In this review, we evaluated venomous snakes in Turkey, as well as the symptoms related with these venomations and principles of current first aid and treatments and possible complications. Geographically, mostly vipers as most venomous snakes are present in Turkey. The people who work or travel in agricultural areas should be aware of venomous snakebites in this country. Generally the symptoms of victims depend on neurotoxicity, myotoxicity and coagulopathy in vipera envenomation. Especially, in addition to emergency room physicians, general surgeons and hand surgeons must be familiar with the principles of diagnosis and current treatment modalities to prevent complications as well as death or limb amputations.

Key words: Snake bite, venomous snakes, antivenom, toxicity, Turkey

INTRODUCTION
Snakes are reptiles, and are closely related to lizards, tortoises, turtles and crocodiles. Generally, they are harmless and play important environmental roles in the fragile ecosystems of the wildlife areas (1-4). Most accidental bites usually occur whenever a snake is encountered and does not have time or space to slip away. Generally, the victims were found to be bitten in the fields for example when harvesting grapes. So everyone must be aware of potential dangers posed by venomous snakes when camp, hike, picnic, work or live in snake-inhabited areas. Snake bites still cause significant morbidity and mortality in developing countries. Geographically the climate of southeast region of Turkey is arid and contains mostly vipers as venomous snakes (3-6).

Venomation of vipera (Viperidea) was mostly encountered in rural areas of Turkey. Local symptoms of victims were swelling (generally appear within two hours), pain and tenderness of regional lymph nodes, bruises and necrosis on the bite side, and sometimes compartment syndromes develop (digits, anterior tibial or thigh). Systemic effects of envenomation: Generally epistaxis, haematemesis, echimoses, haemoptysis; subconjunctival, retroperitoneal and intracranial haemorrhage may occur in case of serious clothing defects. In addition, some neurotoxicity (ptosis, weakness, paresthesia, dysphagia, sweating, respiratory depression, paralysis) and myotoxicity symptoms may develop in envenomed patients (3,5-7).

Snakebite first aid
In warm climates, snakes were found to be more active. Despite many of them are non-venomous, a few of them are venomous and mostly are found to be inhabit in some cities in Turkey. Generally, when they suddenly confronted by human beings, and if there is not enough time or space to slip away, they bite to defend themselves. Anyone who is helping an envenomed victim, should be aware of the envenomous snakes of the region and have a profound knowledge about the first aid approaches. Only 10 out of the more than 40 indigenous species in Turkey were found to be venomous (2).

First of all, the helper should determine whether the victim is envenomed or not. The symptoms and signs depends on the type and amount of venom injected, location of the bite, and the victim’s age, body size and general health conditions. Usually, sense of extreme fright is the common reaction to a snake bite. The use of local ice packs, incision and suction and alcohol or sedative drugs for sedation of victim and pain killers such as aspirin and non-steroid anti-inflammatory drugs should be strictly discouraged. Typically, these patients may become emotionally unstable with thoughts of imminent death, or conversely, the victim may become in extreme withdrawal or lethargy state. Because of fear, victim present some symptoms and
signs such as nausea, vomiting, diarrhea, dizziness, fainting, cold and clammy skin and tachycardia. In this regard, it is important that autonomic reactions must not be mistaken for systemic symptoms and signs resulting from the snakebite. Therefore, local and systemic signs must be evaluated profoundly (4, 8-10). In addition, an envenomed one should be reassured and a firm immobilization must be strictly applied to the bitted limb and it must be kept below the heart level. Then any jewel or constricting cloth should be removed before the development of edema.

A passive transportation to a safe zone can aid to calm the victim and can also diminish the spread of venom by circulation. With applying a 5-15cm creep bandage proximal to the wound can impede lymphatic flow. Generally compressive bands are not advocated for retarding the arterial and venous circulation (4, 7, 10-13). However, Bates recommended the tight (arterial) tourniquets for rapidly acting neurotoxic venoms (for example, bites by the mamba, krait, coral snake, Egyptian and Cape cobras) (4, 7). Ralidis recommended that the use of various incisions can only be allowed when prompt medical treatment is more than 30 minutes away (10). Sutherland et al showed that pressure alone or immobilization alone did not delay venom movement in their study with monkeys. It could be possible to diminish the venom movement only with pressure application and immobilization of the victims bitten limb (14).

Generally electric shock therapy (often with a stun gun) is of no use, and could cause serious injury and was discouraged by many authors (8, 12, 15, 16). Venom pump extractor can be beneficial, if applied in few minutes (3-5min) after the snakebite (8, 10, 12, 17). Bush et al studied about the negative effects of venom extraction device, and no benefit was demonstrated, but skin necrosis occurred associated with the device (18).

Despite the snakes in Turkey are usually not so venomous to kill a victim, but many complications may occur such as local necrosis, neurotoxicity, myotoxicity and serious clothing defects (2, 3).

At the hospital, the victim must have supportive care as ABC management, pain medication (avoid sedatives that may obscure neurotoxicity symptoms), wound care, and broad-spectrum antibiotics, also tetanus prophylaxis should be considered for both immunized and non-immunized cases. A detailed recommendation for laboratory evaluation for a snakebite victim should be accomplished routinely, as summarized in Table 1 (12). Gold et al presented a useful list of indications for antivenom treatment (Table 2) (19). If obvious local and systemic signs of envenomation have been found, the victims must have antivenin that is selected according to VDK (Venomous Detection Kite) as an antidote immediately (20).

### Table 1. Laboratory evaluation in snakebite

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count*</td>
<td>Prothrombin time*</td>
</tr>
<tr>
<td>Partial thromboplastin time*</td>
<td>Fibrinogen*</td>
</tr>
<tr>
<td>Fibrin degradation products*</td>
<td>Blood type and cross match</td>
</tr>
<tr>
<td>Serum electrolytes</td>
<td>Glucose</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>Platelet count</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>Bilirubin</td>
</tr>
<tr>
<td>Creatine kinase</td>
<td>Creatinine</td>
</tr>
<tr>
<td>Urinalysis*</td>
<td>Stool hemoccult</td>
</tr>
<tr>
<td>ECG§</td>
<td>Arterial blood gas</td>
</tr>
</tbody>
</table>

*Should be performed as soon as possible and repeated within 12 hours
± Including free protein, hemoglobin, and myoglobin
§For patients older than 50 years and for patients with a history of heart disease

### Table 2. Principal indications for antivenom therapy

1- Impaired consciousness
2- Neurotoxicity
3- Abnormal EKG; hypotension and shock
4- Homeostatic abnormalities (spontaneous systemic bleeding and coagulopathy
5- Generalized rhabdomyolysis
6- Evidence of severe intravascular haemolysis
7- Evidence of renal failure such as uraemia and oliguria or anuria
Envenomation grading and antivenin administration

Antivenin is derived from antibodies created in a horse’s serum after this animal has been injected with the snake venom. Anyone who is using this drug in an envenomated victim can encounter some rare but unavoidable allergic conditions such as fatal anaphylactic shock (1). The patient’s bitten area in the limb must be followed closely, and should be graded according to severity of symptoms related with extremity edema, and laboratory abnormalities during the first day following the snakebite (Table 3) (9). Antivenin constitutes the major role especially in envenomed grade II-IV victims (9,21). In addition to moderate and severe grade victims; antivenin can be used for mild bites with progression of local symptoms (22).

The use of polyvalent antivenom is found to be safe and effective, associated with prompt improvement in the patient’s condition. Acute allergic reactions were found to be generally mild and usually of urticaria in clinical trials (23,24). In the last decade we encountered some developments in antivenin drugs.

The new antivenin, called CroFab, (Savage Laboratories, Melville, NY) was found to cause mild acute reaction (urticaria/broncospasm and hypotension and delayed reactions (serum sickness) less frequently compared to polyvalent antivenin (25). Skin testing was generally recommended by many authors. Because of the possibility of a simple allergy such as urticaria or a fatal anaphylactic reaction to the horse serum used in skin testing, this test should be applied in the intensive care units (12). Some authors recommend skin test for envenomed victims, and atopic patients who have been severely envenomed can have antivenin treatment with prophylactic adrenaline, as well as antihistamines and hydrocortisone administration (4,21,26,27).

Shaw et al demonstrated that they could be treated by aggressive use of polyvalent equine antivenin safely, which prevented the need for surgery in sixteen of nineteen envenomed children, and recommended that moderate to severe rattle snake envenomations should be treated primarily with antivenin in an intensive care unit with an initially slow rate infusion and compartment pressures should be measured selectively. They concluded that surgery for rattle snake envenomations should be indicated for the patients with confirmed compartment syndrome that is refractory to antivenin treatment (28). Some authors also supported the treatment of snakebite envenomations, mainly by antivenins with superior survival and preservation of muscle function (29,30).

In this regard, Gold et al reported that an envenomed patient who had a compartment syndrome (detected intracompartmental pressure was 55mm Hg) that could be treated by large doses of neutralizing antivenom given concomitantly with mannitol and hyperbaric oxygen (31). Better et al showed the amelioration of intracompartmental pressure by using IV hypertonic mannitol in an experimental study in dogs (32).

**Table 3. Grading of envenomation**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Degree of envenomation</th>
<th>Signs and symptoms</th>
<th>Initial dose of antivenin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
<td>Mild to moderate pain Edema 4 to 5 inches from bite site in first 12 hours after bite No systemic signs of envenomation No laboratory abnormalities</td>
<td>4 to 5 vials</td>
</tr>
<tr>
<td>2</td>
<td>Moderate to severe</td>
<td>Severe pain Edeme extending 6 to 12 inches or more in first 12 hours after bite Nausea, vomiting, diplopia, perioral paresthesia and other signs Laboratory abnormalities</td>
<td>10-15 vials</td>
</tr>
<tr>
<td>3</td>
<td>Severe to very severe</td>
<td>Very severe pain Edema rapidly extending to trunk Severe systemic signs Severe laboratory abnormalities</td>
<td>15-20 vials</td>
</tr>
</tbody>
</table>

Venomous snake bite in Turkey
see a blister and erythema on the bite location as a soft tissue respond to snakebite that may appears immediate or delayed up to 2 or 3 days. Radiation from this small blister is a zone of erythema of 2 to 3 cm with the bite mark becoming the center of the “bull’s eye”. Generally, instead of cellulitis, this erythema represents a local immune response. The erythematous process may spread up to 3 to 5 cm and over the ensuing days, the blister will turn into a necrotic eschar (generally 5 to 7 days after the envenomation injury) (35).

Fasciotomies are generally recommended in case of the clinical symptoms related with compartment syndromes (marked swelling, hyperesthesia, tenseness, and pain on passive finger stretching of the lesion. However, routine intracompartmental pressure at the snake-bitten limb should be measured with catheters in most clinical practice. If this measurement is greater than 30-45 mmHg, fasciotomy can be accomplished for surgical decompression (7,9,21,36).

Complications

Serum sickness, because of the deposition of immune complexes, is a recognized complication of the administration of foreign solutions such as antivenins. The possibility of this complication and its related symptoms and signs should be explained to the patients

Prophylactic antibiotic administration

Most physicians recommend a broad spectrum antibiotic use especially moderate and severe grade envenomations victim (8,9). Blaylock recommended antibiotic ointment on localized lesions (13).

However, LoVecchio et al treated fifty-six patients with rattlesnake envenomations and only 6% of the patients had needed antibiotic treatment and they concluded that prophylactic antibiotics are not indicated in patients with rattlesnake bites (33). Also Kerrigan et al concluded that there was no use of prophylactic antibiotics for prevention of infectious complications of crotalid envenomation (34). Breiner especially emphasized on wound hygiene unless documented cellulitis was found. He does not ratify both ice packs and heating packs as they were found to be more harmful rather than beneficial (35).

Surgical treatment

Nowadays, better first aid and emergency department treatment facilities, new better antivenoms with low side effects and wound healing factors were decreased the number of surgical interventions. However surgery is still indicated occasionally. Breiner emphasized that too urgent debridement may cause more harm than good. Generally, we see a blister and erythema on the bite location as a soft tissue respond to snakebite that may appears immediate or delayed up to 2 or 3 days. Radiation from this small blister is a zone of erythema of 2 to 3 cm with the bite mark becoming the center of the “bull’s eye”. Generally, instead of cellulitis, this erythema represents a local immune response. The erythematous process may spread up to 3 to 5 cm and over the ensuing days, the blister will turn into a necrotic eschar (generally 5 to 7 days after the envenomation injury) (35).

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Table 4. The other rare complications related with snakebites

<table>
<thead>
<tr>
<th>Complications</th>
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<tbody>
<tr>
<td>1- Cardiac arrest (38)</td>
</tr>
<tr>
<td>2- Airway obstruction (39)</td>
</tr>
<tr>
<td>3- Local and systemic bleeding (40,41)</td>
</tr>
<tr>
<td>4- Pulmonary emboli and parenchymal infection (empyema) (42)</td>
</tr>
<tr>
<td>5- Recurrent and persistent coagulopathy (43,44)</td>
</tr>
<tr>
<td>6- Biphasic venom-induced thrombocytopenia (45)</td>
</tr>
<tr>
<td>7- Disseminated intravascular coagulation (46)</td>
</tr>
<tr>
<td>8- Squamous cell carcinoma (47)</td>
</tr>
<tr>
<td>9- Osteomyelitis of the foot (48)</td>
</tr>
<tr>
<td>10-Intracerebral infarction and hematomas (49,50)</td>
</tr>
<tr>
<td>11-Ghost cell glaucoma and vitreous hemorrhage (51)</td>
</tr>
<tr>
<td>12-Tetanus (52)</td>
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</tbody>
</table>

Table 5. Potential errors in the treatment of snakebites

<table>
<thead>
<tr>
<th>Errors in the treatment of snakebites</th>
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<tbody>
<tr>
<td>1- Administration of inadequate quantities of antivenin, particularly in children</td>
</tr>
<tr>
<td>2- Not considering envenomation in children who present dusky, swollen extremities, when the etiology is not clear</td>
</tr>
<tr>
<td>3- Improper administration of antivenin, i.e. intramuscularly or direct bite-side application</td>
</tr>
<tr>
<td>4- Unnecessary skin testing, i.e. when there is no intention to administer antivenin</td>
</tr>
<tr>
<td>5- Improper use of tourniquets and cryotherapy</td>
</tr>
<tr>
<td>6- Failure to provide thorough irrigation of fang puncture wounds</td>
</tr>
<tr>
<td>7- Surgical intervention( fasciotomy) without demonstrating elevated intracompartmental pressure</td>
</tr>
</tbody>
</table>
clearly who had antivenin treatment before to discharge, so it can be recognized and treated more early. The most frequently encountered late complication is serum sickness (type III hypersensitivity) that occur approximately 5-24 days after the administration of antivenom and generally manifested by fever, urticaria, itching, periarticular swelling, albuminuria, rashes, arthralgias, and lymphadenopathy as well as rarely a peripheral neuritis, pericarditis, or encephalitis (4,8,37). The other rare complications related with snakebites are summarized in Table 4.

Errors in Treatment
There are some mistreatment approaches that may influence the victim’s morbidity badly. Forhs et al emphasized some errors about the treatment of snakebite that summarized in Table 5 (9).

Conclusion
In addition to emergency room physicians, general surgeons and hand surgeons must be familiar with the principles of diagnosis and current treatment modalities to prevent serious complications as well as death or limb amputations.

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