **A,** The fastest and safest way out of a deep wilderness setting may entail helicopter evacuation, where available. **B,** Specialized techniques, such as hoisting, may be required to rescue a snakebite victim out of a tenuous situation. *(**A** courtesy Jeff Grange; **B** courtesy Carlos Quezada.)*

Urinalysis should be performed to identify hematuria. Proteinuria and glycosuria may be seen.[217] Each time the patient voids, the urine should be evaluated with bedside testing strips for the presence of blood.

If envenomation is severe or if the patient has significant underlying medical problems (e.g., cardiovascular or respiratory disease), an electrocardiogram (ECG), arterial blood gases (ABGs), and chest radiograph should be obtained. The ECG may reveal evidence of myocardial ischemia. ABGs give important information regarding adequacy of tissue perfusion and respiratory status, but caution should be used in performing arterial puncture in the setting of potential coagulopathy. Pulmonary vascular congestion or frank pulmonary edema may be confirmed radiographically or by bedside ultrasound.

Coral Snakes

Given their less efficient venom delivery system, coral snakes effectively envenomate their victims only about 40% of the time.[214] After envenomation, the effects are predominantly neurotoxic. In the United States, bites by the eastern coral snake (*Micrurus fulvius*) tend to be more severe than those by Texas coral snakes (*Micrurus tener*), and both are significantly more severe than those of the Sonoran coral snake (*Micruroides euryxanthus*).[185,211,220] The victim may have variable, early, and transient pain of the bitten extremity.[213] Local swelling may be absent and is rarely significant. Fang marks may be difficult to see and should be carefully sought.[190] Systemic signs and symptoms may be delayed as long as 13 hours after significant bites and can then progress rapidly.[133] The earliest findings may be nausea and vomiting, followed by headache, abdominal pain, diaphoresis, and pallor.[72] Patients may complain of paresthesias or numbness. They may have altered mental status, such as drowsiness or euphoria.[174] The patient may develop cranial nerve dysfunction (e.g., ptosis, difficulty speaking, difficulty swallowing), followed by peripheral motor nerve dysfunction.[174] In severe cases, respiratory insufficiency and aspiration are significant risks.[133] Cardiovascular insufficiency may also be seen.[217] Unlike with many crotaline envenomations, coagulopathy is not a feature of coral snake envenomation.

Laboratory studies are of little value in evaluation of a victim of coral snake bite. Occasionally, a rise in serum CK and myoglobinuria occur, reflecting myotoxicity.[133] ABGs may be useful in evaluating the patient's respiratory status if endotracheal intubation is considered or performed. A chest radiograph is indicated in the setting of apparent cardiac dysfunction or after endotracheal intubation.

MANAGEMENT

Prehospital Care

Pit Vipers. The factors that most reduce venomous snakebite–related injury and mortality in the United States are rapid transport, antivenom therapy, and intensive care.[30] All patients should be transported to the hospital as expeditiously and safely as possible, preferably through activating the emergency 911 system (where available). Increasing the area of coverage for cellular phone services provides snakebite victims with easier access to ambulance or helicopter rescue (Figure 35-29).

Attempts to kill the snake are not recommended because of the risk for additional bites to the victim or rescuer and because precious time can be wasted. All emergency responders should be able to distinguish native venomous from nonvenomous snakes. However, if rescuers are uncertain about whether a particular snake is venomous, photographs may be taken of the snake from a safe distance (at least 2 m [6.5 feet]) using a digital camera. These images may help facilitate clinical decisions, especially if clinicians have herpetologists preidentified to examine electronically transmitted images. Although helpful in identifying the species of snake,[32,34] transporting it (alive or dead) is discouraged because of inherent dangers. On scene, snakes should be moved or contained only if absolutely necessary (i.e., for safety). A snake hook or long shovel may be helpful to move a snake into a large, empty trash canister, where it can be recovered by a professional, such as an animal control agent. Serious morbidity and even death have been reported after envenomation by decapitated rattlesnake heads.[53,132,235] Again, a recently killed snake or severed snake head can maintain a bite reflex for at least 1 hour after its death. Emergency personnel and hospital care providers should exercise extreme caution in handling any specimen accompanying the patient, even if it appears dead.

Recommendations for first-aid and prehospital treatment of pit viper envenomation have historically been based on intuition and anecdotal experience, although better evidence is accumulating in the literature. In one large retrospective series, first-aid treatment had no relationship to ultimate envenomation severity.[259] Some first-aid measures recommended in the past have caused more injury than have the bites, and delays in care have been shown to increase morbidity and mortality.[71,106] It is inappropriate to use any technique that could injure the patient or delay travel to the nearest facility where antivenom is available. General support of the airway, breathing, and circulation should be provided, depending on the capabilities at hand. Oxygen, cardiac monitoring, and intravenous (IV) fluids should be used in the field when available. Although it may be necessary for the victim to hike out from the scene of the incident, exertion should be minimized as much as possible. Alternative methods (e.g., stretcher, helicopter, boat) of extracting the victim from a wilderness setting can be used when available and when conditions such as weather and terrain allow. Jewelry and tight-fitting clothing are removed from the involved extremity in anticipation of swelling. The border of advancing edema is marked with a pen every 15 minutes so that emergency personnel can estimate the severity of envenomation by following the rate of progression. These measures suffice as adequate prehospital care for the vast

majority of pit viper bites in the United States. Measures such as incision, suction, tourniquets, electric shock, ice, alcohol, and folk therapies should be avoided.

Incising the bite site is contraindicated. This creates additional injury and has never been shown to be effective. Because pit viper fangs are curved, incisions may miss the track along which venom is actually injected. Incisions made by laypersons can cause serious injury to underlying blood vessels, nerves, or tendons. Because of venom-induced coagulopathy, bleeding from such incisions can be severe.[104] Furthermore, the lack of sterile conditions in the field increases the risk for infection.

Although use of the Sawyer Extractor Pump to apply mechanical suction was recommended for a number of years, at least three studies using different methodologies independently found that the Extractor does not work for venomous snakebite and can exacerbate tissue damage.[3,31,35,36] Mouth suction is contraindicated for the additional concern of potentially contaminating the wound with oral flora.

Venom sequestration techniques, such as application of a lymphatic or superficial venous constriction band or pressure immobilization, may inhibit the systemic spread of venom.[29,236] It is not clear, however, whether such measures improve outcome after pit viper envenomation. Some argue that restricting the spread of potentially necrotizing venom to local tissues may intensify injury.[105] Because local sequelae are the predominant complications after pit viper envenomation (see Morbidity and Mortality, later), and because permanent systemic injury and death are rare, especially in North America, any attempt strictly to limit venom to the bite site is not advised.[71] Tourniquets have worsened injury when used for snakebite and are contraindicated.[104]

Pressure immobilization (P-I) has been used effectively in Australia for field management of elapid snakebites (see Chapter 36).[237] This technique involves immediately wrapping the entire bitten extremity with an elastic wrap or crepe bandage as tightly as would be done for a sprain, then splinting and immobilizing the extremity (Figure 35-30). P-I resulted in significantly longer survival but higher intracompartmental pressures after artificial, intramuscular western diamondback rattlesnake (*C. atrox*) envenomation in a pig model.[33] In a separate small porcine study using *C. atrox* venom, P-I again prolonged survival without evidence of worsening local tissue sequelae.[178] Additional conclusive research is necessary to assess definitively the risk/benefit ratio of using P-I in bites by snakes with necrotizing venoms. Furthermore, studies have shown that laypeople as well as physicians have difficulty properly applying the bandage, generally underestimating the necessary tightness for effective application.[50,191] Further complicating the clinical use of P-I is that the victim must be carried out of the field after application of pressure immobilization, because walking stimulates muscular pumping of venom into the systemic circulation and negates any benefit, even in upper-extremity bites.[122] For these reasons, P-I is not routinely recommended at this time for use in pit viper bites. Certain scenarios may, however, warrant consideration of its use. Although it is difficult to predict snakebite severity at the time of the bite, certain factors may suggest an increased likelihood of a more severe envenomation: large snake size, particularly dangerous snake species, small patient size, prolonged fang contact, previous venomous snakebites (treated or not) or exposures to snakes, and delays to medical care and antivenom administration.[125] Individuals who consider using P-I must thoroughly familiarize themselves with the technique and must assess risks, benefits, and alternatives on a case-by-case basis. If P-I is applied after a snakebite, however, the wrap should not be removed until a source of definitive care is reached. Loosening the wrap may result in release of a venom bolus into the systemic circulation. Antivenom must be immediately available to treat such an event, and medications and equipment available to treat an immediate hypersensitivity reaction (see Allergy to Reptile Venom, later).

Electrotherapy was proposed in the late 1980s for first-aid treatment of snakebites and subsequently was popularized by the lay press.[98,117] Early proponents recommended application of high-voltage, low-amperage, direct current (DC) shocks to the bite site using a source such as an outboard motor or lawn mower engine.[97] A "stun gun," typically designed for self-defense, was even modified by one company and marketed for snakebite

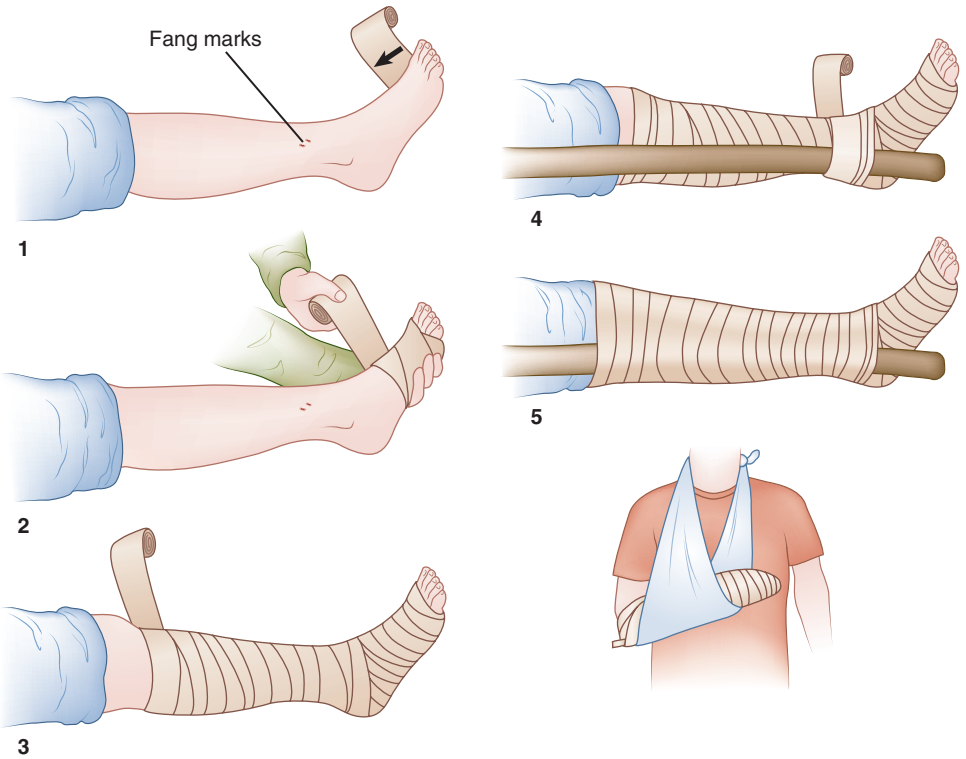


FIGURE 35-30 Australian pressure-immobilization technique. This technique has proved effective in the management of elapid and sea snake envenomations. Its efficacy in viperid bites has yet to be fully evaluated clinically.

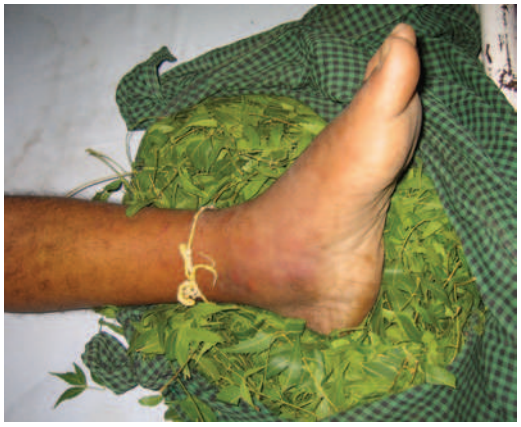


FIGURE 35-31 Neem leaves (*Azadirachta indica*) applied by a victim in an effort to treat saw-scaled viper (*Echis sochureki*) bite in Rajasthan, India. *(Courtesy Robert L. Norris, Jr., MD.)*

treatment.[104] This marketing was halted by the U.S. Food and Drug Administration (FDA) in 1990 because of total lack of testing or evidence of efficacy. In subsequent controlled animal studies, electric shock showed no efficacy in reducing morbidity or mortality after rattlesnake venom injection in mice, rats, or rabbits.[123,127,233] In humans, application of electric shock for snakebite has been associated with acute myocardial infarction and increased local tissue damage secondary to electrical burns.[69,70,215] Because of its lack of efficacy and inherent risks, electric shock should not be used in the treatment of snakebites.

Local application of ice to the bite wound as a first-aid measure has not been adequately studied in terms of its benefits or risks. This should not be confused with "cryotherapy," or packing the injured limb in ice for extended periods. This form of treatment was popularized in the 1950s and 1960s. Use of cryotherapy resulted in a significant increase in tissue loss and amputation rates after pit viper bites, and it has now been completely abandoned.[213] Whether brief (e.g., <1 hour) local application of ice is beneficial (by reducing venom activity or decreasing pain and inflammation) or harmful (by worsening local ischemia and resulting necrosis) is unknown. In any case, ice should not be applied directly to the skin for any prolonged period.

Although indigenous peoples in many parts of the world have long used plants (Figure 35-31), either topically or systemically, for treatment of snakebite, little formal research has been done in this area. No current data support the use of any plants in the management of snakebite.[121]

Other first-aid measures that lack therapeutic value or have potential for being more harmful than the snakebite itself include scarification of the bite wound, ingestion of alcohol, use of stimulants, and various folk remedies, such as application of ammonia, silver nitrate, oil, potassium permanganate, or saliva. Similarly ineffective is application of poultices made from various parts of the offending reptile (or other creatures), such as the snake's crushed head, bile or fat, or use of snake stones.[214]

Insufficient evidence exists regarding efficacy of splinting or specific positioning (e.g., above or below heart level) of the limb. Theoretically, elevation may hasten systemic spread of venom, whereas lowering the extremity may worsen swelling. In the absence of any reliable data, the extremity should be maintained in a neutral position of comfort until it can be ascertained whether the predominant effects of the bite will be systemic or local.

For the victim of a pit viper bite who is many hours or days from medical care, the best course of action depends on the situation. If present, a companion may hike out for help, if conditions allow for prompt return of a rescue team. At times, if sufficient rescuers are available, the victim can be carried out. The victim who must hike out should use a makeshift crutch (for a lower-extremity bite) or sling (for an upper-extremity bite), rest frequently, and maximize oral intake of clear liquids as tolerated.

Antivenom use in the field can be recommended only when a qualified medical provider is on scene and when all equipment (including definitive airway management equipment) and drugs are available to manage acute reaction to the antiserum. Although studies and clinical experience show that newer, purified Fab and $F(ab')_2$ fragment antivenoms may be safer than whole-immunoglobulin products (see Antivenom Production, later), adverse reactions still occur.[143] Antivenom has been shown to retain activity for at least 60 days under conditions of increased heat and motion (as might be encountered in a field setting).[74] With the safety profile and stability of new antivenoms, field use may be worth reconsidering, although acquisition costs for the antivenom may be prohibitive.

Coral Snakes. When a bite by a coral snake is suspected, the animal's skin color pattern should be noted, and if possible the snake should be photographed from a safe distance. Because of the potential delay in onset of signs and symptoms after coral snake envenomation, distinguishing between a coral snake and a harmless mimic is important.

Recent research suggests that the Australian P-I technique may be useful in the field management of coral snake bites. This technique has been shown to be effective in one small-animal study using *Micrurus fulvius* venom.[84] Being elapids, coral snakes are related to the venomous snakes in Australia, for which this technique has been shown in animal models to be effective in limiting venom absorption (see Chapter 36). This intervention remains problematic, however, because rescuers frequently have difficulty applying this technique with the precision required for it to be effective,[191] and because the victim must be fully immobilized and carried out of the field.

Hospital Care

Pit Vipers

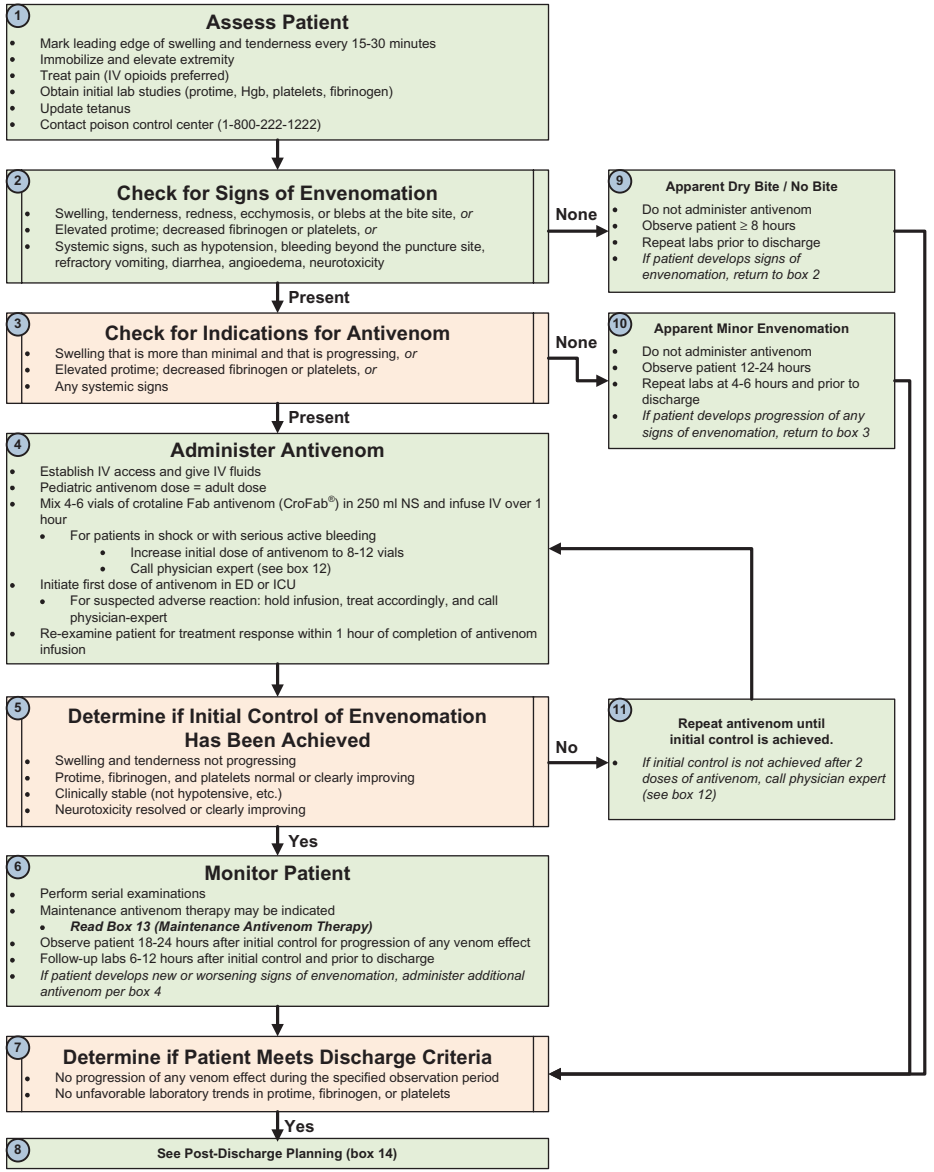
Initial Management. Initial focus of emergency medical care for a pit viper bite is on the victim's airway, breathing, and circulation (Figure 35-32). Patients should receive supplemental oxygen until it is clear that they are stable. Patients with bites to the face or neck may require early endotracheal intubation to prevent loss of the airway caused by severe swelling. Pulse oximetry and cardiac monitoring should be instituted and two large-bore IV lines established. In the setting of potential coagulopathy, venipuncture attempts should be minimized, and non-compressible entry sites (e.g., subclavian vein) should be avoided. As lines are placed, blood is drawn for initial laboratory analysis (complete blood count, coagulation studies, electrolytes, renal and hepatic function studies, and blood typing and screening).

Initial management of hypotension or shock should include vigorous fluid resuscitation with crystalloid (normal saline or Ringer's lactate) infusion and prompt antivenom administration. If organ perfusion remains inadequate after aggressive crystalloid infusion (e.g., 2 L in an adult, 20 to 40 mL/kg in a child) and antivenom, a trial infusion of 5% human albumin can be started (e.g., 250 to 500 mL for older children and adults and 15 to 20 mL/kg for infants and young children, given intravenously and repeated in 30 minutes as needed). Evidence supports the usefulness of adding albumin early in this setting because of the rapid onset of increased vascular permeability after significant pit viper envenomation.[222] Vasopressors (e.g., dopamine) should be used to treat venom-induced shock only after adequate volume infusion and initiation of antivenom therapy. Prolonged, inadequately treated hypotension has been strongly implicated in fatal cases of envenomation.[71,105]

The mainstay of medical management of significant snake envenomation is prompt administration of appropriate antivenom in order to bind deleterious venom components that are being absorbed and circulated from the bite site.[129] Time is of the essence, because venom components can only be bound and deactivated before they attach to target tissues. Once attachment occurs, they cannot be displaced and will inflict damage. The goal is to halt the deleterious effects of circulating venom as quickly as possible. The medical team responsible for a snakebite victim should expeditiously begin the process of locating and obtaining appropriate antivenom. Hospitals in regions where snakebites are likely to occur should maintain a stock of

Emergency Department and Hospital Management of Pit Viper Snakebite

Includes: Rattlesnakes, Copperheads, and Cottonmouths (Water Moccasins)



12 When to Call a Physician-Expert

Direct consultation with a physician-expert is recommended in certain high-risk clinical situations:

- **Life-threatening envenomation**
  - Shock
  - Serious active bleeding
  - Facial or airway swelling
- **Hard to control envenomation**
  - Envenomation that requires more than 2 doses of antivenom for initial control
- **Recurrence or delayed-onset of venom effects**
  - Worsening swelling or abnormal labs (protime, fibrinogen, platelets, or hemoglobin) on follow-up visits
- **Allergic reactions to antivenom**
- **If transfusion is considered**
- **Uncommon clinical situations**
  - Bites to the head and neck
  - Rhabdomyolysis
  - Suspected compartment syndrome
  - Venom-induced hives and angioedema
- **Complicated wound issues**

If no local expert is available, a physician-expert can be reached through a certified poison center (1-800-222-1222) or the antivenom manufacturer's line (1-877-377-3784).

13 Maintenance Antivenom Therapy

- Maintenance therapy is additional antivenom given after initial control to prevent recurrence of limb swelling
  - Maintenance therapy is 2 vials of antivenom Q6H x 3 (given 6, 12, and 18 hours after initial control)
- Maintenance therapy may not be indicated in certain situations, such as
  - Minor envenomations
  - Facilities where close observation by a physician-expert is available.
- Follow local protocol or contact a poison center or physician-expert for advice.

14 Post-Discharge Planning

- Instruct patient to return for
  - Worsening swelling that is not relieved by elevation
  - Abnormal bleeding (gums, easy bruising, melena, etc.)
- Instruct patient where to seek care if symptoms of serum sickness (fever, rash, muscle/joint pains) develop
- Bleeding precautions (no contact sports, elective surgery or dental work, etc.) for 2 weeks in patients with
  - Rattlesnake envenomation
  - Abnormal protime, fibrinogen, or platelet count at any time
- Follow-up visits:
  - Antivenom not given:
    - PRN only
  - Antivenom given:
    - Copperhead victims: PRN only
    - Other snakes: Follow up with labs (protime, fibrinogen, platelets, hemoglobin) twice (2- 3 days and 5-7 days), then PRN

15 Treatments to Avoid in Pit Viper Snakebite

- Cutting and/or suctioning of the wound
- Ice
- NSAIDs
- Prophylactic antibiotics
- Prophylactic fasciotomy
- Routine use of blood products
- Shock therapy (electricity)
- Steroids (except for allergic phenomena)
- Tourniquets

16 Notes:

- **All treatment recommendations in this algorithm refer to Crotalidae polyvalent immune Fab (ovine) (CroFab®).**
- This worksheet represents general advice from a panel of US snakebite experts convened in May, 2010. No algorithm can anticipate all clinical situations. Other valid approaches exist, and deviations from this worksheet based on individual patient needs, local resources, local treatment guidelines, and patient preferences are expected. **This document is not intended to represent a standard of care.** For more information, please see the accompanying manuscript, available at www.biomedcentral.com.

FIGURE 35-32 Unified treatment algorithm for the management of pit viper snakebite in the United States. *(From Lavonas EJ, Ruha AM, Banner B, et al: Unified treatment algorithm for the management of crotaline snakebite in the United States: Results of an evidence-informed consensus workshop,* BMC Emerg Med *11:2, 2011. With permission.* http://www.biomedcentral.com/1471-227X/11/2.*)*

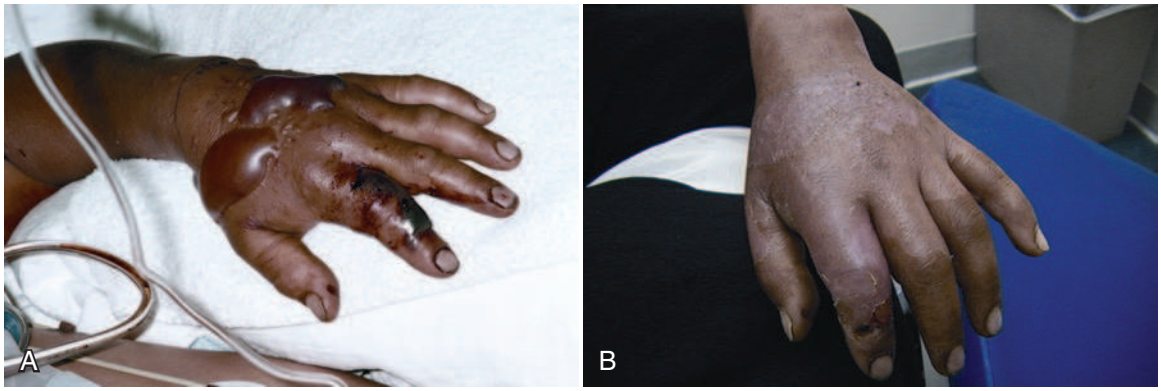


FIGURE 35-33 **A,** This patient was bitten by a 0.9-m-long (3-foot-long) southern Pacific rattlesnake (*Crotalus oreganus helleri*) 72 hours earlier. The snake hung on for 15 seconds, and the patient suffered an extraordinarily severe systemic envenomation. Prolonged fang contact is a factor associated with increased snakebite severity. These bullae were left in place, and the hand ultimately healed with no surgical intervention. **B,** Patient's hand at 3-week follow-up. At 1-year follow-up, this patient had nothing more than a slightly stiff index finger. *(Courtesy Sean P. Bush, MD.)*

antivenom at least sufficient to begin therapy and have plans in place to procure more as needed.

Figure 35-32 summarizes guidelines for managing pit viper bites in North America with CroFab Crotalidae Polyvalent Immune Fab (Ovine).[142] Initial control of envenomation may require larger doses of antivenom in the setting of thrombocytopenia, bleeding, neurologic abnormalities, or an otherwise severe bite.[263] Further details regarding antivenom use, including adverse reactions and their management, are found later in General Concepts of Antivenom Therapy.

Snake envenomation is a complex and dynamic syndrome best managed under the guidance of a physician experienced with the use of antivenom.[129] Regional poison control centers throughout the United States, under the auspices of the AAPCC, are staffed by trained personnel who maintain a list of physician toxinology experts available for consultation to assist with managing cases of native or exotic snakebite. The central emergency phone number is 1-800-222-1222. Centers that handle snakebite cases regularly include the University of Arizona Poison and Drug Information Center, Rocky Mountain Poison and Drug Center, and California Poison Control System, San Diego Division. The *Antivenom Index*, published jointly by the AAPCC and the American Zoo and Aquarium Association, lists antivenom sources within the United States. This list is readily available to poison control center personnel.

Analgesia and Wound Care. Pain can be substantial after pit viper envenomation. Analgesia is best obtained using titrated doses of narcotics. In the presence of hypotension, it may be prudent to start with a short-acting, easily titratable agent, such as fentanyl, until blood pressure stabilizes. Aspirin and nonsteroidal antiinflammatory drugs (NSAIDs) should be avoided because they may exacerbate coagulopathy.

Wound care for pit viper envenomation follows standard principles. Tetanus immunization is recommended if the patient's immunization is not up to date. Any wounds should be cleaned. The extremity is then kept above heart level to reduce swelling.

Wound infections from venomous snakebites are uncommon in North America, and prophylactic antibiotics are unnecessary in most cases.[60,250] A variety of bacteria, including *Clostridium* spp., *Bacteroides fragilis*, *Pseudomonas* spp., *Proteus* spp. and *Staphylococcus aureus,* have been isolated from the oral cavities of pit vipers.[92] *Aeromonas hydrophila* has been reported to cause necrotizing fasciitis after cottonmouth water moccasin (*Agkistrodon piscivorus*) bite.[6] If infection occurs, initial antibiotic choice should be broad to cover gram-positive and gram-negative bacteria, aerobes, and anaerobes and should be further guided by wound cultures and sensitivities.

Intact blisters should be protected as much as possible from rupture (Figure 35-33). Debridement of clearly necrotic tissue or ruptured blebs and bullae should await full reversal of any ongoing coagulopathy. The patient should begin a physical therapy regimen as soon as possible to expedite return of function.

Swelling of the bitten extremity can be quite severe after pit viper envenomation and is often accompanied by discoloration, tenderness, and pain on range of motion of the digits. This may raise clinical concern for a compartment syndrome. In most cases, however, most swelling occurs in the subcutaneous tissues. Compartment syndrome is an uncommon complication.[82,189] Muscle necrosis after pit viper envenomation is primarily caused by direct myotoxic venom effects rather than increased intracompartmental pressures.[83] Differentiating subcutaneous swelling from intramuscular swelling is achieved by objectively measuring intracompartmental pressures using a digital readout device. If compartmental pressure exceeds 30 to 40 mm Hg, antivenom should be started or continued while the extremity is elevated. The hemodynamically stable patient should receive IV mannitol (1 to 2 g/kg) over 30 minutes. These measures may reduce pressures to safe levels.[66] If pressures fail to decrease within 60 minutes and ischemia within the compartment is suspected, fasciotomy is required (Figure 35-34). Although animal evidence suggests that myonecrosis associated with venomous snakebite may actually be worsened by fasciotomy,[238] surgical decompression is necessary to prevent pressure necrosis of intracompartmental nerves.[109] A knowledgeable surgical consultant (hand, orthopedic, plastic, or general) should be involved if compartment syndrome is a possibility. Prophylactic fasciotomy is not recommended. In some patients with finger bites, if the vascular

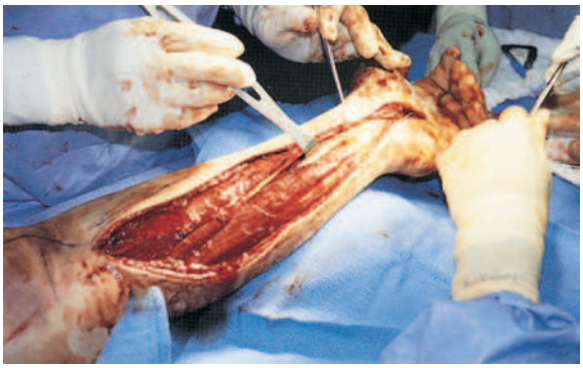


FIGURE 35-34 Rarely indicated fasciotomy in a victim of a severe bite from a rattlesnake (*Crotalus oreganus helleri*). Compartment pressures were greater than 60 mm Hg despite aggressive antivenom therapy. *(Courtesy Robert L. Norris Jr., MD.)*

supply to the digit is compromised despite antivenom and elevation of the extremity, digital dermotomy may be needed.

Occasionally, after a bite to a digit, severe necrosis results, requiring eventual amputation of the appendage. Such an extreme procedure should be delayed until a confident level of demarcation of damage can be ascertained. A digit may also require amputation if the bite results in severe contracture deformity and chronic, severe pain.

Disposition. Disposition decisions for patients bitten by pit vipers are generally straightforward. Admission to the hospital should be strongly considered for all persons with apparent envenomation. In one series, 53% of persons with minimal or no signs of envenomation at presentation subsequently developed significant envenomation with moderate to severe swelling, elevated PT, or thrombocytopenia.[124] Approximately 25% of these persons deteriorated more than 8 hours after envenomation. Even with apparent resolution of swelling, victims may later develop severe toxicity.[99]

Because onset and progression of signs and symptoms after a pit viper bite vary greatly, all potential victims should be closely watched in the emergency department (ED) for a minimum of 8 hours if not admitted to the hospital. Discharge may be considered after 8 hours for patients with no symptoms or signs other than puncture wounds. All laboratory studies and vital signs must be normal. On discharge, such patients should be instructed to return for onset of swelling, increased pain, bleeding, blood in the urine, severe headache, difficulty breathing, rash, joint pain, swollen lymph nodes, fever, or signs of wound infection. The patient should be scheduled for a follow-up reexamination in 24 to 48 hours and should be accompanied and assisted by another responsible adult. Because of the delayed onset of findings with some Mohave rattlesnake (*Crotalus scutulatus*) bites, all persons with suspected bites by this snake should be admitted to the hospital for 24 hours of observation. Admission is also highly recommended for children with potentially venomous snakebites.

Admission to an intensive care unit (ICU) is prudent for victims with severe envenomation or with progressive clinical findings despite initial antivenom administration. Persons bitten in the head, neck, or trunk should be monitored in an ICU because of the greater risks associated with these bites. Any patient who develops a serious acute reaction to antivenom should also be admitted to the ICU (see Adverse Reactions to Antivenoms, later). Patients who require a higher level of care than is available at the treating institution should be transferred to an appropriate facility, but antivenom therapy should be initiated before transfer. After antivenom infusion and clinical stabilization, patients with mild or moderate envenomation can be admitted to a regular hospital floor, but they should be carefully watched, particularly if repeat doses of antivenom are planned.

At hospital discharge, patients who received antivenom should be reminded about the possibility of developing serum sickness (see Adverse Reactions to Antivenoms, later) and the need for prompt medical attention if they develop fever, rash, arthralgias, myalgias, urticaria, or other findings consistent with serum sickness within the first few weeks after treatment. Patients should be warned of potential delayed onset or recurrence of coagulopathy for at least 2 weeks after envenomation and should have follow-up arranged for repeat testing within 2 to 3 days of their last dose of antivenom and again at 5 to 7 days (Figure 35-35). (see Antivenom Administration, later). They should be told to return if they experience any bleeding and to avoid high-risk activities (e.g., contact sports, mountain climbing) and elective surgical procedures during this time. Patients with substantial local tissue effects should have follow-up arranged for ongoing wound management and physical therapy.

Discharge instructions to patients should also include information on ways to prevent venomous snakebite. More than one-half of bites occur during intentional interactions with snakes.[184] These usually involve attempts to handle, harass, capture, or kill the animal. Typically, the bite is inflicted by a specimen in captivity. Avoiding intentional interaction with venomous snakes can prevent many injuries. Wearing shoes and long pants can prevent some strikes.[116] Children should be closely supervised in the outdoors and educated to be cautious around snakes. Animal control services should be called to remove snakes found close to human habitation. If a snake is encountered in the wilderness, people should carefully move a safe distance away as they enjoy the experience.

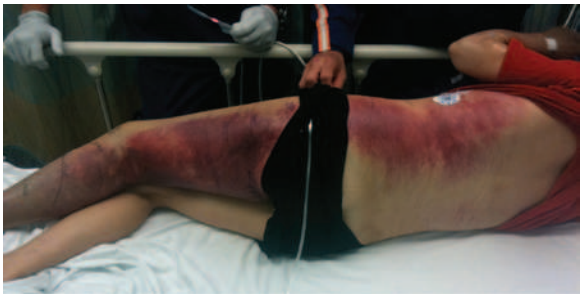


FIGURE 35-35 Victims of rattlesnake bite often develop delayed recurrence of coagulopathy up to 2 weeks after envenomation. This patient was bitten by a large northern Pacific rattlesnake (*Crotalus oreganus oreganus*) to the left foot. Her initial platelet count was 73,000/μL, and she received four vials of CroFab 2 hours after the bite. Platelet count improved to 238,000/μL 1 hour later. Laboratory results were otherwise normal, including hemoglobin and fibrinogen. Sixteen vials of antivenom were given during the hospital course, and the patient was discharged after 2 days with normal platelets, hemoglobin, and fibrinogen as well as regression of local effects. The patient returned 2.5 days after the last dose of antivenom and last laboratory blood draw with profound thrombocytopenia (platelets, 1000/μL), anemia (hemoglobin, 4 g/dL) and extensive ecchymosis (see photo). At no time did she develop hypofibrinogenemia. *(Courtesy Sean P. Bush, MD.)*

Coral Snakes. Hospital management of coral snake bite victims can be challenging (Figure 35-36). The first priority in the stable victim is to determine that a coral snake was actually the culprit. Photographs of coral snakes and nonvenomous mimics indigenous to the area can be useful. If a coral snake is identified and appears to have inflicted an effective bite, management should proceed in anticipation of a significant envenomation, even if systemic abnormalities are currently absent.

The patient should receive cardiac and pulse oximetry monitoring, and an IV line should be established. A history and careful physical examination should be performed; local findings are minimal, and fang marks can be difficult to see.[190] The patient typically has little or no swelling and variable local pain. The patient should be carefully assessed for any neurologic abnormalities. Aggressive airway management is essential with any sign of respiratory dysfunction or difficulty swallowing secretions. Early endotracheal intubation in such cases may prevent pulmonary aspiration and its complications. Bedside spirometry testing can be helpful in monitoring the respiratory status of these patients. Laboratory studies have little benefit, except for ABGs if respiratory insufficiency is suspected or endotracheal intubation is required.

The preferred therapy for an effective coral snake bite includes administration of appropriate coral snake antivenom. The only currently approved antivenom for coral snakes in the United States, Wyeth Antivenin (*Micrurus fulvius*) (equine), also known as North American Coral Snake Antivenin, has been discontinued by the manufacturer. At the time of this writing, there remains a single lot of this product with an extended expiration date of April 30, 2015. The first documented coral snake–related human death in the United States since the Wyeth Antivenin was initially released occurred in 2006.[192] Although this victim did not seek medical care, the case emphasizes the lethal potential in bites by these snakes and the need for an efficacious antiserum. Plans are reportedly in place for Pfizer to resume manufacturing a coral snake antivenom,[77] while research using other potential foreign coral snake antivenoms is underway. Physicians treating victims of coral snake bite in the United States should consult a poison control center for advice regarding availability of antivenom. In the absence of antivenom, treatment is supportive and includes

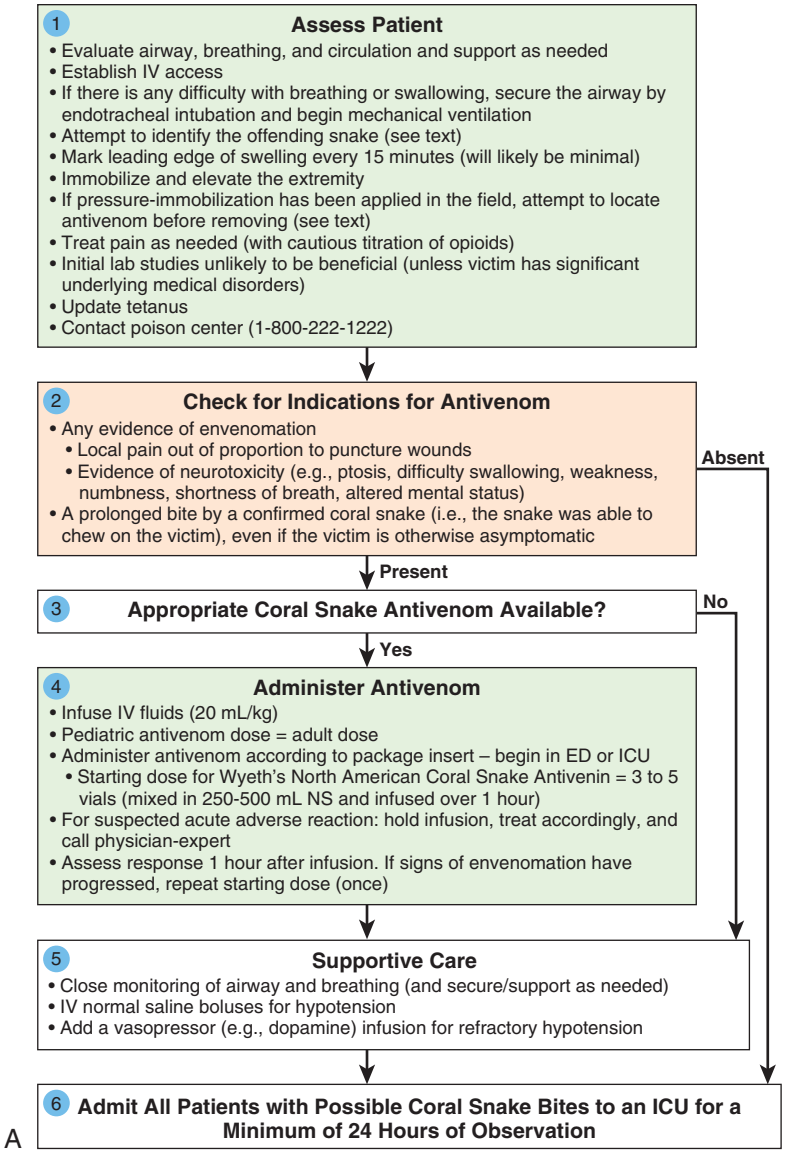


FIGURE 35-36 Emergency department and hospital management of possible coral snake bite in North America. Includes patients bitten by a brightly colored, unidentified snake in areas where coral snakes are indigenous.

ICU admission and early intubation at any sign of respiratory distress or difficulty swallowing oral secretions. Close observation for such complications should occur for at least 24 hours after the bite of a coral snake. If intubation is required, respiratory support may be required for as long as 1 week.[133]

Bites by the Sonoran coral snake (*Micruroides euryxanthus*) have always been managed supportively. There has never been an antivenom for this small, inoffensive species, and no deaths have been reported after its bite.[72]

The role for anticholinesterase agents in the management of bites by coral snakes remains to be determined. These agents have been used in some parts of the world to reverse postsynaptic neurotoxicity in patients envenomated by elapids (see Chapter 36).[244] Anticholinesterase drugs are not, however, a substitute for antivenom administration, and their use does not obviate the need for close monitoring of respiratory and cardiovascular status or airway control with ventilator support if the patient's status worsens.

In the unusual case of hypotension following coral snake bite, the victim should be initially resuscitated with intravascular crystalloids and antivenom if available. Once intravascular volume is expanded, vasopressors may be added as needed (e.g., dopamine, starting dosage 2.5 to 5 mcg/kg/min by IV infusion).

All patients who have possibly been bitten by a coral snake, even if asymptomatic, should be admitted to an ICU for 24 hours of close cardiac and respiratory monitoring.

GENERAL CONCEPTS OF ANTIVENOM THERAPY

Brief History

Antivenoms are immunobiologics designed to neutralize venoms. Scholars of ancient Greek history believe that King Mithridates VI of Pontus (132–63 BC) was the first documented user of immunotherapeutic principles. He ingested sublethal doses of numerous venoms in attempts to render himself immune to the toxins.[73] However, it was not until 1895 that French scientist Albert Calmette developed the first therapeutic antivenom, against the monocellate cobra, *Naja kaouthia*.[43]

In the early 1900s, Brazilian physician Vital Brazil worked to develop and distribute antivenoms for various venomous snakes in South and Central America.[103] To ensure a sufficient venom supply to conduct his research, Dr. Brazil worked with the Brazilian government to provide free rail passage for all snakes shipped to his institute. Participants sending snakes received free snake-capture equipment and transport crates, as well as one vial of antivenom per snake.[103] His work greatly decreased Brazil's snakebite mortality,[19,103] and he subsequently founded the now-famous Instituto Butantan in São Paulo, which still produces antivenoms.

These products were historically termed *antivenins*, derived from *venin,* the French word for "venom." In 1981, however, the World Health Organization (WHO) declared that the preferred term in the English language is *antivenom*.[261] Although modern purification processes have improved tremendously over the years, the basic principles of antivenom production remain the same. Antivenom continues to be the mainstay of treatment for bites and stings of many venomous creatures. Antivenoms exist for various species of snakes (see also Chapter 36), spiders (discussed in Chapter 43), scorpions (discussed in Chapter 44), and for some marine creatures (discussed in Chapters 74 and 75).

Antivenom Production

Antivenoms are currently produced by injecting animals, such as sheep or horses, with sublethal doses of venom. This is done repeatedly and with gradual escalation in dose until the animals develop antibodies directed against the venom proteins. Serum is then removed and purified to extract the useful IgG antibodies while filtering out potentially harmful foreign proteins. Antivenoms are generally lyophilized and require reconstitution before administration. Some antivenoms are available as liquids and require a cold chain for storage. After it is given to a snakebite victim, antivenom imparts immediate passive immunity against venom antigens circulating in the body. Most antivenoms are administered intravenously, although a few may be given intramuscularly (e.g., widow spider [*Latrodectus*] antivenom and box jellyfish [*Chironex fleckeri*] antivenom [see Chapters 43 and 74]).

Antivenom may be produced by immunizing an animal against a single species of venomous creature, in which case it is referred to as "monovalent." It may also be made by immunizing an animal against several different species, making it "polyvalent." Mixing several monovalent products together produces a "mixed monovalent" product that covers all species included in the mix. Monovalent antivenoms provide antibodies against the venom of one particular species and therefore necessitate precise identification of the offending snake. Polyvalent and mixed monovalent antivenoms contain antibodies against a number of different species; exact identification is not as important, as long as the offending species is covered by the product chosen. Use of a broad-spectrum antivenom results in administration of extraneous, potentially allergenic foreign proteins that are of no benefit to the victim. Antivenoms often provide some cross-protection among species with closely related venoms. For example, CroFab, an antivenom derived from four North American pit viper species, has an FDA-approved indication for all North American pit vipers; however, cross-protection has not been studied for all species, and efficacy may vary from snake to snake.[34,62,63] In contrast, specimens of the same species of snake from different regions may have substantial venom differences that limit the efficacy of antivenoms produced with specimens outside the region where the bite occurred. Good examples of this include Russell's vipers (*Daboia russelii*) in Asia and carpet and saw-scaled vipers (*Echis* spp.) of middle Asia and Africa.[262]

An IgG antibody molecule contains two functional domains (Figure 35-37). The desired effects of antivenom administration, binding and neutralization of venom, are achieved by the two Fab fragments. The IgG molecule also contains an Fc or effector region, which activates the immune system and may lead to immediate hypersensitivity reactions. The fear of allergic reaction is a reason why many physicians unfamiliar with the treatment of envenomation may be hesitant to use antivenom, even in situations where it is clearly indicated.

Newer methods of antivenom production attempt to retain the useful Fab fragments of the IgG molecule while eliminating the allergenic Fc fragment. Two different methods of cleaving the IgG molecule are used. Cleavage with pepsin or trypsin yields a single $F(ab')_2$ fragment and an Fc fragment (Figure 35-38), whereas cleavage with papain yields two Fab fragments and an Fc fragment (Figure 35-39). The various fragments have different

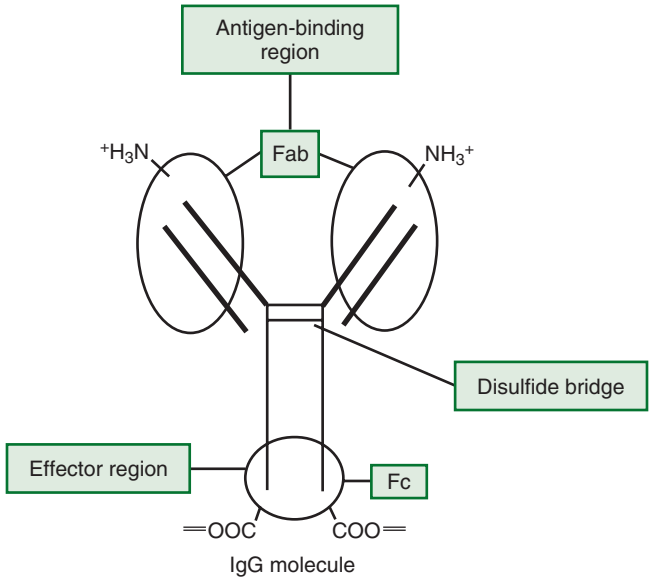


FIGURE 35-37 Schematic diagram of immunoglobulin G (IgG) molecule. The antigen-binding region (Fab portion) is present at the amino-terminal end. The effector region (Fc portion) interacts with the immune system cells and resides at the carboxyl end of IgG. Note the disulfide bridge.

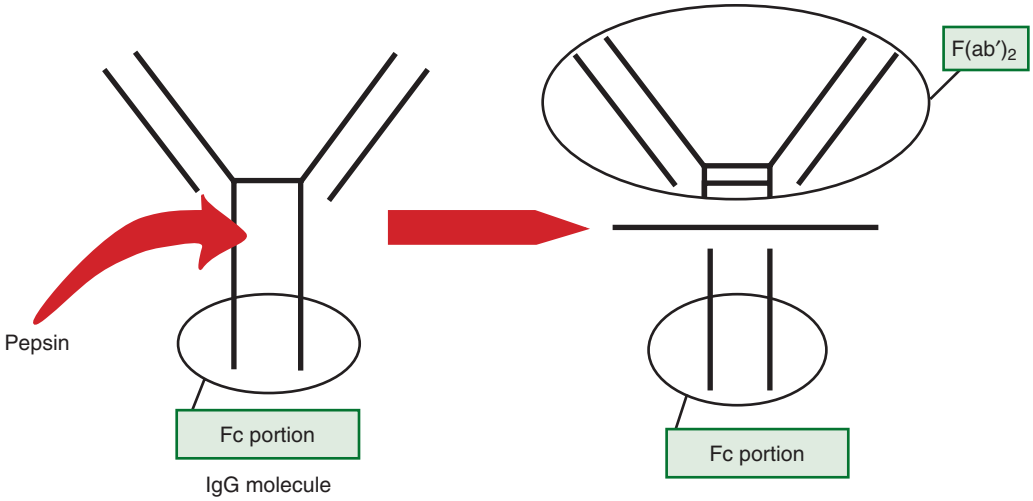


FIGURE 35-38 Proteolytic cleavage of IgG results in predictable substituent fractions. Pepsin digestion produces Fc and $F(ab')_2$ fractions for each IgG molecule. $F(ab')_2$ consists of two Fab portions connected by a disulfide bridge. The molecular weight of $F(ab')_2$ is 100,000 daltons.

advantages and disadvantages when compared with one another and with the parent IgG molecule.

An ideal antivenom would have pharmacokinetics and dynamics similar to those of venom. A whole IgG molecule has a long half-life, and the venom-antivenom complex is slowly removed by the reticuloendothelial system (RES). Because venom may be slowly absorbed into the circulation over time from a "depot" of venom at the bite site, the persistence of whole IgG may help to prevent the phenomena of recurrent or delayed venom effects requiring repeat antivenom dosing. However, this persistence also leads to increased rates and severity of delayed hypersensitivity reactions. The longer the antigen-antibody (i.e., venom component-antivenom) complex circulates, the more likely that host antibodies will be formed against this foreign complex. These host antibody-antivenom immune complexes may then precipitate in susceptible tissues (e.g., skin, synovium, glomeruli) to cause serum sickness (see Adverse Reactions to Antivenoms, later). Additionally, the fact that the whole IgG molecule retains the immunogenic Fc fragment (as well as other non–venom-neutralizing proteins) leads to an increased risk for immediate hypersensitivity reactions.

These principles are supported by clinical data. Antivenin (Crotalidae) Polyvalent (ACP) (equine), a whole IgG product that is no longer available, was reported in the literature to have at least a 20% rate of immediate hypersensitivity reactions, and at least 50% of patients who received it developed delayed serum sickness.[70] Acute reactions were often persistent and difficult to treat. A meta-analysis of the incidence of acute and delayed immunologic reactions to CroFab suggest that these numbers are approximately 8% and 13%, respectively.[223]

Reaction rates also appear to be relatively low with quality $F(ab')_2$ products. A study evaluating acute reaction rates with Thai green pit viper (*Trimeresurus albolabris*) and cobra (*Naja kaouthia*) equine $F(ab')_2$ antivenoms revealed rates of 2.3% and 12.5%, respectively.[239]

Another potential benefit of Fab fragment antivenoms is that their smaller molecular sizes may allow better penetration into tissue compartments and larger volumes of distribution compared

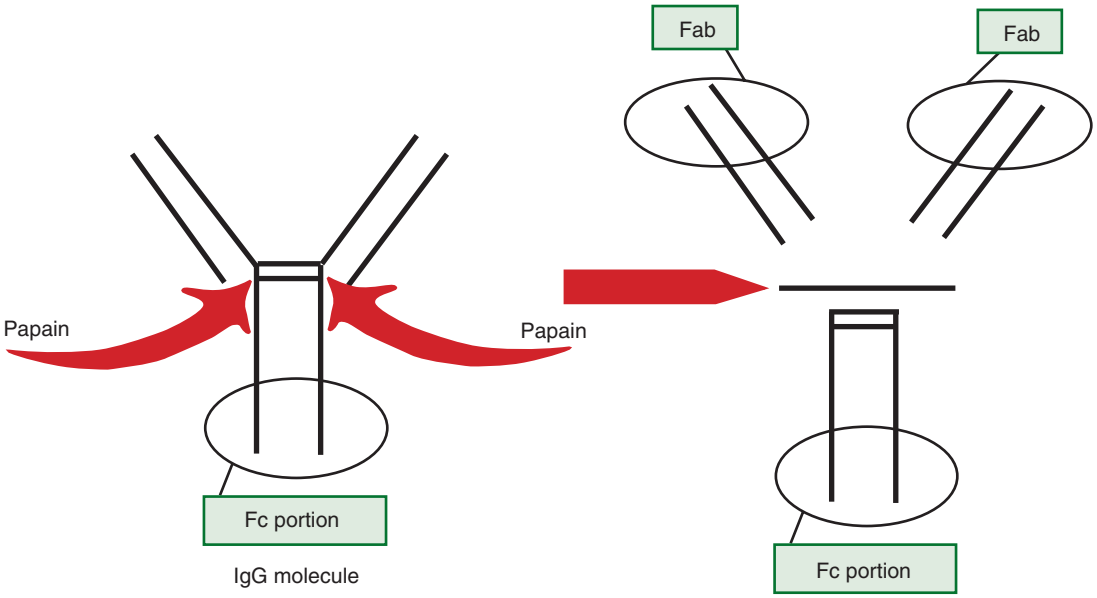


FIGURE 35-39 Proteolytic cleavage of IgG results in predictable substituent fractions. Papain digestion yields the Fc and two Fab segments for each IgG molecule. The molecular weight of Fab is 50,000 daltons.

to whole-IgG antivenoms.[225] Further work is needed to elucidate the clinical importance of this potential size advantage.

One clear drawback to Fab antivenoms is that they are cleared more quickly by the kidneys, resulting in a shorter half-life than whole-IgG antivenoms cleared by the RES.[225] The half-life for whole-IgG antivenoms is 61 to 194 hours, whereas that of a Fab product such as CroFab is probably less than 12 hours.[18] This is likely responsible, to some degree, for the recurrence of venom effects that often follows initial control with Fab antivenoms, necessitating repeat or maintenance antivenom dosing. With CroFab, recommended maintenance dosing after initial control of the envenomation process is two vials every 6 hours for three additional doses (see Figure 35-32).[63] Even with such redosing, however, rattlesnake bite victims have a significant rate of recurrent thrombocytopenia and/or coagulopathy, which may be relatively unresponsive to further doses of CroFab and difficult to manage.[17,225] Patients may develop severe thrombocytopenia (platelet counts <10,000/mm^3) and/or complete defibrination (undetectable fibrinogen and elevations in PT) about 2 to 12 days after initial treatment. Clinical bleeding is rare, although recent case reports have emerged of patients with delayed life-threatening or even fatal bleeding after initial stabilization with CroFab.[78,131,141,181,194] The risk of bleeding, including severe bleeding, appears to be further increased if the patient is receiving antiplatelet or anticoagulant therapy when bitten.[144]

Research is ongoing in an effort to find ways effectively to prevent or mitigate delayed or recurrent coagulopathy. For example, alternative dosing regimens for Fab antivenom, such as by continuous infusion, are being explored.[40] Use of larger-molecular-weight F(ab′)$_2$ antivenom, with its longer circulation half-life compared to an Fab product, may also reduce the risk of delayed or recurrent coagulation problems.[16] In a recent prospective, blinded, multicenter, randomized controlled clinical trial, a Crotalidae equine immune F(ab′)$_2$ antivenom (Anavip) was compared to CroFab. This study of 114 patients bitten by pit vipers in the United States demonstrated a 20% to 25% absolute risk reduction in recurrent and late-onset coagulopathy in the F(ab′)$_2$ group.[39] In the study, the only patients who, after initial control of envenomation, developed fibrinogen levels less than 60 mg/dL or platelet counts less than 50,000/mm^3, or evidence of medically significant late bleeding, were in the Fab group. There were no differences in immediate or delayed hypersensitivity reactions between the two antivenoms.[39] At the time of this writing, Anavip is still pending FDA approval, and a patent infringement lawsuit settlement stipulates that it will not be commercially available until 2018.[254] Once available, the starting dose for Anavip will be 10 vials, with each vial reconstituted in 10 mL of normal saline, then added to a 250-mL bag of normal saline and infused over 60 minutes. Additional 10-vial doses may be infused as needed to gain initial control of envenomation. Maintenance dosing will likely not be necessary; however, if reemerging symptoms occur, including coagulopathies, they can be suppressed with additional 4-vial doses as needed. Having a second choice of antivenom available for treating pit viper envenomation in the United States and Canada may help reduce the current high financial costs of treating these bites.

One drawback with current antivenom production techniques using sheep or horses is the expense of maintaining the animals and the laborious nature of extracting and purifying animal sera. Research is being done using chicken hens immunized against snake venoms as a source of antivenoms. Anti–snake venom antibodies (IgY) can then be extracted from the yolks of the hens' eggs.[2] The costs associated with obtaining and maintaining chickens is much lower than that of large mammals, and the antibody extraction process is less labor intensive. Each egg produces between 80 and 120 mg of antibodies, and the antibodies remain present in the eggs for 100 days after immunization.[75,171] Preliminary studies (animal models and neutralization studies) using avian antivenoms produced against the Russell's viper (*Daboia russelii*), saw-scaled viper (*Echis carinatus*), Indian cobra (*Naja naja*), and the banded krait (*Bungarus caeruleus*) have demonstrated efficacy.[176,177]

In addition to traditional methods of antivenom production, researchers are studying polymer nanoparticle technology to create synthetic plastic antibodies. Nanoparticles are polymerized in the presence of a target molecule (i.e., venom components) in a process known as "imprinting." The resultant polymers bind to target proteins with affinity similar to antibodies produced in animals. The particles are inert and have low affinity for molecules other than the ones with which they are imprinted. The cost of production would likely be relatively low compared with animal-derived antivenoms. Thus far, researchers have created nanoparticles that successfully bind to mellitin, a key component of honeybee venom.[120]

Indications for Antivenom

With regard to pit viper bites, antivenom is indicated for patients presenting with progressive local findings or any evidence of systemic envenomation. This includes evidence of worsening local injury or presence of thrombocytopenia, coagulopathy, or other systemic effects (e.g., hypotension, muscle weakness). Antivenom can generally prevent progression of venom effects, but cannot reverse all effects (e.g., tissue damage) that have already been set in motion. For this reason, antivenom is usually more effective the earlier it is administered. However, if ongoing venom effects, such as persistent thrombocytopenia or coagulopathy, are noted, antivenom may still provide benefit when administered late in the course of envenomation.[8] Of note, antivenom, not blood products, is the first-line treatment in patients with venom-induced coagulopathy or thrombocytopenia. Although blood products may be indicated in patients with severe active bleeding,[28] antivenom should always be administered first to avoid fueling an ongoing consumptive coagulopathy.

Different recommendations exist when antivenom is indicated for late recurrence of thrombocytopenia and coagulopathy, to some extent based on bleeding risks in patients with other bleeding disorders, such as leukemia, congenital hypofibrinogenemia, and overtreatment with oral anticoagulants. It is generally accepted that severe thrombocytopenia (platelet counts <25,000/mm^3) or combined thrombocytopenia and significant coagulopathy should be treated with repeat antivenom dosing. There is controversy, however, as to whether isolated delayed coagulopathy or hypofibrinogenemia without thrombocytopenia requires treatment, as well as how many vials should be administered.[17,46] A reasonable approach is to follow patients who developed coagulopathy during their acute envenomation with repeat blood work at 2 to 3 days after antivenom therapy and again at 5 to 7 days. Thereafter, follow-up should be as needed (ongoing until hematologic disturbances have resolved and wounds are healing). On follow-up, if hematologic derangements have developed or recurred, antivenom should be repeated for any of the conditions in Box 35-1.[17] Large doses (up to 10 vials of CroFab) may be required to reverse delayed hematologic effects, which appear to become less responsive to antivenom over time.[227] If significant active bleeding is present, it may necessitate transfusion with platelets, packed RBCs, fresh-frozen plasma, and/or cryoprecipitate in addition to antivenom. Patients who must receive aspirin or anticoagulants may also require more aggressive treatment.

BOX 35-1 Indications for Administration of Additional Antivenom in Patients with Recurrent Coagulopathy or Thrombocytopenia After Initial Control*

- Evidence of clinically significant bleeding
- Platelet count below 25,000/mm^3
- INR greater than 3
- aPTT greater than 50 seconds
- Fibrinogen less than 50 mg/dL
- Presence of multicomponent coagulopathy
- Worsening trend in a patient with prior severe coagulopathy
- High-risk behavior for trauma
- Certain comorbid conditions (e.g., systemic vasculitis, seizure disorders, prior stroke)

aPTT, Activated partial thromboplastin time; *INR*, international normalized ratio.
*See Indications for Antivenom section.

Antivenom Administration

When possible, it is prudent to obtain informed consent from the patient before administering antivenom because of the risks of adverse reactions (see Adverse Reactions to Antivenoms, next). Snake antivenoms should be administered intravenously.[173] Other routes of administration are inadequate to allow effective circulation of the antiserum for quickly binding venom components. Many antivenoms, including CroFab, are supplied in lyophilized form and require reconstitution before administration. Although the manufacturer of CroFab recommends reconstituting each vial to be given with 18 mL of sterile water for dilution, it appears that using 25 mL per vial and hand-mixing by continuous rolling and inverting of vials significantly reduces the amount of time it takes to get the product into solution and ready for administration.[206] All reconstituted vials that are to be administered should then be injected into a 250-mL bag of normal saline for IV infusion. The infusion should be started slowly, with the attending physician at the bedside to intervene at the first evidence of any acute adverse reaction. All drugs and equipment needed to treat acute anaphylaxis should be immediately available. The infusion is run slowly over the first 10 minutes, and in the absence of an acute reaction, the rate is increased to achieve the total starting dose administered over 1 hour.

Adverse Reactions to Antivenoms

The most common adverse reactions associated with antivenom administration are immediate and delayed hypersensitivity reactions. Immediate hypersensitivity reactions include type I allergic anaphylaxis and clinically indistinguishable, nonallergic anaphylaxis (anaphylactoid reaction). Allergic anaphylaxis results from IgE-mediated mast cell and basophil degranulation and requires prior sensitization. Clinical manifestations may include urticaria, angioedema, laryngeal edema, bronchospasm, and hypotension. Anaphylactoid reactions produce the same clinical findings through direct mast cell and basophil degranulation or complement activation by heterologous antivenom proteins, without involvement of IgE, and thus do not require prior sensitization. Such reactions may be related to the dose, concentration, and infusion rate of the antivenom and are more common than true allergic anaphylaxis after antivenom administration.

Whenever antivenom administration is first started, the treating physician should be at the bedside to recognize the first signs of anaphylaxis and to intervene as needed. Immediate hypersensitivity reactions are managed by temporarily stopping the antivenom infusion and immediately treating with epinephrine. The safest and most effective route of administration of epinephrine is 0.01 mg/kg (up to 0.5 mg) given intramuscularly into the thigh. Epinephrine should only be administered intravenously if hypotension is profound, via slow infusion, and titrated to clinical effect (see Anaphylaxis, Chapter 67). Crystalloid fluid infusions should also be used if hypotension is present. Antihistamines (both H_1 and H_2 blockers) and corticosteroids should be administered intravenously as second-line therapy for anaphylaxis. Once the reaction has been reversed, the antivenom infusion should be restarted. If the reaction was particularly severe and more life threatening than the envenomation, it may be necessary to proceed with management of the envenomation without further antivenom. In all such cases, an expert in envenomation medicine should be consulted for assistance.

It is not possible accurately to predict patients who will have an acute reaction to antivenom. Skin testing is of no benefit in this regard and should not be used.[239,257] Patients who have previously received antivenom may be at some increased risk for allergic reaction, but this is not a contraindication to antivenom use.[59] Other patients at increased risk include those with known allergy to horse or sheep serum (depending on which animal was used to prepare the antivenom), and those with known allergy to papaya or papain. Patients taking β-adrenergic blocking agents are also of concern, because this may predispose to refractory anaphylactic reactions. In all these patients, a careful risk/benefit analysis should be done based on severity of envenomation before deciding whether to proceed with antivenom therapy. If the risk for reaction is deemed high, extra care should be taken and pretreatment with antihistamines may be considered, although this strategy is unproven.

Delayed, type III hypersensitivity reactions, or serum sickness, may occur a few days to a few weeks after antivenom administration.[80] Such reactions result from vascular deposition of immune complexes (host antibody-antivenom) in tissues such as the skin, kidneys, and synovium. Clinical findings may include fever, rash, arthralgias, neuropathies, and renal dysfunction. The presence of non-neutralizing proteins in whole-IgG antivenoms and their prolonged elimination half-life make serum sickness more likely and often more severe than that with Fab or $F(ab')_2$ fragment products.[70] Delayed hypersensitivity reactions are generally not life threatening, although they may be quite debilitating. Serum sickness should be treated with oral corticosteroids (e.g., prednisone, 1 mg/kg/day) until the symptoms have resolved and then tapered over approximately 1 week. Symptomatic relief can be further provided with oral antihistamines and acetaminophen. Clinical illness usually resolves in 1 to 2 weeks with appropriate therapy.

SPECIAL SNAKEBITE SCENARIOS

Allergy to Reptile Venom

Snake (and lizard) venoms are highly immunogenic substances. Occasionally, a bitten victim presents with an acute, allergic anaphylactic reaction.[27,95,204] The risk for such reactions increases in persons previously bitten by venomous reptiles or those who work with venoms (e.g., in a venom-extraction or research facility, particularly if they work with lyophilized venoms that may become airborne and lead to respiratory or mucous membrane exposure). In addition, snake venoms can trigger an autopharmacologic response in victims, with resulting release of vasoactive compounds (e.g., histamine, bradykinin) that cause nonallergic anaphylactic (anaphylactoid) reactions.[45,224] The presentation in either scenario can be typical for anaphylaxis, with bronchospasm, laryngeal edema, hypotension, and urticaria, but differentiating between an acute immunologic reaction to venom and severe, direct venom toxicity can be difficult. If the precise etiology for hypotension or respiratory distress is unclear, treatment can be rendered for anaphylaxis (beginning with intramuscular aqueous epinephrine 1:1000, 0.01 mg/kg up to 0.5 mg) while antivenom preparation (in the case of snakebite) and supportive care proceed.

Bites in Children

When children are bitten by venomous snakes, they receive venom loads similar to those received by adults, resulting in higher relative venom doses per unit body weight. It remains unclear, however, whether children sustain more severe envenomations.[64,195,226,249] Dosing of antivenom in pediatric victims is the same as for adults. Antivenom is not dosed with any weight-based formula. With adequate antivenom administration, children do not appear any more susceptible to systemic venom effects than adults.[71]

The total volume of diluent used in administering antivenom in children can become a factor, particularly in very small children (<10 kg) or those with underlying cardiovascular, pulmonary, or renal disease.[195] In such patients, the total volume of diluent can be reduced as needed. For CroFab, the recommended dilution of the total initial dose in 250 mL of saline is a reasonable volume tolerated by most children weighing more than 10 kg.

CroFab appears to be safe and effective in children.[205] Although CroFab is preserved using thimerosal, an organic mercury-containing preservative, its benefit far outweighs any mercury toxicity risks when used in young children, because the maximum total mercury contained in a vial is 104.5 mcg, resulting in a total exposure of no more than 1.9 mg of mercury in a child receiving a large (18-vial) total dose of this product.[63,96,195]

Bites in Pregnant Women

Snakebites are uncommon in pregnant women. Although likely influenced by publication bias, a review of worldwide reports of such cases found the rate of maternal death to be approximately

4% and fetal loss to approach 20%.[138] Preterm labor, abruptio placentae, and fetal and neonatal deaths have been reported after pit viper envenomation.[138,198,266] Anticoagulant and proteolytic actions in many crotaline venoms are probably responsible for disrupting the integrity of placental attachment to the uterus. To inhibit these systemic venom effects, antivenom administration is important, even though all U.S. antivenoms carry an FDA Category C designation for safety in pregnancy. Fetal malformations after antivenom use have been described,[167] but the benefits of antivenom outweigh the risks in this population (although informed consent should be obtained if possible). Standard doses of antivenom should be used.

If an acute allergic reaction develops during antivenom administration, antivenom should be temporarily stopped. Epinephrine should be avoided, if possible, because of its adverse effects on uterine blood flow. Instead, ephedrine should be given at a dose of 5 to 25 mg by slow IV push.[199] This dose can be repeated every 5 to 10 minutes as needed (maximum, 150 mg in 24 hours). If the reaction is refractory to ephedrine, however, epinephrine should be used. Other drugs (e.g., antihistamines, corticosteroids) should be given as for the nonpregnant patient. Antivenom administration can usually be restarted in a more dilute concentration and at a slower rate. Additional consultation with an envenomation specialist is advisable.

Other management principles for snakebitten pregnant women include early obstetric consultation, fetal monitoring, and early ultrasonography for fetal and placental assessment.

Exotic Snakebites

Traditional zoos and animal parks usually maintain popular collections of exotic venomous snakes. Given strict safety measures, however, zoo personnel are rarely bitten. When such a bite occurs, most institutions have well-developed response plans that include transporting the victim, with an appropriate antivenom drawn from its stock, to a specific hospital for treatment. Given that many of these antivenoms are foreign products sourced from outside the local hospital, it is advantageous for zoos to have a prearranged plan with the medical facility for how such cases will be handled. Failure to do so could result in costly delays in administration of an exotic antivenom with which the treating provider is unfamiliar and uncomfortable.

More problematic are private individuals in the United States and other countries who keep exotic venomous snakes in "underground" collections, often in their homes. As a result, a physician anywhere in North America may see a victim who has been bitten by a king cobra (*Ophiophagus hannah*), a black mamba (*Dendroaspis polylepis*), or some other exotic species. In 2013, 86 exotic snakebites were reported to the AAPCC, with 49 of these confirmed as venomous.[187] Management principles in these cases are similar to those outlined earlier (see also Chapter 36). Such cases present unique clinical challenges, however, given the potential lack of readily available antivenoms for exotic species (most private collectors do not maintain a supply of antivenoms). The online *Antivenom Index* is a helpful resource to locate U.S. stores of exotic antivenoms. This resource can be accessed through a regional poison control center. Additionally, the Miami-Dade Fire Rescue Venom Response Program stocks rare and exotic antivenoms and may be willing to ship or transport antivenom to other locations when needed.[180]

Injuries Caused by Giant Snakes

Snakes of the family Boidae (subfamily Boinae, the boas; subfamily Pythoninae, the pythons) have become quite popular as exotic pets in the United States. Although not venomous, larger boids can cause serious bites and even deaths in humans. Bites by large snakes can be quite painful, with substantial local bleeding from multiple puncture wounds inflicted from numerous fine, sharp teeth in the upper and lower jaws. If the victim reflexively jerks the bitten body part away from the snake, substantial skin tears can occur. Teeth may be dislodged and remain embedded in the victim's soft tissues. Bleeding generally stops quickly with direct pressure. Management includes cleaning the wounds, updating tetanus status as needed, and attempting to rule out retained teeth. Soft tissue radiographs or ultrasound can be used for this purpose. If teeth are not seen, the patient should still be warned of the possibility of retained teeth and instructed to return with any evidence of secondary infection. Antibiotics are not indicated unless an infection occurs.

The boids kill prey by constriction. Every 1 or 2 years, a person is killed in North America by a large, captive boid. Implicated species include the Indian and Burmese pythons (*Python molurus* ssp.), African rock python (*P. sebae*), reticulated python (*P. reticulatus*), amethystine python (*Morelia amethistina*), and anaconda (*Eunectes murinus*). In human fatalities, the constriction may occur in several situations. Victims, including adults, may be killed by a snake that is draped over their shoulders as they clean its cage, or as they sleep in a house with a snake that has escaped from its enclosure or been allowed to roam freely. In all such cases, the snake wraps the victim's neck and body in its coils, and the victim dies as a result of asphyxiation.[172,196] Precautions against such tragic events include maintaining the animal in a secure, escape-proof, and locked enclosure; never cleaning or feeding a large boid while alone; never keeping large boids in the home of a small child; and never allowing children to handle large boids unsupervised. Any boid in excess of 2 m (6.5 feet) in length should be handled with caution. There are no documented cases of humans actually being consumed by giant snakes in the United States, and if this occurs in regions of the world where these animals are found in the wild, it is an exceptionally rare occurrence.

MORBIDITY AND MORTALITY

Pit Vipers

Reliable numbers for morbidity and mortality from snakebite in North America are not available, but it is generally accepted that deaths in the United States and Canada are uncommon. Recent assessments suggest that annual snake-related fatalities average fewer than six per year (range, 0 to 12) in the United States, ranking snakes far behind dogs and stinging insects in terms of animal-related fatalities.[137,139] Another source of information on snakebite-associated morbidity and mortality is the AAPCC. Over a 31-year period (1983 to 2013), 50 deaths from endemic venomous snakes were reported to the AAPCC[21-26,136,145-162,186, 187,242,245-247] (Table 35-4). When the reptile implicated was identified, it was most often a rattlesnake. These numbers are underestimates and can be used only as a rough gauge of incidence and mortality. Not all venomous snakebites, even fatal ones, are reported to the AAPCC. Snakebite is not classified as a reportable disease, and no reliable government statistics exist.

Although causes of death vary following venomous snakebite, delay in reaching emergency medical care is a major contributing factor.[107] When death results, it may rarely occur within a few minutes, or more frequently, it can take several hours to days. A quick death can be caused by anaphylactic or anaphylactoid reactions to venom or antivenom (see Allergy to Reptile Venom and Adverse Reactions to Antivenoms, earlier), by venom-induced respiratory insufficiency, or by airway obstruction after bites to the head or neck. Prolonged hypotension, shock, and tissue hypoxia can lead to hypoxic encephalopathy, cerebral edema, and herniation. Venom-induced coagulopathies can lead to life-threatening bleeding complications, such as intracranial or gastrointestinal bleeding. Multiinfarct encephalopathy has been observed to occur in patients with true disseminated intravascular coagulation (DIC), which is very rare. Similarly rare is true ischemic stroke following pit viper envenomation in the United States.[38] Renal failure may take several days to manifest and can cause death if untreated. Comorbidities, such as coronary artery disease, can affect the chances of succumbing to snakebite. Iatrogenic complications, such as adverse drug reactions or nosocomial infections, can also lead to death. Before the introduction of Wyeth's pit viper antivenom in 1954, mortality rates were estimated to be as high as 5% to 25%.[201] After that time, mortality rates in patients treated without antivenom declined to approximately 2.6%, largely because of improvements in other aspects of care (e.g., development of ICUs and fluid resuscitation principles). Antivenom, however, further reduced the mortality rate

Text continued on p. 757

TABLE 35-4 Snakebite-Related Deaths Reported to the AAPCC, 1983-2013

Year	Total Bites Reported*	Deaths	Specifics of Deaths
1983	717	1	*1 rattlesnake*
1984	1347	1	*1 rattlesnake*
1985	1676	0	—
1986	2416	0	—
1987	2701	1	*1 rattlesnake*
1988	3076	0	—
1989	3851	1	*1 prairie rattlesnake*: A 27-year-old man was bitten on two fingertips by a 2-foot-long prairie rattlesnake (*Crotalus viridis*, formerly *C. v. viridis*). He arrived in the ED 15 minutes later. Swelling rapidly progressed to the upper arm over the next 2.5 hours. He was pretreated with diphenhydramine, epinephrine, and methylprednisolone, and 5 vials of antivenom in 250 mL of D_5W were started. Twenty minutes later, 60% of the antivenom had been given, and he developed anaphylaxis. He was given IV epinephrine, and a cricothyroidotomy was performed; he could not be intubated because of laryngospasm. He suffered cardiac arrest. Autopsy revealed bronchospasm but no swelling of the upper airway.
1990	4461	0	—
1991	5255	1	*1 unidentified rattlesnake:* A 52-year-old man was bitten on his thumb by an unidentified rattlesnake in central Oregon at high altitude. In the ED 20 minutes later, he complained of circumoral numbness, tingling, and flushing. BP was 140/94 mm Hg, HR was 92, RR was 16. On his thumb were "two entrance wounds and minimal swelling." He had been given 6 mL of a solution of 5 vials of antivenom in 500 mL D_5W when he became diaphoretic and dyspneic with increased pulmonary secretions. He became near-syncopal. The antivenom was discontinued, and he was intubated and given epinephrine and steroids. He became hypotensive and developed asystole within 15 minutes. Laboratory values showed acidosis, hemoconcentration, and mild coagulopathy. Autopsy revealed extensive coronary artery disease.
1992	1055	2	*1 northern Pacific rattlesnake:* A 20-year-old man was handling a northern Pacific rattlesnake (*Crotalus oreganus oreganus*, formerly *C. viridis oreganus*) when it bit him on the lips. He collapsed, began vomiting, and was driven 3 miles to the hospital. He was intubated 40 minutes later, but he suffered cardiac arrest during the procedure. He was resuscitated for 30 minutes with epinephrine, atropine, and 5 vials of antivenom before recovering a sinus rhythm and BP of 100/60 mm Hg. He developed profound coagulopathy and was given 30 vials of antivenom. He was later determined to be brain dead. Autopsy showed brain edema and herniation. Blood alcohol level was 207 mg/dL. *1 black Indian cobra:* A 25-year-old male "snake expert" was bitten on the toe by his captive, pregnant black Indian cobra. He died within minutes. Autopsy revealed bloody pulmonary exudate, cerebral edema, and a fine petechial rash.
1993	5653	0	—
1994	6317	2	*1 presumptive Mohave "green" rattlesnake:* A 40-year-old man was bitten while working in bushes. He collapsed 20 minutes later. In the ED 4.5 hours later, he was comatose and in atrial fibrillation with labile BP. He was intubated for poor respiratory effort. Fasciculations and metabolic acidosis were noted. Two small puncture wounds, which had been initially overlooked, were noted 1 cm apart on the forearm and lower leg. The presumptive diagnosis of Mohave "green" rattlesnake (*Crotalus scutulatus scutulatus*) was made, and antivenom was administered. He was cardioverted to normal sinus rhythm and dopamine was started, but he remained hypotensive. He developed disseminated intravascular coagulopathy and died on day 8. *1 rattlesnake:* A 34-year-old male "snake handler" was bitten on the hand when he picked up a rattlesnake on the road. He collapsed 10 minutes later, and his family began CPR. When medics arrived 30 minutes later, he was in full cardiopulmonary arrest. He was intubated and given IV fluids, dopamine, antivenom, and hydrocortisone. He died within 3 hours. Autopsy revealed hemorrhage in the myocardium, alveoli, pancreas, and kidneys. The airway was patent, but there was laryngeal edema, pulmonary edema, and evidence of aspiration. His right coronary artery was 75% stenosed. Blood alcohol level was 118 mg/dL.
1995	7100	2	*1 canebrake rattlesnake:* A 35-year-old man was bitten near the radial artery while playing with a *Crotalus horridus atricaudatus* (now classified as *C. horridus*). He was asystolic when medics arrived 30 minutes later. At autopsy, no necrosis was noted. Blood alcohol level was 250 mg/dL. *1 unknown reptile*
1996	7494	0	—
1997	7045	2	*1 rattlesnake:* A 4-year-old boy bitten on the thigh was treated with 5 vials of antivenom and transferred. He was intubated en route and subsequently developed massive extremity swelling. He suffered cardiac arrest, was resuscitated and given additional antivenom, and then arrested again in the PICU 7 hours after envenomation. *1 venomous exotic snake*
1998	7194	0	—

Continued

TABLE 35-4 Snakebite-Related Deaths Reported to the AAPCC, 1983-2013—cont'd

Year	Total Bites Reported*	Deaths	Specifics of Deaths
1999	6832	2	*1 rattlesnake:* A 43-year-old man who was drinking with his friends was bitten on the hand by a rattlesnake presumed to be dead. After further ethanol consumption, he presented 1 hour later with complaints of hand pain and mild abdominal cramping. His HR was 134, RR 28, and BP 81/46 mm Hg. Tongue swelling, fang marks, and minimal edema of the hand were noted. Hypotension necessitated vasopressor therapy, and increased tongue edema was treated with diphenhydramine and corticosteroids. Unsuccessful attempts at intubation were complicated by hypoxia, and cricothyroidotomy was performed. Further treatment included sodium bicarbonate for metabolic acidosis, 1 unit of polyvalent antivenom, and fresh-frozen plasma. The course was complicated by acute renal failure secondary to hemolysis requiring hemodialysis, rhabdomyolysis, and prolonged ventilatory support. On day 13 in the hospital, cardiac arrest secondary to pulmonary embolism occurred, after which the patient was declared brain dead. *1 unknown snake*
2000	7316	2	*1 eastern diamondback rattlesnake:* A 2-year-old boy was bitten just proximal to the knee by an eastern diamondback rattlesnake (*Crotalus adamanteus*). Findings included one fang mark and minimal local signs. On arrival at the hospital, BP was 98/48 mm Hg and HR was 130. Listlessness, progressive swelling at the site of the bite, hypotension, and bleeding from his cutdown site, nose, mouth, and gastrointestinal tract ensued. Treatment included 90 vials of polyvalent Crotalidae antivenom, vasopressors, and blood products. Within 24 hours, he had fixed, dilated pupils and no response to pain. A CT brain scan revealed bilateral cerebral infarctions, and he was declared brain dead. *1 timber rattlesnake:* A 45-year-old man was bitten under the right nipple by a timber rattlesnake (*Crotalus horridus horridus,* now classified as *C. horridus*) during a snake-handling congregational meeting. Church members reportedly prayed over him for the next 2 days until he died. At autopsy, systemic petechiae, marked ecchymosis of his anterior chest wall, and hemorrhagic mediastinitis were noted.
2001	7463	2	*1 rattlesnake:* A 30-year-old man was comatose after a bite from his pet rattlesnake. In the ED, he was found to have coagulopathy and a subarachnoid hemorrhage. On admission, his INR was 5.5, and his platelet count was 7000/μL. He received 10 to 20 vials of crotalid antivenom and was admitted to the ICU. His condition continued to worsen, and life support was withdrawn on the day after admission. *1 unknown crotaline*
2002	7829	2	*1 timber rattlesnake:* A 43-year-old man was reportedly bitten by a timber rattlesnake (*Crotalus horridus horridus,* now classified as *C. horridus*) while he was trying to capture it. He was unstable in the ED 1 hour after the bite, requiring endotracheal intubation and epinephrine for a BP of 60/47 mm Hg. He was treated with 10 vials of crotaline polyvalent antivenom, diphenhydramine, corticosteroids, morphine, and diazepam. He was transferred to another hospital. An additional 16 vials of antivenom were administered. Dopamine and epinephrine were administered for hypotension. Four hours after the admission, there was laboratory evidence of coagulopathy. Six vials of Fab antivenom were given. Over the next few hours, he appeared to stabilize, and vasopressors were discontinued. Several hours later, epistaxis and bleeding from his mouth began. An additional 7 vials of antivenom, fresh-frozen plasma, platelets, and cryoprecipitate were given. Renal failure developed and required hemodialysis. By the third day, he had developed multisystem organ failure. He died on day 10 in the hospital. *1 rattlesnake*
2003	7952	2	*1 rattlesnake:* A 33-year-old man was hospitalized for a bite to his hand by a *Crotalus viridis lutosus* (now classified as *C. oreganus lutosus*). He was treated with CroFab and discharged within 24 hours after developing minimal symptoms. He was given a prescription for acetaminophen/oxycodone on discharge. That night he was noted to be snoring in bed and was difficult to arouse, and in the morning he was found dead in bed. Autopsy revealed pulmonary edema, thick secretions occluding the trachea and bronchi, and cerebral edema. Postmortem heart blood had an oxycodone concentration of 200 ng/mL. The medical examiner attributed the death to respiratory arrest from an opiate intoxication. *1 venomous exotic snake*
2004	8313	3	*1 canebrake rattlesnake:* A 55-year-old man was bitten on his hand by a captive canebrake rattlesnake (*Crotalus horridus horridus,* now classified as *C. horridus*) while feeding the snake. He became dizzy within seconds of the bite. He drove himself to a nearby ED, where he immediately became hypotensive and unresponsive. He was intubated, intravenous access was obtained, and pressors were started. He had a single puncture wound. The treating facility had no antivenom, so he was transferred to a regional referral hospital. He remained hypotensive most of the 2 hours from the time of the bite to arrival at the referral hospital. He was given 14 vials of CroFab and further resuscitation. However, he ultimately developed circulatory collapse, coagulopathy, and renal failure. He died 7 hours after the bite.

TABLE 35-4 Snakebite-Related Deaths Reported to the AAPCC, 1983-2013—cont'd

Year	Total Bites Reported*	Deaths	Specifics of Deaths
			1 unknown crotaline (*presumed copperhead*): A 50-year-old man was bitten on the finger by a snake presumed to be a copperhead (although not positively identified). He was treated with CroFab, digit dermotomy, and fasciotomy of his arm. He became thrombocytopenic down to a platelet count of 51,000/μL and was transfused. Past medical history was significant for alcoholism, hepatitis C, cirrhosis and chronic thrombocytopenia. The patient was also given lorazepam for alcohol withdrawal; however, he became increasingly agitated and was given diazepam, haloperidol, and fentanyl. He subsequently had a respiratory arrest, which responded to naloxone. He was intubated and put on mechanical ventilation, but was later extubated. He was then taken back to the operating room for debridement of his wounds. During the procedure, he had another respiratory arrest and was reintubated. He appeared to have aspirated during this episode. Later he developed adult respiratory distress syndrome. He also had myoglobinuria. Eventually life support was withdrawn, and the patient died.
			1 venomous exotic snake
2005	7714	6	*1 eastern diamondback rattlesnake:* A 55-year-old man was bitten on the hand by an eastern diamondback rattlesnake (*Crotalus adamanteus*). He had immediate dyspnea and aphonia. On arrival at the ED, he was hypotensive and diaphoretic. Cardiac monitoring showed ectopy. Swelling extended into his forearm. He was given 4 vials of CroFab and amiodarone and showed clinical improvement. Laboratory results: PT 17 sec; platelet count 109,000/μL. Approximately 27 hours after presentation, 16 vials of antivenom had been given. Labs: PT 20 sec; fibrinogen 195 mg/dL. On the sixth hospitalized day, he had coagulopathy recurrence. Labs: platelet count 93,000/μL; fibrinogen <35 mg/dL; PT and PTT both >150 sec. It is not clear whether blood products or additional antivenom were given. Later that day he developed focal neurologic deficits and became unresponsive. Head CT showed intracranial hemorrhage. He died the following day.
			1 rattlesnake (*Crotalus horridus horridus*): A 25-year-old man was bitten on the hand by a rattlesnake (*C. horridus horridus,* now classified as *C. horridus*). He was being driven to a rural hospital when the car had a flat tire. The patient became unconscious and was taken on to the hospital by a passing motorist. He was dead on arrival to the ED. Autopsy revealed a bite mark on the back of the hand, with hemorrhagic necrosis of the underlying soft tissue. A blood ethanol level was 290 mg/dL.
			1 rattlesnake: A 32-year-old man with a history of snakebites in the past was bitten by a rattlesnake. On arrival to the ED 10 minutes later, he had a respiratory arrest due to anaphylaxis. His pupils were fixed and dilated. The patient was resuscitated and antivenom given. Oxygen saturation improved to 98%, and BP stabilized. He was transferred to a higher level of care hospital. Labs: PT and PTT were slightly prolonged; platelet count 120,000/μL. Additional antivenom was given. His neurologic status throughout hospitalization was consistent with anoxic brain injury, confirmed by head CT and EEG. The patient died on day 4.
			1 presumed crotaline: A 44-year-old man saw a 4-foot long snake (presumed crotaline) and chased it into a wooded ravine to catch it. His body was found 2 days later. Autopsy showed 4 puncture marks on his hand with swelling, discoloration, and cellular lysis of the surrounding muscle and tissue. Marked edema of the larynx, epiglottis, and surrounding upper airway was noted as well. A blood ethanol level was 120 mg/dL.
			2 unknown crotalines
			3 rattlesnakes
2006	7311	4	*1 unknown crotaline*
2007	7330	0	
2008	7098	3	*1 rattlesnake:* A 37-year-old man was bitten on his thumb by a rattlesnake at home. He called his wife, who arrived 30 minutes later and found him cyanotic and unresponsive after vomiting. EMS personnel defibrillated and intubated the victim and started CPR. His past medical history included asthma and two prior rattlesnake bites with reported "allergy" to rattlesnake venom. Physical exam revealed him to be unresponsive with fixed and dilated pupils and a small (<1 cm) laceration on his thumb. He had respiratory and metabolic acidosis, and cardiac rhythms during his resuscitation included asystole, VF, and VT. His T was 35.6° C (96.1° F). In the ED, he received IV fluids, sodium bicarbonate, epinephrine, atropine, methylprednisolone, diphenhydramine, 6 vials of antivenom, norepinephrine, lidocaine, clindamycin, levoquinalone, midazolam, vecuronium, naloxone, and vitamin K. Laboratory data approximately 4 hours after the bite demonstrated PT 19.6 seconds; fibrinogen 155 mg/dL; platelets 232,000/μL; and Hgb 19.1. The patient was flown to a tertiary hospital. Six more vials of antivenom were given. No ecchymosis or oozing was noted. On day 2, he was still on a ventilator and shaking; swelling was present in his hand, and the thumb was black. He was on an insulin infusion and antibiotics, and diphenhydramine and 4 units of fresh-frozen plasma were given. On day 2 his platelets were 142,000/μL; INR 1.5; fibrinogen 223 mg/dL; and fibrin degradation products >40 mcg/mL. On day 3 he had a GCS of 5T. He remained on insulin and received nebulized albuterol, morphine, hydrocortisone, antibiotics, and vitamin K. He developed poor urine output and was started on NG feedings. The tip of his thumb became necrotic. His platelets were 84,000/μL, fibrinogen 330 mg/dL; and Hgb 11.5. On day 4, he had no cough or gag reflex, and his GCS was 3T. On day 5, the patient's family requested comfort measures only; he expired on day 6.
			2 unknown crotalines

Continued

TABLE 35-4 Snakebite-Related Deaths Reported to the AAPCC, 1983-2013—cont'd

Year	Total Bites Reported*	Deaths	Specifics of Deaths
2009	7296	3	*3 rattlesnakes*
2010	7013	1	*1 rattlesnake:* A 23-month-old female screamed while playing on a slide near her family's vacation home; she was found crying with blood on her ankle with a small rattlesnake nearby. EMS was notified. She began vomiting, became somnolent, and had a generalized tonic-clonic seizure. She was given O_2 via NRB and IV fluids en route. Physical exam: BP 106/85, HR 224, RR 46, O_2 saturation 100% on NRB. The patient was vomiting blood and had generalized petechiae. There were 4 puncture marks anterior to her medial left ankle with mild ecchymosis and little to no swelling. Clinical course: 2 hours after bite, patient arrived at ED, was promptly intubated after premedication with atropine, etomidate, and rocuronium, and received 6 vials of Crotalidae polyvalent immune Fab. Laboratory data: ABG-pH 7.09, PCO_2 31, PO_2 116 after intubation. WBC 33, Hct 22, platelets 10 with hemolysis on peripheral smear. INR 19, PTT >300 sec, fibrinogen <70 mcg/mL, D-dimer >22 mcg/mL, FDP 320 mcg/mL. Initial CXR revealed right main bronchus intubation. Repeat CXR revealed appropriate positioning with pronounced pulmonary edema. Patient was transferred to ICU and at 3 hours became hypotensive and was resuscitated with CPR, epinephrine, calcium gluconate, and HCO_3^- and maintained on pressors. She received a total of 4 units PRBC, 5 units FFP, 2 units platelets, 10 units cryoprecipitate, and 1 dose of factor VII. Poison control was consulted 4.5 hours after exposure and recommended additional crotaline Fab. Before repeat Fab administration, patient became pulseless and could not be resuscitated. She expired less than 5 hours after the bite. Autopsy findings: 4 fang marks anterior to left medial malleolus; cutaneous and serous petechiae; and acute hemorrhagic pancreatitis and gastritis. The cause of death was listed as "hemorrhagic diathesis due to snake bite(s)."
2011	7219	2	*1 rattlesnake:* A physician reported that a 54-year-old male was bitten by a Mohave rattlesnake (*Crotalus scutulatus*) 2 days earlier. The patient had been working at a railroad in a rural area late at night picking up trash when he was bitten. He developed symptoms consistent with an allergic reaction and was treated by EMS with diphenhydramine and epinephrine. His co-worker reported that he had an altered mental status soon after the bite. Past medical history: hypertension, diabetes, hyperlipidemia, previous traumatic brain injury, posttraumatic stress disorder. Physical exam: bilateral puncture wounds to the hands with bilateral hand swelling. Laboratory data: BUN 59, Cr 3.6, INR "normal"; day 2 after envenomation: Cr 6.7, phosphate 6.08, lactate 4.0, ionized Ca 3.3, PT 14.4, INR 1.49, Mg 1.7. Clinical course: patient was treated with antivenom (polyvalent immune Fab, 4 vials on day 1 and 10 vials on day 2). He had no further coagulation abnormalities or significant progression of swelling. When he arrived at the ED, he had a large upper GI bleed and developed multiorgan system failure, including acute renal failure and hypoxia refractory to intubation and ventilation with 100% O_2. CT chest scan showed no pulmonary emboli. The patient expired of multiorgan system failure on day 6. No autopsy was performed. *1 cottonmouth*
2012	7362	2	*1 rattlesnake* *1 venomous exotic snake*
2013	6861	3	*2 rattlesnakes* A 53-year-old 57-kg male was bitten while attempting to cut the rattle off a rattlesnake, which he presumed was dead. He developed an anaphylactic reaction with cardiopulmonary arrest. He received CPR measures including cardioversion, intubation, and ventilation. Physical exam: after resuscitation, HR 110, BP 94/50; he had an edematous right hand with 3 puncture marks. Laboratory data: 5 hours after bite: Na 145, K 4.1, CO_2 17, glucose 41, WBC 37, Hgb 19.4, Hct 58, platelets 268, CK 9196, Cr 1.6, BUN 7, AST 2018, ALT 1031, alkaline phosphate 225, troponin 4.3, albumin 2.8 g/dL, D-dimer >20. At 6.5 hours after exposure: glucose 109, fibrinogen 30 mg/dL, INR 2.1, PTT 47, CK 5000. Day 2: WBC 23.7, Hgb 15, platelets 131, INR 2.8, PTT 56.3, fibrinogen 104 mg/dL, Cr 3.8, AST 2275, ALT 800. Day 3: WBC 18, platelets 58, Hgb 13.9, Hct 40.8, Cr 3.2, BUN 32, INR 1.9, PTT 44, CK 5176, fibrinogen 367 mg/dL. Day 4: WBC 4.7, platelets 42, Hgb 13.6, Hct 38.7, Cr 3.3, BUN 31, INR 1.4, PTT 149, fibrinogen 564 mg/dL, AST 2797, ALT 1972. Clinical course: patient was given dopamine, 6 vials of antivenom (Fab fragment), tetanus toxoid, epinephrine, methylprednisolone, and diphenhydramine. He was transferred to a tertiary care hospital and admitted to ICU 3 hours after exposure. He was ventilated with 100% oxygen with 5 cm of PEEP. He had no pupillary response. Bite site was slightly swollen with no apparent progression. At 20 hours after bite (14 vials of antivenom), he remained on the ventilator, receiving IV norepinephrine. Pupils were pinpoint and nonreactive. The affected hand measured 19.5 cm and was ecchymotic and blistering. By 24 hours after bite (26 vials antivenom), HR 123 and BP 115/63, a femoral catheter was placed and dialysis started for acute kidney injury. On day 3 (34 vials of antivenom), there were no neurologic changes. On day 4, his entire body was mottled, and he was purple from his nipple line up. The affected arm was ecchymotic and blistered up to his bicep. Right pupil was 3 mm and left pupil 4 mm and nonreactive. EEG showed "severe brain damage," gag reflex was absent, and he had negative doll's-eye reflex. He was receiving multiple vasopressors and IV NS. On day 5, based on the prognosis, the family chose institution of comfort measures, and he expired later that day. *1 unknown crotaline*

TABLE 35-4 Snakebite-Related Deaths Reported to the AAPCC, 1983-2013—cont'd

Year	Total Bites Reported*	Deaths	Specifics of Deaths
Totals:	178,267	50	*Of the cases where circumstances were described:* • With one exception, all victims were male. • Ages (in years) were 2, 4, 20, 25 (two), 27, 30, 32, 33, 35, 37, 40, 43 (two), 44, 45, 50, 52, 53, 54, and 55 (two). The youngest patient was 23 months old. • 34 rattlesnakes, 8 unidentified crotalines, 5 exotics, 2 unknown, and 1 cottonmouth. • Time to death varied from minutes to 10 days. • At least 6 bites were associated with alcohol ingestion. • *Crotalus horridus* was the most commonly implicated snake (5 cases) when species was reported. • 1 appeared to be related to coagulopathy recurrence. • 1 appeared to be related to self-overmedication with opiates.

From references 21-26, 136, 145-162, 186, 187, 242, and 245-247.
AAPCC, American Association of Poison Control Centers; *ABG*, arterial blood gases; *ALT*, alanine transaminase; *ALP*, alkaline phosphatase; *AST*, aspartate transaminase; *bpm*, beats/min; *BP*, blood pressure (mm Hg); *BUN*, blood urea nitrogen; *CBC*, complete blood count; *CK*, creatine kinase; *CPR*, cardiopulmonary resuscitation; *Cr*, creatinine; *CT*, computed tomography; *CXR*, chest x-ray film; *D_5W*, 5% dextrose in water solution; *DIC*, disseminated intravascular coagulation; *ED*, emergency department; *EEG*, electroencephalogram; *EMS*, emergency medical services; *FabAV*, Fab fragment antivenom; *FDP*, fibrin degradation products; *FFP*, fresh-frozen plasma; *GCS*, Glasgow Coma Scale; *GI*, gastrointestinal; *HR*, heart rate (beats per minute); *Hgb*, hemoglobin (g/dL); *ICU*, intensive care unit; *INR*, international normalized ratio; *IV*, intravenous; *NG*, nasogastric; *NRB*, nonrebreather mask; *NS*, normal saline; *NSR*, normal sinus rhythm; *PEEP*, positive end-expiratory pressure; *PICU*, pediatric ICU; *PRBC*, packed red blood cells; *PT*, prothrombin time; *PTT*, partial thromboplastin time; *RR*, respiratory rate (breaths per minute); *RCA*, right coronary artery; *T*, temperature; *VF*, ventricular fibrillation; *VT*, ventricular tachycardia; *WBC*, white blood cell count.
*Includes all bites by reptiles (including exotics, nonvenomous, and unknowns).

to 0.28%, a statistically and clinically significant tenfold reduction.[201] The challenge and focus of future research are likely to shift from mortality issues to measures that reduce morbidity, disability, pain, and inconvenience (e.g., issues associated with prolonged monitoring after treatment).[67]

Other than death, permanent systemic morbidity after pit viper envenomation is rare.[71] Local sequelae, such as the partial or complete loss of a limb or digit, loss of function at a joint (Figure 35-40), or permanent sensory loss, are more common.[71] The reported incidence of permanent local morbidity is less than 10%, although this does not include complications that may follow surgical interventions.[93] Most patients recover fully after rattlesnake envenomation in the United States, but the incidence of local complications is probably underestimated. Unless careful follow-up is done, including objective range-of-motion and sensory testing, permanent disabilities that impact lifestyle and occupation can be missed.[229]

Although not clearly substantiated, it has been suggested that children are more susceptible than adults to systemic morbidity and mortality from snakebites (see Bites in Children, earlier).[64,195,249] However, of the 178,267 snakebite exposures and 50 deaths (including endemic and exotic snakes) described by the AAPCC since its first report in 1983, only three deaths were in pediatric patients.[21-26, 136,145-162,186,187,242,245-247] Better pediatric supportive care and improved understanding of how antivenom should be administered have blurred any distinction between pediatric and adult prognosis.[71] Older adult patients appear to have a higher case fatality rate, probably related to comorbid conditions.[71]

Morbidity and mortality from snakebites can also result from efforts to treat the victim. Significant wound complications can follow ill-advised incisions in and around the bite site and application of mouth suction.[85,260] Serious burns and systemic complications, such as myocardial infarction, can follow application of electric shocks to the wound.[215] Tourniquets or ice may increase the risk for tissue damage. Antivenoms can precipitate early anaphylactic or anaphylactoid reactions that can add to morbidity and even result in death (see Adverse Reactions to Antivenoms, earlier).

Coral Snakes

Deaths from coral snake bites are quite rare, but the potential should not be underestimated. In fact, the mortality rate for an untreated bite has been estimated to be approximately 10%.[202] Although animal research suggests that death can result from cardiovascular collapse,[207] the cause of death is much more likely to be related to paralysis and respiratory failure. Victims with respiratory compromise may require mechanical ventilation for many days, and muscle weakness after severe envenomation may persist for months.[133] There are no reports of permanent sequelae in patients who survive coral snake envenomation.

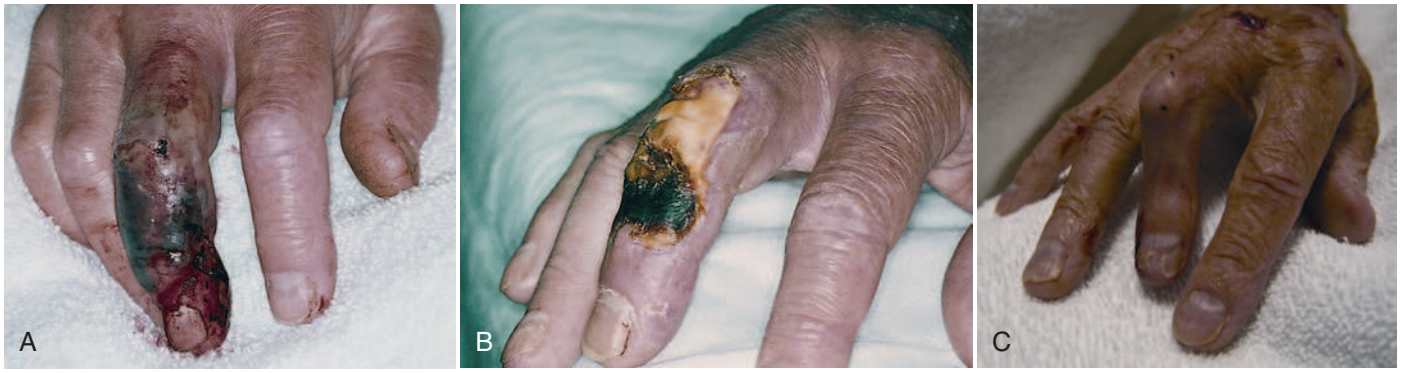


FIGURE 35-40 **A,** Soft tissue swelling, hemorrhagic blebs, and early necrosis after red diamond rattlesnake (*Crotalus ruber*) bite to the long finger (day 2). Victim received 10 vials of antivenom (Crotalidae) polyvalent 6 hours after the bite and 10 more vials for severe thrombocytopenia on day 2. **B,** Seven weeks later. Note the degree of necrosis. **C,** Five years later. Extensor function was never regained. (***A*** *and* ***B*** *courtesy Sean P. Bush, MD;* ***C*** *courtesy Kent Denmark, MD.)*

FIGURE 35-41 Gila monster (*Heloderma suspectum*) is one of only two known venomous lizards and the only species found in the United States. *(Courtesy Michael Cardwell, Extreme Wildlife Photography.)*

FIGURE 35-43 Teeth of the helodermatid lizards are grooved to aid instillation of venom during a bite. These teeth are loosely adherent and may become dislodged in the bite wound. *(Courtesy Michael Cardwell, Extreme Wildlife Photography.)*

VENOMOUS LIZARDS

The only two known species of venomous lizards in the New World are found in North and Central America, and they belong to the genus *Heloderma*. The Gila monster (*Heloderma suspectum*) is found in the southwestern United States (Arizona, western New Mexico, southeastern California, southern tip of Nevada, extreme southwestern Utah) and northwestern Mexico (Figure 35-41).[234] The range of the beaded lizard (*Heloderma horridum*) is south of that of the Gila monster, along the Pacific drainage of mainland Mexico and throughout most of Guatemala (Figure 35-42).[218] Biologists have recently proposed elevating the four long-standing subspecies of *Heloderma horridum* to full species status.[209] Thus, literature in the near future may include five species of *Heloderma* rather than two.

SCOPE OF THE PROBLEM

Establishing credible estimates of the incidence of venomous lizard bites is even more difficult than for snakes. The vast majority of victims are bitten while intentionally interacting with the lizard, and truly accidental bites are rare. Because these creatures are legally protected and serious sequelae are rare, many bites are probably never reported.

ANATOMY

The two New World venomous lizards are impressive creatures about which much misinformation has been spread for centuries. They have been thought to possess supernatural features such as poisonous breath, a stinging tail, and the ability to spit their venom.[214] The Gila monster (*Heloderma suspectum*) reaches a maximum length of approximately 50 cm (20 inches), whereas the beaded lizard (*Heloderma horridum*) is larger, reaching almost 1 m (3.3 feet). They are both heavily built with massive muscles of mastication and powerful biting capacity. The venom delivery apparatus consists of a pair of anterior, multilobed glands that open through one duct (*H. horridum*)[135] or a series of ducts (*H. suspectum*)[231] into the labial mucosa of the lower jaw. Their teeth are lancet shaped, grooved, and loosely attached to the surface of the mandibles without alveoli (Figure 35-43). When the lizard becomes agitated, it salivates heavily, producing a flow of venom into the labial mucosa. It bites with a powerful, chewing motion, instilling venom into the wounds by capillary action along the grooves of the teeth. Teeth may be left in the wounds, especially if the animal must be forcefully removed from the victim. The tenacious creature may still be attached when help arrives. Effective envenomation occurs in about 70% of bites.[15]

FIGURE 35-42 Mexican beaded lizard (*Heloderma horridum*) is located south of the Gila monster's range in Mexico. *(Courtesy Michael Cardwell, Extreme Wildlife Photography.)*

VENOMS

Gila monster and beaded lizard venoms are similar in composition.[231] They possess enzymatic components, including hyaluronidase (spreading factor), protease, phospholipase A_2, kallikrein-like substances, and nonenzymatic substances such as serotonin. Venom kallikreins stimulate the release of vasoactive kinins, such as bradykinin, which may be responsible for occasional hypotension seen after helodermatid bites.[234] These venoms contain no neurotoxic components and no components that directly interfere with coagulation.[175] Of note, Gila monster venom inspired production of a drug that helps diabetic patients obtain better control of their blood glucose levels.[230]

CLINICAL PRESENTATION

A review of the 17 cases of helodermatid bite reported in peer-reviewed journals between 1953 and 2003 indicated the most common effects were local pain and swelling (82% of cases), nausea (65%), hypotension (47%), diaphoresis (47%), tachycardia (35%), and vomiting (35%), with other signs and symptoms being less common.[9] Bleeding usually occurs from punctured and torn tissues, but it is generally not excessive.[175] Throbbing or burning pain may radiate proximally along the bitten extremity and may be severe. Local edema may be progressive (Figures 35-44 and 35-45). Victims may complain of generalized weakness, nausea and vomiting, difficulty breathing, profuse sweating, dizziness, and paresthesias.[7,119,214,234] On examination, the patient may be tachycardic, hypotensive (related to kinin release), and diaphoretic.[7,119] Some systemic symptoms may be related to neurally mediated hypotension and bradycardia secondary to pain and fear resulting from the bite. There may be significant local tissue trauma. The site may be cyanotic or ecchymotic with local

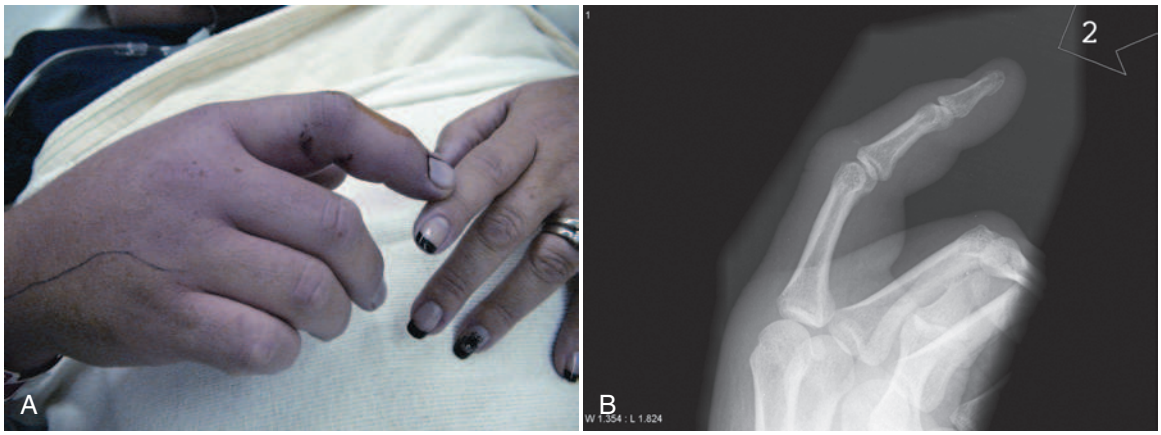


FIGURE 35-44 **A,** This patient sustained a bite by a captive subadult Gila monster (*Heloderma suspectum*) after she touched the lizard's tail. It took approximately 40 seconds to pry the reptile off with tongs. Immediately afterward, the patient complained of "10 out of 10" pain. Shortly after, she developed swelling and redness extending to her midforearm, as well as nausea and vomiting. **B,** A tooth was retained in the wound for over 2 months before it was spontaneously expelled. *(Courtesy Sean P. Bush, MD.)*

vasospasm.[214] Regional lymphadenopathy may be present.[15] Apparent anaphylactic reactions to helodermatid venom have been reported.[51,204]

MANAGEMENT

Prehospital Care

Data are minimal regarding prehospital care of venomous lizard bites. In some cases, the first priority is to detach the lizard from the victim. The lizard can be placed under running hot water, or the jaws can be pried apart using a stick or metal instrument.[234] Care must be taken not to injure the victim further and to avoid a second bite, perhaps to the rescuer.

Once freed from the lizard, the patient should be placed at rest and the bite site rinsed and cleaned as much as possible. Any bleeding should be stopped with direct pressure. There is no evidence to support the use of suction devices, ligatures, or pressure immobilization, and incisions and electrotherapy should be strictly avoided. Local application of ice may be harmful because it may increase the risk for vasospasm and tissue damage.[216] A bandage to stop bleeding and a splint to limit movement may be beneficial. The patient should be expeditiously transported to a medical facility.

Hospital Care

Assuming the lizard has been detached before arrival at the hospital, the patient's airway, breathing, and circulation are assessed. Vital signs should be obtained while the patient is being placed on oxygen and cardiac and pulse oximetry monitoring.

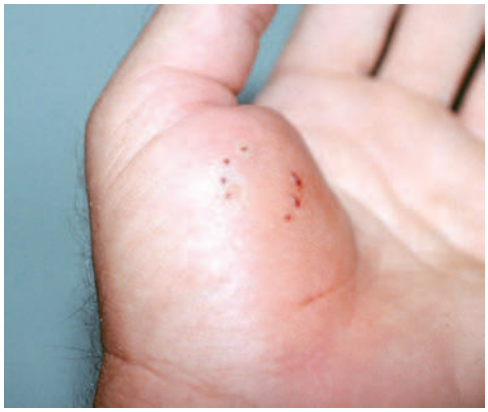


FIGURE 35-45 Bite of a captive beaded lizard (*Heloderma horridum*). *(Courtesy Michael Cardwell.)*

At least one large-bore IV line should be established with normal saline. If the patient is hypotensive or tachycardic, a second line should be placed, and physiologic saline should be given (1 to 2 L for adult, 20 to 40 mL/kg for child). Hypotension rarely persists after volume resuscitation. If necessary, vasopressors can be added after the patient's intravascular volume has been repleted.[234]

Laboratory testing should include a complete blood count, serum electrolytes, renal function studies, and coagulation studies. Total WBC count may be elevated, and in severe cases, platelets may be decreased.[214] Although lizard venoms do not appear to possess anticoagulant fractions, rare hemostatic abnormalities have been reported after severe bites and are probably related to endothelial cell damage.[15,234] Urinalysis is useful to assess for microscopic hematuria or renal casts.

Helodermatid bites can cause transient ECG abnormalities, such as T-wave anomalies and conduction delays.[15,119] A single case of apparent myocardial infarction after a Gila monster bite has been reported in a patient with a history of cocaine abuse.[15] It is reasonable to obtain an ECG and markers of cardiac ischemia if the patient shows any sign or symptom of envenomation.

Once the patient's overall status is stabilized, attention focuses on wound care. A soft tissue radiograph or ultrasound of the bite site may identify retained lizard teeth (see Figure 35-44B) but does not replace careful exploration of the wounds.[119] After assessment of functional status, the wound can be anesthetized using a local or regional block. The bite site should then be carefully explored for damage to underlying vital structures and for retained teeth. Thorough cleansing and irrigation should follow exploration. The wounds are dressed and splinted with generous padding. The extremity is then elevated to reduce swelling and discomfort. Narcotics may be necessary for pain management during the initial evaluation and for any pain not controlled by local or regional anesthesia. The patient's tetanus immunization status should be updated as needed. Infections are uncommon, and prophylactic antibiotics are not required.[234] If secondary infection occurs, cultures should be obtained and the patient started on broad-spectrum antibiotic coverage for both gram-positive cocci and gram-negative rods. Culture and sensitivity results should guide further treatment. Daily wound care should include cleansing with soap and water, followed by saline irrigation, application of a topical antiseptic, and redressing. Physical therapy is helpful in returning the patient more rapidly to full function.

Patients who are relatively asymptomatic, with normal vital signs and diagnostic studies, may have received a dry bite and can be discharged home after 8 hours of medical observation. These patients must have proper resources for care at home and the ability to return if they worsen. Proper wound care instructions should be given and patients scheduled for reevaluation in approximately 24 to 48 hours. An oral narcotic analgesic may be

prescribed. Evidence of envenomation (i.e., signs or symptoms besides simple wounds; laboratory or ECG abnormalities) necessitates admission. Systemic findings (e.g., chest pain, ECG changes, hypotension, rare coagulopathy) require monitoring for at least 24 hours.[234] There is no antivenom for venomous lizard bites, and given the almost complete lack of long-term venom-related morbidity or mortality, none is needed.

MORBIDITY AND MORTALITY

About the beginning of the 20th century, mortality from Gila monster bites was reported in the popular press as about 32%, but steadily declined thereafter, with most reports containing few objective observations and numerous unverifiable claims.[9,13] The last report of a fatality appeared in the *Arizona Republic* newspaper in 1930.[9] An early scholarly review of Gila monster biology and case reports of its bites describes no fatalities.[216] No deaths have been documented in peer-reviewed literature to date, but a bite could possibly prove fatal if a large lizard were to hang on to a victim and deposit a large volume of venom. Bites to children are especially concerning because of a potentially larger venom load per body mass compared with adults. Likewise, given their complicating comorbidities, chronically ill or older adult victims may be at higher risk for a serious outcome.

Pain and tenderness may be prolonged for days or weeks after these bites,[216] although necrosis is rare.[175,214] The vast majority of bites resolve without permanent sequelae.

CONSIDERATIONS BEFORE GOING INTO THE WILDERNESS

Before leaving on a trip into habitat where venomous reptiles may be encountered, it is important to plan the steps to be taken should a bite occur. The traveler should become familiar with local dangerous fauna, using field guides or Internet resources. A plan should be developed for field management of a bite. How will a victim be evacuated from the location? What will be the destination hospital? Does the hospital have antivenom and personnel knowledgeable in the management of snakebite? Appropriate supplies should be gathered, such as dressings and splints (e.g., SAM splints are lightweight and easily carried).

The question often arises of whether to carry antivenom on a trip to a remote location. If this is considered, an appropriate, preferably broad-spectrum polyspecific product is ideal. Such products are best purchased in the destination country, because advance importation of exotic antivenoms into the United States is time-consuming and difficult. If a foreign product is to be carried, its package insert should be translated, if necessary, before the trip begins. If traveling to Central or South America, it is likely that CroFab would provide broad enough coverage for most pit vipers that might be encountered (although further research is needed in this area, and it is certainly more expensive than antivenoms produced by Latin American countries). CroFab has been studied and found to be relatively stable despite prolonged exposure to high temperatures and rough handling.[70] It should stand up to the punishment of vigorous hiking in tropical regions. If antivenom is to be taken into the field, all equipment necessary for its administration (IV supplies, bag of normal saline, airway equipment, and drugs needed to adequately treat an acute reaction) must also be carried, and an expedition member must have the skills needed to give the drug and treat adverse reactions. Although it may be possible to administer CroFab intramuscularly,[225] the IV route is preferred. Further research is needed to determine whether the smaller molecular size of Fab fragments allows adequate distribution by the intramuscular route to be of any benefit in field management of snake envenomation.

The most important consideration when entering the field is prevention. Long pants and boots should be worn in snake country, and team members should be especially vigilant about visually clearing any location where they will place hands and feet when hiking, climbing, or gathering firewood. If going outside in the dark for any reason, each expedition member should wear proper footwear and carry a flashlight, because many venomous snakes are more active after dark. If a snake or venomous lizard is encountered, it is best appreciated and photographed from a safe distance.

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CHAPTER 36

Bites by Venomous and Nonvenomous Reptiles Worldwide

DAVID A. WARRELL

DANGEROUS REPTILES

Some species of alligators and crocodiles (order Crocodylia), notably the Nile crocodile (*Crocodilus niloticus*) and saltwater crocodile (*C. porosus*), grow large and powerful enough to kill and eat humans (see Chapter 33). Large sea turtles (order Testudines) can be dangerous. Leatherback turtles (*Dermochelys coriacea*), which can reach 3 m (9.8 feet) in length and 900 kg (1984 lb) in weight, are reported to have capsized small boats. Giant pythons and Komodo dragons occasionally prey on humans (see later text). However, reptiles' greatest threat to human life is through the lethal venoms of many species of the clade Toxicofera, constituting 60% of the Squamata (snakes and lizards),[73] including snakes of Canada, the United States, and Mexico, and helodermatid lizards of the southern United States and Mexico, discussed in Chapter 35. This chapter covers dangerous snakes and lizards, venomous and nonvenomous, found in the rest of the world and therefore considered "exotic" in North and Middle America.

VENOMOUS SNAKES

TAXONOMIC REVOLUTION

Snake taxonomy is based on morphologic features, such as numbers and arrangement of scales (lepidosis), dentition, osteology,

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myology, sensory organs, form of the hemipenes (paired male genital organs), and increasingly, sequence analysis of DNA encoding important mitochondrial and other enzymes.[192,264,265] The accelerating pace of taxonomic revision of medically important taxa has left clinicians and nonherpetologists breathless, confused, and frustrated. To change familiar names and split genera and species of medically important taxa can be misleading, even though it may be well justified on evolutionary and taxonomic grounds. Correct identification and designation of species responsible for bites is important for optimal clinical management and choice of appropriate antivenom. Therefore, the latest taxonomic designations are employed in this chapter. Use of correct taxonomy is essential when designing regional antivenoms and selecting appropriate venoms for their manufacture. It is also crucial for laboratory toxinologists who work on venoms that are sometimes of uncertain provenance.

Studies of green pit viper venoms in Thailand in the 1970s attributed to "*Trimeresurus erythrurus* and *T. popeorum*" are uninterpretable because of the misuse of these scientific names.[163,164] Ignorance of the correct nomenclature for the source species has been responsible for misnaming of several toxins. For instance, "ceruleotoxin" was named after *Bungarus caeruleus,* although its true origin was *Bungarus fasciatus*. "Grambin" and "gramineleysin" were named after *Trimeresurus (Craspedocephalus) gramineus*, but were obtained from *Trimeresurus* (*Viridovipera*) *stejnegeri*.

In an attempt to improve the flow of information among taxonomists, toxinologists, and clinicians, an important series of reviews was published in *Toxicon*,[327,328] followed by an invaluable website (http://www.bangor.ac.uk/~bss166/update.htm). Some published work on toxins can never be reproduced because the venoms used, with their origin shrouded in incorrect snake nomenclature, can never be identified.[329]

Fortunately, nomenclature and identification have been clarified for several groups of medically important snakes: African spitting cobras,[326,332] Afro-Asian saw-scaled vipers,[185] Asian cobras,[324,326,331,334] Russell's vipers,[330] *Bothrops atrox*,[333] and arboreal pit vipers.[51,148,203]

Taxonomic revision of the mainly arboreal Southeast Asian pit vipers, formerly placed in a single genus, *Trimeresurus,* has been particularly tortuous and circuitous. Based on molecular analyses, the morphology of hemipenes, and the condition of the first upper labial and nasal scale, Malhotra and Thorpe[148] split the genus *Trimeresurus* into seven genera: *Trimeresurus, Cryptelytrops, Parias, Viridovipera, Himalayophis, Popeia,* and *Peltopelor*. This scheme has been largely adopted by most subsequent authors and was used in the previous edition of this chapter. However, careful research of the older literature led David and colleagues[51] to conclude that the status of nucleo (type) species of the genus *Trimeresurus* had been wrongly identified as Indian *T. gramineus*; it was in fact Timorean *T. insularis*. The authors suggest that the subgeneric nomen *Trimeresurus* should no longer be used for the Indian and Indomalayan taxa related to *Trimeresurus gramineus* (Shaw, 1802), but for taxa of the *T. albolabris* group that was referred to as the genus *Cryptelytrops*.[148] This chapter uses the changes suggested by David and associates.[51]

Most of the species responsible for snakebites in each country have been identified and their geographic distributions mapped (http://www.who.int/bloodproducts/snake_antivenoms/en/). New species of both clinical and toxinologic interest continue to be discovered, including New Guinea small-eyed snake (*Micropechis ikaheka*),[299] Indo-Chinese spitting cobra (*Naja siamensis*),[334] hump-nosed pit viper (*Hypnale hypnale*) in India,[114,145] the greater black krait (*Bungarus niger*) in Bangladesh,[63] Wall's and Sind krait in Nepal and Bangladesh,[127] Ashe's cobra (*Naja ashei*) in Kenya, Mandalay spitting cobra (*Naja mandalayensis*) in Myanmar,[221] Senegal cobra (*Naja senegalensis*) in West Africa,[251] and the southern African swamp adder (*Proatheris superciliaris*).[288]

Based on their nuclear and mitochondrial genes, highly evolved (advanced) snakes (Caenophidia), including all venomous snakes, are now classified by some taxonomists into the following three superfamilies[264,265]:

FIGURE 36-1 Eastern bearded dragon (*Pogona barbata*: family Agamidae) (Australia) showing eyelids and external ear orifice typical of lizards. *(Copyright D.A. Warrell.)*

- Colubroidea—including families Natricidae (e.g., Asiatic keelbacks of genus *Rhabdophis*), Colubridae (e.g., African boomslang *Dispholidus typus* and twig snakes genus *Thelotornis*) and Dipsadidae (e.g., South American racers of genus *Philodryas*)
- Elapoidea—including families Lamprophiidae (subfamily Atractaspidinae, burrowing asps of genus *Atractaspis*) and Elapidae (terrestrial elapids, sea snakes, and sea kraits)
- Viperoidea—including Viperidae, subfamilies Viperinae (Old World vipers) and Crotalinae (pit vipers)

IDENTIFICATION OF VENOMOUS SNAKES

DISTINGUISHING SNAKES FROM LEGLESS LIZARDS, AMPHIBIANS, AND SNAKE-LIKE FISH

Most lizards have eyelids, external ear orifices (Figure 36-1, *Pogona barbata*), thick and fleshy tongues that are forked and snake-like in Varanidae, Teiidae, Lacertidae, and Anguidae, and very long friable tails; they lack the enlarged ventral scales of snakes. Legless lizards include slow worms and glass lizards (family Anguidae), worm-like geckos (family Pygopodidae) (Figure 36-2, *Lialis jicari*), and skinks (family Scincidae), some of which have vestigial limbs (Figure 36-3, *Chalcides armitagei*) and may be confused with snakes unless these features are detected. The fossorial amphisbaenid lizards have worm-like annular grooves along the length of their bodies (Figure 36-4, *Amphisbaena fuliginosa*; Figure 36-5, *Amphisbaena mertensii*). Caecilians (legless amphibians) (Figure 36-6, *Dermophis mexicanus*) have no obvious eyes or scales. Eels and pipe-shaped fish are easily distinguished from snakes by their gills and fins.

FIGURE 36-2 Papuan snake-lizard (*Lialis jicari*: family Pygopodidae) (Madang, Papua New Guinea), a legless lizard, showing external ear opening, distinguishing it from snakes. *(Copyright D.A. Warrell.)*

FIGURE 36-3 Armitage's cylindrical skink (*Chalcides armitagei*: family Scincidae) (The Gambia) showing vestigial limbs. *(Copyright D.A. Warrell.)*

FIGURE 36-4 Speckled worm lizard (amphisbaenid) (*Amphisbaena fuliginosa*: family Amphisbaenidae) (Peru) showing distinctive annular rings, distinguishing it from snakes. *(Copyright D.A. Warrell.)*

DISTINGUISHING VENOMOUS FROM NONVENOMOUS SNAKES

There is no quick, simple, and absolutely reliable method for distinguishing venomous from nonvenomous snakes. The venom-conducting fangs may be very small in elapids, or they may be

FIGURE 36-5 Mertens' worm lizard (*Amphisbaena mertensii*: family Amphisbaenidae) (Brazil). *(Copyright D.A. Warrell.)*

FIGURE 36-6 Mexican caecilian (*Dermophis mexicanus*: family Caeciliidae). *(Copyright D.A. Warrell.)*

folded back against the jaw inside a sheath in vipers (Figure 36-7, *Bothrops atrox*). In a dead snake, a needle may be drawn along the upper jaw from the angle of the jaw to the snout to catch on and reveal the fangs. Some key morphologic features are subtle. Most elapid snakes lack the loreal scale (between the preocular and nasal scales) possessed by most colubroid snakes (Figure 36-8, *Dendroaspis angusticeps* and *Philothamnus hoplogaster*). Pit vipers (Crotalinae) possess a heat-sensitive (infrared-sensitive) pit organ, situated between the eyes and nostrils, whose functions include heat regulation and detection of warm-blooded prey and predators (Figure 36-9A, *Porthidium dunni*). Pythons and boas have labial heat-sensitive organs (Figure 36-9B, *Corallus caninus*). Snakes of the subfamily Viperinae, the Old World vipers and adders, have no pit organ.

Fortunately, the most dangerous species of snakes tend to be well known in the areas where they are medically important. The characteristic hood of cobras and some other elapids is visible only when the snake is rearing up in a defensive attitude (Figure 36-10, *Naja mossambica*). Vipers and pit vipers are often identifiable by their striking and sometimes colorful dorsal pattern

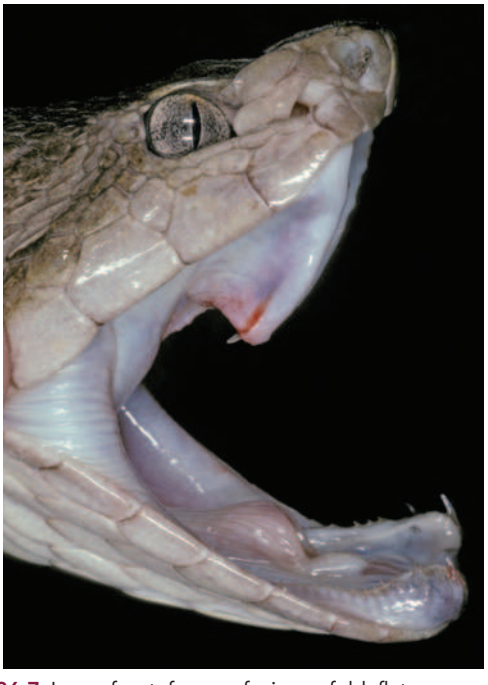


FIGURE 36-7 Long front fangs of vipers fold flat, concealed by a sheath. Common lancehead (*Bothrops atrox*: family Viperidae) (Icoaraci, Brazil). *(Copyright D.A. Warrell.)*

FIGURE 36-8 A, Eastern green mamba (*Dendroaspis angusticeps*: family Elapidae) (KwaZulu-Natal, South Africa) showing the absence of a loreal scale between the preocular and nasal scales typical of elapid snakes. **B,** African South-Eastern green water snake (*Philothamnus hoplogaster*: family Colubridae) (Watamu, Kenya) showing loreal scale (*arrow*) lacking in most elapid snakes. *(Copyright D.A. Warrell.)*

(Figure 36-11, *Bitis arietans*; Figure 36-12, *Deinagkistrodon acutus*). Russell's vipers (*Daboia russelii*) (Figure 36-13A, *Daboia siamensis* (Figure 36-13B), and puff adders (*B. arietans*; see Figure 36-11) hiss loudly by expelling air through their large nostrils. The saw-scaled or carpet vipers (genus *Echis*) and some other desert vipers produce a characteristic rasping sound by rubbing their coils together continuously (Figure 36-14A, *Echis pyramidum*, and Figure 36-14, *B*, *Cerastes cerastes*), and king

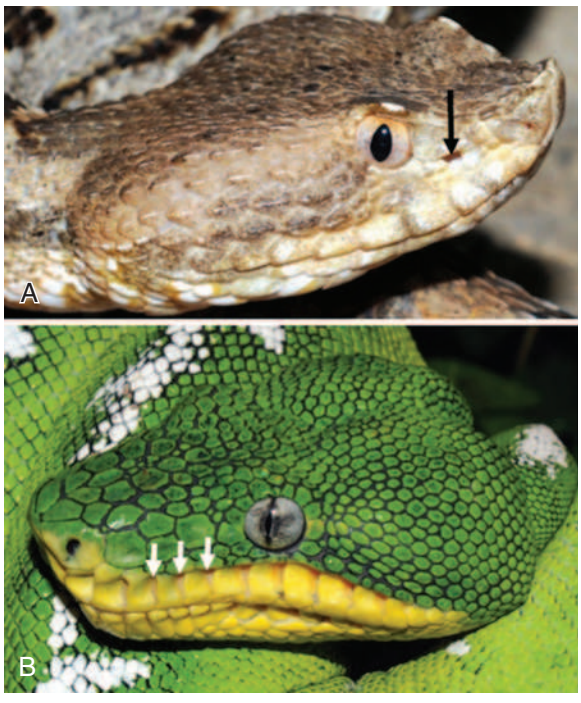


FIGURE 36-9 Heat-sensitive pit organs in snakes. **A,** Between nasal and preocular scales (*arrow*) in Dunn's hognosed pitviper (*Porthidium dunni*: family Viperidae; subfamily Crotalinae) (Oaxaca, Mexico). **B,** On the upper lip (*arrows*) in Emerald tree boa (*Corallus caninus*: family Pythonidae) (Peru). *(Copyright D.A. Warrell.)*

FIGURE 36-10 Mozambican spitting cobra (*Naja mossambica*: family Elapidae) (Harare, Zimbabwe) showing the hood spread in a threatening/defensive attitude and sensing forked tongue. *(Copyright D.A. Warrell.)*

FIGURE 36-11 Puff adder (*Bitis arietans*) (Kenya) showing the distinctive repeated U (chevron) dorsal pattern. *(Copyright D.A. Warrell.)*

cobras (Figure 36-15, *Ophiophagus hannah*) are said to "growl." The tail tip series of interlocking and resonating modified scales of rattlesnakes produce their familiar castanet-like warning sound (Figure 36-16, *Crotalus durissus cumanensis*). However, in a world increasingly densely inhabited by humans, this sound may no longer be protective to these snakes, but rather, attract lethal attention. There is some evidence that natural selection now favors rattlesnakes that are more reticent about sounding their

FIGURE 36-12 Juvenile hundred-pacer (*Deinagkistrodon acutus*) (China) showing the striking dorsal pattern. *(Copyright D.A. Warrell.)*

FIGURE 36-13 Russell's vipers. **A,** Western species (*Daboia russelii*) from Anuradhapura, Sri Lanka. **B,** Eastern species (*Daboia siamensis*) from Eastern Java, Indonesia. *(Copyright D.A. Warrell.)*

rattles. Less spectacularly, several genera of South American pit vipers (*Agkistrodon, Bothrops, Lachesis*), especially their juveniles, vibrate the tips of their tails when aroused, producing a whirring sound by agitating leaves in the undergrowth and leading to the misnomer "cascavel" (rattlesnake).

FIGURE 36-14 Desert snakes. **A,** Saudi Arabian saw-scaled or carpet viper (*Echis pyramidum*) showing its defensive coiling movement, during which the rough lateral scales rub together to produce a characteristic rasping sound. **B,** Algerian Saharan horned viper (*Cerastes cerastes*); this specimen without horns. *(Copyright D.A. Warrell.)*

FIGURE 36-15 King cobra (*Ophiophagus hannah*) (Thailand). *(Copyright D.A. Warrell.)*

Mimics, Misidentification, and Mismanagement

Some nonvenomous or less-venomous colubroid snakes closely resemble highly venomous species in their appearance and behavior. This is probably an example of Batesian mimicry. There are examples from all continents: in Europe, *Hemorrhois nummifer* (coin-marked snake) mimics *Macrovipera lebetina* (Levantine viper) (Figure 36-17); in Africa, *Telescopus variegatus* (tiger snake) (Figure 36-18A) and *Dasypeltis scabra* (egg-eating snake) (Figure 36-18B) mimic *Echis* spp. (saw-scaled viper) (Figure 36-18C); in Southeast Asia, *Boiga multomaculata* (Figure 36-19A) mimics *D. siamensis* (Eastern Russell's viper) (Figure 36-19B), various species of *Dryocalamus* (e.g., *D. davisonii,* Figure 36-20A) and *Lycodon* (e.g., *L. aulicus,* Figure 36-21A) mimic kraits (*Bungarus candidus,* Figure 36-20B; and *Bungarus caeruleus,* Figure 36-21B); and in the Americas, *Dipsas* (Figure 36-22A, *D. indica*), *Xenodon* (Figure 36-22B, *X. neuwiedii*; Figure 36-22C, *X. severus*), *Waglerophis merremi* (Figure 36-22D), and many others mimic *Bothrops* spp. (Figure 36-22E, *B. brazili*). The best known examples are mimics of coral snakes (*Micrurus*) (Figure 36-23: *M. corallinus, M. decoratus, M. frontalis, M. mipartitus, M. spixii obscurus*), which include *Oxyrhopus, Rhinobothryum*, and *Simophis* spp. (Figure 36-24). The familiar jingle "red on yellow kills a fellow, red on black venom lack" (or, "OK Jack") safely distinguishes North American coral snakes (*Micruroides euryxanthus, Micrurus fulvius, M. tener* [Figure 36-25]) from harmless scarlet snakes (*Cemophora coccinea*), king snakes, and milk snakes (*Lampropeltis* spp.). This does not apply in Central and South America, however, because many species of *Micrurus* have "red on black" (see Figure 36-23).

Similarities between the superficial appearances of venomous and nonvenomous species, or even between different venomous species, may lead to choice of the wrong antivenom or inappropriate use of antivenom. For example, in a study of 860 snakebites in Sri Lanka,[10] snakes were misidentified by the hospital staff on 51 occasions, resulting in unnecessary use of antivenom. Hump-nosed pit vipers (*Hypnale hypnale*, Figure 36-26)

FIGURE 36-16 South American rattlesnake (*Crotalus durissus cumanensis*) showing rattle (Colombia). *(Copyright D.A. Warrell.)*

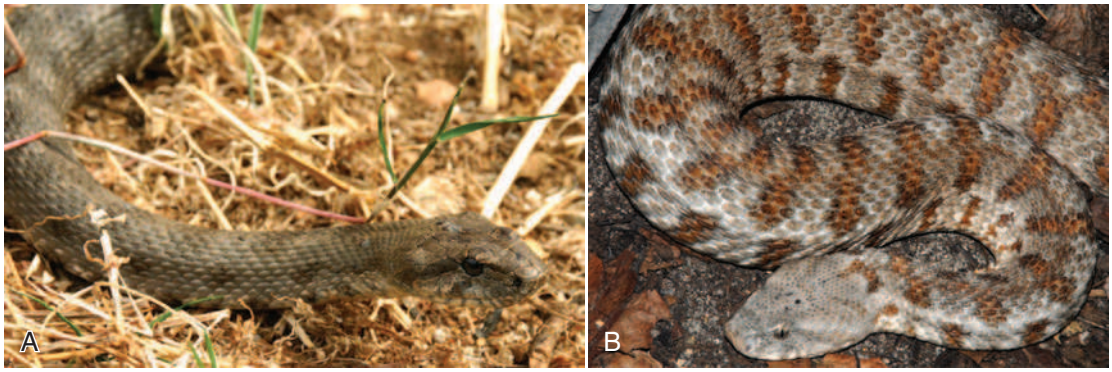


FIGURE 36-17 Mimicry—Europe. **A,** Coin-marked snake (*Hemorrhois* [*Coluber*] *nummifer*: family Colubridae) (Symi). **B,** Levantine viper (*Macrovipera lebetina*: family Viperidae) (Cyprus). *(**A** courtesy Matt Wilson; **B** copyright D.A. Warrell.)*

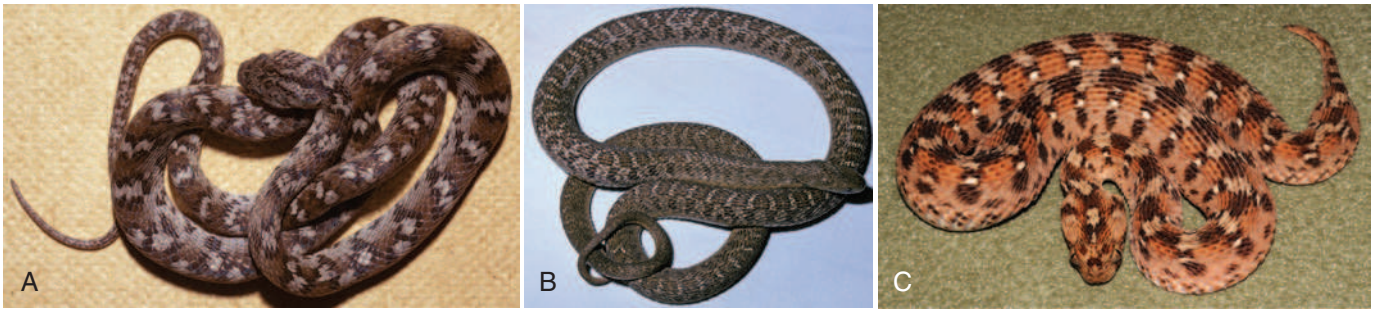


FIGURE 36-18 Mimicry—Africa. **A,** Tiger snake (*Telescopus variegatus*: family Colubridae) (Nigeria). **B,** Egg-eating snake (*Dasypeltis scabra*: family Colubridae) (Kenya). **C,** West African carpet viper (*Echis ocellatus*: family Viperidae) (Nigeria). *(Copyright D.A. Warrell.)*

FIGURE 36-19 Mimicry—Asia. **A,** Spotted cat snake (*Boiga multomaculata*: family Colubridae) (Thailand). **B,** Eastern Russell's viper (*Daboia siamensis*: family Viperidae) (Supanburi, Thailand). *(Copyright D.A. Warrell.)*

FIGURE 36-20 **A,** Blanford's bridal snake (*Dryocalamus davisonii*: family Colubridae) (Thailand). **B,** Malayan krait (*Bungarus candidus*) (Thailand). **C,** Banded krait (*Bungarus fasciatus*) (Thailand). *(Copyright D.A. Warrell.)*

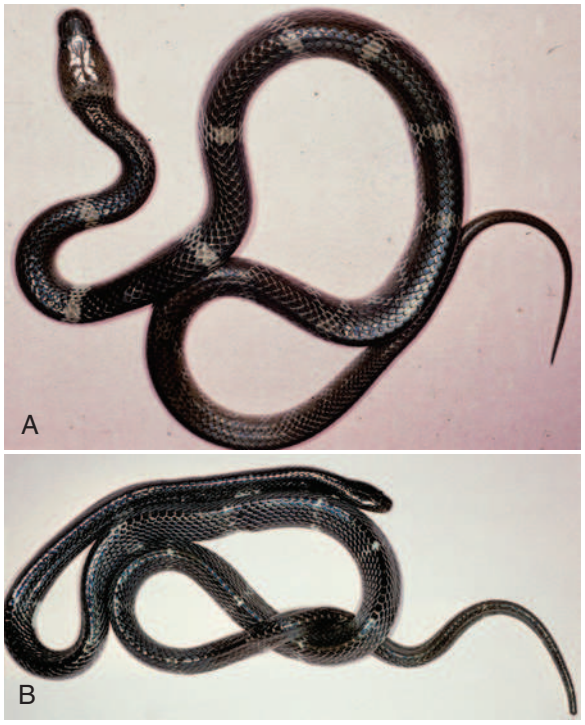


FIGURE 36-21 Mimicry—kraits. **A,** Wolf snake (*Lycodon aulicus*: family Colubridae) (Sri Lanka). **B,** Ceylon krait (*Bungarus ceylonicus*: family Elapidae) (Sri Lanka). *(Copyright D.A. Warrell.)*

were misidentified as Russell's vipers (*Daboia russelii*, see Figure 36-13A) on 36 occasions; cat snakes (*Boiga ceylonensis,* Figure 36-27, and *B. trigonata trigonata*) were misidentified as hump-nosed pit vipers twice, as Russell's vipers three times, and as a saw-scaled viper (*Echis carinatus*, Figure 36-28) once; pythons were misidentified as Russell's vipers twice; wolf snakes banded phase (*L. aulicus* [see Figure 36-21A] and *L. striatus sinhalayus*) were misidentified as common kraits (*B. caeruleus*) five times and rat snakes (*Ptyas mucosus*) as cobras twice. Antivenom was given inappropriately on 13 occasions because a nonvenomous species or a hump-nosed viper had been mistaken for one of the four species covered by Indian polyspecific antivenom. In a study of 1631 snakebites in Thailand,[266] *Oligodon dorsolateralis* was mistaken for *Calloselasma rhosostoma* twice and for *D. siamensis* once, common kukri snakes (*O. cyclurus*) for *C. rhodostoma* on six occasions, *B. multomaculata* (see Figure 36-19A) for *D. siamensis* on seven occasions, *Lycodon laoensis* for *B. candidus* once, *Rhabdophis subminiatus* for *C. rhodostoma* once, and *Dryocalamus davisonii* (see Figure 36-20A) for *B. candidus* (see Figure 36-20B) or *B. fasciatus* (see Figure 36-20C) on four occasions. *Bungarus candidus* was confused with *B. fasciatus* on five occasions, with the result that inappropriate monospecific *B. fasciatus* antivenom was given.

FANGS AND VENOM APPARATUS[126,313]

Venomous snakes have one or more pairs of enlarged teeth (fangs) in their upper jaws. The fangs usually contain grooves or venom channels through which venom is injected through the skin of their prey or human victim or inoculated by chewing. One or two reserve fangs may be situated immediately behind the active fang on each side.

Colubroidea: Natricidae, Colubridae, Dipsadidae

Venom from supralabial (Duvernoy's) glands is inoculated by enlarged posteriorly situated (opisthoglyphous) maxillary teeth that can be formidably long (thus the term "rear-fanged snake") (Figure 36-29, *Tomodon dorsatus*). These teeth may have anterior grooves or be solid. To envenom a human, the snake must seize, hold onto, and chew the finger of its victim, often a herpetologist. Duvernoy's glands are surrounded by muscles (adductores superficialis, medialis, and profundus and retractor quadrati) that may help to express the secretions.

FIGURE 36-22 Mimicry—South American pit vipers. **A,** Amazonian snail eater (*Dipsas indica*: family Dipsadidae) (Amparo Granja, Sao Jose, Brazil). **B,** Neuwied's false fer de lance (*Xenodon neuwiedii*: family Dipsadidae) (Cajamar, Brazil). **C,** Amazon false fer de lance (*Xenodon severus*: family Dipsadidae) (Porto Velho, Brazil). **D,** Wagler's snake (*Waglerophis merremi*: family Dipsadidae) (Brazil). **E,** Brazil's lancehead (*Bothrops brazili*: family Viperidae) (Moreno Santiago, Ecuador). *(Copyright D.A. Warrell.)*

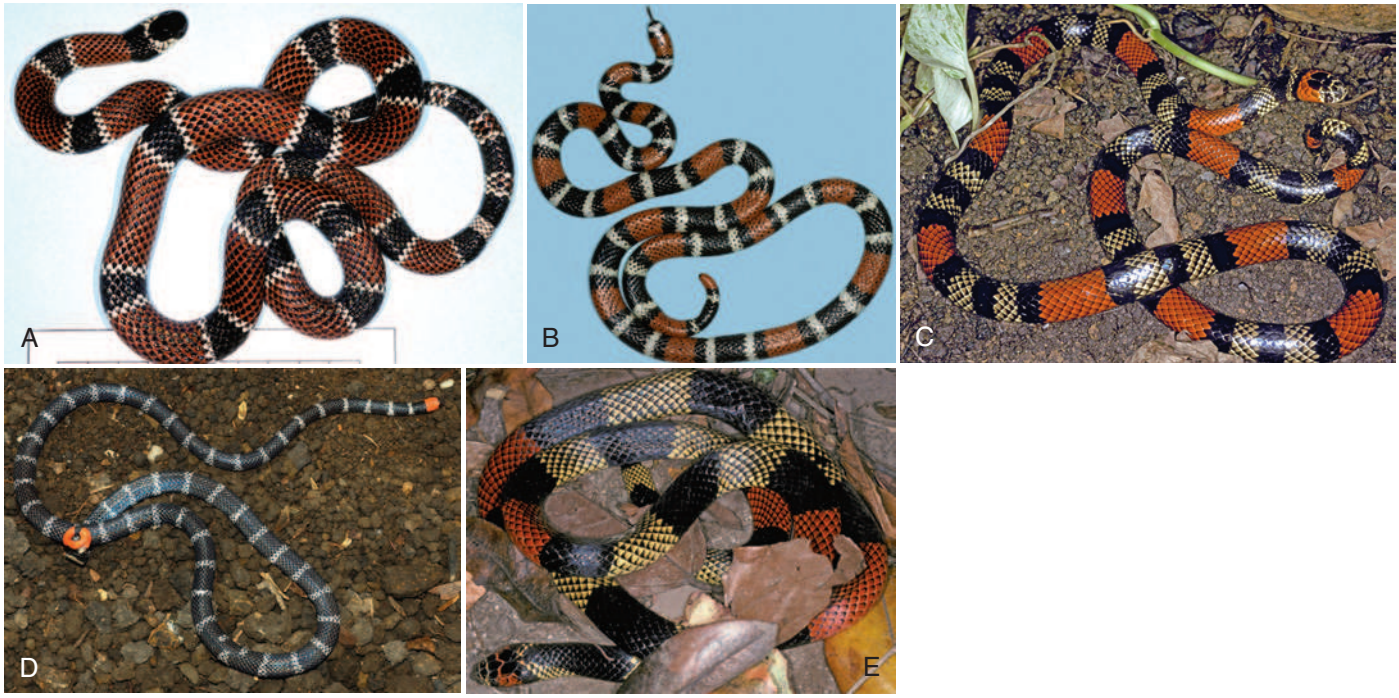


FIGURE 36-23 South American coral snakes (family Elapidae). **A,** Painted coral snake (*Micrurus corallinus*) (Brazil). **B,** Decorated coral snake (*M. decoratus*) (Brazil). **C,** Cerrado coral snake (*M. frontalis*) (Brazil). **D,** Red-tailed coral snake (*M. mipartitus*) (Colombia) showing tail curling display. **E,** Amazonian coral snake (*M. spixii obscurus*) (Ecuador). *(Copyright D.A. Warrell.)*

FIGURE 36-24 Coral snakes mimics (family Dipsadidae). **A,** Duméril's false coral snake (*Oxyrhopus clathratus*) (Juquitiba, Brazil). **B,** Brazilian false coral snake (*Oxyrhopus trigeminus*) (northeast Brazil). **C,** *Rhinobothryum bovallii* (Rio Bogota, Esmeraldas, Ecuador). **D,** *Simophis rhinostoma* (Brazil). *(Copyright D.A. Warrell.)*

FIGURE 36-25 Texas coral snake (*Micrurus tener*) (Kingsville, Texas) showing "red on yellow" pattern. *(Copyright D.A. Warrell.)*

FIGURE 36-26 Sri Lankan hump-nosed pit viper (*Hypnale hypnale*: family Viperidae; subfamily Crotalinae; scale in cm). *(Copyright D.A. Warrell.)*

FIGURE 36-27 Ceylon cat snakes (*Boiga ceylonensis*). *(Copyright D.A. Warrell.)*

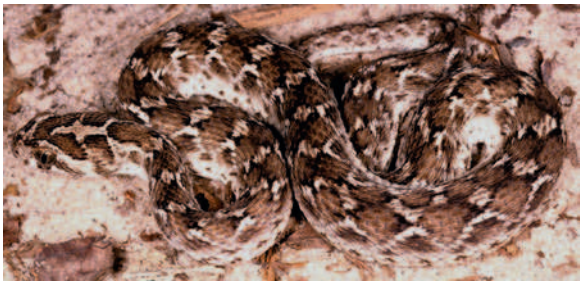


FIGURE 36-28 Sri Lankan saw-scaled viper (*Echis carinatus*). *(Copyright D.A. Warrell.)*

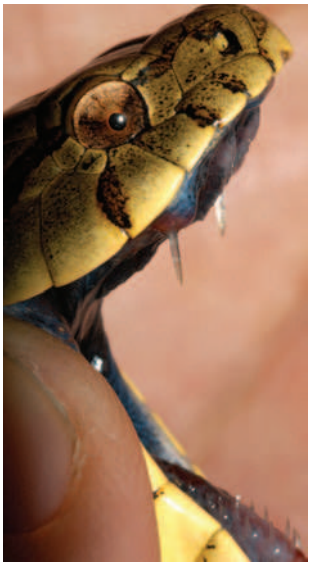


FIGURE 36-29 Long maxillary fangs of Pampas snake (*Tomodon dorsatus*: family Dipsadidae) (Ibiuna, Brazil). *(Copyright D.A. Warrell.)*

Elapoidea: Lamprophiidae, Subfamily Atractaspidinae

The genus *Atractaspis* (African and Middle Eastern burrowing asps, stiletto snakes, burrowing or mole vipers or adders, false vipers, or side-stabbing snakes) have long front fangs on which they impale their victims by a side-swiping motion of the fang protruding from the corner of the partially closed mouth (Figure 36-30, *Atractaspis aterrima*). In some species, the venom glands are very long—perhaps one-sixth of the snake's total length. The Natal black snake (*Macrelaps microlepidotus*) possesses two very large, grooved opisthoglyphous fangs at the posterior ends of its maxillae.

Elapoidea: Elapidae

Cobras—*Naja*; kraits—*Bungarus*; mambas—*Dendroaspis*; shield-nosed and African coral snakes—*Aspidelaps*; Asian coral snakes—*Calliophis*; African garter snakes—*Elapsoidea*; terrestrial venomous Australasian snakes (e.g., *Acanthophis, Pseudechis, Pseudonaja, Oxyuranus, Notechis*); and sea snakes (e.g., *Laticauda*, *Enhydrina*, *Hydrophis*, *Lapemis*) have relatively short, proteroglyphous (fixed) front fangs mounted on a relatively fixed maxilla so that they cannot be folded flat against the jaw (Figure 36-31, *Oxyuranus scutellatus canni*). However, mambas can rotate their

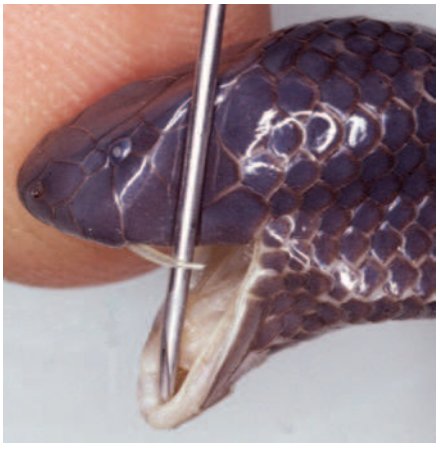


FIGURE 36-30 Long front fang of a slender burrowing asp (*Atractaspis aterrima*: subfamily Atractaspidinae) (Zaria, Nigeria). *(Copyright D.A. Warrell.)*

FIGURE 36-31 Short front fangs of a Papuan taipan (*Oxyuranus scutellatus*: family Elapidae) (Port Moresby, Papua New Guinea). *(Copyright D.A. Warrell.)*

fangs in the sagittal plane because the maxilla has a posterior articulation with the prefrontal bone (Figure 36-32, *Dendroaspis angusticeps*). This allows the snake to close its mouth despite having unusually long elapid type of fangs and to increase its gape when striking at large prey. Venom glands are situated behind the eyes and are compressed by *adductor externus superficialis* (equivalent to *levator anguli oris*) muscles. Some coral snakes possess inferolabial glands in the lower jaw that also secrete venom conducted by shallow grooves in the mandibular teeth.

Spitting Elapids.[46] The fangs of African and Asian spitting cobras and the South African ringhals or rinkhals (*Hemachatus haemachatus*) have venom channels that turn forward at their point of exit near the tips of the fangs. Compressor muscles produce a stream of venom under high pressure so that a spray of venom can be ejected forward for 1 m (3.3 feet) or more into the eyes of an aggressor (Figure 36-33, *Naja nigricollis*).[25,46,331,332] This is a defensive strategy that temporarily blinds the aggressor, usually a large, threatening mammal, and allows the snake to escape. To eject venom 2 m (6.6 feet), pressures of 1.5 kg/cm^2 (21.3 psi) are required.

Viperidae

Viperidae (vipers, adders, and pit vipers) have highly evolved, long, curved front solenoglyphous (hinged, venom-conducting) fangs, mounted on a rotatable maxilla that allows them to be erected when the snake strikes and folded flat against the jaw in a protective membrane when not in use. They contain a closed

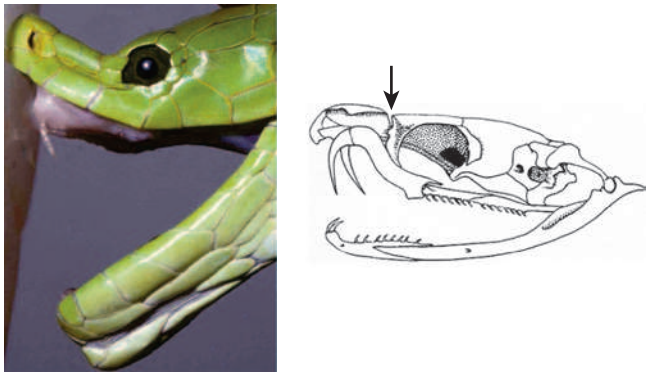


FIGURE 36-32 Eastern green mamba (*Dendroaspis angusticeps*) (coastal Kenya) showing articulation of the maxilla (bearing the fangs) on the prefrontal bone (*arrow*), allowing rotation of the long, elapid type of fangs. *(Copyright D.A. Warrell.)*

FIGURE 36-33 Black-necked spitting cobra (*Naja nigricollis*) (Zaria, Nigeria) in the act of "spitting" venom from its fang tips toward the snake charmer's hand. *(Copyright D.A. Warrell.)*

venom channel and resemble hypodermic needles (Figure 36-34A, *Bothrops jararacussu;* and B, *Bitis rhinoceros*). The venom glands are squeezed by compressor glandulae, adductor externus profundus, and pterygoideus muscles.

VENOM COMPOSITION[93,144,159,293]

Snakes have evolved the most complex of all venoms. The venom of each species contains more than 100 different components. The evolutionary origins of these molecules are of increasing interest.[70,76] More than 90% of the dry weight is protein, comprising a variety of enzymes, nonenzymatic polypeptide toxins, and nontoxic proteins. Nonprotein ingredients include carbohydrates and metals (often part of glycoprotein metalloprotein enzymes), lipids, free amino acids, nucleosides, and biogenic amines such as serotonin and acetylcholine.

ENZYMES

From 80% to 95% of viperid and 25% to 70% of elapid venoms consist of enzymes (molecular weight, 13 to 15 kilodaltons), including digestive hydrolases (proteinases, exopeptidase, endopeptidases, phosphodiesterases, metalloproteinases, and phospholipases), hyaluronidase,[120,190,191] and activators or inactivators of physiologic processes. Most venoms contain L-amino acid oxidase (containing riboflavin 5′-phosphate prosthetic group, which confers the yellow color of many venoms), which may have a digestive function,[234] phosphomonoesterase, diesterase, 5′-nucleotidase, deoxyribonuclease, nicotinamide adenine dinucleotide nucleosidase,[55] phospholipase A_2 (PLA_2), and peptidases.

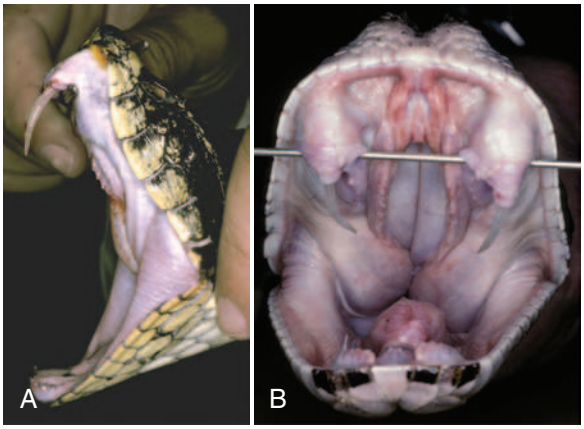


FIGURE 36-34 Erectile front fangs of Viperidae. **A,** Large front fangs of jararacuçu (*Bothrops jararacussu*: subfamily Crotalinae, Brazil). **B,** Enormous solenoglyphous front fangs of a West African Gaboon viper/adder (*Bitis rhinoceros*: subfamily Viperinae, Cameroun) erected as when the snake strikes its prey. Gaboon vipers have longer fangs than do other snakes, up to 8 cm (3.2 inches) in length. *(Copyright D.A. Warrell.)*

Elapid venoms also contain acetylcholine esterase,[3] phospholipase B, and glycerophosphatase, whereas viperid venoms have endopeptidase, arginine ester hydrolase, kininogenase (which releases bradykinin from bradykininogen), procoagulants (thrombin-like serine proteinases),[142] and factor V, factor X, and prothrombin-activating enzymes, which cause disseminated intravascular coagulation (DIC), leading to consumption coagulopathy. PLA_2s are the most widespread and extensively studied of all venom enzymes.[56,144] Under experimental conditions, they damage mitochondria, red blood cells, leukocytes, platelets, peripheral nerve endings, skeletal muscle, vascular endothelium, and other membranes and produce presynaptic neurotoxic activity, opiate-like sedative effects, and autopharmacologic release of histamine. Hyaluronidase promotes spread of venom through tissues. Proteolytic enzymes (endopeptidases or hydrolases) are responsible for local changes in vascular permeability, leading to edema, blistering, bruising, and necrosis. Metalloproteinases cause local and systemic hemorrhage and local myonecrosis, blistering, and edema through their actions on vascular endothelium, platelets,[115] muscle, and other tissues.[66,86]

NECROTOXINS

Many snake venoms contain myotoxic and cytolytic factors that contribute to tissue destruction around the site of the bite. These include zinc-dependent metalloproteinases and myotoxic PLA_2s, other digestive hydrolases, and hyaluronidase. Myotoxins are proteins that can damage the muscle cell plasma membrane directly. Most are PLA_2s, either enzymatically active (aspartate-49) or enzymatically inactive (lysine-49).[86] Cobra cardiotoxins are low-molecular-weight polypeptides with cytotoxic action.

NEUROTOXINS

Postsynaptic Three-Finger-Fold Neurotoxins[159]

These polypeptide curarimimetic neurotoxins or α-neurotoxins are low-molecular-weight, nonenzymatic proteins found in elapid and some colubroid venoms.[71,143,179] They are termed "short" (60 to 62 amino acids) or "long" (66 to 74 amino acids), such as α-bungarotoxin and cobrotoxin. They bind to the nicotinic acetylcholine (ACh) binding sites of motor end plates of skeletal muscles, at the interfaces between the α/ε and the α/δ subunits of the ACh receptor, thereby preventing interaction between ACh and the receptor, to cause a rapidly developing neuromuscular paralysis and eventually death from bulbar and respiratory muscle weakness. These neurotoxins have a distinctive "three-finger-fold" structure, complementary in shape to their receptor, and have also been found in some colubrid venoms.

Presynaptic Phospholipase A_2 Neurotoxins

These β-neurotoxins, such as β-bungarotoxin, crotoxin, and taipoxin, contain about 120 to 140 amino acid residues and a phospholipase A subunit. They damage nerve endings at neuromuscular junctions, targeting voltage-gated potassium channels and causing sequential suppression, enhancement, and finally complete failure of ACh release. The resulting paralysis is clinically indistinguishable from that caused by postsynaptic toxins, except that the latter may be ameliorated by anticholinesterases, such as edrophonium or neostigmine. Many neurotoxic PLA_2s and other phospholipases have myotoxic activity.

MAMBA TOXINS

Mamba (*Dendroaspis*) venoms contain a number of distinctive neurotoxins.[93,159] Dendrotoxins (7-kDa, 57- to 60-amino-acid proteins), such as α-dendrotoxin from eastern green mamba (*Dendroaspis angusticeps*) (see Figure 36-8) venom, which binds to some classes of voltage-gated potassium channels at nerve endings to cause polarizing block by ACh release, and calcicludine, which blocks calcium channels, are "pear"-fold structures. Two "three-finger-fold" neurotoxins are unique to mamba venoms. Fasciculins (61-amino-acid residues) inhibit some acetylcholinesterases, causing persistent muscle fasciculations,[93] whereas calciseptine binds to calcium channels.

KRAIT BUNGAROTOXINS

In the venoms of kraits (*Bungarus* spp.), a number of neurotoxins have been identified that have proved useful to neurophysiologists and neuropharmacologists. They include β-bungarotoxins (β-BTXs) that act presynaptically, α-bungarotoxins (α-BTXs) and γ-bungarotoxins (γ-BTXs) that antagonize binding of ACh postsynaptically at peripheral neuromuscular junctions, and κ-bungarotoxins (κ-BTXs) that block neuronal nicotinic receptors. β-BTXs are heterodimeric neurotoxins consisting of a PLA_2 chain and a Kunitz type of protease inhibitor chain. As with most neurotoxic PLA_2s, BTXs have been shown to cause significant loss of labeling by antisynaptophysin (reflecting loss of synaptic vesicles) at the mammalian neuromuscular junction and degeneration of intramuscular branches of the terminal motor axon. BTXs are implicated in the resistance of the neuromuscular weakness of krait bite victims to antivenom and anticholinesterases.

CARDIOVASCULAR TOXINS

Shock in snakebites victims is attributable to permeability factors causing hypovolemia from extravasation of plasma and toxins acting directly or indirectly on cardiac muscle, vascular smooth muscle, and other tissues.

ACE Inhibitors and Bradykinin-Potentiating Peptides

Oligopeptides (molecular weight, 600 to 1600 daltons) from venom of the Brazilian jararaca (*Bothrops jararaca*) activate bradykinin and, through bradykinin-potentiating peptide (BPP) activity, prolong bradykinin's hypotensive effect by inactivating the peptidyl dipeptidase that destroys bradykinin and converts angiotensin I to angiotensin II. This provided the structural model for captopril, the first of the synthetic angiotensin-converting enzyme (ACE) inhibitors. BPPs and ACE-inhibiting peptides have been found in several other crotaline and viperine venoms.[57]

Sarafotoxins[19,59,27]

Venoms of the Israeli burrowing asp (*Atractaspis engaddensis*: Atractaspidinae) and some other members of this genus contain endothelin-like sarafotoxins. These are 21-amino-acid polypeptides that cause coronary artery vasoconstriction and prolonged atrioventricular conduction, and that are positively inotropic.

Natriuretic Peptides

Natriuretic peptides been found in many viperid and *Dendroaspis, Bungarus,* and *Micrurus* venoms. A B-type natriuretic peptide from eastern green mamba venom (*Dendroaspis angusticeps*) is under therapeutic trial for treatment of congestive cardiac failure.

PAIN-PRODUCING TOXINS

The clinical observation that Texas coral snake (*Micrurus tener tener*) bites produced intense and unremitting pain led to the discovery of a heteromeric complex between Kunitz-like and PLA_2-like proteins in this species' venom that functioned together in a potent, persistent, and selective agonistic manner for a subtype of acid-sensing ion channel (ASIC), ASIC1, on capsaicin-sensitive nerve fibres.[26,27] It is not known whether this painful toxin evolved as a predatory or defensive strategy.[175] Envenoming by tropical coral snakes (*Micrurus lemniscatus*) also produces excruciating pain.[151]

BIOGENIC AMINES

Biogenic amines, such as histamine and 5-hydroxytryptamine (5-HT, serotonin), found particularly in viper venoms, may contribute to local pain and permeability changes at the site of a snakebite.

VENOM POTENCY AND LETHALITY

The activities of different venoms can be compared in the laboratory using in vitro and animal in vivo assays. The only practicable index of lethality is the median lethal dose (LD_{50}) measured in mice of specified strain and size (Table 36-1). However, this value

TABLE 36-1 Venom Yield on Milking and Mouse Lethality of Selected Venoms in Declining Order of Lethal Potency in Mice

Species	Venom Yield: (Dry Weight) (mg)			Mouse Median Lethal Dose (LD_{50}) (mg/kg)
	Range	Average	Maximum	
Papuan taipan (*Oxyuranus scutellatus*)	90-420		420	0.0023 ±0.006 (IP*)
				0.0047 ±0.006 (IV*)
			400	0.05 (subcutaneous)[232]
Beaked sea snake (*Hydrophis schistosus*, formerly *Enhydrina schistosa*)	7-20			0.01 (0.164) (IV)
Australian (Eastern) taipan (*Oxyuranus scutellatus*)	40	120		0.015 (IV)
				0.099 (subcutaneous)
Western/inland taipan or small-scaled snake (*Oxyuranus microlepidotus*)	44	110		0.025 (subcutaneous)
Eastern brown snake (*Pseudonaja textilis*)		8	67	0.053 (IV)
Russell's viper (*Daboia russelii*)	130-250			0.08 (IV)
Common krait (*Bungarus caeruleus*)	8-20			0.09 (IV)
Mainland tiger snake (*Notechis scutatus*)		35	189	0.118 (IV)
Indian cobra (*Naja naja*)		169	610	0.13-0.42 (IV)
Tropical rattlesnake (*Crotalus durissus terrificus*)			220	0.17 (IV)
Mohave rattlesnake (*Crotalus scutulatus*)			141	0.18 (IV)
Florida coral snake (*Micrurus fulvius*)			38	0.21 (IV)
Black mamba (*Dendroaspis polylepis*)				0.26-2.9 (IV)
Common lancehead (*Bothrops atrox*)			300	0.35 (IV)
Hundred pacer (*Deinagkistrodon acutus*)				0.38 (IV)
Green mamba (*Dendroaspis angusticeps*)	60-95			0.45 (IV)
European adder (*Vipera berus*)	6-18			0.55 (IV)
Southern Pacific rattlesnake [*Crotalus (oreganus) helleri*]			390	0.84 (IV)
West African carpet viper (*Echis ocellatus*)	1.4-24.8		25	0.99 (95% CI, 0.83-1.20) (IV†)
Terciopelo (*Bothrops asper*)		485	1530	1.10 (IV)
Eastern diamondback rattlesnake (*Crotalus adamanteus*)	370-720	410	848	1.2 (IV)
Cerrado coral snake (*Micrurus frontalis*)			53	1.5 (subcutaneous)
Jararacuçu (*Bothrops jararacussu*)			830	1.75 (IV)
King cobra (*Ophiophagus hannah*)		421	1000	1.80 (IV)
Central American rattlesnake (*Crotalus simus*)		159	360	1.84 (IV)
Indian saw-scaled viper (*Echis carinatus*)	20-35			2.30 (IV)
Bushmaster (*Lachesis muta*)			1760	5.6 (IV)

From Bolaños R: Toxicity of Costa Rican snake venoms for the white mouse, *Am J Trop Med Hyg* 21:360, 1972; Broad AJ, Sutherland SK, Coulter AR: The lethality in mice of dangerous Australian and other snake venom, *Toxicon* 17:661, 1979; and Mebs D: Pharmacology of reptilian venoms. In Gans C, editor: *Biology of the reptilia*, vol 8, London, 1978, Academic Press, pp 437-560.
CI, Confidence interval; *IP*, intraperitoneal; *IV*, intravenous.
*Data from Vargas M, Segura A, Herrera M, et al: Preclinical evaluation of caprylic acid-fractionated IgG antivenom for the treatment of Taipan (*Oxyuranus scutellatus*) envenoming in Papua New Guinea, *PLoS Negl Trop Dis* 5:e1144, 2011.
†Data from Theakston RDG: Personal communication, August 2010.

cannot be extrapolated easily to give a reliable idea of the lethal dose or even the relative lethality of different venoms in humans. Quite apart from the marked species variations in vulnerability to venoms, the mode of death in different animals may not be the same. In mice, for example, venom of the black-necked spitting cobra (*N. nigricollis*) causes death with convulsions following paralysis (intravenous LD_{50}, 0.40 to 1.37 mg/kg), but humans envenomed by this species do not show neurotoxicity.[248,298] However, a recent proteomic study of African spitting cobra venoms found no neurotoxic 3FTxs, such as the well-known "*Naja nigricollis* toxin-α" in the venom of this species. It was originally purified from the venom of *N. nigricollis* "collected in Ethiopia in 1961,"[117] but the donor snake may have been a misidentified *Naja nubiae* because only this species' venom contains a relatively high content of a type-1 α-neurotoxin.[181]

A portfolio of standard World Health Organization (WHO) assays for assessing different aspects of venom activity has been developed.[239] It is hoped that an assay in insensate chick embryos,[214] as well as increasing use of tissue culture assays, may reduce the need for studies in living animals.

VARIATIONS IN QUANTITY AND COMPOSITION OF VENOM INJECTED BY SNAKEBITE

In human victims of snakebites, the amount and composition of venom injected by the snake are the most important, but obviously indeterminate, factors influencing evolution of envenoming and prognosis. Apart from inferring the quantity and quality of injected venom from the range and severity of clinical manifestations of envenoming, the only currently available objective method of assessment is to measure venom antigenemia on the patient's hospital admission (not venom concentration, which cannot be assessed by enzyme immunoassay because many of the smaller but pathophysiologically important molecules, such as oligopeptides, are poorly immunogenic and therefore are not detected by the test antiserum). This has been found to correlate with clinical severity in the case of several different species of snake, including European vipers,[14,260] Martinican lancehead (*Bothrops lanceolatus*),[246] jararaca (*B. jararaca*),[68] and common lancehead (*B. atrox*).[222]

Box 36-1 summarizes the factors that determine severity of envenoming. Clinical assessment suggests that the amount of venom injected by a bite is extremely variable. A proportion of human victims of snakebites, more than one-half in some series, show negligible or no signs of envenoming, even though the snake was identified as being venomous, and there were obvious puncture marks indicating that the fangs had penetrated the skin.[168,182] These "dry bites" have led to the belief that snakes can somehow control the amount of venom injected, according to the size of their natural prey,[97] and that they can inflict an intentionally "defensive bite," choosing not to expend venom when they strike at an enemy. However, when humans are

BOX 36-1 Determinants of Snakebite Incidence and Severity of Envenoming

Incidence of Bites

Frequency/intensity of snake-human encounters, depending on:
- Population densities (snake, human) and their spatial/temporal coincidence
- Diurnal and seasonal variations in activity
- Types of behavior (e.g., human agricultural)

Snakes' "irritability"—readiness to strike when disturbed, alarmed or provoked—varies with species

Severity of Envenoming

Dose of venom injected—depends on mechanical efficiency of bite, species and size of snake, and number of strikes ("dry bite" phenomenon)

Composition and thus potency of venom—depends on species and, within a species, the geographic location, season, and age of the snake

Health, age, size, and specific immunity of human victim

Nature and timing of first aid and medical treatment

bitten, the usual circumstances of the bite—the victim inadvertently picking up or stepping on a snake in foliage—may mitigate against mechanical efficiency of the snake's venom apparatus in injecting venom, because humans are unexpected and abnormal targets. The idea that a snake might exhaust its supply of venom by a recent strike and therefore be less venomous after killing and swallowing its natural prey or after striking another person has been refuted. Snakes do not exhaust the contents of their venom glands during the first strike. The proportion of unexpended venom after the first strike was found to be 0% to 85% for Australian death adder (*Acanthophis*), 5% to 81% for Australian tiger snakes (*Notechis*), 40% for the Indian cobra (*Naja naja*), and 30% for the saw-scaled viper (*Echis carinatus*).[126] Palestine vipers (*Daboia palaestinae*) continue to deliver substantial quantities of venom even after nine or more consecutive strikes.[126] In several reports of consecutive strikes by a single snake on several human victims, the first victim was not always the most severely envenomed. In the case of Russell's viper bites in Burma (Myanmar), snakes that had recently fed (those in which a rodent was found in the stomach) inflicted bites that were no less venomous than those with an empty stomach.[260]Although the largest snakes do necessarily inflict the most highly venomous bites, there is a tendency, in most species that have been studied, for the severity of local and systemic envenoming to increase with size of the individual snake responsible.[260] Venom yield has been shown to increase with ambient temperature, but no definite seasonal variation has been documented.

INTRASPECIES VARIATION IN VENOM COMPOSITION

In many snake species, venom composition has been found to change as the snake grows older, presumably to accommodate a changing range of prey species. Most of the species that have been studied are from the Americas (see Chapter 35), but in the rest of the world, Indian cobra (*Naja naja*) venom has been shown to have decreasing lethality with increasing age, whereas venoms of the saw-scaled viper (*Echis carinatus*) and black-necked spitting cobra (*Naja nigricollis*) show decreasing lethality despite increasing protein concentration.[281] Seasonal variation in venom composition of a particular species has been suspected but not proved. There is abundant literature describing variations in venom lethality, composition, and activities between individuals of a particular species at the same geographic focus or from different places within the snake's geographic range.[50,187,281] In the case of the Malayan pit viper (*Calloselasma rhodostoma*),[50] *Echis* spp.,[18,38] and *Sistrurus* spp.,[81] available prey species seemed to have had a major evolutionary influence on venom composition in different parts of the snake's geographic range.

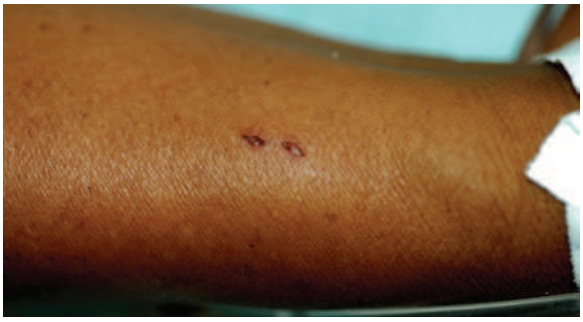


FIGURE 36-35 Common lancehead (*Bothrops atrox*) bite (Iquitos, Peru) in which the fang puncture marks were over the cephalic vein above the wrist. There were no signs of local envenoming, but severe systemic venom evolved rapidly, implying intravenous injection of venom. *(Copyright D.A. Warrell.)*

EFFECT OF THE SITE, DEPTH, AND NUMBER OF BITES

In experimental animals, the route of venom administration (topical, intradermal, subcutaneous, intramuscular, intraperitoneal, intravenous, intracerebral) affects the speed, pattern, and lethality of envenoming. This is virtually impossible to study clinically, but in anecdotal cases of human envenoming, in which systemic effects develop rapidly after a bite with minimal local signs, it has been assumed that venom entered the bloodstream directly as a result of a fortuitous intravenous puncture (Figure 36-35, *Bothrops atrox* bite). As might be expected, multiple bites, revealed by the number of fang punctures, have been associated with more severe envenoming (Figure 36-36).

EPIDEMIOLOGY OF SNAKEBITE

SNAKE SPECIES RESPONSIBLE FOR MOST BITES

Table 36-2 lists the species responsible for most snakebite deaths and severe morbidity outside North America. Fortunately, some species notorious for the potency of their venom (e.g., sea snakes and reclusive Australian inland taipan, *Oxyuranus microlepidotus*) or their great size (e.g., south Asian king cobra, *Ophiophagus hannah* [see Figure 36-15], which can grow longer than 5.8 m [19 feet]; Gaboon vipers, *Bitis gabonica* and *B. rhinoceros* [see Figure 36-34B], which may exceed 2 m [6.6 feet] in total length and weigh more than 8 kg [17.6 lb]; and bushmasters [genus *Lachesis*] that grow to more than 4 m [13 feet] [Figure 36-37, *Lachesis stenophrys*]) rarely bite humans. African night adders and burrowing asps (genera *Causus,* Figure 36-38; and *Atractaspis,* Figure 36-39),[297] Asian green pit

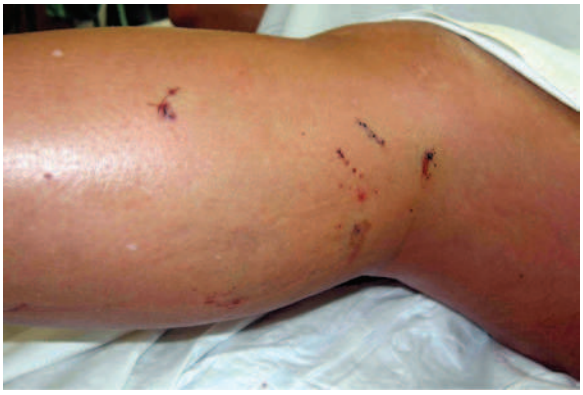


FIGURE 36-36 Multiple puncture marks resulting from repeated strikes by bushmaster (*Lachesis muta*) in Trinidad. *(Courtesy Ms. H. Hansen.)*

TABLE 36-2 Species of Snake Probably Responsible for Most Deaths and Morbidity Outside North America and Mexico

Geographic Area	Scientific Name	Common Name
Europe	Vipera and *Macrovipera* spp.	Vipers, adders
	Vipera ammodytes	Long-nosed viper
Africa	*Naja nigricollis, N. mossambica*, etc.	African spitting cobras
	Naja haje, N. senegalensis, N. annulifera, N. anchietae	Egyptian and snouted cobras
	Dendroaspis spp.	Mambas
	Echis ocellatus, E. jogeri, E. leucogaster, E. pyramidum, etc.	Saw-scaled or carpet vipers
	Bitis arietans	Puff adder
Asia, Middle East	*Naja oxiana*	Oxus cobra
	Echis spp.	Saw-scaled or carpet vipers
	Macrovipera lebetina	Levantine viper
	Daboia palaestinae	Palestine viper
Asia, Indian Subcontinent, Southeast Asia	*Naja naja, N. kaouthia, N. siamensis*	Asian cobras
	Bungarus spp.	Kraits
	Daboia russelii, D. siamensis	Russell's vipers
	Calloselasma rhodostoma	Malayan pit viper
	Echis carinatus	Saw-scaled or carpet vipers
	Hypnale hypnale	Hump-nosed pit viper
	Trimeresurus (*Trimeresurus, Craspedocephalus, Viridovipera*, etc.) and related genera	Arboreal and other pit vipers
Asia, Far East	*Naja atra*	Chinese cobra
	Bungarus multicinctus	Chinese krait
	Protobothrops flavoviridis	Japanese habu
	Protobothrops mucrosquamatus	Chinese habu
	Gloydius blomhoffii and *G. brevicaudus*	Mamushis
Australasia, New Guinea	*Acanthophis* spp.	Death adders
	Pseudonaja spp.	Brown snakes
	Pseudechis spp.	Black snakes
	Notechis spp.	Tiger snakes
	Oxyuranus scutellatus	Taipan
	Micropechis ikaheka	New Guinean small-eyed snake
Central America, South America	*Micrurus* spp.	Coral snakes
	Bothrops atrox	Common lancehead
	Bothrops asper	Terciopelo
	Bothrops jararaca	Jararaca
	Bothrops bilineatus (*Bothriopsis bilineata*)	Papagaio
	Agkistrodon, Bothriechis, Porthidium, and related genera	Cantils and other pit vipers
	Lachesis spp.	Bushmasters, surucucu
Caribbean	*Micrurus lemniscatus, M. circinalis*	Coral snakes (Trinidad)
	Bothrops asper	Mapepire (Trinidad)
	Bothrops caribbaeus	Serpent (St Lucia)
	Bothrops lanceolatus	Fer de lance (Martinique)
	Crotalus durissus	Colebre (Aruba), Islas Los Testigos
	Lachesis muta	Mapepire zanana (Trinidad)

vipers (e.g., genera *Trimeresurus* [*Trimeresurus*] [Figure 36-40], *Trimeresurus* [*Craspedocephalus*], *Trimeresurus* [*Viridovipera*] [Figure 36-41],[106,266] and Sri Lankan and southwest Indian hump-nosed pit vipers [*H. hypnale*])[13,54,114] are responsible for many bites, but severe envenoming is relatively uncommon.

DISTRIBUTION OF VENOMOUS SNAKES

Venomous snakes are distributed from sea level to high altitudes. The Himalayan pit viper, *Gloydius himalayanus,* normally confined below 1500 m (4921 feet), has been recorded at the base of the Dharamsala glacier in northern India as high as 4877 m (16,000 feet).[212] The rattlesnake (*Crotalus triseriatus triseriatus,* Figure 36-42A) has been found on Mt Popocatepetl and Ajusco and Volcán Pico de Orizaba in Mexico at altitudes up to 4600 m (15,092 feet).The European adder, *Vipera berus*, is widely distributed, from England, Scotland, and Wales in the west, across Europe and Asia to North Korea and Sakhalin Island in the east, and north into Scandinavia and the Arctic Circle (Figure 36-42B and Figure 36-43). No other venomous species is found in the Arctic, and none occurs in the Antarctic, Crete, Ireland, Iceland, Madagascar, New Caledonia, New Zealand, or Hawaii. Most of the islands of the western Mediterranean Sea, Atlantic Ocean, and Pacific Ocean are free of venomous snakes (Figure 36-44).

Sea snakes occur in the Persian Gulf, Indian Ocean, and Pacific Ocean between latitudes 30 degrees north and 30 degrees south, as far south as New Zealand and Tasmania, and as far north as Siberia (yellow-bellied or pelagic sea snake *Pelamis platura*)[154,197,277] (Figure 36-45). The beaked sea snake (*Enhydrina schistosa,* also known as *Hydrophis schistosus*) and *Hydrophis* spp. frequent estuaries and have been found 130 to 160 km (80 to 100 miles) up rivers. In Papua New Guinea, *E. schistosa* was taken in the Ramu River, 30 km (18.6 miles) from the sea, where it had caused fatal envenoming (Figure 36-46). In freshwater lakes, *Hydrophis semperi* occurs in Lake Taal (also called Lake Bombon) (Figure 36-47) in the Philippines and *E. schistosa* in Tonle Sap in Cambodia. There are no sea snakes in the Atlantic Ocean or the Red Sea.[277]

FIGURE 36-37 Bushmasters (genus *Lachesis*). **A,** South American bushmaster (*L. muta*) (Brazil). **B,** Central American bushmaster (*L. stenophrys*) (Costa Rica). *(Copyright D.A. Warrell.)*

FIGURE 36-38 Velvety-green night adder (*Causus resimus*: subfamily Viperinae) (Watamu, Kenya). *(Copyright D.A. Warrell.)*

FIGURE 36-39 Burrowing asp (*Atractaspis fallax*: subfamily Atractaspidinae) (Watamu, Kenya). *(Copyright D.A. Warrell.)*

FIGURE 36-40 White-lipped green pit viper (*Trimeresurus* [*Trimeresurus*] *albolabris*: subfamily: Crotalinae) (Thailand). *(Copyright D.A. Warrell.)*

SNAKEBITE MORTALITY AND MORBIDITY

In the tropical countries where snakebite is most common, few reliable data exist. There have been only three serious attempts to assess global snakebite mortality.[43,119,233] However, community-based studies have revealed gross underreporting of deaths in these studies. One reason is that records of patients treated by traditional methods are missing from official hospital-based statistics, and deaths reported at the hamlet or district level may not be sent on to ministry headquarters. Population surveys have given a far more accurate picture of snakebite incidence, morbidity, and mortality.[67,95,165,185,189,224,252,294] The prevalence of chronic morbidity after snakebite is unknown, but for every person killed by snakebite, one or two may survive with a long-term physical handicap.

AMERICAS (CENTRAL, SOUTH, AND THE CARIBBEAN)

Estimates of the total number of deaths caused by snakebites each year in Central and South America (including Mexico) were as follows: in 1954, between 3000 and 4000;[233] in 1998, 5000 out of 300,000 bites;[43] and in 2008, 3300 to 4500 deaths out of 81,427 to 137,123 bites.[119] The incidence is high among indigenous Amerindian tribes. In Acre, western Brazil, snakebite accounted for 3.3% of all deaths and 24% of deaths in the 15- to 44-year-old age-group among 100 families of Kaxinawa of the Rio Tejo, Upper Juruá rubber extraction area.[28] A survey of forest-dwelling Amazonian Indians and rubber tappers of the Juruá Valley found that 30% of the population had been bitten during their lifetime.

FIGURE 36-41 Chinese bamboo viper (*Trimeresurus* [*Viridovipera*] *stejnegeri*: subfamily Crotalinae) (China). *(Copyright D.A. Warrell.)*

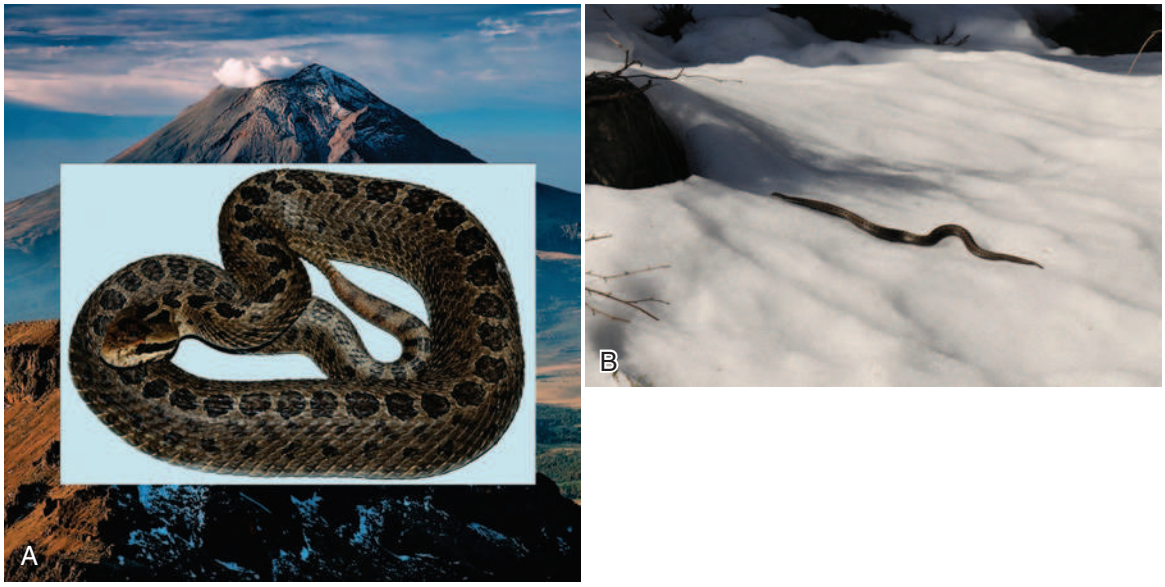


FIGURE 36-42 Venomous snakes at environmental extremes. **A,** High-altitude rattlesnake. Mexican dusky rattlesnake (*Crotalus triseriatus*) found on Mt Popocatepetl and Ajusco and Volcán Pico de Orizaba in Mexico at altitudes up to 4600 m (15,092 feet). **B,** European adder (*Vipera berus*) within the Arctic Circle in Norway. (***A,*** *Copyright D.A. Warrell;* ***B,*** *Courtesy Øyvind Syrrist, Oslo.)*

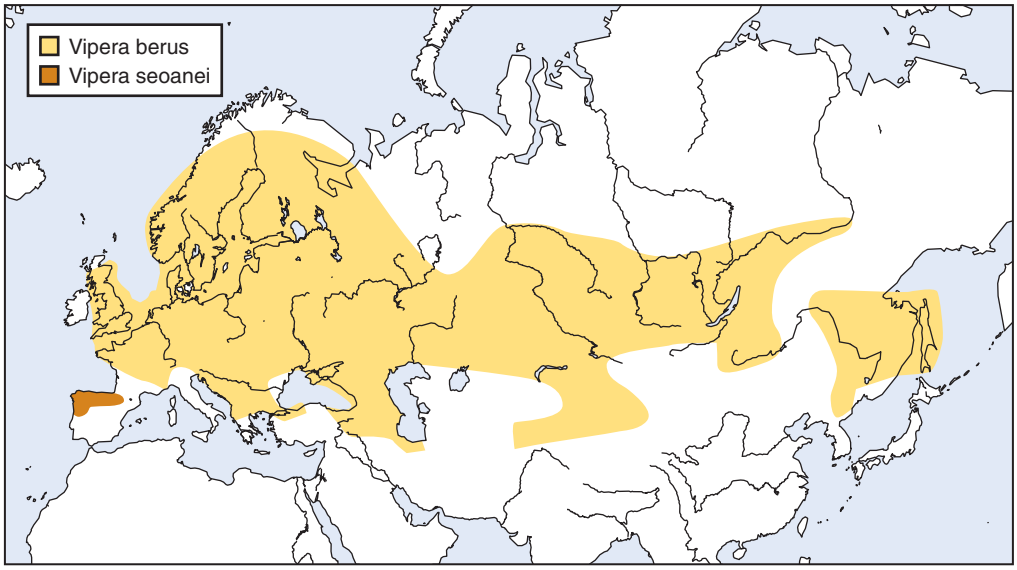


FIGURE 36-43 Global distribution of the European adder (*Vipera berus*). *(Courtesy Goran Nilson.)*

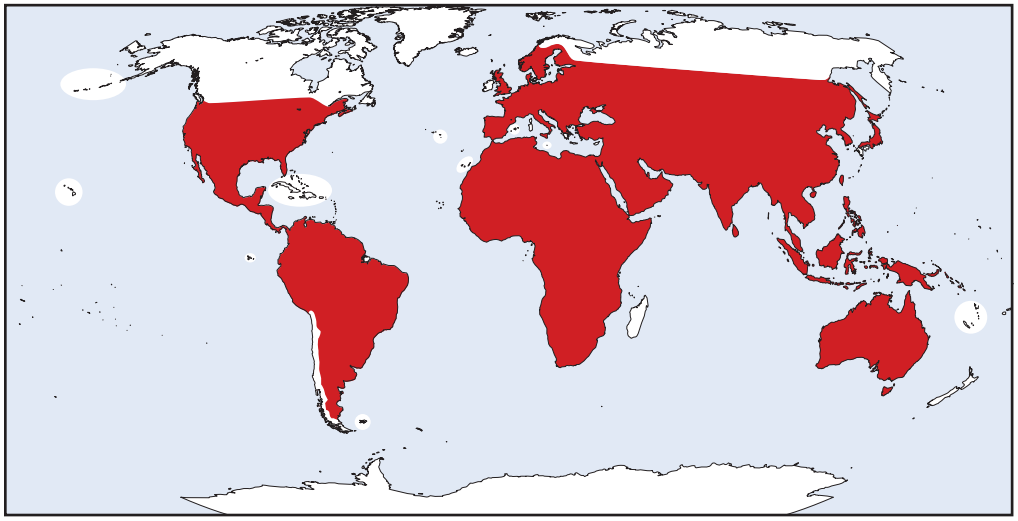


FIGURE 36-44 Global distribution of terrestrial venomous snakes.

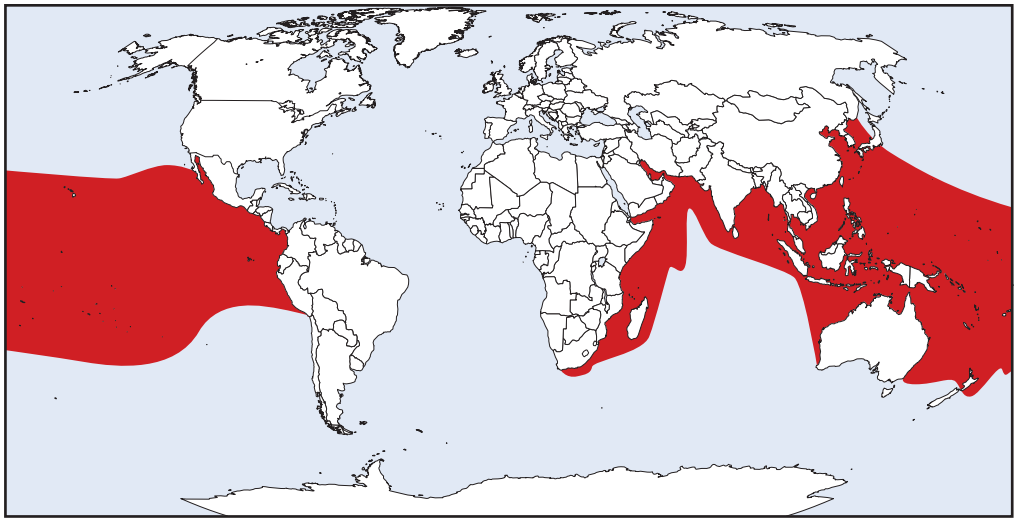


FIGURE 36-45 Global distribution of sea snakes.

FIGURE 36-46 Beaked sea snake (*Enhydrina schistosa*, also known as *Hydrophis schistosus*: subfamily Hydrophiinae) found in estuaries and up rivers (Bunapas Mission, Ramu River, Papua New Guinea). *(Copyright D.A. Warrell.)*

FIGURE 36-47 Freshwater sea snake. **A,** Lake Taal (Lake Bombon), Luzon, Philippines home of Garman's sea snake (*Hydrophis semperi*) (**B**). *(**A** copyright D.A. Warrell; **B** courtesy George Watt.)*

Mortality was estimated at about 400 deaths per 100,000 population per lifetime.[183]

Brazil

At the beginning of the 20th century, Vital Brazil estimated that, among 19,200 probable bites in Brazil, there were 4800 deaths. In 1949, 2000 deaths were estimated.[233] During the period 1990 to 1993, there was an average of 27,200 cases per year with 120 deaths per year, the overall case fatality being 0.4%. In 2005, 28,711 snakebites were reported (15 per 100,000 population) with 114 deaths.

Costa Rica

In 1943, 24 deaths were attributed to attacks by venomous animals.[233] Annual mortality (per 100,000 population) has declined, from about five in 1952 to 0.15 in 1996. Currently, there are an estimated 600 bites, with two to five deaths each year (J-M Gutiérrez, personal communication).

ASIA

Estimates of snakebite deaths in Asia range between 15,000 and 100,000 per year,[38,119] reflecting the difficulty in assessing an occupational and environmental disease that exacts so much of its mortality outside hospitals. The highest recorded incidence was 162 deaths per 100,000 population per year, determined in the Eastern Terai area of Nepal.[217] In this study, only 20% of deaths occurred in hospitals. Increased risk for fatality was associated with being bitten inside the house while resting between midnight and 6:00 AM, which suggests bites by the common krait (*B. caeruleus*) (see later discussion). Other risk factors were an initial visit to a traditional healer and delayed transport to the hospital. In Bardhaman (Burdwan) District, West Bengal, a field survey in randomly selected villages suggested that among the total population of almost 5 million people, nearly 8000 were bitten and 800 killed by snakes each year.[95]

Bangladesh

About 19,000 people in 4000 randomly selected households throughout the country provided information about snakebites. National totals of approximately 600,000 bites and approximately 6000 deaths per year were calculated by extrapolating to the total population of rural Bangladesh.[193]

India

From 1869, when Joseph Fayrer first solicited data from "British India," approximately 20,000 human deaths each year were attributed to snakebite. The Registrar General's "Million Death Study" directly estimated that 46,000 people (99% confidence interval [CI], 41,000 to 51,000) died from snakebite in 2005, a

figure based on verbal autopsy of all deaths in 6671 randomly chosen sample areas (average population, ~1000 each) throughout the entire country. Snakebite was responsible for 0.5% of all deaths, notably 3% in the age-group 5 to 14 years; 97% of the victims died in rural areas, only 23% in a health facility.[165]

Japan

In the Amami and Okinawa Islands of Japan, there were 5488 bites by the habu (*Protobothrops* [*Trimeresurus*] *flavoviridis*), resulting in 50 deaths during 9 years from 1962 to 1970.[209] The highest incidence of bites on one of the islands was 4.6 per 1000 population per year.

Myanmar (Burma)

In the 1930s, the annual snakebite mortality reported in Burma (now Myanmar) exceeded 2000 (15.4 per 100,000 population per year). Russell's viper (*Daboia siamensis*) bite was once the 5th and is now the 12th single leading cause of death in the country. In 1991, there were 14,000 bites with 1000 deaths, and in 1997, 8000 bites with 500 deaths. From 2005 until 2008, 8994 to 11,172 bites were reported annually, with 748 to 794 deaths. The average case fatality is 7.9%. Underreporting is estimated to be about 12%. In some townships in the Irrawaddy division, case fatality still ranges from 10% to 40% and may be increasing. About 90% of bites are caused by Russell's vipers (*D. siamensis*).

Sri Lanka

Snakebite numbers increased from 12,175 per year in 1991 to peak at 37,244 in 2002 and 36,861 in 2005. Fatalities peaked at 194 in 2000, and there were 134 in 2005. There are currently 30,000 to 35,000 bites and 100 to 150 deaths each year in Sri Lanka. In hospitals, case fatality decreased from 3.5% in 1985 to 0.2% in 2006.

Thailand

Improved surveillance explained the reporting of increasing numbers of snakebite cases in Thailand from an average of 2316 per year in the 1950s to 9071 (14.5 per 100,000) in 2002 and 8299 (13.25 per 100,000) in 2006. Mortality has declined from an average of 178 deaths per year in the 1950s to fewer than 10 per year recently. Over the last 5 years, both incidence and case fatality have declined to 8000 to 10,000 bites per year (12 to 18 per 100,000 population per year), with an admirably low case fatality of 0.5%.

AFRICA

There are probably more than 100,000 envenomings and 5000 snakebite deaths in Africa each year. However, Chippaux[43,44] has estimated fivefold higher figures of 1 million bites, 500,000 envenomings, and 20,000 deaths.

Burkina Faso

Snakebites (*Echis leucogaster*) are said to be common in Burkina Faso, even in the suburbs of Ouagadougou (7.5 envenomings per 100,000 population per year). In rural areas, the incidence is 35 to 120 per 100,000 population per year, with a case fatality of 3%. Health services claim 7000 to 10,000 envenomings and 200 fatalities. Few patients are admitted to hospitals, and there is virtually no antivenom available.

Nigeria

In Nigeria, 74 snakebites per 100,000 population per year are reported.[169] The saw-scaled or carpet viper (*Echis ocellatus*) is responsible for 90% of bites and 60% of deaths.[169] In the Benue Valley of northeastern Nigeria, the incidence of snakebite was found to be about 500 per 100,000 population per year with a mortality of 12.2%.[294] A community survey of snakebites by the black-necked spitting cobra (*Naja nigricollis*) in Malumfashi, northern Nigeria, found that in a population of 43,500; there were 15 to 20 bites per 100,000 population per year. Only 8.5% of the victims had visited a hospital. The case fatality rate was 5%, and 19% of survivors had persistent physical disability from locally necrotic venom effects of the venom.[189]

Senegal

In Bandafassi, southeastern Senegal, in a population of 10,509, snakebite mortality was 14 per 100,000 population per year. Saw-scaled vipers (*E. jogeri*), puff adders (*B. arietans*), and spitting cobras (*Naja katiensis*) were implicated.[252]

Kenya

In Kenya, a preliminary survey based on Ministry of Health, hospital, clinic, and dispensary records in Kakamega and western Kenya, Lake Baringo, Laikipia, Kilifi, Malindi, and northern Kenya suggested an overall average frequency of snakebite of 14 (range, 2 to 68) per 100,000 population per year, with a minimum death rate of 0.45 per 100,000 per year. Puff adders, black mambas, and spitting cobras were responsible for the fatalities.[48] However, a community-based study on the coast in the Kilifi district discovered 15 adult snakebite fatalities per 100,000 population per year.[224]

South Africa

Three hospital-based studies in KwaZulu-Natal reported bite incidences of 31 to 89 per 100,000 population per year, and a study from Transvaal reported an incidence of 34 per 100,000 per year. There were few deaths. The species responsible included *Bitis arietans, Naja nivea, Naja mossambica, Dendroaspis polylepis, Causus rhombeatus*, and *Atractaspis bibronii*.

OCEANIA

In Australia, 1000 to 2000 bites occur per year, with an average of two to three deaths. In Papua New Guinea, the incidence of bites was 215 and of deaths 7.9 per 100,000 population per year in Central Province, whereas in Kairuku subprovince, there were 526 bites per 100,000 per year.[137] The number of deaths may have increased recently because of inadequate antivenom supplies. It seems likely that 200 to 300 people die each year of snakebite in Papua New Guinea.

EUROPE

In Britain, there are more than 200 adder (*Vipera berus*) bites each year, but there have been only 14 deaths during the last hundred years, the last in 1975.[196,286] There were 44 deaths caused by this species in Sweden between 1911 and 1978; in Finland, there were 21 deaths in 25 years with an annual incidence of almost 200 bites.

SNAKEBITE AS AN OCCUPATIONAL DISEASE

In tropical countries, farmers, plantation workers, herders, and hunters are those most frequently bitten. Rice farmers in Burma, Sri Lanka, and central Thailand tread on Russell's vipers or inadvertently pick them up in a handful of paddy during the harvest[168] (Figure 36-48A). Cobras (*Naja philippinensis*) are an occupational hazard to rice farmers in the Philippines.[309] The Chinese predilection for snakes and their organs, both as food and medicines, has resulted in many bites in snake restaurants and snake farms in China and Southeast Asia. In the savanna of West Africa, farmers are bitten by *Echis* spp. as they dig the fields at the start of the rainy season[265] (Figure 36-48B). Rubber tappers in Southeast Asia tread on Malayan pit vipers (*Calloselasma rhodostoma*) in the dark and are bitten as they make their early-morning rounds of the rubber trees (Figure 36-48C).[301] This species is also responsible for numerous fatal bites among coffee and rubber plantation workers in Vietnam, especially in Song Be province.

Sea-snake bites were an occupational hazard of fishermen in Southeast Asia where hand nets were used.[199] Mechanization of fishing methods in this region has resulted in a dramatic decrease in sea-snake bites, but they still occur along the coast of South Vietnam (Figure 36-48D).[277] The beaked sea snake (*Enhydrina schistosa*; also known as *Hydrophis schistosus*) has caused most bites and deaths (see Figure 36-46). Other common and medically important species are *Hydrophis cyanocinctus, Hydrophis spiralis,* and *Lapemis curtus*.

FIGURE 36-48 Snakebite as an occupational hazard. **A,** Rice harvest, Sri Lanka. **B,** Early tilling, Kaltungo, Nigeria. **C,** Rubber tapping, Trang, Southern Thailand. **D,** Fishermen, Long Hai, Vietnam. *(Copyright D.A. Warrell.)*

BITES BY SNAKES KEPT IN CAPTIVITY

Especially in more industrialized countries, venomous snakes and other dangerous animals are increasingly popular exotic pets. Many are kept illegally. Most bites are inflicted on the hands when the animal is picked up by an owner who is under the influence of alcohol or recreational drugs.[4,290]

RISK TO WILDERNESS TRAVELERS

The risk for snakebite is a major anxiety among members of expeditions and wilderness travelers. Provided that sensible precautions are taken (see later text), the risk is small. However, for field biologists working in snake-infested areas, especially those who are interested specifically in finding and capturing snakes, the risk is much higher. The death of Joe Slowinski in 2001 illustrated the mortal danger of handling snakes in places far from medical help. He was an expert herpetologist from the California Academy of Sciences who died at Rat Baw in remote northern Burma, 32 hours after being bitten by a 30-cm (12-inch) juvenile krait (*Bungarus* near *multicinctus*) that he pulled out of a bag with his bare hand, believing it to be the harmless krait-mimic *Dinodon septentrionalis.*[140] Snakebite is a rare accident for ordinary backpackers, but people have been bitten even while walking down the main trail into the Grand Canyon.

CIRCUMSTANCES IN WHICH SNAKEBITES OCCUR

Most people are bitten after inadvertent contact with snakes while doing agricultural work in fields or plantations or while walking to and from work along unlit paths after dusk. Unprovoked attacks are unusual, but snakes will bite if they are cornered or feel threatened. Asian kraits, notably *Bungarus caeruleus* (Figure 36-49) in Pakistan, India,[202] Nepal, Bangladesh, and Sri Lanka;[11] *B. candidus* and *B. multicinctus* in Southeast Asia;[104,244,257,302] African spitting cobras, *Naja nigricollis,* in western Africa;[298] and *N. mossambica* in South Africa,[48] enter human dwellings at night in pursuit of their prey (rodents, lizards, toads) and may strike at a sleeping person who moves. Epidemics of snakebite can be caused by flooding, building of new roads through jungles, and implementation of irrigation schemes. In Western countries, a larger proportion of people, especially young men, are bitten on their hands, either in the wild (including such bizarre events as rattlesnake roundups in the United States) or

FIGURE 36-49 Common krait (*Bungarus caeruleus*) (Hyderabad, India). *(Copyright D.A. Warrell.)*

TABLE 36-3 Clinical Manifestations of Snakebite Envenoming with Suggested Pathophysiologic Mechanisms

Sign or Symptom	Proposed Mechanism
Local Envenoming	
Swelling, bruising, and blistering	Increased vascular permeability (digestive enzymes, metalloproteinases, PLA_2 myotoxins)
Severe local/regional pain (coral snake envenoming)	Cystine knot peptides activating noxious transient receptor potentiating V1 receptor, agonists for acid-sensing ion channels
Enlarged, painful, and tender lymph nodes draining the bitten area	Absorption and passage of larger-molecular-weight venom toxins via the lymphatic system
Tissue necrosis/gangrene	Venom myotoxins, cytotoxins, metalloproteinases, etc; secondary ischemia (iatrogenic from tourniquet, or thrombosis, intracompartmental syndrome)
Peripheral nerve lesion	Iatrogenic from pressure of tourniquet (e.g., lateral popliteal nerve), compartment syndrome, hematoma
Systemic Envenoming	
Hypotension and shock	Hypovolemia from extravasation of blood/plasma into the swollen limb and generally ("capillary leak")
	Vasodilatation by venom toxins and autacoids (ACE inhibitors and bradykinin-potentiating peptides)
	Myocardial damage, cardiac arrhythmias, (rarely) venom hypersensitivity anaphylaxis
	Acute pituitary-adrenal insufficiency (Russell's vipers: Sheehan's-type syndrome)
Bleeding, coagulopathy, thrombosis	Vascular endothelial activation and damage by metalloproteinase hemorrhagins, consumption coagulopathy by venom procoagulant enzymes, fibrinolysis/fibrinogenolysis by venom toxins and endogenous plasmin, anticoagulant effects of venom PLA_2, platelet activation and inhibition by venom C-type lectins, fibrin deposition in small to large arteries
Intravascular hemolysis	PLA_2-mediated, complement (cobra venom C3b) activation or microangiopathic (endothelial activated)
Acute kidney injury: acute tubular necrosis	Hypotension, disseminated intravascular coagulation, direct nephrotoxicity, pigment nephropathy (hemoglobinuria, myoglobinuria), associated with microangiopathic hemolysis, secondary to hyperkalemia
Neurotoxicity	Presynaptic and/or postsynaptic neuromuscular block
Autonomic hyperactivity	Release of adrenergic/cholinergic mediators
Abdominal pain (krait bite envenoming)	Hyperalgesic AVIT sequence cysteine-rich protein (e.g., mamba intestinal toxin—prokineticin)
Fasciculation	Anticholinesterases (mamba fasciculin), *Crotalus* toxins
Generalized rhabdomyolysis	Myotoxic phospholipases A_2

ACE, Angiotensin-converting enzyme; *PLA_2*, phospholipase A_2.

by captive specimens, while showing off under the influence of alcohol or other recreational drugs.

CLINICAL FEATURES OF ENVENOMING AND PATHOPHYSIOLOGIC MECHANISMS

Fear, direct and indirect effects of venom, results of prehospital treatment, and later complications all contribute to the symptomatology and clinical picture in a snake-bitten patient by the time he or she presents for medical treatment[157,278,279,321,322] (Table 36-3).

LOCAL SIGNS AT THE SITE OF THE BITE

Local swelling at the site of the bite is the most common feature of envenoming, but a constricting band applied as first aid may cause misleading swelling ("factitious swelling") that is not necessarily indicative of envenoming. Other "fashionable" first-aid methods, such as suction pumps, incisions, tattooing, application of herbs and chemicals, electric shocks, ice, or fire, may create their own dramatic signs and obscure the evidence of envenoming.

Puncture wounds can be useful evidence, but they are not diagnostic of snakebite and do not help distinguish venomous snakebites from those of nonvenomous snakes. Bites that are responsible for fatal envenoming may leave no discernable mark. The differential diagnosis includes bites and stings by other animals, including Hymenoptera, spiders, scorpions, centipedes, rodents, and, in estuaries and the sea, fish bites and various aquatic stingers (Figure 36-50). Fang and other teeth punctures may be the sites of persistent bleeding, suggesting coagulopathy (Figure 36-51). Multiple punctures may indicate repeated strikes with a higher risk of severe envenoming (Figure 36-50B).

Local signs of envenoming include progressive swelling, tender painful enlargement of lymph nodes draining the bite site, bruising, red lymphangitic lines, inflammation and erythema resembling cellulitis, blistering, and signs of necrosis, such as an anesthetic hyperpigmented or hypopigmented area smelling of putrefaction (Figure 36-52). Complications include ischemia secondary to raised intracompartmental pressure or thrombosis, and wound infection or local abscess.

Pathophysiology

Increased vascular permeability leads to swelling and bruising. The factors responsible include endopeptidases, metalloproteinase hemorrhagins, membrane-damaging polypeptide toxins, phospholipases, and endogenous autacoids released by the venom, such as histamine, 5-HT, and kinins. Venoms of some Viperidae, such as *D. russelii, D. siamensis*, and *V. berus*, can also produce generalized increase in vascular permeability, resulting in pulmonary edema, serous effusions, conjunctival and facial edema, albuminuria, and hemoconcentration. Local tissue necrosis results from the direct action of myotoxins and cytotoxins, and ischemia caused by thrombosis; compression of blood vessels by first-aid methods such as tight tourniquets; or by swollen muscle within a tight fascial compartment. Myotoxins damage the muscle cell plasma membrane directly. Most are PA_2s, either enzymatically active (aspartate-49) or enzymatically inactive (lysine-49).[86] Cobra cardiotoxins are low-molecular-weight polypeptides with cytotoxic action.

SIGNS OF SYSTEMIC ENVENOMING

Hypotension and Shock

Usually, blood pressure falls and shock develops within hours of the bite as a result of hypovolemia (Figure 36-53A). However, patients may suffer shock within minutes of the bite, manifested

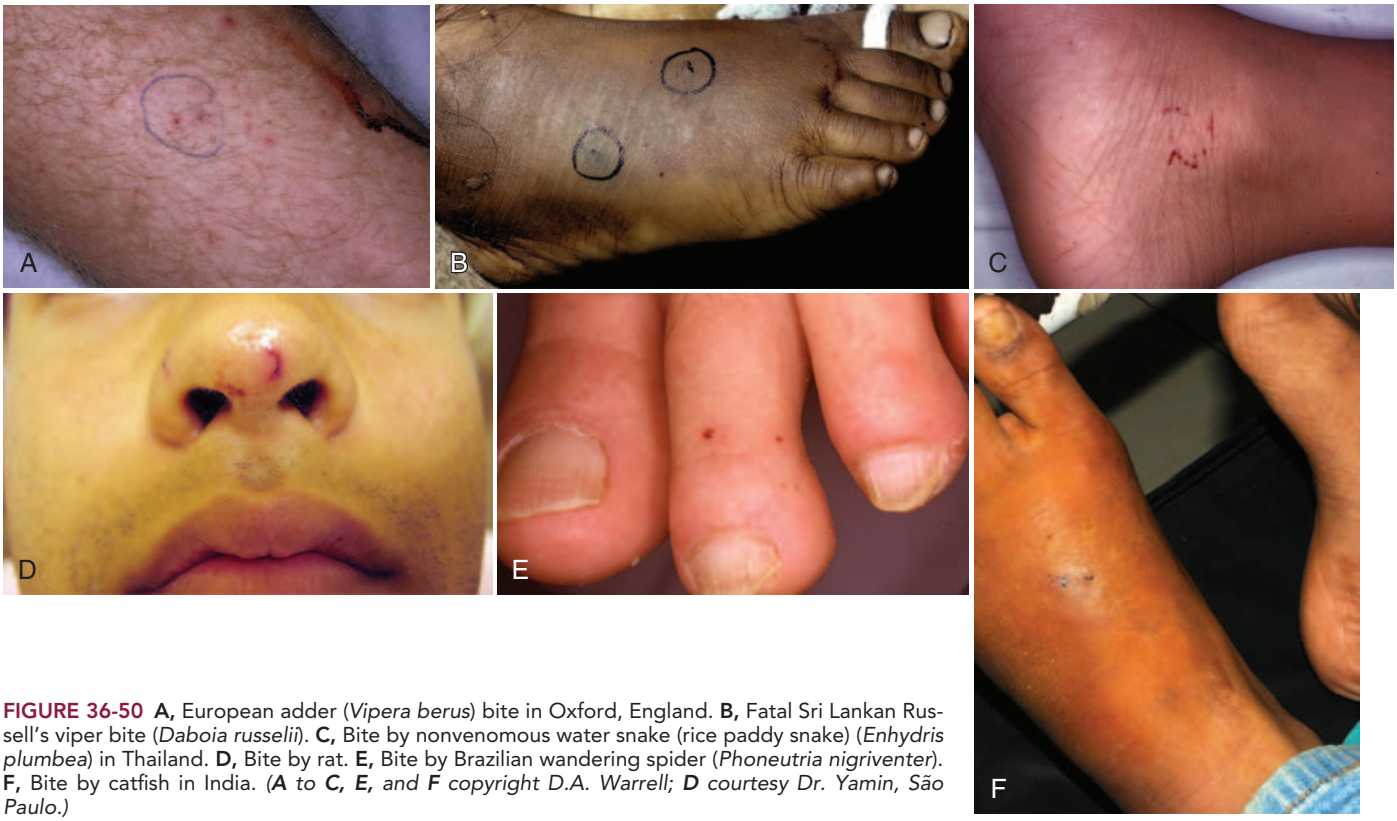


FIGURE 36-50 **A,** European adder (*Vipera berus*) bite in Oxford, England. **B,** Fatal Sri Lankan Russell's viper bite (*Daboia russelii*). **C,** Bite by nonvenomous water snake (rice paddy snake) (*Enhydris plumbea*) in Thailand. **D,** Bite by rat. **E,** Bite by Brazilian wandering spider (*Phoneutria nigriventer*). **F,** Bite by catfish in India. *(**A** to **C, E,** and **F** copyright D.A. Warrell; **D** courtesy Dr. Yamin, São Paulo.)*

by faintness, loss of vision, collapse, and unconsciousness, which is usually transient. Victims may injure themselves falling during syncopal attacks. There may be associated features of anaphylaxis, such as following envenoming by vipers (*Vipera berus, V. aspis*): urticaria, angioedema, bronchospasm, nausea, vomiting, and abdominal colic. People who have become hypersensitive to snake venoms, usually habitual snake handlers, may develop anaphylactic shock soon after exposure.

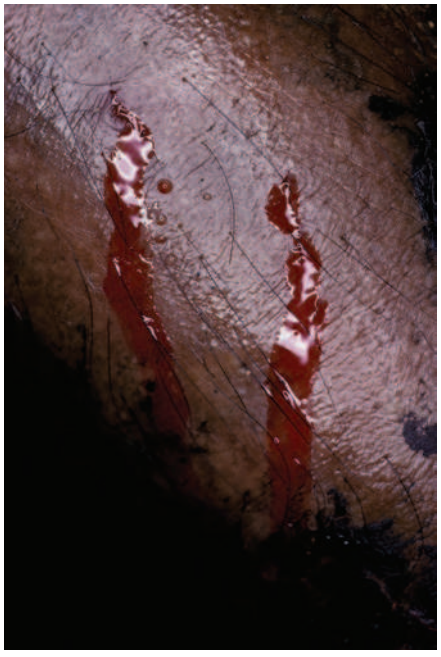


FIGURE 36-51 Persistent bleeding from fang marks 40 minutes after bite by Malayan pit viper (*Calloselasma rhodostoma*) in Thailand. *(Copyright D.A. Warrell.)*

Pathophysiology. Leakage of plasma or blood into the bitten limb and elsewhere, or massive gastrointestinal (GI) hemorrhage, may cause hypovolemia after viper bites. Vasodilation, especially of splanchnic vessels, and a direct effect on the myocardium may contribute to hypotension after viper bites. Profound hypotension is part of the autopharmacologic syndrome that occurs within minutes of bites by European *Vipera, Daboia palaestinae, D. siamensis, D. russelii*, burrowing asps (*Actractaspis engaddensis*), and Australian elapids. Presumably, this is caused by oligopeptides (ACE inhibitors and BPPs) and vasodilating autacoids (see earlier discussion), but massive clot formation in the heart and great vessels has been suggested as an explanation for early collapse in victims of Australian elapid envenoming.[232] Hypotensive collapse associated with bradycardia in a susceptible person might be explained by vasovagal syncope. This might occur even in the absence of envenoming. In some cases, direct myocardial effects of venom may be suggested by electrocardiographic (ECG) changes and autopsy findings of epicardial or endocardial hemorrhages and histopathologic evidence of cardiac myonecrosis (Figure 36-53B and C, and Figure 36-54D).

Bleeding and Clotting Disturbances[107,115,142,317]

Hemostatic disturbances are an important feature of envenoming by vipers, pit vipers, Australasian elapids, and dangerously venomous colubrids. These manifest clinically as persistent bleeding from the fang punctures (see Figure 36-51) and other sites of acute or recent trauma (e.g., partially healed wounds) and spontaneous systemic bleeding from gums, nose, GI and genitourinary tracts, and into skin, conjunctivae, the brain, and other tissues (Figure 36-55).

Pathophysiology. Snake venoms affect hemostasis in several ways.

Procoagulant Enzymes. These activate intravascular coagulation, producing consumption coagulopathy and incoagulable blood. For example, procoagulants in the venoms of Colubridae, *Notechis scutatus, Oyuranus scutellatus* and other Australasian Elapidae, *Echis, Daboia russelii,*[235] and *Bothrops* spp.[216] activate prothrombin, whereas those in venoms of *Daboia russelii* and

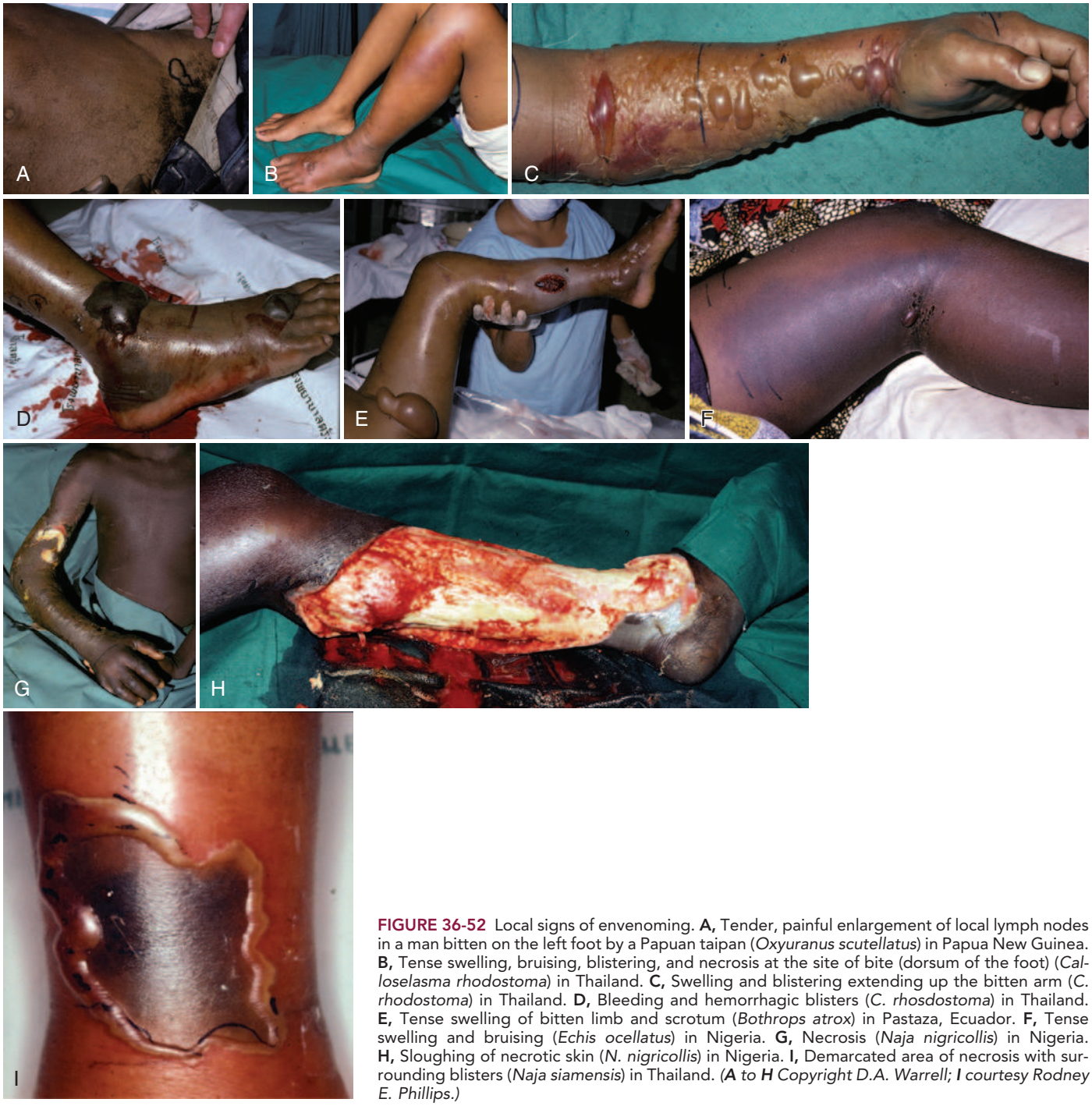


FIGURE 36-52 Local signs of envenoming. **A,** Tender, painful enlargement of local lymph nodes in a man bitten on the left foot by a Papuan taipan (*Oxyuranus scutellatus*) in Papua New Guinea. **B,** Tense swelling, bruising, blistering, and necrosis at the site of bite (dorsum of the foot) (*Calloselasma rhodostoma*) in Thailand. **C,** Swelling and blistering extending up the bitten arm (*C. rhodostoma*) in Thailand. **D,** Bleeding and hemorrhagic blisters (*C. rhosdostoma*) in Thailand. **E,** Tense swelling of bitten limb and scrotum (*Bothrops atrox*) in Pastaza, Ecuador. **F,** Tense swelling and bruising (*Echis ocellatus*) in Nigeria. **G,** Necrosis (*Naja nigricollis*) in Nigeria. **H,** Sloughing of necrotic skin (*N. nigricollis*) in Nigeria. **I,** Demarcated area of necrosis with surrounding blisters (*Naja siamensis*) in Thailand. (***A*** *to* ***H*** *Copyright D.A. Warrell;* ***I*** *courtesy Rodney E. Phillips.*)

D. siamensis also activate factors V and X (see earlier discussion).

Thrombin-like Enzymes. In venoms of many crotaline snakes, thrombin-like enzymes have a direct action on fibrinogen. Some venoms cause defibrinogenation by activating the endogenous fibrinolytic (plasmin) system.

Anticoagulant Activity. This is attributable to venom phospholipases.

Platelet Activation or Inhibition and Thrombocytopenia. These are common accompaniments of systemic envenoming. Activators of platelet agglutination are C-type lectins of viperid and elapid venoms.[142] Mucrocetin (*Protobothrops* [*Trimeresurus*] *mucrosquamatus*), ophioluxin (*Ophiophagus hannah*), and stejnulxin (*Viridovipera stejnegeri*) target platelet glycoprotein receptor GPIb. Alboaggregin A and alboluxin (*Cryptelytrops* [*Trimeresurus*] *albolabris*) and convulxin (*Crotalus durissus terrificus*) act through both receptors GPIb and GPVI. Aggretin (*Calloselasma rhodostoma*) activates platelet receptor CLEC2 and agkaggregin (*Deinagkistrodon acutus*), and rhodoaggretin (*C. rhodostoma*) and crotacetin (*Crotalus durissus terrificus*) are platelet agonists acting through an undetermined receptor. Proatherocytin (*Proatheris superciliaris*) is a platelet receptor PAR-1 agonist.[208]

Platelet inhibitors also include C-type lectin. Dabocetin (*Daboia siamensis*) binds with GPIb and rhodocetin (*C. rhodostoma*) and inhibits platelets via interaction with $\alpha_2\beta_1$ integrin receptor. Mocarhagin (*Naja mossambica*) and jararhagin (*Bothrops jararaca*) are metalloproteinases that cleave GPIbα and GPIa-IIa, respectively, thus inhibiting platelet responses depending on those receptors. Arg-Gly-Asp (RGD) tripeptide sequence–containing venom peptides, such as trigramin, echistatin, contortrostatin, and flavoviridin, are powerful inhibitors of the

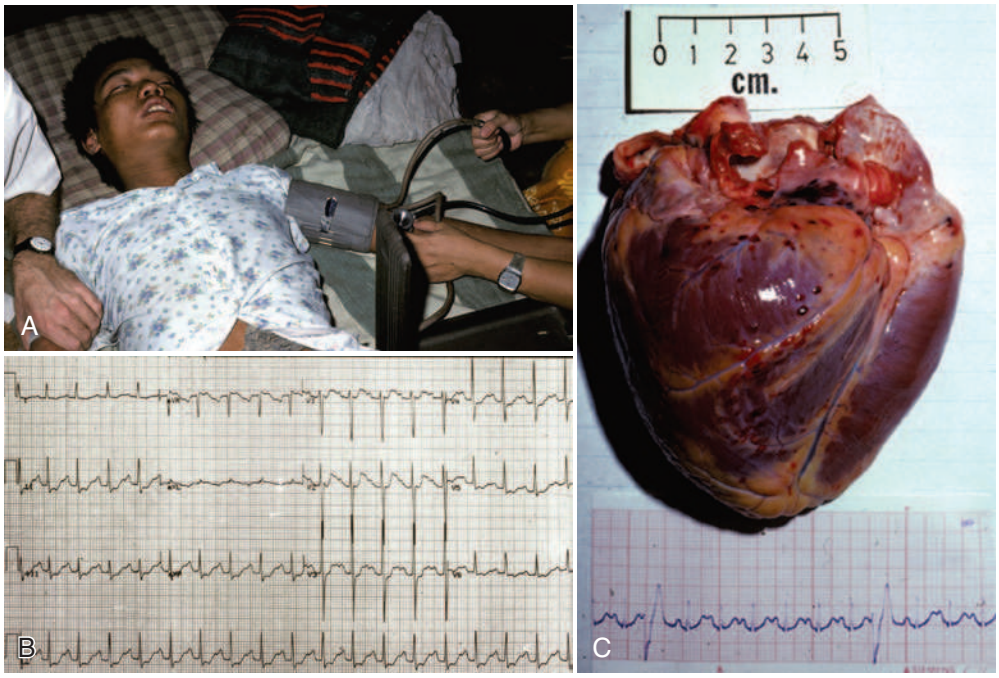


FIGURE 36-53 **A,** Shock (*Daboia russelii*) (Myanmar/Burma). **B,** ECG changes caused by European adder (*Vipera berus*) envenoming in England. **C,** Premortem tachyarrhythmia, epicardial hemorrhages at autopsy (*Daboia siamensis*) (Myanmar). *(Copyright D.A. Warrell.)*

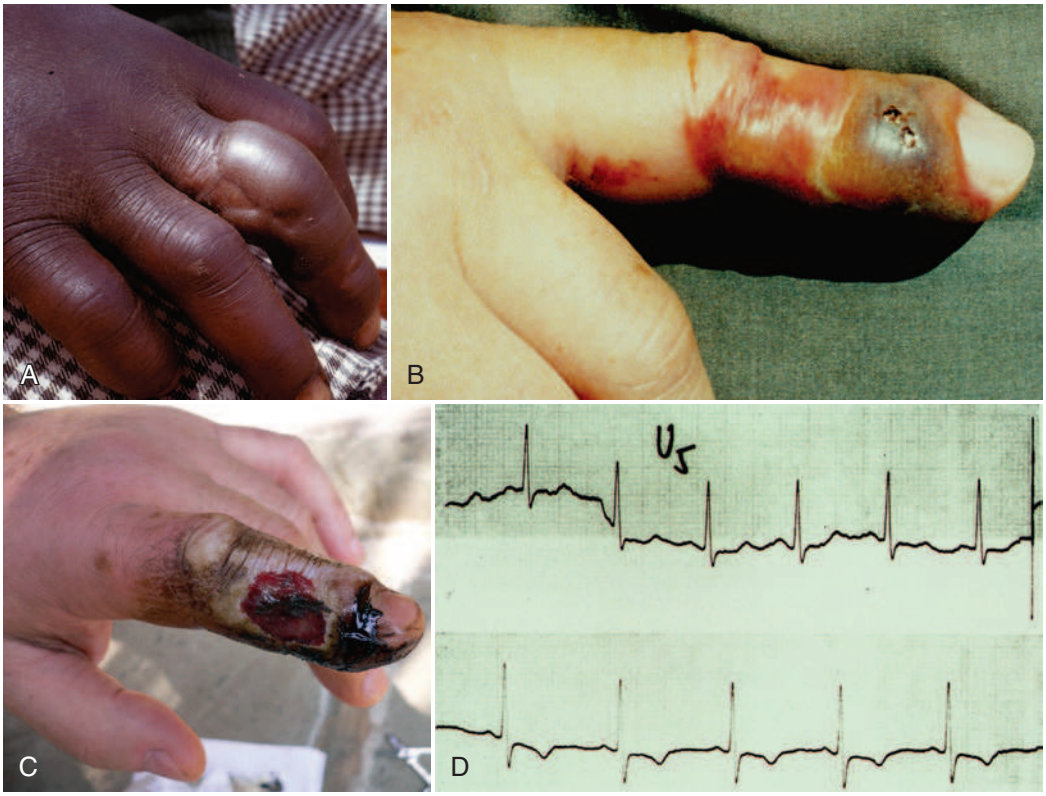


FIGURE 36-54 Envenoming by burrowing asps. **A,** Local blistering at site of bite by slender burrowing asp (*Atractaspis aterrima*) in Nigeria. **B,** *Atractaspis engaddensis* bite in Israel. **C,** *Atractaspis fallax* bite, Diani Beach, Kenya. **D,** ECG changes after *A. engaddensis* bite in Israel. *(**A** copyright D.A.Warrell; **B** and **D** courtesy Elazar Kochva;[126] **C** courtesy Thomas Sollacher.)*

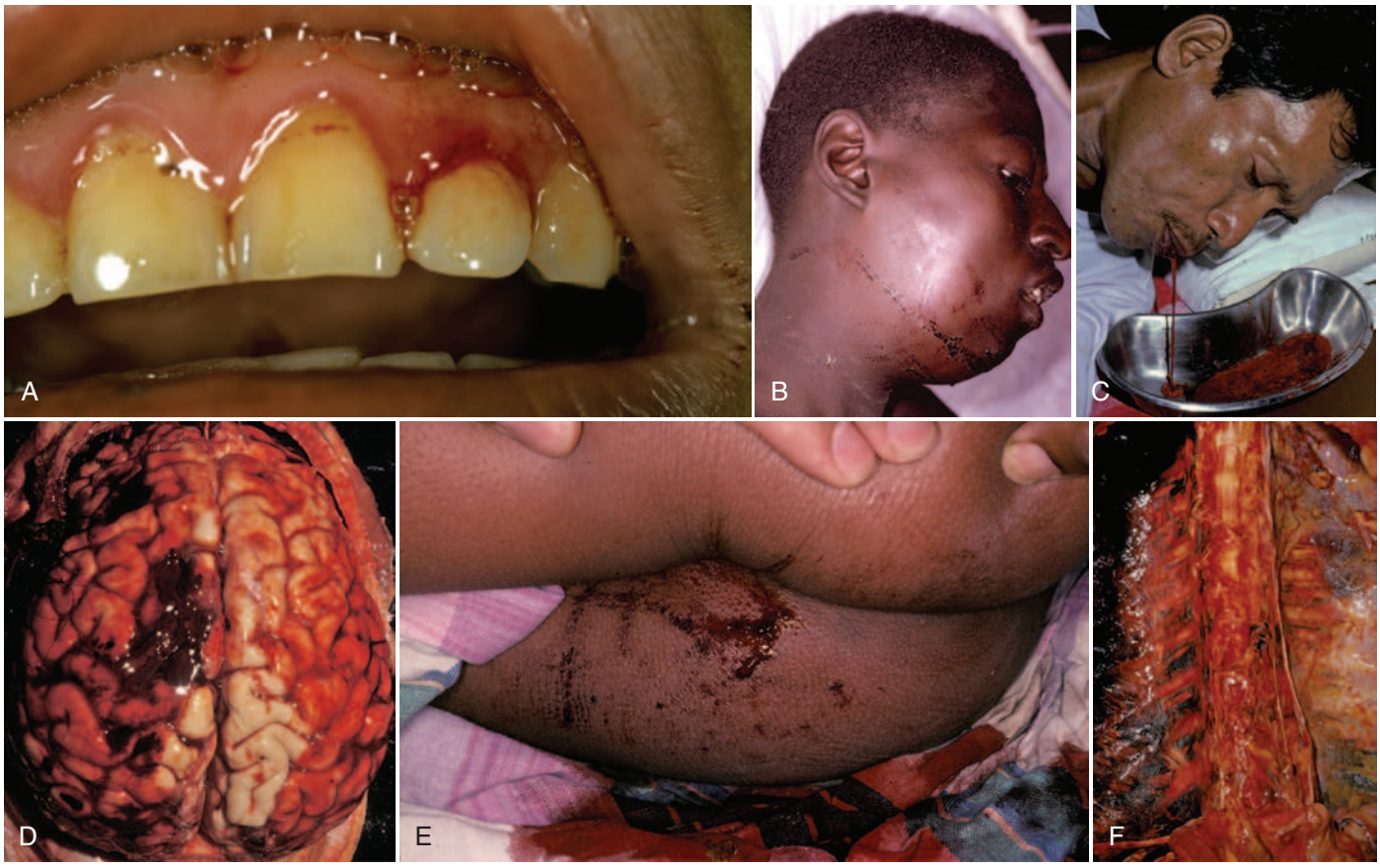


FIGURE 36-55 Spontaneous systemic bleeding after snakebites. **A,** Gums (*Bothrops atrox,* Ecuador). **B,** Floor of mouth (*Echis ocellatus,* Nigeria). **C,** Hemoptysis from a tuberculous cavity (*Calloselasma rhodostoma,* Thailand). **D,** Brain (*Daboia siamensis,* Myanmar). **E,** Rectal (*D. russelii,* Sri Lanka). **F,** Generalized (*E. ocellatus,* Nigeria). (***A*** *to* ***C, E,*** *and* ***F*** *copyright D.A.Warrell;* ***D*** *courtesy Hla Mon.)*

fibrinogen receptor GPIIb-IIIa. Few studies of platelet function have been attempted in envenomed humans. In patients bitten by Malayan pit vipers and green pit vipers (*Cryptelytrops albolabris*), there was initially inhibition of platelet agglutination, followed by activation and appearance of circulating clumps of platelets.[106,107]

Hemorrhagins. In the absence of trauma, defibrination/defibrinogenation induced by venom coagulants, such as ancrod (Arvin, Arwin) from *C. rhodostoma* venom, is a relatively benign state.[198] Potentially lethal spontaneous systemic bleeding is attributable to distinct venom components, known as hemorrhagins, which damage vascular endothelium. These metalloproteinases are zinc metalloendopeptidases (reprolysins), some of which have disintegrin-like, cysteine-rich, and lectin domains.[115] The combination of incoagulable blood, thrombocytopenia, and vessel wall damage result in massive bleeding, a common cause of death from viper bite.

Complement Activation. Elapid and some colubroid venoms activate complement via the alternative pathway ("cobra venom factor" is the snake's C3b), whereas some viperid venoms activate the classic pathway.[269] This has been documented in human victims of snakebite.[172,298] Complement activation could in turn affect platelets, the blood coagulation system, and other humoral mediators.[241]

Neurotoxicity

Paralytic symptoms may emerge within 15 to 30 minutes of the bite, or they may be delayed for 9 or more hours. Preparalytic symptoms include nausea, vomiting, abnormal taste sensations, paresthesias, hyperacusis, blurred vision, feeling of eyelid heaviness, and drowsiness. Ptosis, external ophthalmoplegia, mydriasis, and paralysis of muscles innervated by the facial and other cranial nerves ensue, eventually involving muscles of deglutition and respiration, the trunk, and limbs (Figure 36-56). Autonomic nervous system symptoms include sweating, hypersalivation, GI symptoms, and changes in blood pressure and pulse rate. These symptoms are characteristic of envenoming by most elapids, such as kraits, coral snakes, mambas, cobras and the king cobra, but not of African spitting cobras, whose venoms are not paralytic in humans. Venoms of terrestrial Australasian snakes,[47,33,34,35,232] sea snakes, and a few species of Viperidae, notably the Chinese and Japanese mamushis (*Gloydius* [*Agkistrodon*] *blomhoffii* and *G. brevicaudus*), Sri Lankan and South Indian *D. russelii*, the southern African berg adder (*Bitis atropos*), and some other small *Bitis* spp. of southern Africa (*B. peringueyi, B. xeropaga*), are also neurotoxic in humans.

Pathophysiology. Neurotoxic polypeptides and PA_2s of snake venoms cause paralysis by blocking transmission at the neuromuscular junction.[47,255] Patients with paralysis of the bulbar muscles may die of upper airway obstruction or aspiration, but the most common mode of death after neurotoxic envenoming is respiratory paralysis. By prolonging activity of ACh at neuromuscular junctions, anticholinesterase drugs may improve paralytic symptoms in patients bitten by snakes with neurotoxins that are predominantly postsynaptic in their action (e.g., Asian cobras and Australasian death adders [genus *Acanthophis*]). Some patients bitten by elapids or vipers are unphysiologically drowsy in the absence of respiratory or circulatory failure. This is unlikely to be an effect of neurotoxic polypeptides, which do not cross the blood-brain barrier. It may be caused by endogenous opiates released by a venom component. Intracerebral injection of β-RTX (a receptor-active protein), a potent antagonist of opiate receptors from *D. russelii* venom, produced sedation in rats.[94]

FIGURE 36-56 Neurotoxicity after snakebite. **A,** Ptosis (*Bungarus caeruleus,* Sri Lanka). **B** and **C,** Ptosis and external ophthalmoplegia (*Oxyuranus scutellatus,* Papua New Guinea). Patient is trying to look at the finger. **D,** Restricted jaw opening (*O. scutellatus,* Papua New Guinea). **E,** Ptsosis and jaw hanging open caused by paralysis of masseter muscles (*Crotalus durissus terrificus,* Brazil). **F,** Late generalized flaccid paralysis (*B. caeruleus,* Sri Lanka). **G,** Persistent mydriasis unresponsive to light 25 days after a bite by *Bungarus multicinctus* on the right index finger in Hanoi, Vietnam. White line indicates pupillary diameter before (above) and 20 minutes after (below) instillation of 1% pilocarpine drops. *(Copyright D.A. Warrell.)*

Myotoxicity

Patients with generalized rhabdomyolysis develop myalgia, muscle tenderness on palpation or passive stretching, and trismus, and they pass dark-brown or black urine (Figure 36-57).

Pathogenesis. PLA_2 myotoxins and metalloproteinases are principally responsible.[86,87] They are present in venoms of most species of sea snakes,[197] many terrestrial Australasian elapids such as tiger snakes (*Notechis scutatus* and *N. ater*), king brown or mulga snake (*Pseudechis australis*), taipan (*O. scutellatus*), rough-scaled snake (*Tropidechis carinatus*), Australian small-eyed snake (*Rhinoplocephalus/Cryptophis nigrescens*),[232] some species of krait (*Bungarus*),[63,104,257] coral snakes (*Micrurus*),[123,151] and Viperidae, such as the Sri Lankan Russell's viper (*D. russelii*),[182] tropical rattlesnakes (*Crotalus durissus*),[16,17,285] and North American rattlesnakes.[122] Release into the bloodstream of myoglobin, muscle enzymes, uric acid, potassium, and other muscle constituents is an effect in humans of presynaptic neurotoxins. Patients may die of bulbar and respiratory muscle weakness, acute hyperkalemia, or renal failure.

ACUTE KIDNEY INJURY

Acute kidney injury is a common event and cause of death following bites by Russell's vipers[168,220,245,250] and sea snakes,[197,277] and is not uncommon following bites by South American rattlesnakes (*Crotalus durissus terrificus*)[16] and some *Bothrops* spp. It can complicate severe envenoming, even by species that usually cause only mild envenoming, such as *Trimeresurus (T.) albolabris*, the hump-nosed pit viper (*H. hypnale*),[13,54] *V. berus*,[196,286] and *Cerastes cerastes*.[211]

Clinical presentation may be dramatic and is often associated with a period of profound hypotension (Figure 36-58A). The patient claims to have passed no urine since the moment of being bitten. More often, there is declining urine output and, much more rarely, polyuria. Some patients present late with symptoms of uremia. There may be evidence of pigment nephropathy associated with myotoxicity (see earlier discussion) or intravascular hemolysis, as in victims of envenoming by the colubroid genera *Dispholidus*, *Thelotornis*, and *Rhabdophis* who develop hemoglobinemia, hemoglobinuria, and mild jaundice. Acute kidney injury associated with features suggestive of hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP) has been recognized in patients envenomed by Australian elapids, especially brown snakes (genus *Pseudonaja*),[108] and several vipers, including *Cerastes cerastes*.[211] Severe and often refractory renal failure is associated with thrombocytopenia, and intravascular hemolysis with the presence of circulating schistocytes (helmet cells, fragmented erythrocytes) (Figure 36-59), indicating microangiopathic hemolysis with or without consumption coagulopathy. Preexisting chronic renal disease and the effects of antivenom (serum sickness) may confuse clinical and histopathologic interpretations.

Pathophysiology

A wide range of renal histologic changes has been described after snakebite (Box 36-2). Acute tubular necrosis is the most common, but proliferative glomerulonephritis, toxic mesangiolysis with platelet agglutination, fibrin deposition, ischemic changes, and distal tubular damage ("lower nephron nephrosis"), suggesting direct venom nephrotoxicity, and bilateral renal cortical necrosis with subsequent calcification are also reported.[220] Acute tubular necrosis may result from prolonged hypotension and hypovolemia (see Figure 36-58A), DIC, direct toxic effect of the venom on the renal tubules, hemoglobinuria, myoglobinuria, and hyperkalemia. Russell's viper venom produces hypotension, DIC, direct nephrotoxicity,[194] and, in Sri Lanka and India, intravascular

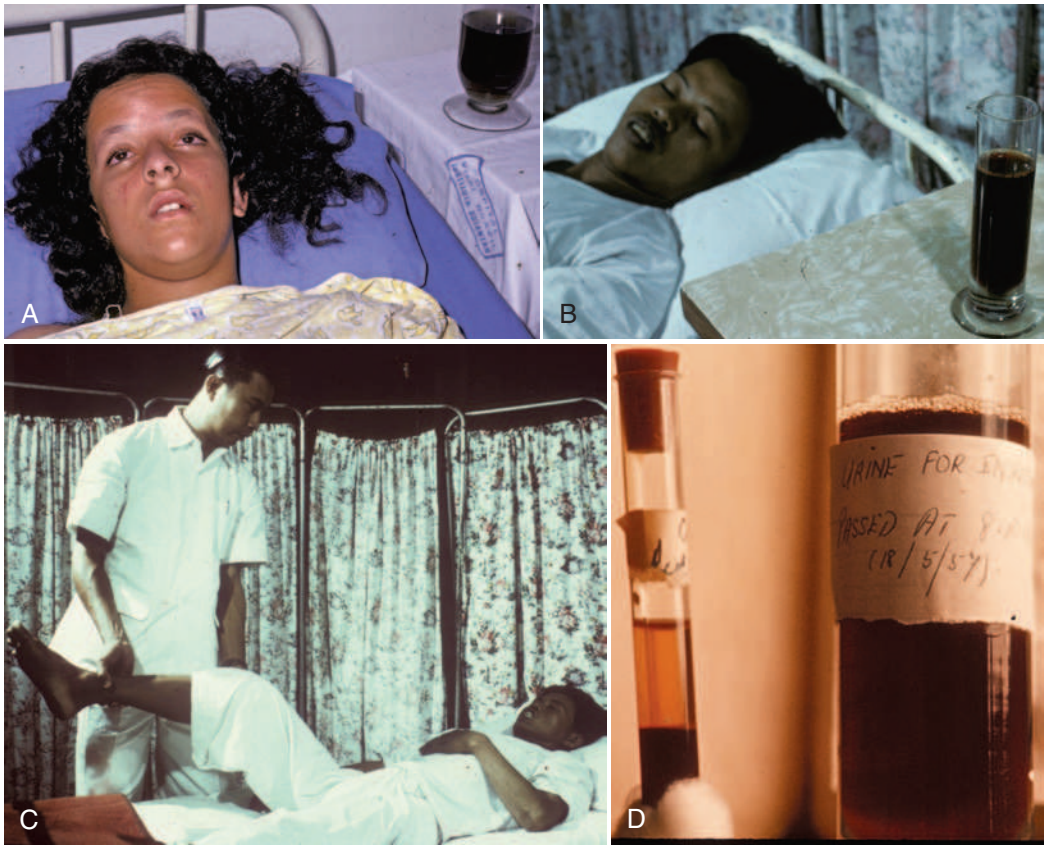


FIGURE 36-57 Myotoxicity after snakebite showing myopathic facies, pain on passive stretching of muscles, brown staining of plasma (myoglobinemia), and myoglobinuria. **A,** *Crotalus durissus terrificus,* São Paulo, Brazil. **B** to **D,** Sea snake, western Malaysia. *(**A** copyright D.A. Warrell; **B** to **D** courtesy the late H. Alistair Reid.)*

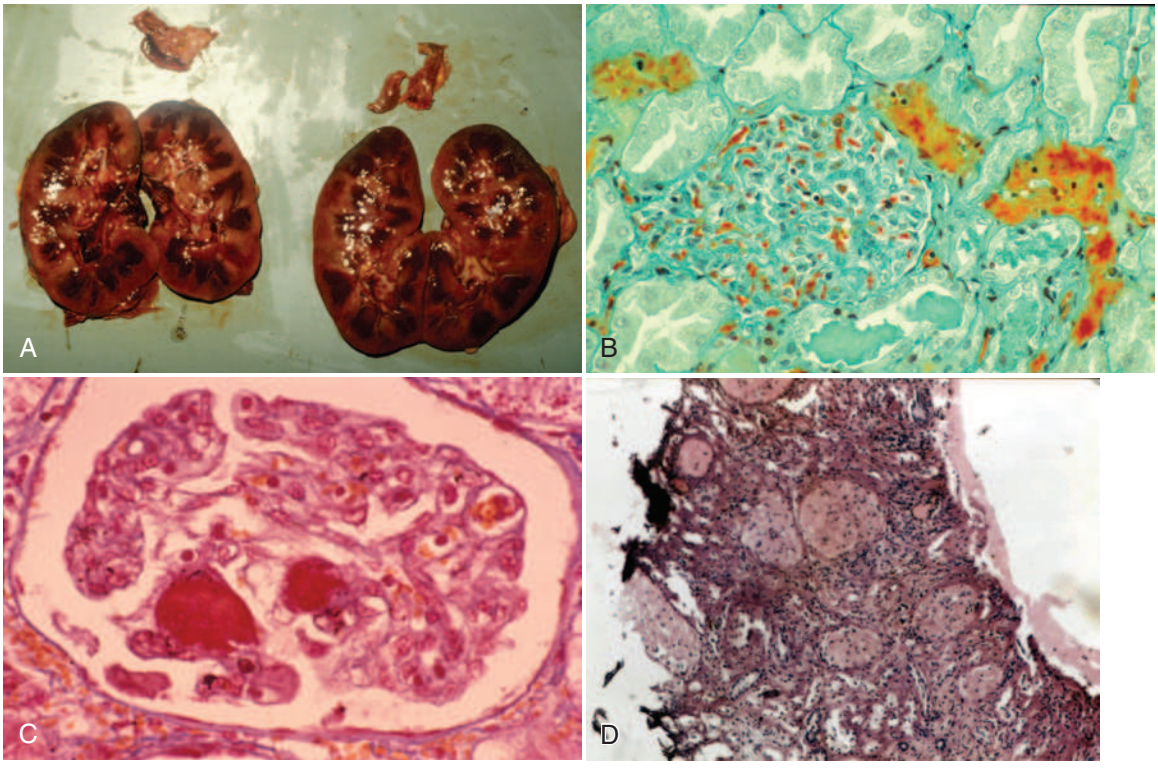


FIGURE 36-58 Acute kidney injury following snakebite. **A,** Shocked kidneys (demarcation between cortex and medulla) after *Daboia siamensis* bite in Myanmar. **B,** Fibrin (stained *red*) deposition in glomerular and peritubular vessels after *D. siamensis* bite in Myanmar. **C,** Fibrin deposition after *Bothrops jararaca* bite. **D,** Chronic renal failure after *Hypnale hypnale* bite in Sri Lanka showing glomerular sclerosis, tubular atrophy and necrosis, and inflammatory interstitial infiltrate. *(**A** courtesy Hla Mon; **B** courtesy Nicholas Francis; **C** courtesy Carlos Amaral; **D** courtesy Christeine Gnanathasan.)*

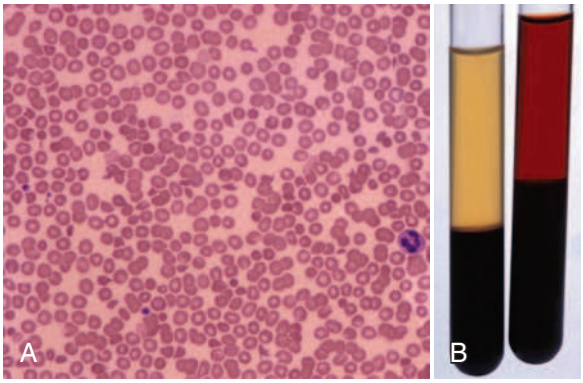


FIGURE 36-59 Microangiopathic hemolysis following *Cerastes cerastes* bite. **A,** Blood film showing schistocytes (helmet cells). **B,** Showing hemoglobinemia (*right*) compared with control (*left*). *(Copyright D.A. Warrell.)*

BOX 36-2 Renal Histopathologic Changes in Human Snakebite Victims

Glomerular Changes

Toxic mesangiolysis, platelet aggregation, mesangial proliferation
Proliferative glomerulonephritis; endocapillary, exocapillary, mesangiocapillary
Fibrin deposition
Ischemia

Tubular Changes

Direct nephrotoxicity: "lower nephron nephrosis"
Secondary ischemic changes (fibrin deposition)
Acute tubular necrosis (prerenal)
Cortical infarction, calcification

hemolysis and rhabdomyolysis.[182] In Burmese patients envenomed by Russell's vipers (*D. siamensis*), high urinary concentrations of β_2-microglobulin, retinal binding protein, and *N*-acetyl glucosaminidase suggested failure of proximal tubular reabsorption and tubular damage.[250] High plasma concentrations of active renin suggested that renal ischemia with activation of the renin-angiotensin system was involved in development of renal failure. A marked but transient capillary and glomerular leak of albumin was an early sign of oliguric renal failure.[245] Snake venom–induced DIC may result in deposition of fibrin on vascular endothelium (see Figure 36-58B and C) that has been activated by, for example, metalloproteinases, producing microangiopathic hemolysis. Although the clinical picture (see earlier discussion) is reminiscent of HUS, there is no reason to postulate autoantibodies (as in some forms of TTP) and no justification for plasmapheresis.

CLINICAL PATTERN OF ENVENOMING BY DIFFERENT TAXA OF VENOMOUS SNAKES

COLUBROIDEA (BACK-FANGED SNAKES)[278,279,285,314]

Species Capable of Causing Fatal Envenoming

Five species of non-front-fanged colubroid (NFFC) snakes—African boomslang (*Dispholidus typus*, Colubridae, Colubrinae); African twig, vine, tree, or bird snakes (*Thelotornis kirtlandii* and *Thelotornis capensis*, Colubridae, Colubrinae); Asian red-necked keelback (*Rhabdophis subminiatus*, Natricidae); and tiger keelback or yamakagashi (*Rhabdophis tigrinus*, Natricidae)[98]—have caused life-threatening or fatal envenoming in human victims. *D. typus* (Figure 36-60) and *T. kirtlandii* and *T. capensis* (Figure 36-61) have caused fatalities, including among their victims two famous herpetologists, Karl P. Schmidt (bitten by *D. typus*) and Robert Mertens (bitten by *T. kirtlandii*). *R. tigrinus* and *R. subminiatus* have caused severe or fatal envenoming (Figures 36-62 and 36-63).

If these colubroid snakes are able to engage their rear fangs and chew for 15 seconds or longer, severe envenoming may result. Envenoming by these species gives rise to similar symptoms, sometimes delayed for many hours or even days after the bite.[278,279] There is nausea, vomiting, colicky abdominal pain, and headache. Bleeding develops from old and recent wounds, such as venipunctures, and there is spontaneous gingival bleeding, epistaxis, hematemesis, melena, subarachnoid or intracerebral hemorrhage (Figure 36-64A), hematuria, and extensive ecchymoses (Figure 36-64B). Intravascular and microangiopathic hemolysis have been described. Most fatalities followed acute kidney injury from acute tubular necrosis many days after the bite. Local effects of the venom are usually trivial (Figure 36-65), but several patients showed local swelling; one person bitten by *D. typus* had massive swelling with blood-filled bullae. Investigations reveal incoagulable blood, defibrination, elevated fibrin/fibrinogen degradation products (FDPs), severe thrombocytopenia, and anemia. These clinical features are explained by DIC triggered by a venom prothrombin activator. There is complement activation.[172]

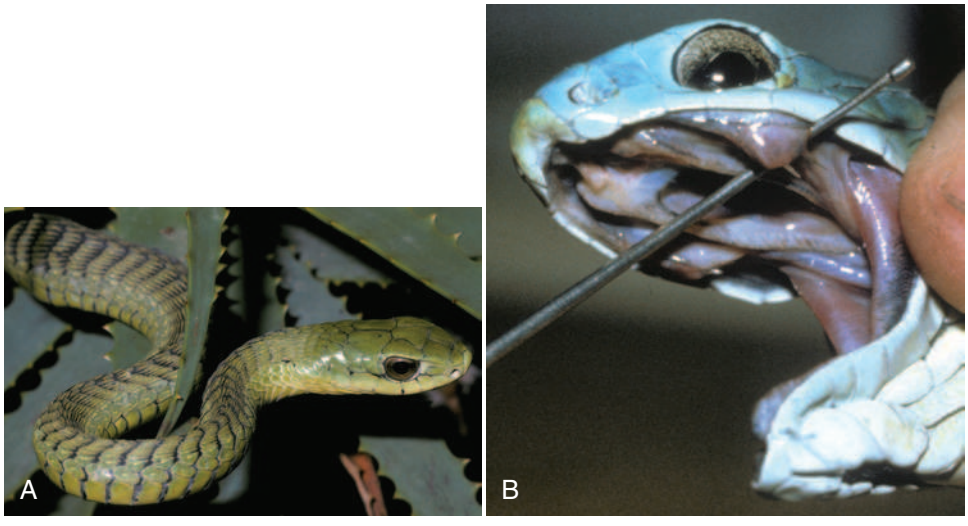


FIGURE 36-60 Boomslang (*Dispholidus typus*), an arboreal colubrid snake capable of fatally envenoming humans. **A,** South African specimen (Johannesburg, South Africa). **B,** Showing large back fangs. *(**A** copyright D.A. Warrell; **B** courtesy Dave Ball.)*

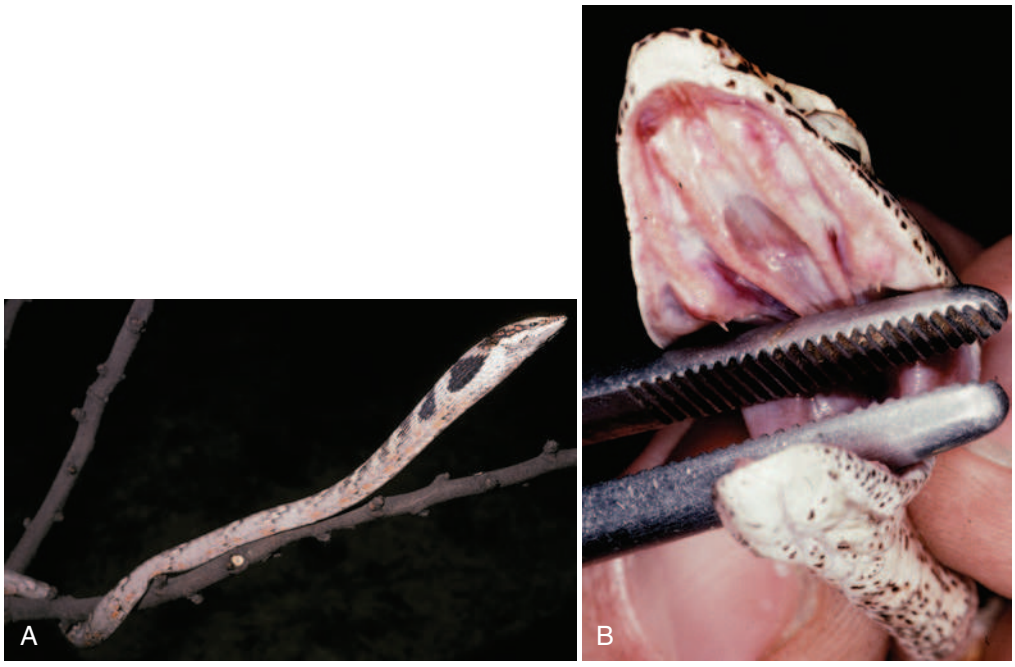


FIGURE 36-61 Bird, twig, vine, or tree snake (*Thelotornis capensis*), an arboreal colubrid snake capable of fatally envenoming humans. **A,** South African specimen. **B,** Showing back fangs (Johannesburg, South Africa). *(Copyright D.A. Warrell.)*

FIGURE 36-62 Yamakagashi (*Rhabdophis tigrinus tigrinus*). Japanese specimens. *(Courtesy S. Mishima and the late Yoshio Sawai:* The Snake *6:cover, 1974.)*

Other Species Capable of Causing Systemic Envenoming

In Europe, the Montpellier snake (*Malpolon monspessulanus*) has been reported to cause neurotoxic symptoms (Figure 36-66). In Oceania, the brown tree snake (*Boiga irregularis*), exported from Australia and New Guinea to Guam, has been known to attack and possibly envenom infants[69] (Figure 36-67). In South America, a green racer (*Philodryas olfersii*) (Figure 36-68A and B) and possibly other members of this genus can cause systemic hemostatic disturbance with ecchymoses distant from the bite (Figure 36-68C and D).[285]

In Sri Lanka, envenoming by *Balanophis ceylonensis* (Natricidae) caused severe occipital headache, photophobia, chills, transient loss of consciousness, vomiting of blood-stained gastric contents, and bleeding from venipuncture sites. The victim had greatly elevated international normalized ratio (INR) and positive D-dimer test.[65]

Implication of other colubroid species in cases of severe systemic envenoming may have been caused by confusion with

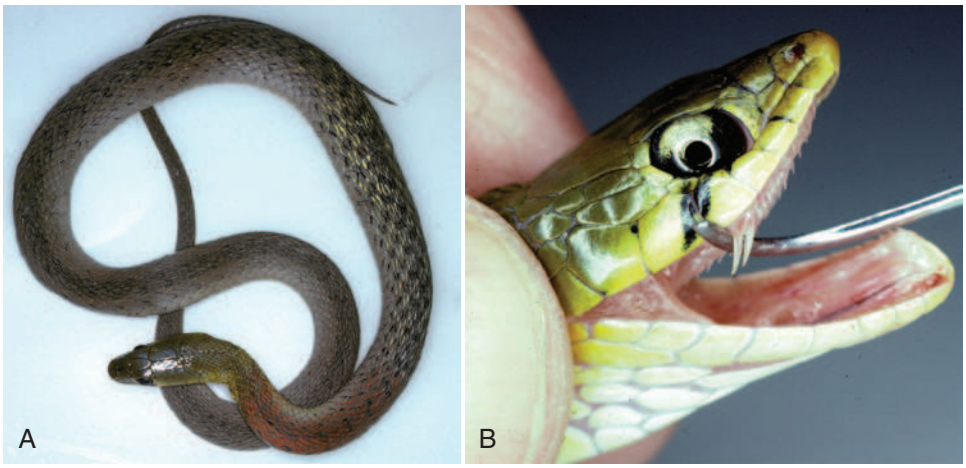


FIGURE 36-63 **A,** Red-necked keelback (*Rhabdophid subminiatus*) (Chanthaburi, Thailand), a dangerously venomous colubrid snake of Southeast Asia. **B,** Showing back fangs. *(Copyright D.A. Warrell.)*

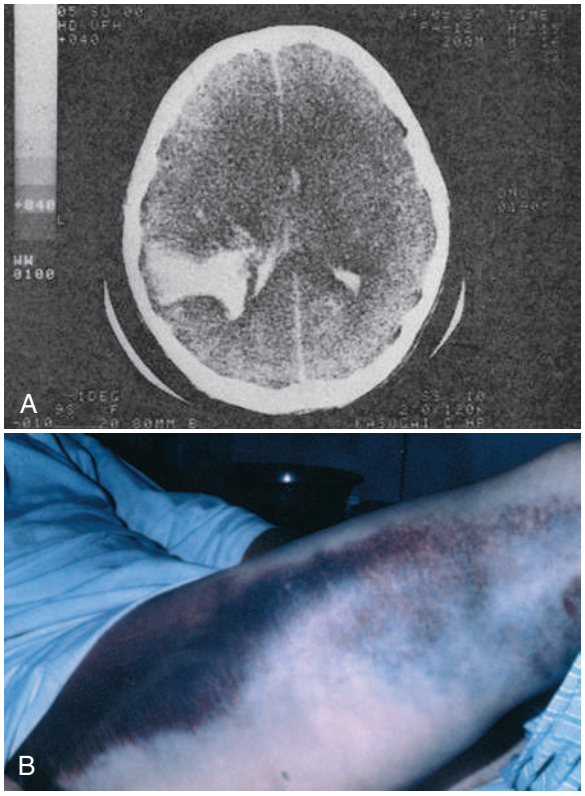


FIGURE 36-64 Yamakagashi (*Rhabdophis tigrinus*) bite in Japan. **A,** Cerebral hemorrhage. **B,** Extensive ecchymoses on bitten leg. *(Courtesy the late Yoshio Sawai.)*

venomous species of similar appearance that are present in the same geographic areas.[315]

Species Capable of Causing Local Envenoming

A large and increasing variety of colubroid species is capable of causing local pain, swelling, bruising, local bleeding, regional lymphadenopathy, and mild constitutional symptoms.[285,314] Many accounts of these cases are written by nonmedical authors, often the victims themselves. They tend to be highly subjective and remain controversial among clinical toxinologists. However, convincing recent descriptions of envenoming included bites by *Boiga dendrophila* (Colubridae), *Rhamphiophis oxyrhynchus* (Lamprophiidae), *Leptodeira frenata* (Dipsadidae),[312] and *Hydrodynastes gigas* (Dipsadidae).

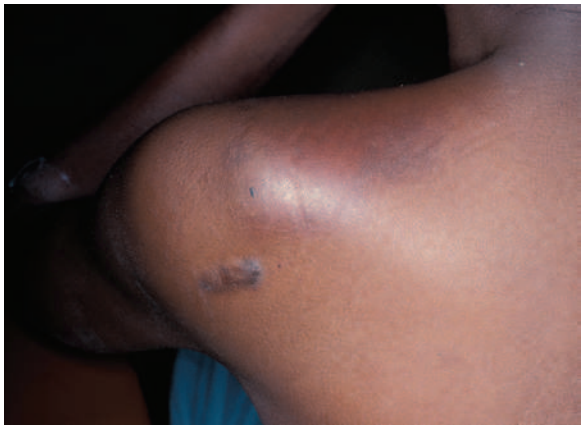


FIGURE 36-65 Healing bite from a boomslang (*Dispholidus typus*) in Zimbabwe. Local effects of the venom are usually trivial. *(Courtesy Professor Jimmy Thomas.)*

FIGURE 36-66 Montpellier snake (*Malpolon monspessulanus*), 180-cm-long (71-inch-long) male in Cartagena, Spain. *(Courtesy Matt Wilson.)*

ATRACTASPIDINAE, GENUS *ATRACTASPIS* (BURROWING ASPS OR STILETTO SNAKES)

(See Figures 36-30 and 36-38)

Fatal envenoming has been reported from the Sudan (Kassala and Kordofan) ("*Atractaspis microlepidota*"*), Nigeria (*A. irregularis*), and Arabian peninsula ("*A. microlepidota andersoni*").[305,278] However, in many parts of Africa and the Middle East, bites by the approximately 17 species of burrowing asp are common but rarely cause more than local symptoms.[276,278,305] There is local pain, swelling, blistering, necrosis (especially of bitten fingers) (see Figure 36-54A to C), tender enlargement of local lymph nodes, local numbness, and paresthesias. The most common systemic symptom is fever. Most of the fatal cases died soon after the bite, suffering vomiting, profuse salivation, and coma.[305] In Israel, severe envenoming by *A. engaddensis* may produce violent autonomic symptoms (nausea, vomiting, abdominal pain,

*The taxonomic status of Arabian and Sudanese "*Atractaspis microlepidota*" is currently uncertain.

FIGURE 36-67 Brown tree snake (*Boiga irregularis*) (Papua New Guinea). *(Copyright D.A. Warrell.)*

FIGURE 36-68 Brazilian green racer (*Philodryas olfersii*). **A,** Specimen from Brazil. **B,** Details of back fangs. **C** and **D,** Bruising distant from the bite. (***A*** *and* ***B*** *copyright D.A.Warrell;* ***C*** *and* ***D*** *courtesy João Luiz Costa Cardoso.)*

diarrhea, sweating, profuse salivation) within minutes of the bite. One patient developed severe dyspnea with acute respiratory failure; one had weakness, impaired consciousness, and transient hypertension; and three showed ECG abnormalities (ST-T changes, prolonged PR interval) (see Figure 36-54D).[129] Mild abnormalities of blood coagulation and liver function have also been described.

Atractaspis venoms have high lethal toxicity. The venom of *A. engaddensis* contains four 21-amino-acid peptides, sarafotoxins, that have 60% sequence homology with endogenous endothelins. They can cause coronary vasoconstriction and atrioventricular block.[19,59,227] The venom also contains hemorrhagic and necrotic factors, but no true neurotoxins. Bites by the Natal black snake (*M. microlepidotus*) are said in two cases to have resulted in collapse and loss of consciousness for up to 30 minutes.

ELAPIDAE

Elapidae comprise cobras, kraits, mambas, African shield-nosed snakes, garter snakes (*Elapsoidea*), coral snakes (*Aspidelaps*), Asian coral snakes (*Calliophis* [including *Maticora*], *Sinomicrurus, Hemibungarus*), American coral snakes (*Micruroides, Micrurus*), sea kraits (genus *Laticauda*), and true sea snakes (subfamily Hydrophiinae). They are best known for systemic neurotoxic effects, but cytotoxic elapids, such as African spitting cobras and Asian spitting and nonspitting cobras, produce severe local envenoming (see later discussion).

Neurotoxic Elapidae

Kraits,[11,104,243,257] mambas, most of the Australasian elapids (see later text), some of the cobras (e.g., Philippine cobra, *Naja philippinensis*[279,308]), Cape cobra *Naja nivea*, and sea snakes[197,277] cause minimal local effects. Rapidly evolving neurotoxicity is the dominant clinical feature of envenoming by many elapid species, including African mambas, some African and Asian cobras, king cobras and kraits, Australasian elapids, American coral snakes, and sea snakes.

The earliest symptom of systemic envenoming is repeated vomiting, but sometimes use of emetic herbal medicines confuses interpretation of this symptom. Other early preparalytic symptoms include contraction of the frontalis muscle (before there is demonstrable ptosis), blurred vision and loss of visual accommodation attributable to mydriasis, paresthesias (especially around the mouth), hyperacusis, loss of smell and taste, headache, dizziness, vertigo, and signs of autonomic nervous stimulation, such as hypersalivation, congested conjunctivae, and piloerection ("goose bumps"). Paralysis is first detectable as ptosis and external ophthalmoplegia, because ocular muscles are most sensitive to neuromuscular blockade (see Figure 36-56A to C). These signs may appear as early as 15 minutes after the bite (cobras and mambas), but may be delayed for 10 hours or more

following krait and cobra snakebites. Later, facial muscles, palate, jaws, tongue, vocal cords, neck muscles, and muscles of deglutition may become paralyzed. Pupils are usually dilated. Many patients are unable to open their mouth, but this can be overcome by force. In a minority, the jaw hangs open (see Figure 36-56E). Respiratory arrest may be precipitated by obstruction of the upper airway by the paralyzed tongue or inhaled vomitus. Intercostal muscles are affected before limbs, diaphragm, and superficial muscles, and the pattern of breathing becomes abdominal or paradoxical (protrusion of abdomen during inspiration). Even in patients with generalized flaccid paralysis (see Figure 36-56F), slight movements of the digits may be possible, allowing the patients to signal. Loss of consciousness and generalized convulsions are caused by respiratory paralysis, shock, or massive cerebral hemorrhage or thrombosis. Drowsiness may develop before significant paralysis. Drooping eyelids from tiredness may be misconstrued as ptosis, unless the extent of lid retraction with upward gaze is formally assessed. Patients with systemic envenoming suffer from headache, malaise, and generalized myalgia.[5] Intractable hypotension may occur in patients envenomed by Asian and Australasian elapids, despite adequate respiratory support.

Neurotoxic effects are completely reversible, either acutely in response to antivenom (e.g., in Asian cobra and Australasian death adder bites) or to anticholinesterases,[133,255,302,307,311] or they may slowly wear off spontaneously.[33,34,134,243] In the absence of specific antivenom, patients supported by mechanical ventilators usually recover sufficient respiratory muscle function to breathe adequately in 1 to 4 days; ocular muscles recover in 2 to 4 days, and there is usually full recovery of motor function in 3 to 7 days.[34,35,134] However, especially in the absence of antivenom treatment, paralysis may persist. Patients have recovered after 30 days of manual ventilation (in a case of envenoming by the Chinese krait, *B. multicinctus*) and after 10 weeks of mechanical ventilation (Australian rough-scaled snake, *Tropidechis carinatus*). Neurotoxic deaths are claimed to have occurred as soon as 15 minutes after the bite in the case of *N. naja* and from 1.25 to 60 (mean 12.6) hours in the case of *N. kaouthia*.[141,267]

Envenoming by Asian Nonspitting Cobras (*Naja naja, N. kaouthia , N. oxiana, N. philippinensis, N. atra,* etc.) and Spitting Cobras

The relative frequency of neurotoxic and cytotoxic effects (see later) varies from *N. philippinensis* (predominantly neurotoxic) to *N. siamensis* (predominantly cytotoxic).[243,267] Typical neurotoxic features are those previously described, sometimes with lost ability to taste chili. Unlike krait bites, cobra bites are locally painful, but abdominal pain is not a feature. Paralysis may resolve dramatically in response to anticholinesterase drugs such as neostigmine and within 30 to 60 minutes after antivenom administration.

Envenoming by Mambas (Genus *Dendroaspis*)

Mambas are justifiably the most dreaded snakes in Africa. All four species—*Dendroaspis polylepis, D. angusticeps, D. jamesoni, and D. viridis*—are capable of causing rapidly progressive and fatal respiratory paralysis (Figure 36-69A to E; see also Figures 36-8 and 36-32). Mamba venom toxins (see earlier discussion) are responsible for a distinct clinical syndrome of envenoming: paresthesias, signs of autonomic nervous system stimulation, muscular fasciculations, and paralysis (Figure 36-70).

The speed of evolution of envenoming is well illustrated by a patient seen in Harare, Zimbabwe. After a bite by a 3-m-long (9.8-foot-long) black mamba (*D. polylepis*), the victim noticed tingling of the tongue and lips within 1 minute, followed by generalized tingling, abdominal pain, and lightheadedness. Within 20 minutes, he was sweating profusely, had dilated pupils, and was too weak to stand up. He became nauseated and vomited 30 minutes after the bite, by which time he was unable to pass urine and had detectable ptosis. He became breathless and found it difficult to clear his throat of thick secretions. Forty minutes after the bite, he felt cold all over and noticed

FIGURE 36-69 Mambas (genus *Dendroaspis*). **A,** Black mamba (*D. polylepis*) (Zimbabwe). **B,** Showing long fangs and black lining of mouth, which gives this species its name (specimen from Watamu, Kenya). **C,** Eastern green mamba (*D. angusticeps*). **D,** Showing fangs (Watamu, Kenya). **E,** Western green mamba (*D. jamesoni kaemosi*) (Kakamega, Kenya). **F,** Western green mamba (*D. viridis*) (Sierra Leone). *(Copyright D.A. Warrell.)*

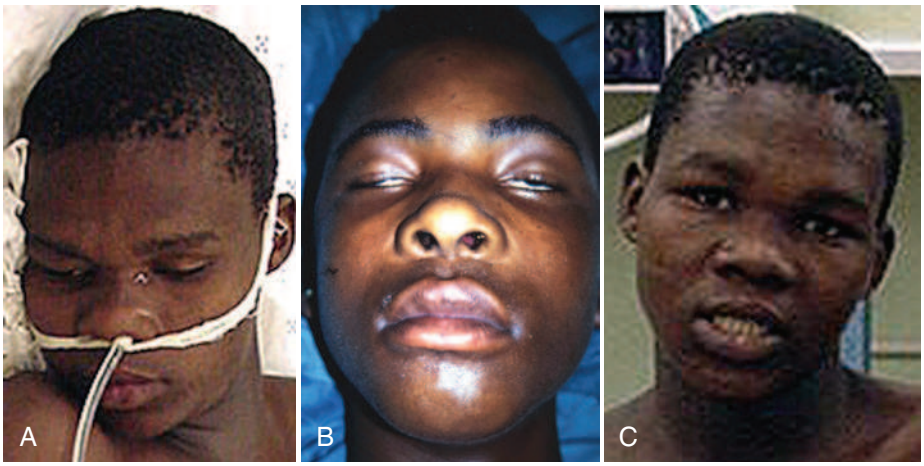


FIGURE 36-70 Envenoming by black mamba (*Dendroaspis polylepis*) bite in KwaZulu-Natal, South Africa. **A** and **B,** Eight hours after bite on leg—no local signs, drooling saliva, ptosis, but still breathing well. **C,** Improved after antivenom treatment. *(Courtesy Iain Thirsk.)*

gooseflesh, his conjunctivae were congested, and he was unable to open his mouth or protrude his tongue. There was then rapid deterioration in his breathing and level of consciousness. Generalized fasciculations were noticed. He was treated with antivenom after 75 minutes and, 4.5 hours after the bite, was intubated and mechanically ventilated for 40 hours, after which he made a complete recovery.[278]

Several patients bitten by captive eastern green mambas (*D. angusticeps*) in Western countries developed atypical envenoming: extensive local swelling, blistering, and mild antihemostatic disturbances in the absence of classic neurotoxicity.

Envenoming by African Neurotoxic Cobras (*Naja anchietae, N. annulifera, N. haje, N. melanoleuca, N. nivea,* and *N. senegalensis*) (Figure 36-71)

Bites may cause some local swelling, but no necrosis develops unless the bite is on a finger pulp. Classic neurotoxic symptoms develop as early as 30 minutes after the bite and can evolve to the point of fatal respiratory paralysis 2 to 16 hours after the bite[278,295,322] (Figure 36-72).

Envenoming by the King Cobra (*Ophiophagus hannah*) (See Figure 36-15)

Bites by the world's largest venomous snake can cause extensive local swelling, but neurotoxicity is the most prominent feature, reputedly capable of leading to death "soon" or in a "few minutes" after the bite. One patient, bitten by a 2-m (6.6-foot) specimen in Myanmar, began to feel dizzy 15 minutes after the bite, had difficulties with speech and breathing after 30 minutes, showed bilateral ptosis after 40 minutes, and at 90 minutes suffered respiratory arrest requiring 38 hours of mechanical ventilation (Figure 36-73A to D). He made a full recovery[249] (Figure 36-73E). Severe envenoming by the king cobra (*O. hannah*) results in swelling of the whole limb and formation of bullae at the site of the bite, but local necrosis is minimal or absent[249,263,279] (Figure 36-73F).

Envenoming by Asian Kraits (Genus *Bungarus*) (See Figures 36-20B and C, and Figure 36-21B)

The common Indian krait (*B. caeruleus*) (see Figure 36-49) is considered to be the most dangerous species of venomous snake in the Indian subcontinent, along with *N. naja.*[243] It is responsible for 22% to 44% of snakebite deaths in Anuradhapura, Sri Lanka, and for 33% of venomous snakebites in West Bengal.

The epidemiologic pattern is distinctive.[11] Most patients are bitten while asleep on the floors of their huts. The victims may roll over in their sleep, inadvertently touching or trapping a snake that is prowling around their home in search of its natural prey. Because people are bitten while lying down, the target may be any part of the body, including the head, neck, and shoulders. In one series of 88 cases of proven *B. caeruleus* envenoming in Sri Lanka, all patients were bitten while sleeping on the ground, at night indoors. Only 23% of bites were on the lower limbs (compared with 82% by other species). Only 9% of patients had any sign of local envenoming, but 64% developed respiratory paralysis, and the case fatality rate was 6%, twice as high as with other species.[11] Krait bites usually produce invisible or scarcely perceptible puncture marks; no local symptoms apart from mild tenderness, itchiness, numbness, or some other paresthesia; and negligible or no local swelling. As a result, snakebite may not be suspected, and patients commonly present to the hospital after waking in the morning with descending paralysis ("early morning paralysis").[202]

A virtually identical syndrome has been described following Malayan krait (*B. candidus*) (see Figure 36-20B) bites in Southeast Asia, Ceylon krait (*B. ceylonicus*) (see Figure 36-21B) bites in Sri Lanka, and bites by the banded krait (*B. fasciatus*) (see Figure 36-20C) and the Chinese krait (*B. multicinctus*) (Figure 36-74). Patients envenomed by *B. candidus* and *B. multicinctus* in Vietnam often develop persistent mydriasis (see Figure 36-56G).[104,257] Rare differential diagnoses of this type of neurologic presentation would include acute idiopathic inflammatory polyneuropathy (Guillain-Barré syndrome, especially its variants, Miller Fisher syndrome and polyneuritis cranialis), Bickerstaff brainstem encephalitis, myasthenia gravis, and botulism. Rarely, local lymph nodes may be painfully enlarged. Noncolicky, increasing (crescendo) pain (resembling classic gallstone or renal "colic"), epigastric or central in location, is a prominent and characteristic early symptom of *B. caeruleus* envenoming, which may be the manifesting feature before development of neurotoxicity.[11] This symptom seems to be less prominent in *B. candidus* and *B. multicinctus* envenoming. AVIT-sequence cysteine-rich proteins, as with mamba intestinal toxin (prokineticin), which cause painful gut spasm and hyperalgesia, may be responsible. Paralysis may develop within 2 hours or be delayed for 7 to 12 hours. Severe generalized muscle pains were noticed by a few patients in whom moderately elevated plasma myoglobin concentrations suggested the possibility of generalized rhabdomyolysis.[52] Rhabdomyolysis and acute kidney injury have been described in victims of greater black krait (*B. niger*) bite in Bangladesh,[63] and, combined with profound hyponatremia, in patients envenomed by *B. multicinctus* and *B. candidus* in Vietnam.[102,104,257] *Bungarus sindanus* and *B. walli* have caused cases of severe neurotoxic envenoming in Nepal and Bangladesh.[127] Reported

FIGURE 36-71 African neurotoxic cobras (genus *Naja*). **A,** Snouted cobra (*N. annulifera,* South Africa). **B,** Egyptian cobra ("asp") (*N. haje,* Nigeria). **C,** Arabian cobra (*N. arabica,* Saudi Arabia). **D,** Forest cobra (*N. melanoleuca*). **E,** Cape cobra (*N. nivea,* South Africa). **F,** Senegalese cobra (*N. senegalensis*). (***A*** *to* ***D*** *copyright D.A.Warrell;* ***E*** *courtesy of the late John D. Visser;* ***F*** *courtesy Jean-François Trape.)*

case fatality rates in the absence of antivenom treatment and assisted ventilation were as high as 77% in India and 100% in Sri Lanka.

Envenoming by Australian and New Guinean Elapids[33-35,47,132-137,232,316] (Figure 36-75)

Venoms of these snakes cause a distinctive triad of symptoms: neurotoxicity similar to that seen with other elapid bites, generalized rhabdomyolysis, and hemostatic disturbances (Figure 36-76). Local signs are usually mild, but extensive local swelling and bruising with necrosis have been reported, especially after bites by the king brown or mulga snake (*Pseudechis australis*). Painful and tender local lymph nodes are a common feature in patients developing systemic envenoming.

Early symptoms include vomiting, headache, and syncopal attacks similar to those experienced after some viper bites. ECG changes were common in patients envenomed by taipans (*Oxyuranus scutellatus canni*) (see Figure 36-31) in Papua New Guinea, and some had elevated cardiac troponin-T levels, suggesting myocardial damage.[134,135] In dogs, common brown snake (*Pseudonaja textilis*) venom caused myocardial depression attributed to DIC, and tiger snake (*Notechis scutatus*) venom caused

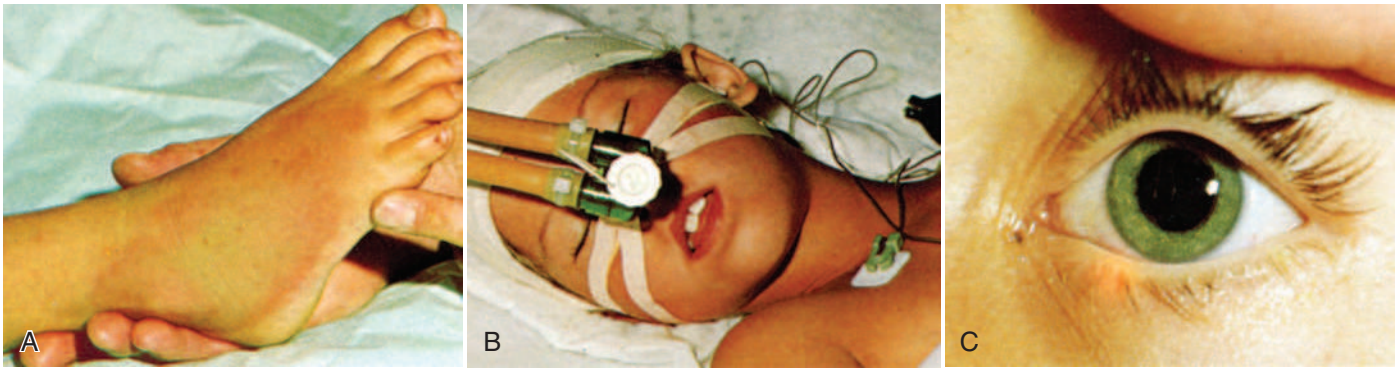


FIGURE 36-72 Envenoming by Cape cobra (*Naja nivea*). **A,** Negligible local envenoming after 5 days. **B,** Respiratory paralysis on ventilator after 8 hours. **C,** Mydriasis. *(Courtesy the late John D. Visser.)*

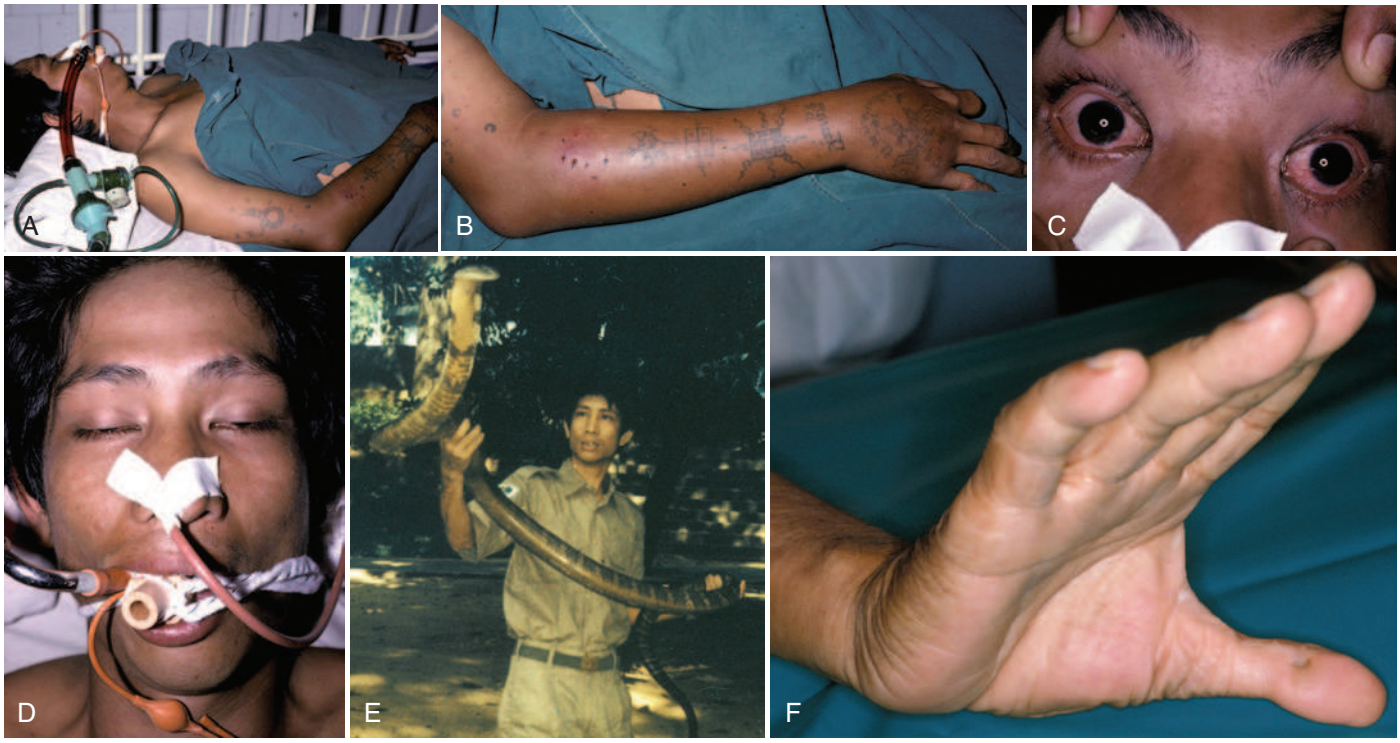


FIGURE 36-73 Envenoming by king cobra (*Ophiophagus hannah*). **A,** Patient became paralyzed and required ventilation 30 minutes after the bite. **B,** Local swelling and multiple fang marks. **C,** Bilateral ptosis. **D,** Conjunctival congestion. **E,** After recovery, back at work with the snake responsible for the bite. **F,** Minimal local necrosis at the site of a bite on the thumb in another reptile handler in Bangkok. *(Copyright D.A. Warrell.)*[249]

formation of thrombi within the heart, leading to pulmonary and coronary artery thromboembolism.[232]

All Australian elapid venoms are potentially neurotoxic to humans.[253] Some patients lose their senses of smell and taste, in a few cases permanently, which is reminiscent of bites by the African berg adder, *Bitis atropos* (see later text). Many of the venoms contain myolytic PLA_2s,[228,232,299] and generalized rhabdomyolysis has been confirmed after bites by *Notechis, Pseudechis, Oxyuranus, Austrelaps, Tropidechis, Rhinoplocephalus/Cryptophis nigrescens, Micropechis ikaheka*, and *Acanthophis*.[133,299,316]

Persistent bleeding from wounds and spontaneous systemic bleeding from gums and the GI tract are found in association with incoagulable blood after bites by many Australasian species. Venoms of 15 out of 19 species exhibited procoagulant activity in vitro.[232] Some venoms (e.g., *Pseudechis, Acanthophis, Micropechis ikaheka*, *Pseudonaja*) are anticoagulant and might cause incoagulable blood without evidence of activation of coagulation and fibrinolysis.[116,133,229,299] Hemostatic abnormalities are particularly frequent and serious in patients bitten by tiger snakes (*Notechis* spp.), taipans (*Oxyuranus* spp.), and brown snakes (*Pseudonaja* spp.); uncommon with bites by black snakes (*Pseudechis* spp.); and rare with bites by death adders (*Acanthophis* spp.).[133]

FIGURE 36-74 Chinese many-banded krait (*Bungarus multicinctus*) (China). *(Copyright D.A. Warrell.)*

Envenoming by American Coral Snakes (See Figures 36-23 and 36-25)

Local signs are usually reported as minimal, consisting of mild swelling and some erythema, or are entirely absent (Figure 36-77A and E) However, local symptoms may be severe and persistent, including pain that may be excruciating (*Micrurus lemniscatus*),[151] and sometimes generalized to bones, joints, and tooth sockets, paresthesias such as numbness radiating up the bitten limb, and in some cases, extensive swelling. The earliest symptom of systemic envenoming may be nausea, retching, and repeated vomiting, sometimes with abdominal pain. Other early preparalytic symptoms include euphoria (*M. fulvius*), blurred vision, perioral paresthesias, hyperacusis, loss of the senses of smell and taste, headache, dizziness, vertigo, and signs of autonomic nervous system stimulation, such as hypersalivation producing unusually sticky secretions, congestion of the conjunctivae, and piloerection. Descending paralysis is usually first detectable as ptosis and external ophthalmoplegia, appearing as early as 15 minutes but sometimes as late as many hours after the bite, progressing to total flaccid paralysis (Figure 36-77B, C, D, and F). Symptoms of systemic envenoming include headache, malaise, and generalized myalgia with, in rare cases, evidence of generalized rhabdomyolysis (*M. fulvius, M. lemniscatus helleri, M. laticollaris*), hemolysis,[8] mild coagulopathy, and bleeding into GI and urinary tracts.[123,151,285]

Envenoming by Sea Snakes (Hydrophiinae) and Sea Kraits (Laticaudinae) (Figures 36-78 and 36-79; see also Figures 36-46 to 36-48)

The bite is usually painless and may not be noticed by the wader or swimmer. Fangs and other teeth may be left in the wound. There is minimal or no local swelling (Figure 36-79A), and involvement of local lymph nodes is unusual. Generalized

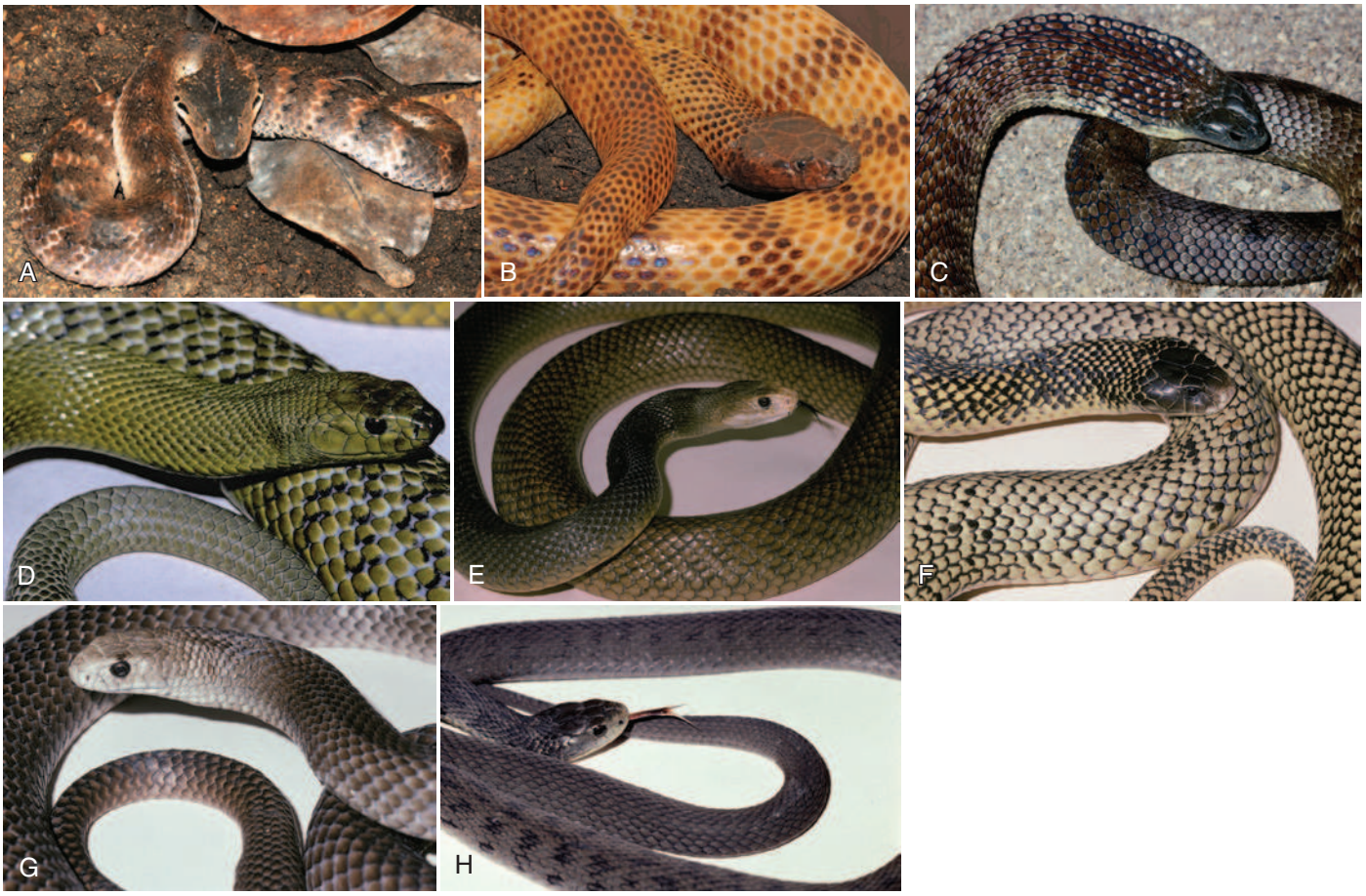


FIGURE 36-75 Australasian elapid snakes. **A,** Death adder (*Acanthophis laevis*) (Papua New Guinea). **B,** New Guinea small-eyed snake (*Micropechis ikaheka*). **C,** Tiger snake (*Notechis scutatus*) spreading hood. **D,** Inland taipan (*Oxyuranus microlepidota*). **E,** Eastern taipan (*Oxyuranus scutellatus*). **F,** King brown or mulga snake (*Pseudechis australis*). **G,** Eastern brown snake (*Pseudonaja textilis*). **H,** Rough-scaled snake (*Tropidechis carinatus*). *(Copyright D.A. Warrell.)*

rhabdomyolysis is the dominant effect of envenoming by many species. Early symptoms include headache, a thick feeling of the tongue, thirst, sweating, and vomiting. Generalized aching, stiffness, and tenderness of the muscles become noticeable between 30 minutes and 210 minutes after the bite. Trismus is common (Figure 36-79B). Passive stretching of the muscles is painful (see Figure 36-57C). Later, there is progressive flaccid paralysis starting with ptosis, as in other neurotoxic envenomings (Figure 36-79). The patient remains conscious until the respiratory muscles are sufficiently affected to cause respiratory failure. Myoglobinemia and myoglobinuria develop 3 to 8 hours after the bite (see Figure 36-57B to D, sea-snake bite). These are suspected when the serum/plasma appears brownish and the urine dark reddish brown. Bedside "stix" tests will appear positive for hemoglobin/blood in urine containing myoglobin. Myoglobin and potassium released from damaged skeletal muscles may cause acute kidney injury, whereas hyperkalemia developing within 6 to 12 hours of the bite may precipitate cardiac arrest.[197,199,232,277,316]

Sea-snake bites are rarely reported since the decline of hand-net fishing, but there have been recent reports from Sri Lanka of severe and fatal envenoming by *Enhydrina schistosa* (also known as *Hydrophis schistosus*).[128,268]

Cytotoxic Elapidae

Envenoming by African Spitting Cobras (Genus *Naja*) (Figure 36-80; See Figures 36-10 and 36-33)**.** Bites by *Naja ashei, N. katiensis, N. mossambica, N. pallida, N. nigricincta, N. nigricollis,* and *N. nubiae* cause severe local envenoming without neurotoxicity.[248,271,278,298] Most bites occur at night inside homes while the victims are asleep. There is immediate pain, followed by vomiting within 6 hours and extensive local swelling, blistering (60%), and tissue necrosis (70%) (see Figure 36-52G and H, *N. nigricollis* bite). A ring of initially small blisters surround a demarcated pale or blackened anesthetic area of necrotic skin. There is associated regional lymphadenopathy. The lesion smells putrid and eventually breaks down with extensive loss of skin and subcutaneous tissue. There may be the appearance of skip lesions, in which areas of necrosis are separated by strips of apparently normal skin. There is leukocytosis and evidence of complement activation, principally by the alternative pathway[271,298] (Figure 36-81). Prolonged morbidity may result. Some patients may lose a digit or the affected limb if there is secondary infection, whereas malignant change (Marjolin's ulcer) may occur in chronic ulcerative lesions.

Envenoming by Asian Cobras (Genus *Naja*) (Figure 36-82)**.** In victims of spitting and nonspitting Asian cobras, severe local effects, as described for African spitting cobras, can develop, but with classic elapid neurotoxicity (Figure 36-83). Species include Chinese cobra (*N. atra*), monocellate cobra (*N. kaouthia*), Indian spectacled cobra (*N. naja*),[243] and Southeast Asian spitting cobras (*N. siamensis,*[334] and *N. sumatrana*). The Philippine cobra, which is responsible for about one-half of all snakebites in Luzon Island, rarely causes local swelling or necrosis.[308,309]

Snake Venom Ophthalmia.[46] Venom ophthalmia results when venom of the spitting elapids (African and Asian spitting cobras, genus *Naja*; southern African rinkhal, *Hemachatus haemachatus*) enters the eye. There is intense local pain,

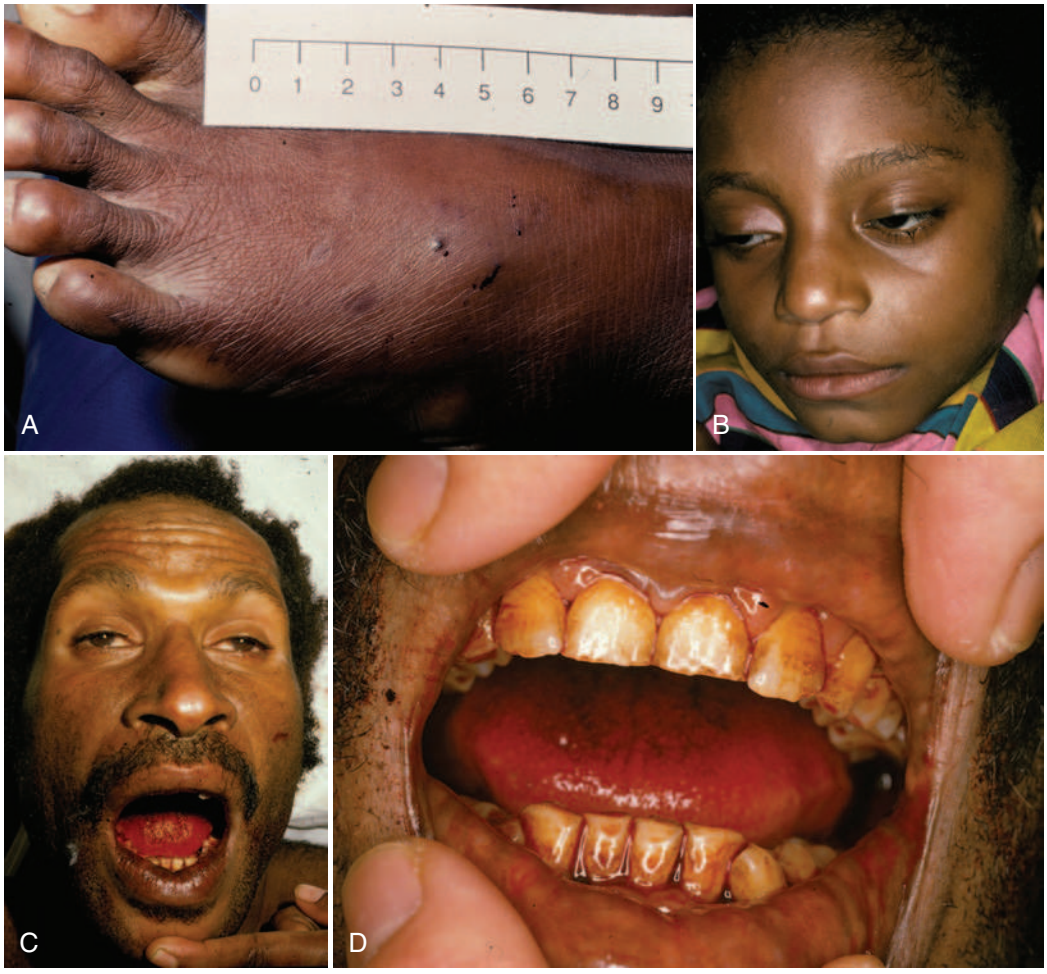


FIGURE 36-76 Envenoming by Papua New Guinean elapids. **A,** Negligible local envenoming after Papuan taipan (*Oxyuranus scutellatus*) bite. **B,** Ptosis after death adder (*Acanthophis laevis*) bite. **C,** Paralytic and hemorrhagic signs after Papuan taipan bite. **D,** Bleeding gums after Papuan taipan bite. *(Copyright D.A. Warrell.)*

blepharospasm, palpebral edema, and leukorrhea (Figure 36-84A to C, *N. nigricollis* spit). Slit-lamp or fluorescein examination reveals corneal erosions in more than one-half the patients spat at by *N. nigricollis*.[189,271,303] Secondary infection of the corneal lesions may result in permanent opacities (Figure 36-84F), causing blindness or panophthalmitis with destruction of the eye (Figure 36-84E). Rarely, venom is absorbed into the anterior chamber, causing hypopyon and anterior uveitis (Figure 36-84D).[180] Seventh (facial) cranial nerve paralysis is a rare complication that results from tracking of venom from the conjunctival sac through lymphatics posteriorly to the superficially situated seventh cranial nerve.

VIPERIDAE (OLD WORLD VIPERS AND ADDERS, ASIAN AND LATIN AMERICAN PIT VIPERS)[285,293]

Local envenoming is usually more severe than that caused by other snakebites. Swelling may develop immediately, typically within 2 hours, but is rarely delayed for several hours. It may spread rapidly, sometimes involving the whole limb and adjacent trunk (see Figure 36-52B, C, E, and F). There is associated pain, tenderness, and enlargement of regional lymph nodes. Bruising is common, especially along the path of superficial lymphatics and over regional lymph nodes. Persistent bleeding from the fang marks suggests coagulopathy (see Figure 36-51, *C. rhodostoma* bite). Swollen limbs can accommodate many liters of extravasated blood, leading to hypovolemic shock. Blistering may appear at the bite site within a few hours after the bite (see Figure 36-52C and D). These contain clear or bloodstained fluid. Necrosis of skin, subcutaneous tissue, and muscle develops in up to 10% of hospitalized cases, especially following bites by Asian pit vipers (e.g., *Calloselasma rhodostoma, Deinagkistrodon acutus*, *Protobothrops flavoviridis*), African vipers (genus *Bitis*), saw-scaled vipers (genus *Echis*), and the Palestine viper (*Daboia palaestinae*). Bites on the digits and in areas draining into tight fascial compartments, such as the anterior tibial compartment, are particularly likely to result in necrosis. High intracompartmental pressure may cause ischemia that contributes, together with direct effects of the venom, to muscle necrosis.[77] Severe pain associated with tense swelling, segmental anesthesia, and pain on stretching the intracompartmental muscles (e.g., dorsiflexion of the foot in the case of the anterior tibial compartment) should raise the possibility of increased intracompartmental pressure. Sudden severe pain, absence of arterial pulses, and a demarcated cold segment of limb suggest thrombosis of a major artery. Deep vein thrombosis has been described but is rare. Absence of detectable local swelling 2 hours after a viper bite usually means that no venom has been injected, but fatal systemic envenoming by the Burmese Russell's viper (*D. siamensis*) and tropical rattlesnake (*Crotalus durissus* subspp.) may occur in the absence of local signs of envenoming.

Systemic Envenoming: Hemostatic Abnormalities

Hemostatic abnormalities are characteristic of envenoming by Viperidae but are usually absent in patients bitten by the smaller European vipers (e.g., *V. berus, V. aspis, V. ammodytes*).[196,286]

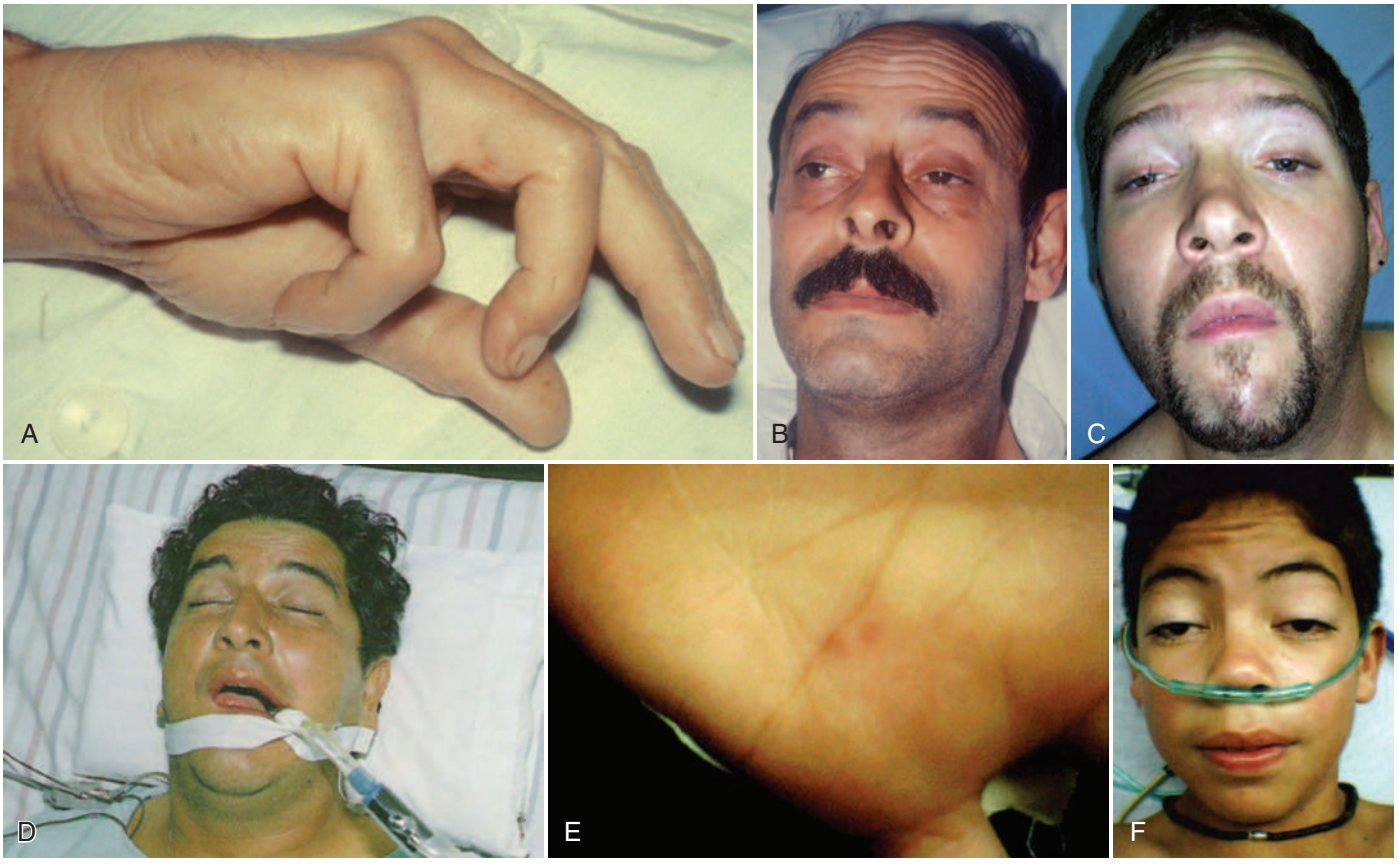


FIGURE 36-77 Envenoming by American coral snakes. **A,** Showing lack of local envenoming (*Micrurus corallinus*). **B,** Neurotoxic signs (*M. corallinus*). **C,** Neurotoxic signs appearing first 15 hours after bite (*Micrurus lemniscatus helleri*). **D,** Ptosis and facial paralysis during first day after bite (*Micrurus mipartitus*) (Colombia). **E,** Bite site on palm of hand showing lack of local envenoming. **F,** Neurotoxicity after bite by *M. mipartitus* in Colombia. (***A*** *and* ***B*** *courtesy Instituto Butantan, São Paulo;* ***C*** *courtesy Steve Manoch;*[151] ***D*** *to* ***F*** *courtesy Rafael Otero-Patiño.)*

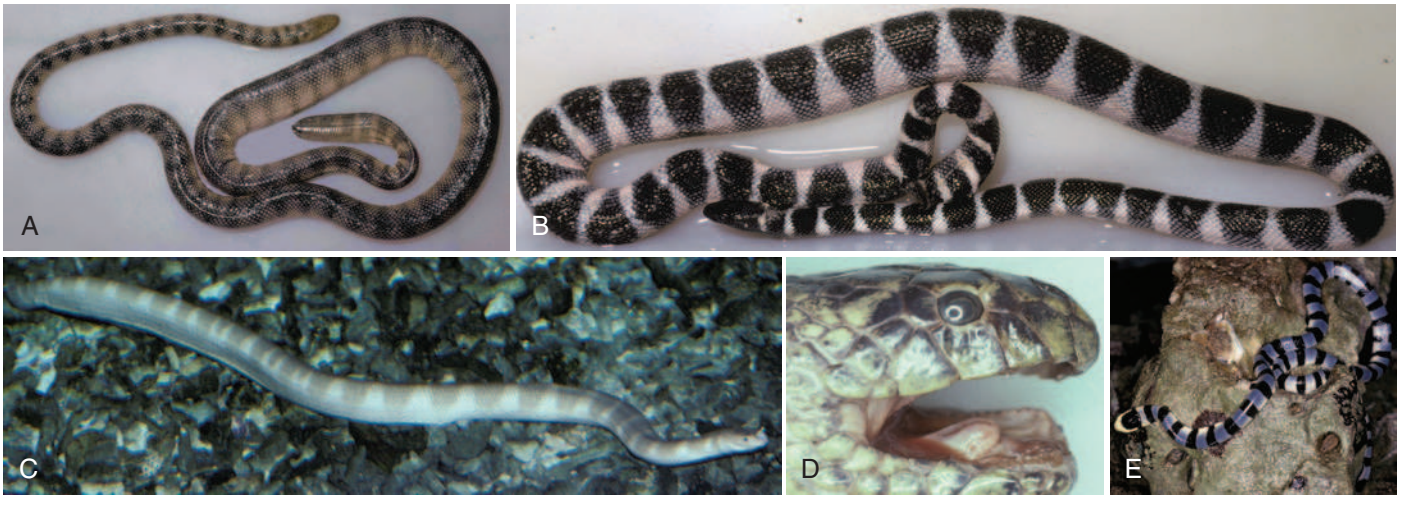


FIGURE 36-78 Sea snakes. **A,** Blue-spotted sea snake (*Hydrophis cyanocinctus*) (Tachalab, Thailand). **B,** *Hydrophis fasciatus atriceps* (Thailand). **C** and **D,** Hardwick's sea snake (*Lapemis curtus*) showing tiny fangs. **E,** Sea krait (*Laticauda colubrina*) (Madang, Papua New Guinea). *(Copyright D.A. Warrell.)*

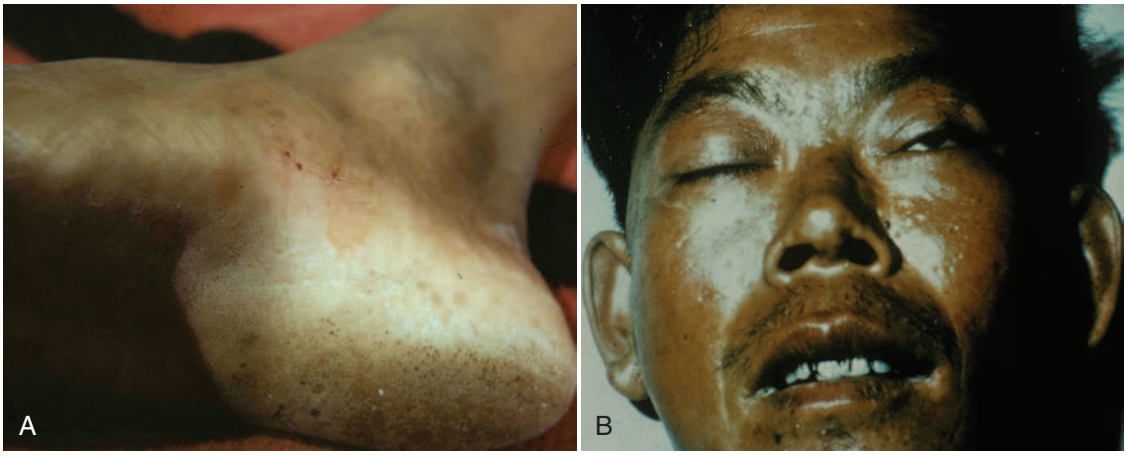


FIGURE 36-79 Sea-snake bite. **A,** Fang marks; note lack of local envenoming. **B,** Ptosis, external ophthalmoplegia, facial paralysis, and trismus in a Malaysian fisherman bitten 24 hours previously by a beaked sea snake (*Enhydrina schistosa*). *(Courtesy the late H. Alistair Reid.)*

FIGURE 36-80 African spitting cobras (genus *Naja*). **A,** *N. ashei* (Watamu, Kenya). **B,** *N. nigricollis* (Abuja, Nigeria). **C,** *N. nubiae* (Egypt). **D,** *N. pallida* (Kenya). *(Copyright D.A. Warrell.)*

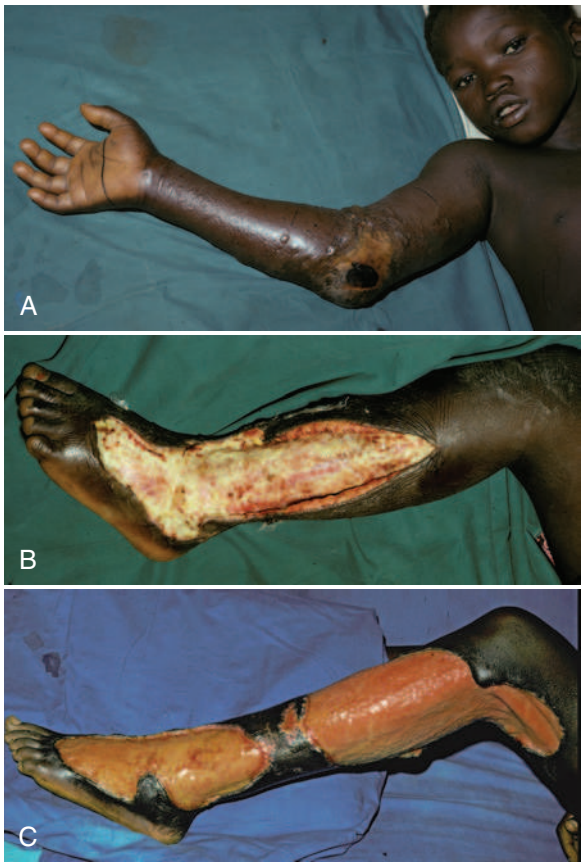


FIGURE 36-81 Envenoming by African black-necked spitting cobra (*Naja nigricollis*). **A,** Swelling, blistering, and necrosis after bite on elbow. **B,** Loss of skin and subcutaneous tissue after bite on dorsum of foot. **C,** Extensive necrosis of skin and subcutaneous tissues in a Mende woman in Sierra Leone bitten 2 weeks earlier. Note the "skip lesions"—areas of necrosis separated by intact skin. *(Copyright D.A. Warrell.)*

Persistent bleeding (>10 minutes) from fang puncture wounds and from new injuries such as venipuncture sites and old, partially healed wounds is the first clinical evidence of consumption coagulopathy. Spontaneous systemic hemorrhage is most often detected in the gingival sulci (see Figure 36-55A). Bloodstained saliva and sputum usually reflect bleeding gums or epistaxis. True hemoptysis is rare. Hematuria may be detected a few hours after the bite. Other types of spontaneous bleeding are ecchymoses; intracranial and subconjunctival hemorrhages; bleeding into the floor of the mouth, tympanic membrane, and GI and genitourinary tracts; petechiae; and larger discoid and follicular hemorrhages. Bleeding into the iliacus muscle may result in weakness of hip flexion. Hemorrhagic infarction of the anterior pituitary (resembling postpartum Sheehan's syndrome) may complicate envenoming. The first, but still unique case was described in Brazil, allegedly caused by *Bothrops jararacussu*. Russell's viper bites in Myanmar (*D. siamensis*),[261] as well as in India and Sri Lanka (*D. russelii*),[7,111] are more common causes. Menorrhagia and antepartum and postpartum hemorrhage have been described after envenoming by vipers. Severe headache and meningism suggest subarachnoid hemorrhage. Evidence of a developing central nervous system lesion (e.g., hemiplegia), irritability, loss of consciousness, and convulsions suggest intracranial hemorrhage (see Figure 36-55D) or cerebral thrombosis. Abdominal distention, tenderness, and peritonitis with signs of hemorrhagic shock but no external blood loss (hematemesis or melena) suggest retroperitoneal or intraperitoneal hemorrhage. Incoagulable blood resulting from defibrination or DIC is a common and important finding in patients systemically envenomed by members of the following genera: *Atheris, Daboia, Vipera, Echis, Gloydius, Calloselasma, Deinagkistrodon,* and *Trimeresurus (sensu lato).*

Intravascular hemolysis causing hemoglobinemia (pink plasma) and black or grayish urine (hemoglobinuria or methemoglobinuria) has been convincingly described in patients bitten by Sri Lankan Russell's viper (*Daboia russelii*),[182] the Saharan horned viper (*Cerastes cerastes*)[211] (see Figure 36-59), and Australian western brown snakes (*Pseudonaja* spp.).[108] Features of microangiopathic hemolysis, which have suggested hemolytic uremic syndrome, may progress to severe anemia and acute kidney injury.[211]

Circulatory Shock (Hypotensive) Syndromes

Falling blood pressure is a common and serious event in patients bitten by vipers, especially in the case of some of the Old World Viperinae (e.g., *D. russelii, D. siamensis, D. palaestinae, V. berus, Bitis arietans, B. gabonica, B. rhinoceros*)[155,168,304] (see Figure 36-53). Sinus tachycardia suggests hypovolemia resulting from external hemorrhage, blood loss into the tissues, or local or generalized increase in capillary permeability ("capillary leak syndrome"). Patients envenomed by Burmese Russell's viper (*D. siamensis*) may develop conjunctival edema, serous effusions, pulmonary edema, hemoconcentration, and decrease in serum albumin concentration, all evidence of increased vascular permeability (see later discussion).[168,245] Pulse rate may be slow or irregular if the venom affects the heart directly or reflexly (e.g., *V. berus, B. arietans, Calloselasma rhodostoma*). Vasovagal syncope may be precipitated by fear and pain. Early, repeated, and usually transient syncopal attacks with features of anaphylaxis develop in patients bitten by some Viperidae (e.g., *D. palaestinae, V. berus, V. aspis, D. siamensis, D. russelii*). Vomiting, sweating, colic, diarrhea (with incontinence), shock, bronchospasm, urticaria, and angioedema of the face, lips, gums, tongue, and throat may appear as early as 5 minutes or as late as many hours after the bite. Hypotension is an important feature of anaphylactic reactions to antivenom (see later text). Acute kidney injury can complicate severe envenoming by any species of snake, but it is common and the most frequent cause of death in victims of Russell's viper. People bitten by Russell's viper may become oliguric within a few hours of the bite. Loin pain and tenderness may be experienced within the first 24 hours, and in 3 or 4 days the victim may become irritable, comatose, or convulsing, with hypertension and evidence of metabolic acidosis.

Neurotoxicity

Neurotoxicity, attributable to venom PLA_2s, is a feature of envenoming by a few species of Old World Viperidae (e.g., *Gloydius blomhoffii, G. brevicaudus, Bitis atropos*, other small South African *Bitis* spp., Sri Lankan and south Indian Russell's vipers), some populations of *Vipera aspis and V. berus*,[149,150] and New World tropical rattlesnakes (*Crotalus durissus* subspp.). The clinical features are the same as with elapid envenoming (Figure 36-85; see also Figures 36-56E and 36-57A). Progression to respiratory or generalized paralysis is unusual but has been described. Associated generalized myalgia suggests the possibility of rhabdomyolysis. Pupillary dilatation, causing visual disturbance from loss of accommodation, is a feature of severe envenoming by small *Bitis* spp. (e.g., *B. peringueyi*) and may be a permanent neurologic sequela that can be corrected transiently by instillation of pilocarpine, as in some cases of krait bite envenoming.

VIPERINAE

Europe

Envenoming by European Vipers[24,118,157,196,251,283,286] (Figure 36-86)**.** The common viper, or adder (*Vipera berus*) (Figure 36-86C), the only venomous snake found in Britain, occurs in England, Wales, Scotland, and northern Europe (Figure 36-86D and E), extending into the Arctic Circle and through Asia as far east as Sakhalin Island and south to northern Korea (see Figure 36-43). Four other vipers are widely distributed in mainland Europe: the nose-horned or sand viper (*V. ammodytes*) (Figure 36-86A and B) in the Balkans, Italy, Austria, and Romania; the asp viper (*V. aspis*) in France (south of Paris), Spain, Germany, Switzerland, and Italy; Lataste's viper (*V. latastei*) in Spain and Portugal; and Orsini's viper (*V. ursinii*) in southeastern France,

FIGURE 36-82 Asian cobras. **A,** Chinese cobra (*Naja atra*) (Hong Kong). **B,** Monocellate cobra (*N. kaouthia*) (Thailand). **C,** Indian spectacled cobra (*N. naja*) (Sri Lanka). Black and white (**D**) and brown (**E**) phases of Indo-Chinese spitting cobra (*N. siamensis*) (Thailand). **F,** Equatorial spitting cobra (*N. sumatrana*) (Singapore). *(Copyright D.A. Warrell.)*

central Italy, and Eastern Europe. The Ottoman viper (*Montivipera xanthina*) (Figure 36-86G) occurs around Istanbul and in some eastern Aegean islands, northern Greece, and Asia Minor. The Milos viper (*Macrovipera schweizeri*) (Figure 36-86F) inhabits some of the Cyclades Islands, southeast of Greece, whereas the Levantine viper (*Macrovipera lebetina*) occurs on Cyprus.

Clinical Features of the European Adder (*Vipera berus*) Bite. Pain usually develops quickly at the site of the bite, and local swelling is evident within a few minutes but is sometimes delayed for 30 minutes or longer. Local blisters containing blood are uncommon (Figure 36-87A). Swelling and bruising with lymphangitis may advance to involve the whole limb within 24 hours, extend to the trunk, and in children become generalized (Figure 36-87B to D). A few cases of compartment syndromes and necrosis have been described. Pain, tenderness, and enlargement of local lymph nodes are sometimes noticeable within hours. Dramatic early systemic symptoms may appear within 5 minutes of the bite or may be delayed for many hours. These include retching; vomiting; abdominal colic; diarrhea; incontinence of urine and feces; sweating; vasoconstriction; tachycardia; shock; angioedema of the face, lips, gums, tongue, throat, and epiglottis; urticaria; and bronchospasm. These symptoms may persist for as long as 48 hours. Hypotension is the most important sign. It usually develops within 2 hours. It may be transient, resolving spontaneously within 2 hours, persistent and recurrent, or progressive and fatal. ECG changes (see Figure 36-53B) include flattening or inversion of T waves, ST-segment elevation, second-degree heart block, bradyarrhythmias or tachyarrhythmias, atrial fibrillation, and myocardial infarction. Defibrination (incoagulable blood) or milder degrees of coagulopathy and spontaneous bleeding into the GI tract, lungs (see Figure 36-87E), or urinary tract are uncommon.

Other clinical features include fever, drowsiness, and rarely, coma and seizures secondary to hypotension or cerebral edema, respiratory distress/pulmonary edema (in children), acute kidney injury, cardiac arrest, intrauterine death, acute gastric dilation, paralytic ileus, and acute pancreatitis. Laboratory findings include neutrophil leukocytosis (>20 × 10^9/L in severe cases), thrombocytopenia, initial hemoconcentration and later anemia, resulting from leakage of plasma and blood cells out of blood vessels into the bitten limb, and rarely, hemolysis, elevation of serum creatine kinase, and metabolic acidosis. Deaths usually occur from 6 to 60 (average 34) hours after the bite. Most adder bites cause only trivial symptoms; patients must be assessed individually. Children may be severely envenomed; in a French series, there were three deaths in a group of seven children between 2.5 and 10 years of age. The dangers of adder bite should not be underestimated.

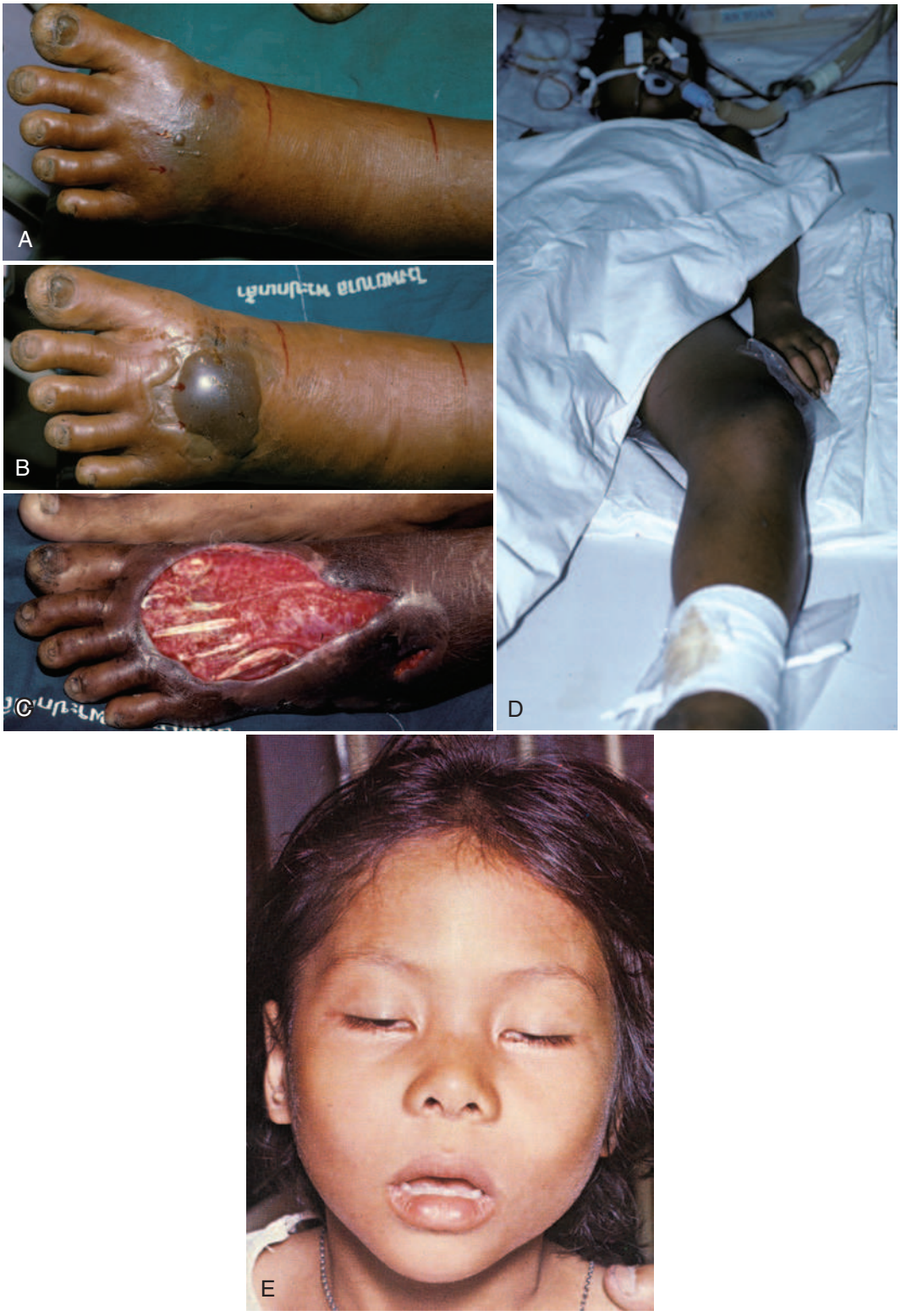


FIGURE 36-83 Envenoming by monocellate Asian cobra (*Naja kaouthia*). **A,** Local swelling and early darkening. **B,** Blistering and demarcated necrotic area. **C,** After debridement of necrotic tissue. **D,** Severe hypoxic brain damage in a boy bitten on his left ankle in Vietnam. There was a delay in resuscitating him after development of respiratory paralysis. **E**, Bilateral ptosis, facial paralysis, and other early signs of neurotoxicity in a girl in Thailand. *(**A** to **D** copyright D.A. Warrell; **E** courtesy Professor Mukda Trishnananda.)*

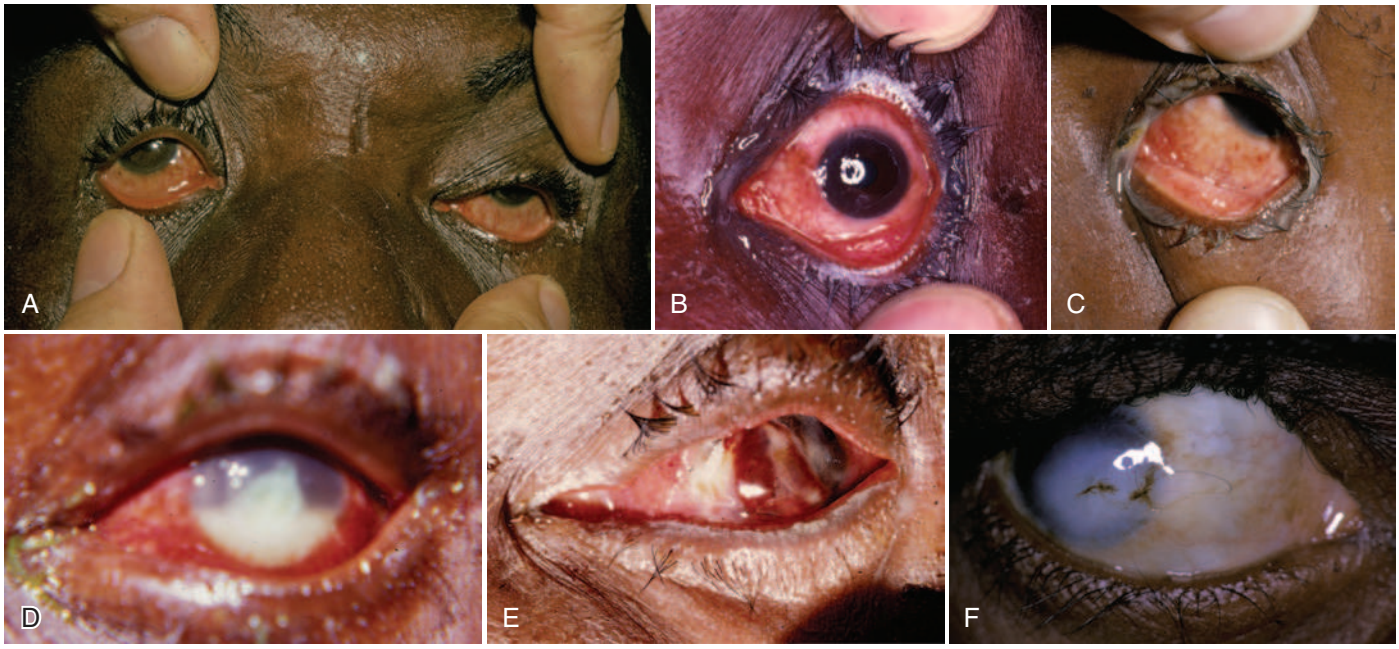


FIGURE 36-84 Venom ophthalmia after venom "spitting" by black-necked spitting cobra (*Naja nigricollis*) in Nigeria. **A** to **C,** Acute effects—blepharospasm, inflammation, leukorrhea, epiphora. **D,** Hypopyon. **E,** Panophthalmitis following neglected corneal abrasion. **F,** Corneal opacity causing blindness. *(Copyright D.A. Warrell.)*

Envenoming by other European and Mediterranean vipera produces similar features, most severe in the case of *M. lebetina* (Cyprus), *V. ammodytes*, and *V. aspis* bites, and least severe in *V. ursinii* and *V. latastei* bites. It is surprising that bites by *M. schweizeri* (Cyclades Islands, Greece) do not appear to result in severe envenoming. Some populations of *V. aspis zinnikeri* and *V. aspis* in southeastern France and of *V. berus* in Hungary can cause mild neurotoxic envenoming.[149,150]

Guillain-Barré syndrome developing after *V. aspis* envenoming was attributed to cross-reactivities between venom proteins and the patient's GM2 gangliosides.[170]

Africa

Envenoming by Saw-Scaled or Carpet Vipers (Genus *Echis*)[279,294] (Figure 36-88; see also Figures 36-14A and 36-18C)**.** This genus of vipers is of great medical importance. *Echis* is widely distributed in the northern third of Africa from Senegal in the west to the Tana River in Kenya in the south and through the Middle East. Throughout this range, *Echis* is usually the most important cause of human snakebite morbidity and mortality. Bites are most common in West Africa, where *E. ocellatus* (see Figure 36-18C) is the most important species.[61,271,296,297] In Nigeria, only 4% of patients admitted to the hospital lacked signs of envenoming, the lowest rate of "dry bites" reported in any large case series. The remainder had both local and systemic envenoming; 12% developed local blistering, and 9% developed necrosis (Figure 36-89A and B). Coagulopathy (attributable to venom prothrombin activators and factor X activators) was universal; 55% of victims showed spontaneous systemic bleeding (see Figures 36-55A, B, E, and F and 36-89C to G), usually from the gingival sulci (Figure 36-89C), but thrombocytopenia (platelet count $<103 \times 10^9$/L, or 103,000/mm^3) was detected in only 7%. Soluble fibrin complexes and fibrin/fibrinogen breakdown products were detected, but heparin does not inhibit *Echis* thrombin in vitro or in patients.[61,107,296] The case fatality rate of 3.6% was attributable to hemorrhagic shock (three cases) (Figure 36-89E to G; see Figure 36-55F) and intracerebral hemorrhage (two cases) (Figure 36-89D). Envenoming by eastern and North African *E. pyramidum* is generally less severe, but fatalities are reported in Turkana and Wajir in northern Kenya and in Somalia. One patient bitten by a Tunisian *E. leucogaster* developed transient ptosis.[82,293] *Echis* species cause most fatal snakebites in the Middle East.[276,278,282]

Envenoming by African Puff Adders (*Bitis arietans*)[278] (Figure 36-90; see also Figure 36-11)**.** This species (or species

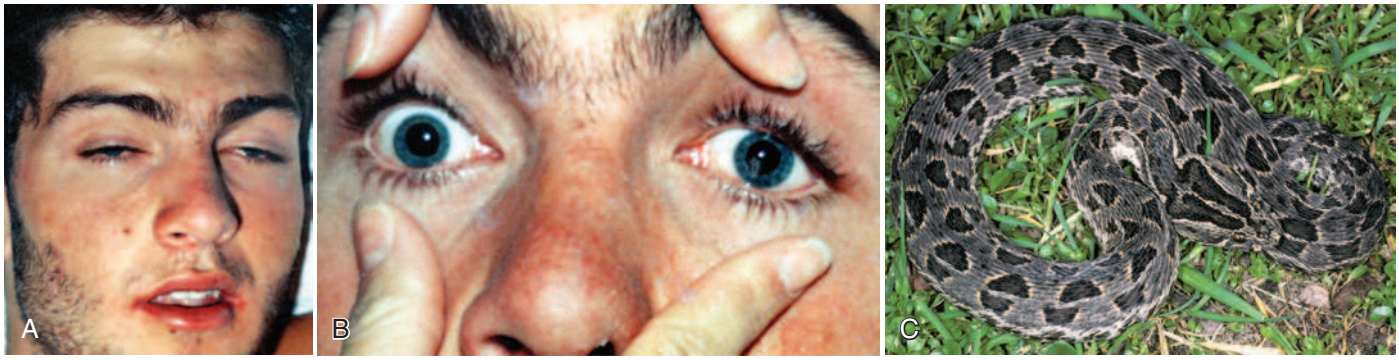


FIGURE 36-85 Neurotoxic envenoming by Viperidae. Ptosis (**A**) and mydriasis (**B**) after berg adder (*Bitis atropos*) bite in Drakensberg, South Africa. **C,** *B. atropos* specimen from South Africa. *(**A** and **B** courtesy Craig Smith; **C** copyright D.A. Warrell.)*

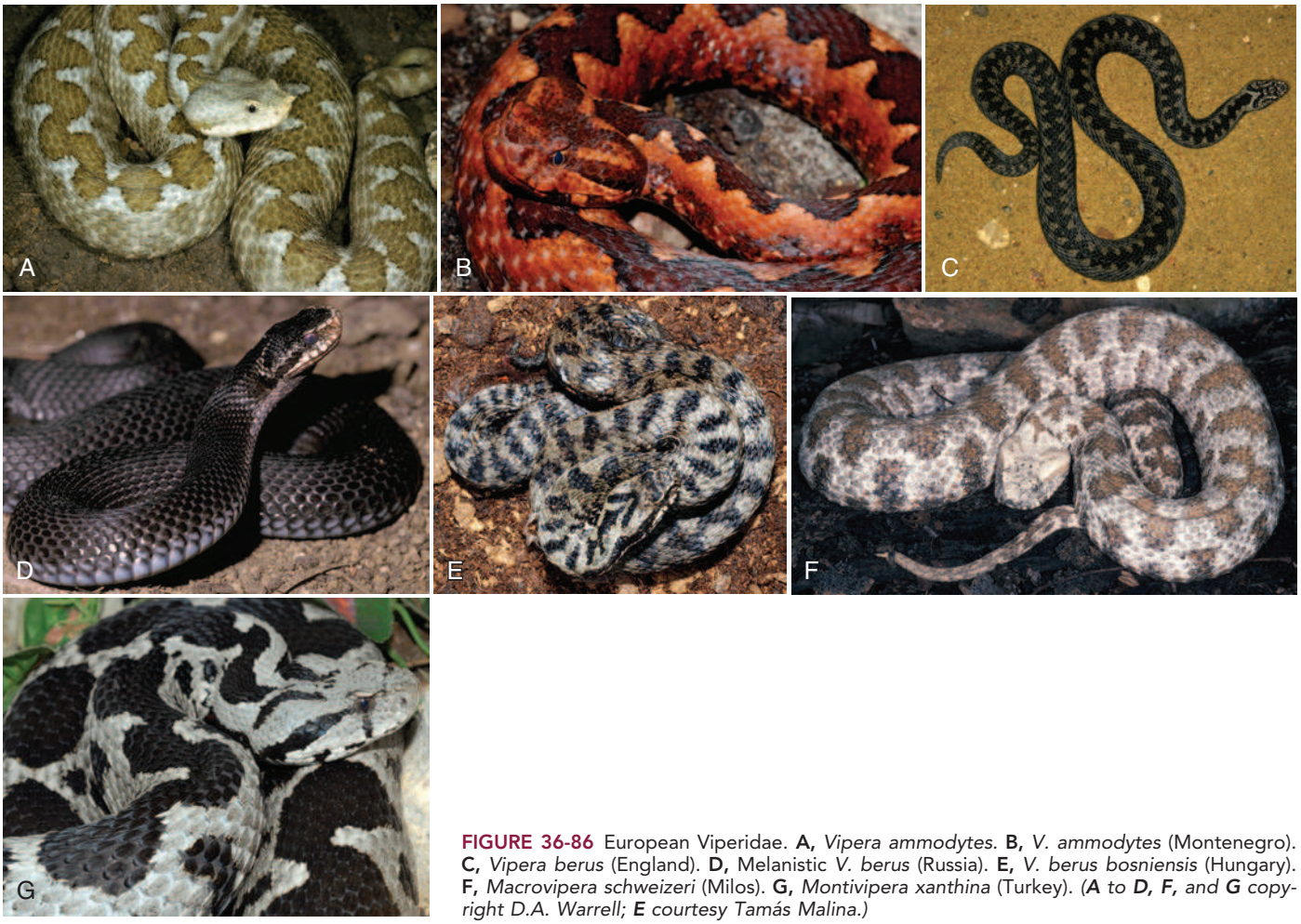


FIGURE 36-86 European Viperidae. **A,** *Vipera ammodytes*. **B,** *V. ammodytes* (Montenegro). **C,** *Vipera berus* (England). **D,** Melanistic *V. berus* (Russia). **E,** *V. berus bosniensis* (Hungary). **F,** *Macrovipera schweizeri* (Milos). **G,** *Montivipera xanthina* (Turkey). (***A*** *to* ***D, F,*** *and* ***G*** *copyright D.A. Warrell;* ***E*** *courtesy Tamás Malina.)*

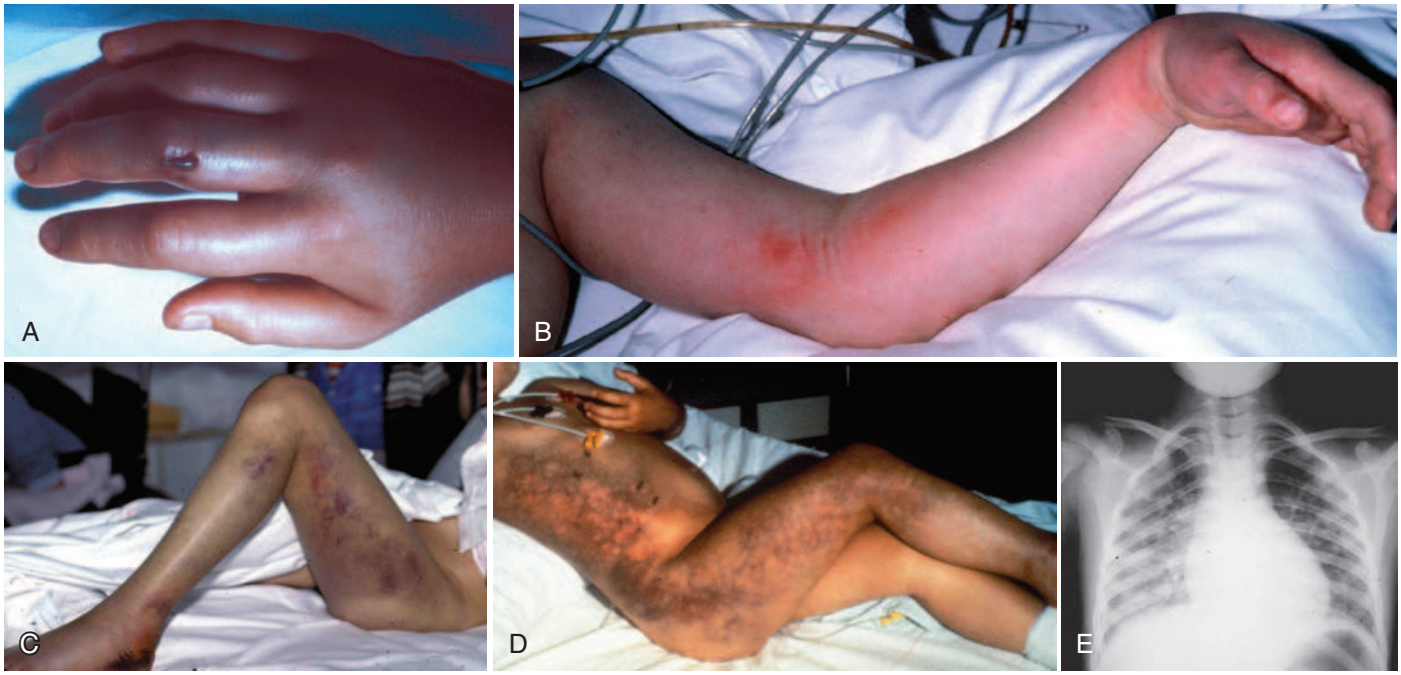


FIGURE 36-87 Envenoming by *Vipera berus*. **A,** Hemorrhagic blister at site of bite. **B,** Swelling of bitten limb. **C,** Bruising of bitten limb. **D,** Generalized swelling and bruising in a 4-year-old child in Sweden. **E,** Chest radiograph showing extensive intrapulmonary bleeding. (***A*** *copyright D.A. Warrell;* ***B*** *courtesy Mark Brueton;* ***C*** *and* ***E*** *courtesy H. Bowker;* ***D*** *courtesy Hans Persson.)*

FIGURE 36-88 Saw-scaled or carpet vipers. **A,** *Echis carinatus carinatus* (Tamil Nadu, India). **B,** *Echis carinatus multisquamatus* (Russia). **C,** *Echis carinatus sochureki*. **D,** *Echis coloratus* (Saudi Arabia). **E,** *Echis jogeri* (Senegal). **F,** *Echis pyramidum leakeyi* (Baringo, Kenya). *(**A** to **D, F,** and **G** copyright D.A. Warrell; **E** courtesy Wolfgang Wüster.)*

complex) is thought to be responsible for many of the bites throughout the African savanna region. Local swelling is often very extensive, often extending to involve the entire bitten limb and spreading to the trunk[304] (Figure 36-91A). This extravasation of plasma causes hypovolemic shock, a common manifesting feature. Local blistering and necrosis may be extensive, requiring amputation of the bitten digit or even part or all of the bitten limb (Figure 36-91B). Major arteries may become thrombosed or entrapped by swollen tissue in the bitten limb,[23] increasing local tissue damage. Compartment syndromes may develop, especially involving the anterior tibial compartment after bites on the feet and ankles. These may lead to ischemic muscle necrosis, as in Volkmann's ischemic contracture of the forearm. Direct myocardial effects and arrhythmias, commonly sinus bradycardia, may contribute to hypotension. In West Africa, envenoming by *B. arietans* causes spontaneous bleeding, bruising, and petechial hemorrhages on serosal surfaces, attributable to thrombocytopenia but not coagulopathy. However, in East and South Africa, coagulopathy, and rarely even cerebral thrombosis, have been reported. This regional variation in the pattern of envenoming suggests that there may be different species of puff adder.

Envenoming by Giant Rain Forest Vipers or Adders (*Bitis gabonica, Bitis rhinoceros,* and *Bitis nasicornis*)[278,293] (Figure 36-92; see also Figure 36-34B)**.** These giant rain forest species are the commonest cause of snakebite in some areas of Africa, for example in southern Nigeria and the eastern Democratic Republic of Congo. In light of their wide distribution, prodigious size, enormous fangs, and massive yield of highly potent venom, it is surprising that so few cases of envenoming have been reported. Local effects of envenoming may be less severe than those produced by puff adder bites, but swelling, bruising, blistering, and necrosis are common (Figure 36-93). Systemic symptoms may be early and dramatic, including dizziness, chest tightness, nausea, and vomiting. In one case, there was deafness and early paralysis of visual accommodation, suggesting neurotoxicity. Cardiovascular abnormalities, including hypotension, hypovolemic and cardiogenic shock, arrhythmias, and ECG changes, are reported. Spontaneous systemic bleeding is a common feature, whereas hemostatic abnormalities include thrombocytopenia, inhibition of platelet aggregation, and evidence of thrombin-like and fibrinolytic activities.[155]

Envenoming by the Berg Adder (*Bitis atropos*). This mountain species has been responsible for envenoming rock climbers and mountain travelers in Zimbabwe and South Africa. It is the most neurotoxic of African vipers and can cause other unusual symptoms. After initial severe pain and rapidly spreading local swelling (with rare development of necrosis), there are paresthesias of the tongue and lips, blurring of vision, loss of the senses of taste and smell, nausea, vomiting, and dizziness. In one series of cases, ptosis, external/internal ophthalmoplegia, dilated pupils, loss of visual accommodation, and anosmia were reported in 93% of cases (see Figure 36-85). There was respiratory paralysis in 72%, hyponatremia (attributed to a natriuretic hormone–like toxin), and dysphagia in 64%, and convulsions in 29%.[166] Only one fatal case has been reported.

Envenoming by Bush Vipers (Genera *Atheris, Proatheris,* and Others)[158,186,288,291] (Figure 36-94)**.** These mainly arboreal species seem more likely to bite Western snake

FIGURE 36-89 Envenoming by West African carpet viper (*Echis ocellatus*) in northern Nigeria. **A** and **B,** Local necrosis. **C,** Bleeding from gums and into floor of mouth. **D,** Subarachnoid hemorrhage causing meningism. **E** to **G,** Autopsy finding of bleeding into the lungs, kidneys, and bladder. *(Copyright D.A. Warrell.)*

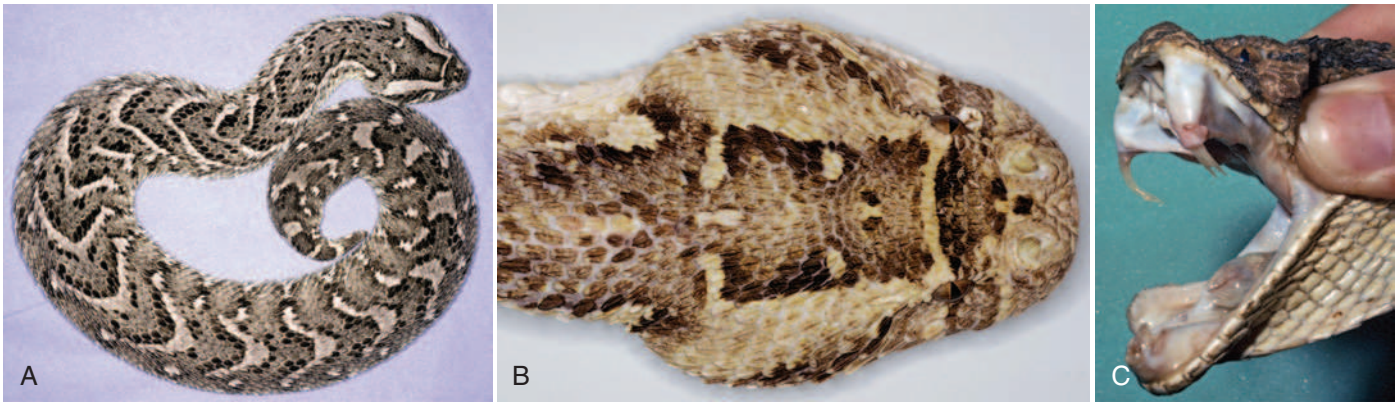


FIGURE 36-90 African puff adder (*Bitis arietans*). **A,** Specimen from Saudi Arabia. **B,** Dorsal view of head showing large nostrils. **C,** Showing fangs. *(Copyright D.A. Warrell.)*

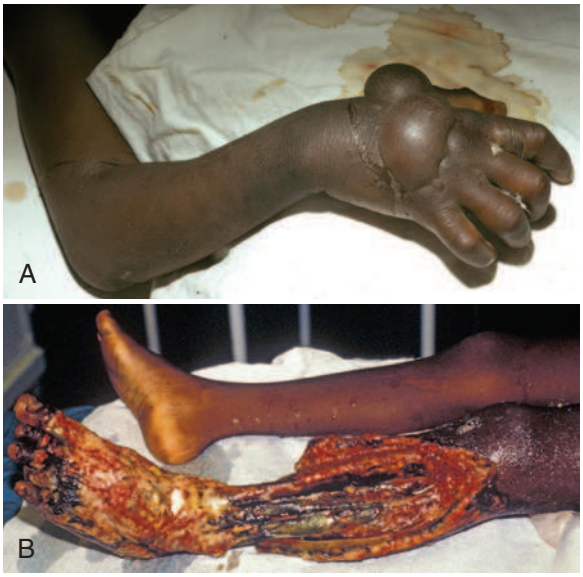


FIGURE 36-91 Envenoming by puff adder (*Bitis arietans*). **A,** Swelling and blistering of bitten limb. **B,** Necrosis in neglected case (KwaZulu Natal, South Africa). (***A*** *copyright D.A. Warrell;* ***B*** *courtesy Paul Rollinson.)*

enthusiasts than indigenous Africans. Envenoming by them has been underestimated. Bites by *Atheris* ceratophora and *A. desaixi* caused only local effects: transient pain, swelling, bruising, and residual arthrodesis. However, a prominent feature of severe envenoming by *A. squamigera and A. chlorechis* was hypotension, perhaps attributable to a new class of peptides containing small poly-His and poly-Gly segments identified in venoms of *A. squamigera, A. chlorechis,* and *A. nitschei.*

A man bitten by a large green bush viper (*A. squamigera*) developed massive swelling of the bitten limb and incoagulable blood. He died 6 days later in hemorrhagic shock following hematemesis. Other victims of bites by this species experienced immediate severe pain, swelling, local bruising, dizziness, shivering, nausea, and local lymphadenopathy. A man bitten on the hand by an adult great lakes bush viper (*A. nitschei*) developed swelling of the arm with ecchymoses in the axilla and bleeding from the bite site and from the oral mucosa. He had anemia, thrombocytopenia, coagulopathy, and hypofibrinoginemia but survived after treatment with blood products.[96] A man bitten by a Western bush viper (*A. chlorechis*) developed a severe bleeding diathesis, hypotension, acute kidney injury, and hemolysis, but survived.

Three men were bitten by captive specimens of lowland or swamp adders (*P. superciliaris*). All experienced severe and persistent pain, initially in the bitten limb but later spreading to the trunk and back; local swelling (local necrosis in one); intravascular hemolysis (schistocytes in one) with hyperbilirubinemia; thrombocytopenia; fibrinolysis (elevated D-dimer); elevated aspartate aminotransferase and other serum enzymes; oliguric acute kidney injury requiring dialysis in two cases; and slow recovery over several weeks. One presented with severe persistent nausea, vomiting, and diarrhea. Two had consumptive coagulopathy, two had hematuria or hemoglobinuria, and two became hypertensive and developed pulmonary congestion with arterial desaturation. In one case, imaging suggested bilateral intrarenal vascular occlusion that progressed to renal cortical necrosis, and later myocardial ischemia, leaving him with intractable renal failure.[186,288]

Envenoming by Desert Vipers (Genus *Cerastes*) (Figure 36-95)**.** *Cerastes cerastes, C. gasperettii, C. vipera,* and *Pseudocerastes persicus* inhabit the vast arid deserts of North Africa and the Middle East, where they are the most common cause of snakebite. A few fatal cases were reported in the 19th-century French colonial military literature, but there have been no recent reports. Envenoming usually results in local pain and swelling, complicated by necrosis in some cases. Nausea, vomiting, spontaneous bleeding, and coagulopathy have been observed in some cases. Recently, DIC, microangiopathic hemolysis, and acute tubular necrosis were described in two proven cases of envenoming by *C. cerastes* (see Figure 36-59).[211]

Asia

Envenoming by Saw-Scaled or Carpet Vipers (Genus *Echis*)[279,293] (See Figure 36-89A to C)**.** *Echis carinatus* occurs in western Asia, as far north as the Aral Sea, and throughout the Indian subcontinent, including Sri Lanka, as far as the border of

FIGURE 36-92 Giant rain forest vipers or adders. **A,** Eastern Gaboon/Gabon viper (*Bitis gabonica*) (South Africa). **B** and **C,** Western rhinoceros viper (*Bitis rhinoceros*) (Ghana). **D** to **F,** Rhinoceros-horned viper or river jack showing nasal horns (*B. nasicornis*) (Cameroon). *(Copyright D.A. Warrell.)*

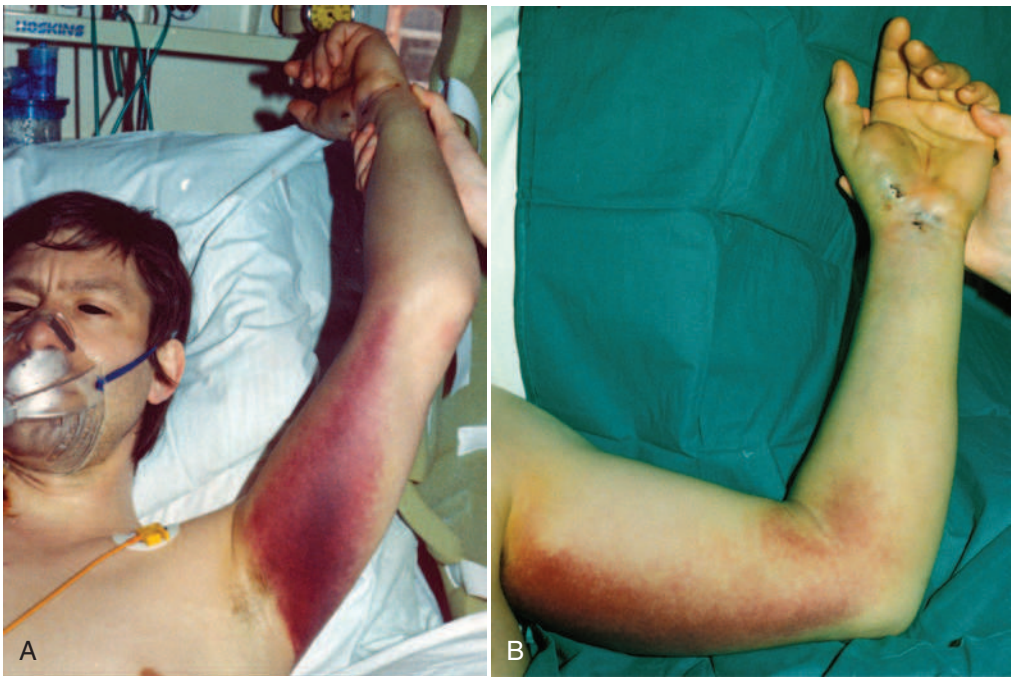


FIGURE 36-93 **A** and **B,** Envenoming by Gaboon viper (*Bitis gabonica*) showing pulmonary edema, swelling, and bruising after a bite on the wrist.[155] *(Copyright D.A. Warrell).*

West Bengal. It is prodigiously common in some areas of India and Pakistan (e.g., in Sind and Jammu), where it is the major cause of snakebite morbidity and mortality.[20,111,265] In northern India (Jammu) and in western India (Rajasthan), envenoming by *E. carinatus sochureki* caused symptoms similar to those observed in Nigeria (see Figures 36-52F; 36-55B and F; and 36-89D to G).[21,125]

Envenoming by Western and Eastern Russell's Vipers (*Daboia russelii* and *D. siamensis*)[273,293] (See Figure 36-13)**.** These medically important species occur from Pakistan in the west through India and Sri Lanka, north into Nepal[22] and Bhutan (*D. russelii*), and as far east as West Bengal; and in Southeast Asia, southern China, Taiwan, and in parts of Indonesia (*D. siamensis*)[20] (Figure 36-96). Throughout this range, there are

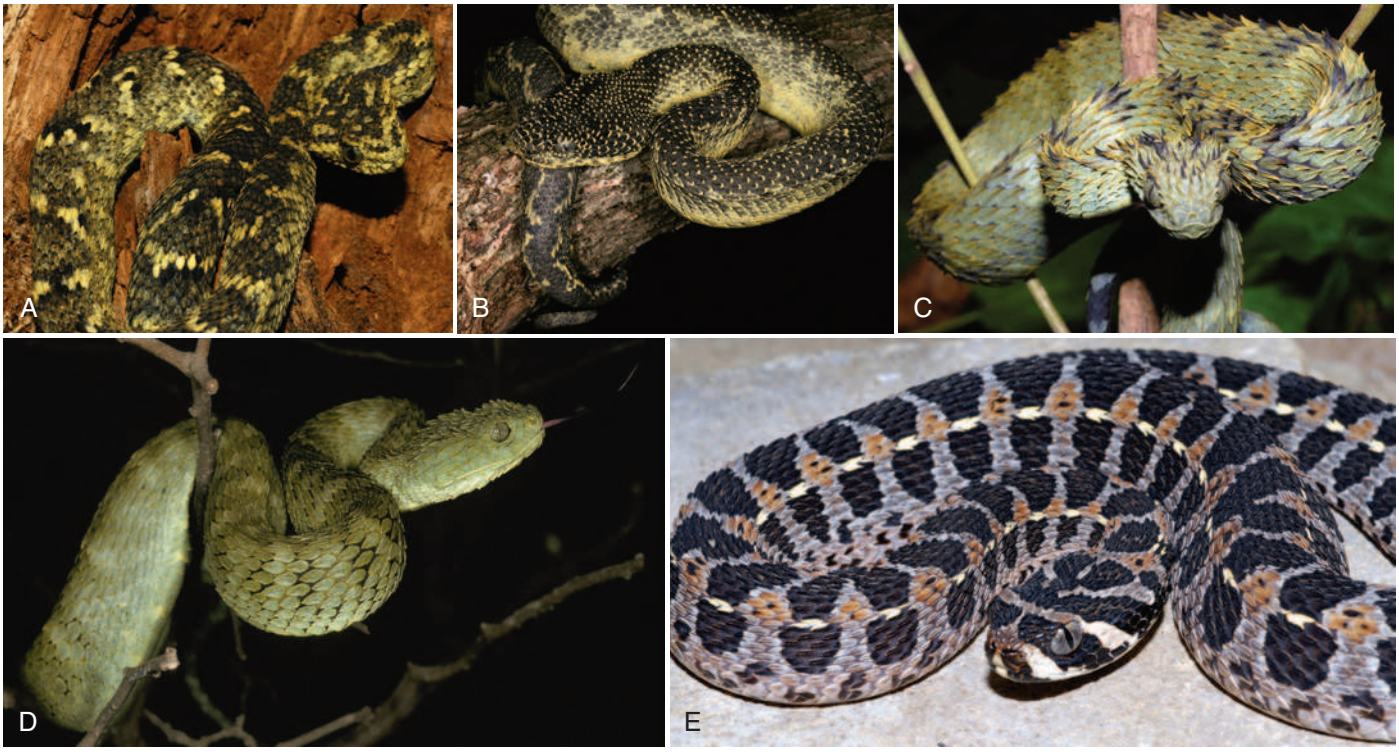


FIGURE 36-94 African bush vipers. **A,** Usambara bush viper (*Atheris ceratophora*) (Tanzania). **B,** Mt Kenya bush viper (*A. desaixi*) (Kenya). **C,** Rough-scaled bush viper (*A. hispida*) (Kakamega, Kenya). **D,** *A. squamigera*. **E,** Swamp adder (*Proatheris superciliaris*) (Malawi). *(Copyright D.A. Warrell.)*

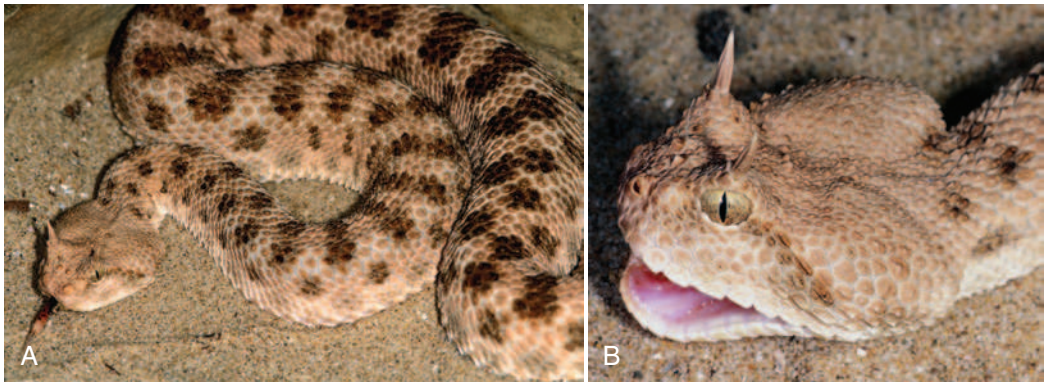


FIGURE 36-95 **A** and **B,** Sahara horned viper (*Cerastes cerastes*) (Algeria) showing supraocular horns. *(Copyright D.A. Warrell.)*

intriguing geographic variations in the clinical manifestations of envenoming, reflecting differences in venom composition.[62,162,258,272,273]

Sri Lanka. *D. russelii* is a major cause of venomous snakebites (see Figure 36-13A). Of patients bitten by this species, 28% showed no clinical evidence of envenoming.[9,12,182] Apart from typical features of viperine envenoming (local envenoming, coagulopathy, bleeding, and sometimes shock; see Figures 36-52B to F and 36-53), there were distinctive features of neuromyotoxicity attributable to venom PLA_2: ptosis (77%), external ophthalmoplegia (82%) (Figure 36-97A), inability to open the mouth (23%) or to swallow and protrude the tongue, generalized muscle tenderness (32%), and myoglobinuria (27%) (Figure 36-97B). Most patients showed evidence of intravascular hemolysis. Acute kidney injury was a common feature of severe envenoming. Single or multiple, medium to large cerebral arterial thromboses have been described,[78] as well as the more familiar hemorrhagic strokes. Similar findings have been reported from envenoming by *D. siamensis* in Taiwan.[105] Two cases of hypopituitarism have been detected in Sri Lanka.[7,111]

India. In most parts of the country, *D. russelii* is an important cause of snakebite, but in Jammu in the northeast, only 4 of 310 identified viperine bites were caused by this species.[21] Clinical manifestations of envenoming vary in different parts of India. In Tamil Nadu, in the south, neurotoxic signs, such as ptosis and ophthalmoplegia, associated with hemostatic disorders, are common. In Kerala, generalized increase in capillary permeability is a dreaded feature. Bilateral parotid enlargement is also described.[60] Features of panhypopituitarism, manifesting between 1 month and 1 year after the bite, were observed in 7 of 1000 cases of snakebite, and there was one case of diabetes insipidus. Especially in the south, Russell's viper bite is the most common cause of acute kidney injury in both adults and children.

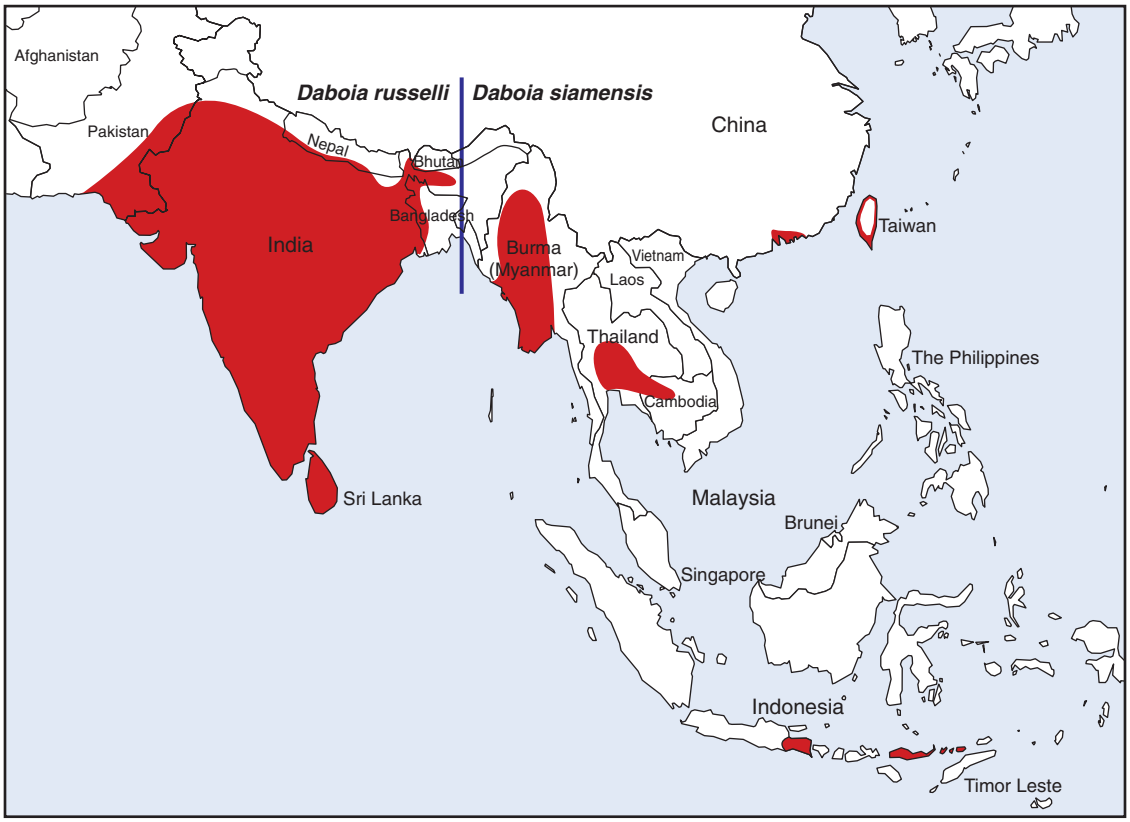


FIGURE 36-96 Western and Eastern Russell's vipers (*Daboia russelii* and *Daboia siamensis*). *(Courtesy David J. Williams.)*

Myanmar. Russell's viper (*D. siamensis*) is the most important cause of snakebite morbidity and mortality in Myanmar (formerly Burma). However, about one-third of all patients hospitalized after proven Russell's viper bites develop no clinical evidence of envenoming at any stage. In Tharrawaddy, north of Yangon, two distinct populations of Russell's vipers were found to be responsible for bites during the November to January rice harvest. Smaller snakes (125 to 375 mm [4.9 to 14.8 inches] in total length) had probably been born that year, whereas the larger snakes (500 to 1125 mm [19.7 to 44.3 inches] in total length) had been born in previous years.[260] Bites by larger snakes were associated with more intense local swelling (Figure 36-97C) and higher risk of systemic envenoming.[260] Severe systemic envenoming can result, despite minimal or no local evidence of envenoming. Spontaneous bleeding (gums, epistaxis, hemoptysis, hematemesis, hematuria) develops within a few hours and may result in fatal cerebral hemorrhage (see Figure 36-55D). Orbital and conjunctival edema with conjunctival hemorrhages (Figure 36-97D and E) develops in severe cases and is evidence of generalized increase in capillary permeability. Other manifestations of this permeability syndrome are facial edema, pleural effusions, ascites, pulmonary edema (Figure 36-97F), macular edema, glaucoma, and transient massive albuminuria leading to hypoalbuminemia.[245]

Other clinical features include hypotension and shock (see Figure 36-53A and C), epigastric and chest pain, and acute kidney injury within 3 to 4 days of the bite (see Figure 36-58A and B). This is associated with bilateral loin tenderness and hypertension, attributable to renal ischemia and associated with increased plasma renin concentrations.[250] In some cases, spontaneous diuresis began within 7 to 10 days, followed by complete recovery without residual renal abnormalities. A late polyuric phase can be life threatening. Persistent or recurrent bleeding and shock may be attributable to hemorrhagic infarction of the anterior pituitary (Figure 36-97G) and/or adrenal glands. There may be intracranial hemorrhage and swollen hemorrhagic kidneys.[7,261] Renal angle tenderness predicted the development of oliguria (sensitivity 0.7, specificity 0.9).[245,250]

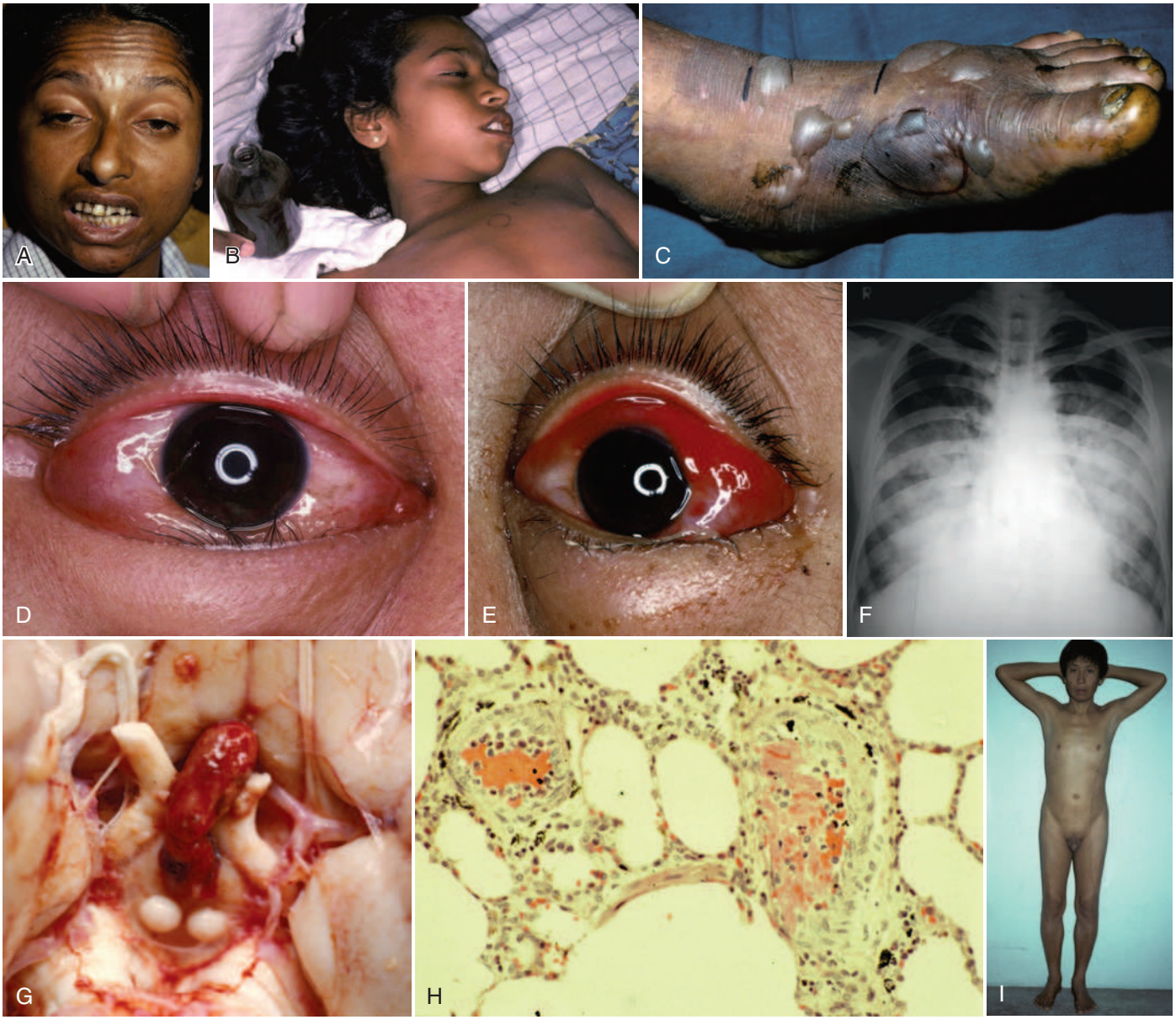


FIGURE 36-97 Envenoming by Russell's vipers in Sri Lanka (*Daboia russelii*): **A,** neurotoxicity; **B,** myotoxicity. In Myanmar (*Daboia siamensis*): **C,** local swelling, blistering, and necrosis; **D** and **E,** chemosis and subconjunctival hemorrhage; **F,** pulmonary edema; **G,** hemorrhagic infarction of anterior pituitary; **H,** fibrin deposition in pulmonary blood vessels; **I,** chronic panhypopituitarism showing loss of secondary sexual hair and testicular atrophy. *(A to G and I copyright D.A. Warrell; H courtesy Nicholas Francis.)*

Russell's viper venom contains a number of different components that affect hemostasis, including procoagulants (activating factors X, IX, and V and protein C), fibrinolytic agents, platelet aggregating and inhibiting factors, an anticoagulant, and a hemorrhagin.[107] In human patients, the most striking laboratory features are depletion of fibrinogen, factors V, X, and XIIIa, antithrombin III, plasminogen, antiplasmin, protein C, and platelets. There are high levels of fibrin/fibrinogen-related antigen, mostly cross-linked in the form of D-dimer.[237,238] At autopsy, there is widespread evidence of bleeding but also fibrin deposition, occluding small blood vessels in the pituitary, lungs (Figure 36-97H), and kidneys.[236] Some patients who survived the acute pituitary adrenal crisis presented later with more insidious symptoms of panhypopituitarism, including loss of libido, impotence, loss of secondary sexual hair, hypotension, amenorrhea, and features of hypothyroidism[261] (Figure 36-97I).

Thailand. Russell's viper bites are common in the central rice-growing area of Thailand, but although the snake is the same species (*D. siamensis*) as in adjacent Myanmar, clinical features are generally less severe, although there have been deaths attributed to shock, cerebral hemorrhage, and acute kidney injury.[141]

PIT VIPERS (CROTALINAE)[279,285]

Envenoming by Japanese and Chinese Mamushis (*Gloydius [Agkistrodon] blomhoffii, G. brevicaudus,* and others) (Figure 36-98)

In Japan, bites by the Japanese mamushi (*G. blomhoffii*) are mainly inflicted on the hands. There is local swelling with blistering, nausea, vomiting, fever, headache, abdominal and lumbar pain, shock, acute renal failure, bleeding gums, and ecchymoses. Neurotoxic features are confined to ptosis and external ophthalmoplegia, which can develop between one and 48 hours after the bite.

In China north of latitude 25 degrees north, the Chinese mamushi (*G. brevicaudus*) is the most common cause of snakebite. There is local swelling, together with neurotoxic symptoms, such as blurring of vision, ptosis, and diplopia within 24 hours of the bite. Breathlessness, dysphagia, and difficulty opening the mouth are associated with symptoms suggesting generalized rhabdomyolysis. Some patients require assisted ventilation.

FIGURE 36-98 Chinese (short-tailed) mamushi (*Gloydius brevicaudus*) (Beijing). *(Copyright D.A. Warrell.)*

Envenoming by the Malayan Pit Viper (*Calloselasma rhodostoma*)[198,200,301] (Figure 36-99)

This species is an important cause of snakebite in northwestern Malaysia, Thailand, Laos, Cambodia, Vietnam, and Java (see Figure 36-99A). *C. rhodostoma* inhabits coffee and rubber plantations and rice fields in areas of cleared jungle. Bites are a major occupational hazard of plantation workers (see Figure 36-48C). About one-half the patients develop minimal or no envenoming, but in the remainder, local swelling starts within minutes and reaches its maximum after 24 to 72 hours (see Figure 36-52B to

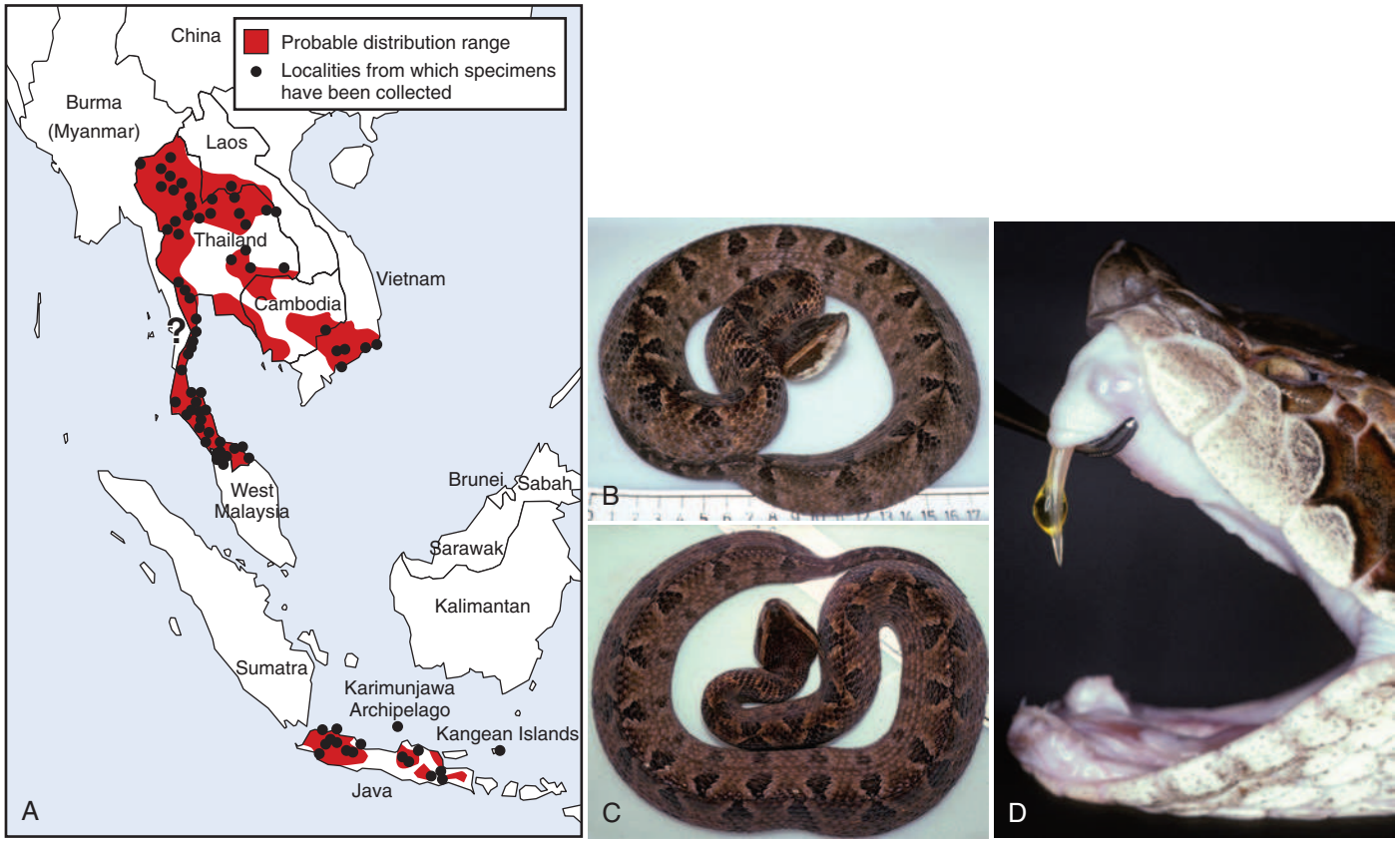


FIGURE 36-99 Malayan pit viper (*Calloselasma rhodostoma*). **A,** Distribution. **B** to **D,** Specimens from Thailand showing dorsal pattern and fangs. *(**A** courtesy Jenny Daltry; **B** to **D** copyright D.A. Warrell.)*

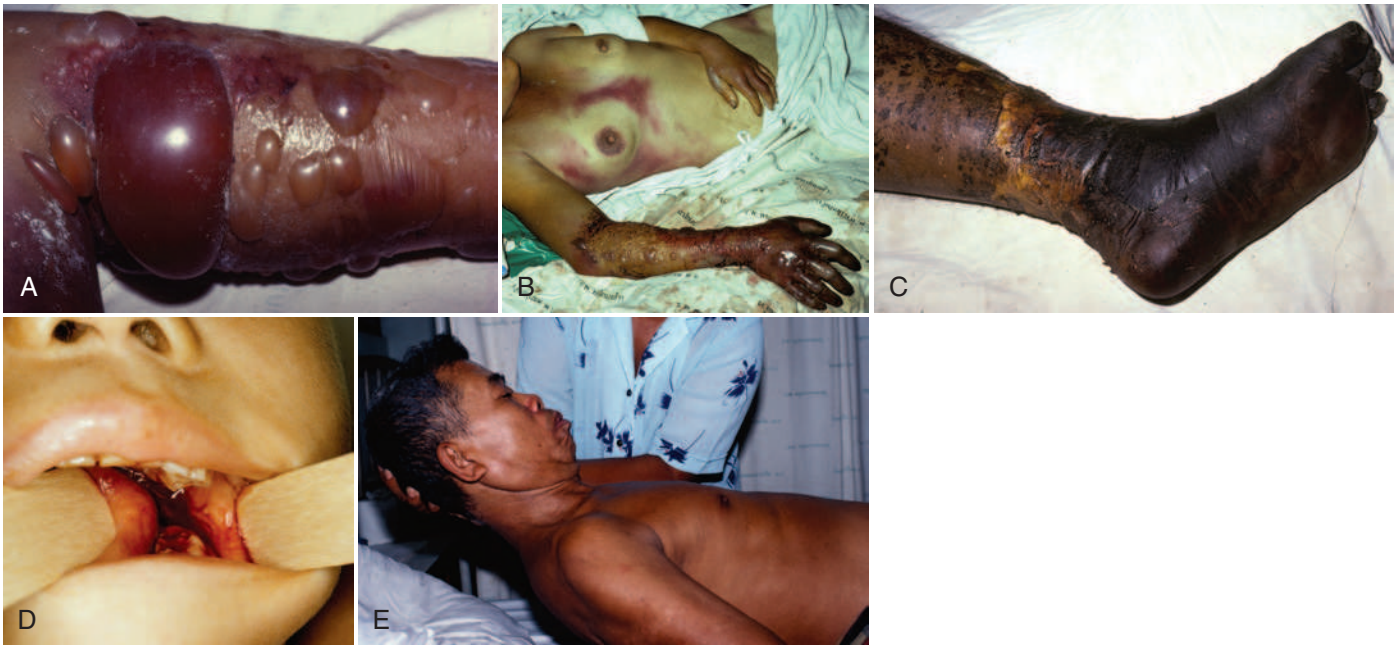


FIGURE 36-100 Envenoming by Malayan pit viper (*Calloselasma rhodostoma*). **A,** Severe blistering and bruising. **B,** Diffuse ecchymoses, shock, and gangrene of the bitten arm 4 days after the bite, when the patient was finally brought to the hospital. **C,** Gangrene. **D,** Bleeding gums. **E,** Tetanus complicating snakebite wound infection. *(Copyright D.A. Warrell.)*

D). Local necrosis develops in 11% of victims and is always preceded by blistering (Figure 36-100A to C). Secondary infection by bacteria peculiar to the venom and oral cavity of the snakes is common, and fatal tetanus may ensue (Figure 36-100E).[242] Blood becomes incoagulable as early as 30 minutes after the bite and, in untreated patients, may persist for 1 to 26 days.[198] There is associated bleeding from sites of trauma (see Figure 36-51), gums, ecchymoses, and elsewhere (see Figures 36-52D, and 36-55B and D). Most patients have profound thrombocytopenia, probably resulting from sequestration. Fatal cases in Thailand were attributed to cerebral hemorrhage, shock, tetanus, septicemia, and anaphylaxis.[141]

Envenoming by Asian Arboreal Pit Vipers (Genera *Trimeresurus* [*Trimeresurus*], *Trimeresurus* [*Viridovipera*], *Trimeresurus* [*Craspedocephalus*], *Protobothrops*, and Others)[106,279,300] (See Figures 36-40 and 36-41)

In Thailand, the white-lipped green pit viper (*Trimeresurus* [*Trimeresurus*] *albolabris*) is the most widely distributed venomous snake and the second most common cause of snakebite (27% of cases).[266] Pain and swelling develop early after the bite, spreading to involve more than one-half of the bitten limb in 46% of cases. Local bruising and tender enlargement of local lymph nodes are common, whereas local blistering and necrosis are rare (Figure 36-101A to C). Coagulopathy, thrombocytopenia, and leukocytosis may develop.

In Myanmar, *Trimeresurus* [*Trimeresurus*] *erythrurus* bites resulted in no evidence of envenoming in 65% of cases. In the rest, there was local swelling without necrosis, incoagulable blood, thrombocytopenia, and in one case, acute kidney injury.

In Bangladesh, most victims of bites by this species show no coagulopathy and recover without antivenom treatment. Although the Indian bamboo viper (*Trimeresurus* [*Craspedocephalus*] *gramineus*) is the most abundant pit viper in the southern half of India, there is little reliable information about the effects of envenoming. In south India, the Malabar pit viper (*Trimesurus* [*Craspedocephalus*] *malabaricus*) is said to be a common cause of local necrosis.[106]

In Thailand, the dark-green pit viper (*Trimeresurus* [*Trimeresurus*] *macrops*) is a common cause of mild envenoming in some areas, notably in gardens in central Bangkok, whereas the Kanchanaburi pit viper (*Trimeresurus* [*Trimeresurus*] *kanburiensis*) is capable of causing severe envenoming[300] (Figure 36-101D).

The Chinese habu (*Protobothrops mucrosquamatus*) causes about one-third of venomous snakebites in Taiwan and results in an 8% case fatality rate, whereas the Chinese green pit viper (*Trimeresurus* [*Viridovipera*] *stejnegeri*), although responsible for 53% of bites in Taiwan, carries a case fatality rate of only1%. Bites by *P. mucrosquamatus* are more likely to cause local necrosis and rhabdomyolysis.[41]

Envenoming by Latin American Pit Vipers (Genera *Bothrops, Bothriopsis, Crotalus, Lachesis*)[285]

***Agkistrodon, Bothrops* (Bothriopsis), and Others** (Figure 36-102; see also Figures 36-7, 36-22E and 36-34A)**.** Local envenoming may appear within 15 minutes but rarely may be delayed for several hours. Swelling spreads rapidly, sometimes to involve the entire bitten limb and adjacent areas of the trunk (see Figure 36-52E). There is associated pain, tenderness, and enlargement of regional lymph nodes. Bruising may extend up the bitten limb, especially in lines along the path of superficial lymphatics and over regional lymph nodes. There may be persistent bleeding from the fang marks if the blood is incoagulable. Blistering may appear at the site of the bite within the first 12 hours, and necrosis of skin, subcutaneous tissue, and muscle develops in up to 10% of hospitalized cases (Figure 36-103A to F). Bites on the digits (fingers and toes) and in areas draining into the tight fascial compartments, such as the anterior tibial compartment, are particularly likely to cause necrosis. Absence of detectable local swelling 2 hours after a viper bite usually means that no venom has been injected. Secondary bacterial infections may manifest as subcutaneous abscesses or more diffuse cellulitis (Figure 36-103G). Spontaneous systemic hemorrhage occurs from the gingival sulci (see Figures 36-55A, and 36-103H and I), as well as epistaxis, hematemesis, hematuria, intracranial (Figure 36-103J) and subconjunctival hemorrhages and bleeding into the GI and genitourinary tracts. Women may develop menorrhagia and pregnant women antepartum or postpartum may develop hemorrhages with hemorrhagic abortion of the fetus. Severe headache and meningism suggest subarachnoid hemorrhage, whereas hemiplegia and other lateralizing neurologic signs, irritability, loss

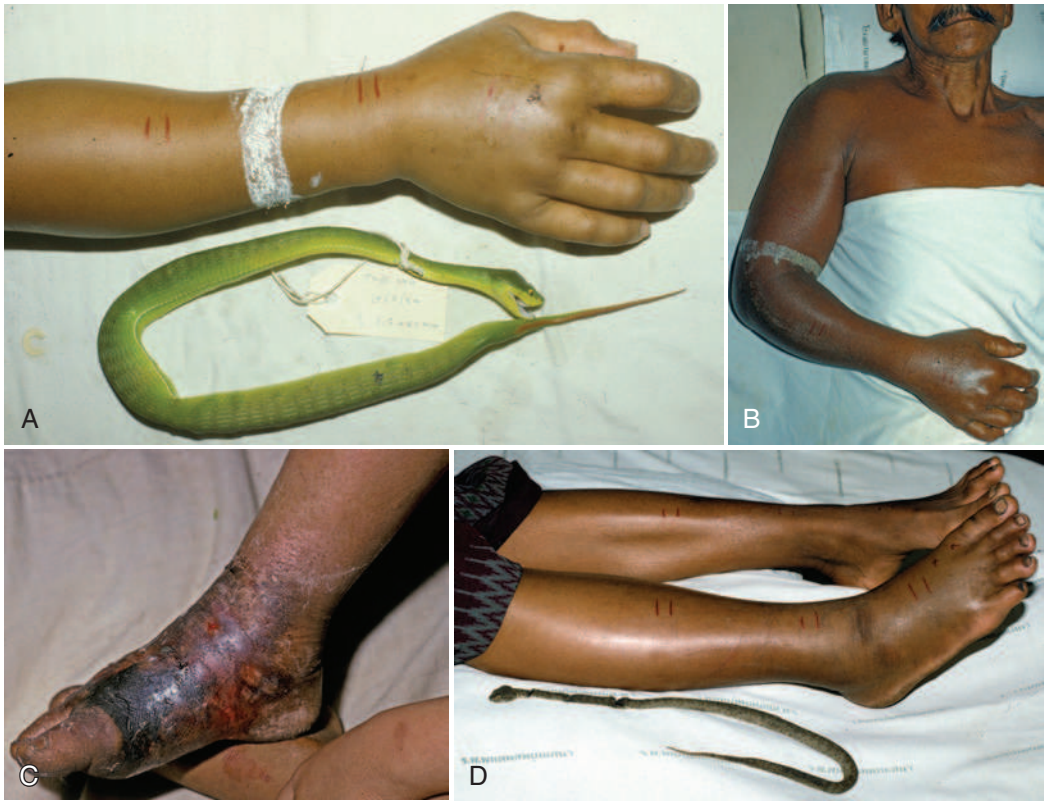


FIGURE 36-101 Envenoming by arboreal green pit vipers (genus *Trimeresurus*). Bites by white-lipped green pit viper [*T.* (*T.*) *albolabris*]. **A** and **B,** Swelling of bitten arm and the snake responsible (Thailand). **C,** Local necrosis (Vietnam). **D,** Local swelling after a bite by a Kanchanaburi pit viper [*T.* (*T.*) *kanburiensis*] (Thailand). *(Copyright D.A. Warrell.)*

of consciousness, and convulsions suggest intracranial hemorrhage or cerebral thrombosis. Abdominal distention, tenderness, and peritonism with signs of hemorrhagic shock but no external blood loss suggest retroperitoneal or intraperitoneal hemorrhage. Hypotension and circulatory shock causing loss of vision and then consciousness may occur a short time after the bite. Acute kidney injury can complicate cases of severe envenoming (see Figure 36-58C). Thromboses of small to medium-sized cerebral, pulmonary, coronary, or mesenteric arteries are features of envenoming by the fer de lance of Martinique (*Bothrops lanceolatus*) and the serpent of St Lucia (*Bothrops caribbaeus*) (see Figure 36-102I).[88,147,246] Cerebral thrombosis has also been described in patients envenomed by *Daboia russelii* in Sri Lanka, *D. siamensis* in Taiwan, *Bitis arietans* in South Africa, and some species of North American rattlesnakes (e.g., *Crotalus oreganus helleri*).

The terciopelo (*Bothrops asper*) and common lancehead (*Bothrops atrox*) are responsible for many cases of severe envenoming in Central and South America, resulting in death or permanent disability.[177] The larger *B. asper* (exceptionally, up to 2.5 m [8.2 feet] in total length), seems even more inclined than *B. atrox* to strike if cornered, molested, or inadvertently trodden upon or touched. Its habit of raising its head high off the ground can result in bites above knee level. The jararaca (*Bothrops jararaca*) is an important cause of envenoming in southeastern Brazil and in adjacent northeastern Paraguay and northern Argentina. Clinical effects are generally less severe than with *B. asper* and *B. atrox* envenoming, but coagulopathy, bleeding, and local necrosis are common.[201,206,285] The jararacuçu (*Bothrops jararacussu*) is a bulky snake with a high yield of unusually potent venom. It has a formidable reputation for causing severe bleeding, fibrin deposition, local necrosis, shock, and acute kidney injury that often prove fatal.[161]

Crotalus (Figure 36-104; see also Figure 36-16)**.** The two species of Latin American (tropical) rattlesnake, *Crotalus simus* in Central America and *C. durissus* in South America, pose a serious medical problem in many parts of their ranges. Severe systemic envenoming by the tropical rattlesnake (*C. durissus terrificus*) may occur in the absence of local signs. Neurotoxic envenoming develops only in victims of populations of some subspecies of *C. durissus*, such as *C. d. terrificus, C. d. collilineatus*, and *C.d. cascavella.* Typical elapid-type descending paralysis (Figure 36-105A; see also Figure 36-56E) may result in life-threatening respiratory paralysis. Venom myotoxins cause myoglobinemia and myoglobinuria (see Figure 36-57A), which may result in acute kidney injury.[16,17] Other life-threatening clinical effects include coagulopathy and spontaneous systemic hemorrhage,[205,285] hypotension, and shock. Local envenoming, however, is usually trivial, and restricted to pain, mild swelling, and erythema (Figure 36-105B and C). In contrast, envenoming by *C. simus* in Central America produces clinical effects more reminiscent of rattlesnake bites in North America: severe local envenoming with massive swelling, blistering, and necrosis. Systemic envenoming involves hemostatic disorders such as hypofibrinogenemia, but spontaneous systemic bleeding is unusual, acute kidney injury has rarely been reported, and neurotoxicity is controversial.

Lachesis (See Figure 36-36)**.** Bushmasters may reach a length of almost 4 m (13.2 feet) and are the longest venomous snakes in the western hemisphere. Envenoming by all four species may cause local swelling, blistering, bruising, and necrosis with coagulopathy, spontaneous systemic bleeding, shock, and acute kidney injury reminiscent of other pit vipers. However, a distinctive syndrome has been described in a proportion of cases. Within 10 to 15 minutes of the bite, there is nausea, abdominal colic, repeated bilious vomiting, watery diarrhea with profuse sweating, hypersalivation, and other features of autonomic hyperactivity, bradycardia, visual disturbances, profound shock, and syncope. Local effects of envenoming may leave permanent impairment.[113]

FIGURE 36-102 Latin American pit vipers. **A,** Cantil (*Agkistrodon bilineatus*) (Mexico). **B,** Central American jumping viper (*Atropoides mexicanus*) (Guatemala). **C,** Small-eyed toad-headed pit viper (*Bothrocophias microphthalmus*) (Garagoa, Boyaca, Colombia). **D,** Terciopelo (*Bothrops asper*) (Caucasia, Colombia). **E,** Common lancehead (*Bothrops atrox*) (Para, Brazil). **F,** Papagaio (*Bothrops bilineatus smaragdinus/Bothriopsis bilineata smaragdina*) (Napo, Ecuador). **G,** Jararaca (*Bothrops jararaca*). **H,** Jararacuçu (*Bothrops jararacussu*) (Brazil). **I,** Serpent of St Lucia (*Bothrops caribbaeus*). *(Copyright D.A. Warrell.)*

COURSE AND SEQUELAE OF ENVENOMING

RISK OF ENVENOMING: THE "DRY BITE" PHENOMENON

Even when the fangs of a venomous snake have pierced the skin, envenoming is not inevitable. About 20% of patients bitten by *Calloselasma rhodostoma* and *Daboia russelii* show absolutely no evidence of envenoming, and as many as 80% of persons bitten by sea snakes and Australasian eastern brown snakes (*Pseudonaja textilis*) and 50% by *C. rhodostoma* or Russell's vipers have trivial or no envenoming. These are the so-called dry bites.

RISK OF DEATH

Untreated snakebite mortality is difficult to assess, because hospital admissions include a disproportionate number of severe cases, and data for untreated snakebites are available only from the preantivenom era or from occasions when antivenom supply is limited, an antivenom of low potency is used,[294] or when antivenom is withheld by physicians who doubt its efficacy. The mortality rate of *Echis ocellatus* bites has been reduced from about 20% to 3% with antivenom.[294,296] In Brazil, untreated and treated case fatalities for *Bothrops* and *Crotalus durissus terrificus* envenoming were estimated as 8% and 0.7%, and 72% and 12%, respectively.[201] In Australia, case fatality before development of antivenom was 50% for *Acanthophis*, 45% for *Notechis*, and 19% for *Pseudonaja*.[247] Prognosis appears to be the worst in infants and older adults, but there is no convincing evidence that older children have a worse prognosis than young adults, despite the larger dose of venom they may receive relative to their body weight.

INTERVAL BETWEEN BITE AND DEATH

Death after snakebite may occur as rapidly as within a few minutes (reputedly after a bite by the king cobra, *O. hannah*) or as long as 41 days after a bite by the saw-scaled or carpet viper (*E. carinatus*). However, the speed of killing has been exaggerated. Most elapid deaths occur within hours of the bite, most sea-snake bite deaths between 12 and 24 hours, and viper bite deaths within days.

RATE OF EVOLUTION AND RECOVERY OF ENVENOMING

Local swelling is usually evident within 2 to 4 hours of bites by vipers and cytotoxic cobras. Swelling is maximal and most extensive on the second or third day after the bite. Resolution of swelling and restoration of normal function in the bitten limb may be delayed for months, especially in older people (e.g., after bites by the European adder *V. berus*). The earliest systemic symptoms, such as vomiting and syncope, may develop within minutes of the bite, but even in the case of rapidly absorbed elapid venoms, patients rarely die less than 1 hour after the bite. Defibrination may be complete within 1 to 2 hours of the bite (e.g., saw-scaled or carpet viper *E. ocellatus*).[271,296] Neurotoxic signs may progress to generalized flaccid paralysis and

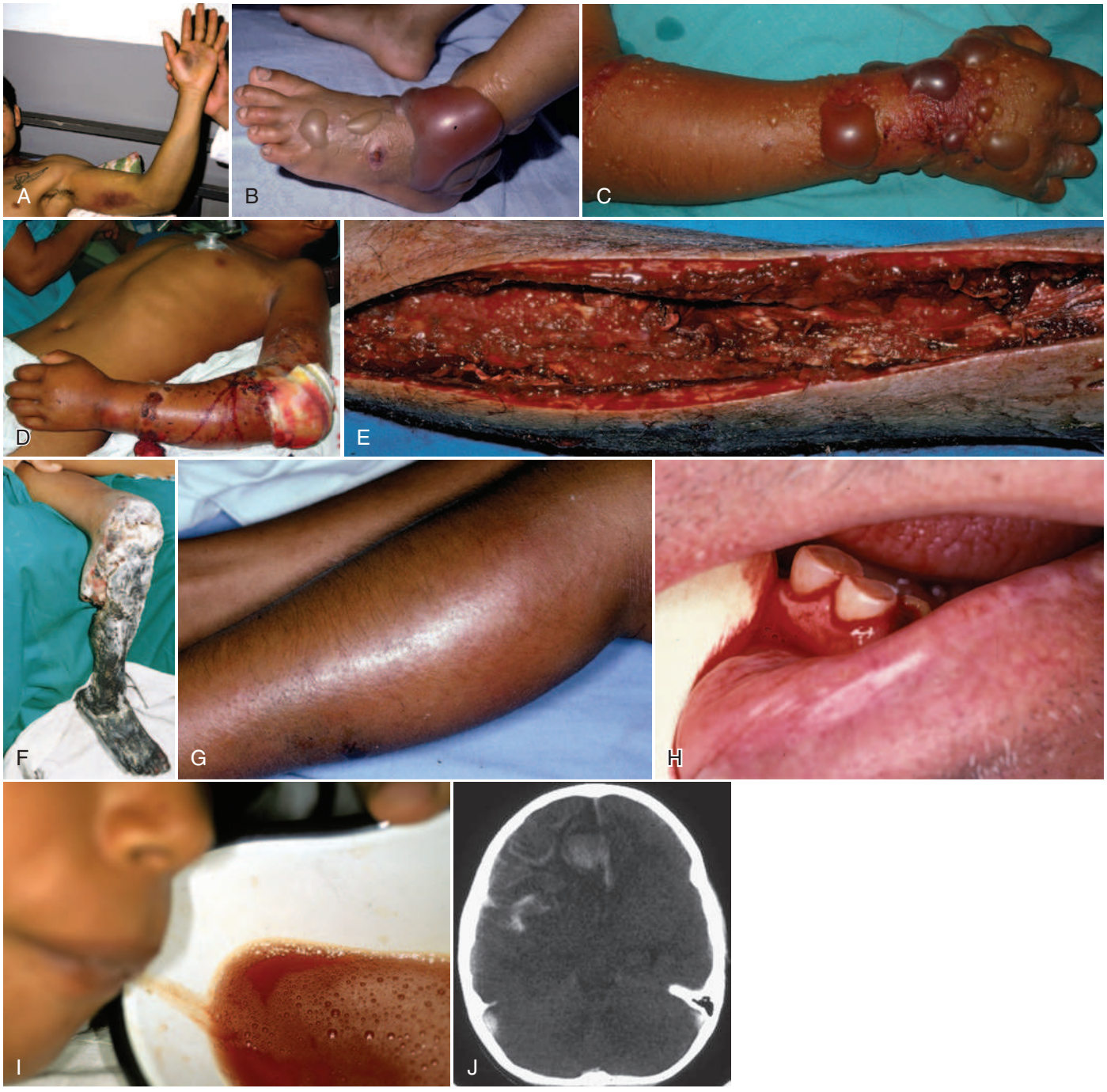


FIGURE 36-103 Envenoming by South American lanceheads (genus *Bothrops*). **A,** Swelling and bruising after bite on hand by papagaio (*B. bilineatus smaragdinus*) (Largo Agrio, Ecuador). **B,** Local blistering after bite by jararaca (*B. jararaca*) (São Paulo, Brazil). **C,** Severe blistering after bite by common lancehead (*B. atrox*) (Pucallpa, Peru). **D,** Blistering and necrosis after bite by *B. atrox* (Pucallpa, Peru). **E,** Liquefaction-necrosis of anterior tibial compartment after bite by *B. marajoensis* (Marajo, Brazil). **F,** Gangrene after bite by terciopelo (*B. asper*) (Pedro Vicente Maldonado, Ecuador). **G,** Abscess developing 5 days after bite by *B. atrox* (Pastaza, Ecuador). **H,** Bleeding gums after bite by *B. jararaca* (São Paulo, Brazil). **I,** Spitting out blood in sputum after *B. atrox* bite (Pastaza, Ecuador). **J,** Cerebral hemorrhage after bite by *B. atrox* (Pastaza, Ecuador). *(**A** to **E** and **G** to **J** copyright D.A. Warrell; **F** courtesy David Gaus.)*

respiratory arrest within a few hours. If the venom is not neutralized by antivenom, these effects may be prolonged. Defibrination can persist for weeks (*Echis* spp. and *C. rhodostoma*).[198,271,296] Patients with neurotoxic envenoming have recovered after being artificially ventilated for up to 10 weeks. Tissue necrosis usually manifests within 1 week of the bite. Sloughing of necrotic tissue and secondary infections, including osteomyelitis, may occur during subsequent weeks or months.

Deaths occurring from neurotoxic envenoming are caused by airway obstruction or respiratory paralysis, whereas later deaths may result from technical complications of mechanical ventilation or intractable hypotension. Late deaths, more than 5 days after the bite, are usually the result of acute kidney injury. Delayed shock with recurrent spontaneous hemorrhage has been described in victims of Burmese Russell's viper; pituitary and other intracranial hemorrhages have been found at autopsy.

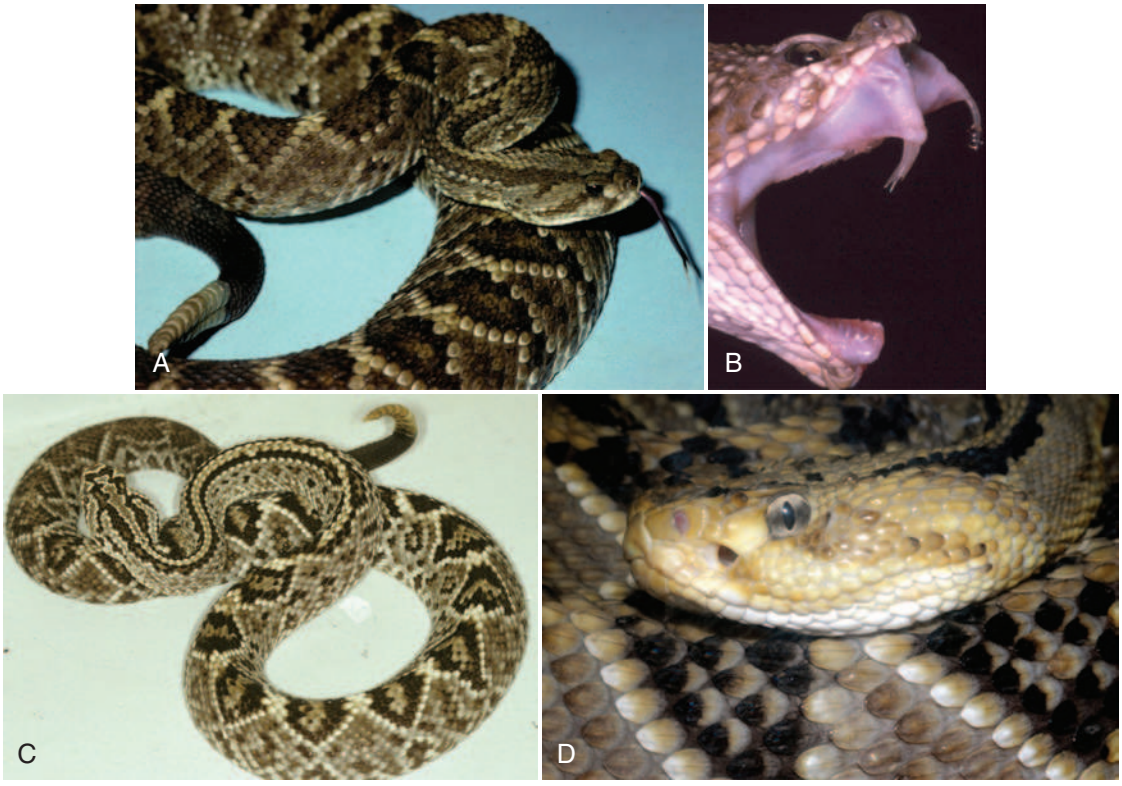


FIGURE 36-104 Latin American rattlesnakes (genus *Crotalus*). Tropical rattlesnakes (Brazil). **A,** *C. durissus cascavella.* **B,** *C. durissus collilineatus.* **C,** *C. durissus ruruima.* **D,** Central American rattlesnake (*C. simus*) (Guerrero, Mexico). *(Copyright D.A. Warrell.)*

CHRONIC SEQUELAE OF SNAKEBITE

Tissue loss, amputations, contractures, arthrodeses, hypertrophic and keloid scars, tendon damage, and complications of surgery are the most common causes of persistent morbidity in survivors of snakebite (Figure 36-106A). Chronic ulcers, pyogenic arthritis, and osteomyelitis are described. Malignant transformation (Marjolin's ulcer) has been seen in patients with chronic ulceration after bites by *N. nigricollis*[298] and *C. rhodostoma*[100,301] (Figure 36-106B). Chronic renal failure (bilateral cortical necrosis) and panhypopituitarism (from Sheehan's-like syndrome) are reported

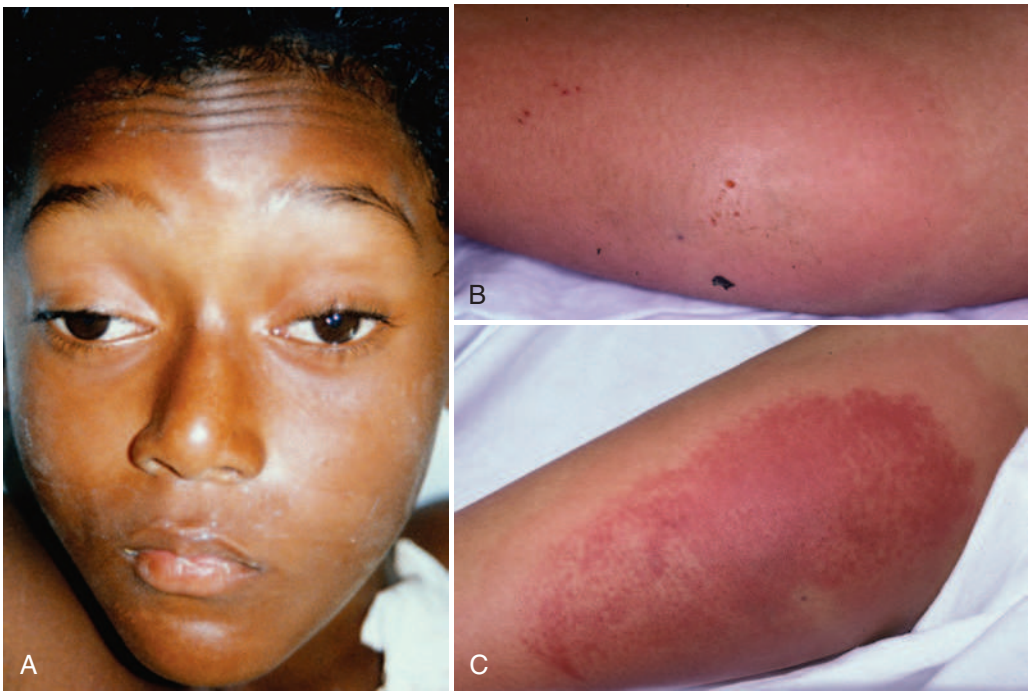


FIGURE 36-105 Envenoming by tropical rattlesnakes (*Crotalus durissus*) in Brazil. **A,** Neurotoxicity (*C. durissus marajoensis*) (Marajo, Brazil). **B** and **C,** Evolution of local swelling and demarcated erythema after bite by *C. durissus terrificus* (São Paulo, Brazil). *(**A** courtesy Pedro Pardal; **B** and **C** copyright D.A. Warrell.)*

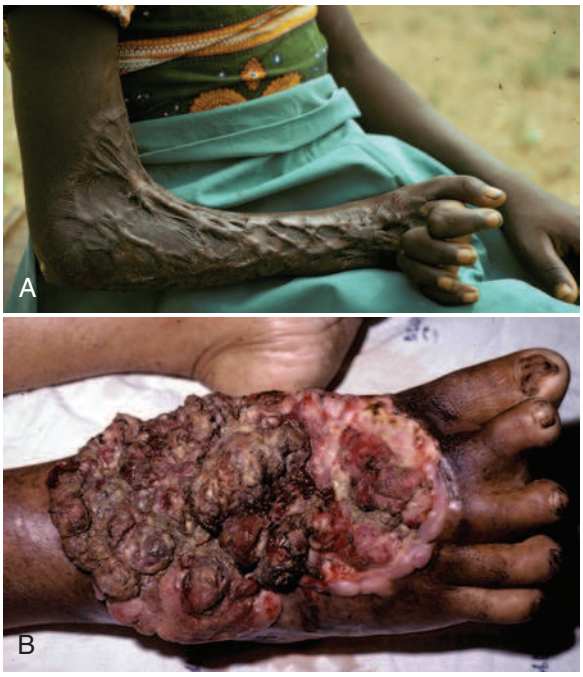


FIGURE 36-106 Permanent sequelae of snakebite. **A,** Hypertrophic scar with contractures and arthrodeses at site of spitting cobra bite (*Naja nigricollis*, Nigeria). **B,** Marjolin's ulcer: malignant transformation to squamous cell carcinoma at site of chronic osteomyelitis following bite by *Calloselasma rhodostoma* in Thailand. *(Copyright D.A. Warrell.)*

complications of Russell's viper bites.[7,261,273] An unknown number of patients who develop acute bilateral renal cortical necrosis after viper bite envenoming, even by small species such as *Hypnale hypnale*, may be left with chronic renal failure.[13] Cerebral hemorrhage complicating viperid, colubrid, and Australasian elapid bites may result in chronic neurologic deficits, and survivors of severe presynaptic neurotoxicity (e.g., from krait and Australasian elapid envenoming) may be susceptible to a late poliomyelitis-like syndrome. Apart from these purely objective abnormalities, snakebite victims may complain of chronic or recurrent symptoms in the bitten limb and attribute a wide variety of physical and mental problems to that unforgettable, dramatic, and traumatic event of their snakebite.

LABORATORY INVESTIGATIONS

HEMATOLOGY

Systemic envenoming is usually associated with a neutrophil leukocytosis: counts above 20×10^9/L indicate severe envenoming. Initially, hematocrit may be high from hemoconcentration when there is generalized increase in capillary permeability (e.g., Burmese *D. siamensis*). Later, hematocrit falls because of bleeding into the bitten limb and elsewhere, and from intravascular hemolysis or microangiopathic hemolysis in patients with DIC. Thrombocytopenia is common (e.g., *D. russelii, C. rhodostoma, B. arietans*).

Twenty-Minute Whole-Blood Clotting Test[204,297]

Incoagulable blood is a cardinal sign of systemic envenoming by most of the Viperidae, many of the Australasian elapids, and the medically important Colubridae. For clinical purposes, a simple bedside test of blood coagulability is all that is currently available in most parts of the world where snakebites are common. The 20-minute whole-blood clotting test (not "time") (20WBCT) is a simple indication of blood coagulability that has been used in developing countries for at least 50 years. Two milliliters of venous blood taken by venipuncture is placed in a new, clean, dry, glass vessel; left undisturbed at room temperature for 20 minutes; then tipped once to see if there is clotting (Figure 36-107).

A recent critique of the method[109] has stimulated reconsideration of the strengths and weaknesses of the 20WBCT. The 20WBCT is certainly less sensitive to milder degrees of coagulopathy than many of the tests widely available in laboratories in Western hospitals, such as prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen and other clotting factor assays, and D-dimer, but whether this matters in practical clinical decision making has not been proved.[184] The main technical problem is the type and condition of glass vessels used. Activation of Hageman factor (factor XII) at the blood-glass interface is crucial. If this is lacking because the vessel is made of plastic or some other inactive material, or if the glass vessel has been cleaned with detergent, soap, or washing liquid, the blood will not clot within 20 minutes, and the result of the test will be falsely positive.

A recent study in Papua New Guinea demonstrated that in soda-lime glass vessels at ambient temperatures of 24°, 28°, 32°, and 36° C (75.2°, 82.4°, 89.6°, and 96.8° F),whole blood from 30 volunteers with normal hemostasis (mean INR, 1.0; range, 0.9 to 1.2) clotted within 20 minutes, whereas borosilicate glass and BD Vacutainer glass tubes were unreliable at some temperatures.[178] In patients envenomed by taipans (*Oxyuranus scutellatus*), PT and aPTT were significantly higher (p <0.001) and fibrinogen levels significantly lower (p <0.001) in 29 patients with positive (nonclotting) 20WBCT compared to 31 patients with a negative (clotting) 20WBCT. In clinical practice, a positive 20WBCT protocol was associated with median PT of 120.0 seconds (IQR = 24.4 to 200 sec), median aPTT of 132 seconds (IQR = 69.1 to 180 sec), and median fibrinogen concentration of 0.01 g/L (IQR = 0.01 to 0.18 g/L). A positive 20WBCT had a positive predictive value (PPV) of 89.7%, negative predictive value (NPV) of 93.5%, sensitivity of 92.9%, and specificity of 90.6% for fibrinogen concentrations of less than 0.5 g/L.[178]

Variants of the 20WBCT have been developed in some countries because of difficulty in obtaining suitable new glass vessels. These include glass syringe tests that involve tipping every 30 seconds (e.g. the "2-3-5 test" in Myanmar) and a capillary tube clotting test. None has been validated.

OTHER TESTS OF HEMOSTASIS

More sensitive laboratory tests that are rapid and relatively simple to perform are whole-blood or plasma PTs and detection of

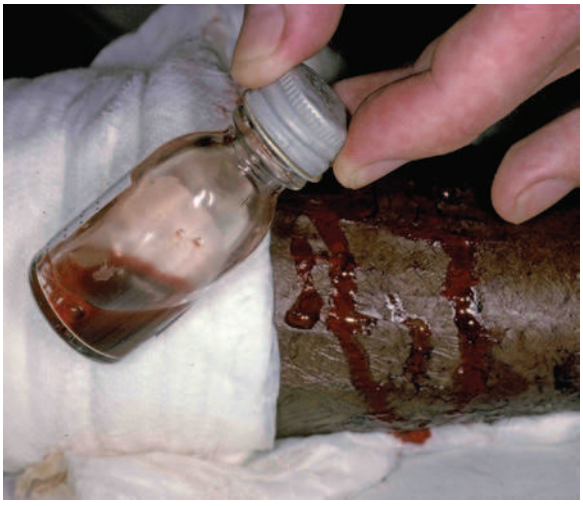


FIGURE 36-107 Twenty-minute whole-blood clotting test. Blood taken by venipuncture from a patient bitten by Papuan taipan (*Oxyuranus scutellatus*), placed in a new, clean, dry glass tube and left for 20 minutes undisturbed has failed to clot, indicating consumption coagulopathy or presence of venom anticoagulants. *(Copyright D.A. Warrell.)*

elevated concentration of FDPs by agglutination of sensitized latex particles, or of D-dimer (cross-linked fibrin fragments) by assays using monoclonal antibodies that detect an epitope that is present in the factor XIIIa–cross-linked fragment D domain of fibrin. Thromboelastography has been suggested as a simple bedside method for assessing coagulopathy in snakebite victims.[5]

Serum concentrations of creatine kinase, aspartate aminotransferase, and blood urea are frequently elevated in patients with severe envenoming because of local muscle damage at the site of the bite.

Evidence of Muscle Damage

Generalized rhabdomyolysis caused by sea snake, Australasian elapid, tropical rattlesnake, and Sri Lankan Russell's viper bites causes a steep rise in serum creatine kinase and other muscle-derived enzymes, myoglobin, and potassium concentrations. Plasma is stained brownish by myoglobin and pink by hemoglobin. Heparinized blood should be allowed to sediment spontaneously (without centrifugation) to reveal these pigments.

Evidence of Intravascular Hemolysis

Patients with intravascular hemolysis have black urine (as in malarial "blackwater fever"). It is brownish, pinkish, or reddish in patients with hematuria or myoglobinuria. Blood films should be examined for evidence of microangiopathic hemolysis.

EVIDENCE OF RENAL DYSFUNCTION AND ACID-BASE IMBALANCE

Blood urea nitrogen, or serum creatinine, and potassium concentrations should be measured in patients who become oliguric, especially in cases with a high risk for renal failure (e.g., *D. russelii*, terrestrial Australasian snakes, sea snakes, Colubridae). All snake-bitten patients should be encouraged to empty their bladder on admission. Urine should be examined for blood/hemoglobin and protein (by dipstick test) and for microscopic hematuria and red cell casts. Severely sick and hypotensive patients will develop lactic acidosis (suggested by increased anion gap). Those with renal failure will also develop metabolic acidosis (decreased plasma pH and bicarbonate concentration, reduced arterial P_{CO_2}), and patients with respiratory paralysis will develop respiratory acidosis (low pH, high arterial P_{CO_2}, decreased P_{O_2}), or respiratory alkalosis if they are mechanically overventilated.

ELECTROCARDIOGRAPHIC ABNORMALITIES[134,135,196,271,283,286,296]

The ECG abnormalities include sinus bradycardia, ST-T wave changes, varying degrees of atrioventricular block, and evidence of hyperkalemia (see Figures 36-53B and C and 36-54D). Shock may induce myocardial ischemia or infarction in patients with diseased coronary arteries.

CHEST RADIOGRAPHY

Chest radiography is useful for detecting pulmonary edema (e.g., European *Vipera* and *D. russelii/D. siamensis*), pulmonary hemorrhages and infarcts, pleural effusions, and secondary bronchopneumonia (see Figures 36-87E and 36-97F).

IMAGING

Computed tomography (CT) and magnetic resonance imaging (MRI) are increasingly available in the developing world, where snakebites are most common. Images have revealed hemorrhages and ischemic infarcts in the brain (subarachnoid, subdural, cerebral, cerebellar, brainstem), spinal cord, peritoneum, and elsewhere. Cerebral imaging has shown pituitary shrinkage in cases of chronic panhypopituitarism after Russell's viper bites and also unexplained hemorrhagic and demyelinating leukoencephalopathies. Imaging can show edema and hemorrhage within muscle-containing compartments defined by fascial boundaries, as well as the degree of osteomyelitis and soft tissue changes in chronic snakebite ulcers that have undergone malignant change to squamous cell carcinomas (Marjolin's ulcers).

ULTRASOUND

Ultrasonography is useful for assessing local envenoming.[270] It may reveal deep vein thrombosis and detect pleural or pericardial effusion and bleeding into serous cavities. Echocardiography has proved useful in demonstrating reduced left ventricular ejection fraction as a cause of hypotension in envenomed patients.

IMMUNODIAGNOSIS

Detection of venom antigens in body fluids of snakebite victims using enzyme immunoassays has proved a valuable research tool for confirming the species responsible for envenoming (immunodiagnosis), as a prognostic index of the severity of envenoming, and to assess efficacy of antivenom treatment.* Venom gland mRNA has been detected in stored venom samples using reverse transcription–polymerase chain reaction (RT-PCR).[40] Of the various techniques used, enzyme immunoassay has proved the most rapid, sensitive, and specific. However, commercial venom detection kits for clinical diagnosis are available only in Australia (Venom Detection Kit).[232] They are highly sensitive, but specificity may be inadequate to distinguish between envenoming by different species in the same genus or in closely related genera.[232,256] Envenomed patients develop persisting levels of antibodies to venom antigens, including individual toxins,[215] detectable by enzyme immunoassay, but they have proved insufficiently specific to allow reliable retrospective diagnosis.[100,267]

MANAGEMENT OF SNAKEBITE[34,138,157,232,253,284,293,316]

FIRST-AID TREATMENT[42,274,275,287,293]

Principles of First Aid

- Reassure the victim, who is often terrified.
- Do not tamper with the bite wound in any way, but immobilize the bitten limb using a splint or sling. If the patient is thought to have been bitten by a dangerously neurotoxic elapid snake (including sea snakes), consider a pressure-immobilization method (see next section).
- Take the patient as quickly as possible to the nearest medical care facility. The entire patient should be immobilized, especially the bitten limb, because any muscle contractions will promote spread of venom. Ideally, the patient should be transported by motor vehicle, bicycle (as a passenger), boat, or litter.
- Avoid harmful and time-wasting treatments (see later section).
- Because species diagnosis is critically important, the snake should be taken along to the hospital if it has already been killed. However, if the snake is still at large, do not risk further bites and waste time by searching for it. Even snakes that appear to be dead should not be touched with bare hands, but carried in a bag or dangling across a stick. Some species (e.g., *Hemachatus haemachatus*) sham death, and even a severed head can inject venom. An image of the dead snake may be taken and sent by mobile phone to a local or national snake expert or Poisons Information Centre for expert identification.

Pressure-Immobilization Methods

Anker's (Monash) Pressure-Pad Method (Figure 36-108A)**.** This simple method of local compression was developed by Anker and colleagues,[6] and tested in Burmese Russell's viper bite cases by Tun-Pe and colleagues in Myanmar.[259] Application of a foam rubber pad directly over the bite wound, at a pressure of about 70 mm Hg, delayed systemic envenoming, as assessed by measurements of venom antigenemia, and the method appeared safe and effective in a preliminary field trial.[259] The pad may be

*References 84, 100, 101, 174, 219, 240, 241, 263.

made of any available material, such as a folded bandage or piece of material approximately 5 × 5 × 3 cm.

Sutherland's Pressure-Immobilization Bandage Method (Figure 36-108B)**.** The splinting and pressure-immobilization (P-I) bandaging method developed and advocated by the late Struan Sutherland in Australia proved effective in limiting absorption of Australian elapid toxins in restrained monkeys.[251] A series of long, 10-cm-wide (4-inch-wide) elastic bandages are wrapped firmly ("as firmly as for a sprained ankle") around the bitten limb, starting distal to the bite site and continued up to the groin or axilla. Although never subjected to formal clinical trials, the method has proved successful and safe, as judged by anecdotal reports of delayed systemic envenoming and rapid deterioration after release of the bandage, in some cases supported by measurements of venom antigenemia. However, there have been practical difficulties in implementing this discovery, and even in Australia, only 18% to 53% of the bandages in place when patients arrived in the hospital had been correctly and effectively applied. Some experienced physicians still regard the method as having unproven benefit.[42] Bandaging aims to exert a pressure of about 55 mm Hg (1.06 psi), that of a venous tourniquet. In practice, it is difficult to judge how tightly the bandage should be applied and difficult for the patient to put it on unaided,[287] explaining why so many are incorrectly applied.[42]

A recent study found that Sutherland's P-I technique was difficult to teach and that elasticized bandages were superior to traditional crepe bandages.[293] External compression increases intracompartmental pressure and may accentuate the effects of some necrotic snake venoms, but animal studies found little evidence that this was deleterious and reinforced the lifesaving effects of lymphatic/venous compression.[29,80,156,] If a patient is bitten by a dangerously neurotoxic elapid (e.g., mamba, king cobra, taipan) or sea snake, respiratory paralysis might develop en route to the hospital. In these patients, it is recommended that an elastic bandage and splint be applied firmly, but not so tightly as to obliterate the peripheral arterial pulse.

In a porcine model, survival after challenge with Eastern coral snake (*Micrurus fulvius*) venom measured at 8 hours and 21 days was prolonged by long-term application of P-I bandages.[80,223] In human volunteers, lymphoscintigraphy studies in simulated envenoming showed that excessive pressure (>70 mm Hg [1.35 psi]) and movement of the other limbs increased lymphatic flow.[103] The patient should lie down and remain as immobile as possible during the journey to the hospital.

Transcutaneous Glyceryl Trinitrate

A study of lymphatic flow in human volunteers and in rats showed that nitric oxide (NO)–donating drugs, such as glyceryl trinitrate (GTN), applied topically to the bitten limb, slowed lymphatic flow substantially, presumably by inhibiting the intrinsic lymphatic pump, despite movement of the limb. In rats challenged with Eastern brown snake venom, death was delayed. It is suggested that topical application of NO-donating drugs might prove to be a useful adjunct to pressure-pad or P-I first-aid methods.[207]

A

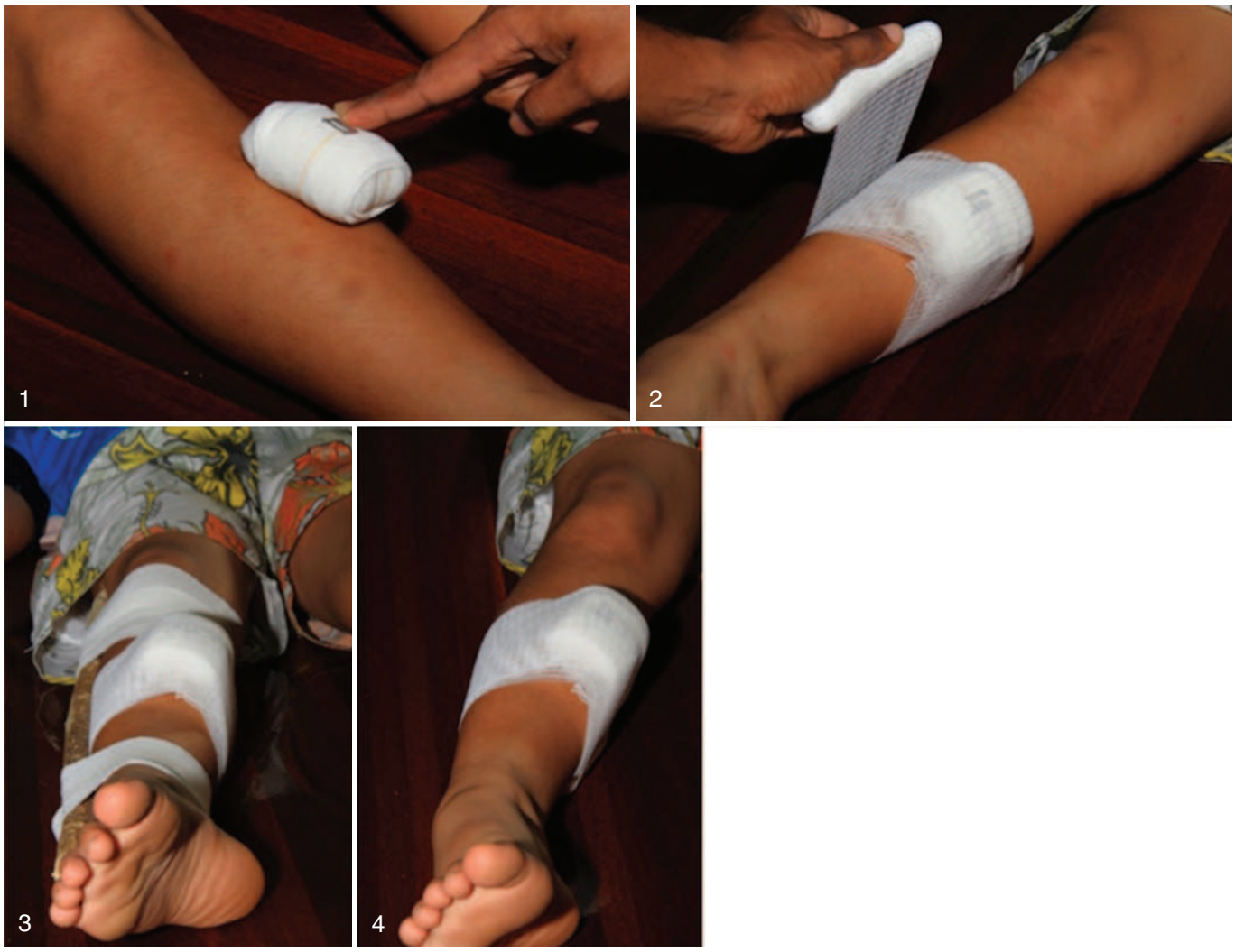
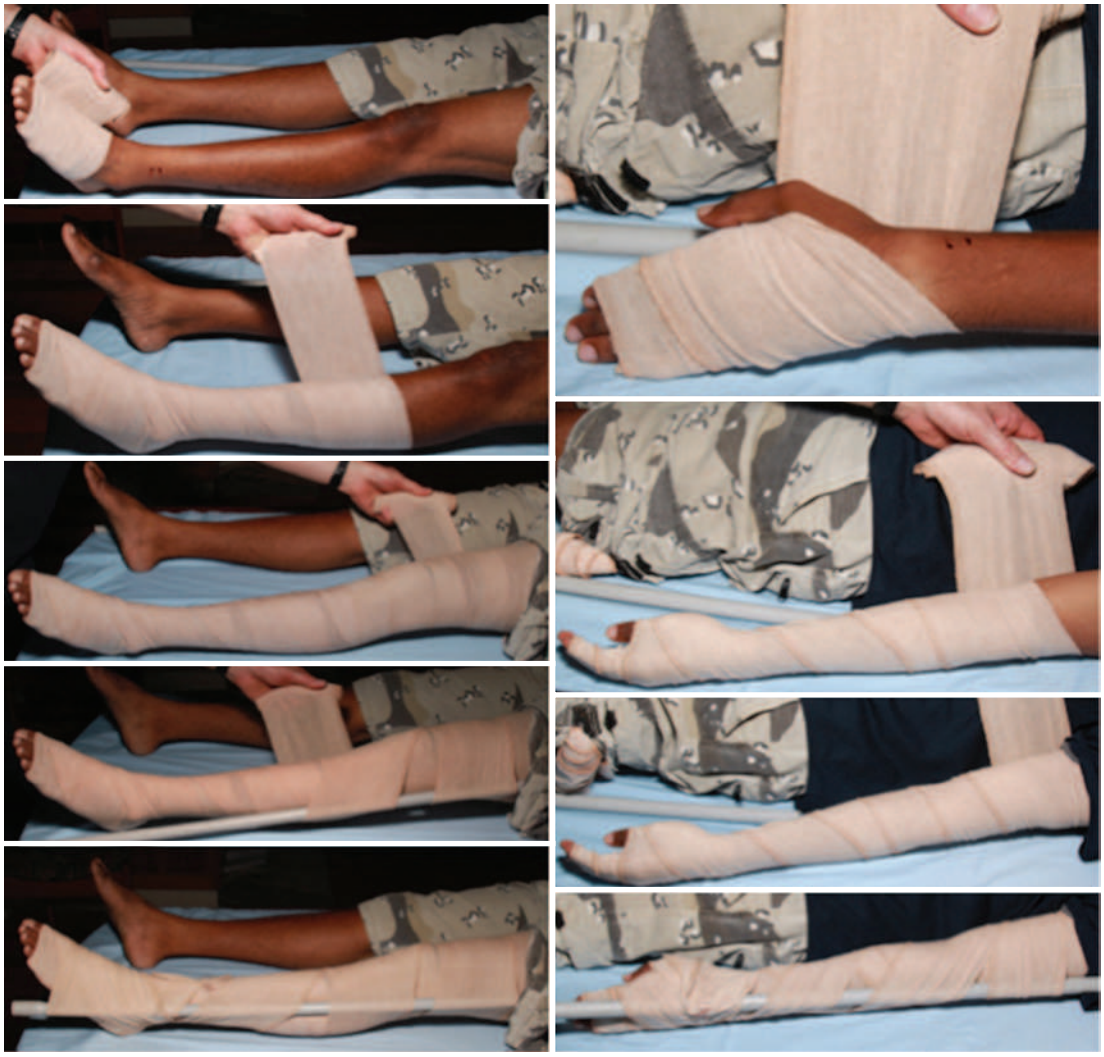


FIGURE 36-108 Pressure-immobilization first-aid methods. **A,** Anker's pressure-pad method. *Continued*



B

FIGURE 36-108, cont'd **B,** Sutherland's pressure-bandage method. *(Courtesy Dr David J Williams)*

Rejected or Controversial First-Aid Methods[275,286]

Traditional snakebite treatments are widely preferred by inhabitants of rural parts of the developing world.[171] However, even in the West, tourniquets, constriction bands, wound cauterization, incision or excision, amputation of the bitten digit, suction by mouth, vacuum pumps[30] or "venom-ex" apparatus, instillation of chemical compounds (e.g., potassium permanganate), application of ice packs (cryotherapy), "snake stones," electric shocks, and many other outlandish first-aid treatments have been advocated. These are absolutely contraindicated in that they are harmful and have no proven benefit.[91,275]

Incisions can provoke uncontrolled bleeding when the blood is incoagulable; may damage nerves, blood vessels, or tendons; and may introduce infection.[21] Suction, chemicals, and cryotherapy can cause tissue necrosis. Snake stones do not remove venom from the wound and usually require an incision to make them adhere. This can result in persistent bleeding and infection.

Dangers of Tight Tourniquets

Tight (arterial) tourniquets have been responsible for serious morbidity and even mortality in snakebite victims and should never be advocated or used. Dangers of tourniquets include ischemia and gangrene if they are applied for more than about 2 hours, damage to peripheral nerves (especially the lateral popliteal [common peroneal] nerve when a tourniquet presses against neck of fibula), increased fibrinolytic activity, congestion, swelling, increased bleeding, increased local effects of venom, and shock, rapid development of life-threatening systemic envenoming, or even pulmonary embolism after their release (see later text).[274,275]

TREATMENT BEFORE PATIENT REACHES THE HOSPITAL

Early Symptoms

Distressing and dangerous manifestations of envenoming may appear before the patient reaches the hospital.

Local Pain. This may be intense. Oral acetaminophen is preferable to aspirin or nonsteroidal antiinflammatory drugs (NSAIDs), which carry the risk of gastric bleeding in patients with incoagulable blood. Severe pain should be treated with opiates.

Vomiting. This is a common early symptom of systemic envenoming. Patients should be laid in the recovery position (on their left side) with the head down to avoid aspiration. Persistent vomiting can be treated with intravenous (IV) promethazine (12.5 to 25 mg in adults, 0.1 to 0.25 mg/kg in children older than 2 years).

Syncopal Attacks and Anaphylactic Shock. Patients who collapse within minutes of the bite may show features of either a vasovagal attack with profound bradycardia or of anaphylaxis with angioedema, urticaria, asthma, abdominal colic, and diarrhea. Anaphylaxis should be treated with aqueous epinephrine 0.1% (1:1000) (0.3 to 0.5 mL in adults, 0.01 mL/kg in children) by intramuscular (IM) injection, followed by a histamine H_1-blocker such as chlorphenamine maleate (10 mg in adults,

0.2 mg/kg in children) given by IV or IM injection. In patients with incoagulable blood, injections can cause hematomas. Pressure dressings should be applied to all injection sites to prevent oozing.

Respiratory Distress. This may result from upper airway obstruction, if the jaw, tongue, and bulbar muscles are paralyzed, or from paralysis of the respiratory muscles. Patients should be placed in the recovery position, the airway cleared if possible using a suction pump, an oral airway inserted, and the jaw elevated. If the patient is cyanotic or respiratory movements are weak, oxygen should be given by any available means. If clearing the airway does not produce immediate relief, artificial ventilation must be initiated. In the absence of any equipment, mouth-to-mouth or mouth-to-nose ventilation can be lifesaving. Manual ventilation by bag-valve-mask device is rarely effective for a prolonged period. Ideally, a cuffed endotracheal tube should be introduced using a laryngoscope, a tracheal mask airway, or i-gel supraglottic airway (http://www.i-gel.com/), or a cuffed tracheostomy tube should be inserted. The patient can then be ventilated by bag. If no femoral or carotid pulse can be felt, external cardiac massage should be instituted.

Examination of Pregnant Women

Potential complications of envenoming in pregnancy include antepartum and postpartum hemorrhage indicated by vaginal bleeding, premature labor, abortion/stillbirth, and fetal distress.[89,90] If possible, uterine contractions and fetal heart rate should be monitored continuously. Fetal distress may be signaled by fetal bradycardia, tachycardia, or late deceleration after each uterine contraction. If there is vaginal bleeding or the need for imminent surgery, correction of antihemostatic abnormalities after antivenom treatment should be accelerated using blood products. Lactating women should be encouraged to continue breastfeeding.

MEDICAL TREATMENT IN THE HOSPITAL

Snakebite is a medical emergency. The history, symptoms, and signs must be assessed rapidly to direct urgent appropriate treatment. Patients may arrive at the hospital soon, or in some cases many days, after being bitten. They may therefore show early or late signs of envenoming or its complications. It is essential that all patients with a history of snakebite be assessed rapidly; they may be moribund but still salvageable by appropriate resuscitation. Cardiopulmonary resuscitation may be needed, including clearance of the airway, oxygen administration by face mask or nasal catheter, and establishment of IV access to allow treatment with drugs and IV fluids. Airway, respiratory movements (breathing), and arterial pulse (circulation) must be checked immediately. Vital signs must be recorded: blood pressure, pulse rate, and respiratory rate.

Need for Rapid Assessment and Resuscitation

Patients with severe envenoming may present with the following problems requiring urgent intervention:

- Profound hypotension and shock, resulting from:
  - Direct cardiovascular effects of the venom (e.g., *V. berus*, *D. russelii*, *D. siamensis*, *B. arietans*, *O. scutellatus*)
  - Hypovolemia secondary to blood loss, persistent vomiting, or other causes of dehydration
  - Autopharmacologic effects of the venom (activation/inhibition of physiologic vasomotor systems, such as angiotensin-renin-bradykinin systems, by venom toxins)
  - Rarely, anaphylaxis provoked by antivenom given outside the hospital and, even more rarely, provoked by venom in habitual snake handlers who have been sensitized by previous exposure
- Sudden deterioration after release of a tourniquet or compression bandage, resulting in shock, bleeding, or respiratory paralysis.[310,321,322] These bands, bandages, bindings, tourniquets, or ligatures are often removed too hastily by hospital staff before antivenom treatment has been initiated and before appropriate staff and equipment are on hand in the event that resuscitation is needed.
- Airway obstruction, resulting from aspirated vomitus, foreign body, or tongue blocking the upper airway, especially in patients with evolving bulbar paralysis who have not been transported to hospital in the left lateral (recovery) position. Vomiting can be the result of systemic envenoming or ingestion of emetic herbal remedies.
- Terminal respiratory failure from progressive neurotoxic envenoming that has led to paralysis of respiratory muscles
- (Hours after the bite) Cardiac arrest resulting from hyperkalemia in patients with massive generalized skeletal muscle breakdown (rhabdomyolysis) after sea-snake bites
- (Days after the bite) Acute kidney injury
- (Days after the bite) Septicemia complicating aspiration pneumonia (see earlier text) or infection of incisions made at the site of the bite

Clinical Assessment

Four important preliminary questions for the snakebite victim are as follows:

1. In which part of your body have you been bitten?
2. When and under what circumstances were you bitten?
3. Where is the snake that bit you? Did you bring it, and if not, what did it look like?
4. How are you feeling now?

If the snake has been killed but not brought, someone should be dispatched to collect it. Alternatively, a high-quality digital photograph(s) may be obtained. Only if the snake can be identified confidently as nonvenomous can the bitten patient be discharged after a booster dose of tetanus toxoid. Patients should be asked whether they have taken any drugs or alcohol; whether they have vomited, fainted, or noticed any bleeding or other ill effects of the bite; and whether they have passed urine since being bitten. Physical signs should be assessed before any compression bandage or tourniquet is removed. Fang marks are sometimes invisible and rarely help the diagnosis, although the discovery of only two or three discrete puncture marks suggests a bite by a venomous snake. Local swelling, tenderness, and lymph node involvement are early signs of envenoming. The gingival sulci are usually the earliest site of detectable spontaneous bleeding (see Figures 36-55A, 36-76C and D, 36-89C, 36-100D, and 36-103H). Bleeding from venipuncture sites, recent wounds, and skin lesions suggests incoagulable blood.

If the patient is in shock (collapsed, sweating, cool cyanotic extremities, low blood pressure, tachycardia), the foot of the bed should be raised and an IV infusion of isotonic saline started immediately. The central venous pressure should be observed. The earliest symptoms of neurotoxicity after elapid bites are often blurred vision, feeling of heaviness in the eyelids, and drowsiness. The earliest sign is contraction of the frontalis muscle (raised eyebrows and puckered forehead), even before true ptosis can be demonstrated. Signs of respiratory muscle paralysis (dyspnea, "paradoxical" abdominal respiration, and cyanosis) are ominous. Patients with generalized rhabdomyolysis may have trismus and muscles that are stiff, tender, and resistant to passive stretch. Urine output may dwindle very early in the course of Russell's viper bite. Dark urine suggests myoglobinuria or hemoglobinuria.

If there is initially no evidence of envenoming, the patient should be admitted for observation, ideally for 24 hours.[92] Every hour, symptoms, level of consciousness, degree of ptosis, pulse rate and rhythm, blood pressure, respiratory rate, extent of local swelling, and other new signs should be recorded. If there is any evidence of neurotoxicity, ventilatory capacity should be recorded every hour. Useful investigations include the 20WBCT (or other tests of coagulation), peripheral leukocyte count, hematocrit, urine microscopy and dipstick testing, and electrocardiography.

If a tourniquet or tight compression bandage is in place, it may create distal edema through venous congestion even in the absence of envenoming and, if applied tightly enough to prevent arterial perfusion, might cause a cold, pulseless, and cyanotic extremity. Blockage of venous drainage from a limb in the presence of a powerfully procoagulant venom that has been injected by the snake may promote deep vein thrombosis and subsequent pulmonary embolism when the tourniquet is released. Ideally,

such occlusive devices should not be released until IV access has been established and antivenom, plasma expanders, and adequate medical staff are available to cope with the dramatic deterioration that may follow.

Early Clues That a Patient May Be Severely Envenomed

- The snake is identified as a dangerously venomous species and was perhaps a large specimen.
- There are multiple fang punctures, suggesting repeated strikes.
- Rapid early spread of local swelling from the site of the bite is seen.
- Enlarged, painful, and tender lymph nodes draining the site of the bite indicate early spread of larger-molecular-weight venom components into the lymphatic system.
- Early symptoms of systemic envenoming include collapse (hypotension, shock); nausea, vomiting, and diarrhea; severe headache; heaviness of the eyelids; pathologic drowsiness; or early ptosis/ophthalmoplegia.
- Early spontaneous systemic bleeding occurs, for example, from the gums or nose, or in vomitus, feces, or urine.
- Urine is dark brown or black.

ANTIVENOM

Antivenom (Antivenene, Antisnake venom [ASV], Antisnakebite Serum) is the concentrated whole gamma immunoglobulin (IgG) or enzyme-refined gamma IgG fragments (F[ab′]$_2$ or Fab) of horses or sheep, which have been immunized with venom.[85,176,244,320,323] It is the only specific treatment available and has proved effective against many of the lethal and damaging effects of venoms. In the management of snakebite, the most important clinical decision is whether or not to give antivenom, because only a minority of snake-bitten patients need it, it may produce severe reactions, and it is expensive and often in short supply.

Clinical testing of effectiveness and safety of antivenoms in human patients has been generally neglected in favor of inadequate testing in animals, usually mice. Recently, attempts have been made to encourage routine preclinical and Phase I (equivalent) and Phase II/III clinical trials.[1,2,5,222,244,323]

Indications for Antivenom

Systemic Envenoming

- Hemostatic abnormalities: spontaneous systemic bleeding, incoagulable blood or prolonged clotting time, severe thrombocytopenia
- Cardiovascular abnormalities: hypotension, shock, abnormal ECG, cardiac arrhythmia
- Neurotoxicity
- Generalized rhabdomyolysis
- In patients with definite signs of local envenoming, the following indicate significant systemic envenoming: neutrophil leukocytosis, elevated serum enzymes such as creatine kinase and aminotransferases, hemoconcentration, uremia, increased serum creatinine, oliguria, hypoxemia, acidosis, and vomiting in the absence of a history of ingesting emetic agents.

Severe Local Envenoming

- Local swelling that is spreading rapidly or that extends more than halfway up the bitten limb
- Extensive blistering or bruising, especially in patients bitten by species known to cause local necrosis (e.g., Viperidae, Asian cobras, African spitting cobras)
- Bites by these species inflicted on the digits carry a high risk for necrosis and warrant antivenom treatment.
- In Europe, to improve the rate of recovery after bites by *V. berus*, antivenom has been recommended in adults with swelling extending beyond the wrist or ankle within 2 hours of a bite.[196,280,283,286]

Special Indications for Antivenom in Specific Areas

Europe (Adder [Vipera berus] and Other European Vipera). Protherics ViperaTAb or Sanofi-Pasteur Viperfav is indicated to prevent morbidity and reduce the length of convalescence in patients with moderately severe envenoming, as well as to save the lives of severely envenomed patients (see Table 36-4). Indications are as follows[118,280,283,286]:

- Fall in blood pressure with or without signs of shock
- Other signs of systemic envenoming, including spontaneous bleeding, coagulopathy, pulmonary edema or hemorrhage (shown by chest radiograph), ECG abnormalities, peripheral leukocytosis, profound anemia, and elevated serum creatine kinase
- Severe local envenoming—swelling of more than one-half the bitten limb developing within 48 hours of the bite—even in the absence of systemic envenoming
- In adults, early swelling extending within 4 hours of the bite beyond the wrist after bites on the hand or beyond the ankle after bites on the foot

Patients bitten by European *Vipera* who show any evidence of envenoming should be admitted to a hospital for observation for at least 24 hours. Antivenom should be given whenever there is evidence of systemic envenoming (see earlier text), even if its appearance is delayed for several days after the bite.

Contraindications to Antivenom Treatment

There are no absolute contraindications to antivenom in cases of life-threatening envenoming. However, patients with atopic asthma and those who have reacted to equine antiserum on previous occasions have an increased risk for developing severe antivenom reactions. In such patients, antivenom should not be given unless there is evidence of systemic envenoming. If antivenom is given, pretreatment with adrenaline (epinephrine), an antihistamine, and a corticosteroid is recommended. Rapid desensitization is not recommended.

Choice of Antivenom in a Particular Case: Monovalent and Polyvalent Antivenoms

The range of venoms neutralized by an antivenom is usually stated on the package insert and can be found in compendia of antivenoms.[157,316,321,322] If the biting species is known or strongly suspected, the appropriate monovalent (monospecific) antivenom should be used.

Monovalent antivenom is raised against the venom of a single species and is effective for treating envenoming by that species of snake alone, or in some cases for envenoming by a few closely related species. Monovalent antivenoms are generally less expensive than polyvalent antivenoms,[253,256] but this is no longer true for CSL taipan and polyvalent antivenoms. In cases of known taipan envenoming, CSL polyvalent antivenom is preferred. In parts of the world where several species produce identical signs, patients who fail to bring the dead snake (or, in Australia, who cannot be diagnosed by venom detection kits) must be treated with polyvalent (polyspecific) antivenom.

Polyvalent antivenom is raised against the venoms of a selection of the most important species of snakes in a particular geographic region. Polyvalent antivenoms do not necessarily contain lower concentrations of species-specific antibody per unit volume (or total protein content) than do monovalent antivenoms, because immunizing animals with the venoms of two or more related species may produce an augmented antibody response to conserved epitopes.[195] Polyvalent antivenoms do not necessarily carry a higher risk for reactions than monovalent antivenoms. The chosen antivenom must have demonstrated ability to protect against the venom of the species thought to have been responsible. Nonspecific antivenom is generally of no benefit to the patient and may cause reactions (see later text). Some antivenom manufacturers claim a wide range of "paraspecific" neutralization for their products, but mere immunologic cross-reactivity in the laboratory is inadequate grounds for relying on an antivenom to be effective clinically.[181]

Table 36-4 lists some important antivenoms for regions outside the Americas. In some cases, clinical trials have established an average initial dose.

Conservation of Antivenom and Expiration Dates

Liquid antivenoms stored at temperatures below 8° C (46.4° F) usually retain most of their activity for 5 years or more.[320] Freeze-dried (lyophilized) antivenoms are even more stable. Under expedition conditions, liquid antivenoms can be expected to retain their activity even if exposed to environmental

TABLE 36-4 Guide to Initial Dosage of Some Antivenoms for Treating Bites by Medically Important Snakes Outside the Americas

Species		Manufacturer, Antivenom	Approximate Average Initial Dose (reference)
Latin Name	**English Name**		
Acanthophis spp.	Death adder	CSL* Death Adder or Polyvalent Antivenom	1-3 vials[316]
Bitis arietans, Africa	Puff adder	Sanofi-Pasteur ("Fav-Afrique" or "Favirept") polyvalent#; SAVP† polyvalent; ICP§ EchiTAb-plus-ICP	80 mL[304]
Bitis arietans, Middle East	Puff adder	NAVPC‡ Polyvalent Snake Antivenom	80 mL[276,282]
		Vacsera Polyvalent or Anti-Viper Venom Antiserum	80 mL
Bothrops asper	Terciopelo	ICP§ polyvalent, LBS‖ Antivipmyn TRI	5-20 vials[176]
Bothrops atrox	Common lancehead	Butantan, FED¶ Antibotropico polyvalent	2-12 vials[222]
Bothrops bilineatus	Papagaio	Butantan polyvalent	2-4 vials[222]
Bothrops jararaca	Jararaca	Butantan polyvalent	2-12 vials††
Bothrops lanceolatus, B. caribbaeus	Lesser Antillean fer de lance	Sanofi-Pasteur Bothrofav	2-6 vials[246]
Bungarus caeruleus	Common krait	Indian manufacturers** polyvalent	100 mL
Bungarus candidus	Malayan krait	TRC†† Malayan Krait Antivenin monovalent or neuro-polyvalent	50 mL
Bungarus fasciatus	Banded krait	TRC†† Banded Krait Antivenin Monovalent or neuro-polyvalent	50 mL
Bungarus multicinctus	Chinese krait	Shanghai Vaccine & Serum Institute Antivenom of *Bungarus multicinctus*	
		Blyth Taiwan	5 vials
		NIPM Taipei *Naja-Bungarus* antivenin	5 vials
Calloselasma (Agkistrodon) rhodostoma	Malayan pit viper	TRC†† Malayan Pit Viper Antivenin monovalent or haemato-polyvalent	100 mL[301]
Cerastes spp.	Desert (horned) vipers	NAVPC‡ Polyvalent	30-50 mL
		Vacsera Anti-Viper or Polyvalent	30-50 mL
Crotalus durissus	Tropical rattlesnakes	Butantan or FED¶ Anticrotalico or Antibotropico-crotalico	5-20 vials
Crotalus simus	Central American	ICP§ LBS‖ polyvalent	5-15 vials
Cryptelytrops albolabris, C macrops see below *Trimeresurus (Trimeresurus) albolabris etc.*	Green pit vipers	TRC†† Green Pit Viper Antivenin or haemato-polyvalent	100 mL[106]
Daboia (Vipera) palaestinae	Palestine viper	Rogoff Medical Research Institute, Tel Aviv, Palestine viper monovalent	50-80 mL
Daboia (Vipera) russelii, D siamensis	Russell's vipers	Myanmar Pharmaceutical Factory, monovalent	80 mL[168]
		Indian manufacturers** polyvalent	100 mL[9,12]
		TRC†† Russell's Viper Antivenin monovalent or haemato-polyvalent	50 mL
Dendroaspis spp.	East/South African mambas	SAVP† Dendroaspis or Polyvalent Antivenoms	50-100 mL
Dispholidus typus	African boomslang	SAVP† Boomslang Antivenom	1-2 vials
Echis spp., Africa	Saw-scaled or carpet Vipers	SAVP†, Echis, monovalent	20 mL[296]
		Sanofi-Pasteur ("Fav-Afrique")#	100 mL
		MicroPharm Echi-TAb G	1 vial[1,2]
		ICP§ EchiTAb-plus-ICP	3 vials[1,2]
Echis spp., Middle East	– – – – – – – – –	NAVPC‡ Polyvalent Snake Antivenom	50 mL
		Vacsera Polyvalent and Anti-Viper Venom Antiserum	50 mL
Echis carinatus, India	– – – – – – – – –	Indian manufacturers‖ polyvalent	50 mL
Gloydius (Agkistrodon) blomhoffii	Chinese Mamushi	Shanghai Vaccine & Serum Institute Mamushi antivenom	5 vials
Hydrophiinae	Sea snakes	CSL* Sea Snake Antivenom	1-10 vials
Lachesis spp.	Bushmasters	ICP§ polyspecific, FED¶ Antibotropico laquetico, Butantan Antiofidico	10-20 vials
Micropechis ikaheka	New Guinean small-eyed snake	CSL* Polyvalent Antivenom	?2 vials
Micrurus corallinus, M. frontalis	Brazilian coral snakes	Butantan "Antielapidico"	1-5 vials
M. nigrocinctus, M. mipartitus, M. multifasciatus	Central American coral snakes	ICP§ monovalent	1-5 vials
Naja kaouthia	Monocellate Thai cobra	TRC†† Cobra Antivenin monovalent or neuro-polyvalent	100 mL
Naja naja, N. oxiana	Indian cobras	Indian manufacturers** polyvalent	100 mL

Continued

TABLE 36-4 Guide to Initial Dosage of Some Antivenoms for Treating Bites by Medically Important Snakes Outside the Americas—cont'd

Species		Manufacturer, Antivenom	Approximate Average Initial Dose (reference)
Latin Name	**English Name**		
Naja haje, N. anchietae, N. annulifera, N. melanoleuca, cobras, *N. nivea, N. senegalensis*	African neurotoxic	SAVP2 and Sanofi-Pasteur# Polyvalent	100 mL
Naja haje (Middle East)	Egyptian cobra	Vacsera Polyvalent Venom Antiserum	100 mL
Naja haje arabica	Arabian cobra	NAVPC‡ Bivalent Naja/Walterinnesia or Polyvalent Snake Antivenom	100 mL
Naja nigricollis, N. mossambica, etc.	African spitting cobras	SAVP† and Sanofi-Pasteur Polyvalent# ICP§ Echi-TAb G	100 mL[298]
Naja nubiae	Egyptian spitting cobra	Vacsera Polyvalent Venom Antiserum	100 mL
Naja siamensis, N. sumatrana	Indo-Chinese and other SE Asian spitting cobras	TRC†† neuro-polyvalent antivenom	100 mL
Notechis scutatus	Tiger snake	CSL* Tiger Snake or Polyvalent Antivenom	1-3+ vials[316]
Ophiophagus hannah	King cobra	TRC†† King Cobra Antivenin or neuro-polyvalent	100-200 mL
Oxyuranus scutellatus	Australian/Papuan taipans	CSL* Polvalent (or Taipan) Antivenom	1-6+ vials[316]
Pseudonaja species	Australian brown snakes	CSL* Brown Snake or Polyvalent Antivenom	1-6+ vials[316]
Pseudechis spp.	Australian black snakes	CSL* Black Snake Antivenom	1-3 vials[316]
Rhabdophis tigrinus	Japanese yamakagashi	Japanese Snake Institute, Nitta-gun	1-2 vials[98]
R. subminiatus	SE Asian red-necked keelback	Yamakagashi antivenom	
Trimeresurus (Trimeresurus) albolabris, T. macrops	Green pit vipers	TRC†† Green Pit Viper Antivenin or haemato-polyvalent	100 mL[106]
Vipera berus and other European *Vipera*	European adder	"ViperaTAb" MicroPharm Fab monovalent	100-200 mg[286]
		Sanofi-Pasteur Viperfav	4 mL[24]
Walterinnesia aegyptia	Black desert cobra	NAVPC‡ Bivalent Naja/Walterinnesia or Polyvalent Snake Antivenom	50 mL

*Commonwealth Serum Laboratories, Parkville, Australia.
†South African Vaccine Producers, formerly SAIMR, Johannesburg.
‡National Antivenom and Vaccine Production Center, National Guard Health Affairs, Riyadh, KSA.
§Instituto Clodomiro Picado, San Jose, Costa Rica.
‖Laboratorios Bioclon, Silanes, Mexico.
¶Fundação Ezequiel Dias, Belo Horizonte, Brazil.
**Indian Manufacturers: Bharat Serums and Vaccines, Mumbai, Biological E (Evans), Vins Bioproducts, Hyderabad.
††Thai Red Cross Society, Bangkok.
#Sanofi-Pasteur announced that they have stopped production of FavAfrique and FaviRept antivenoms.

temperatures above 30° C (86° F).[320] Antivenoms retain much of their activity well beyond stated expiration dates. Although the use of such out-of-date material could never be recommended, situations may arise in the developing world when there is no alternative.[174] Opaque solutions should not be administered, because precipitation of protein indicates denaturing, with loss of activity and increased risk for adverse reactions.

Supply of Antivenoms

Antivenom manufacturers and suppliers change often, so availability of antivenom is uncertain. For this reason, a timely Internet search (see Internet Resources, later) followed by confirmation of clinical efficacy and safety, as well as immediate availability, are essential, well in advance of the time when antivenom is needed. In urgent cases, some national poison centers (e.g., London) and zoo networks hold stocks of antivenoms covering most exotic and local species. Europe, Asia, and Australia are reasonably well supplied with antivenoms, but there is currently a crisis in antivenom supply to the sub-Saharan countries of Africa and to New Guinea.[85,130,131,318] This problem may be relieved by production of new "pan-African" polyvalent antivenoms, raised against appropriate African venoms, by manufacturers outside Africa.[32,85,130,131,213]

Purchasers of antivenom should be aware that some clinically ineffective, nonspecific, but highly reactogenic antivenoms raised against Indian venoms (e.g., *Naja, Echis*) are sold in African and Asian countries and in Papua New Guinea, where they are purported to be effective against venoms of the local snakes.[289]

Antivenom Reactions

Antivenom treatment may be complicated by early anaphylactic-type, pyrogenic, or late (serum sickness–type) reactions.[139]

Early Anaphylactic Type of Reactions. These reactions usually develop within 10 to 180 minutes of starting antivenom, with itching, urticaria, fever, tachycardia, palpitations, cough, nausea, and vomiting. Up to 40% of patients with early reactions show features of severe systemic anaphylaxis—bronchospasm, hypotension, or angioedema—but deaths are rare. The reported incidence of reactions, which varies between antivenoms and according to dose, ranges from 3% to 84%. Safety can be improved by attention to the manufacturing processes.[244,323] These reactions are usually not type I IgE-mediated hypersensitivity reactions to equine serum proteins and are therefore not predicted by hypersensitivity tests.[49,146] For this reason, it is inappropriate and misleading to apply the adjectives *immediate*, *allergic*, or *hypersensitivity* to early antivenom reactions in general.

Antivenoms activate complement in vitro,[230] whereas the clinically similar reactions to homologous serum are associated with complement activation and immune complex formation in vivo. The complement system is probably activated by aggregates of IgG or its fragments, but there is little evidence that pepsin digestion, which removes complement-activating Fc fragments, reduces the incidence of reactions.[176] Unless patients are watched carefully for 3 hours after treatment, mild reactions may be missed and deaths misattributed to the envenoming itself. Early reactions should be treated as for anaphylaxis of any cause.[225,226] They respond readily to aqueous epinephrine/adrenaline given by IM

injection of 0.5 to 1.0 mL of 0.1% (1:1000, 1 mg/mL) in adults (children, 0.01 mL/kg) at the first sign of trouble. Antihistamines, such as chlorpheniramine maleate (adult dose, 10 mg; children, 0.2 mg/kg), should be given by IV injection to combat the effects of histamine released during the reaction.

Pyrogenic Reactions. Pyrogenic reactions result from contamination of the antivenom by endotoxin-like compounds. High body temperature develops 1 to 2 hours after treatment and is associated with rigors, followed by vasodilation and decreased blood pressure. Febrile convulsions may be precipitated in children. Patients should be physically cooled and given an antipyretic drug, such as acetaminophen, by mouth, nasogastric tube, or suppository. Aspirin and NSAIDs are not safe in patients with hemostatic problems.

Late (Serum Sickness–Type) Reactions. Late reactions develop 5 to 24 (mean 7) days after treatment. Their incidence and speed of development increase with the dose of antivenom. Symptoms include fever, itching, urticaria, arthralgias (which may involve the temporomandibular joint), lymphadenopathy, periarticular swellings, mononeuritis multiplex, albuminuria, and (rarely) encephalopathy. This immune complex disorder responds to an antihistamine such as chlorpheniramine (adults, 2 mg four times daily; children, 0.25 mg/kg/day in divided doses), or, in more severe cases, to corticosteroids such as prednisolone (adults, 5 mg four times daily for 5 days; children, 0.7 mg/kg/day in divided doses for 5 days).

Prediction of Antivenom Reactions. Hypersensitivity testing by intradermal or subcutaneous injection or intraconjunctival instillation of diluted antivenom has been widely practiced in the past. However, these tests delay the start of antivenom treatment, are not without risk, and have no predictive value for early (anaphylactic) or late (serum sickness–type) antivenom reactions, which are not usually manifestations of IgE-mediated type I hypersensitivity.[49,146]

Prevention of Early Antivenom Reactions. Prophylactic antihistamines (anti-H_1 and anti-H_2), corticosteroids, and epinephrine have been widely used, singly or in combination, on empirical grounds, but not without risk. A few randomized controlled trials have now been completed, and several more are in progress. IM promethazine proved ineffective,[64] but in two published studies, subcutaneous epinephrine (adrenaline) (0.1%, adult dose 0.25 mg) reduced the incidence of early antivenom reactions.[188,319] A study purporting to demonstrate the efficacy of combined hydrocortisone and antihistamine infusion was underpowered.[79] A review of 10 years of experience with various premedication regimens in Papua New Guinea[319] illustrated the heterogeneity and lack of standardization of snakebite victim care in developing countries while suggesting efficacy of some prophylactic regimens, as did the study of Caron and colleagues[37] in Ecuador. Premedication of 1007 Sri Lankan snakebite victims with promethazine, hydrocortisone, and epinephrine in a subcutaneous dose of 0.25 mL of 1:1000 was compared, each alone and in various combinations. Compared with placebo, adrenaline significantly reduced severe reactions to antivenom by 43% (95% CI, 25 to 67) at 1 hour and by 38% (95% CI, 26 to 49) up to and at 48 hours after antivenom administration. Hydrocortisone and promethazine were ineffective, and addition of hydrocortisone negated the benefit of adrenaline.[53] Routine prophylaxis with low-dose subcutaneous epinephrine (adult dose, 0.25 mg of 1:1,000 solution), given before starting antivenom infusion, should now be generally recommended based on this convincing evidence.

Antivenom Administration

Antivenom should be given as soon as it is indicated, but it remains potentially effective as long as signs of systemic envenoming persist (e.g., up to 2 days after a sea-snake bite and many days or even weeks for prolonged defibrination after bites by Viperidae).[198,296,297] In contrast, local effects of venoms are probably not reversible by antivenom delayed for more than 1 to 2 hours after the bite.[248,298,304]

Route of Administration. The IV route is most effective. Although IM injection is associated with a lower rate of early anaphylactoid reactions, absorption is very slow, especially when the gluteal site is used (however, see next section). An infusion over 30 to 60 minutes of antivenom diluted in isotonic fluid may be easier to control than an IV "push" injection of reconstituted but undiluted antivenom given over 10 to 20 minutes. There is no difference in the incidence of severity of antivenom reactions in patients treated by these two methods,[146] but greater dilution and slower infusion should be tested.[34] However, there was no difference in the incidence of reactions when 20-minute and 2-hour infusions were compared.[110]

Snakebite in Remote (Wilderness) Locations. If someone is bitten by a snake in a remote location and signs of envenoming develop, but no one in the group is capable of giving an IV injection, antivenom may be given by deep IM injection at multiple sites into the anterolateral aspect of the thighs (not into the gluteal region, from which absorption is exceptionally slow), followed by massage to promote absorption. An algorithm has been developed to guide the use of antivenom in these circumstances (Figure 36-109). However, the volumes of antivenom normally required would make this route impractical, as would the risk for hematoma formation in patients with incoagulable blood.

Dose of Antivenom. Ideally, the initial dose of a particular antivenom should be based on results of clinical studies when available, depending on species of snake responsible and severity of envenoming. However, most manufacturers' recommendations are based on mouse assays, which may not correlate with clinical findings.[307] Clinical trials of antivenom have been carried out since 1973,[297] but are inappropriately neglected, even though they are the only reliable means of obtaining efficacy and safety data. Initial doses of some important antivenoms are given in Table 36-4. The apparent serum half-lives of antivenoms in envenomed patients range from 26 to 95 hours, depending on which IgG fragment they contain.[99,240] Children must be given the same doses of antivenom as adults.

Recurrent Envenoming. Recurrence of clinical and laboratory features of systemic envenoming, including recurrent venom antigenemia, several days after an initially good response to antivenom, was clearly documented in patients envenomed by Malayan pit vipers (*C. rhodostoma*) in Thailand in the 1980s, and later after the introduction of CroFab in the United States.[31,100,275,301] Recurrent envenoming is probably the result of continuing absorption of venom from the injection site after antivenom has been largely cleared from the circulation, or perhaps by redistribution of venom from tissue in response to antivenom.[14,100] Paradoxically, venom absorption may increase after a hypotensive, shocked patient has been resuscitated. It is more likely to occur when a rapidly eliminated, small-IgG-fragment antivenom, such as Fab, is used.[9,31,160] This suggests that an initial dose of antivenom, however large, may not prevent late or recurrent envenoming.

Repeated Dosing. The response to antivenom will determine whether further doses should be given. Neurotoxic signs may improve within 30 minutes of antivenom treatment, but this usually takes several hours. Hypotension, sinus bradycardia, and spontaneous systemic bleeding may respond within 10 to 20 minutes. Blood coagulability is usually restored between 1 and 6 hours, provided sufficient antivenom has been given. A second dose of antivenom should be given if severe cardiorespiratory symptoms persist for more than about 30 minutes, and when incoagulable blood persists for more than 6 hours after the start of the first dose.

The "6-Hour Rule." Studies of envenoming by several species of snakes whose venoms cause coagulopathy have demonstrated that once an adequate neutralizing dose of antivenom has been given, blood coagulability (assessed by 20WBCT) will be restored within a median of 6 hours.[293] This reflects the ability of the liver, highly activated by circulating fibrin/fibrinogen breakdown products, to restore coagulable levels of clotting factors in patients with consumption coagulopathy. This important observation is the basis for a simple method of titrating antivenom dosage in individual patients whose blood is initially incoagulable. The 20WBCT is performed at 6-hour intervals, and the initial dose of antivenom is repeated every 6 hours until blood coagulability is restored. After that, the 20WBCT is checked at

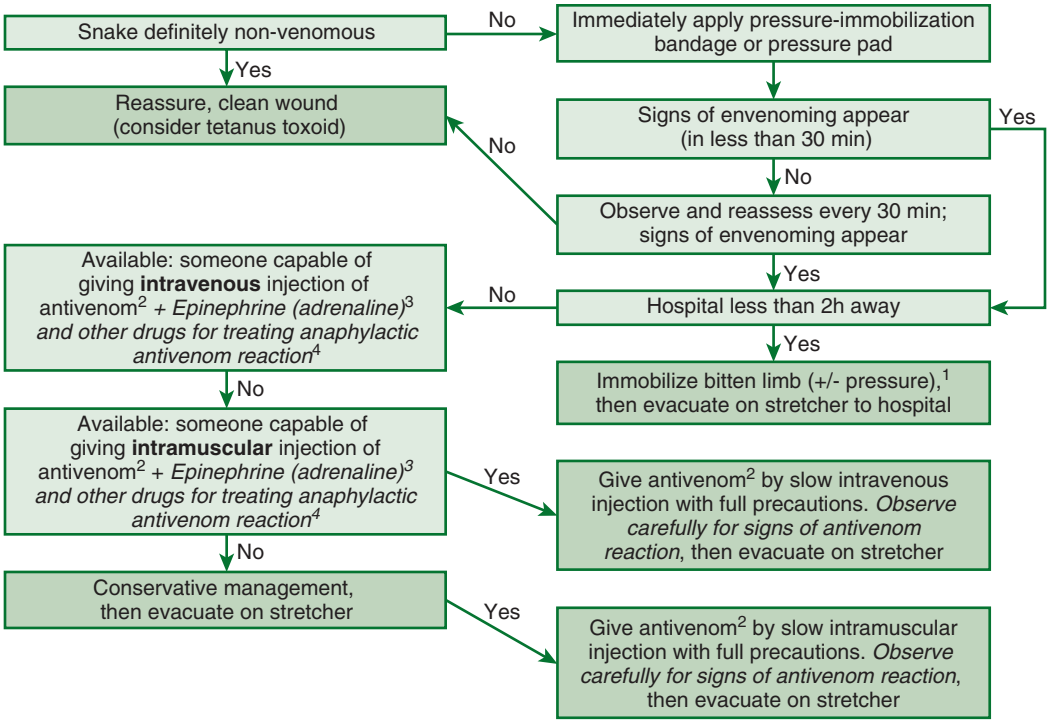


FIGURE 36-109 Algorithm indicating appropriate management for snakebite in a patient while in a remote wilderness location. *(From Johnson C, Anderson S, Dallimore J, et al, editors:* Oxford handbook of expedition and wilderness medicine, *2nd ed, New York, 2015, Oxford University Press, pp 541-576.)*

12-hour intervals for at least 48 hours to detect recurrent envenoming.

Very large doses of antivenom may be required to treat patients bitten by species capable of injecting enormous amounts of venom or extremely potent venom. A patient bitten by the king cobra (*O. hannah*) was given 1150 mL of specific antivenom and prolonged artificial ventilation and survived.[249]

SUPPORTIVE TREATMENT

The following supportive care measures are provided assuming that an adequate initial dose of antivenom has been given.

Neurotoxic Envenoming

Artificial Ventilation. This was first suggested for neurotoxic envenoming more than 130 years ago, but patients continue to die because of a lack of vital respiratory support.

Bulbar and Respiratory Muscle Paralysis. Inability to swallow is indicated by accumulation of secretions in the pharynx. Stridor indicates paralysis of the vocal cords; it can be accentuated by extending the neck. Early paralysis of intercostal respiratory muscles is suggested by "abdominal breathing" (or "paradoxical respiration") in which exaggerated compensatory contraction of the diaphragm causes the paralyzed abdomen (rather than the chest) to expand on inspiration.

Objective measurement of ventilatory capacity is very useful to monitor respiratory paralysis. This can be achieved with a peak flow meter, spirometer, or respirometer (if the patient is using a face mask or is intubated) or by asking the patient to blow into the tube of a sphygmomanometer to record the maximum expiratory pressure. If patients are adequately oxygenated, even those with profound generalized flaccid paralysis from neurotoxic envenoming are fully conscious. However, because their eyes are closed (ptosis) and they do not move or speak, they are commonly assumed to be unconscious, and their level of consciousness cannot be properly assessed by the conventional Glasgow Coma Scale. Tactless remarks made by medical staff can be heard by the apparently comatose patient. Opening the eyes so that the patient can see the surroundings is very reassuring for a ptotic and completely paralyzed patient. Patients may still be able to flex a finger or toe, allowing simple "yes or no" communication. It is very important *not* to assume that patients with snakebite neurotoxicity have irreversible brain damage, although they may be areflexic, unresponsive to painful stimuli, and may have fixed, dilated pupils.

Neurotoxic effects are fully reversible with time. A patient bitten by *B. multicinctus* in Canton recovered completely after being ventilated manually for 30 days, and a patient probably envenomed by *Tropidechis carinatus* recovered after 10 weeks of mechanical ventilation in Queensland, Australia. Endotracheal intubation or tracheostomy using a cuffed tube is needed. The patient can be ventilated manually with an anesthesia bag or, preferably, with a mechanical ventilator. For technical details of airway management and assisted ventilation, see http://www.searo.who.int/EN/Section10/Section17.htm.

Anticholinesterase Drugs.* Anticholinesterase drugs have limited usefulness in neurotoxic envenoming but may produce rapid improvement in neuromuscular transmission in patients suffering the effects of postsynaptic neurotoxins, for example, from envenoming by some species of Asian and African cobras,

*CAUTION: The doses of anticholinesterase drugs suggested in this text are, in some cases, higher than those stated as being maximum doses in literature dealing with other applications of these agents.

mambas, death adders (*Acanthophis* spp.), and kraits.[133,302,307,311] Recent claims that intranasal neostigmine might provide a universal first-aid method for snakebite victims have achieved a high media profile but are unsubstantiated, misleading, and fanciful.

It is worth trying the "Tensilon test" in all cases of severe neurotoxic envenoming, as for a patient with suspected myasthenia gravis. Baseline observations or measurements are made against which to assess the effectiveness of the anticholinesterase. Atropine sulfate (0.6 mg for adults, 50 mcg/kg for children) or glycopyrronium is given by IV injection followed by neostigmine bromide or methylsulfate (Prostigmin) (or distigmine, pyridostigmine, ambenomium, and others in appropriate doses) by IM injection (0.02 mg/kg for adults, 0.04 mg/kg for children). Short-acting edrophonium chloride (Tensilon) is ideal for this test but is rarely available in the region. It is given by slow IV injection in an adult dose of 10 mg, or 0.25 mg/kg for children. The patient is observed over the next 30 to 60 minutes (neostigmine) or 10 to 20 minutes (edrophonium) for signs of improved neuromuscular transmission. Ptosis may disappear and ventilatory capacity (peak flow, forced expiratory volume in 1 second [FEV_1], or maximum expiratory pressure) may improve.

The "ice test" is a possible alternative to the Tensilon test.[83] In patients with myasthenia gravis who have bilateral ptosis, application of an ice-filled plastic glove to one eye for 2 minutes resulted in improvement in ptosis on that side, due to inhibition of anticholinesterase. This quick and simple test might obviate the need for the Tensilon test. However, it has not yet been evaluated in patients with neurotoxic snake envenoming.

Patients who respond convincingly can be maintained on neostigmine methylsulfate, 0.5 to 2.5 mg every 1 to 3 hours (up to 10 mg/24 hours maximum) for adults, or 0.01 to 0.04 mg/kg every 2 to 4 hours for children, by IM, IV, or subcutaneous injection, together with atropine to block muscarinic side effects. Patients able to swallow tablets may be maintained on atropine (0.6 mg twice daily), neostigmine (15 mg four times daily), or pyridostigmine (60 mg four times daily). Patients must be observed closely for symptoms of cholinergic crisis.

Hypotension and Shock

Hypovolemia is a common cause of hypotension and shock and should be treated by infusing a plasma expander. Central venous pressure is the safest way to monitor volume replacement. Hypotensive patients envenomed by the Burmese Russell's viper responded to dopamine, 2.5 mcg/kg per minute by IV infusion; however, methylprednisolone, 30 mg/kg, and naloxone were not effective.[168] Anaphylaxis, whether a primary response to envenoming, the result of hypersensitization, or a reaction to antivenom, should be treated promptly with epinephrine/adrenaline.[225,226]

Acute Kidney Injury

If urine output drops below 400 mL/24 hours, urethral and central venous catheters should be inserted. If urine flow fails to increase after cautious rehydration, the patient should be placed on strict fluid balance. Peritoneal dialysis or hemodialysis will be required in most patients with established renal failure.[220,321] For technical details of assessment and treatment of acute kidney injury, see http://www.searo.who.int/EN/Section10/Section17.htm.

Local Infection

A booster dose of tetanus toxoid should be given. Following bites by Latin American pit vipers[112] and some other species, such as Malayan pit vipers (*C. rhodostoma*),[242] local bacterial infections with formation of wound abscesses occur in about 10% of patients. A wide range of bacteria have been implicated, some peculiar to snakes' oral cavities and venom.[218] Even a case of Buruli ulcer (*Mycobacterium ulcerans*) has been attributed to snakebite. Prophylactic antibiotics are not justified unless the wound has been incised or there is evidence of necrosis.[112] Penicillin, erythromycin, or chloramphenicol is appropriate, as well as an antibiotic effective against the bacterial flora of the buccal cavity and venoms of local snakes.[242] An aminoglycoside such as gentamicin should be added for 48 hours. Bullae are best left intact.

SNAKE-BITTEN LIMBS

Excessive elevation of snake-bitten limbs should be avoided, as it has been shown to increase the risk of compartment syndromes.[153]

Surgical Management[306]

Necrotic tissue should be debrided as soon as possible and the denuded area covered with split-thickness skin grafts. Muscle should not be excised just because it looks dark or even black, because intense hemorrhage may produce this appearance in viable muscle and damaged muscle can regenerate.

Compartment Syndrome and Fasciotomy.[321] In a snake-bitten limb, swelling of muscles within tight fascial compartments, such as the anterior tibial compartment, may raise tissue pressure to such an extent that perfusion is impaired and ischemic damage (as in Volkmann's contracture of the forearm) is added to the effects of the venom. Risk factors include pressure bandaging and excessive elevation of the limb that reduce arterial perfusion pressure in the compartment but cannot reduce local venous pressure below tissue pressure. Reduction of the arteriovenous pressure gradient was associated with decreased muscle PO_2 and nerve conduction velocity.[153]

The classic signs of compartment syndrome include excessive pain, weakness of the compartment muscles and pain when they are passively stretched, hypoesthesia of areas of skin supplied by nerves running through the compartment, and obvious tenseness of the compartment.[153] These features have been characterized as "the seven P's": pain at rest, pain with movement, paralysis, pallor, paresthesia, poikilothermia, and pulselessness. However, local effects of envenoming often result in a painful, tender, immobile, pale, cyanotic, cold, tensely swollen, and apparently pulseless limb with poor capillary refill in the absence of a demonstrable compartment syndrome. These appearances may mislead inexperienced surgeons into diagnosing compartment syndrome without objective evidence and encourage them to proceed to fasciotomy. Discovery of dark or even black-looking muscle tissue may reassure the surgeon that the surgery was necessary, but envenomed yet viable muscle often looks black because of hemorrhage.

Dangers of fasciotomy include neglect of early adequate antivenom treatment, severe persistent bleeding if the venom-induced hemostatic abnormalities have not been corrected by adequate doses of antivenom, delayed recovery of function, prolonged hospital admission, persistent morbidity from damage to sensory nerves, and contractures from keloid formation or hypertrophic scarring in some ethnic groups. Palpation of peripheral pulses or their detection by Doppler ultrasound does not exclude compartmental ischemia. However, direct measurement of intracompartmental pressure is reasonably simple, using a perfusion pump and saline manometer system or a commercial transducer such as the Stryker apparatus. An intracompartmental pressure of more than 45 mm Hg in an adult or 30 mm Hg in a child indicates a high risk for ischemic necrosis.[152] In these circumstances, fasciotomy may be justified to relieve the pressure in the compartment, but this treatment did not prove effective in saving envenomed muscle in animal experiments.[77] Necrosis occurs most frequently after digital bites. Fasciotomy must never be undertaken until blood coagulability has been restored by adequate doses of specific antivenom, followed by transfusion of fresh whole blood, clotting factors, or platelets as required.

INAPPROPRIATE TREATMENTS

Corticosteroids, heparin, antifibrinolytic agents such as aprotinin (Trasylol) and ε-aminocaproic acid, antihistamines, trypsin, and a variety of traditional herbal remedies have been used and advocated for snakebite. Most are potentially harmful, and none has been proved to be effective.

TREATMENT OF SNAKE VENOM OPHTHALMIA[46,284,303]

Management of venom ophthalmia consists of the following:

1. Urgent decontamination by copious irrigation: The "spat" venom should be washed from the eye or mucous membrane as soon as possible using large volumes of water or any other available bland fluid. Even urine is better than nothing.
2. Analgesia by vasoconstrictors with weak mydriatic activity (e.g., 0.5% adrenaline/epinephrine) or a single topical administration of local anesthetic such as 0.4% oxybuprocaine hydrochloride (Novesin), 4% lidocaine hydrochloride, or tetracaine hydrochloride (Dicaine)
3. Exclusion of corneal abrasions by fluorescein staining and/or slit-lamp examination and application of a prophylactic topical antibiotic such as tetracycline, chloramphenicol, soframycin, ciprofloxacin, gatifloxacin, penicillin-streptomycin, or polymyxin B sulfate
4. Prevention of posterior synechiae, ciliary spasm, and discomfort with a topical cycloplegic such as 2% atropine, scopolamine, or homatropine
5. Antihistamines in case of allergic keratoconjunctivitis

Topical or IV antivenom and topical corticosteroids are contraindicated. Topical heparin proved promising experimentally but has been untested clinically.

PREVENTION OF SNAKEBITE

The risk for snakebite can be reduced by simple precautions. Snakes should never be disturbed, attacked, or handled unnecessarily, even if they are thought to be harmless species or appear to be dead. Some venomous species, such as the ringhals (*Hemachatus haemachatus*), a South African spitting elapid, sham death (Figure 36-110). Venomous species should never be kept as pets or as performing animals. Protective clothing—boots (not open sandals), socks, and long pants (trousers)—should be worn when walking in undergrowth or deep sand, and a flashlight should always be carried at night. Particular care should be taken while collecting firewood; moving logs, boulders, boxes, or debris likely to conceal a snake; climbing rocks and trees covered with dense foliage; or swimming in overgrown lakes and rivers. Where there are sea snakes, wading in the sea, especially in sand or near coral reefs, is a dangerous pastime and should be avoided if possible. Shuffling is safer than a high-stepping gait. Divers should keep clear of sea snakes. Fishermen who catch sea snakes in nets or on lines should return them to their element without touching them; their heads and tails may be difficult to differentiate.

In the camp, sleep off the ground in a hammock, on a camp bed or in a tent with a sewn-in ground sheet, especially in krait country. A study in Nepal proved that a well tucked-in mosquito net afforded good protection against snakebites.[39] Remove unnecessary junk and litter that might attract rodents, because rodents attract snakes. Various toxic chemicals, such as naphthalene, sulfur, insecticides (e.g., DDT, dieldrin, pyrethrins), and fumigants (e.g., methyl bromide, formaldehyde, tetrachloroethane), are lethal to snakes, but no true repellent has been identified that is acceptably safe for peridomestic use where there are children, domestic animals, and valuable wildlife.

Prophylactic immunization against snakebite using venom toxoids has been attempted, for example, against habu (*Protobothrops flavoviridis*) among farmers in the Amami and Ryuku Islands of southern Japan, where it proved ineffective.[208] The analogy with immunization against infectious diseases is misleading, because the immunized person would not have time to develop an enhanced secondary (anamnestic) response to the venom after being bitten. Protection would depend solely on levels of neutralizing antibody circulating at the time of the bite.

FIGURE 36-110 South African ringhals, a spitting elapid (*Hemachatus haemachatus*: family Elapidae), shamming death. *(Copyright D.A. Warrell.)*

FIGURE 36-111 Lizards whose saliva contains toxins.[74] **A,** Asian water monitor (*Varanus salvator*: family Varanidae) (Muda Ganga, Balapitiya, Sri Lanka). **B,** Chinese crocodile lizard (*Shinisaurus crododilurus*: family Shinisauridae) (Yao Shan E Xi, China). *(Copyright D.A. Warrell.)*

VENOMOUS LIZARDS

The overtly venomous helodermatid lizards (Gila monster and Mexican beaded lizard) are discussed in Chapter 35. Recently, evidence has been published that the saliva of other groups of lizards contains toxins: Iguania (e.g., iguanas and agamids) (see Figure 36-1, *Pogona*) and Anguimorpha (e.g., varanid or monitor lizards) (Figure 36-111A, *Varanus salvator*).[72] These lizards have mandibular glands, but only those of Varanidae/Lanthanotidae and Helodermatidae are segregated into specialized serous protein-secreting glands with thick capsules. Glands of members of four Anguimorph families (Anguidae, Lanthanotidae, Shinisauridae [Figure 36-111B], and Varanidae) were shown to secrete a variety of toxins, including cysteine-rich secretory proteins (CRiSP), kallikrein, helokinestatin, hyaluronidase, lectin, natriuretic peptides, PLA_2s, and new cardiopetides.[74] The clinical significance of these findings is doubtful, because lizard bites rarely cause more than mild trauma, transient pain, and swelling. However, it has been claimed that envenoming might contribute to the massively traumatic predatory attacks launched by Komodo dragons against large mammals and occasionally humans (see later text).

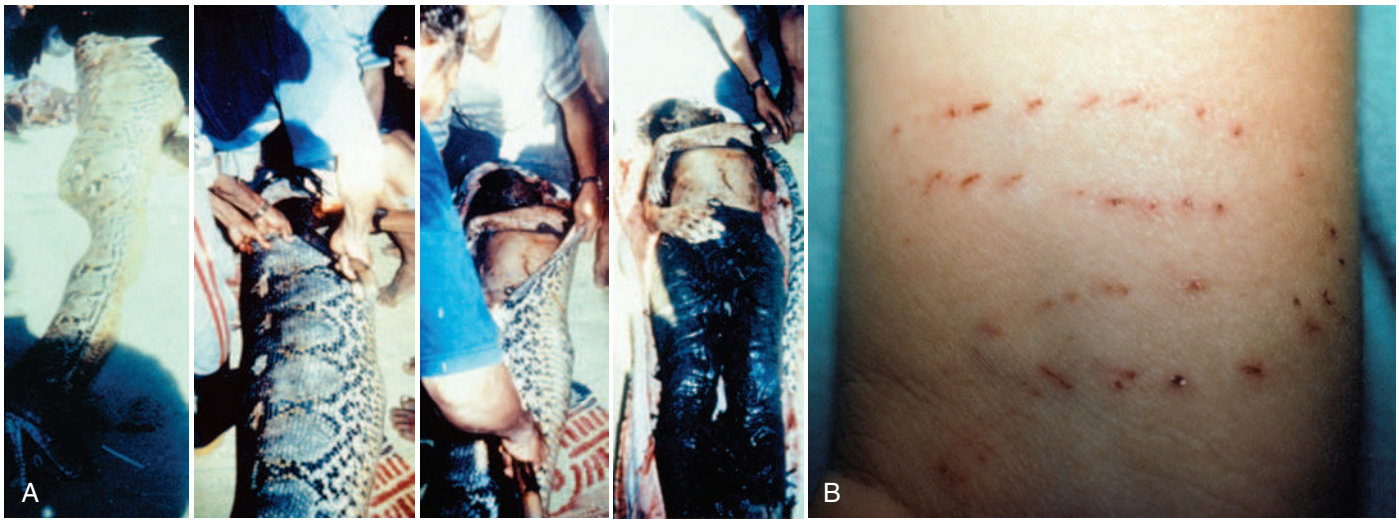


FIGURE 36-112 Attacks by pythons. **A,** Man killed and swallowed by a large reticulated python (*Python reticulatus*). **B,** Tooth marks made by a brown water python (*Liasis fuscus*) that seized a 7-year-old child while she was asleep near the Adelaide River in Australia. *(**A** courtesy Exel Sawuwu; **B** courtesy Bart Currie.)*

DANGEROUS LARGE REPTILES

GIANT PYTHONS (FAMILY BOIDAE)

Bites by most species of python can be locally traumatic and sometimes complicated by infection (Figure 36-112B). Several species have been responsible for rare fatal attacks reported from South America (anaconda, *Eunectes murinus*) (Figure 36-113A); Africa (rock python, *Python sebae*) (Figure 36-113B to D); south and Southeast Asia, especially Indonesia (reticulated python, *Python reticulatus* [Figure 36-113E], and the Indian python, *Python molurus*); and Australia, where a 5.2-m (17-foot) scrub python, *Morelia amethistina,* killed its keeper.[62] The victims were asphyxiated and crushed by constriction and in some cases swallowed after the clavicles had been broken[167,292] (Figure 36-112A). In 1974, a man attacked by *P. sebae* near Harrar, Ethiopia, died 48 hours later as a result of perinephric hematomas resulting from crush injuries. Recently, a 34-year-old man in the United States was strangled to death by his 2.7-m (9-foot), 11.3-kg (25-lb) boa constrictor, reemphasizing the danger posed by even modest-sized pythons.

KOMODO DRAGON (MONITOR)

This giant lizard, *Varanus komodoensis,* which can reach 3.1 m (10.2 feet) in length and 166 kg (366 lb) in weight, is restricted

FIGURE 36-113 Giant pythons. **A,** Anaconda (*Eunectes murinus*), Brazil. **B** to **D,** African rock python (*Python sebae*), showing head (note supralabial heat-sensitive pit organs) and multiple teeth. **E,** Reticulated python (*Python reticulatus*). *(Courtesy D.A.Warrell.)*

to Komodo, Rinca, Flores, and Gili Motang Islands in Indonesia. Until recently, it was believed that the Komodo dragon killed its prey (deer, cattle, pig, and occasionally humans) by brute force or through debilitation through contamination of bite wounds with pathogenic bacteria, such as *Pasteurella multocida*.[15] Recently, Fry and associates[75] found that these monitors possessed compound mandibular venom glands whose six compartments ducted to openings between the serrated pleurodont teeth. The venom contains toxins capable of causing hypotension (CRiSP, kallikrein, and natriuretic toxins), bleeding (PLA_2 toxins), and hyperalgesia (cramping AVIT toxins), which, the authors argue, contribute to the predation strategy. In support of envenoming, they note that prey animals are reported to be unusually quiet after being bitten and that they rapidly go into shock. There are anecdotal reports of persistent bleeding in human victims after bites by *V. komodoensis*.

INTERNET RESOURCES

Snakebite Management and Antivenoms

Africa: <http://www.afro.who.int/en/clusters-a-programmes/hss/essential-medicines/edm-publications/2731-guidelines-for-the-prevention-and-clinical-management-of-snakebite-in-africa.html>.

South and Southeast Asia: <http://www.searo.who.int/EN/Section10/Section17.htm> (see under Technical Guidelines).

Global ("Antivenoms website" [Venomous Snakes Distribution and Species Risk Categories] and "WHO Guidelines" [for the Production, Control and Regulation of Snake Antivenom Immunoglobulins]): <http://www.who.int/bloodproducts/snake_antivenoms/en/>.

Global (especially Australasia): <http://www.toxinology.com/>.

Global VAPA Guide: <https://www.vapaguide.info/>.

Antivenoms Only

Munich AntiVenomINdex (MAVIN): <http://www.toxinfo.org/antivenoms/>.

CSL Australian antivenoms: <http://www.toxinology.com/generic_static_files/cslb_index.html>.

Global crisis solutions center: <http://globalcrisis.info/latestantivenom.htm>.

Venomous Snake Taxonomy Updates

<http://pages.bangor.ac.uk/~bss166/update.htm>.

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Complete references used in this text are available online at expertconsult.inkling.com.

CHAPTER 37

Ranch and Rodeo Medicine

MARK A. BRANDENBURG, MARK LAFAVE, AND DALE J. BUTTERWICK

RANCH MEDICINE

HISTORY AND PERSPECTIVE

For as long as there have been farms and ranches in North America, there have been dedicated, empathetic medical professionals tending to workers and family members in these rugged environments. Often cited as among the most dangerous professions of the modern age, farming and ranching are synonymous with rural trauma. Rural trauma has been called the "neglected disease" of the 21st century.[164]

In addition to easily identifiable, unique, and statistically evident health care challenges on farms and ranches, more abstract and cultural issues are no less critical. As in most of medicine, the approach to injured ranch workers requires cultural understanding and adjustment; in this case the European-American culture of rural America.[182]

Understanding the midwestern U.S. ethos is an important component of the health care provider's communication skills set (Figures 37-1 and 37-2). Talking with, not down to, the rural patient is essential. This is especially true for the cowboy, in whom self-respect, individualism, and perseverance in adverse situations are characteristic. In particular, dealing with issues of pain, disability, and loss of autonomy require deference to the cultural milieu. For example, asking a cowboy with a shoulder injury, "Does it hurt?" might not elicit the expected response. However, asking the same cowboy, "Can you use that arm?" will be more likely to elicit congruent dialog.

EPIDEMIOLOGY OF AGRICULTURAL DISEASE AND INJURY

Agriculture ranks among the most hazardous industries in the world. Farmers are at high risk of sustaining fatal and nonfatal injuries, work-related lung diseases, noise-induced hearing loss, skin diseases, and certain cancers associated with chemical use, in addition to repetitive-use injuries and prolonged sun exposure. Farming is one of the few industries in which all family members, who often share the work and live on the premises, are at increased risk for injuries, illness, and death.[75,77] In 2014, 568 deaths were reported to have occurred in the U.S. agricultural industry.[188a] On-the-job mortality rates in agriculture, forestry, and fishing industries are 36 times greater than in other industries.[190]

This chapter addresses primarily acute injuries, but a variety of repetitive-use injuries are well known to occur in the farm setting. Farming is a physically arduous occupation that places workers at risk for injuries such as osteoarthritis, neck and lower-back disorders, and hand-arm vibration syndromes.[201]

A variety of acute farmyard injuries caused by environmental and human factors regularly cause permanent disability and even death. Common injuries include lacerations, amputations, farm animal bites, fractures, and dislocations.[15] Raising livestock, heavy equipment, exposure to dust and gas, noise, chemicals and pesticides, and activities that involve heavy lifting are common risk factors for injury on ranches and farms. Certain characteristics surrounding farm-related injuries serve as risk factors and can be used to predict and prevent injuries, yet there remains need for development and evaluation of injury control interventions.[87] Personal contributing factors in most injuries include young age, advanced age, hurried work activities, fatigue, and stress.[156] In the elderly rancher, aging and health impairments, such as arthritis and hearing difficulties, are risk factors for falls that accommodations and preventive strategies can address.[181]

Eye injuries on the farm are also very common and can be serious. One-quarter of farm-related eye injuries requiring treatment occur during the activity of grinding or cutting metal, resulting in metallic foreign bodies in the eye.[181] The largest

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FIGURE 37-1 Oklahoma farmer. *(Courtesy Mark Brandenburg, MD.)*

proportion of eye injuries, however, result from a more diverse set of work activities. The use of appropriate eye protection can prevent the majority of these injuries.

PEDIATRIC INJURIES

The discussion of farm injuries includes pediatric injuries, which account for one-fifth of all agricultural injury fatalities and hospitalizations.[48] A multitude of hazards on ranches and farms exist for children; 80% of those injured are boys, with a small proportion of the injuries being work related; 80% of pediatric farm injuries are not work related, but rather often involve large animals and vehicles.[141]

In 2012, 7780 children were injured on U.S. farms.[141] Hand injuries in children, often complex and requiring tendon repair, fracture fixation, grafting, and skin flaps, are well known to occur on farms, most frequently a result of machinery and tractors.[185] The most prevalent causes of death in children on the ranch, 45% of whom are less than 16 years of age, involve machinery (25%), motor vehicles (17%), and drowning (16%).[78] Falls from buildings, haylofts, and horses account for a significant proportion of these injuries. Approximately one-third of the farm-related pediatric injuries involve head injuries (36.4%), with more than half of these involving skull fractures.[178]

FIGURE 37-2 The farmer shown in Figure 37-1 with two friends working on an antique planter pulled by a small tractor. *(Courtesy Mark Brandenburg, MD.)*

EMERGENCY MEDICAL SERVICES AND TRIAGE

Extrication and rescue can be the most difficult parts of an agricultural rescue operation, because farmers and ranchers work in isolated locations, and agricultural equipment and the resulting injuries are unique and complex. For these reasons, preincident planning and preparation are critical components to a successful rural emergency medical services (EMS) system.

The safety of the rescuers should always be addressed and clarified when discussing and planning agricultural rescue operations. Emergency personnel safety takes priority over the victim being rescued. If a rescuer is injured, it not only takes the person out of the rescue but also generates another patient in need of emergency response. Scene safety applies as well to bystanders, co-workers, assisting mechanics, and other persons likely to at the scene of a serious agricultural incident. Assigning the initial bystanders the task of securing scene safety accomplishes two of these objectives.

In the rural setting, resources are usually lacking, and health care providers are in short supply. This translates into an overwhelmed health care system that often cannot meet the same standards of care expected in larger, urban settings. Moreover, there are vast differences in the quality of health care systems between rural regions, making it difficult to predict how a particular type of injury or illness might be managed in the rural setting. The health care provider must allow for a variety of EMS responses when planning for medical emergencies in this setting. The astute clinician will investigate in advance the availability of local and regional health care services and EMS protocols in the area.

Identification and Understanding of Illness and Injury

In an emergency, appropriate triage from the ranch environment enhances survival and minimizes morbidity and mortality of the acutely injured patient. Patient outcome is directly related to time from injury to proper definitive care.[11] Early recognition of multisystem, life- and limb-threatening injuries is necessary before directing the EMS transport system to a particular hospital.

Local Medical Care and Regional Tertiary Care Centers

Understanding the capabilities of nearby hospitals is an essential element in making the right triage choice.[11] Often, patients with more complex injuries and illnesses cannot receive definitive medical or surgical care in the rural setting. In many regions, online medical direction or standing orders will be available to assist determination of how and where to transport a patient from the ranch setting to the most appropriate medical care facility. Nonetheless, if a patient is unstable, transport to the nearest hospital regardless of specialty care availability might be necessary to stabilize the patient before transport to a facility with higher levels of expertise and specialty care.

Emergency Medical Services Activation

Activation of EMS for local and long-distance transportation should be accomplished as soon as possible. In some situations, it will benefit the patient to have advanced-level paramedics and nurses brought by aircraft to the scene so that early stabilization can be achieved, also providing for safer transport to a tertiary medical center for definitive care.

In communicating with medical control, the rescuer should provide a concise description of the patient, current set of vital signs, mechanism of injury or medical condition, neurologic findings, and the nearest location where EMS personnel can safely pick up the patient. If time permits, the secondary survey can be communicated to the online medical control officer, but this should not delay initiation of EMS dispatch. Patients with respiratory or hemodynamic instability, decreased level of consciousness, or open wounds of the head, neck, chest, or abdomen may require advanced treatment in the field or initial evaluation and

stabilization at a local emergency department (ED) before long-distance travel.[164]

UNIQUE INJURIES AND MEDICAL MANAGEMENT

Confined Spaces

The National Institute for Occupational Safety and Health (NIOSH) defines *confined space* as a "space with limited openings for entry and exit, with unfavorable natural ventilation that could contain or produce dangerous air contaminants, and that is not intended for continuous worker occupancy."[139] Manure pits and silos are dangerous, gas-containing, confined spaces that can generate hazardous levels of hydrogen sulfide (H_2S) and nitrogen dioxide (NO_2), respectively.[175] Methane (CH_4) and carbon dioxide (CO_2) concentrations can also reach toxic levels in manure storage facilities.

Specific gases accumulating in confined spaces can be categorized as simple asphyxiants or pulmonary irritants.[183] Simple asphyxiants, such as CO_2 and nitrogen, when present in high enough concentrations, produce toxicity by lowering the fraction of inspired oxygen (FIO_2), placing the exposed individual at risk of hypoxia. Pulmonary irritants represent a large group of noxious agents and produce severe irritation of the respiratory tract mucous membranes.[146] Clinical presentation of the patient from a confined-space accident frequently depends on the type of asphyxiant and severity of exposure.

Simple Asphyxiants

Manure Pits and Grain Bins. All mammalian life requires oxygen. Normal air is approximately 21% oxygen, 79% nitrogen, and 0.03% CO_2. The human response to lower levels of oxygen includes increased breathing and pulse rate, mild muscular incoordination (12% to 16% oxygen); emotional upset, abnormal fatigue on exertion, disturbed respiration (10% to 14%); nausea and vomiting, inability to move freely, loss of consciousness, collapse, and inability to move or cry out (6% to 10%). Less frequent symptoms are seizures and severe respiratory distress leading to full cardiopulmonary arrest (<6%).[148]

Fatalities caused by asphyxiation or poisoning associated with confined-space manure storage facilities are tragic. Manure pits and other confined-space storage structures are characterized by limited openings and ventilation, allowing for buildup of gases and placing workers at risk of asphyxiation. In one case series of 91 fatalities and 21 severe injuries resulting from livestock manure–related incidents, with more than 50% at dairy operations, 21% involved persons under age 16, with more than half occurring to persons conducting repair/maintenance activities on manure-handling equipment or attempting to rescue another person.[21]

Silos. A silo is a storage structure that holds harvested crops with moisture content of 50% to 65% for the purpose of fermentation and future use as feed (Figure 37-3). Usually, the entire plant has been harvested and chopped into segments up to several inches long before being placed in the storage structure to ferment. The two basic types of silos are upright and trench.

FIGURE 37-3 Grain silos. *(Courtesy Mark Brandenburg, MD.)*

FIGURE 37-4 Silo involved in a fatal explosion incident. *(Courtesy Centers for Disease Control and Prevention.)*

Upright, or tower, silos are cylindrical structures 6 to 9 m (20 to 30 feet) in diameter and up to 24 m (80 feet) tall. Forage is unloaded and blown into the silo by specialized equipment. The silage is later unloaded from the silo with another machine that removes the top layer from the silo and blows it down into a wagon or conveyor for delivery to livestock (Figure 37-4).

Oxygen-limiting, or airtight/sealed, silos are intended to provide an oxygen-deficient environment to enhance fermentation and allow convenient unloading of silage as it sloughs from the bottom of the feed column and then is removed by conveyor. There is little need for the farmer to enter an oxygen-limiting silo, except for maintenance and repair. Nonetheless, oxygen-limiting silos have been responsible for the asphyxiation deaths of many farmers as well as responding medical/fire rescue personnel.

Oxygen-limiting silos can explode during a fire, especially on initiation of firefighting activities. This results from sudden entry of outside, ambient oxygen into a carbon monoxide (CO)–rich environment, which creates a high-density, flammable, gaseous fuel. No person other than members of expert fire and EMS rescue crews should be anywhere near a silo fire. A variety of silo types and emergency situations require specialized training by rescue personnel.

Clinical Presentation. The on-scene presentation of an individual poisoned by a simple asphyxiant can range from mild symptoms of hypoxia (e.g., tachypnea, tachycardia, dyspnea) to more severe symptoms of ischemic brain injury (e.g., ataxia, dizziness, confusion, coma). Simply removing the patient from the toxic environment often results in dramatic clinical improvement. This indicates a milder, reversible condition. Failure to improve indicates the possibility of complications from hypoxia and ischemia, such as myocardial infarction, cerebrovascular accident, seizures, or coma, particularly in patients with risk factors for cardiovascular disease.

Carbon dioxide and pulmonary irritant gases can be present simultaneously within the same grain bin. Although grain bins are most often known to produce pulmonary irritant gases, simple asphyxiation can also occur in these confined spaces because of CO_2 excess during fermentation of stored, wet grain.

Differential Diagnosis. The patient presenting with tachycardia, tachypnea, and dyspnea who quickly recovers after being removed from the environment is more likely to have been exposed only to a simple asphyxiant. Difficulties in making a diagnosis can arise when a patient presents with ongoing symptoms of dyspnea, altered level of consciousness, or even coma.

For these patients, a broader differential diagnosis must be entertained to determine whether secondary medical conditions, such as cardiovascular complications or seizures, might exist. In these patients, eyewitness accounts of the immediate symptoms and signs experienced by the patient can be important for identification of the inciting agent.

Treatment. Patients exposed to a simple asphyxiant usually respond to removal from the exposure and administration of supplemental oxygen. All patients should be given oxygen and cardiorespiratory monitoring while symptomatic; otherwise, management of the exposed patient rarely requires specific therapy.

Fire departments and other emergency responders should be trained to recognize confined-space hazards on farms, understand associated dangers, know how to test air quality in a confined space, and have a pressure-demand supplied-air respirator with long air hose as part of the emergency equipment for silo rescues. For "immediately dangerous to life and health" (IDLH) atmospheres, this type of respirator must be equipped with a small cylinder of escape air.[148]

Self-contained breathing apparatus (SCBA) equipment may not be suitable for some silo rescues because the air tank can be too bulky for climbing the silo chute or outside ladder or for negotiating the inside of the silo. Wearing SCBA equipment is essential for all rescue personnel who enter a manure pit where a victim is lying down. Before entering a manure pit or silo, restoring ventilation to the structure as rapidly as possible enhances the likelihood of safe ingress/egress. Fire departments and other emergency responders should develop and implement a written respiratory protection program that complies with requirements of OSHA standards and General Industry Safety Standard, Part 74, Firefighting.[148]

Emergency rescue personnel should always wear a lifeline and harness and have an extra person with radio communication monitoring the rescue from outside the silo. The patient should be provided oxygen and then lifted from the ground, ideally with a backboard, to limit further irritant gas exposure.

Sequelae and Aftercare. The asymptomatic patient who previously experienced symptoms consistent with a simple asphyxiant, and who has normal vital signs, physical examination, and pulse oximetry, need not undergo further testing after receiving a brief period of observation.

Pulmonary Irritants (Manure Pits, Silos, Grain Bins)

A broad array of irritant gases, such as NO_2 (silos) and H_2S (manure pits), is produced on farms and ranches. The clinical presentation of pulmonary irritant toxicity depends in part on water solubility of the agent, which reacts with water to form a highly caustic acid (usually nitric or sulfuric acid). The more water soluble the agent, the quicker and more proximally in the body it will react with respiratory tract mucus and lacrimal moisture to incite symptoms of irritation (e.g., eyes, nasal mucosal, oral mucosal, pharyngeal, upper respiratory tract) in the patient.

When the acid-producing reaction occurs in the upper respiratory tract, there will generally be less alveolar injury but still possibly life-threatening laryngeal edema, or laryngeal spasm and bronchospasm. Agents with less water solubility travel a greater distance into the pulmonary tree before reacting with mucosal water molecules, resulting in delayed (2 to 24 hours) symptoms, and causing greater and more irreversible damage to alveoli and lung parenchyma. In addition, victims may remain in the toxic environment with ongoing exposure to water-insoluble irritant gases for a longer duration (Figure 37-5).

Manure Pits. Manure pits can produce H_2S, a colorless, poisonous gas. In low concentrations, the smell of sulfur (similar to rotten eggs) is sometimes noted; in higher concentrations, H_2S overwhelms the olfactory nerve such that the victim cannot smell the gas, and the gas can quickly kill nearby animals and humans. Detection of any dead animals, or animals dying or struggling in or around a manure pit, should prompt all individuals to evacuate the area immediately.

Silo Filler's Disease

Silo filler's disease results from acute pulmonary exposure to NO_2, a reddish brown gas with odor similar to that of household bleach. This toxic gas is produced by fermentation within hours of filling a farm silo with fresh, organic material, such as corn, grains, oats, alfalfa, and hay. NO_2 is heavier than air and may concentrate along the top of the silage or the floor of the silo entrance. Silage is a high-moisture product usually made from grass crops, sorghum, or corn by using the entire green plant in the fermentation process by silo storage. Silage is then used to feed cattle or sheep. After a silo is stocked with silage (usually September and October), NO_2 is released into the air, with maximum concentrations being reached in 1 to 2 days.

FIGURE 37-5 In-ground manure pit. *(Courtesy National Pork Board.)*

Clinical Presentation. Silo filler's disease usually occurs around harvest season in the months of September and October. Exposed individuals usually experience minor symptoms, such as eye irritation, cough, and nausea, but can have more serious symptoms, such as pulmonary edema, bronchiolitis obliterans, rapid asphyxiation, respiratory collapse, and death, within minutes when exposed to high concentrations.

The most common symptom is cough, but other symptoms, such as dyspnea, wheezing, nausea, lightheadedness, chest tightness, diaphoresis, and throat/eye irritation, are also common. Less frequent symptoms include myalgias, palpitations, hemoptysis, and cyanosis. These symptoms usually indicate acute exposure when the history is consistent; however, persistent or delayed symptoms can also occur for days or even weeks after a single exposure.

Examination of the patient with silo filler's disease may uncover predominantly pulmonary abnormalities, such as rales, rhonchi, wheezes, and decreased breath sounds. Hypotension can be a result of nitric oxide (NO) formation in the vascular system, which reduces systemic vascular resistance and causes vasodilation.[97] Cyanosis indicates either methemoglobinemia or hypoxemia. Hemoptysis indicates severe inflammatory reaction within the respiratory tract. Conjunctival injection (erythema) can be a sign of direct exposure to a highly water-soluble irritant gas.

Differential Diagnosis. Differentiating between simple and irritant gas exposure in a patient presenting with dyspnea relies on initial symptoms and signs. For example, a confined-space patient presenting with immediate burning and tearing of the eyes, nose, and mouth is likely to have been exposed to a highly water-soluble irritant gas typically found in grain silos and bins. Immediate dyspnea, tachycardia, and tachypnea are more consistent with simple asphyxia.

With general presenting symptoms, silo filler's disease has a broad differential diagnosis that includes asthma, chronic obstructive pulmonary disease (COPD), farmer's lung, hantavirus pulmonary syndrome, chemical pneumonitis, smoke inhalation, toxic organic dust syndrome, miliary tuberculosis, angina pectoris, myocardial infarction, infectious pneumonias of all types, pulmonary embolism, and pulmonary toxicity from a variety of noxious gases (e.g., CO, chlorine gas, H_2S, carbamate, phosgene, ozone, cyanide, organophosphate, salicylate).[97]

Diagnostic Tests. The patient who exhibits ongoing symptoms of irritant asphyxiation needs monitoring of vital signs,

pulse oximetry, and chest radiography. Persistent pulmonary symptoms of a sensation of burning in the airways, cough, or dyspnea mandate hospital admission. Evaluation for other entities can be undertaken as indicated. Arterial blood gas (ABG) monitoring might be required in the patient with hypoxemia. Persistent cyanosis not responding to oxygen therapy might indicate the presence of methemoglobinemia.

Treatment. Decontamination is necessary when the victim's clothing is contaminated with nitrogen oxides in solid or liquid form, which can secondarily contaminate others by direct contact or off-gassing.[5] Rescue personnel should have proper training and equipment before entering a "hot zone" where nitrogen oxides are a potential threat. Otherwise, assistance should be obtained from a regional hazardous materials (hazmat) team. Victims who can walk should be led away from the hot zone to the "decontamination zone" and asked to assist with their own decontamination. Victims exposed to N_2O gases should undergo decontamination procedures that assume clothing and skin have been exposed. The clothing and personal belongings of each victim should be collected and double-bagged. Water can be used to irrigate eyes (for at least 20 minutes) and wash the skin of contaminated victims.

Supportive care is indicated for the patient with severe respiratory symptoms. Patients exposed to pulmonary irritants usually require oxygen administration and sometimes β-agonist bronchodilator therapy, although the latter is not evidence based. Supportive care, such as suctioning and pulmonary toilet, is usually the mainstay treatment strategy.

Sequelae and Aftercare. Any evidence that the patient is experiencing pulmonary irritation (e.g., rales, wheezing, rhonchi) or respiratory distress (e.g., tachypnea, tachycardia, anxiety, dyspnea) should result in admission or transfer to a higher level of care. Hospitalization for minimum 12-hour observation is prudent, because the patient could experience rebound or worsening pulmonary symptoms.

Prevention. Forced ventilation into confined-space storage facilities can reduce concentrations of noxious gases to levels safe for human entry.[151] Educating agricultural workers about the mechanisms of work-related asphyxia and the symptoms and signs of toxicity will enable earlier recognition of exposure and should allow earlier escape (Box 37-1).

Grain Storage Bin Entrapment

Entrapment in bins containing loose agricultural material, usually corn or other grains, is a well-known cause of serious injury and fatality. More than 200 people have been killed and another 300 injured in the past 30 years as a result of grain suffocation. High-capacity augers are usually implicated in these accidents (Figure 37-6). Severe entrapment injuries and fatalities can occur when suspended materials or crusted surfaces of stored material suddenly break loose and collapse beneath the worker.[141] Crusting at the surface of stored grain, called *bridging*, is more likely to occur when moist grain is stored, typically in rainy harvest seasons. Moisture collects at the surface of the stacked grain and later dries, forming a crusty surface on which workers are tempted to walk. Bridged grain is extremely hazardous because it prevents grain flow and hides underlying pockets of air, which allow the surface to collapse (Figure 37-7).

Farm workers may also be buried by stored grain when it is emptied from the bottom of the bin. Flowing grain can very quickly pull an adult completely down and into the bin. Once the knees are covered by flowing grain, it is extremely difficult to free oneself without assistance.[27]

In a 2001 retrospective study, 16% of grain bin entrapment fatalities were children younger than 16, and 77% of fatalities involved unloading the bin at the time of injury.[100] Children should never be allowed in or around a grain bin, even when operation has ceased. The entrance to the grain bin should always be locked to exclude children. Injury prevention is key.

Clinical Presentation. A majority of grain bin entrapment injuries occur during the unloading process.[100] Suffocation occurs if an individual becomes caught in flowing grain and is pulled under. The victim inhales and swallows so much grain that

BOX 37-1 Safety Tips Regarding Silos, Grain Bins, and Manure Pits

To Prevent Asphyxiation

1. Never enter a confined space without doing the following:
   - Confirming sufficient oxygen
   - Verifying adequate ventilation
   - Posting a second person outside the area with whom you can communicate by sight, sound, or signal line
   - Wearing a safety harness attached to be able to hoist
2. Have rescue equipment (ropes, ladders, lifts) available in case someone is overcome by gas.
3. Wear one of the several types of masks and respirators available for use:
   - Dust-mask respirator
   - Dust mask
   - Half-face cartridge respirator
   - Self-contained breathing apparatus (SCBA)—for fire department and rescue personnel

Silos

1. Do not enter a silo for 4 to 6 weeks after filling; dangerous gases are produced as forage ferments during this time. Be aware that even after 6 weeks it may not be safe to enter a silo, and that SCBA-equipped respirators should be worn anytime you are entering full or partially full silos.
2. Before entering a silo, set up and run the blower to force air into the silo for at least 30 minutes to minimize the possibility that hazardous gases coalesce about the silage.
3. The blower should be left running while inside the silo.
4. Be alert for silo gas odors or yellowish-brown or reddish fumes in or near the silo. These gases are nitrogen oxides (pulmonary irritants).
5. If you must enter silos during the first 4 to 6 weeks after filling, or at the time the silo is full or partially full, wear an SCBA-equipped respirator. A regular respirator or dust mask will not protect you from an oxygen-deficient atmosphere.
6. Never enter a silo alone.
7. If you start coughing or experiencing throat irritation, remove yourself from the area immediately and seek medical attention.

Manure Pits

1. Never enter a manure pit unless you are wearing an SCBA respirator and a lifeline and harness.
2. Never enter a manure pit unless you are monitored by a standby person who is equipped and trained to rescue you.
3. Secure the end of your lifeline to the mechanical lifting equipment outside the pit. Mechanical lifting equipment should have a clutch that will prevent exerting excessive force on the person being retrieved.
4. Do not try to rescue someone from a manure pit unless you have been trained and are wearing the proper equipment. Call the local fire department or rescue squad immediately. They have the training and equipment necessary to accomplish such a rescue without endangering other lives.

Modified from Youth in Agriculture: Confined spaces, US Department of Agriculture, Occupational Safety and Health Administration. http://www.osha.gov/SLTC/youth/agriculture/confinedspaces.html.

FIGURE 37-6 Auger inside a grain silo. *(Courtesy of Mark Brandenburg, MD.)*

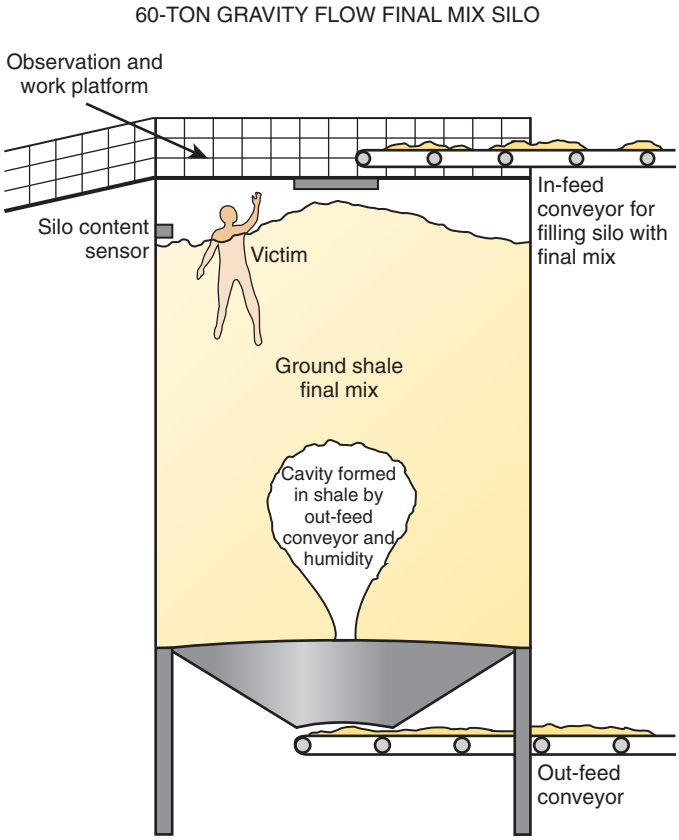

FIGURE 37-7 Sketch of silo involved in suffocation incident. *(Courtesy Centers for Disease Control and Prevention.)*

normal oxygenation cannot occur. Asphyxiation by chest wall restriction is another mechanism of death.

Diagnostic Tests. Other than pulse oximetry, diagnostic testing at the scene is generally not indicated. Persons who survive grain entrapment may have organic foreign bodies in the respiratory tract. Chest and soft tissue neck radiography might identify this material, although bronchoscopy is often necessary. Persons who suffer severe respiratory insufficiency might have acid-base disturbances best characterized by ABG and electrolyte analysis.

Grain Bin Rescue. If the victim is found before succumbing to hypoxia, there may be a lifesaving opportunity, so always assume an individual trapped in a grain bin is still alive. Emergency rescue personnel must be summoned immediately. Establishing that there are no toxic gases in the storage bin is the first priority at the accident scene. On entering the scene where a victim is submerged by grain, the bin aeration fans should be turned on to supply the patient additional oxygen and ventilate the area. Safe removal of grain from the bin in a rapid, orderly manner will help rescuers gain access to the victim. Grain removal requires training and expertise. On reaching the victim, removing grain from the airway and administering oxygen should be done immediately.

Sequelae and Aftercare. Depending on the degree of entrapment, chest wall compression and injury, and respiratory tract obstruction, the victim will require any duration of monitoring from several hours of observation to weeks in the hospital. On discharge, the patient should be advised to return if fever or respiratory symptoms occur. Foreign material in the pulmonary tree will eventually create a suppurative process that can become life threatening.

Hypersensitivity Pneumonitis

Hypersensitivity pneumonitis, also known as *farmer's lung* or *extrinsic allergic alveolitis,* involves terminal airways and is triggered by exposure to organic dust that consists of a large variety of particles of varying sizes and microbial cell wall components.[122] Thermophilic *Actinomyces* and *Aspergillus* are the more common antigens responsible for this pulmonary reaction.[205] Exposure to antigenic organisms in a wide variety of agricultural occupations can be responsible for hypersensitivity pneumonitis.

Contaminated hay, straw, and grain are the most common sources of antigen inhalation. When these crops are stored in moist environments, molds proliferate, allowing for aerosolization when the material is disturbed. The fine dust is inhaled into the lower respiratory system, where immune complexes damage distal bronchioles and alveoli. Dairy farmers and other cattle ranchers who handle large amounts of hay are at greatest risk in the winter months, when they are more likely to be around stored hay.

Clinical Presentation. Hypersensitivity pneumonitis can be acute, subacute, or chronic.[173] The acute form develops after exposure to high concentrations of contaminated hay or compost. Onset of fever, chills, cough, dyspnea, and chest pain usually occurs 4 to 8 hours after exposure to the antigen and may last for several days or longer if antigen exposure continues.[122] However, inhalation of very large amounts of the organic antigen can induce acute respiratory failure. The chronic form of this disease generally follows repeated exposure to the inciting antigen and can lead to irreversible lung damage and chronic dyspnea.[122]

Physical examination of the patient with acute disease reveals nonproductive cough, rales, fever, tachycardia, and rarely, wheezes. Patients with subacute and chronic farmer's lung can exhibit cough and rales, as well as weight loss, fatigue, clubbing, anorexia, and dyspnea.

Differential Diagnosis. A variety of pulmonary infections and aerosolized antigens can cause similar presentations. Organic dust toxic syndrome (ODTS), discussed next, results from inhaling the dust of feed and stored organic material. Acute symptoms of ODTS are identical to acute farmer's lung; however, ODTS is not allergic in nature, and most patients achieve complete recovery without irreversible pulmonary damage. Sarcoidosis, idiopathic pulmonary fibrosis, COPD, pulmonary embolism, and myocardial ischemia are more common general medical conditions with similar presenting symptoms and signs. Other agents that trigger similar pulmonary reactions include allergens, chemicals, toxic gases, and infectious agents.

Diagnostic Tests. Detailed environmental and occupational histories comprise the best diagnostic tool used to suspect hypersensitivity pneumonitis. Chest radiography may reveal diffuse consolidations (acute antigen exposure), nodular or reticulonodular changes (subacute disease), or fibrotic changes (chronic scarring) but is usually normal between acute episodes. Pulmonary function tests, peak-flow measurement, allergy skin tests, and serum radioallergosorbent testing for suspected hypersensitivity pneumonitis should all be considered when attempting to make the diagnosis. Sputum and blood cultures should be obtained when a zoonotic infection is suspected. If the diagnosis remains elusive, lung biopsy may be required.[107] High-resolution computed tomography (CT) scanning may reveal or rule out pulmonary fibrosis, pulmonary emboli, malignancy, and pneumonia. Referral to a pulmonologist is indicated if the diagnosis remains elusive.

Treatment. Early diagnosis and antigen avoidance are key actions in management of hypersensitivity pneumonitis. Primary treatment involves administration of systemic corticosteroids.[173] Severe and permanent damage to lung parenchyma can result from repeated exposure to the antigen.

Organic Dust Toxic Syndrome

Organic dust toxic syndrome, also known as *toxic alveolitis, inhalation fever,* or *pulmonary mycotoxosis,* is a common respiratory condition of farmers, with an estimated incidence of 6% to 8%.[13] ODTS results from inhaling high concentrations of bioaerosol components found in the dust of feed, seeds, and stored organic material.[118] Inhalation of organic dust laden with microorganisms, such as fungal spores, molds, bacteria and endotoxins, and resultant inflammation are believed to be the pathogenesis of ODTS.[200] Pig farmers, particularly those who use wood shavings as bedding in hog barns, are at particular risk.[199]

Clinical Presentation. ODTS is characterized by fever occurring 4 to 12 hours after exposure, along with general weakness, dyspnea, headache, chills, body aches, and cough.[138] Physical examination, lung auscultation, and chest radiography are usually normal. Lower respiratory system illness, such as reactive airway symptoms, dyspnea, and chest tightness, are consistent with ODTS.

Differential Diagnosis. Similar clinical presentations include acute bronchitis, farmer's lung, influenza, and mild pneumonia.

Diagnostic Tests. No specific diagnostic test is required to make this diagnosis, although chest x-ray film is often performed and found to be normal. Taking an accurate and thorough history of occupational exposures, in addition to physical examination, is usually adequate to make the diagnosis.

Treatment and Prevention. There is no specific therapy for ODTS other than supportive care. However, prevention of future episodes can be successful by having the farmer properly use an N-95 respirator (readily available in hardware stores).

Sequelae and Aftercare. The symptoms of ODTS usually subside within 24 to 72 hours, but can last 5 to 7 days.[118] Recurrence is possible if the farmer sustains repeated exposure to the inciting organic dust.

Lacerations

General wound care is covered in Chapter 21, but there are environmentally specific management enhancements to consider when treating acute, open wounds that might have soil and range-animal fecal contamination. Extra attention to thorough wound cleaning is essential when managing open wounds occurring in the farm or ranch setting. Very few data-driven guidelines exist for use of prophylactic antibiotics in management of contaminated wounds;[71] in principle, however, use of prophylactic antibiotics should match the pathogens most likely to cause wound infections in the same setting. It is well known that open wounds from the agricultural setting can become infected with aerobic, anaerobic, and fungal organisms.[8] The most common bacterial infections are noted in the Differential Diagnosis discussion later. Clinical syndromes are produced by wound infections with *Clostridium tetani* and *C. botulinum,* both of which are toxin-producing, anaerobic, spore-bearing, gram-positive bacteria.[20]

Clinical Presentation. The clinical presentation of patients with contaminated wounds will often be self-evident on examination, but a thorough history is required to gain a full appreciation of the circumstances in which the patient was injured, including the potential for soil and fecal contamination.

Patients with wound infections or cellulitis usually present with the typical symptoms of wound inflammation, purulent drainage, and sometimes fever. Evaluation for fasciitis and osteomyelitis often requires closer scrutiny for history and physical examination findings consistent with deep tissue infections. Subcutaneous crepitus around the wound can sometimes be palpated in patients with anaerobic bacterial soft tissue infections. Osteomyelitis often presents in patients with nonhealing wound infections; patients with vascular disease or a compromised immune system are particularly at risk.

Localized tetanus is underdiagnosed and may present as fixed muscle contractions lasting for weeks. Cephalic tetanus occurs most often in patients with head and neck wounds and is named for its common physical findings of trismus, dysphagia, and other focal cranial neuropathies.[20] Although rare in the United States, cephalic tetanus has worldwide incidence of approximately 250,000 cases annually, occurring most frequently in neonates. Botulism is characterized by symmetric, descending paresis or paralysis, often presenting with acute, bilateral cranial neuropathies. Infant botulism often presents with upper airway obstruction, general weakness, and feeding difficulties.[20]

Differential Diagnosis. A contaminated farm wound that has developed infection deserves a broader microbiologic differential diagnosis than do ordinary wounds. Aerobic bacteria in these wounds, based on wound infection studies, may include coagulase-negative *Staphylococcus, Enterobacter, Stenotrophomonas, Pseudomonas,* and *Serratia* spp. Anaerobic bacteria are often *Clostridium perfringens, Peptostreptococcus,* and *Propionibacterium*.[20]

Diagnostic Tests. In addition to following standard wound care principles, the clinician should consider obtaining plain radiographs to assess for open fractures. If wound infection develops, plain radiography can identify subcutaneous gas, often found with deep tissue infections caused by anaerobic bacteria, whereas CT has greater sensitivity in detecting subcutaneous gas.

Treatment and Prevention. Any wound contaminated with soil from a horse or cow pasture should be managed with appropriate, sufficiently high-pressure irrigation using sterile water or saline solution, and removal of foreign matter found within the wound. Tap water should be used if sterile irrigant is not available. The decision about whether a patient should be managed in the operating room (OR) or the ED or office setting should be based on the characteristics of the patient and injuries, such as length and complexity of wound, degree of contamination, vascularity of the surrounding tissue, timeliness of presentation for treatment, immunocompetence, and likelihood of compliance. Tetanus prophylaxis should always be given when indicated.

A small collection of evidence-based research on the efficacy of antibiotic prophylaxis in patients with contaminated open fractures is found in the orthopedic surgery literature. Current guidelines for minor open fractures include coverage for common gram-positive bacteria and for wounds exposed to soil or range-animal feces (e.g., animal pastures, rodeo arenas, horse stalls), in addition to gram-negative and anaerobic bacterial species.[68,196] *Clostridium* is the particular anaerobe of concern, against which high-dose intravenous (IV) penicillin, 10 to 40 million international units (IU) daily, is recommended for administration no longer than 24 hours after closure of open fractures.[71] A single IV dose (adult, 8 to 12 million IU; pediatric, 200,000 IU/kg) can suffice when fracture does not coexist with the wound.[67]

Sequelae and Aftercare. Close follow-up of the patient with a contaminated wound from the ranch or farm should be occur no later than 72 hours after initial treatment, or earlier if infection is suspected.

FARM EQUIPMENT

The majority of farm equipment–related injuries involve tractors and combines but may involve augers, balers, power takeoffs, feeders, and grinders,[98] as well as the popular all-terrain vehicle.

All-Terrain Vehicles

All-terrain vehicles (ATVs) are very popular in the United States. They are marketed and advertised for off-road travel and are used for recreation and competition racing and as work tools on the ranch. Size, power, and ruggedness of these vehicles make them very useful, but riding them is a high-risk activity. One study showed that 35% of ATV crashes occur on farms and ranches.[35] The impact force of these vehicles during a rollover event leads to severe head, face, and torso crush injuries, in addition to orthopedic injuries.

During the 1980s, researchers found ATVs to be quite dangerous to operators. In 1988, the U.S. Consumer Product Safety Commission and ATV industry agreed to cease manufacturing three-wheeled ATVs (but not four-wheeled ATVs) in a consent decree negotiated in Federal District Court.[192,195] Since that time, only four-wheeled ATVs have been manufactured and sold to consumers; however, residual three-wheeled ATVs are still in operation. In the years during this consent decree, U.S. consumers continued to be at great risk of injury while riding ATVs.[90,113,117]

In 1998, the consent decree expired, and ATV manufacturers began increasing speed, power, and size of ATVs. In 1998, there were approximately 4 million ATVs in use in the United States,[192] and by 2003, approximately 7 million.[171] Since 2003, the ATV industry has increased production of large-engine ATVs threefold. Some ATVs can attain speeds of up to 55 miles/hr (88 km/hr) and weigh 800 lb (360 kg). Advertising for these vehicles

increased greatly after 1997; concurrently, the Consumer Product Safety Commission (CPSC) reported a significant increase in ATV-related injuries.[171,194] As of December 31, 2012, CPSC staff received reports of 12,391 ATV-related fatalities occurring between 1982 and 2012.[187]

It is widely accepted among experts that children are in extreme danger when riding ATVs.[9,10,39,59,94,163,176] Children under age 16 years are disproportionately injured and killed.[194] Children younger than 16 represent only 14% of all ATV riders but continue to account for up to 47% of ATV-related injuries.[192] Despite these alarming statistics, popularity of this activity among children is increasing.[26] The most common types of ATV-related injuries are soft tissue injuries, extremity fractures, and head injuries,[39] with 38% of children requiring surgery for their injuries in one study, and 69% of children requiring either an orthopedic procedure (40%) or a general surgical procedure (29%).[113] Approximately 50% of ATV-injured patients sustain head injuries.[4] In children, approximately 25% to 35% of ATV-related injuries involve brain and/or spinal cord injury.[59,120] In one study, during an 11-year period, 45% of ATV-related fatalities due to central nervous system injuries were in children under 16 years of age.[35] In response to these disturbing statistics, professional pediatric and orthopedic organizations have been urging parents not to let children operate four-wheeled ATVs.[3,7,9,10]

Risk factors associated with ATV morbidity and mortality include lack of ATV safety training, inadequate driver experience, young age, vehicle characteristics, and lack of protective headgear.[64,159,160] The risk for ATV-related injury is greatest among children younger than 16, males, riders of three-wheeled ATVs, and inexperienced riders; additionally, the risk of injury increases substantially as the ATV engine size increases, especially for three-wheeled ATVs.[160]

Prevention. Studies in both Canada and the United States have concluded that wearing protective headgear can significantly decrease mortality and resulting head injuries in ATV crashes.[30,150] Using ATVs with the minimum cubic-centimeter motor should diminish the likelihood of high-speed impacts and rollover crashes. Unfortunately, helmet use by ATV riders is not universal, and unsafe riding practices remain common in North America, prompting strong position statements for legislation that would mandate safety training and age requirements for young riders.[208]

Given the large percentage of ATV injuries resulting from rollovers, consideration must be given to the possibility that some ATV models might be predisposed to roll. Significantly higher incidences of backward and rightward rollovers indicate that nonrandom factors are likely involved; these factors might be subject to modification. Modifiable factors include vehicle speed when traveling uphill or turning, vehicle center of gravity, and change of center of gravity with passengers of specific weight and height. Rollover proclivity studies could be used to assist manufacturers in designing safer ATV models.

Tractors

Tractors are associated with tens of thousands of injuries annually in North America and are the principal source of fatal injuries on U.S. and Canadian farms.[66,131] Severe injuries result from agricultural tractor run-over accidents and traffic collisions.[131,152,155] Tractor turnovers are the leading cause of agricultural-related occupational deaths in the United States. The direction of a tractor rollover depends on the terrain. Sideways rollovers are more likely when driving across a slope or at the edge of a ditch bordering a roadway; backwards rollovers occur when the tractor is driven up an incline, towing or extracting stuck machines, pulling stumps or trees, or towing implements or logs.[66] Farmers age 55 and older have been identified as having a higher risk of severe injuries from tractor rollover.[132]

Clinical Presentation. Significant differences do not exist between tractor rollover injuries and other injuries involving similar dynamic forces. These include pelvic, rib, and long-bone fractures and pneumothoraces. There might be increased possibility of gram-negative and anaerobic bacterial infections resulting from wounds contaminated by soil and animal feces. Tractor overturn injuries also include chemical burns from fluids that leak from a hot radiator, hydraulic system, or battery.[112]

Rescue. Rural rescue and EMS personnel should have specific training for care of tractor accident victims, beginning with safe extrication at the scene. At the minimum, basic mechanical knowledge of tractors is required in order for rescue personnel to fully disengage a running tractor engine.

Treatment. One unique complication is potential for wound contamination with soil and livestock fecal material, increasing potential for gram-negative and anaerobic wound infections. This concern should prompt the physician to consider high-pressure pulse irrigation in the OR as well as broad-spectrum prophylactic antibiotics when dealing with complex soft tissue and orthopedic wounds.

Prevention. Along with proper maintenance and operation of the tractor, using rollover protective structures (ROPS) and seat belts is the best method for preventing these injuries. First introduced by tractor designers in 1966, the heavy steel ROPS frame mounted to the rear axle and tractor frame is designed to prevent a complete rollover and to support the weight of the tractor in the event of a rollover. Without this protective equipment, the driver of the tractor that rolls over is at great risk of being crushed (Figure 37-8).

Improper hitching of tractors to other equipment can cause tractors suddenly to flip backward, resulting in severe injuries or death. Specific steps for preventing these accidents have been recommended, as follows[137]:

1. Use farm tractors equipped with ROPS, and wear a safety belt.
2. Be familiar with safe use of the equipment.
3. Select a strong tow chain with a length sufficient to allow adequate stopping distance between the towed object and the towing vehicle, to avoid collision and rear rollover.
4. Ensure a cleared work area for maneuvering.
5. Use slow, steady pull.
6. When using a tractor to free an embedded vehicle, hitch the vehicles front-to-front and drive the towing tractor in reverse to minimize the risk of rollover.
7. Carefully select a hitching point to the tractor.
   - Do not alter the drawbar by raising or shortening it.
   - Never attach the load directly to the axle.
   - Never use a two- or three-point hitch as a single-point hitch instead of the drawbar.
   - If the load attaches by a single point, attach it only to the drawbar.

Drivelines, Augers, and Power Takeoffs

Combines, augers, corn pickers, and other grain-harvesting machines have many moving parts that can be lethal to a person interacting with this equipment while in operation. The rotating mechanical shaft with two or more universal joints and splined couplings is called a *power takeoff* (PTO) and has been standard equipment on tractors for several decades. The PTO driveline is

FIGURE 37-8 Tractor with rollover protection structure (ROPS). *(Courtesy Mark Brandenburg, MD.)*

FIGURE 37-9 Auger with shielding. *(Courtesy Mark Brandenburg, MD.)*

the most common means of transferring power from a tractor to towed machinery and stationary equipment (Figures 37-9 and 37-10). Driveline accidents result from clothing entanglement in the rotating shaft that rapidly and violently draws in the body part.[186] These incidents often result in catastrophic injuries such as amputation, spinal cord injuries, compound fractures, and disruption of ligaments and musculotendinous units.

Equipment manufacturers install shielding devices to protect operators and bystanders from coming into contact with PTO components. Still, agricultural equipment driveline-related incidents represent a significant cause of farm-related injury resulting in death or disability. Male youths, with 13-year-olds having the highest frequency of accidents, represent greater than 50% of all patients injured by agricultural drivelines.[22] Lighter clothing materials, such as cotton thread, and loosely fitted clothing have higher probabilities of becoming entangled in a PTO driveline.[76]

Clinical Presentation. These injuries are often devastating to soft tissues of the upper limb caught in the rotating, mechanical shaft of the PTO. Deep, stellate and spiral lacerations with partial or complete distal extremity degloving often result.

Treatment. These wounds should be considered contaminated with soil and petroleum lubricant and highly suspect for foreign bodies such as clothing fibers and organic material, including livestock feces, that may have been on the clothing of the patient or on the equipment.

Sequelae and Aftercare. Although large prospective studies have not been conducted regarding management of PTO injuries, it is reasonable to anticipate that surgical care will be necessary. Broad-spectrum prophylactic antibiotics with anaerobic coverage are helpful to prevent severe wound infections during the postoperative period.

Prevention. Evidence suggests that an alternative mechanism using fluid power to drive a tractor PTO would diminish the risk in terms of frequency and severity of these injuries.[186]

FIGURE 37-10 Tractor power takeoff. *(Courtesy Mark Brandenburg, MD.)*

FIGURE 37-11 Chemical sprayer. *(Courtesy Mark Brandenburg, MD.)*

FARM SUPPLIES

Chemicals

Modern farms and ranches often utilize a wide variety of industrial-strength chemicals (Figure 37-11). Seasonal release of hazardous substances in the agricultural setting indicates a strong association with the planting operation.

Fertilizer

Anhydrous Ammonia. Anhydrous ammonia is a widely used source of nitrogen fertilizer and is one of the most dangerous chemicals used in agriculture. Ammonia is the chemical most frequently implicated in farming accidents, resulting in respiratory, ocular, and traumatic injuries. Compressed into a liquid state, ammonia can be stored in specially designed, pressurized tanks. Once released into the air or soil at room temperature, ammonia enters the gaseous state as a colorless, highly irritating gas with a pungent, suffocating odor, although it can also first create an ammonia cloud with a white, opaque appearance.[119] When ammonia gas reacts with mucous membrane moisture, it forms a strongly alkaline solution, ammonium hydroxide.[96]

Clinical Presentation. Ammonia in any form can be caustic to body tissues. Severe eye irritation can lead to rapid and permanent loss of vision. Higher concentrations in the gaseous phase can cause severe burns to the respiratory tract.

Differential Diagnosis. History of an obvious exposure to ammonia often accompanies the patient; however, lack of such information may prompt the clinician to consider other causes, such as acute respiratory distress syndrome, anaphylaxis, other toxic inhalations, reactive airway disease, and chemical exposures to the skin.

Diagnostic Tests. Cardiac and respiratory monitoring and ABGs are necessary in patients who have suffered acute inhalation and severe respiratory distress or failure. Chest radiography may reveal interstitial infiltrates but can also be normal during early stages of exposure-induced respiratory distress. Bronchoscopy is sometimes required to assess severity of injury. In the event of ocular injury, slit-lamp examination with fluorescein staining and conjunctival pH measurement provide assessment of corneal epithelial injury and need for further irrigation.

Treatment. Immediate removal of the victim from the environment of inhalation exposure should be performed by an experienced team of rescue personnel. All contaminated clothing should be removed and then large volumes of cool water used to irrigate the skin and eyes for a minimum of 15 minutes.[6] If the victim has become unresponsive, standard cardiopulmonary resuscitation (CPR) can be administered, with precautions for secondary exposure taken by those in immediate contact with the patient.

In the event of acute bronchospasm, bronchodilator therapy with β_2-adrenergic agonists can provide immediate relief to the patient. Oxygen therapy remains critical for acute management of any patient in respiratory distress from inhalation exposure.

Sequelae and Aftercare. Any patient showing persistent signs of ammonia exposure should be admitted to the hospital and observed for at least 24 hours. Patients exposed to small

amounts of household ammonia generally have very mild symptoms and can be safely discharged once they are asymptomatic.

Prevention. The most common causes of toxic ammonia exposure are equipment failure and operator error.[24] When working with anhydrous ammonia, always have clean water available for decontamination. Always use heavy-duty protective clothing, rubber gloves, and goggles and a face mask when working with anhydrous ammonia. Never fill a tank beyond 85% liquid capacity. Never wear contact lenses when working with ammonia; the chemical might get under the lenses and cause permanent eye damage.[6] Keep a safe distance and stand upwind from valve and hose openings when transferring liquid ammonia. Use caution when hauling an ammonia tank behind a motorized vehicle.

Pesticides

The term *pesticide* is generic and represents a category of various chemicals intended for use as insecticides, herbicides, rodenticides, fungicides, and fumigants.[1] Most of these agents are found on typical American farms and ranches, and occupational toxicity can occur through a wide variety of mechanisms because of the broad array of applications in which pesticides are used in the agricultural setting.[62] Respiratory, gastrointestinal (GI), allergic, and neurologic symptoms are known to occur in acute pesticide exposure poisoning.[53] The Environmental Protection Agency (EPA) estimates that 10,000 to 20,000 physician-diagnosed pesticide poisonings occur annually in U.S. agricultural workers.[74] In 2008, pesticides were the ninth most common substance reported to poison control centers, and approximately 45% of all reports of pesticide poisoning were for children.[161] General principles of toxicity of the most common agents and early clinical management are described here.

Herbicides

Glyphosate. Glyphosate, commercially known and available as Roundup, is a nonselective herbicide manufactured by Monsanto Agricultural Company (St Louis, Missouri). The primary active chemical is a non–cholinesterase-inhibiting organophosphate agent used to control broad-leaf weeds in both residential and commercial markets.

Clinical Presentation. Ingestion of glyphosate, often by children, is the usual route of toxicity and leads to GI illness. Milder symptoms of nausea, vomiting, and diarrhea result from the typical small ingestions. Patients who ingest larger quantities or industrial-strength concentrations of glyphosate are more likely to have abdominal pain, respiratory distress, noncardiogenic pulmonary edema, dysrhythmias, cardiovascular shock, and coma.

Diagnostic Tests. Early recognition of lactic acidosis and respiratory compromise allow the health care provider to manage the patient more aggressively.

Treatment. The mainstay of treatment is supportive care. Intubation and ventilatory support are sometimes required to prevent aspiration pneumonitis and provide adequate oxygenation in the face of noncardiogenic pulmonary edema.

Sequelae and Aftercare. The person who ingests only a small amount of a relatively dilute formulation of glyphosate may be observed and discharged after 6 hours if symptoms have resolved completely. Persistent pain in the throat or chest can indicate corrosive esophagitis, requiring admission and evaluation by a gastroenterologist. Ongoing supportive management is required for patients with respiratory or hemodynamic compromise.

Insecticides

Organophosphates and Carbamates. Organophosphate and carbamate insecticides are two classes of acetylcholinesterase inhibitors with identical signs and symptoms of toxicity, the notable exception being a much shorter duration of illness with the carbamates.

Pharmacology. Organophosphates and carbamates are highly lipid soluble and therefore easily and quickly absorbed into the body by dermal, respiratory, and GI systems. Storage of these compounds in adipose tissue allows for delayed or long-term toxicity from chronic, low-dose exposure.

The mechanism of toxicity is enzymatic inactivation of the ubiquitous neurotransmitter acetylcholine. The primary difference between organophosphates and carbamates is a much longer duration of symptomatology with organophosphates, resulting from irreversible acetylcholinesterase inactivation. Carbamate-induced acetylcholinesterase inactivation is reversible, often self-limited, and generally responsive to antidotal therapy.

Clinical Presentation. Inactivation of acetylcholinesterase at neurotransmitter receptors results in accumulation of excessive acetylcholine, which promulgates excessive activity at the neuromuscular junction. The clinical, syndromic manifestation of this abnormal synaptic activity is described by the mnemonic DUMBELS (defecation, urination, muscle weakness, bradycardia, bronchorrhea, bronchospasm, emesis, lacrimation, salivation). Other physical examination findings in severely poisoned patients can include pupillary miosis, bradycardia, and seizures.

Management. Identification of this constellation of symptoms and signs in a patient from a ranch or farm environment where insecticides are used is virtually pathognomonic for organophosphate or carbamate poisoning.

Decontamination procedures should be instituted immediately on recognition of toxicity for the sake of both patient and emergency responder. Gross contamination of the patient or environment can result in poisoning of rescue personnel and health care workers. Removal of clothing and washing of the skin when dermal exposure has occurred is generally sufficient to prevent contamination of others. GI decontamination is not useful, because the poisoned patient will usually have vomiting and diarrhea. Supportive care is first focused on airway and breathing, with orotracheal intubation sometimes required to prevent aspiration and provide adequate oxygen. Agitation and seizures can occur, and diazepam is a first-line therapy for either of these.[104]

Antidotes. Eventual recovery of the poisoned patient depends on reaccumulation of acetylcholinesterase at synaptic junctions throughout the body, resulting either from reversing the enzymatic inactivation or resupplying newly formed enzyme. Symptomatic improvement can be elicited by administration of atropine. Very large doses of atropine administered intravenously (IV) are sometimes required, with the optimum dosing, 0.6- to 3-mg boluses, depending on severity of toxicity.[25] An atropine infusion can next be initiated with the aim to restore and maintain cardiorespiratory function and treat the symptoms of toxicity.

Another pharmaceutical treatment for organophosphate poisoning (but not carbamate poisoning) is pralidoxime (2-PAM, Protopam), which brings about dissociation of the organophosphate-acetylcholinesterase complex, allowing enzyme reactivation. The recommended starting dose of pralidoxime is 1 to 2 g IV (pediatric dose, 25 to 50 mg/kg IV, up to 1 g). Subsequent doses and infusions of both medications can be given depending on the clinical picture.

Sequelae and Aftercare. Most persons with symptoms of acetylcholinesterase inhibition require hospital admission for ongoing treatment, supportive care, and observation. Rebound toxicity several days after initial symptomatic improvement should be anticipated in patients with acute exposure.

Pyrethroid Pesticides

Pyrethrins are naturally occurring chemicals produced by the yellow *Chrysanthemum cinerariifolium* and *Tanacetum cinerariifolium* flowers. Synthetic derivatives of pyrethrins known as pyrethroids are produced in mass quantities for use in commercially available insecticides. Pyrethroids have greater chemical stability and can be much more toxic and dangerous to humans than pyrethrins. Pyrethroid insecticides act on the afferent nerve fibers of both insects and higher animals, caused by transient increase in sodium permeability of the nerve membrane during excitation. This action results in relatively short bursts of repetitive sensory nerve impulses.[207]

Clinical Presentation. Manifestations of toxicity depend on route of exposure, with inhalation being the most common, and may result from using pyrethroid-containing aerosols in poorly ventilated spaces. Large applications of pyrethroid insecticides in farm fields can create airborne clouds capable of drifting into neighboring fields, where unsuspecting workers are vulnerable

to exposure.[52] Pyrethroid exposure of oral and upper respiratory mucous membranes can induce lacrimation, rhinorrhea, sneezing, and laryngeal edema. The lower respiratory tract is also susceptible to the inflammatory effects of pyrethroids, usually manifested as coughing, wheezing, dyspnea, and chest pain.

Dermal toxicity can include contact dermatitis, allergic dermatitis, and photosensitivity reactions. General neurologic syndromes resulting from severe exposure can include nonspecific symptoms of headaches and malaise; paresthesias and seizures have also been documented.[157,179]

Diagnostic Tests. There are no known methods of testing or laboratory monitoring for toxicologic exposure to pyrethroids.

Treatment. All patients believed to have the toxicologic effects of pyrethroids should be considered for dermal decontamination, including clothing removal and thorough washing of skin with soap and water. Supportive care for respiratory and neurologic symptoms is the primary management strategy. The prognosis of acute, occupational poisonings from pyrethroids is usually good, without chronic or long-term consequences.[208]

RODEO MEDICINE

HISTORY AND PERSPECTIVE

"Rodeo" originated from early Spanish settlers in California and is a Spanish word meaning "roundup."[170] Rodeo has a long history in America, with the first modern rodeo emerging in 1888 in Prescott, Arizona. American rodeo events evolved from the cowboy skills commonly employed on ranches. Skills such as roping, wild bronc riding, steer wrestling, and horseback agility were all valuable to the working ranch in early American history. In modern rodeo, competitors come from a more varied background and may belong to three categories: a rodeo competitor, urban cowboy, or rancher.[149]

Major rodeo events include bareback riding, saddle bronc riding, steer wrestling, tie-down roping, team roping, ladies' barrel racing, and bull riding (Figure 37-12). The United States has the largest number of professional rodeos, bull ridings, and cowboys in the world. Canada has the closest professional rodeo links to the United States, and Mexico, Brazil, Australia, and New Zealand all have bull ridings and bull riders striving to reach the pinnacle in rodeo by competing in Professional Rodeo Cowboys Association (PRCA) events throughout the United States. The world's best cowboys participate in the National Finals Rodeo (NFR) every year. The world's best bull riders participate in Professional Bull Riders events across the United States, the finals of which are held every year.

Rodeo athletes often compete and then pack up gear and horse(s) and immediately travel to distant locations, competing in three to five rodeos in as many afternoons. It is not a coincidence that rodeo's busiest season (June through August) in North America is the time at which seasonal ranch and farm work subsides. When the crops are growing and calving and branding season has passed, many cowboys and cowgirls find time to hit the road for competitions.

FIGURE 37-12 Bull rider thrown from a bull, striking his face against the ground. *(Courtesy Mark Brandenburg, MD.)*

The time commitment involved with farming and ranching, especially when combined with rodeo, makes on-site, medical care for rodeo athletes an important component of rural health care. On-site health care providers are typically local volunteers and may also be part of a larger team, such as the Justin Sportsmedicine Team. Health care providers (e.g., physicians, athletic therapists/trainers, chiropractors) provide treatment for injuries, offer suggestions to help mitigate risks specific to rodeo events, and facilitate rodeo athletes' wide-ranging travel, work, and competition goals.

HEALTH CARE PROVIDERS AND MEDICAL COVERAGE AT RODEOS

Since the inception of organized rodeo medicine in the early 1980s, there has been commitment and fellowship among these medical professionals, and a willingness to coordinate care for the injured cowboys and cowgirls. Providing adequate care to the athletes who travel across the continent to compete is a challenge to organizations devoted to the practice of rodeo medicine. The Justin Sportsmedicine Team was the first to provide care at rodeos; the International Pro Rodeo Association and Canadian Professional Rodeo Association followed their model of care and delivery of service.

Justin Sportsmedicine Team

In 1980, Dr. J. Pat Evans and Don Andrews envisioned a nationwide network of clinics, medical centers, physicians, and athletic trainers dedicated to bringing quality health care to rodeo athletes. The vision became reality in 1981 through the late John Justin of the Justin Boot Company (Fort Worth, Texas). The Justin Sportsmedicine Team (JST), consisting of a fully equipped truck and trailer, became the first mobile rodeo sports medicine facility in North America, appearing first at the 1982 NFR. The following year, the Justin Team traveled 50,000 miles to 25 major rodeos serving 1500 cowboys. The JST now has three mobile centers serving approximately 130 PRCA rodeos (600 performances) and 50 professional bull ridings annually.[99] More than 6000 athletes are treated by these experts every year (>$1.5 million of free service). The extensive injury prevention program serves these rodeo athletes well. The JST staff has traveled more than 2 million miles providing sports medicine coverage at more than 2400 PRCA rodeos and cared for more than 120,000 professional rodeo athletes.[99]

In 1983 in Canada, Dexter Nelson, a certified athletic therapist, and Don Johansen, a Canadian Champion bull rider, created the first organized rodeo sport medicine program. In 1984, Dale Butterwick joined Nelson to expand and grow the program to include athletic therapists, massage therapists, chiropractors, sport medicine physicians, and orthopedic surgeons, working together to serve cowboys injured in rodeo and bull ridings throughout Canada. The Canadian Pro Rodeo Sport Medicine Team provides rodeo medicine services to approximately100 rodeo and bull-riding performances across Canada each year. This coverage leads to medical referral, treatment, and follow-up services to injured rodeo cowboys and cowgirls.[49]

In the eastern half of the United States, the International Pro Rodeo Association (IPRA) is the predominant professional rodeo circuit. In 1988, Dr. Robert Nebergall and Justin Laird, Athletic Trainer (Certified), in Tulsa, Oklahoma, established a rodeo medicine team to serve injured athletes from this rodeo circuit. Dr. Nebergall's legacy continues with a team of athletic trainers, chiropractors, massage therapists, emergency physicians, and orthopedic surgeons who continue to provide on-site and follow-up orthopedic care for injured rodeo athletes from the IPRA.

The founders of the Professional Bull Riders (PBR), Inc. (1994) asked the Justin Boot Company to provide medical coverage through the JST in the early years. Currently, the PBR has a medical director and is staffed full-time by a certified athletic trainer. Both travel with the Ford Built Tough level of competition. There is a tiered system whereby the Ford Built Tough

Series is the top tier, and lower-tiered events feed the upper tier. Medical coverage at the lower tiers is not as well organized as that for the upper tier.

Individual physicians, surgeons, athletic therapists/trainer, and chiropractors who are members of the JST and the Canadian Pro Rodeo Sport Medicine Team and IRPA medical personnel have been a significant source of data collection and research specific to rodeo injuries. Many of these individuals (and more) are part of an international database of rodeo medicine providers available online to assist health care professionals and rodeo athletes in locating the correct health care providers for an athlete in a particular region of North America.[38]

The JST runs an annual rodeo medicine conference at the NFR, where volunteers and medical staff come together to discuss rodeo injury management and prevention strategies. The first international meeting that brought all rodeo medical associations together resulted in an agreement statement on head injuries.[46]

EPIDEMIOLOGY OF RODEO INJURY

Rodeo injuries can be considered catastrophic or noncatastrophic. Butterwick and colleagues[47] were the first to study the impact of catastrophic injuries in rodeo while establishing an international Rodeo Catastrophic Injury Registry at the University of Calgary in 2006. *Catastrophic* injuries were defined as fatal, nonfatal, and serious. The majority of injuries in rodeo are *noncatastrophic*, including simple musculoskeletal injuries, cuts, abrasions, and minor concussions, all of which are important to address. The mission of this worldwide registry is to collect and analyze catastrophic and severe injury incidents specific to rodeo and bull-riding participation. Such rodeo data have never been collected; the registry is designed to accept incidents retrospectively or prospectively. These data help to identify factors that may be modifiable, with the goal of making these athletic events less dangerous. Cases can be reported online at www.rodeoresearch.ca.

The rate of catastrophic injury incidence was categorized into two time frame: 1989 to 2009, with 9.45 per 100,000, and 2007 to 2009, with 19.81 per 100,000.[47] Thirteen of 49 catastrophic injuries were in competitors under age 17. Seven of the 21 deaths in this data set were also younger athletes (≤17 years old). Twelve of 21 fatalities (57%) involved a mechanism of injury that included contact between the competitor and the livestock in the chest, thorax, or abdomen. Five of the 21 fatalities (~24%) died from head injuries, and none was wearing protective headgear at the time. Rough stock events (steer riding, junior bull riding, bull riding, bareback riding, saddle bronc riding) accounted for almost 94% of the catastrophic injuries reported during this period.[47] Livingston and associates[115] published hospital data that supported many of Butterwick's conclusions.[47] Most serious injuries resulted from contact with an animal, particularly being trampled or kicked by a bull.

Protective gear is recommended, but design, development, and research associated with it is still in an early stage. For example, many of the rodeo governing bodies either recommend or require protective vests to be worn.[50,153] There are some estimates that 40% of competitors use protective gear.[70] However, the effectiveness of vests as currently designed is unclear.[47] In fact, 11 of 21 fatalities had injury to the abdomen, chest, or thorax at anatomic locations where competitors were wearing vests (thus questioning their effectiveness). Protective vests are typically made of a leather outer with a combination of Kevlar, foam, and/or plastic inside the leather. The positive aspect of this design is that those materials will likely mitigate sharp, penetrating blows from a bull's horn or the hoof of an animal. However, the magnitude of measured ground impact forces calls for more research and development on vests that can protect against substantial, blunt-force trauma.

INJURY INCIDENCE BY RODEO EVENT

Cowboys are extreme athletes, participating in rodeo events with great risks. Rough stock events, bull riding, bareback riding, and saddle bronc riding have been shown to have the highest injury rates.[45,70,126,177] Understanding the demands of each rodeo event and characterizing injury rates, risks, and types have been some of the early projects of rodeo medicine personnel. A 5-year epidemiologic analysis of rodeo injury in Canada showed bull riding to have the highest injury rate (32.2 per 1000 exposures) and bareback riding the second highest.[41] The conclusion was that cowboys participating in these two events have the greatest likelihood of being injured in rodeo.

Of the modern-day rodeo events, all were born out of important skills on early cattle ranches, except for bull riding. The ability of a cowboy to sit atop a full-grown, ferocious, 2000-lb bull has never been a necessary part of ranch work. Bull riding resulted from machismo competitions between cowboys when the workday was done and ranch hands were looking for a source of entertainment. Even today, the bull-riding competition is reserved as the last event in modern-day rodeos and usually proves to be the most dangerous event of rodeo action. Bull riding is a mainstay event in American competition rodeo, implicated in up to almost 50% of rodeo injuries and making it the most dangerous event in rodeo.[41,70]

In 2007, statistical comparisons were made between the injury rates of bull riders and athletes competing in American football, ice hockey, rugby, boxing, and soccer. The injury rate of bull riders was found to be 1440 injuries per 1000 exposure hours. The bull-riding injury rate was 10.3 times the rate of injury in American football, 13.3 times that in ice hockey, and 1.56 times that in boxing.[36] The rate of injury associated with bull riding has been shown to be two times higher than with other major rodeo events (3.2 vs. 1.39 per 1000 competitor exposures).[41]

INJURY BY BODY REGION

Reports of injuries by body region vary slightly, but generally the most common injuries (in the order of incidence in rodeo and bull riding) include knee, head (including concussion), and shoulder.[41,177] Knee injuries are understandable considering the variables that contribute to the mechanisms of injury: animal forces; uneven arena surfaces made from dirt and clay; metal chutes to move and mount livestock; speed of animals; and strength of competitors (animal and human). Some of these injuries might be prevented by appropriate strength and conditioning programs or educational programs for participants.[19,127,128] Rodeo schools teach novices about common injuries and how to manage and prevent them. In addition, schools teach youth how to dismount and fall from their animal with less chance of injury. The success of these prevention strategies has yet to be measured.

Upper-Body Injuries

Shoulder injuries are common in rodeo.[41,177] There are unique shoulder injuries, such as the combined acromioclavicular sprain and elevated first rib that result from hitting the ground after a dismount.[106] There are also a set of unique muscle-tendon ruptures that are associated with various rodeo events. Tendon ruptures occur to rodeo contestants primarily in bull-riding, steer-wrestling, and bareback-riding events. Pectoralis major, latissimus dorsi, distal biceps, long head of biceps, and finger extensor tendon ruptures have been reported.[43,54,110] Recognition of muscle or tendon rupture requires basic understanding of forces created in rodeo events and detailed anatomic knowledge. Awareness of the magnitude of forces involved may stimulate an appropriate index of suspicion, careful history taking, and thorough observation and examination, including functional muscle testing, ancillary testing, and early referral.[44] The objective portion of the examination requires painstaking palpation and functional assessment to limit false-negative conclusions. The following discussion focuses on tendon injuries that are unusual and present greater diagnostic challenges.

Pectoralis Major Ruptures in Steer Wrestling

Clinical Presentation. Pectoralis major (PM) ruptures found are more often in steer wrestling than in other rodeo events.[110] Bak and associates[17] reported on 112 cases of PM rupture in the general population. Cases presented in the literature seem to be evolving from workplace injury to athletic

endeavors such as steer wrestling, while most are reported in weight lifting.[18] The common denominator in most cases is the forceful, eccentric external rotation and abduction mechanism of injury.[7,110] In a small cohort of nine rodeo steer wrestlers with PM ruptures from 2006 to 2009, two-thirds described the mechanism of injury as occurring when the steer stopped running, slowed down, or veered, resulting in a sudden eccentric force to the PM of the competitor trying to "wrestle" the steer.[110]

Differential Diagnosis. Patients present with pain, loss of palpable continuity of PM tendon, palpable avulsed tendon end on the chest wall, muscle retraction, ecchymosis, inflammation, and weakness in resisted internal rotation, adduction, or horizontal flexion of the shoulder.[18] Tears are classified by muscular rupture at the sternum or clavicle or at the musculotendinous junction. Most tears at the muscular end are treated conservatively with success, whereas tears at the musculotendinous junction are treated surgically.[58] Because of the location of the musculotendinous junction, differential diagnosis may include long head of the bicep tendon injury or rupture. In addition, this injury is occasionally combined with a glenohumeral dislocation.

Diagnostic Tests. Historically, clinical diagnosis led to surgical or nonsurgical treatment. Young, athletic patients (including rodeo contestants) seem to prefer and prosper after surgical repair. However, steer wrestlers with incomplete PM ruptures are known to participate successfully after nonsurgical treatment. Conversely, in PM ruptures to nine Canadian steer wrestlers, four reported previous injury to the same shoulder before PM rupture.[110]

Clinical evaluation shows dramatic differences in resisted isometric testing in shoulder internal rotation, adduction, and horizontal flexion. One can create a position to test all three moments simultaneously.[18,44] Magnetic resonance imaging (MRI) and ultrasound have been used successfully to diagnose and plan a treatment.[211] MRI has been used to classify PM ruptures into complete rupture at the muscle or tendon enthesis junction.[2,211] PM ruptures were classified as (1) complete rupture, (2) high-grade (>50%) tear, and (3) low-grade (<50%) tear. Three surgeons used MRI to direct patients to surgery or nonsurgical treatment. They agreed to perform surgical repair of the PM in 19 of 27 patients, and the majority of their results were quite positive (Figure 37-13).

Ultrasound imaging by experienced sonographers is showing promise diagnostically. It has also been studied in comparison to MRI, and clinical and surgical findings,[203] and as a stand-alone diagnostic tool.[158] MRI assessment compared to clinical assessment has been reported as not significantly affecting the preoperative planning.[18] In isolated or selected rural settings, ultrasonography, which may demonstrate intramuscular injury or loss of tendon continuity, may be a worthwhile alternative to delayed MRI assessment or expert referral.

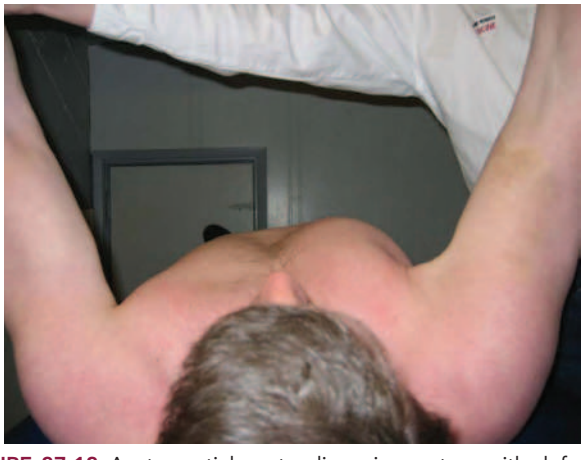

FIGURE 37-13 Acute partial pectoralis major rupture with deformity and ecchymosis. Partial ruptures are usually treated nonsurgically. *(Courtesy Krista Burton.)*

Treatment. Understanding and diagnosis of PM ruptures has evolved considerably over the last 20 years.[58] Specifically, the anatomy of musculotendinous junction at the humeral attachment is complex, with the clavicular and sternal heads twisting and folding over each other like a piece of cloth that has been folded in half, creating a U-shaped structure with both an anterior and a posterior attachment. Understanding the anatomy has led to a newer classification scheme for injury: (1) full-thickness tear involving both anterior and posterior tendon components, (2) partial-thickness tear involving one of the tendon attachments, and (3) incomplete tear involving partial tear of either the anterior or the posterior tendon attachments, but neither is complete.[73] Chiavaras and colleagues[58] advocate for surgical repair on any musculotendinous attachment tears previously described.

Three metrics have been used to classify success in surgical intervention: patient-reported outcome measures, diagnostic ultrasound, and objective strength testing. The majority of surgical interventions across a number of studies have demonstrated success with musculotendinous junction repair.[64,65,73]

Sequelae and Aftercare. Most reported research is focused on classifying PM ruptures and the best surgical technique.[64,65,73] Rehabilitation protocols have yet to be reported but should consist of strengthening and range-of-motion (ROM) exercises. In rural settings, treating cowboys, ranchers, or farmers with home-based rehabilitation protocols should be considered. This model has been successfully studied in rehabilitation after certain knee procedures.[79]

Prevention. Prevention of PM ruptures has only recently been of interest. Based on the mechanism of injury, a number of variables could be targeted to prevent PM ruptures or injury.[110] We believe that strong core muscles, experience as a steer wrestler, shoulder/PM flexibility in horizontal extension, and "eccentric" strength training of abduction and external rotation may be factors worthy of study.

Latissimus Dorsi Muscles in Steer Wrestling

Clinical Presentation. Latissimus dorsi (LD) ruptures have been reported in two rodeo steer wrestlers,[40,92] a professional wrestler,[84] two water skiers,[91,111] a SWAT police team member,[40] a rock climber,[114] and an army officer;[188] all described mechanisms involving supporting body weight with the arm in an overhead position. A case was reported in a 38-year-old golfer,[180] and a case series involved 10 professional baseball pitchers.[167]

Clinical diagnosis is variable. Since some of the cases were initially not recognized, Table 37-1 illustrates the specific diversity reported regarding patient presentation. Many patients can be characterized as presenting with significant axillary pain, a description of burning or tearing sensation, or a tender mass and/or defect in the posterior axillary fold that can be more visible or palpable during isometric testing. Weakness shown in isometric testing of shoulder adduction, internal rotation, and/or extension is common. Some authors warn that athletic patients may maintain surprisingly full ROM and isometric strength due to contraction of other muscles with similar prime-mover functions, particularly in shoulder adduction and internal rotation. Early presentation may include extensive ecchymosis and descriptions of specific functional limitations (Figure 37-14).

To avoid initially dismissing LD tendon rupture as a minor injury, a careful history, including estimation of forces to which the patient may have been subjected during the traumatic event; report of pain with burning, tearing, or popping sensation; and extensive ecchymosis should lead to a high index of suspicion for a major tendon rupture.[44]

Differential Diagnosis. It is often challenging to achieve accurate differential diagnoses that include the exact muscle strain, rotator cuff tear, contusion, and LD avulsion or rupture. Patients may present with additional tendon injuries, particularly the conjoined teres major tendon, in concert with an LD tendon avulsion. Several authors warn about underdiagnosis and failure to recognize this major tendon avulsion or rupture in athletes.[92,180]

Diagnostic Tests. Careful clinical assessment, combined with an index of suspicion for tendon avulsion, is the most

TABLE 37-1 Latissimus Dorsi Ruptures

	Presentation				Signs/Symptoms				Weakness/ROM						Strength			
Study	Felt Pop	Axillary Pain	Burning or Tearing	Ecchymosis	Defect Visible, Palpable	Defect Axillary Fold	Tender Axillary Fold	Palpable Tender Mass	Painful Motion	No ROM Deficit	Weak/ Pain in Internal Rotation	Weak/ Pain in Extension	Weak/ Pain in Adduction	Scapular Dysfunction	Unable to Perform	Overhead Functional Limits	Surprising Strength 4/5	No Strength Deficits
Burks et al.[40] (2006)	x	x			x	x							x		x	x		
Butterwick et al.[43] (2000)			x	x			x	x			x		x		x		x	
Hapa et al.[84] (2008)		x		x	x	x				x				x		x		x
Henry and Scerpella[91] (2000)		x	x				x		x				x				x	
Hiemstra et al.[92] (2007)				x	x		x							x				
Lim et al.[111] (2006)		x	x				x			x			x					
Livesey et al.[114] (2002)			x		x	x	x			x					x	x		
Park et al.[147a] (2008)		x		x								x						
Schikendantz et al.[167] (2009)		x					x				x		x					
Spinner et al.[180] (1998)	x	x	x	x	x		x			x	x	x	x					x
Turner and Stewart[188] (2005)		x				x				x	x			x		x	x	
TOTAL	2	8	5	5	5	4	7	1	1	5	4	2	5	3	2	3	3	2

ROM, Range of motion.

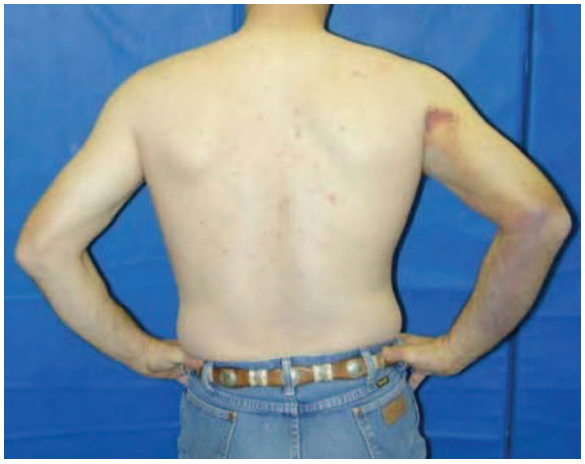

FIGURE 37-14 Extensive ecchymosis of the entire arm with edema over the ruptured latissimus dorsi in a steer wrestler. *(Courtesy Dale Butterwick, ATC(C).)*

important clinical tool. Only one report of LD ruptures mentions a positive radiographic finding, whereas about half of cases report MRI findings consistent with complete tendon avulsion.[180] One case presented with normal MRI findings, but the clinical findings resulted in surgery, with confirmation of a complete avulsion of the LD tendon from the humeral insertion. There has been only one reported diagnosis using ultrasound imaging.[188]

Treatment. One LD rupture in a rodeo steer wrestler was treated nonsurgically with strengthening exercises and athletic taping to restrict the ranges of motion of abduction and external rotation to participate in national finals competition over a short period of time.[45] Winning performances occurred during the Canadian Finals Rodeo, and times equivalent to personal bests were achieved at the National Finals Rodeo approximately 3 weeks later. Unfortunately, due to death from other causes, this athlete was not followed over time. Another steer wrestler with LD rupture was treated with surgical repair of the tendon and is still competing in professional rodeos.[92]

Although there is a case series with 10 baseball pitchers treated nonsurgically with success, we believe that surgical treatment will usually be preferred by most high-performance, high-demand athletes such as rodeo competitors.[167] There are consistent reports of dissatisfaction when athletes cannot perform the overhead tasks required in their occupations, pastimes, or favorite sporting activities. Since many of these athletes work and live in rural farming and ranching settings where manual labor is required, functional outcomes are very important. As in other tendon avulsions or ruptures in these populations, early repair is preferred.

Sequelae and Aftercare. An example of postsurgical treatment includes a sling for 4 weeks, passive and active-assisted ROM exercises without active ROM for 2 weeks, followed by isometric strengthening at 6 weeks. Finally, active resisted exercises are allowed and continued for approximately 6 months. Strength testing can be performed when strength no longer improves. This may occur between 8 months and 1 year after surgery. Burks and associates[40] presented an entire rehabilitation program for patients with LD tendon surgical repairs.

Prevention. Prevention of LD ruptures has not been studied. In rodeo steer wrestlers with either LD or PM rupture, it has been noted that in several cases the mechanism of injury involved a steer that stopped running just as the cowboy jumped from the horse. This likely causes a tremendous eccentric force on the involved muscles. As with PM ruptures, we believe that strong core muscles, experience as a steer wrestler, shoulder/LD flexibility in horizontal extension and abduction, and general upper-body strengthening, including eccentric exercise, may be variables of interest in establishing effective injury prevention strategies.

Distal Biceps Tendon Rupture

Clinical Presentation. Distal biceps rupture has been reported as accounting for approximately 3% of biceps tendon injury.[61] Athletes reporting distal biceps rupture include rodeo bull riders and bareback riders, as well as rock climbers[169] and weight lifters, whereas previously, the typical presentation had been in a 40- to 50-year-old worker in whom chronic tendon degeneration is a risk factor.[29,154] Patients describe a "popping" sensation that may be combined with a sharp, tearing pain immediately following an eccentric load.[28,125,197] Farm and ranch workers are also at risk for this type of injury, in which the typical mechanism involves a sudden eccentric load to a flexed, shortened, and contracted muscle.[165] In workers, these forces have often been "unexpected," but in the rodeo athlete these forces are expected, although occasionally overpowering. Mechanical impingement and hypovascularity have also been hypothesized as causative factors.[172] Smoking has been presented as a significant risk factor[165] for distal biceps tendon rupture, which in some cases have been associated with use of anabolic steroids.[198]

Differential Diagnosis. Similar to patients with rupture of the long head of the biceps, acute distal biceps tendon rupture in healthy, young athletes presents with a history of a "pop" and sudden onset of pain with concomitant weakness in resisted elbow flexion and supination. Point tenderness and palpable and visible loss of continuity of the distal biceps tendon are common. Retraction of the muscle belly and ruptured tendon is appreciated, and the tendon stump is often palpable, particularly when the lacertus fibrosis also ruptures.[197] Ecchymosis is variable, but even at 48 hours may not be present. A biceps crease interval test (unilateral) and a biceps crease interval ratio (left-to-right comparison) have been proposed to aid clinical diagnosis[72] (Figure 37-15).

Diagnostic Tests. Clinical findings include loss of palpable continuity of distal biceps tendon, muscle retraction, palpable retracted tendon stump, and unilateral weakness in elbow flexion and supination. Do not be surprised by resisted strength of elbow flexion, because the brachialis muscle is usually intact in bull riders with distal biceps tendon rupture. Occasionally, ultrasonography or MRI may be used with delayed or unclear presentation. However, these tests usually are not necessary.[154]

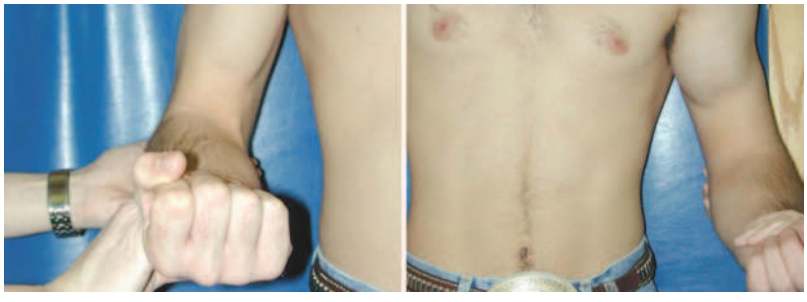

FIGURE 37-15 Acute rupture of left distal biceps tendon in a bull rider with isometric contraction of the brachialis muscle. Uninjured (right) arm in the same bull rider. Note the lacertus fibrosis (biceps aponeurosis) and the distance from the bicipital crease to the muscle belly. *(Courtesy Dale Butterwick, ATC(C).)*

Treatment. Distal biceps tendon rupture in a healthy, young athlete such as a professional bull rider should be referred promptly for surgery. Surgical outcomes over the past two decades are generally excellent[57] and superior to nonsurgical treatment functionally and clinically,[80] especially when surgery is completed in a timely manner. Operative repairs show superior restoration of muscular strength and endurance in elbow flexion and supination.[60] In the rodeo patient, rancher, or farmer, early surgery is the preferred treatment. Supination strength after surgery has been reported as unpredictable and should be discussed with rodeo athletes as a potential outcome.[63,197] The importance of supination strength in rodeo athletes, particularly in bull riders and bareback riders, to our knowledge has not been studied.

Sequelae and Aftercare. Postoperative care typically includes 2 to 4 weeks of immobilization followed by active and passive ROM exercises for 8 weeks. Strength training typically begins after 8 to 12 weeks.[57] In rodeo athletes (bull riders and bareback riders), early return to activity is discouraged. Since the distal biceps rupture occurs in the "riding hand" arm (the hand/arm with which the athlete holds onto the animal) and these animals create tremendous forces while bucking, a 6-month rehabilitation period is desired. Compliance with a conservative return to heavy lifting activities has been a challenge in some patients, because they feel ready to return.[123] Compliance must be emphasized, with the return-to-play protocol proposed for a rodeo competitor after surgery. However, with use of new surgical stabilization techniques such as an EndoButton,[55,80] which has recorded the highest load and stiffness of currently available fixation methods, some of these timelines for ROM, strength training, and return to sport are being challenged.[55] Many professional bull riders elect to wear functional elbow braces that limit full extension by 3 to 5 degrees when they return to bull riding after surgical repair of an avulsed distal biceps tendon.

Prevention. Prevention of distal biceps tendon rupture or rerupture in bull riders has not been studied. Some factors that may warrant investigation as preventive strategies include early strength training in teenaged junior bull riders, strength training in adult bull riders, riding with two hands as youth steer riders, matching of bulls to young participants, and wearing a functional elbow brace that limits elbow extension when returning to bull riding after operative care. Strength-training prevention strategies should focus on eccentric phases of strength, because this is where the majority of these injuries transpire.[100,101] Furthermore, strengthening should also focus on other body parts that support the rodeo competitor during the ride, such as core abdominal and back extensor stabilization or triceps muscle strengthening, to counterbalance what is happening with the elbow flexors. These are only theoretical approaches, combined with observation of elite bull riders who have successfully returned to the sport after surgical care.

Thumb Amputation

Most thumb amputations occur in industrial or agricultural settings involving power machinery.[95,129] Team roping in a rodeo or on a ranch is a unique mechanism of thumb amputation. These injuries are speculated to occur more frequently than is normally appreciated.[130] Because farm and ranch workers often participate in roping cattle for branding or doctoring, thumb amputations are of interest as an occupational hazard.[129]

Team roping involves a "header" who catches the horns of the steer, "dallys" (winds) the rope around the saddle horn, and turns the steer to change the direction of travel. The "heeler" then catches the hind feet (heels) of the steer and dallys the rope around the saddle horn. Both headers and heelers can suffer thumb amputations while performing the dally.[129] Beginning ropers are usually taught to keep their thumbs pointed upward while dallying, because this position is alleged to prevent thumb amputations. However, reports indicate that thumbs can be amputated using either a "thumb up" or "thumb down" technique.

Clinical Presentation. Avulsion or amputation of thumbs in roping-event competitors exhibits elements of crush and avulsion and guillotine amputation.[95,129] Presentation should be obvious. Many patients are aware that reimplantation can be successful and are likely to bring the detached member.

Diagnostic Tests. Partial or near-complete amputation can be difficult to ascertain when there is significant integrity of the epidermis combined with copious bleeding. In the field, no specific diagnostic test on the stump or amputated part is necessary, whereas in the hospital setting, radiographic studies on both might be of benefit to the hand surgeon. The decision to treat with reimplantation is enhanced in cases where minimal arterial and venous debridement is required to achieve vessels with viable anatomy to create an anastomosis.[95]

Treatment. One author reports that thumb reimplantation has become routine, but reconstruction using a toe is also possible.[95] In the event of complete thumb amputation, immediate efforts should be made to control active bleeding from the proximal stump and preserve the amputated digit. Both the stump and the amputated part should be covered with saline-moistened dressings.

The amputated part should be sealed in a dry plastic bag and placed in ice water, such that the ice does not come in direct contact with the amputated part. Both patient and amputated part should be transported together to the nearest facility where a hand surgeon can manage the patient. Cooling the amputated part to 4° C (39.2° F) can extend viability to 12 hours or more.[116]

Team roping has elements of both crush and avulsion, so these injuries may have a poor prognosis for reimplantation. However, thumb reimplantation seems to be the treatment of choice despite the severe mechanism of injury. It is speculated that unsuccessful reimplantation could result from a lack of vein grafts or repair of only one digital artery. Primary digital nerve repair and repair of flexor and extensor tendons are also reported in some of these patients. Successful reimplantation varies in reports on rodeo athletes. In a series of 19 such injuries, five were reported as successful, four as "not available," and 10 as unsuccessful. Many ropers choose reimplantation and return to roping (one participated in the national roping finals 11 weeks after surgery), while others choose not to undergo reimplantation and have been subsequently able to return to roping activities.[95]

Prevention. Discussion of prevention strategies suggests that roping gloves have little if any protective value. Tradition has it that learning to dally with the thumb "up" is protective. Others suggest eliminating the dally or encouraging use of longer ropes as thumb preservation techniques, but these are unlikely in this time-based competitive event for which the world record is less than 4 seconds.[129]

Head Injury and Concussion

Head injury and concussion in sports and society are receiving enormous attention, and rodeo is not immune to this trend. However, what may be unique is the way concussion is managed in rodeo and bull riding. In professional rodeo and bull riding, no rules govern the right to participate, particularly as it relates to return to participation with a post–head-injured athlete. Most major sport organizations now have concussion evaluation and management protocols designed to protect the athlete.[31,103,133,162] Rodeo and bull riding will likely catch up with more education and awareness about the importance of head injury and concussion management protocols. Until rodeo and bull-riding governing bodies mandate appropriate concussion management policies, rodeo medicine personnel can build trust and keep open lines of communication with the riders in hopes of convincing them about the correct course of action after sustaining a concussion.

One retrospective bull-riding survey study researching head injuries estimated the likelihood of a bull rider sustaining a head injury at 15.4 per 1000 exposures, or 684 head injuries per 1000 exposure hours, assuming an 80-second exposure.[36] Bull riders are at risk for both head injury and concussion. An estimated 38.5% of head injuries in bull riding involve concussions, and 19.3% involve facial fractures[37] (Tables 37-2 and 37-3).

Although rodeo head injury research has focused on bull riding, concussion is also a significant problem in bareback

TABLE 37-2 Types of Injury While Not Wearing the Bull Tough Helmet

Type of Injury	Number of Injuries	Percentage
Concussion	42	38
Laceration	31	28
Facial fracture	21	19
Benign closed head injury	7	6
Permanent brain damage	2	2
Skull fracture	2	2
Avulsed ear	2	2
Detached retina	1	1
Loss of eye	1	1
Seizure	1	1
TOTAL	110	100

From Brandenburg MA, Archer P: Mechanisms of head injury in bull riders with and without the Bull Tough Helmet: A case series, *J Okla State Med Assoc* 98:591, 2005.

riding. In the 5-year study of rodeo competitors in Canada, there were 39 concussions, with 15 from bull riding and 10 from bareback riding. In 2012, Mathers and colleagues[121] described ear-mounted triaxial accelerometers and angular rate sensors being worn by nine bull riders and eight bareback riders. Although the sample size was small, interesting data showed very high forces being produced (linear acceleration) during each ride. Much more research needs to be done, but it is conceivable that the coup-contrecoup mechanism typically seen in football is also possible with bareback riding each time the horse bucks, particularly if a competitor makes contact with the horse's rump or spine.[210] Neck strengthening is of particular interest to researchers as a possible strategy in preventing concussion in bareback riders.

Concussion is likely undiagnosed in rodeo because competitors often do not seek evaluation, or the attending clinician does not have a sufficiently high index of suspicion. Furthermore, loss of consciousness is often not present in concussion, and identification of the subtler symptoms and signs requires the performance of a physical examination.

Rodeo is a unique environment relative to other organized sports, and medical personnel may or may not be present. It is critical that signs and symptoms of concussion are shared with the rodeo community so traveling partners, parents, event organizers, and other rodeo stakeholders can help identify concussion when competitors do not recognize it themselves or do not seek further medical attention after rodeo participation.

TABLE 37-3 Mechanisms of Injury While Not Wearing the Bull Tough Helmet

Mechanism of Injury	Number of Injuries	Percentage
Head-to-head impact	47	56
Stepped on by bull	12	14
Head impact with ground	11	13
Kicked by bull	7	8
Thrown against chute gate/wall	4	5
Thrown into arena wall/fence	3	4
TOTAL	84	100

From Brandenburg MA, Archer P: Mechanisms of head injury in bull riders with and without the Bull Tough Helmet: A case series, *J Okla State Med Assoc* 98:591, 2005.

FIGURE 37-16 Bull-riding helmet damaged after impact with bull's hoof. *(Courtesy Mark Brandenburg, MD.)*

The clinical presentation and international evaluation guidelines have been published by the Concussion in Sport Group.[124] One of the tools developed to help evaluate and manage concussion is the Sport Concussion Assessment Tool (SCAT). It has been questioned whether that tool is valid in a rodeo environment.[105] Although most of the SCAT may be relevant and valid for a rodeo environment, on review, some questions in the SCAT needed to be modified for the rodeo environment. Therefore, questions have been customized to a rodeo environment. A copy of the rodeo SCAT can be found on the Justin Sportsmedicine Team website (http://www.justinsportsmedicine.com/firstaid/#).

Protective Headgear

Helmets seem to have a protective benefit.[33,37] A consensus statement of rodeo medicine experts in 2005 endorsed "mandatory" helmet use for junior bull riders (i.e., <18 years old) and only "recommended" it for bull riders over age 18.[46] Adoption of mandatory helmet use for riders under age 18 occurs only in Canada and the United States.[50] Anecdotally, it seems that protective equipment use is on the rise, but more research is need to confirm this. More education from medical and allied health care personnel about the benefits of protective equipment would be helpful.

It has been suggested that protective headgear can decrease the incidence of head and face injury to bull riders.[33] The most common head injuries in bull riders are concussion, lacerations, and facial fractures. The results of one descriptive study demonstrated that the most common mechanisms of head injury in bull riders are the rider's head smashing against the bull's head and impacting the ground. Bull riders not wearing protective headgear who were involved in a head injury incident were more likely to sustain multiple injuries (26%) than were those wearing protective headgear (12%)[37] (Figure 37-16).

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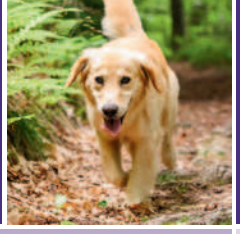

CHAPTER 38

Emergency Veterinary Medicine

S. CHRISTOPHER RALPHS AND CHRISTOPHER R. BYRON

This chapter provides an overview of the physiology of dogs, equids (horses, donkeys, and mules), bovines, and camelids (llamas, alpacas, and camels) that may accompany humans on trips in wilderness or remote areas, along with preventive, diagnostic, and treatment options for specific conditions that may arise in this context. It is not meant as a substitute for adequate veterinary care. The ideal treatment is always to seek qualified veterinary care as soon as possible; the information provided here is intended to be useful when a veterinarian is not readily available.

DOGS

Dogs are frequent companions on wilderness trips as companions, pack animals, or draft animals for sleds. Their athleticism serves them well in the wilderness, but they are susceptible to a wide range of diseases and injuries. Regardless of canine age or breed, care must be taken to ensure animals are fit for service, have had a recent veterinary examination, and are current on preventive care measures, such as vaccinations and anthelmintic drug administration.

CANINE PHYSIOLOGY AND PHYSICAL EXAMINATION

Temperature

Dog temperatures are measured rectally. Normal range is approximately 37° to 39° C (98.6° to 102.5° F). Exercising dogs may safely reach temperatures of 40.5° C (105° F), but a core body temperature higher than that risks inducing heatstroke.

Dogs thermoregulate by panting rather than sweating, so any condition that affects their ability to pant effectively can impair their ability to cool themselves and predispose to heat stress. Brachycephalic breeds, such as bulldogs and pugs, have anatomic anomalies that impair their ability to pant effectively, so they may not be suitable companions for strenuous wilderness expeditions. Obesity and thick or dark-colored fur (coats) in sunny weather impair temperature control. These factors should be taken into account when planning a trip.

Cardiac Evaluation

Normal heart rate for adult dogs is 70 to 180 beats/min in small dogs and 60 to 140 beats/min in larger dogs. As in humans, dogs normally have two heart sounds; a murmur or third heart sound, such as a gallop, indicates cardiac pathology. Dogs have pronounced vagal tone, so they can have a normal sinus arrhythmia such that heart rate varies throughout the respiratory cycle; heart rate is faster during inspiration and slower during expiration. This does not necessarily indicate pathology because it is a normal rhythm for many dogs. To evaluate rhythm, it is important to check an arterial pulse while auscultating the heart to verify that each heart sound is matched by a strong pulsation.

Mucous Membrane Color

This is a subjective evaluation that can yield important information. Normal mucous membranes in the dog should be pink and slightly moist. Anemia or vasoconstrictive shock can cause pale mucous membranes. Vasodilation from systemic inflammatory states and hyperthermia can cause red mucous membranes. Cyanosis can occur with hypoxemia. Icterus from liver disease or hemolysis can result in a yellow color to the mucous membranes and sclera. Petechiae or bleeding can be indicative of coagulopathies. Dry mucous membranes should raise suspicion for dehydration.

Capillary Refill Time

Normal capillary refill time (CRT) in dogs is 1 to 2 seconds. Even recently deceased dogs can have a normal CRT, so this should be interpreted in relation to pulses, respiratory rate, gingiva color, and other clinical parameters. A CRT longer than 2 seconds indicates poor perfusion or peripheral vasoconstriction.

Pulse

The easiest location to check a dog's pulse is in the femoral triangle of the groin just anterior to the proximal femur. The femoral pulse in most dogs is palpable down to a systolic blood pressure of approximately 60 mm Hg. The pedal pulse on the cranial aspect of the foot just below the hock (ankle) is generally palpable at a systolic pressure of 80 mm Hg, although the clinician's experience plays a major role in ability to appreciate the pulse at this location. Bounding pulses indicate a hyperdynamic state, whereas weak pulses correlate with decreased cardiac contractility, peripheral vasoconstriction, or decreased blood pressure.

Hydration Status

A general gauge of hydration can be made with the skin turgor test. However, skin turgor can be unreliable in obese, cachectic, or old animals. As dogs become dehydrated, they lose interstitial fluid in the subcutaneous tissues and lose some skin elasticity. Normally hydrated dogs have extra loose skin at the back of their head and neck, known as the "scruff." In a hydrated dog, this skin can be gently pulled upward and when released, immediately springs back into normal position. With mild to moderate dehydration, this returns to normal position more slowly; with severe dehydration, it may remain standing in a ridge (Figure 38-1).

CANINE FIRST-AID KIT

Items appropriate for a canine first-aid kit vary widely based on type of dog, type of terrain, experience of the dog handler, weather conditions, length of expedition, and other considerations. Box 38-1 lists items that may be of general use for wilderness canine emergencies and is not exhaustive.

BASIC DOG-HANDLING TECHNIQUES

Administering Oral Medications

Most dogs will take pills if these are put inside tasty treats, such as butter, cheese, or any type of meat. If the wily dog is able to separate pills from food, then non–time-release pills can be crushed and mixed into the food. If the dog will not consume pills placed in any manner into food, the handler can grab the dog around the maxilla (upper jaw) with one hand, using the thumb and forefinger on either side of the maxilla and exerting pressure just behind the canine teeth, and use the other hand to pull down on the mandible (lower jaw). After the jaw is opened, the pill should be placed as far back on the tongue as possible, and then the mouth should be helped closed and the throat rubbed to encourage swallowing. Watch for several minutes afterward to ensure the dog does not regurgitate the pill. If it is difficult or dangerous to open the dog's mouth, a pill gun can be used to deliver the pill to the back of the oral cavity. A plunger

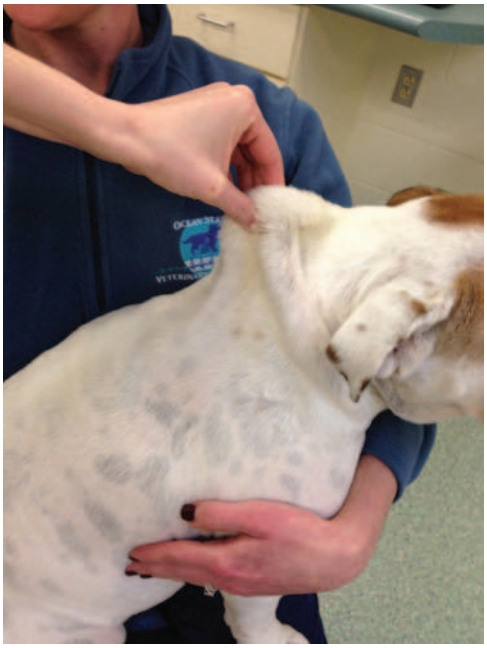

FIGURE 38-1 Canine skin turgor (hydration test).

is depressed to release the pill. The mouth should be held closed until the dog swallows to minimize risk of regurgitation.

Muzzle

It is important to remember that dogs, no matter how cute, friendly, or docile, are efficient predators and, when panicked or in pain, can quickly inflict serious bite wounds on well-meaning caregivers. Even veterinary professionals make mistakes when they trust the "nicest" dogs and breeds not to bite in times of distress; these friendly dogs are often responsible for the worst injuries. A muzzle can mean the difference between successful treatment of a canine patient and having both an untreated canine patient and severe bite wound trauma in a human patient. Muzzles should be used with care in dogs with respiratory distress or heat stress because this will impair their ability to ventilate and cool by panting.

For most dogs, a commercially available nylon muzzle works well if properly fitted. If this is not available, a muzzle can be made from a leash, length of cord, shoelace, or other linear cloth material. Loop the material around the dog's muzzle and tie an overhand knot on the top of the muzzle. Pull the ends down and tie another overhand knot under the jaw, then bring the ends around the back of the neck below the ears, and tie either a bow or a square knot to secure (Figure 38-2).

For brachycephalic dogs, such as bulldogs or pugs, that do not have enough of a muzzle for this technique, the entire head may be wrapped in a shirt or jacket, being careful to allow the animal to breathe while preventing it from biting.

BOX 38-1 Canine First-Aid Kit

- Information card containing veterinarian, emergency clinic, and national poison control numbers as well as the dog's weight for medical dosing to facilitate phone consultation
- Commercial muzzle or length of fabric to improvise one
- Hemostat
- Thumb forceps (e.g., Brown-Adson forceps)
- Battery-operated hair clipper
- Wire cutter
- Toenail clipper (canine)
- Topical disinfectant, such as 2% to 4% chlorhexidine solution or 5% povidone-iodine solution
- Bandaging material, such as gauze pads and rolls, cast padding, nonadhesive dressing, adhesive tape, VetRap, Elastikon, fiberglass casting tape
- Skin stapler and/or tissue glue
- Activated charcoal preparation (ToxiBan)
- Sterile nonlatex examination gloves
- 0.2% Lidocaine with sterile syringes and needles for injection
- Apomorphine (3 mg/mL injectable given at a dose of 0.03 mg/kg IV) and 3% hydrogen peroxide for emesis induction
- Prescription medications and dosages (see Table 38-1)
- Properly fitted booties to protect feet
- Pill gun if it is difficult to administer pills to your dog

Manual Restraint

Examinations and treatments are best accomplished by having a dog in a lateral recumbent position. This is accomplished by sitting next to the dog, reaching across its neck, and grabbing the front foot closest to you. This foot becomes the down leg. You or an assistant can also grab the hind foot on the same side. It is vital to control the down legs to prevent the dog from being able to stand up at will. The handler's forearm is used to push down the dog's neck as the dog is pushed into lateral recumbency with the legs away from the handler. Once the dog is recumbent, this forearm serves to keep the dog's head down and prevents the dog from biting the handler. It is vital to keep control of both legs on the down side (Figure 38-3).

BANDAGING TECHNIQUES

Bandages can be useful in dogs for protecting open wounds or stabilizing injuries. These benefits must be weighed against the possibility that bandages, splints, and casts can create complications or exacerbate injuries. Any bandage that is too tight, is being chewed by the dog, becomes wet, or has a foul odor should be removed or changed immediately. Limb bandages can cause pressure sores or rub sores and can interfere with blood flow, leading to serious complications.

Covering Open Wounds

This bandaging is most likely to be used in a wilderness setting. Bandages can be used to protect an open wound that has been closed or to protect an open wound from further contamination or trauma. High-motion areas, such as the inguinal region and axilla, are difficult to bandage adequately, so bandaging may not be practical in these areas. Wounds on the perineum and head also may be difficult to bandage, and a tie-over bandage may be indicated.

Bandaging of Feet

Commercially made booties work well to protect canine feet from injury, prevent ice balls from forming between toes in winter conditions, and protect feet that have cuts or abrasions. If these are not available, foot bandages can be fashioned from available bandaging material. Because of the abrasion, soiling, and moisture that are common to foot bandages, they must be monitored closely and changed as needed. Foot bandages can be applied with a nonadherent dressing over any open wound, then covered with cast padding, followed by a stretchy outer layer, such as VetRap or Elastikon. White tape or duct tape can be applied to the walking surface for abrasion resistance, but these do not breathe well, so moisture and heat accumulation can be problems. It is important not to apply these bandages too tightly, particularly if there are stretchy outer layers. Leather, fabric, or other abrasion-resistant material can be applied to the walking surface to extend the life of the bandage.

Bandaging of Limbs

Because the legs, particularly the hind legs, of dogs taper from proximal to distal, bandages have a tendency to slip off. This can be partially counteracted by creation of stirrups, using adhesive tape applied directly to skin or fur (Figure 38-4). The tape extends through the distal end of the bandage and then is taped directly to the bandage itself to minimize slippage. A bandage that is applied to a limb in a proximal location is likely to cause edema in the distal limb if the limb is left uncovered, so in most cases, a bandage is applied from the area of interest all the way

FIGURE 38-2 A muzzle can be made from a leash, length of cord, shoelace, or other linear cloth material. **A,** Loop the material around the dog's muzzle and tie an overhand knot on the top of the muzzle. **B,** Pull the ends down and tie another overhand knot under the jaw. **C,** Bring the ends around the back of the neck below the ears and tie either a bow or a square knot to secure.

down the limb distally to cover the foot. If this is not done, one must be careful not to apply the bandage too tightly, which would impair venous and lymphatic return. Limb bandaging generally consists of a nonadherent sterile dressing on open wounds, followed by at least three layers of cast padding or other absorbent layer, followed by a stretchy outer layer, such as VetRap or Elastikon. Duct tape can be used as a substitute for the outer layer, but because it does not breathe, it should not stay on for prolonged periods.

Bandaging of Trunk

Wraps around torso and abdomen require large amounts of bandage material. Because many fit dogs have large chests and narrow waists, thoracic bandages may need to go around the shoulders and front legs to prevent them from migrating toward the hind end of the animal. An alternative for covering a wound in a large-breed dog is to use a T-shirt tied around the waist to remove excess width. This will not apply compression but can help protect a wound from contamination. Abdominal bandages can be a problem in male dogs because the position of the prepuce and penis make it difficult to keep a circumferential abdominal bandage from being contaminated by urine. Wounds in the axillary, inguinal, and perineal areas can be difficult to bandage because of anatomic constraints and the high motion of these areas.

Tie-Over Bandages

Tie-over bandages can be used to cover and protect wounds in areas such as the head, perineum, proximal limbs, or wherever it is difficult to use a normal circumferential bandage. They do not apply compression but can be used to keep a dressing in place and utilize less bandage material than a bandage encompassing the entire trunk. It is tedious and time-consuming to place the suture loops, but once placed, they can be reused for future bandage changes. To place a tie-over bandage, suture loops of approximately 1 to 2 cm (0.4 to 0.8 inch) in diameter are placed in the skin at regular intervals 2 to 3 cm (0.8 to 1.2 inches) from the wound edges (Figure 38-5). The bandage material is then placed over the wound after it has been appropriately cleaned. The material is secured in place by using suture in a

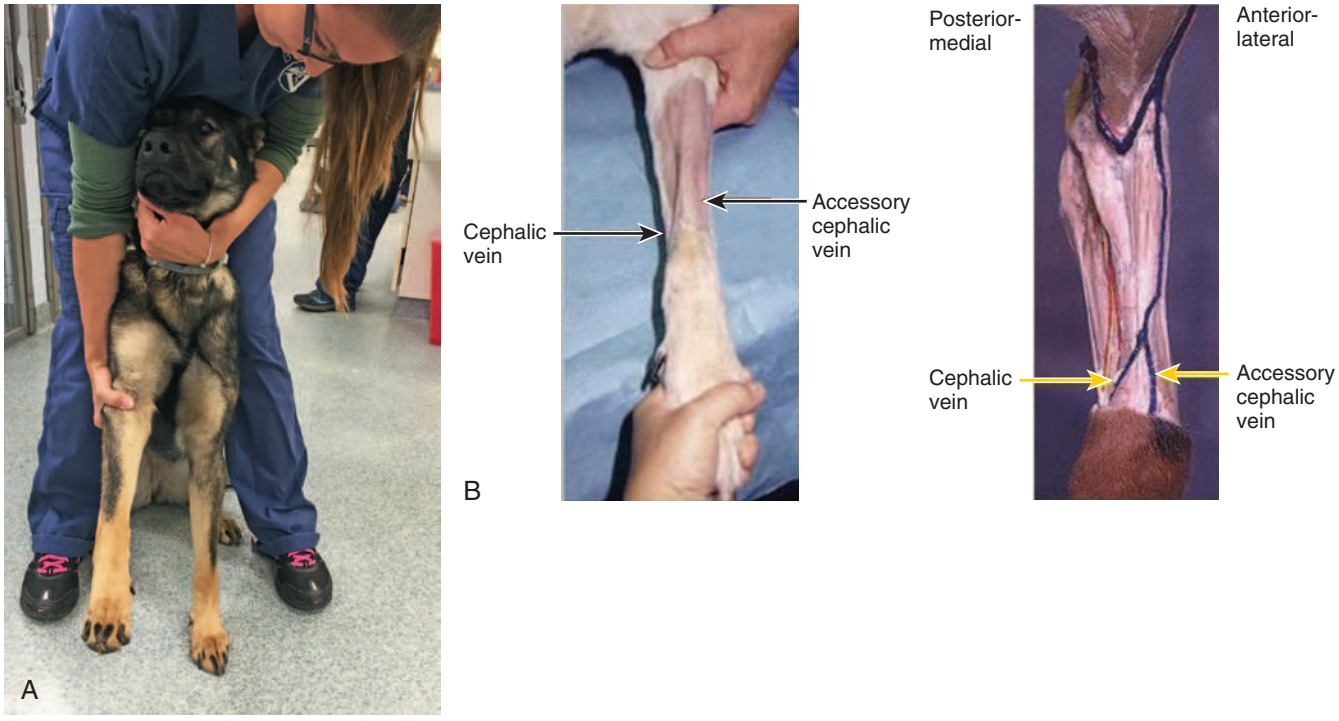

FIGURE 38-3 **A,** Cephalic vein restraint. **B,** Cephalic vein anatomy.

web pattern. We prefer to place the suture through the loop and then through the bandaging material to help prevent the bandaging material from becoming dislodged. To change the bandage, the loops are left in place, and the other suture is cut.

Splints and Casts

Specialized bandages to immobilize the limbs may be difficult to apply correctly and can cause complications if improperly positioned. In most cases, a dog is capable of walking on three legs, and furthermore, a field cast is rarely applied sufficiently well to allow good use of the limb. However, if there is an open fracture or very unstable fracture or dislocation, a cast or splint may help prevent further pain or injury. Casts and splints should not be used to immobilize limbs for femoral fractures, humeral fractures, or hip or shoulder dislocations (Figure 38-6), because these areas usually cannot be immobilized adequately using casts and splints, and the bandage material makes the limbs heavier and ultimately exacerbates the injury.

For instabilities of the limbs below the elbow and knee, rigid material can be added to a bandage to provide stability. This can be casting tape, wood, or multiple layers of less rigid material, such as roll cotton, newspaper, or bubble wrap, applied with an

FIGURE 38-4 Tape stirrups.

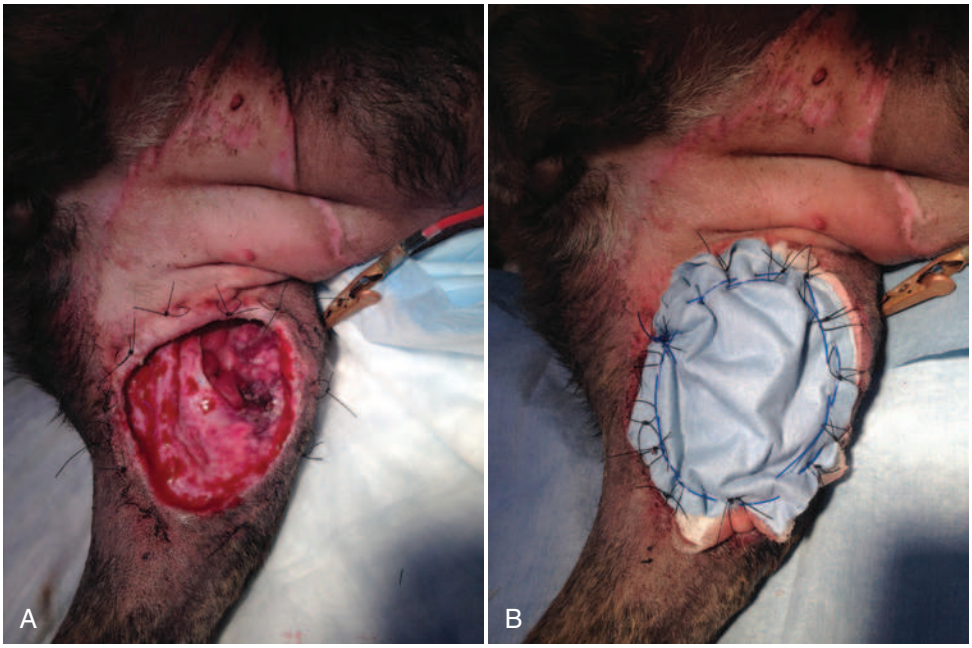

FIGURE 38-5 Tie-over bandage. **A,** Preparation; note the suture loops around the open wound. **B,** Bandage completed.

overlying pressure layer. When applying these bandages, it is important to bandage all the way to the toes to prevent swelling below the bandage. When using casting tape in a wilderness situation, splints or half-casts are more appropriate than full casts because of difficulty removing a full cast without a cast saw.

TOENAIL INJURIES

Toenails can split or fracture, may be extremely painful, and can hemorrhage impressive amounts. Generally, any portion of the toenail that is damaged should be removed with a toenail clipper. The dog may need to be muzzled for this procedure because it can be quite painful. Bleeding can be stopped with styptic powder. Topical blood-stanching products used in humans might work well for hemostasis in animals; there is no harm in attempting their use. If these are not available, the toenail can be pushed into a softened bar of soap to create a solid barrier, or any powder (e.g., baking soda, flour) can be applied to bleeding portions under a pressure bandage to encourage clot formation.

LACERATIONS

Dogs have more mobile skin than humans because of a different arrangement of the vascular supply and loose subcutaneous connective tissue. This allows skin more freedom to move when closing open wounds. If there is avulsion or degloving wounds with flaps of skin, every effort should be made to preserve these flaps if they are not obviously necrotic, to allow more options for definitive closure and healing.

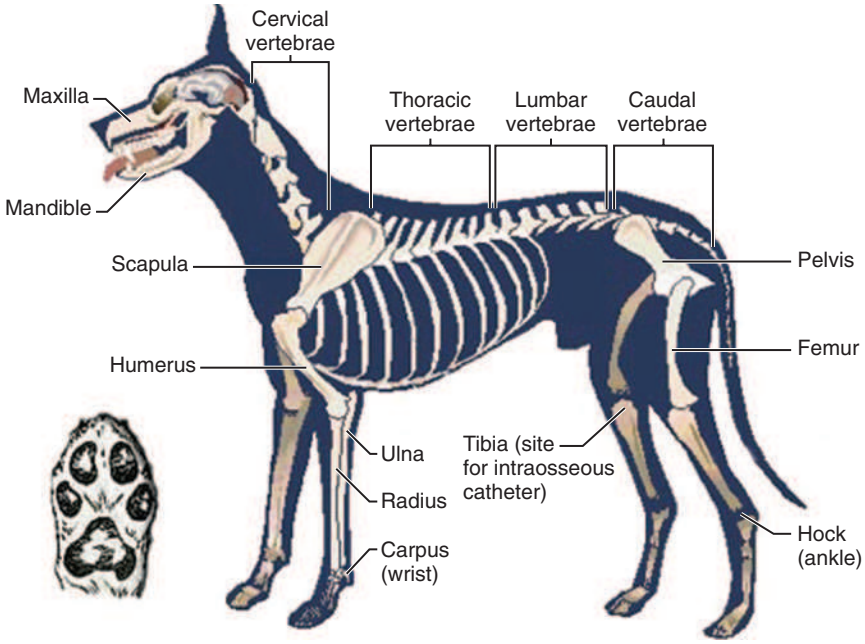

FIGURE 38-6 Canine skeletal anatomy.

STAPLING, SUTURING, AND GLUING WOUNDS

The decision to close or leave open a wound is not straightforward. In general, acute, minimally contaminated wounds with healthy edges should be closed, whereas grossly contaminated, older, grossly infected wounds or wounds with questionably viable tissues should be left open or debrided before closure. Because it may not be possible to clean wounds thoroughly in a wilderness environment, it may be desirable to leave at least the ventral part (lowest point) of the laceration open to allow drainage.

If the decision is made to close a wound primarily, it may be desirable to provide local anesthesia with lidocaine or bupivacaine. This can be infused into the subcutaneous tissue along the edges of the area to be closed. The pain of local anesthetic injections can be minimized by slow injection using a small-gauge needle. Buffering lidocaine with bicarbonate to minimize injection pain, as used in human patients, has not yet been shown useful in animals.

The hair around a laceration should be clipped before cleaning and closing a wound. Shaving is more traumatic and is not necessary. The area should be cleaned of all hair, dirt, and debris before closure. Dog skin is extremely mobile compared to human skin, but still may be closed with staples, sutures, or tissue glue in the same way as human skin would be closed. Because cosmetic outcome is rarely a concern in canines, and because dogs are generally not compliant with activity restriction, sutures or staples are usually left in place for 2 weeks before removal. Nylon or absorbable suture material (e.g., poliglecaprone 25 [Monocryl]) can be used. Advantages of absorbables include absorption and self-removal if suture removal is forgotten and absorption of the subcutaneous portion if the knot is inadvertently cut prematurely.

TAIL INJURIES

Lacerations of the tail, although almost never life threatening, can be a difficult problem because a happy, vigorous dog with a long tail can generate a large amount of centripetal force and repeatedly traumatize the tail with wagging. Because of its tapered shape, bandages are difficult to keep on the tail. A syringe casing or other rigid tube can be used to protect the tip of the tail, and tail hair can be incorporated between layers of adhesive tape to help prevent a bandage from slipping off.

SPINAL INJURIES

Fractures

Clinically recognizing and diagnosing fractures in the field is done by understanding normal anatomy and using standard clinical suspicion based on findings, such as abnormal limb angle, favoring a body part in a way that is indicative of pain, crepitus, or similar condition. Cervical spine injuries are much less common in animals than humans because head size and weight relative to neck size and strength are different. Most cervical trauma is the result of being hit by vehicles or from running headfirst into a tree or other immobile object (very rare). Fractures of the lumbar spine are also almost exclusively the result of vehicular trauma, although they occur occasionally from falls. It can be difficult to restrain adequately a dog with a suspected spinal fracture in a wilderness setting. Sedation and rigid immobilization and transport are ideal if possible.

Spinal injuries will usually cause neurologic deficits, ranging from ataxia to paresis to paralysis in the limbs caudal to the injury. It is important to recognize that even with complete spinal cord transection, a withdrawal reflex might still be present, so it is important that the dog respond to aggressive toe pinching if you are trying to assess whether it still has nociception in a limb.

Myelopathies

Vertebral disk herniations occur most often in chondrodystrophic breeds, such as dachshunds and basset hounds, although they can occur in any dog. With cervical disk herniation, severe pain is typically the most obvious clinical sign, whereas with thoracolumbar herniation, ataxia, paresis, or paralysis is most common. Definitive diagnosis will not be possible in a wilderness setting. Most cases of disk herniation occur without trauma, and onset may be acute, subacute, or insidious.

Vascular events, such as fibrocartilaginous embolus (FCE), can cause myelopathies of varying severity. These events occur most frequently in large-breed dogs, are acute in onset, and often affect one side more than the other. The most common presentation is a dog that is running, suddenly yelps, and becomes acutely paretic or paraplegic. Prognosis correlates with severity of clinical signs. Definitive diagnosis requires magnetic resonance imaging (MRI).

OCULAR AND PERIOCULAR INJURIES

Most ocular injuries are not treatable in a wilderness situation. Sterile saline, or potable water if saline is not available, can be used as a flush to remove foreign bodies and other contaminants. Antiseptic or antibiotic ointment can be used for corneal, scleral, and eyelid trauma. Lacerations involving the eyelid margins should not be repaired in the field, but rather delayed until veterinary management is available.

GUNSHOT WOUNDS

Gunshot wounds in animals are similar in type and trauma to those in humans. These are high-energy injuries where internal damage is often much greater than the external injury. In most cases, these injuries cannot be definitively treated in a wilderness setting; transporting the dog to an appropriate veterinary facility is paramount. An impermeable bandage, such as plastic cut from a baggie, should be used to avoid a tension pneumothorax if there is an open chest wound. Abdominal wounds may damage the gastrointestinal (GI) tract, resulting in sepsis. Even if a dog appears to be stable, seek veterinary care as soon as possible, because signs of GI tract perforation may not be evident for more than 24 hours. Bleeding should be controlled as well as possible with direct pressure. Intravenous (IV) fluids can be administered if available, and if the dog shows signs of shock. Subcutaneous fluids are inadequate in these types of injury because they are absorbed too slowly. Unstable fractures should be stabilized and the dog evacuated as soon as possible.

FLUIDS

There are several ways to administer fluid to a dog, depending on the clinical situation. Fluid types used in dogs are the same as in humans, including crystalloids such as lactated Ringer's solution or normal saline. The "shock dose" that is approximately equal to the animal's blood volume is 90 mL/kg of crystalloid. This is not given as a single bolus, but titrated to effect. There are several methods of fluid administration. The best method is intravenously through a cephalic or lateral saphenous vein catheter. Fluids can also be given subcutaneously (SC), although this should be avoided in cases of severe dehydration, because absorption will be slow or negligible, or in very cold weather, where the fluid could contribute to frostbite. For subcutaneous administration, the skin over the shoulders is tented upward and a needle or catheter placed into the subcutaneous space. In this method, the amount of fluid given per site is 10 to 20 mL/kg and limited by patient comfort. Fluids given subcutaneously are absorbed over 4 to 8 hours.

If available, an intraosseous catheter may be placed by drilling into the proximal-medial aspect of the tibia approximately 5 cm (2 inches) below the stifle joint. At this level, there is very little soft tissue over the bone, and a good amount of metaphyseal bone is available. The skin should be clipped and scrubbed and a local block of the skin and periosteum performed with 2% lidocaine. Fluids can generally be administered through an intraosseous catheter in the same amounts and rates as through an IV catheter. Oral electrolyte-containing hydration solutions (e.g., Pet-A-Lyte, Rebound OES) are available for dogs, but are probably not useful because dogs do not sweat and thus do not develop the same type of electrolyte losses during extremes of exercise as do humans.

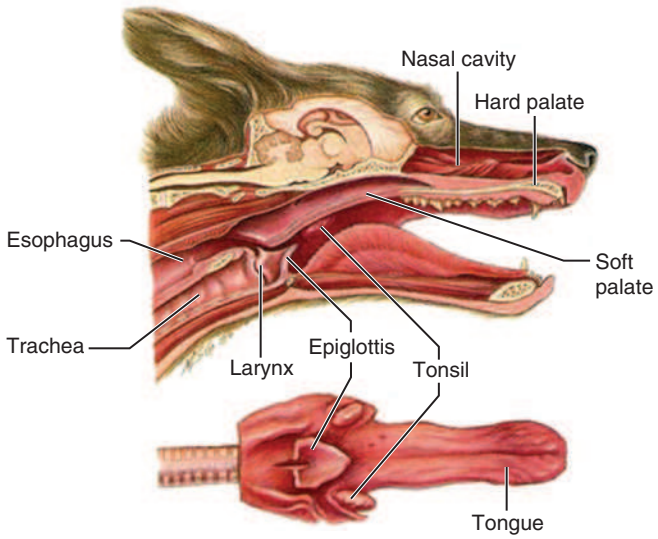

FIGURE 38-7 Canine glottis.

ENDOTRACHEAL INTUBATION

Dogs most easily are endotracheally intubated in sternal recumbency (laying on their sternum). An assistant should hold the upper jaw and use it to lift and extend the head. With the other hand, the assistant should grasp the tongue, pulling it forward and down to extend it and thereby use the tongue to open the jaw. A laryngoscope is very helpful to depress the tongue and hold down the epiglottis as necessary. A size 8 endotracheal tube will comfortably fit inside the trachea of most dogs 15 kg (33 lb) or larger (Figure 38-7).

CARDIOPULMONARY RESUSCITATION

Because dogs rarely have myocardial infarction, most cardiopulmonary arrest in dogs results from severe physiologic stress or injury. If the cause of arrest is not addressed, resuscitation is unlikely to be successful. In a wilderness situation, resuscitation is unlikely with the exceptions of drowning and choking. Check a femoral pulse, or listen to the heart, to confirm cardiac arrest before beginning chest compressions, and monitor every minute during compressions.

Chest Compression Techniques

Small Dog. A small dog is defined one whose chest is small enough that one adult human hand can reach more than 180 degrees around the chest when the palm is on the sternum. Most dogs that fit this description weigh 5 kg (11 lb) or less. Holding the dog in sternal recumbency, cup your hand over the point of the chest just behind the elbow. Squeeze firmly, pressing to compress the chest by 25% to 30% in width. The goal is 80 to 100 compressions per minute.

Medium or Large Dog. Lay the dog in lateral recumbent position on a firm surface. Place one hand on the highest point of the dog's chest—at the junction of the top (dorsal) and middle third of the rib cage. Place the other hand on top of the first, and push down forcefully with both hands, attempting to compress the chest 25% to 30% of its width. Chest compression should be 50% of total cycle time so that the compression phase equals the relaxation phase, with a goal of 70 to 90 compressions/min (Figure 38-8).

Respirations

Assisted breathing can be provided to a dog by holding the mouth closed and placing one's mouth around the dog's nose. Forced blowing into the nose should cause visible chest rise. The rate is 15 to 20 breaths/min for two rescuers, or two breaths alternated with every 10 chest compressions for a single rescuer. Chest compressions without breaths may be just as effective.

TOXICITY

For many cases of toxicosis or suspected toxicosis in a wilderness situation, the two mainstays of treatment are induced emesis and giving activated charcoal (1 to 2 g/kg) to bind the toxin. Several animal poison control hotlines are available to consult for a fee and can be valuable resources. These include American Society for the Prevention of Cruelty to Animals (ASPCA) Poison Control Center (888-426-4435); PROSAR International Animal Poison Center (888-232-8870); and Pet Poison Helpline (800-213-1680). The ideal situation is that an expert will be available and willing to take a telephone call to provide advice. Alternatively, the ASPCA has a free mobile app called *APCC by ASPCA* that gives information about common toxicities.

Emesis can be induced by using apomorphine, either injected (0.03 mL/kg IV or 0.04 mL/kg intramuscularly [IM]) or via subconjunctival (placed in conjunctival sac of eye) administration of a crushed ¼ tablet of 6 mg. If conjunctival administration is used, the eye should be flushed after emesis is achieved. If apomorphine is not available, 1 to 2.2 mL/kg of 3% hydrogen peroxide can be administered orally (not to exceed 45 mL total dose).

Activated charcoal is administered orally as soon as possible after ingestion of a known poison. ToxiBan comes in two formulations: 104 mg activated charcoal and 62.5 mg kaolin per mL, and 100 mg activated charcoal, 62.5 mg kaolin, and 100 mg sorbitol per mL. If available, the formulation with sorbitol is given for a first dose of 10 to 20 mL/kg. In addition to binding toxin to the activated charcoal, sorbitol acts as an osmotic cathartic to decrease intestinal transit time and decrease toxin absorption. A second and third dose of 10 to 20 mL/kg of the non-sorbitol containing formulation can be given every 6 to 8 hours. The formulation without sorbitol should be used to decrease the risk for hypernatremia.

COMMON CANINE TOXINS

Xylitol

This common sweetener is used in chewing gum, mints, toothpaste, and many other products. In dogs, xylitol can cause hypoglycemia at low doses (<100 mg/kg); ingestion of 500 mg/kg can be associated with hepatic failure. With ingestion of 100% xylitol products such as mints, most dogs vomit within 30 minutes and may effectively self-decontaminate. However, with chewing gum or other products containing lower concentrations, clinical signs may not occur until 12 hours later; common signs include vomiting, lethargy, and weakness. At the 12-hour point, only supportive care and monitoring can be provided. Without the ability to determine laboratory test values, no specific therapy exists.

Mushroom Toxicosis

Although many mushrooms are not toxic, ingestion of some types can result in hepatotoxic, neurologic, cardiovascular, hemolytic, muscarinic, GI, and/or nephrotoxic injury, similar to what occurs

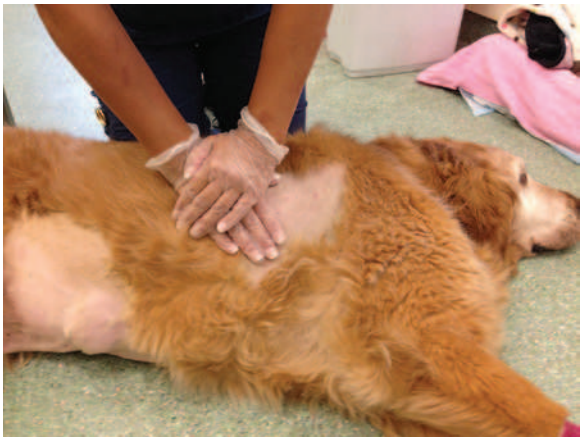

FIGURE 38-8 Canine cardiopulmonary resuscitation: hand placement.

in humans (see Chapter 66). It is safest to assume that ingested mushrooms are toxic and that more than one type might have been ingested. Recommended treatment in the field is induction of emesis followed by activated charcoal administration.[13]

Blue-Green Algae Intoxication

Cyanobacteria or blue-green algae are bacteria found in freshwater ecosystems. They colonize the water, giving it a thick "pea-soup" appearance. They can also be blown by the wind into thick, concentrated mats near the shoreline. They are most abundant during warm weather and in nutrient-rich water. Although most blue-green algae do not produce toxins, it is impossible to tell which ones are toxic without testing, so all "blooms" should be considered toxic. They produce a variety of toxins that can be deadly for dogs, and small exposures can be fatal. Clinical signs depend on the type of toxin involved, but may include vomiting, diarrhea, hematochezia, melena, weakness, icterus, seizures, disorientation, coma, and shock. Signs can occur as soon as 30 to 60 minutes after exposure. Treatment is induction of emesis if ingestion is witnessed, followed by activated charcoal administration.

Castor Bean Toxicosis

Castor bean plants are large, ornamental, Caribbean plants that grow in certain warmer parts of the United States. Seeds are produced in spiny pods that open after drying. The seeds, which contain ricin, have markings that resemble ticks or beetles. Ricin ingestion can result in cell death, causing vomiting, diarrhea, abdominal pain, and coagulopathy. Clinical signs can be observed 12 to 24 hours after ingestion. Ricin can be fatal in very small quantities, but is not likely to be absorbed if the seeds are not masticated, broken, or otherwise damaged. In dogs, as few as one to eight seeds may be fatal. Treatment for suspected ingestion is induction of emesis followed by administration of activated charcoal.

Ethylene Glycol (Antifreeze) Toxicosis

Although antifreeze is not a naturally occurring toxin, off-road vehicles and snowmobiles may be serviced in remote locations. Because ethylene glycol has a sweet taste, dogs may drink it. The fluid is rapidly absorbed, and clinical signs of central nervous system (CNS) depression, ataxia, and weakness occur in 1 to 2 hours. The dog may appear to improve after the initial "drunk phase" subsides. However, polyuria and polydipsia persist and can progress to acute renal failure in 24 to 72 hours. Once renal failure has occurred, the damage is irreversible. In the initial 1 to 8 hours after exposure, treatment is indicated. This includes induction of vomiting within 1 hour after ingestion to decrease absorption.

The antidote fomepizole prevents hepatic conversion of ethylene glycol to its toxic metabolites glycolic acid and oxalate, but it is unlikely to be available in a wilderness environment. Fomepizole or ethanol can be lifesaving if administered within the first 8 hours after ingestion, by competing with ethylene glycol for alcohol dehydrogenase in hepatocytes. Fomepizole is administered as 20 mg/kg IV over 30 minutes for a loading dose, followed by 15 mg/kg IV 12 and 24 hours later, then 5 mg/kg IV at 36 hours. A 7% solution of ethanol in saline can be made by removing 74 mL of fluid from a liter (1-L) bag and injecting 74 mL of 190-proof Everclear (the calculation can be changed for other strengths of ethanol), then administering a 8.8-mL/kg bolus over 30 minutes, followed by 1.43 mL/kg/hr for 48 hours. In a hospital setting, ethanol is given IV, but in a wilderness situation, if alcohol is available in beverage form and the dog is willing to drink it, this might help ethylene glycol to be excreted unchanged and minimize kidney damage. Exact oral dosing and efficacy of ethanol are unknown.

Grape/Raisin Toxicosis

The mechanism by which grapes or raisins cause renal tubular necrosis in dogs is unknown. As few as 10 to 12 grapes or 1 oz of raisins in an 8-kg (17.6-lb) dog have caused acute renal failure. Clinical signs consistent with renal failure begin with 12 to 24 hours after ingestion. Induction of emesis is recommended if there is suspicion of raisin or grape ingestion. Because the renal tubular basement membrane typically remains intact, recovery may be possible with prompt hospitalization and supportive care. Prompt evacuation is recommended if ingestion occurs in the wilderness.

Lead Toxicosis

Lead in birdshot has largely been eliminated in the United States and some European countries, but may still be used in other locations. Lead is also used in fishing weights, which can cause acute lead intoxication in dogs after ingestion. Acute toxicosis is characterized by anorexia and neurologic signs such as lethargy, ataxia, tremors, and seizures. Induction of emesis is recommended if lead is still in the stomach. Otherwise, removal of lead with chelation therapy is needed.

Oleander Toxicosis

Oleander is an ornamental evergreen shrub cultivated worldwide. The plant contains cardiac glycosides similar to digoxin that can cause fatal arrhythmias in dogs. Clinical signs of lethargy, weakness, diarrhea, and tremors may be reported within 6 hours of ingestion. Induction of emesis is recommended, followed by activated charcoal administration. If available, digoxin-specific Fab fragments can be used in dogs. This therapy has been found to be efficacious in treating experimentally induced oleander toxicity at a dose of 60 mg/kg IV.[2]

Onion Toxicosis

Onions, leeks, scallions, garlic, shallots, and chives are cultivated and also grow wild. They contain sulfoxides that can cause anemia by oxidizing red blood cell membranes. Japanese dog breeds, such as Akita, Shiba Inu, and Tosa, are more susceptible to oxidative damage. Most dogs require ingestion of 5 g/kg of onions to develop poisoning, which is unlikely in a wilderness situation. Clinical signs of lethargy, weakness, pale mucous membranes, and discolored urine occur 3 to 5 days after ingestion. Induction of emesis followed by activated charcoal administration is recommended.

Palm (Sago/Cycad) Toxicosis

Cycad palms are native to Japan but cultivated in tropical and temperate regions worldwide. Their leaves, seeds, bark, and roots contain several poisonous compounds that can be fatal to dogs if ingested. Clinical signs, such as vomiting, lethargy, and anorexia, may occur within 24 hours of ingestion. Ataxia, weakness, bleeding, and seizures may occur as acute liver failure and coagulopathy progress 2 to 3 days after ingestion. Induction of emesis followed by activated charcoal administration is recommended soon after ingestion.

Toad Intoxication

Dogs may be poisoned by oral exposure to many species of toads. Severity depends on extent of contact and type of toad. All toads produce toxins from modified parotid glands located dorsal and posterior to the eyes and distributed throughout the skin; potency varies between species and geographic locations and within individual species. The toxin, a thick, creamy white, highly irritating substance, can be expelled quickly when the toad is threatened and contains many components, including bufagenins with digitalis-like effects, and bufotoxins, with actions similar to those of local anesthetics, catecholamines, and serotonin.

The giant or marine toad, *Rhinella marina* (formerly *Bufo marinus*), an introduced species that is established in Florida, Hawaii, and Texas, is the most toxic toad in the United States. This toad is known as the cane toad in Australia, where its range extends across the northeastern half of the continent. Mortality rates are reported from 20% to 100% in untreated cases, depending on exposure circumstances. The Colorado River toad *Incillus* (formerly *Bufo*) *alvarius*, found in the southwestern United States and northern Mexico, is of sufficient size that it can produce a lethal amount of toxin in its skin.

Encounters with toads are most common in warm or mild weather, peaking in the United States from June through

September. Signs of poisoning range from local effects to convulsions and death. Severity depends on host factors, extent of exposure, length of time since exposure, and species of toad. Local effects (profuse and sometimes frothy salivation, accompanied by vigorous head shaking, pawing at the mouth, and retching) are immediate because the toxin is extremely irritating. Vomiting is not unusual, especially in severe cases, and although it may persist for several hours, no further signs may develop in poisoning by common indigenous toads. With more severe intoxication, as from *R. marina* or *I. alvarius,* cardiac arrhythmias, dyspnea, cyanosis, and seizures are characteristic. Cardiac and CNS involvement can be life threatening.

Because an antidote is not available, treatment is directed at minimizing toxin absorption and controlling associated clinical signs. If significant exposure is suspected, the mouth should be thoroughly washed with water. If the toad has been ingested, induction of emesis is indicated. Recognition and treatment of cardiac arrhythmias are unlikely to be feasible in a wilderness situation, but seizure activity can be treated with benzodiazepines or barbiturates.

SLED DOGS

Sled dogs undergo unique training and have physical demands that are far beyond tasks expected of most other, domestic dogs. One problem frequently encountered in sled dogs in a race situation is hemorrhagic colitis. This has been associated with multiple possible causative microbes, such as *Campylobacter* and *Salmonella,* some of which are zoonotic. However, the common causal factor seems to be the extreme physiologic demands of racing rather than bacterial infection. Treatment is with metronidazole (10 to 15 mg/kg orally (PO) twice daily) and supportive care. Metronidazole is effective by an unknown mechanism for treating irritable bowel disease in dogs, perhaps in some way related to the mechanism of action for hemorrhagic colitis. Sled dogs are also prone to carpal (wrist) injuries because of punching through the top snow crust. These injuries generally resolve with rest. Sled dogs are prone to foot injuries; most racing dogs wear preventive booties for this reason. Feet and booties should be inspected regularly.

Although dehydration is a concern in sled dogs because of evaporative losses from panting, it is important to remember that subcutaneous fluid should not be given because of the increased risk of frostbite. In a severely cold weather situation, all necessary supplemental fluid should be given intravenously.

HEATSTROKE

Heatstroke occurs when a dog's body temperature increases beyond the animal's ability to cool. Rectal temperature above 41°C (105.8°F) is considered dangerous and may be life threatening. Prevention is accomplished by avoiding extremes of activity, providing adequate water and shelter, and avoiding high environmental temperature. Heatstroke can be fatal if untreated.

Because dogs thermoregulate by panting, anything that interferes with a dog's ability to pant increases the risk for overheating. These interferences include brachycephalic breeds (e.g., bulldogs, pugs), laryngeal paralysis, wearing a muzzle, and obesity. Dark coloration and long hair can also increase risk.

Treatment for heat illness includes active cooling. In the field, wetting the dog and keeping it in the shade may be the most effective means available. Cool or cold, running or standing water (e.g., river or lake) may be used if available. Monitor temperature every 10 minutes, and stop active cooling when core temperature is between 39.4° and 40°C (103° and 104°F) to avoid overcooling. In the absence of ability to monitor temperature, less reliable indicators ("best guesses") must be used. If the dog has brick-red mucous membranes and is unable to stop panting when in a cooler, shady environment, excessive body temperature should be suspected and active cooling initiated. It will be difficult to determine when cooling goals have been met, but active cooling should be continued until the dog has more normal perfusion (as judged by mucous membrane color and CRT of 1 to 2 seconds) and respiratory pattern.

SNAKEBITE

Snakebite injuries in dogs are similar to those in humans (see Chapters 54 and 55). Envenomation from snakebites can cause neurologic dysfunction or local tissue damage with possible systemic coagulopathy. Because of the hair coat, bite marks can be difficult to find on dogs. Clinical signs of elapid envenomation appear 1 to 7½ hours after the bite and can progress rapidly. Signs range from salivation, vomiting, and nervous behavior to convulsions, paralysis, and death.

Crotalid (rattlesnake) venom causes immediate regional swelling that typically worsens over the first 24 hours after a bite. In severe injuries, tissue may become necrotic within ½ hour of envenomation.

In the field, antivenom can be administered, if available, although this is unlikely so the best treatment is evacuation. Because it can cause anaphylaxis, if antivenom is to be administered, the dog should be pretreated with 2 mg/kg diphenhydramine and the antivenom administered IV slowly. It is diluted in 50 to 200 mL of crystalloid fluid and administered over 1 hour. The antivenom used in most canine patients is Antivenin Crotalidae Polyvalent (ACP), supplied by Fort Dodge Laboratories. Recommended dosage is 1 to 5 vials (10 mL/vial) IV (no per-kg dosages are given). Generally, treatment starts with 1 to 2 vials within 4 hours after envenomation, with additional vials given every 2 hours if needed for symptom progression. CroFab (polyvalent immune Fab-ovine) administration has not been as thoroughly validated in dogs, but has been administered at the same dosage regimen and appears effective. Efforts should be made to minimize the patient's exertion after an envenomation. If possible, the dog should be carried to a veterinary facility for treatment.

LARYNGEAL PARALYSIS

Laryngeal paralysis occurs in older, medium and large-breed dogs, particularly Labrador retrievers. The problem occurs because of degeneration of the recurrent laryngeal nerve that innervates the intrinsic muscles of the larynx. There is mounting evidence that this disease is part of a generalized, slowly progressive peripheral neuropathy.

Laryngeal paralysis manifests as respiratory stridor with increased breathing noise and effort, particularly during the inspiratory phase. Many afflicted dogs have a hoarse bark because they are unable to close the glottis to initiate a normal bark. As the dog attempts to inspire, negative pressure generated in the airway apposes the arytenoid cartilages and closes the glottis. The harder the dog works to breathe, the more difficult breathing becomes. Dogs with laryngeal paralysis can become hypoxic, but the disease is more often life threatening because the dogs are unable to thermoregulate effectively by panting. In a vicious cycle, the hotter the dogs become, the harder they work to breathe, and the more heat they generate. Because they cannot dissipate this heat, heatstroke can result. Many affected dogs do well when relaxed and in a cool environment, but the stress of outdoor activity, particularly in warm weather, can precipitate a crisis. Because this is a disease that affects breeds frequently favored by outdoor recreationalists, it is important to take preventive measures. Dogs should be kept cool and calm. Exercise should be avoided and every effort made to keep the dog from becoming overheated or excited. Sedation can be used. If the dog is in a critical situation, endotracheal intubation or tracheostomy can be performed, although this is rarely feasible in the field.

PORCUPINE QUILLS

Because of their curiosity, dogs can get a face full of porcupine quills. This is rarely fatal but can be very painful. If there are many quills in the face, particularly if they have entered the eye or periorbital structures, it may best to wait for removal attempts until a veterinarian can sedate the dog. Quills can be removed by grasping the base with pliers or a hemostat. Pull straight out with a forceful steady motion, but do not yank, because this could cause the quill to break off. Removal can be very painful, so the dog should be restrained and/or muzzled for the procedure. If quills break off, they need to be removed surgically, but

this can wait until the dog is at a hospital. Cutting off the ends of the quills does not make them easier to remove. Rather, it results in less quill to grab and actually makes them more difficult to remove. Quills can break off under the skin and migrate to the eyes, brain, spine, and thorax. Dogs should be observed for signs of retained foreign bodies for several months after a porcupine exposure. These signs include joint pain, fever, anorexia, and behavioral changes.

GRASS AWNS

Numerous species of grass, such as foxtail, have awns with barbs that may become attached to the dog's hair coat or lodged in the external ear canal, nasal passage, conjunctival sac, or interdigital spaces. Dogs that are outdoors when plants are mature, typically in late summer, when awns are easily dislodged from the seed head, should be inspected frequently for awns in these sites. The purpose is to identify their presence and remove them promptly, before awns migrate further into the animal.

Signs depend on the location of the foreign body. When an awn is within the ear canal, the dog paws at its ear and shakes its head, which may be held tilted. Exudate may flow from the ear. Awns in the nostril cause sneezing and nasal exudate. Awns in the conjunctival sac cause lacrimation, photophobia, and corneal edema and ulceration, and the dog paws at the eye. Awn penetration between the digits or other locations throughout the skin is more difficult to diagnose because the awn may migrate quite a distance from the initial site of penetration.

Awns must be removed physically. Sedation, topical anesthesia, or both may be necessary. Although topical ophthalmic anesthetics are desirable in the eye, lidocaine may be used in an emergency. Small alligator forceps are most suitable for reaching into otherwise inaccessible places. An otoscope may be necessary to visualize awns in the nostril or ear canal. Instillation of an antiseptic or antibiotic ointment is advised after removal of the awn.

ANAPHYLAXIS

Anaphylaxis is a hypersensitivity reaction that results in massive generalized release of inflammatory mediators and can result in urticaria, angioedema, life-threatening cardiovascular collapse, and respiratory distress. Boxers and pit bulls are most often affected by urticaria, but there is no breed or age predilection for other allergic reactions. Recognized causes of anaphylaxis in dogs include antibiotics, parasiticides (antiparasitics), insects, food, and environmental allergens. The most common clinical signs are restlessness, diarrhea, vomiting, cardiovascular collapse, seizures, coma, and death.

In a wilderness situation, treatment is with aqueous epinephrine, if available. It may be given IM at 0.01 mg/kg of 1 mg/kg of the 1:1000 preparation. The easiest and safest place to give injections IM in a dog is in the dorsal paraspinal muscles or the quadriceps. If available, crystalloid fluids may be given at 20 to 30 mL/kg IV. A rapid-acting steroid, such as hydrocortisone sodium succinate (0.1 to 0.25 mg/kg), may be given IV. The antihistamine diphenhydramine may be given PO or IV at 1 to 2 mg/kg.

DROWNING

Scant evidence exists about resuscitation of pets after drowning, particularly in a wilderness environment. Anecdotally, many dogs will make a good recovery if they are able to regain spontaneous ventilation. Abdominal thrust or gravitational drainage offers no survival advantage and may increase risks of regurgitation and aspiration. If the dog is not spontaneously ventilating, mouth-to-nose breathing may be performed (see earlier). If no pulse is present, chest compressions are indicated.

FROSTBITE

Frostbite can be a risk for any dog, but particularly for short-haired breeds or those with very low body fat. Hypothermia increases risks of frostbite caused by vasoconstriction. Pinnae, testicles, and tail are the most frequently affected body parts. Skin may be pale and cool to the touch, or even cyanotic. Tissues should be gently warmed with warm compresses or, if possible, by submerging the affected body part in warm (~39° to 40°C [102° to 104°F]) water, but not rubbed or massaged because this may cause further injury. Debridement should be delayed unless infection is present.

GASTRIC DILATION AND VOLVULUS ("BLOAT")

Gastric dilation and volvulus (GDV), commonly called "bloat," occurs most often in older, large- and giant-breed dogs, particularly deep-chest breeds such as Great Danes. In this condition, the stomach twists around such that both the esophagus and the pyloric outflow become occluded. The stomach distends with gas and stretches until it severely impedes circulatory blood flow with resultant physiologic abnormalities and possible gastric necrosis (Figure 38-9). This condition can be fatal within 6 hours of onset if untreated, and mortality rates are high even with appropriate treatment. Mortality is almost 100% without treatment.

Dogs with GDV are unable to swallow or vomit. They will attempt to vomit and often bring up recently swallowed saliva that looks like uncooked egg whites. Their abdomen becomes progressively distended and tympanitic as the stomach fills with

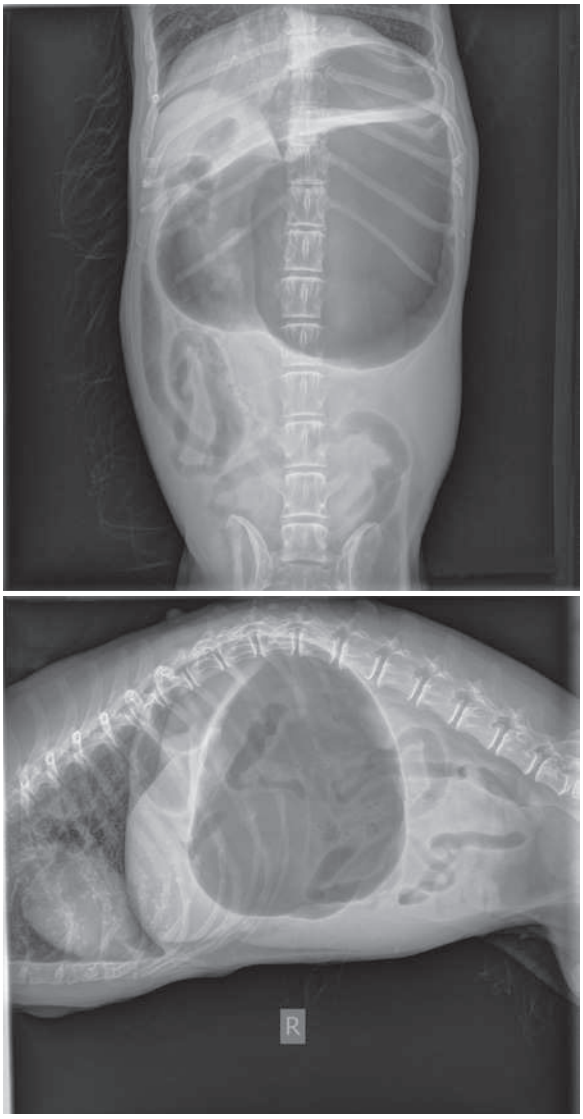

FIGURE 38-9 Gastric dilation and volvulus ("bloat").

gas. Dogs become weak and develop shock as the condition worsens.

Definitive surgical treatment is needed to resolve GDV. All haste should be made in taking the animal to a veterinary facility. While the animal is transported, passing an orogastric tube to decompress the stomach is ideal. However, this can be difficult, even with an anesthetized dog and proper equipment. One way to relieve gaseous distention is to perform trocharization with a large-bore needle, or preferably a large-bore over-the-needle catheter that is less likely to lacerate the stomach as it vents the stomach. This procedure should be attempted only when veterinary care is not immediately available, because of the risk of lacerating abdominal organs. The needle or catheter is inserted approximately a hand's width behind the last rib in the center of the lateral body wall. The operator will hear and smell gas escaping if trocharization is successful. Once the needle is removed, the catheter can be left in place as long as it is releasing gas. The catheter will typically become clogged with semifluid gastric contents as the gas flow decreases. This procedure can be repeated multiple times if necessary while the animal is being transported.

INFECTIOUS DISEASES

Rabies

Rabies is a viral disease that can occur in warm-blooded animals (see Chapter 31). The most commonly reported wild animal carriers are raccoons, skunks, bats, and foxes. All domestic dogs in the United States should have current rabies immunization; thus, their risk of being infected is very low. Onset of clinical signs after exposure is 2 weeks to several months. The disease is 100% fatal in dogs, with most dogs dying within 10 days of onset of clinical signs.

Botulism

Botulism, caused by a toxin produced by *Clostridium botulinum,* may occur in dogs with a history of ingestion of carrion or other source of anaerobic bacteria. The incubation period is hours to 6 days. Botulism causes lower-motor-neuron paresis/paralysis, with loss of tone and reflexes that generally begins in the hind legs and progresses to quadriplegia. Consciousness and pain perception are maintained. In severe cases, the muscles of breathing are affected, and death can occur from respiratory failure. Treatment is supportive. Antitoxin is not widely available and must be given early in the course of disease before toxin binds to the neuromuscular junction. Dosage is 10,000 to 150,000 IU/dog IV or IM for two doses 4 hours apart. Prognosis corresponds to the degree of symptoms with which the dog is affected.

Tetanus

Tetanus is caused by a potent neurotoxin produced by *Clostridium tetani.* The bacteria enter skin through cuts or punctures, as in humans. Signs of hyperesthesia and tonic muscle contraction typically begin 5 to 10 days after exposure, but onset may be delayed by up to 3 weeks.

Tetanus-prone wounds should not be closed to minimize anaerobic conditions. A 10-day course of an antibiotic, such as penicillin G (20,000 to 100,000 U/kg IV, SC, or IM every 8 to 12 hours), metronidazole (10 mg/kg PO every 12 hours), tetracycline (22 mg/kg PO or IV every 8 hours), or clindamycin (5.5 to 33 mg/kg PO, IM, or IV every 12 hours) can be administered if available. The afflicted animal should be kept in a quiet area to minimize stimulation, and veterinary care sought as soon as possible.

Tick Paralysis

Tick paralysis is a rapidly progressive, lower-motor-neuron (flaccid) paralysis caused by a neurotoxin found in saliva of gravid female ticks of *Dermacentor* (North America) and *Ixodes* (Australia) ticks. This can occur worldwide but is most often reported in North America and Australia. Weakness begins in the hind legs 5 to 9 days after tick attachment and progresses in 24 to 72 hours to flaccid paralysis and possibly death from respiratory failure. Reflexes are lost, but mentation and pain sensation are preserved. The paralysis is similar that caused by botulinum toxin or severe myasthenia gravis. Tick removal is both diagnostic and therapeutic because the paralysis often resolves within hours after removal. It is important to remove the tick head because the toxin resides in saliva (see Chapter 42).

Leptospirosis

Leptospirosis is an infectious disease affecting both dogs and humans caused by a gram-negative filamentous spirochete of the genus *Leptospira.* Humans can become infected from contact with infected dogs. Dogs contract the disease through mucous membranes when drinking standing water or transcutaneously through abraded or water-softened skin. Many infections are asymptomatic. With peracute, acute, subacute, and chronic forms, clinical signs include anorexia, lethargy, fever, vomiting, diarrhea, muscle pain, polyuria/polydipsia, icterus, and in severe cases, coagulopathy. Unexplained fever with signs of renal or hepatic disease should raise the possibility of leptospirosis. Untreated leptospirosis can lead to renal or liver failure. Treatment with amoxicillin, 22 mg/kg PO or IV every 8 hours, is generally effective. Early treatment carries a fair prognosis in symptomatic patients.

Rocky Mountain Spotted Fever

Rocky Mountain Spotted Fever is an acute, potentially life threatening tick-borne rickettsial disease affecting dogs and people in North, Central, and South America. This disease cannot be spread directly from dogs to people, although dogs may act as short-term reservoirs. The incubation period is 2 to 14 days after tick exposure. Early clinical signs are vague and may include fever, pain, cough, petechiae, ecchymoses, uveitis, and neurologic abnormalities, such as head tilt and ataxia. Fulminant disease can lead to coagulopathy and death. Treatment is with doxycycline (5 to 10 mg/kg PO twice daily for 14 to 21 days) or enrofloxacin (5 to 10 mg/kg PO twice daily for similar duration). Ciprofloxacin may be substituted, but absorption in dogs is variable, so dosing is unreliable; it is typically dosed at 30 mg/kg PO every 24 hours.

Giardiasis

Giardiasis is caused by *Giardia lamblia*, a flagellate protozoan parasite that can be found in the GI tract of humans and many domestic and wild animals. Although many dogs asymptomatically carry *Giardia,* exposure can result in acute, short-lived or chronic diarrhea. It is possible for dogs to transmit the parasite to other dogs or people. The cysts are excreted in feces, are immediately infective, and can live for weeks in a cool, moist environment. Giardiasis can be treated with fenbendazole (veterinary-specific drug) or metronidazole (15 mg PO twice daily for 5 to 7 days), but metronidazole is less effective than fenbendazole in dogs (Table 38-1).

LARGE ANIMALS

USE AND CARE OF LARGE ANIMALS IN THE WILDERNESS

Equids, including horses, mules, and donkeys, are some of the most popular animals for transport of personnel, supplies, and equipment in the wilderness. Their strength, capability for sustained work, and ability to traverse varied terrain make them extremely useful backcountry companions. These animals are versatile for a variety of uses, including service as pack animals and for riding. New World camelids (llamas, alpacas, and guanacos) are popular pack animals in high-altitude regions, for which they are well adapted. Expeditions in various parts of the world may also encounter camels, bovids (e.g., oxen, yak), elephants, and small-ruminant species (e.g., goats) as pack animals. Although general guidelines are provided for emergency care of large-animal species in the wilderness, it is important to remember that important and substantial medical differences exist among the large-animal species, between large-animal species and small-animal species, and between large-animal species and humans; diseases and treatments vary accordingly.

Regardless of the large-animal species used during an expedition, care must be taken to ensure animals are fit for service,

TABLE 38-1 Medications for Dogs*

Generic Name	Trade Name (Company)	Concentration in Vial	Route of Administration	Dog	Indication and notes
Acepromazine maleate	PromAce (Fort Dodge)	10 mg/mL or tabs	IM, SC, PO	0.05-0.22 mg/kg PO, 0.55 to 1.1 mg/kg IV, IM, or SQ	Tranquilizer
Amoxicillin	Generic	Tabs	PO	10-20 mg/kg q12h	Infections and Lyme disease
Ampicillin sodium	Generic	—	IM	10-30 mg/kg q6-8h	Infection
Apomorphine	Generic	Tabs, injectable	SC, IV, IM, or crushed tab placed in conjunctival sac	0.03 mg/kg IV, 0.04 mg/kg IM	For induction of emesis Rinse conjunctiva after emesis occurs
Aspirin-buffered and enteric-coated forms preferred	Generic		PO with food	10-20 mg/kg q12h	Canine-specific NSAIDs are safer and more effective; inhibit platelet function.
Atropine sulfate	Generic	2 mg/mL	IM, SC	0.04 mg/kg	Bradycardia; antidote for blue-green algae or muscarinic mushroom intoxication
Azithromycin	Zithromax (Pfizer)	Concentration varies with reconstitution	PO	5-10 mg/kg qd for 3-5 d	Infections
Cephalexin	Generic, Keflex	250- and 500-mg capsules	PO	22 mg/kg bid-tid	Infections, skin
Charcoal (activated)	Generic	—	PO	1-4 g/kg as slurry with water	Toxin adsorbent
Ciprofloxacin	Generic	Tabs	PO	10-20 mg/kg qd	Infections
Clindamycin	Antirobe, Cleocin, generic	Tabs	PO	5-11 mg/kg q12h	Infections, abscesses, oral infections
Diazepam	Generic	5 mg/mL	IV, per rectum, intranasal	0.2-1 mg/kg IV, 2 mg/kg per rectum or intranasal for status epilepticus	Sedation or antiepileptic
Diphenhydramine	Generic	Tabs, injectable	PO, SC	2-4 mg/kg q8h	Allergic reactions, motion sickness
Doxycycline	Generic	Tabs	PO	3-5 mg/kg q12h (infection), 10 mg/kg q24h (Lyme disease)	Infection, Lyme disease, ehrlichiosis, Rocky Mountain spotted fever
Famotidine	Pepcid	Tabs, injectable	PO, SC, IM	0.5 mg/kg q12h	Decrease gastric acidity
Hydromorphone	Generic	Injectable	IM, IV, SC	0.05-0.2 mg/kg q2-6h	Pain control, sedation
Lidocaine	Generic	2%		As needed; do not exceed 8 mg/kg total dose	Local anesthesia
Metoclopramide (Reglan)		Tablets, injectable	PO, SC, IM, IV	0.2-0.5 mg/kg q12h	Antiemetic, prokinetic
Metronidazole	Flagyl (Pharmacia)	Tabs	PO	15 mg/kg q12h	Antibacterial, antiprotozoal, and amebicidal agent
Misoprostol	Cytotec (Pfizer)	Tabs	PO	3 mcg/kg q12h	Gastric ulcers, abortifacient
Morphine	Generic	Oral, injectable variable concentrations	IM, SC, IV	0.5-2 mg/kg IM, SQ, or 0.1-0.2 IV q4h	Can cause histamine release particularly with IV injection
Nitenpyram	Capstar	Tabs	PO	Give per label directions.	Very safe, effective, over-the-counter flea adulticide; will not treat larvae or eggs
Omeprazole	Prilosec	Tabs	PO	0.5-1.0 mg/kg q24h	Gastric ulcers
Oxycodone	Generic	Tabs	PO	0.1-0.2 mg/kg q6-8h	Pain, sedation (not well studied in canines)
Prednisone	Generic	Tabs	PO	0.5-1 mg/kg q12-24h	Antiinflammatory
Trimethoprim/ sulfamethoxazole	Tribrissen (Schering-Plough)	Tabs	PO	15-30 mg/kg q12h	Infection
Tramadol	Ultram (Ortho-McNeil)	Tabs	PO	2-4 mg/kg q8h	Analgesic

*Many drugs and/or dosages are not evaluated and approved by the FDA and should be considered off-label usage.
IM, Intramuscular; *IV,* intravenous; *PO,* oral; *q12h,* every 12 hours; *q6-8h,* every 6 to 8 hours; *qd,* once daily; *bid,* twice daily; *tid,* three times daily; *qid,* four times daily; *SC,* subcutaneous.

have had a recent veterinary examination, and are current on preventive care measures, such as vaccinations and anthelmintic drug administration. Equids are particularly susceptible to tetanus, and a toxoid booster should have been administered within the past year. Llamas should be vaccinated against tetanus and *Clostridium perfringens* types C and D. Additional protocols for preventive medicine measures vary with geographic region, and local veterinarians should be consulted on these matters. Personnel should have knowledge of common injuries and diseases that are likely to affect large animals in the wilderness, as well as appropriate emergency treatment measures. Well-equipped and knowledgeable medical personnel can handle many such situations (Box 38-2). However, veterinarians should be consulted for advanced treatments.

Expedition personnel should be aware of local regulations concerning use of large animals in wilderness areas. For example, the U.S. National Park Service publishes and enforces regulations regarding use of stock animals in many wilderness areas under its jurisdiction. These regulations include guidelines for number of animals allowed, number of consecutive days and nights allowed in wilderness areas, and use of grazing areas. In addition, some areas have requirements regarding sources of feed and removal of animal waste; these regulations are intended to prevent introduction of non-native plant species.

Loading Guidelines for Large Animals

Large animals are abundantly useful in the wilderness because they can carry large loads efficiently over long distances. However, overloading can cause fatigue and injuries. Recommendations regarding maximum safe loads vary widely. Personnel should be familiar with local regulations concerning pack-animal use; some jurisdictions have specific weight recommendations based on weight, size, and species of animal. Pack animals in good health can safely carry 25% to 30% of their body weight (Table 38-2). However, terrain (e.g., mountains) and other environmental conditions (e.g., extreme heat or altitude) may require that loads be decreased. Animal caretakers should ensure that loads are evenly distributed and balanced.

Physical Examination

Physical examination should be performed on all animals before beginning a wilderness trip. Indications for physical examination, including signs of illness or injury, may arise during the trip. Examination may include assessment of the cardiovascular, respiratory, GI, musculoskeletal, and nervous systems. Basic assessment should include measurement of rectal temperature, heart rate, respiratory rate, and mucous membrane CRT; auscultation of the thorax and abdomen; and assessment of hydration status (by assessing mucous membranes). For horses with lameness, digital arterial pulse strength should be assessed and major musculoskeletal structures palpated (synovial cavities, tendons, ligaments, and bones). Observation of the amount and consistency of fecal material can be an indication of GI tract health. Observation of the animal in motion may also help detect musculoskeletal issues that could be problematic in the wilderness.

Body temperature is typically measured rectally in large animals. For horses, normal values are 37.2° to 38°C (99.0° to 101.0°F). Normal values for cattle are (38° to 39°C (100.4° to 102.5°F). Lower temperature values may be obtained in normal

BOX 38-2 Equipment and Supplies for Large Animals in the Wilderness

- Lip twitch
- Battery-operated hair clippers
- Wire cutters
- Hoof care equipment: hoof file, nail pullers, shoe pullers, hoof trimmers, hoof knife, hoof testers, clinch cutter, hammer (see Figure 38-12)
- Topical disinfectant such as chlorhexidine gluconate 2% to 4% or povidone-iodine 5% scrub
- Bandaging material: gauze pads, gauze roll, cast padding, nonadhesive dressing, adhesive tape, VetRap, Elastikon, fiberglass casting tape; splinting material (wood boards, PVC pipe)
- Skin stapler and/or tissue glue
- Suture material: monofilament and multifilament, absorbable and nonabsorbable, sizes, 3-0 to No. 2
- Activated charcoal preparation (ToxiBan); must be administered via nasogastric (NG) tube
- Sterile nonlatex surgical gloves
- Lidocaine 2% with epinephrine
- Sterile disposable syringes: 1 to 60 mL
- Sterile needles: 22 to 18 gauge
- Intravenous (IV) catheter: 14 gauge
- Sterile surgical pack
  - Needle holders
  - Thumb forceps
  - Suture scissors
  - Mayo scissors
  - Metzenbaum scissors
  - Hemostats
  - Scalpel handle (No. 3)
  - Scalpel blades (No. 10)
- Tubing
  - Silastic, 1-cm outside diameter, 10 cm (4 inches) long, for nasal tube
  - Large-animal tracheostomy tube
  - Large-animal stomach tube, 1-cm inside diameter, 300 cm (120 inches) long
  - Funnel (plastic) to fit into stomach tube
- Thermometer
- Stethoscope

TABLE 38-2 Vital Statistics of Trek Animals

Animal	Body Weight		Heart Rate (beats/min)	Respiratory Rate (breaths/min)	Body Temperature		Weight Carried by Well-Conditioned Animal*	
	Kg	lb			°C	°F	kg	lb
Horse	360-540	800-1200	28-44	12-24	37.2-38.0	99.0-101.0	110-136	240-300
Mule	275-540	600-1200	28-44	12-24	37.2-38.0	99.0-101.0	82-136	180-300
Donkey	136-275	300-600	28-44	12-24	37.2-38.0	99.0-101.0	40-82	90-180
Llama	136-200	300-450	60-90	10-30	37.2-38.7	99.0-101.8	34-50	75-110
Dog	9-45	20-100	65-120	15-30	37.5-38.6	99.5-102.5	3-14	6-30
Camel	400-550	880-1200	40-50	5-12	36.4-42.0	97.5-107.6	225	500
Elephant	2300-3700	5000-8000	25-35	4-6	36.0-37.0	97.5-99.0	900	2000
Yak	1000	2200	60-80	12-36	37.8-39.2	100.5-102.5	235	550
Ox	499-1361	1000-3000	60-80	12-36	37.8-39.2	100.5-102.5	235	550

*Sustained trekking for 24 to 40 km (15 to 25 miles) per day on moderately difficult trails. The weight includes tack. Animals in training should be expected to carry only one-half to two-thirds of this weight.

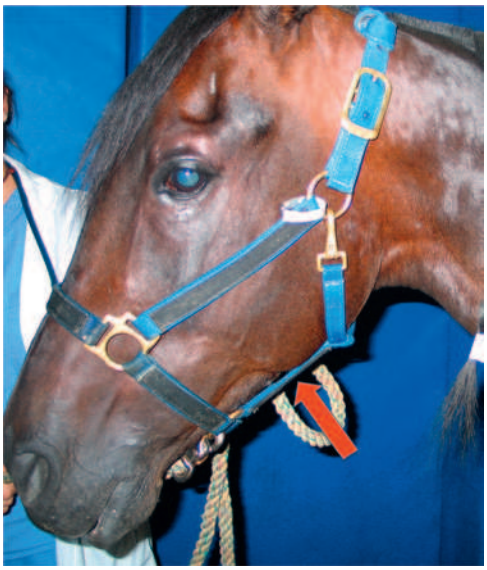

FIGURE 38-10 The external maxillary arterial pulse in equids is easily palpated where the artery crosses the mandible, just rostroventral to the large masseter muscle (*arrow*).

animals if there is gas or feces in the rectum. Elevated rectal temperature values should prompt further investigation to determine a cause; problems with respiratory and GI systems are the most common sources of elevated rectal temperature in animals without other obvious sources, such as superficial abscesses.

The heart should be auscultated on the right and left ventral aspects of the thoracic wall just behind the olecranon process of the ulna in the elbow region. Normal heart rate for horses is 28 to 44 beats/min. Normal heart rate for cattle is 60 to 80 beats/min. Each heartbeat is typically heard as two distinct sounds; however all four sounds (closure of atrioventricular valves, closure of semilunar valves, oscillation of blood in the ventricles, and atrial contraction) may be heard. Some horses may have second degree atrioventricular node block, which is considered normal. However, other arrhythmias (most often atrial fibrillation) are abnormal. Mild early systolic and diastolic murmurs (caused by flow of blood out of the heart during systole or into the heart during diastole) can be heard in horses without cardiac disease, but severe murmurs are cause for concern and may preclude safe performance of animals in the wilderness. Such murmurs are most frequently caused by cardiac valve incompetence and septal defects. The most reliable location for palpation of a pulse is the external maxillary artery under the mandible (Figure 38-10), where the vessel courses just rostroventral to the masseter muscle. Pulses should be palpably strong and synchronous with heart sounds.

The lungs are auscultated in a triangular-shaped field on the lateral aspects of the right and left thoracic walls. The cranioventral boundary of the auscultable lung field is the olecranon process of the ulna (elbow region). The craniodorsal boundary is a point directly dorsal to the cranioventral boundary just below the epaxial musculature. The ventral border of the lung field follows a curved line to a point just below the epaxial musculature in the 16th intercostal space; equids typically have 18 paired ribs, although some breeds (e.g., Arabians) have 17. The audible lung field is much smaller in cattle; these animals have only 13 paired ribs, and the caudodorsal border of the lungs is at the 11th rib. The normal respiratory rate for horses is 12 to 24 breaths/min and for cattle is 12 to 36 breaths/min. Abnormal adventitious sounds may indicate lower respiratory tract inflammation and infection. Horses with chronic obstructive pulmonary disease (equine recurrent obstructive airway syndrome, or "heaves") secondary to allergic reactive airways have increased respiratory effort and may have hypertrophy of abdominal wall musculature, visible as a prominent groove ("heave" line). Animals with this condition will likely have difficulty performing strenuous tasks or traveling long distances. Auscultation of the trachea along the ventral aspect of the neck may reveal evidence of tracheal exudate.

Auscultation of the abdomen can be used to determine character and frequency of GI tract contractions. The abdomen should be auscultated between the last rib and the point of the hip (tuber coxa). Infrequent or absent GI tract sounds can indicate poor motility. Animals with ileus, obstruction, volvulus, or torsion may have obvious abdominal distention and audible tympany (gas ping) heard after snapping a finger over a distended viscus. These conditions usually cause moderate to severe pain and represent emergencies requiring prompt veterinary care.

Skin turgor is not a reliable indicator of hydration status in large animals. Palpation of moist oral gingiva is a more reliable indicator of adequate hydration. CRT of the mucous membranes after release of firm pressure should be less than 2 seconds. Prolonged CRT is an indicator of poor capillary perfusion, and along with reddening of membranes, can be an indication of endotoxemia.

Examination of the musculoskeletal system is vitally important for work animals before undertaking a wilderness trip. Palpation of synovial structures, tendons, and ligaments may reveal injuries that could limit performance and prove dangerous in remote areas (Figure 38-11). Animals should not have obvious lameness in motion. Animals with substantial lameness are not suitable for wilderness travel. Particular emphasis should be placed on examination of all four hooves, because foot problems are very common in equids and can result in substantial lameness. Hooves should have a consistent angle from the ground to the *coronary band,* the soft tissue immediately adjacent to the horny tissue. The solar surface of the foot should be slightly concave and smooth, with no obvious defects or bruising. The *frog* (a triangular section of soft horn toward the back of the sole) should be dry without any exudate. Use of a hoof tester instrument to place pressure on the solar surface should elicit minimal or no withdrawal response. Before traveling into a wilderness area, horses and other equids should have had routine preventive hoof care performed by a farrier. This entails trimming the solar surface and wall of the hoof and, when appropriate, application of metal shoes. Personnel accompanying animals in remote areas should be familiar with basic hoof care procedures, and appropriate tools should be available to accomplish minor trimming and shoe removal (Figure 38-12). Personnel with experience in more advanced hoof care, such as placement of shoes, may be

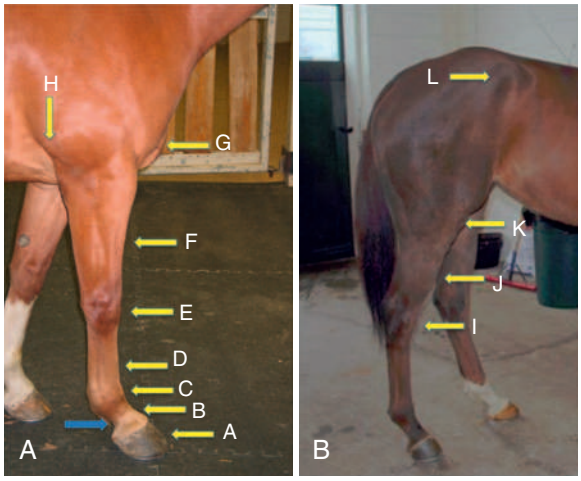

FIGURE 38-11 Common anatomic terms for forelimbs (*A* through *H*) and hind limbs (*I* through *L*) of large animals include the foot (*A*), pastern (*B*), fetlock (*C*), metacarpus or cannon bone (*D*), carpus (*E*), radius (*F*), shoulder (*G*), olecranon or point of the elbow (*H*), hock (*I*), tibia (*J*), stifle (*K*), and tuber coxa or point of the hip (*L*). Anatomic regions are identical in the forelimbs and hind limbs distal to the carpus and hock. *Blue arrow* indicates the location for palpation of the digital arterial pulse in the pastern region.

FIGURE 38-12 Selection of hoof tools that should be carried as equipment for care of large animals in the wilderness. *Left* to *right,* Hoof rasp, hoof testers, shoe pullers, hoof nippers, hammer, clinch cutters (for straightening and removing clinches of nails in the hoof), hoof knife, and nail pullers.

advantageous for longer excursions. Shoes should not be placed by inexperienced personnel.

Food and Water Requirements

It is essential that an adequate source of water be provided for animals in the wilderness. Clean water sources will be more palatable for animals and decrease the risk of secondary illness. At a minimum, sedentary adult horses should drink approximately 20 L (5 gallons) of water per day. Cattle may drink up to 50% more, and camelids may drink less than that amount daily. High workload and environmental temperature can increase the requirement by as much as 200%.

Horses typically consume 2% of their body weight (20 lb of feed for a 1000-lb [450-kg] adult) per day. They can utilize forage or hay, although not as efficiently as ruminants (e.g., cattle, oxen, yak, water buffalo). Rations of grain concentrates should be included to supplement the diet for working equids. Camelids may consume less food as a percentage of body weight (1% to 2%) than equids. Camelids and ruminants can subsist on forage, although concentrates may be added to their diet, particularly in areas with poor quality or small amounts of grazing. If grazing is allowed, personnel should be familiar with local toxic plants to avoid intoxication of the animals.

LARGE-ANIMAL RESTRAINT

Proper physical restraint of large animals is essential for safety of animals and handlers. For most purposes, equids may be controlled by a single handler using an appropriately sized halter and lead rope. The handler should remain on the left side of the animal in front of the shoulder. For medical procedures, additional physical restraint may be required. The handler may manually grab a fold of skin on the lateral side of the neck just cranial to the shoulder. Similarly, the handler may squeeze the left ear; however, the handler should be cautious that he is not pulled off the ground if the animal lifts its head. Use of a lip twitch may be useful to maintain safe control of an equid for certain procedures (Figure 38-13). These devices are quite useful; however, handlers should not let go of the lip switch while it is in place, because if the handle swings rapidly, it can seriously injure personnel or the animal. The muzzle should be grasped through the rope or chain loop of the device; then the handle is twisted until the muzzle is grasped with firm pressure. A lip twitch should not be used on large animals other than equids; physical restraint of other large animals is best accomplished by trained handlers.

If physical restraint is not adequate for completion of a medical procedure, chemical restraint may be required. Sedative medication may be administered IM or IV. Medications are most easily administered IV to equids in the right or left jugular vein,

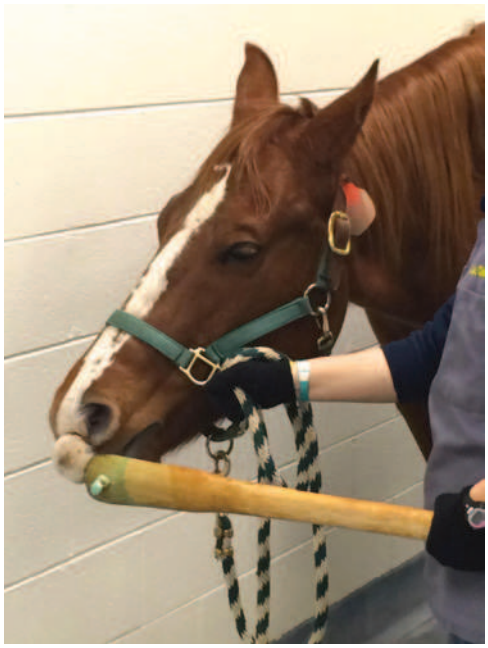

FIGURE 38-13 A lip twitch is useful for manual restraint of horses. The rope or chain of the twitch should be firmly twisted onto the muzzle and securely grasped by the handler.

which runs in the jugular furrow along the ventral aspect of the neck (Figure 38-14). Cattle may be injected in the jugular vein or a ventral tail vein. IV injection in camelids can be extremely challenging. Caution should be used when administering medication because the carotid artery courses just deep to the jugular vein. It is safest to inject the jugular vein in the cranial one-third of the neck, where the vein and artery are separated by more fascia and muscle. Typically, an 18- or 20-gauge needle is used. Needles may be inserted before syringe attachment; if pulsatile arterial blood flow is observed, the needle should be withdrawn and reintroduced at a shallower angle to enter the vein. Most common sedatives used in large animals are veterinary-specific drugs. Doses for equids and other large animals vary substantially, so veterinary guidance should be sought when sedation is required.

LOCAL ANESTHESIA

For procedures that cause cutaneous pain (e.g., laceration repair), local anesthetic techniques should be used in conjunction with

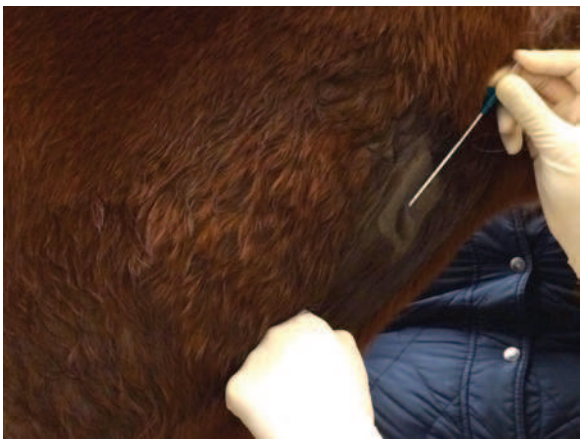

FIGURE 38-14 Intravenous injection in large animals is typically performed via the jugular vein, which lies in a furrow at the ventral aspect of the neck. Injection is performed through a needle (18 or 20 gauge) or 14-gauge catheter (insertion of catheter shown).

restraint techniques to decrease patient discomfort and improve operator safety. Many perineural techniques can be used, and veterinarians can guide use of these techniques. However, for most emergency purposes, simple local infiltration of anesthetic solution (subcutaneous line block at the site or ring block around the site) should be sufficient. Lidocaine (2% solution) is the most commonly used local anesthetic in large animals; it affords rapid onset and reasonably long duration of action, approximately 2 to 2½ hours, that comfortably allows completion of most procedures. Before injection, skin should be prepared to reduce the risk of contamination in deeper tissues. If possible, hair should be clipped around the site. Skin should be cleansed with povidone-iodine 5% solution or chlorhexidine 2% to 4% solution scrub and thoroughly rinsed with saline or potable water before injection, although a full-sterile preparation is not necessary unless a synovial cavity will be injected. Needle gauges vary between 18 and 25 gauge, depending on the site and thickness of skin. Ruminants have much thicker skin than equids, so large needles may be needed for these animals.

MEDICATION GUIDELINES

Many medications for large animals are specific for the particular species. Some common drugs are listed in Table 38-3. Those needed most often for emergency care of large animals are sedatives, antimicrobials, and nonsteroidal antiinflammatory drugs (NSAIDs). Flunixin meglumine (1.1 mg/kg IV or PO once daily) and phenylbutazone (2.2 to 4.4 mg/kg IV or PO twice daily) are common and effective NSAIDs for horses. Use of NSAIDs, particularly phenylbutazone, in food-animal species is strictly controlled in the United States, and a veterinarian should be consulted before such use. Injectable formulations of NSAIDs should only be administered IV; IM administration commonly leads to clostridial myositis with severe local and systemic sequelae. Oral formulations of flunixin meglumine and phenylbutazone are readily available, effective, and convenient for use in a wilderness setting. NSAID treatment duration should be kept to a minimum to avoid adverse effects, especially renal damage and GI ulceration. Phenylbutazone should not be administered to horses at a 4.4-mg/kg twice-daily dosage for more than 2 consecutive days. Total duration of NSAID administration should not exceed 10 days without veterinary consultation.

For some drugs, dosages may differ substantially between species, and care should be taken to ensure that proper amounts are administered. Personnel should also be aware of national regulations concerning approved use of drugs for food-animal species. For example, the Federal Drug Administration (FDA) regulates drug approvals for food animals in the United States. Drugs should be administered in accordance with drug labels specific for the species and the Animal Medicinal Drug Use Clarification Act (AMDUCA). Extralabel use of drugs may be illegal in food animals. Such drugs should be administered under the supervision or direction of a veterinarian.

TRACHEOSTOMY

Other than wound care, tracheostomy is one of the few surgical procedures that is useful and feasible to perform in a wilderness setting for large animals. Other common emergency orthopedic and abdominal procedures require advanced veterinary care in a hospital environment. Tracheostomy can be a lifesaving measure for animals with upper airway obstruction attributable to laryngeal paralysis, space-occupying masses, and severe soft tissue swelling caused by problems such as snakebite. The procedure should be performed at the junction of the cranial one-third and middle-third of the neck on the ventral aspect. If possible, hair should be clipped at the surgical site and local anesthetic solution (~10 to 15 mL of 2% lidocaine) instilled subcutaneously. A 10-cm (4-inch) longitudinal incision is made on the ventral midline of the neck through skin and subcutaneous tissue. The paired sternothyroideus muscles are bluntly separated with scissors until tracheal rings are identified. A 2-cm (0.8-inch) transverse incision is made between two cartilaginous rings into the tracheal lumen. A tracheostomy tube appropriate for use in

TABLE 38-3 Medications for Trek Animals*

Generic Name	Trade Name (Company)	Concentration in Vial	Route of Administration	Dosage		Indication
				Horse	Llama	
Acepromazine maleate	PromAce (Boehringer Ingelheim)	10 mg/mL	IV, IM	0.02-0.05 mg/kg	Not indicated	Tranquilizer
Ampicillin sodium	Generic	—	IV	15-20 mg/kg qid	10-25 mg/kg tid	Infection
Charcoal (activated)	Generic	—	PO via NG intubation	0.5-1 g/kg	0.5-1 g/kg	Toxin ingestion
Dexamethasone	Azium (Schering-Plough)	2 mg/mL	IV, IM	0.02-0.05 mg/kg	0.1 mg/kg	Shock, severe nonseptic inflammation
Epinephrine	Generic	1:1000, 1 mg/mL	IV, IM	0.01-0.02 mg/kg	0.01 mg/kg	Anaphylaxis
Flunixin meglumine	Banamine (Merck Animal Health)	50 mg/mL	IV	1.1 mg/kg daily	1.1 mg/kg daily	Colic pain, inflammation, fever
Lidocaine	Generic	2%	SC, IM	<10 mL/100 lb	< 10 mL/100 lb	Local anesthesia
Penicillin G benzathine	Benzapen (Pfizer)	150,000 units/mL	IM	Not recommended	5000-15,000 units/kg q2d	Infection
Penicillin G procaine	Generic	300,000 IU/mL	IM	22,000 IU/kg bid	22,000 IU/kg bid	Infection
Phenylbutazone	Butazolidin (Schering-Plough)	200 mg/mL; 1-g/tablet	IV, PO	2.2-4.4 mg/kg bid	2.2-4.4 mg/kg daily	Pain, inflammation, fever
Trimethoprim/sulfadiazine	Tribrissen (Schering-Plough)	960-mg/tablet	PO	20-30 mg/kg bid	45 mg/kg bid	Infection
Xylazine	Rompun (Bayer)	100 mg/mL	IV, IM	0.2-0.6 mg/kg	0.2-0.3 mg/kg	Sedation

*Most veterinary-specific drugs are not listed. Doses for food animal species are not listed; such drugs should be administered as directed by a veterinarian. In the United States, drugs should be administered to food animals in accordance with the Animal Medicinal Drug Use Clarification Act (AMDUCA).
IM, Intramuscular; *IV,* intravenous; *NG,* nasogastric; *PO,* oral; *SC,* subcutaneous; *IU,* international units; *bid,* twice daily; *tid,* three times daily; *qid,* four times daily; *q2d,* every 2 days.

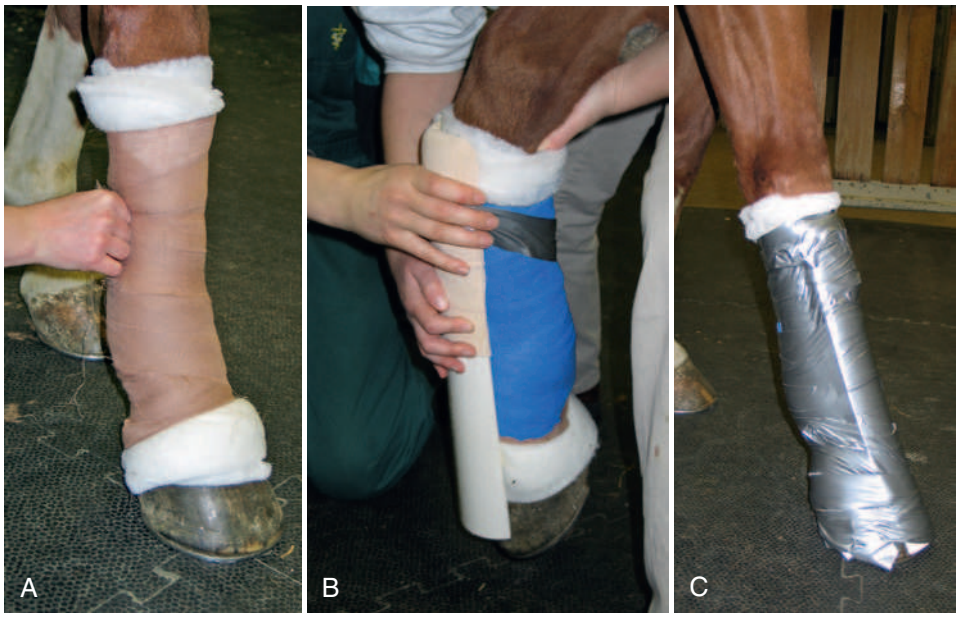

FIGURE 38-15 Bandages in large animals should be applied using a sheet of cotton wrapped around the limb and compressed with wide gauze and an elastic bandage wrap. For animals with a fracture, splints can be applied over the bandage and secured with inelastic tape. For this distal limb splint, notice that the splint is applied dorsally with the limb held straight by an assistant.

large animals should be inserted into the trachea and secured with sutures or tied with string or umbilical tape over the neck. If a tracheostomy tube is not available, the operator may need to improvise with a similar-diameter tube or hose. For example, a 6-mL or 20-mL syringe or syringe casing may be cut to form a tube and inserted instead of a dedicated tracheostomy tube.

LIMB-BANDAGING AND LIMB-SPLINTING TECHNIQUES

Bandages can be easily applied to lower limbs of large animals in the field for covering wounds (Figure 38-15). However, bandages are much more difficult to apply to other areas, and wounds of the chest, abdomen, proximal limbs, and head are often left uncovered. Bandages can be used to protect open wounds after cleaning and debridement and for wounds that have been primarily sutured. Bandages keep wounds clean in contaminated environments and provide support and partial immobilization for soft tissues, which can speed healing.

Bandages should be applied over clean and dry skin. Appropriate dressings should be applied as a contact layer over wounds to prevent outer bandages from adhering. An intermediate layer of padding should be wrapped around the limb in a spiral pattern, ensuring that this layer of bandage is at least 2.5 cm (1 inch) thick after application. Bandage material should be applied without wrinkles, which can cause soft tissue irritation, open sores, and even pressure necrosis. In general, lower-limb bandages should overlap approximately 50% of the hoof wall so that the coronary band is covered and should extend proximally to end just distal to the joint above the wound. This layer should be soft to protect soft tissues and absorptive to contain wound exudate. After application of the intermediate layer of padding, an outer compressive layer is added. Compression of the intermediate layer of bandage padding will prevent slipping, provide soft tissue support and immobilization, minimize migration of foreign contaminants under the bandage, and protect wounds from further trauma. Rolls of self-adhesive elastic material are ideal for this outer layer. The elastic outer bandage should be applied in a spiral manner, overlapping preceding layers by approximately 50%. It is important to keep consistent pressure along the bandage, because focal areas of compression may compromise blood supply to the underlying soft tissues. This compressive layer should not extend past the limits of the intermediate padding bandage layer; direct application of elastic bandage material to skin can compromise blood supply and cause necrosis of skin. If necessary, adhesive tape can be loosely applied to the skin and bandage at the top and bottom to prevent contaminants from entering; skin at the top and bottom of the bandage should be checked daily to ensure soft tissues have not been overly compressed to the extent that there are any signs of ischemia.

Bandages should be changed every 1 to 3 days, depending on wound care requirements and the amount of exudate. Soiled or wet bandages should be changed immediately. At the bandage change, soft tissues should be carefully examined and palpated to ensure pressure sores or other soft tissue problems are not developing related to the bandage.

For animals with hoof wall and solar injuries, a foot bandage may be required. A layer of padding may be placed on the solar surface of the foot extending up the hoof wall on all sides. The padding should be held in place by an elastic compressive bandage layer applied in a figure-of-eight pattern to cover the solar surface and walls of the hoof, extending up to the pastern region just below the fetlock (metacarpophalangeal) joint. Because foot bandages undergo a high amount of wear, an additional layer of abrasion-resistant tape (duct tape) should be applied to the walking surface of the bandage. Foot bandages should be changed every 1 to 2 days, or sooner if they become soiled or worn.

Bandages placed over potential anatomic pressure points, such as the point of the hock or accessory carpal bone, may cause soft tissue necrosis. To avoid this complication, the outer compressive layer of bandage material may be applied so as not to cover the anatomic prominence, or a partial-thickness relief incision may be made in the bandage material over the site, being careful not to cut the soft tissues.

Rigid materials can be applied over bandages to serve as splints. The most common indications for splinting large-animal limbs are fractures and wounds with extensive flexor tendon damage. Unfortunately, such injuries will typically prevent an animal from long-distance travel, and evacuation would likely be required. Bandages for splinting are applied as for wound care. Splint materials should be strong, lightweight, and not too bulky. Lengths of polyvinyl chloride (PVC) pipe, sectioned in thirds or quarters along their long axis, and lumber boards make good splint materials. Alternatively, fiberglass casting tape can be

applied over a thin bandage. For forelimb instability beyond the distal one-fourth of the cannon bone, the bandage should be applied from the hoof to just below the carpus (Figure 38-15). The splint is then applied along the dorsal surface of the limb from the toe of the hoof to the proximal cannon bone. For forelimb fractures proximal to this location up to the elbow joint, a full-limb bandage should be applied, and two splints on the lateral and caudal aspects of the limb should be placed from the ground to the proximal radius. For midshaft radius fractures, the lateral splint should be extended proximally along the body wall; this minimizes the chances of a fracture becoming open because large animals have little medial soft tissue coverage over the radius. Splint configurations for hind limbs are similar, except that splints for distal limb fractures are better placed along the back of the limb in flexion, particularly for equids, because flexion of one joint in these animals causes flexion of all joints due to the arrangement of ligament and tendon attachments.

Because large animals require quadrilateral ambulation for efficient movement, splints should protect limbs only until definitive treatment can be instituted after emergency evacuation and transport to a veterinary hospital. Some injuries may warrant humane euthanasia in the field; it is best to consult with a veterinarian before making the decision for euthanasia (see later discussion).

WOUNDS

The most common injuries sustained by large animals in wilderness settings are wounds. These injuries result from lacerations caused by rocks, tree branches, equipment, or other environmental hazards; bite or kick injuries from other animals in the group; or attacks by wildlife. It is vital that a full assessment be performed to identify damage to deeper structures, which may alter the preferred treatments and suitability of the animal to continue on the trip. Wounds on limbs should be carefully assessed to determine involvement of neurovascular structures. Large animals have poor collateral circulation to the distal limbs. Beginning at the level of the fetlock joint, the medial and lateral palmar/plantar digital neurovascular structures provide the primary vascular supply to the foot. Therefore, transection of both the medial and the lateral neurovascular structures in the pastern region presents a dire situation. Knowledge of large-animal limb anatomy will help personnel determine the likelihood of neurovascular damage.

Involvement of synovial structures (joints, tendon sheaths, and bursae) is also of great concern. When open to a wound, these structures rapidly develop sepsis, which can debilitate large animals and make ambulation extremely difficult. In addition, substantial lameness increases risk of contralateral limb laminitis in the feet, particularly in equids. Therefore, identification of synovial damage is important for determination of a treatment plan. Consultation with a veterinarian would be extremely beneficial in such cases. Briefly, after sterile preparation, a needle may be introduced into the joint at a location distant from the wound. Sterile isotonic fluid solution is injected until the joint is distended and resistance to further injection is felt. If the joint holds fluid under pressure and no leakage is observed from the wound, the joint is not likely to be open. If fluid is observed to leak from the wound during injection, the joint is open to the wound. Open joints should be lavaged with sterile isotonic fluid (at least 1 L) during debridement. If contamination remains, it is best to leave the wound open until definitive treatment can be instituted at a veterinary hospital.

Laceration of flexor tendons and ligaments presents a serious situation for large animals. The flexor tendons (deep and superficial digital flexor tendons) and suspensory ligaments course along the back of the limbs from the carpal joints distally. Because these structures are under tension during weight bearing, disruption causes lameness and lack of support for distal limb joints. After wound debridement, these structures may be sutured; however, gap formation is likely, and definitive treatment is best conducted at a veterinary hospital. Animals with partial disruption of these structures may be temporarily treated by wound debridement and application of a bandage; a splint may be applied over the bandage if hyperextension of the lower-limb joints is apparent. Animals with complete disruption of all flexor tendons and ligaments are candidates for immediate euthanasia.

Wounds of the thoracic body wall should be evaluated to determine whether the pleural cavity has been penetrated. Covering the wound with an impermeable occlusive bandage or plastic wrap can prevent air from entering the thorax and worsening pneumothorax. Pneumothorax may be diagnosed in moderate to severe cases by auscultation of the dorsal aspect of the cavity; loss of audible lung sounds is suggestive of free air. If respiratory effort is increased, pneumothorax should be resolved by repeated aspiration of air with a large-volume syringe from the dorsal aspect of the chest. This is done high on the thorax in the 13th or 14th intercostal space, just below the epaxial musculature. Wounds of the abdominal body wall should be explored to determine whether the abdominal cavity has been penetrated. If the peritoneum has been penetrated, local debridement and wound closure along with systemic antimicrobial administration are indicated. If bowel has been penetrated, rapid onset of peritonitis and septicemia are likely, and euthanasia should be considered unless rapid evacuation of the animal is possible.

Wounds of the head should be assessed to identify damage to deeper structures. Involvement of the globe should be considered an ocular emergency and immediate veterinary care sought. Involvement of the brain is a serious emergency, and animals with such injuries should be rapidly evacuated. If severe neurologic abnormalities develop, euthanasia should be considered. These abnormalities include inability to rise (recumbency or tetraparesis), seizures, and dementia. All large animals, and horses in particular, have an extensive network of air-filled sinuses in the head. Traumatic injuries with bone fractures involving sinuses can be temporarily managed in the field. Bone fragments should be manually elevated into place and wounds debrided and closed. Subcutaneous emphysema may develop because of communication with air-filled sinuses. Mild cases should spontaneously resolve; however, severe subcutaneous emphysema may migrate and in rare instances cause respiratory distress. Bandaging to decrease subcutaneous dead space, strict rest, and timely evacuation for veterinary care are indicated in these cases.

Adequate treatment of many wounds can be accomplished in the field with basic equipment and supplies. Distal limb wounds in particular are likely to be grossly contaminated. Successful primary closure is possible if wounds are rapidly addressed. Wounds should be lavaged with a high volume of fluids (sterile isotonic fluids, if available) and thoroughly debrided of contaminated tissue. Skin edges should be only minimally debrided, because large animals do not have abundant soft tissue in their limbs, and primary wound closure may be difficult if a substantial amount of skin is lost from injury or aggressive debridement. When possible, primary closure is preferred to speed healing, protect underlying bone and soft tissues, and decrease risk of exuberant granulation tissue formation. Horses are prone to develop such tissue during second-intention healing of wounds distal to the hock and carpal joints. Nonetheless, heavily contaminated wounds and those with excessive dead space may be best treated by debridement with partial or no closure to allow drainage of exudate. Lacerations of the body wall and proximal limbs may require suturing of deep tissues to decrease dead space. Wounds of distal limbs typically only require skin closure, since there is little deep tissue in these areas. Because lacerations typically occur over high-motion areas and soft tissues may be under tension when closed, tension-relieving suture patterns (e.g., vertical and horizontal mattress) are often incorporated in wound repairs. Tissues that are not under tension, or for which tension has been relieved with mattress sutures or relief incisions, may be closed with appositional interrupted suture patterns. Typical suture sizes for wound closure in large animals range from 2 to 2-0. Absorbable suture material is recommended for deep tissues, and absorbable or nonabsorbable monofilament suture material is typically used for closure of skin. When possible, bandages should be placed to protect and support wounds after closure.

Administration of antiinflammatory, analgesic, and antimicrobial medication is appropriate for large animals with wounds. Oral formulations of antimicrobial drugs are most convenient for use in wilderness situations.

Saddle, Cinch, and Rigging Sores

Large animals used for pulling, carrying packs, or riding are susceptible to injuries from equipment. The tail base, withers, breast, shoulder, girth, and back are the most common locations of wounds attributable to pack equipment. These wounds result from poorly fitting equipment, poor padding, and rope abrasion. Ropes with a narrow diameter (particularly synthetic ropes), tightly applied ropes, and dirty ropes are most likely to cause problems. Injury to the tuber coxae (hip bones) may occur because of poor equipment fit or direct trauma. Wounds should be cleansed with antiseptic (2% to 4% chlorhexidine gluconate solution or povidone-iodine 5% solution) and thoroughly rinsed with saline. Severe injuries can induce abscess formation; although ventral drainage is often difficult to achieve in upper portions of the body, superficial abscesses should be surgically opened and lavaged. It is exceedingly difficult to bandage wounds on the upper body of an animal. These injuries will usually heal well if wound care is continued daily and the area left open to air, as long as the inciting cause is removed. Alternately, a tie-over bandage can be used to protect wounds from environmental contaminants and insects. Wound care is important to protect from myiasis. If sores develop, equipment should be cleaned, padding added or replaced to reduce pressure on affected areas, and loads redistributed.

MUSCULOSKELETAL INJURIES AND LAMENESS

Lameness is a common problem in large animals. Definitive diagnosis and treatment of large-animal lameness can be difficult in a wilderness setting. Administration of an analgesic or antiinflammatory medication, application of ice or cold water, and redistribution of loads can allow resumption of a trip after musculoskeletal injury.

Foot problems are the most common cause of lameness in large animals. Bruises and abscesses can develop on the solar foot surface. Diagnosis is achieved by application of a hoof tester that applies pressure to the sole of the hoof. Animals with bruises or abscesses typically have a vigorous reaction to pressure and try to withdraw the limb. Careful paring of the sole with a hoof knife usually helps determine whether the animal has a foot bruise or abscess. Bruised areas have a dark-red appearance within the sole of the hoof. Abscessed areas have purulent discharge that ranges from white to black in color. Bruises should be treated by immersing the foot in ice water for 30 to 60 minutes every 8 to 12 hours and applying a foot pad. Foot pads that protect the sole of the foot are commercially available. They can also be fashioned from foam insulation, saddle blankets, or bandage material cut to size and taped to the hoof wall. If possible, animals should also be relieved of pack duties, and exercise should be restricted by housing them in a small area until clinical signs have resolved. Abscesses should be treated by creation of a drainage portal in the sole using a hoof knife. Soaking in hypertonic antiseptic solution (Epsom salts and povidone-iodine solution in warm water; final concentration, 0.05%) twice daily can help accelerate healing of the abscess. After paring the sole, application of a foot bandage may be indicated to keep the area clean. Administration of NSAIDs is indicated for foot bruises and abscesses. Administration of antimicrobials is usually not required for animals with a foot abscess, provided adequate drainage of purulent exudate can be obtained. Rarely, cellulitis can develop in the limb; antimicrobials should be administered in such cases, and transport to a veterinary facility may be warranted if symptoms are severe.

The third phalanx (coffin bone) of equids is suspended in the hoof by interdigitations called laminae. *Laminitis* (founder) is a debilitating condition of equids in which these laminae become inflamed and lameness ensues. Laminitis is usually a bilateral condition of forelimb feet, but any or all feet can be affected. In equids with severe laminitis, the laminar interdigitations between the third phalangeal bone and hoof wall may separate, leading to rotation of bone within the hoof from tension exerted by the deep digital flexor tendon. The third phalangeal bone can also completely detach from the hoof wall and sink. These conditions may render an animal recumbent and can be life threatening. Laminitis can be induced by endotoxemia as a result of systemic diseases, overeating of grain, or repeated concussion of the hooves. Animals with laminitis have a stiff gait with walking and may be reluctant to move. Palpation of the palmar digital arteries at the back of the fetlock joint and pastern region reveals a bounding character to the pulse that is much more prominent than digital pulses in healthy animals. Animals with laminitis require strict rest (i.e., housing in a small pen, <6-m [20-foot] diameter, with no forced exercise). Administration of NSAIDs is warranted. In addition, submerging the affected feet in ice-water slurry may help relieve inflammation and prevent progression of the condition. Horses can withstand continuous submersion of feet in ice for at least 48 hours with no apparent adverse effects. Animals with moderate to severe laminitis should be transported to a veterinary facility for further care.

Osteoarthritis affects animals in much the same way as humans. Animals with severe arthritis are poor candidates for wilderness use because they typically have lameness that precludes such travel. Animals with mild arthritis may be suitable for packing or riding provided they do not have substantial lameness and symptoms do not worsen with use. Mild symptoms of osteoarthritis typically improve with rest and administration of NSAIDs.

Large animals used for pack transport and riding may develop or have preexisting *tendonitis* or *desmitis*. The most common structures involved are the superficial digital flexor tendon, deep digital flexor tendon, and suspensory ligament. These can be easily palpated behind the third metacarpal/metatarsal (cannon) bone from the carpal/tarsal joint region to the fetlock joint region. Signs of inflammation include swelling, heat, and pain during palpation of the structures. Administration of NSAIDs and application of ice or cold water can decrease symptoms. However, continued use is likely to worsen the injury, and animals with active tendonitis or desmitis should be rested.

Myositis can develop with sustained or strenuous exercise. Clinical signs include lameness, muscle tremors, palpably firm musculature, and pain during palpation of musculature. Gluteal and hamstring muscles are most frequently affected. Dehydration worsens signs and can increase risk of renal damage from circulating myoglobin. Dark-red or reddish brown urine is a sign of myoglobinuria, and these animals should be aggressively treated with fluids by either nasogastric (NG) tube or IV administration. Large animals with myositis should maintain strict rest. Administration of NSAIDs may alleviate muscle pain and inflammation. However, there is a risk of increased renal damage with these medications if the animal has myoglobinuria or is dehydrated.

COLIC

Abdominal pain in equids has many causes. Mild signs of colic include anorexia and flank watching (looking at the abdomen). Moderate signs of colic include repeated pawing at the ground, general restlessness, and recumbency. Equids with severe signs of colic may repeatedly become recumbent and rise or violently roll. When rolling, they can injure themselves or humans, and caution should be exercised by personnel. Pyrexia is an uncommon physical examination finding for equids with colic. Tachycardia is frequently detected. More severe problems may cause visible abdominal distention detectable in the paralumbar fossa between the last ribs and hind limbs. It can be difficult to determine the cause of colic symptoms without more advanced methods (e.g., radiographic and ultrasonographic imaging, laboratory analysis of blood and peritoneal fluid samples, exploratory laparotomy), although manual examination per rectum by veterinary personnel can be useful to determine differential diagnoses. There is risk of rectal trauma during this procedure, so it should be performed only by a trained veterinarian.

Although colic symptoms may be caused by any structure in the abdomen, the GI tract is most often involved. Serious stomach

problems are rare, although equids can develop stomach ulcers that cause mild colic symptoms, such as intermittent anorexia. Gastric impactions can develop secondary to ingestion of poor-quality roughage and reduced water intake. Horses have extensive jejunum, approximately 30 m (100 feet) in length. Small intestine lesions include volvulus, intussusception, impaction, entrapment in mesenteric rents or potential peritoneal spaces in the abdomen, and strangulation by lipomas. Other than simple impaction, anatomic problems of the small intestine are typically strangulating; these animals develop severe pain and are unlikely to survive without prompt treatment at a veterinary surgical facility. Gastric outflow or small intestine obstruction causes gastric accumulation of intraluminal fluids. Equids are unable to relieve fluids causing gastric dilation through emesis; stomach rupture may result, which is fatal.

If small intestine obstruction is suspected on the basis of moderate to severe clinical signs of pain, veterinary personnel can perform emergency NG intubation to relieve stomach distention. A purpose-made stomach tube is passed through the ventral aspect of either nasal passage until it reaches the nasopharynx. Other types of tubing are not suitable, so the procedure should not be attempted if a stomach tube is not available. Passage of a tube along the dorsal aspect of the nasal passages may cause trauma to the ethmoid turbinates, which causes profuse hemorrhage. Once in the nasopharynx, the tube should be advanced into the esophagus in coordination with swallowing. It is important to confirm that the NG tube is in the esophagus and not the trachea, because instillation of fluid into the trachea will cause aspiration pneumonia and may be fatal. Application of suction by mouth should result in negative pressure if the tube is in the esophagus; negative pressure will not be felt if the tube has been passed into the trachea. In addition, the tube can be observed and palpated as it is passed through the cervical portion of the esophagus; in most equids, the esophagus courses on the left side of the neck in the jugular furrow. Once it has been confirmed that the tube is in the esophagus, it should be advanced into the stomach; application of positive pressure through the tube by mouth may be necessary. Firm resistance is often felt as the tube passes through the gastroesophageal sphincter. Gas may emit through the tube, but spontaneous flow of fluid is unusual, even in animals with gastric distention. The tube should be primed by passing 1 to 2 L of water into the stomach with a pump or funnel; when using a pump, overdistention of the stomach is possible, and caution should be used so that excess fluid is not introduced. After priming the tube, the end should be lowered into a bucket. Excess stomach fluid should flow freely from the tube.

The gastric siphoning and lavage procedure may need to be repeated several times to ensure adequate evacuation of stomach contents. The net amount of fluid returned should be estimated. It is normal for approximately 2 L of gastric fluid to be returned. The capacity of the stomach in a full-size (450-kg [1000-lb]) horse is approximately 20 L. If a large volume of gastric fluid is removed and the animal's symptoms of pain greatly improve, a nonstrangulating, small intestine obstruction or physiologic ileus is the likely cause of colic; the procedure should be repeated every 2 to 4 hours for these animals until they can be evacuated to a veterinary hospital. Animals with strangulating obstruction typically do not have substantial relief after removal of excess gastric fluid, and immediate evacuation for surgical treatment is warranted.

Equids ferment ingested material in the cecum and ascending colon. The ascending colon is freely mobile in the abdomen, with minimal mesenteric attachments. Because of this anatomic arrangement, the ascending colon may become displaced (nonstrangulating lesion), or strangulating torsion may develop. In either case, the lumen becomes partially or completely obstructed, resulting in gas accumulation. Equids with nonstrangulating displacement typically have less severe signs of colic than animals with strangulating torsion, although it can be difficult to determine a diagnosis without surgical exploration. Nonstrangulating displacement can resolve with exercise, although surgical correction is often required. Animals with strangulating torsion of the ascending colon require prompt surgical attention. Impaction of the ascending colon may develop secondary to low water intake or ingestion of poor-quality roughage. This is the most common cause of colic in equids. Mild cases may be treated in the field. Signs include mild to moderate colic and decreased output of feces; fecal piles may be smaller than normal. In a wilderness situation, mild impactions may be treated by administration of NSAIDs and fluids through an NG tube. For animals with a confirmed diagnosis of impaction (based on rectal examination by veterinarian), mineral oil (4 L [1 gallon]) may also be administered via NG tube to ease passage of firm ingested material, and a solution of magnesium sulfate (Epsom salts) can be administered by the NG route to retain fluids osmotically in the lumen and rehydrate the impacted material. These treatments for colic should be administered only by NG tube to avoid aspiration pneumonia, which is particularly serious after aspiration of mineral oil. Worsening signs of colic indicate that evacuation for advanced treatment is warranted.

Equids may develop impaction of the descending (small) colon and rectum. Signs include mild to moderate colic symptoms and decreased frequency and amount of feces. Fecal balls may be small, dry, and covered with mucoid material. Animals with less severe impaction can be successfully treated in the field as for ascending colon impaction. If fecal production has stopped, if colic symptoms are severe, or if signs of endotoxemia develop, immediate evacuation for veterinary care is warranted.

Other species of large animals can also develop GI problems. In particular, bovids can develop tympany, displacement, and torsion of portions of the GI tract. Clinical signs, including pain, elevated heart and respiratory rates, and an audible ping on the right or left side of the abdomen, indicate serious GI tract problems. Such animals should be hydrated and treated with analgesic medication. Lack of improvement or worsening signs indicate that evacuation for veterinary care is warranted, and surgical treatment by a veterinarian is often required.

ESOPHAGEAL OBSTRUCTION

Large animals can develop esophageal obstruction. These animals rarely swallow inappropriate objects, so obstruction is usually attributable to feed material. Large objects, such as corn cobs, that are difficult to chew can cause obstruction. Dry feed material, such as hay, can also cause esophageal obstruction, particularly if animals have poor dentition. The most obvious clinical sign is water and feed material in the nares. Physical obstruction of the esophagus can be difficult to differentiate from neurologic causes of dysphagia without using an endoscope. Inability to pass an NG tube may indicate the level of esophageal obstruction. Obstructions can pass with time without direct manipulation. Animals should receive IV fluids. All oral feed and water should be withheld. Sedation may allow esophageal relaxation and passage of the impacted feed bolus. Water lavage through a NG tube can be used to dislodge the obstruction and allow its passage into the stomach; this carries a high risk of aspiration and subsequent pneumonia.

INTERNAL AND EXTERNAL PARASITES

Internal parasites most often affect the GI tract of large animals. External parasites may cause dermatologic problems. Infectious diseases caused by organisms such as *Borrelia burgdorferi* (borreliosis, Lyme disease) can be transmitted to horses through tick bites. Tick paralysis can affect horses and llamas in various geographic areas, including North America, Europe, Africa, Australia, and Russia. Multiple species of ticks produce a toxin that causes ataxia, progressing to paresis that ascends from hind limbs to forelimbs. Signs may progress cephalad, causing difficulty masticating, dysphagia, respiratory failure, and ultimately death. Diagnosis of tick paralysis is made on the basis of progressive clinical signs. The animal should be thoroughly examined and all ticks removed.

Other types of parasites and specific clinical signs in large animals vary substantially around the world. Personnel should familiarize themselves with geographic-specific parasitic diseases of animal companions before embarking.[19] Appropriate husbandry and prophylactic administration of anthelmintic medications

can prevent many medical problems attributable to parasites in animals.

RESPIRATORY SYSTEM

Large animals can develop upper respiratory obstruction from acute laryngeal paralysis, space-occupying masses, or severe soft tissue swelling. Passing an endotracheal tube or segment of NG tube through the nares may relieve respiratory distress from nasal passage obstruction. The tube can be passed into the trachea to relieve dyspnea in animals with laryngeal paralysis, although this procedure can be difficult. If passage of a nasal tube cannot be accomplished or does not relieve distress, tracheostomy should be performed.

Pneumonia can develop in large animals, particularly after shipping. Clinical signs include fever, depression, and audible abnormalities in the trachea and lung fields. Antimicrobials and an antiinflammatory medication should be administered. Selection of antimicrobial drugs is difficult without culture and sensitivity results. Until such diagnostic testing can be performed, broad-spectrum antibacterial coverage with one or more drugs is warranted. Initial treatment for equids often includes β-lactams and aminoglycosides. Metronidazole may be required for animals with severe pneumonia with anaerobic involvement in necrotic tissue. Animals with severe pneumonia require transport to a veterinary facility for further diagnosis and treatment.

GUNSHOT WOUNDS

Gunshot injuries may be sustained by livestock as a result of malicious or mistaken targeting and bullet ricochet in close quarters. Entry wounds are typically small, so superficial examination may not indicate the full extent of tissue damage. Wounds are contaminated because of deep penetration of skin and introduction into the wound of hair, cutaneous foreign material, and the projectile. Gunshot wounds may be mistaken for simple puncture wounds if the incident was not witnessed; in such cases, diagnosis is difficult without diagnostic imaging. The animal should be carefully examined for exit wounds. If no exit wound is found, the bullet is likely lodged in deep tissues. Unless the bullet was traveling at extremely low velocity, locating the projectile by surgical exploration of the wound is usually impractical. In addition, access to deep tissues may be limited even under the best conditions, and surgical trauma can cause further injury. Removal of the projectile is usually not attempted. A successful outcome can be attained without bullet removal.[15] Animals with injury of deep vital structures have a guarded prognosis.[22] The extent of deep injury may be estimated based on type of firearm, type of projectile, distance traveled, and whether the bullet impacted the animal directly or after ricochet or passing through other material.[16]

Knowledge of large-animal anatomy, combined with the location of entry and exit wounds, is invaluable to determine potential deep structure damage. Fractures of long limb bones can be diagnosed by palpation alone. Involvement of superficial neurovascular structures may be identified by direct observation and careful wound exploration. Damage to deep neural structures is evident based on characteristics of limb gait or, in the case of head wounds, level of consciousness. Bullets that penetrate the abdomen or thorax typically do not exit.

A presumptive diagnosis of major blood vessel or cardiac hemorrhage, pneumothorax, or pleural or peritoneal cavity sepsis can be made on the basis of clinical signs, such as those that accompany shock. Ligating superficial blood vessels and packing soft tissue wound cavities can sometimes be effective to stop hemorrhage. Progression of pneumothorax can be slowed or stopped by application of an airtight bandage; continued worsening of pneumothorax after application of the bandage and evacuation of pleural cavity air may indicate bronchial involvement. Animals with penetration of GI viscera typically develop systemic signs of peritonitis (including signs of colic) and septicemia (elevated heart rate, fever, increased mucous membrane CRT, and purple or red discoloration of mucous membranes) within several hours after injury. Projectiles may pass through a hemithorax before penetrating the diaphragm and coming to rest in the abdominal cavity.

Gunshot wounds of the head and neck can damage orbital tissues, sinuses, the larynx or trachea, and major blood vessels. Ligating vessels should be attempted if there is profuse hemorrhage. Gunshot damage to the brain is often fatal, so evacuation for intensive care or immediate euthanasia may be warranted. Penetration of paranasal sinuses may cause epistaxis; however, such cases can be successfully managed conservatively. Damage to the orbit may result in eventual loss of the globe, although animals can be kept comfortable with a NSAID and figure-of-eight bandaging around the head.

In general, definitive treatment for major organ damage requires evacuation to a veterinary hospital. However, superficial gunshot injuries and deeper injuries without vital structure involvement may be adequately treated in the field. Conservative debridement and copious lavage of wounds are indicated. Bandages should be placed on limb wounds and wounds associated with suspected thoracic or abdominal cavity penetration. Administration of broad-spectrum antimicrobials, including coverage for anaerobes, is indicated. Animals may be able to travel under their own power but should be transported or carried to the closest veterinary facility for further evaluation and care as soon as feasible.

DROWNING

Although horses and other large animals are capable swimmers, they are at risk for drowning because of fatigue, injury, or fast currents. Rescue can be dangerous for personnel, so extreme caution should be used. A sling may be fashioned from rope and electrical or mechanical winches used to pull the animal to shallow water, where it can stand. If the animal has aspirated water, rapid emergency airway management may be required. The thorax should be auscultated to determine cardiac rate and rhythm. Cardiopulmonary resuscitation is difficult but can be performed with the animal in a lateral recumbent position by rapidly compressing the chest just behind the point of the elbow. A rate of 80 compressions per minute yields greater cardiac output than do lower rates.[11] Evacuation for further treatment with humidified oxygen and surfactant transplant may be beneficial.[12] After aspiration of water, large animals can develop hypoxemia secondary to alveolar edema, similar to acute lung injury and acute respiratory distress syndrome in humans.[3]

HEAT STRESS

Horses thermoregulate primarily by vasodilation and sweating. Ruminants cannot sweat and are therefore more susceptible to heatstroke. Some animals, such as llamas, may also pant. Large animals can develop hyperthermia because of intense muscular exertion. Although altitude may contribute,[6] high heat and humidity are the most important environmental contributing factors.[5] Intense and prolonged exercise in such conditions contributes to dehydration, loss of electrolytes, acid-base abnormalities, and intramuscular glycogen depletion. These contribute to a rise in core body temperature. Other clinical signs include increased heart and respiratory rates, arrhythmias, muscle stiffness from exertional myopathy, weakness, diarrhea, colic, laminitis, diaphragmatic flutter, and changes in mental status. Heatstroke may occur at rectal temperatures near 41°C (106°F). Exercise should be stopped as soon as clinical signs or an increase in rectal temperature are detected. The animal should be moved to shade. Immersion in or repeated dowsing with cold water should be started to decrease body temperature. Cool water may be administered via NG tube. If available, sterile isotonic fluids should be administered IV.

HYPOTHERMIA AND FROSTBITE

Hypothermia can develop in large animals after exposure to extreme cold for extended periods. Clinical signs include weakness, lethargy, dysrhythmias, decreased GI activity, low rectal temperature, and recumbency. Among adult equids, donkeys are

more susceptible to hypothermia than horses.[21] Underweight animals are at increased risk for hypothermia. Animals should be warmed with external heat sources and blankets. Warm, sterile isotonic fluids may be administered IV; 5% dextrose can be added to the infusion if hypoglycemia is suspected.

Frostbite in large animals is rare; it occurs in severely cold conditions and high winds. Contributing factors include lack of shelter, dehydration, poor condition, low food intake, and wet conditions. Large animals are typically affected by frostbite to the tips of their ears. Extremities can be affected in cold and damp conditions. Male equids that are sedated often do not retract the penis, which can develop frostbite rapidly. Special care should be taken to prevent the onset of frostbite in severe conditions, because treatment is difficult, and severe damage to extremities can necessitate euthanasia. As for humans, treatment is focused on maintenance of core body temperature with blankets and rapid rewarming of extremities with water at 37° to 39° C (98.6° to 102.2° F).[14]

ALTITUDE

Anecdotally, equids may have acutely reduced performance after arrival at high altitudes, greater than 1500 m (4921 feet). Equids acutely develop cerebrospinal fluid alkalosis[17] and systemic alkalosis, hypoxia, and hypocapnia[10] at altitudes above 3000 m (9843 feet). Although there is some evidence that mules have slightly better adaptation than do horses to high altitude, both have similar responses.[9] Based on analysis of circulating concentrations of metabolic (glucose, insulin, cortisol, and thyroxine) and osmoregulatory (sodium, potassium, chloride, and total protein) markers, equids seem to acclimatize to high altitude in approximately 3 days.[8] Such animals do not usually develop substantial medical problems related to altitude alone.

Certain bovine species (particularly domestic cattle) kept at high altitude (>1500 m) are at risk for developing pulmonary hypertension caused by hypoxia. Chronic high-altitude hypoxic pulmonary hypertension can cause right ventricular failure, which manifests as edema of the ventral mandibular, thoracic, and abdominal regions ("brisket disease"). This is similar to sequelae of hypoxic pulmonary hypertension in humans.[18] Animals with clinical signs of high-altitude illness should be immediately evacuated to lower altitude. Nasal oxygen administration may aid recovery. Administration of digoxin and diuretics may be of benefit for heart failure in these animals.[19] Cattle with signs of heart failure have a guarded prognosis. Some bovid species, such as yaks (*Bos grunniens*), are native to high-altitude locations (3000 to 5000 m [9843 to 16,404 feet]); these animals are not at risk for pulmonary hypertension and secondary right-sided heart failure. In addition, New World camelids (e.g., llamas) and goats are adapted or can acclimatize well, and they do not usually have medical problems at high altitude.

TOXIC PLANTS

Personnel accompanying animals in the wilderness should be familiar with local toxic plants. Some common toxic plants are listed in Table 38-4. However, species vary with geographic region and climate. Because most large animals subsist primarily on forage, they are quite susceptible to intoxication from these plants. If ingestion is detected early, treatment should be

TABLE 38-4 Poisonous Plants That May Affect Horses or Llamas on a Trek

Common Name	Scientific Name	Poisonous Principle	Signs of Poisoning	Habitat	Species	Therapy*
False hellebore, corn lily	*Veratrum californicum*	Alkaloids	Vomiting, salivation, convulsions, fast irregular pulse	High mountains, meadows	Llama	Symptomatic
Death camas, sandcorn	*Zigadenus* spp.	Alkaloids	Foaming at mouth, convulsions, ataxia, vomiting, fast weak pulse	Hillsides, fields, meadows, in spring of year	Horse, llama	Symptomatic
Water hemlock	*Cicuta douglasii*	Resin	Frothing at mouth, muscle twitching, convulsions, death in 15 to 30 minutes	Standing or running water, obligate aquatic	Horse, llama	Symptomatic
Nightshade	*Solanum* spp.	Alkaloidal glycoside, solanine	Vomiting, weakness, groaning	Ubiquitous	Horse, llama	Symptomatic
Jimson weed	*Datura stramonium*	Alkaloid, atropine	Dry mucous membranes, dilated pupils, mania	Waste places	Horse, llama	Parasympathomimetics
Tobacco, tree tobacco	*Nicotiana* spp.	Alkaloid, nicotine	Stimulation of CNS, then depression; sweating, muscle twitching, convulsions	Waste places	Horse, llama	Symptomatic
Lupine, blue bonnet	*Lupinus* spp.	Alkaloid	CNS depression, dyspnea, muscle twitching, ataxia, frothing, convulsions	Ubiquitous	Horse, llama	Symptomatic
Dogbane, Indian hemp	*Apocynum cannabinum*	Cardioactive glycoside (similar to digitoxin)	Dyspnea, cardiac arrhythmias, agonal convulsions, vomiting, diarrhea	Ubiquitous	Horse, llama	Symptomatic
Oleander	*Nerium oleander*	Same as for dogbane	Same as for dogbane	Ornamental	Horse, llama	Symptomatic, gastrotomy
Castor bean	*Ricinus communis*	Ricin, water solution	Anaphylactic shock, diarrhea	Ornamental	Horse, llama	Treat for shock; fluids
Rhodo-dendron	*Rhododendron* spp.	Andromedotoxin glycoside	Vomiting, colic, severe depression	Shrubs in meadows and moist places	Llama	Activated charcoal, time

*In most cases of poisoning from plants, no specific antidote exists. Victims are treated symptomatically. The critical factor is to empty the digestive tract of the plant material with cathartics, parasympathomimetic stimulation, and enemas. Activated charcoal given orally may be of value.
CNS, Central nervous system.

instituted to remove as much plant material as possible via stomach lavage through an NG tube. Activated charcoal administered by NG tube adsorbs toxins. Clinical signs are treated symptomatically.

EUTHANASIA OF LARGE ANIMALS

Large animals might require euthanasia in the wilderness because of debilitating injuries or illnesses that preclude evacuation, because of conditions with a poor prognosis for survival, or when an animal is suffering without other medical options for relief. Medical personnel should exercise optimal judgment when deciding whether euthanasia is warranted. When possible, a veterinarian should be consulted before making the decision to euthanize and on the method of euthanasia. In all cases, euthanasia should be performed in as humane a manner as possible given the circumstances. Extensive guidelines are available regarding humane euthanasia practices for domestic and wild animals.[1]

The most common method of euthanasia for animals not intended for human consumption is IV administration of an overdose of a barbiturate (e.g., pentobarbital). This method is not suitable for euthanasia of large animals in a wilderness setting because distribution and use of these drugs are strictly controlled (e.g., requirement of U.S. Drug Enforcement Agency registration), and there are unique requirements for disposal of the carcass to prevent ingestion of contaminated tissues by wildlife. IV injection of other uncontrolled chemical agents, such as potassium chloride, magnesium sulfate, nonanesthetic drugs, and other common chemical substances, is not suitable as a sole means of humane euthanasia. Other available methods in such settings, such as drowning and air embolism (i.e., injection of air into the vasculature) are not suitable as a sole means of euthanasia for large animals. Likewise, exsanguination and pithing are only acceptable methods of euthanasia for unconscious animals (typically after induction of general anesthesia).

The most suitable method of euthanasia for large animals in a wilderness setting is gunshot to the brain. Suitable firearms include handguns (.32 or .45 caliber) fired from 30 to 60 cm (1 to 2 feet), shotguns (number 6 or larger birdshot or slugs) fired from 1 to 2 m (1 to 2 yards), or rifles (.223 or larger if fired from >1 m). This method should only be used by personnel who are well trained in use of firearms, have knowledge of anatomic landmarks for safe and effective euthanasia by gunshot, and are using well-maintained equipment. For equids, the gun should be pointed at the intersection of two lines from the outside corner of each eye to the center of the base of the opposite ear (Figure 38-16). For cattle, the gun should be pointed at the intersection of two lines from the outside corner of each eye to the center of the base of the opposite horn; for cattle without horns, the locations of points at the back of the head should be estimated based on knowledge of anatomic locations in horned animals (Figure 38-17).

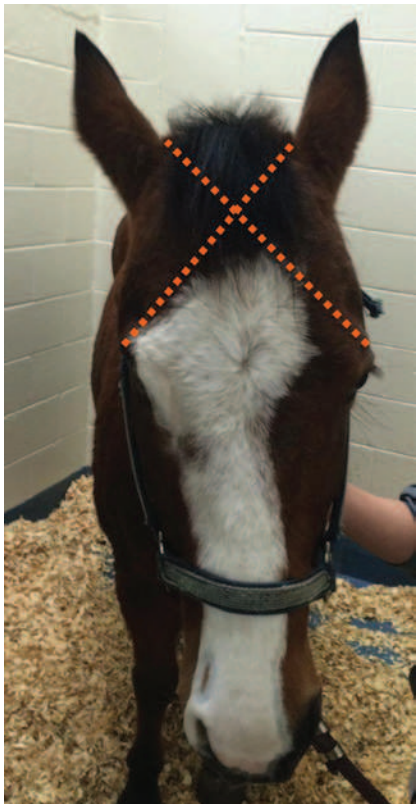

FIGURE 38-16 Anatomic landmarks for firearm euthanasia of horses. For equids, the gun should be pointed at the intersection of two lines drawn from the outside corner of each eye to the center of the base of the opposite ear.

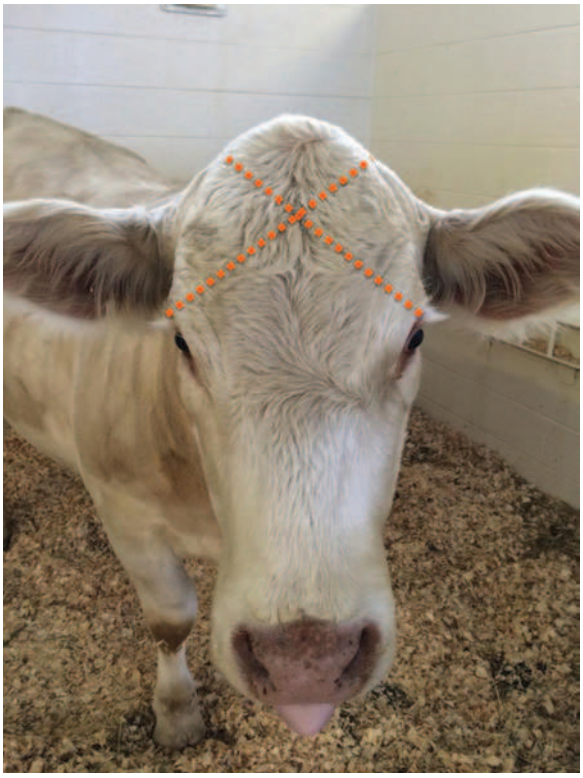

FIGURE 38-17 Anatomic landmarks for firearm euthanasia of cattle. For cattle, the gun should be pointed at the intersection of two lines from the outside corner of each eye to the center of the base of the opposite horn, or an equivalent position for animals without horns (shown).

INFECTIOUS DISEASES

Infectious diseases of large animals vary globally, and personnel should be familiar with those in local wilderness areas. Preventable diseases should be addressed through available prophylactic measures, such as vaccination. Some important infectious diseases of large animals are presented here.

Neurologic Diseases

Central nervous system signs can be caused by a number of organisms that induce encephalitis. West Nile virus (WNV) is an RNA virus, transmitted by mosquitoes, that causes encephalitis in humans and other mammals. Birds are the most important reservoir of the virus. Of the large-animal species, horses are most likely to become infected with WNV. The disease causes many signs, including muscle fasciculations, lameness, colic, fever, anorexia, changes in personality, obtundation, and recumbency. Vaccination against WNV should be performed for animals traveling in endemic areas.

Other viruses that cause neurologic disease in horses include herpesviruses and alphaviruses (eastern, western, and Venezuelan

equine encephalitis viruses); equids should be routinely vaccinated against these viruses.

Numerous organisms cause bacterial meningitis in equids. *Listeria monocytogenes* more frequently affects ruminants than equids. Clinical signs suggestive of listeriosis include circling, head tilt, nystagmus, dysphagia, tongue paralysis, and obtundation. Although definitive diagnosis in a wilderness setting is impossible, animals with suspected listeriosis should be treated with penicillin (potassium penicillin G, 22,000 IU/kg IV three or four times daily, or procaine penicillin G, 22,000 IU/kg IM twice daily, until resolution of clinical signs). Treatment for neurologic signs is symptomatic and consists of NSAIDs and supportive measures, such as IV or oral fluid administration. Recumbent animals are difficult to care for in a wilderness setting, which may necessitate humane euthanasia.

Equine protozoal myeloencephalitis (EPM) is a CNS disease of horses caused by *Sarcocystis neurona*. Many wildlife species can be intermediate hosts of the organism. Clinical signs can result from damage in any CNS tissue, although ataxia and asymmetric muscle atrophy are the most common signs and cerebral signs are rare. Diagnosis is difficult under the best circumstances and is impossible in a wilderness setting. The disease is slowly progressive and unlikely to require emergency treatment, although horses with suspected EPM can be started on a course of sulfonamide antibiotics.

Lyme Disease

Like humans, large animals can contract Lyme disease, caused by infection with the spirochete *Borrelia burgdorferi* after transmission by tick bite. Clinical signs in horses typically include lameness, muscle soreness, stiffness, synovitis, and hyperesthesia. The disease is uncommon in other large-animal species. Horses should be treated with tetracycline (6.6 mg/kg IV every 12 hours) or doxycycline (10 mg/kg PO every 12 hours) for 3 to 4 weeks.

Rabies

As with other mammals, large-animal species can become infected with rabies virus (see Chapter 31 and earlier discussion under Dogs). Rabies is most often transmitted through bite wounds inflicted by infected wildlife. In the United States, the most common carriers are raccoons, skunks, bats, and foxes. Rabies should be considered when animals show rapidly progressive signs of encephalitis. Large animals should be kept current for vaccination against rabies.

Botulism

Large animals can develop botulism, typically after ingestion of preformed *Clostridium botulinum* exotoxin in feed. The disease can also develop after ingestion of bacterial spores or subsequent to wound infection with the organism. Clinical signs progress from decreased tongue tone to dysphagia, decreased skeletal muscle tone, and weakness. Animals may become recumbent 1 to 2 days after the first clinical sign. Multiple animals can be affected; severity is related to amount of toxin exposure. A toxoid vaccine efficacious for prevention is available for horses; administration should be considered for animals traveling in endemic areas. Antitoxin is a good treatment, although it is unlikely to be available in a wilderness environment. Therefore, treatment focuses on supportive care. Evacuation for advanced care is warranted for large animals with progressive signs of botulism.

Tetanus

Large animals usually develop tetanus from growth of *Clostridium tetani* in wounds. Clinical signs begin 2 to 4 weeks after the start of bacterial growth and can progress from colic, bloat, muscle spasm, and rigidity to recumbency. Infection should be eliminated with surgical debridement and administration of potassium penicillin G (22,000 IU/kg IV three or four times daily) or procaine penicillin G (22,000 IU/kg IM twice daily); penicillin should be administered for at least 7 days (or longer) until clinical signs have resolved completely. Affected animals should receive IV and oral fluids, and food should be placed in a location that is easy to access. Affected animals should be evacuated for further veterinary care.

Leptospirosis

Large animals can develop leptospirosis. Clinical signs include fever, anorexia, jaundice, and lethargy. Acute renal failure may occur. Personnel should practice appropriate preventive biosecurity measures because the disease is zoonotic. Affected animals should be treated with procaine penicillin G (22,000 IU/kg IM every 12 hours) or doxycycline (7 to 10 mg/kg PO every 12 hours) until resolution of clinical signs.

Potomac Horse Fever

Potomac horse fever (PHF) is an enterocolitis of horses caused by infection with *Neorickettsia risticii*. Other large animals seem to resist infection. Affected horses develop fever and diarrhea. Treatment with oxytetracycline (7 to 11 mg/kg IV every 12 hours for 4 days) is effective to eliminate the organism. Horses with fever should also receive NSAIDs. Animals with severe diarrhea require aggressive IV fluid therapy, and evacuation to a hospital may be necessary. Clinical signs are similar to those of salmonellosis, and personnel should exercise caution, because *Salmonella* spp. can cause zoonotic infection.

SNAKEBITE

Snakebite in large animals typically occurs on the head in the area of the muzzle, but may occur on the limbs.[4,20] The most common clinical sign is soft tissue swelling at the bite site. For animals with head bites, swelling often progresses into the neck. If animals are in respiratory distress, immediate performance of a tracheostomy is indicated. Other clinical signs include decreased volume and frequency of GI tract sounds, fever, tachycardia, cardiac arrhythmia, tachypnea, and spontaneous hemorrhage from eyes, ears, nostrils, or the tracheostomy site. Equids should be monitored closely for development of laminitis. Standard treatments include broad-spectrum antimicrobials and NSAIDs. Fluids may be administered IV and, if available, plasma or whole blood obtained from a healthy animal of the same species. If available and the treatment is not cost-prohibitive, antivenom can be administered IV. Equine-derived antivenin products are most often used, similar to treatment for humans. Antivenom treatment improves survival rate for large animals with envenomation, although prognosis is fair to good without this treatment. The mortality rate for horses with envenomation that receive antivenin is very low (0%); it is 10% for horses that do not receive antivenom. New World camelids have mortality rates of 17% and 36% with and without antivenin treatment, respectively. Animals that survive should be monitored for development of sequelae related to myocardial damage.[7]

OPHTHALMOLOGIC EMERGENCIES

Ocular and periocular injuries are best treated in a hospital setting by a veterinary ophthalmologist. Emergency management in a wilderness environment can be critical to preventing further damage and increasing the chance of preserving ocular function. In the event of injury, the eye and exposed periorbital soft tissues should be thoroughly lavaged with saline solution. For animals with suspected globe rupture, tissues may be gently lavaged; however, irrigation and handling should be kept to a minimum until examination by a veterinary ophthalmologist. Neomycin, polymyxin B, and bacitracin ointment can be applied to the orbit to prevent bacterial growth in corneal ulcers. Ointments containing corticosteroids should not be applied to the cornea after a wound, because bacterial growth is likely to be potentiated and corneal ulcers can worsen rapidly. Ointments should not be used in cases of suspected globe rupture. The orbit can be bandaged with a soft cotton pad and elastic bandage tape (Elastikon) in a figure-of-eight pattern around the head until definitive treatment can be performed.

REFERENCES

Complete references used in this text are available online at expertconsult.inkling.com.