

VIPER SNAKEBITES

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Snakebites are a common problem in human and veterinary medicine. Vipers are member of the family Viperidae, a group of snakes found all over the world, except in Madagascar and Australia.

The viper family includes 223 species of venomous snakes that are divided into four subfamilies: pit vipers (subfamily Crotalinae), true vipers (subfamily Viperinae), Fea's viper (subfamily Azemiopinae) and night adder (subfamily Causinae). Vipers are characterized by a pair of long, hollow, venom-injecting fangs. They feed on small animals and hunt by striking and envenomating their prey. Pit vipers are the largest group of venomous snakes with 151 species and are responsible for ~150,000 envenomations of dogs and cats in the United States annually (1). The other major subfamily, the true vipers, include 66 species, and is also known as pitless vipers. They are distinguished by their lack of the heat-sensing pit organs that characterize their sister group. Among them, *Vipera berus* is found from Western Europe and Great Britain to the Far East (2). *Vipera palaestinae* (Vp) is the most common venomous snake in the Middle East. It is responsible for most envenomations in humans and domestic animals in Israel (3). The snake is endemic to Israel, can be found in all country parts except the desert, and has adapted to life in agricultural and suburban areas. Envenomations were reported in people, dogs, cats, horses and a ram (3, 4). In the present article experiences with Vp envenomations are reviewed.

The viper's venom contains about 30 components, 16 of which were identified, with the most important ones being proteases, hemorrhagins (metaloproteinases), amino acid esterases, phospholipase-A2, phospholipase-B and neurotoxins (5). The hemorrhagins activity leads to endothelial cell damage, causing high vascular permeability, bleeding and fluid extravasation into inflamed tissues. Phospholipase-A2 is considered the most important component in many snake venoms. It has both pro-coagulant and anti-coagulant activities as reflected by inhibition of the prothrombinase, inhibition and activation of platelet aggregation, and activation of Factor V and plasminogen (5). The amount of venom injected in a single bite increases with increased ambient temperatures, and may reach as much as one gram (dry weight); nevertheless, bites may contain no venom at all (6).

Most of canine Vp envenomations in Israel occur between

May and October and between 14:00 – 22:00, and parallel the viper's seasonal and diurnal activity. This pattern, however, may also result from increased seasonal and diurnal dog activity (4).

The onset of clinical signs following envenomation may be delayed for several hours. This phenomenon is highlighted by the fact that 40% of all severe envenomations in humans are graded as mild to nonenvenomating upon admission. In humans, 20% of all pit viper bites are dry envenomations (venom free) with an additional 25% classified as mild envenomations (1). The severity of the envenomation is influenced by species and victim factors such as the bite location, victim body mass, post-bite excitability, the species and snake size, its age and motivation and the degree of venom regeneration since last bite (1). For the aforementioned reasons, one can find among the risk factors for mortality causes such as envenomation during the first summer months and low body weight (<15kg). Additional risk factors include envenomations in the limbs and identification of the snake's bite as well as shock and bleeding tendencies (4).

Most canine Vp envenomations in dogs are in the head and neck area (80%) and less frequently in the limbs (20%) (3, 4). In a study on dogs with Vp envenomation, skin marks consistent of snakebite were identified in only 51% of the dogs (4). The most common local signs in canine snakebite include swelling, edema and hematoma which are attributed mostly to venom hemorrhagin activity. Acute lameness with pain may appear when limb envenomations occur (3). Reported systemic signs include anaphylactic, hemorrhagic or neurogenic shock, tachypnea, tachycardia, local lymphadenomegaly and cardiac arrhythmias (3). To date, no specific cardiotoxin has been identified in the viper's venom, although myocardial necrosis as a rare complication was reported in dogs and horses following Vp envenomation (7). A recent study demonstrated cardiac injury in Vp envenomed dogs as was reflected by increased serum cardiac troponin T and I (biomarkers of myocardial damage) (8). In the study, serum cardiac troponins concentration were increased in 65% of the dogs envenomed by Vp. Dogs with increased cardiac troponin were found to have a significantly higher occurrence of arrhythmias (58% vs. 19%).

The most common hematological findings in Vp

envenomation include hemoconcentration, leucocytosis and thrombocytopenia and nucleated red blood cells in the peripheral circulation. Drastic drop of total solids in the first 24 h after envenomation is very common, as well as mild prolongation of prothrombin (PT) and activated partial thromboplastin (aPTT) times and decrease in antithrombin activity. The most common biochemical abnormalities observed include increased activities of muscle enzymes: lactate dehydrogenase, creatine kinase and aspartate aminotransferase. Additional abnormalities included hypertriglyceridemia, mild hyperglycemia, hyperbilirubinemia, hyperglobulinemia and hypocholesterolemia (4).

The most common complications reported in dogs with viper snakebites include bacterial infections (clostridial or other), local necrosis, upper respiratory airway obstruction due to laryngeal edema, disseminated intravascular coagulation (DIC), acute renal failure, severe thrombocytopenia and death (3). For dogs with Vp envenomation, the reported mortality rate in the literature is relatively low (3.7-4%) (3, 4).

The veterinary literature on viper snakebites in cats is limited to a few case reports (9). Cats are considered more resistant to snakebites than other animals. In our emergency department we see 2-6 cases of cat's snakebites a year, as compared to 30-40 cases of dogs with snakebite. The explanation for the limited cases might be the caution and the ability of cats to cope with snakes, and the fact that many cats are not referred for medical treatment since they do not show clinical signs or are outdoor cats. Based on our limited experience, the diagnosis of snake bites in cats is not as obvious as in dogs. As the time lag from the snakebite to admission in cats is usually longer than in dogs, the most common clinical signs are local swelling with severe hematoma, which might develop over the 24-48 hour post snakebite, depression and shock. Hematological findings are hemoconcentration, thrombocytopenia, hypoproteinemia, hemolysis and consequent anemia, and the appearance of peripheral nucleated red blood cells. Disseminated intravascular coagulation also is a common complication in cats with snakebites with dramatic prolongation of the PT and aPTT but relatively mild clinical signs that are characteristic to DIC in other species.

Different treatment regimes are used for Vp envenomation in different (human or veterinary) institutions. These include antibiotics, antihistamines, steroids and specific antivenom (10). Dosing and timing are controversial, and may vary in different medical institutions. The Hebrew University Veterinary Treating Hospital (HUVTH) treatment protocol includes:

1. Fluid therapy
 - Crystalloids- 20 mL/kg as a bolus.
 - Colloids / Fresh frozen plasma when DIC is suspected or when total solids (TS) are low (below 4 g/dL), as needed.
2. Antimicrobial therapy (ampicillin 25 mg/kg q8h for 5 days) to prevent clostridial or other infection that may have been transferred by the snake's teeth.

3. Antihistamine - Diphenhydramine (2 mg/kg q8h for 24 h), only after hypersensitivity skin test for the antivenom has been completed.
4. Steroids - The use of glucocorticosteroids in snakebites has always been controversial. They are used in cases of shock and severe edema, particularly when in the larynx area, as they may minimize and/or prevent further endothelial damage. However, steroids may slow and diminish antivenom activity and increase the risk for bacterial infection. Some clinicians believe that the use of steroids is contraindicated in snakebites (10). In a retrospective study of 327 dogs with snakebite it has been shown that glucocorticoid therapy was significantly associated with mortality ($p=0.002$) (4). Therefore, the use of steroids in HUVTH is limited to cases in which laryngeal edema is severe and may prevent tracheostomy.
5. Antivenom- It has been shown that treatment with low specific antivenom dose (10 mL) did not decrease the mortality rate (4). However, in humans, the mortality is reported to decrease sharply from 6-10% to 0.5-2% since the introduction of the specific antivenom (12). Our recommendations, based on the findings in human medicine and our clinical experience, are that antivenom is to be administered to effect in cases of:
 - (a) Clinical signs of shock.
 - (b) Severe swelling at the site of the bite.
 - (c) Abnormal coagulation parameters, including thrombocytopenia.
 - (d) Owner's financial abilities (10 mL of antivenom in Israel costs approximately \$250).
6. Monitoring for 24 h. This includes complete blood count (CBC), creatinine (q12h), PT and aPTT (q12h), PCV/TS (q12h), ECG (q2h), and blood pressure.

In conclusion, we summarize that Vp, a member of the viper family, viper snakebite has relatively low mortality rate both in human and in dogs. Further investigation of snakebites in cats is needed. Risk factors for mortality include the first months of the summer, low patient body weight, limb envenomation, systemic clinical signs and coagulation disorders. Treatment with steroid is controversial and should be further investigated, while antivenom should be considered in cases in which one of the risk factors to death is present and not as a fixed dose but rather to effect.

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