Viper bites: treat or ignore?

Review of a series of 99 patients bitten by Vipera aspis in an alpine Swiss area

Jacques Petite

Hôpital Régional, Martigny, Switzerland

Summary

In a well defined alpine area of Switzerland (Valais, about 300000 inhabitants, tourists included) we studied retrospectively over 32 years, 99 patients bitten by vipers (*Vipera aspis*, the likely unique species in this area). The annual incidence was estimated at 3/100000, as in other European countries. The mortality was 0% for the adults. The patients, 72 adults and 17 children (13 years and less), were classified in four groups: grade 0 no envenomation (8%), grade 1 minimal (42%), grade 2 moderate (40%), and grade 3 severe envenoma-

tion (10%). The 10 patients of grade 3 showed impressive clinical signs and blood abnormalities, as exemplified by our three most severe cases. Only patients of grade 3 must be treated with antivenom and other intensive treatments, but all patients, even grade 1, especially small children, must be observed for several hours.

Key words: viper bites; Vipera aspis; Valais; Switzerland

Introduction

In Europe, despite many medical reports attesting their general benignity, the public's fear of snake bites is still vivid. The severity of envenomation has been poorly evaluated, because of the difficulty in collecting cases in large areas and of the lack of reliable epidemiological data [6]. Over the past 100 years, several reports on snake bites have been published in Switzerland [12, 14, 18, 33], Italy [24] and France [1, 8]. Our country provides the habitat for three species of viper: Vipera berus, most common in the north, as in central and northern Europe, Vipera aspis common in the south and alpine part of Switzerland, as well as in France and southern Europe, Vipera ammodytes, is found, albeit rarely, in canton Ticino. The composition of their venom is similar, although some variations might exist with possible different clinical consequences which could not be ascertained in previous Swiss series because of their heterogeneity (mixtures of cases from different parts of the country, bites from three viper species).

The canton Valais is a well-outlined alpine region, with an native population of 290000 (plus 40-50000 tourists in the summer). It has the peculiarity of housing only one species of viper (Vipera aspis), with some very rare exceptions (Vipera berus). We thus took the opportunity to conduct a retrospective and prospective study of all patients bitten in Valais by Vipera aspis over a 32 year period. The aim of this work is to define, in a homogenous group of patients, the risks, the criteria of severity, the prognosis, and the treatment of severe envenomation. We insist on the latter situation by describing clinical cases exemplifying the importance of treatment. Our conclusions might be extrapolated to patients bitten by other European vipers but not for other continents, where the bites by crotalids and other snakes can induce severe complications, such as neurotoxicity, coagulopathy and renal failure [5, 9, 16, 20].

Patients and methods

Patients were collected in two groups: for the region A, Martigny-Entremont, all patients admitted in the regional hospital from 1973 to 2004, had a complete chart, with clinical and biological parameters, prospectively defined. Practitioners reported three more ambulatory cases from this area. This group makes half of the series. For the rest of the canton Valais, region B, we collected cases registered from 4 other regional hospitals (complete data since 1992 only), from all private practitioners (standard questionnaire) and for 4 cases from Toxzentrum Zurich.

No financial support to declare. In this second group, the severity of cases is quite similar to the first group, despite likely deficient reporting from this region (see Results).

For the clinical evaluation, we adopted, with small modifications, the grading scale from Fr. Audebert et al. [1].

Blood tests, done in only 69 of 99 patients, included: haemoglobin, leucocytes, thrombocytes, creatinine, prothrombin time (PT), partial thromboplastin time (PTT) and fibrinogen (14 patients only).

Results

For the region A, Martigny-Entremont (39000 inhabitants + about 15000 tourists in summer), we treated 47 cases from 1973 to 2004. For the rest of canton Valais, region B (240000 inhabitants + about 30000 tourists), during the same period, we collected only 53 cases. This means that, despite the fact that snakes are probably more abundant in region A, the number of bites for the whole country was likely to be underreported.

One patient from region B, bitten in 1996 by an exotic snake (*Naja*), was excluded from the study. Thus the total number was 99 patients: 17 children (13 years and less) and 82 adults, 55 males and 27 females, aged between 16 and 85 years. The average age for the adults was 36 years.

The annual incidence (morbidity), calculated in Region A (where collecting was complete and precise), was 3/100000 inhabitants, a number similar to that reported in other European countries.

A 2 year-old child died 3 days after what was most probably a viper bite. Forensic investigation could not demonstrate venom, but the history and clinical status were characteristic. The mortality in our series is therefore 1%, but 0% for the adults. As shown in figure 1, viper bites occurred from March to September.

All patients were bitten during the day (between 8.30 am and 9.30 pm), with a peak between 2 and 4 pm. The annual incidence was very variable, from 0 cases to 9 cases in 1990. We did not find any correlation with the average daily temperature (only 2 cases in the very hot 2003 summer). The site of accident is shown in the map of canton Valais (figure 2). Some areas may appear more dangerous, probably in relationship to the patients' work in the vineyards on the right bank of the Rhone.

Vipera aspis likes a mountainous habitat: 52

bites out of the 93 where the location of the event could be determined occurred at an altitude of 1000 m and above (up to 2300 m). The snake likes warm and sunny typical biotopes. Several bites occurred when snakes lying under stones were disturbed. 68 bites were on the hand or forearm, when trying to handle the snake and more rarely, 27 times, on the foot or ankle generally when treading on the viper. Four patients were bitten on other parts of the body. Nobody was "attacked" by a snake.

Clinically, the 96 patients (99 minus 3 patients with unreliable grading), 79 adults and 17 children, can be classified as showed in table 1.

The majority of patients, even with grade 0 bites, were seen in hospital after 4 hours or more. Only 9 patients were examined by a physician and sent home without subsequent follow-up. Probably some patients did not consult a doctor after being bitten and can be assumed to have had a benign progress. Their number is impossible to evaluate, but we can assume that it is not as high as in the past, when the agricultural way of life was predominant.

As shown in table 2, the consequences of viper bites were slightly more severe in children than in adults.

Among the 8 patients with suspicion of snake bite (grade 0), only 4 had typical marks of fangs. In patients with minimal envenomation (grade 1), the local signs of bite were constant, the pain frequently reported and the inflammation only transient (no more than 2 days). In cases of moderate envenomation, the limb oedema, characterising grade 2, developed after a minimal delay of two hours progressing to a maximal level after 24 to 48 hours, especially when complicated by haema-

Figure 1 Seasonal incidence of 97 viper bites.



Figure 2 Site of accident (97 patients).



Table 1

Table 2

Clinical of 96 pa

Clinical gradation after viper-bite.

| Grade | 0 | no envenomation | fang-marks, no oedema |
|-------|---|-----------------------|--|
| | 1 | minimal envenomation | local oedema around the bite, no systemic symptoms |
| | 2 | moderate envenomation | oedema of the limb, mild systemic symptoms (vomiting, transient hypotension, etc) |
| | 3 | severe envenomation | extensive oedema spreading to the trunk, shock or prolonged hypotension, bleeding and other systemic signs |

| classification | Grade of envenoming | Adults | Children | Total |
|----------------|------------------------|--------|----------|----------|
| tients. | 0 | 5 | 3 | 8 (8%) |
| | 1 | 35 | 5 | 40 (42%) |
| | 2 | 33 | 5 | 38 (40%) |
| | 3 | 6 | 4 | 10 (10%) |
| | Total | 79 | 17 | 96 (100% |

toma (ecchymosis). Fainting, hypotension and vagal symptoms could occur even in mild envenomation (grade 1 and 2). They should not be confused with shock found in grade 3.

The dramatic symptoms of severe envenomation (grade 3) occurred generally very early after the bite, and were accompanied in all cases by blood abnormalities. The clinical presentation and the complications of these cases were complex. It is therefore worthwhile giving a more detailed account of three cases.

Case Nr 1

A 63 year-old woman was bitten by a viper on the ankle at 1 pm, on the 10th of August, while walking on the lawn around her chalet (altitude 900 m). She immediately fainted with violent pain at the ankle, abdominal cramps and nausea. Her husband drove her rapidly to the hospital (20 minutes travel time). She was conscious, but in shock (blood pressure 60/35 mm Hg), pale and sweating, complaining of strong abdominal pain. Temperature was 37.5 °C heart-rate 120/min, regular. Palpation and auscultation of the abdomen were normal. The bite was easily visible on the retromalleolar left ankle, with two marks of fangs and mild local oedema. Laboratory values were: Haemoglobin 12.5 g/l (5.2 g/l 4 days later), thrombocytes 250 g/l (44 g/l one day later), PT 100%, then 61%. PTT 20 sec. Fibrinogen 1.79 g/l, then 1.44 g/l (12 hours later), Haptoglobin 0.86 g/l.

Despite massive saline infusion (8 litres/48 h) and adrenaline, she remained in shock for 36 hours. Following the advice of several specialists, we did not administer antivenom. She developed oliguria, a progressive violaceous oedema of the whole left part of the trunk, a large left pleural effusion, which turned out to be a transudate, anaemia (due to interstitial bleeding and haemodilution without signs of haemolysis) treated by transfusions, renal failure (creatinine 264 umol/l) and mild hepatic damage (bilirubin 58 umol/l, alkaline phosphatase 490 U/l, gamma glutamyl transferase 227 /l, SGOT 62 U/l, SGPT 98 U/l). Renal and hepatic lesions, probably due to the prolonged shock, were reversible.

Progress was very slow but favourable. The patient was discharged after 5 weeks in hospital with only two sequelae: residual oedema of the left lower limb which finally resolved 2 months later and a right radial palsy related to the use of a walking-stick.

After this dramatic case, the attitude towards the treatment of snake bites in our country radically changed and since 1995 all Swiss hospitals have a reserve of antivenom.

Case Nr 2

A 41 year-old man, who bred snakes, was bitten for the first time in 1985, by an alpine viper (local oedema, no complications, no antivenom). Three years later, in the same location known for its numerous snakes (at an elevation of 1600 m) he was bitten on the 3rd left finger, while attempting to catch a viper. His friends saw him collapse (unconscious for about 10 minutes); they transported him with great difficulty on an improvised stretcher to reach a road and finally the hospital 2 hours later. He was conscious but in shock (blood pressure 90/60 mm Hg), bleeding from the nose, the mouth (haematemesis, plus haemoptysis) and the anus (haematochesis). He had an ecchymotic oedema of the left arm and hemiface. A diagnosis of coagulopathy (disseminated intravascular coagulation DIVC) was rapidly confirmed: Haemoglobin 9 g/dl, Thrombocytes 3 g/l, PT 27%, PTT 58 seconds, Fibrinogen 0.5 g/l. Administration of fluids and corticosteroids had no effect. The patient was rapidly transferred by helicopter to the University Hospital of Lausanne (CHUV): he was still in shock, dyspnoeic, bleeding from all orifices; he received blood transfusions (5 units) and, very cautiously, small and repeated doses of antivenom. After many complications, he was discharged, without any sequelae. To the best of our knowledge he is now in good health but has nothing to do with snakes anymore.

The severity of the clinical presentation and of the coagulopathy was explained by anaphylactic shock due to prior sensitisation with snake proteins [13]. This physiopathological mechanism was proved by the detection in the blood of the patient of specific IgE against venom from *Vipera aspis* but not against *Vipera berus* [19].

Case Nr 3

A 66 year-old woman with a history of atopia and hypertension, was wandering on a mountain path (altitude 1600 m) in June. At 9 am she trod on a viper and was bitten on the left ankle. The pain was slight. She walked back to her car and reached the doctor's surgery 15 minutes later. She was conscious, not anxious, but diaphoretic and discretely hypotensive. 5 minutes later, the patient became dyspnoeic and more hypotensive. She was transported to hospital by helicopter.

On admission she was shocked (TA 65/40 mm Hg), very dyspnoeic, with oedema of the face. The pulmonary auscultation revealed the presence of diffuse wheezing, a prolonged exspirium and decreased breath sounds. The left ankle was swollen, but not the limb. She was intubated and mechanically ventilated for 3 hours. She received corticos-

teroids and intravenous adrenaline, very successfully. She had no signs of coagulopathy, or renal failure. 24 hrs later, she was eupnoeic, with a swollen and bruised left limb. Eventually, she had to be be transfused because of anaemia (haematoma, plus bleeding gastric ulcer) and cardioverted due to paroxysmal supraventricular tachycardia. She left the hospital without sequelae.

This patient known for allergy, showed a typical anaphylactic reaction to the venom, with shock, Quincke's facial oedema, respiratory failure quickly treated with adrenaline and corticosteroids.

Comment on the laboratory abnormalities

Typical allergic manifestations (oedema of lips, tongue or larynx, with various asthmatic symptoms) were encountered in 5 patients, among whom 3 with moderate envenomation (grade 2). These three patients were known for allergy to hymenopters, proved in one subject by the detection of specific IgE against wasp venom [27]. On the other hand, two patients known to be allergic to hymenopters tolerated the viper's bite well.

A renal lesion was seen in 3 patients and was always reversible, even in the case Nr 1 with transient renal failure due to shock. Hepatic biological abnormalities were seen in only 2 cases, including case Nr 1, and were completely reversible.

Among the 75 complete charts, we found blood abnormalities in all patients of grade 3 (6 adults and 4 children), very rarely in patients of grade 2 (2 adults and 1 child), but never in patients of grade 0 or 1.

Anaemia, sometimes severe, was manifest one or more days after the bite. Except for case Nr 2 (massive bleeding with DIVC), nobody was anaemic on admission. The anaemia was explained by haematoma (bleeding in the swollen limb) and massive saline infusions. The anaemia was aggravated by intestinal bleeding in one case (Nr 3). No sign of haemolysis could be detected.

A neutrophilic hyperleucocytosis (more than 20 G/l) was found in 5 cases with severe envenomation (3 adults and 2 children). A very severe thrombocytopenia was present only in case Nr 2 with DIVC. A moderate thrombocytopenia (60 to 150 G/l) was noted in 6 other cases (case Nr 3) on admission or later (accompanying the haemorrhage), always transitory and reversible.

Disorders of coagulation were rare in our series. Fibrinogen, measured in 49 cases, was abnormal in only 2 cases (number 2 and one case with grade 3: 1,85 g/l). In other patients with severe envenomation, fibrinogen was minimally and transiently decreased, often during the period of haemorrhage. PT and PTT were measured several times for 75 patients. A true disseminated intravascular coagulopathy (DIVC) was diagnosed in 2 cases (numbers 2 and 3), accompanied by thrombocytopenia and hypofibrinogenaemia. In other 3 patients with grade 3, PT was abnormal at the admission. In all other patients with severe enven-

Table 3

Clinical and biological symptoms in 79 adults and 17 children (numbers in brackets) bitten by Vipera aspis.

| Grade | 0 | 1 | 2 | 3 |
|-----------------------------|----------|--------|--------|-------|
| Number of patients 79 (17) | 5 (3) | 35 (5) | 33 (5) | 6 (4) |
| Clinical symptoms | | | | |
| pain | 4 (3) | 18 (5) | 25 (4) | 5 (3) |
| bite marks | 2 (2) | 32 (5) | 31 (5) | 5 (4) |
| oedema of the limbs | | | 33 (5) | 6 (4) |
| extensive oedema, effusions | | | 2* | 3 (3) |
| ecchymosis | | | 5 (1) | 3 (2) |
| bullae, necrosis | | | 6 (1) | |
| vomiting, abdominal pain | | | 6 (4) | 4 (4) |
| fainting, vagal symptoms | | 3 | 8 (1) | 2 |
| dyspnoea | | | 2* | |
| shock | | | | 5 (3) |
| Blood abnormalities 64 co | mplete c | harts | | |
| anaemia | | | 2 (1) | 5 (2) |
| leucocytosis >20 G/l | | | 2 | 5 (1) |
| thrombocytopenia <100 G/l | | | 2 | 5 (1) |
| coagulation disorder | | | | 4 |

omation, changes of PT and PTT were minimal, and not correlated with thrombocytopenia.

As shown in table 3, the clinical and biological manifestations after viper bite were slightly more severe in the children than in the adults. Case 4 exemplifies that point: A 9 year-old boy, playing on an August morning in the mountains (altitude 1700 m), fell from a rock in a small grassy place, where he was bitten by a viper (the snake was not seen but typical marks of fangs were identified by his mother, a nurse). The oedema of the hand increasing, the boy was transported to hospital 2 hours later. On admission, the clinical status and the blood analysis are reassuring (except for the

leucocytosis at 26 G/l). The day after, the oedema has reached the right hemithorax; the child was dyspnoeic, with clinical and radiological signs of pulmonary oedema. A pericardial effusion was detected by echocardiography. Corticosteroids and diuretics were given but no antivenom (on the advice of a specialist). Dyspnoea and oliguria regressed slowly. The haemoglobin fell to 8.2 g/dl from 13.9 g/dl, probably because of a haematoma, and the thrombocytes to 102 G/l, without coagulation abnormalities. The child left the hospital with a residual swollen right arm (complete recovery 2 weeks later).

The attitude of patients and parents at the scene of the bite was very variable. Many attempted suction, with or without prior incision. Only two patients used a special instrument (Aspivenin®). A tourniquet was placed in 10 cases, without any complication. The great majority were transported by car. The delay between the accident and medical examination varied from 15 minutes to 7 hours (mean, calculated from only 38 cases with precise data, was 90 minutes and median 75 minutes). 4 patients were admitted 2 and 3 days after the bite, because of a swollen limb. Only 9 patients (Grade 1 and 2) were treated on an outpatient basis. For the others, the hospital stay lasted 4 to 72 hours, except for the few patients with grade 3 (severe envenomation) who were hospitalised for prolonged periods.

Antivenin was administrated in only 2 patients of grade 3 (see Discussion). All 10 patients with severe envenomation were admitted in an intensive care unit and received aggressive supportive care (cases 1, 2 and 3).

Discussion

The snake Vipera aspis, probably the only species in our series, is also the most common viper causing bites in France [8]. Its venom, a complex mixture of proteins and peptides acting as enzymes and ligand, is quite similar to that of the other European vipers (V. berus and V. ammodytes). Among the 26 enzymes discovered in snake venom, 12 are common to all species in the world. The main enzymes are phospholipase A2 (absent in Vipera berus), hyaluronidase, metalloproteinases and proteases [10, 28, 30, 34]. Their astonishingly high number seems to have been conserved in all venomous snakes for a double aim. The first is paralysis and the second digestion of the prey, the latter being more important as snakes eat animals that are alive and sometimes very large only intermittently with very long intervals between feeding. The viper is poikilothermic and needs solar heat to elevate its temperature and become active for hunting and catching prey. During digestion vipers sleep but when aroused, respond very aggressively. This reaction is only defensive and, contrary to

some mythical accounts, the viper being very sensitive to vibration chooses to flee and never "attacks".

In humans (and animals), the snakebite has two major effects. Locally, the venom causes an intense inflammation and destroys by proteolytic enzymes the vascular walls, inducing oedema, sometimes over a large area, often with blood loss. The venom proteins, when in high concentrations in the blood, cause shock, generalised symptoms such as hypotension and abdominal cramps, allergic sensitisation, coagulopathy and, rarely, death. When injected intravenously in rabbits [2] viper venom has a half-life of 0.7 hours for distribution, and of 12 hours for elimination (only 5% by renal route). By the intramuscular route the venom is rapidly absorbed, the blood level of venom is low but it persists for 72 hours. The venom of other snakes (crotalids, Russel's viper) induces immediate shock, when injected intravenously in the dog, and subsequent disseminated coagulopathy and death within 3 days [20, 36].

| Table 4Comparative severityof snakebites in | | Kaufmann 1892 n = 60 | Pozio 1988 n = 286 | Audebert 1992 n = 102 | Stahel 1995 n = 113 | Meier 2003 n = 161 | This study 2004 n = 99 |
|--|---------|----------------------------|--------------------------|-----------------------------|---------------------------|--------------------------|------------------------------|
| Switzerland (Kauf- mann [12], Stahel et | Grade 0 | 6 (10%) | 46% | 20 (20%) | 13 (12%) | 15 (9%) | 8 (8%) |
| al. [33], Meier et al. | Grade 1 | 21 (35%) | 30% | 48 (47%) | 62 (55%) | 73 (46%) | 40 (41%) |
| [18], our study), in Italy (Pozio [24]) and | Grade 2 | 13 (22%) | 14% | 28 (28%) | 24 (21%) | 50 (31%) | 38 (30%) |
| in France (Audebert | Grade 3 | 12 (20%) | 10% | 5 (5%) | 14 (12%) | 23 (14%) | 10 (10%) |
| L • 1/• | Deaths | 8 (13%) | 3 (1%) | 1* (1%) | 0 | 0 | 1*(1%) |

The incidence of snakebite, 3/100000 in our series, is identical to that reported in France, Sweden, Finland, and North America [6]. Comparatively, the incidence seems much higher in Africa and Asia, for example in Nepal 1'162/100000 [31]. However, as already mentioned, precise and reliable data are very difficult to obtain.

The circumstances of accidents are typical: bite on the hand or forearm when handling or touching the viper (mostly in children), bite at the foot or ankle when treading on the snake (more frequent in the adults). A peculiarity in our series is the higher risk for people working in vineyards (Vipera aspis does not climb vines but lives around the vineyard in typical rocky and sunny biotopes).

The clinical presentation and the severity of viper bites have not changed during the last 100 years, in Switzerland as in France, as shown in table 4. The mortality was high in 1892 [10] but has been effectively null over many decades. As noted in other studies [15, 17], snakebite has more severe consequences in small children, probably because of the higher dose of venom to weight ratio.

The symptoms and signs of viper bite were well described, with their timing, by Jackson in his personal observation [11]): pain, local oedematous inflammation, and, after a delay of several hours, oedema of the limb, are characteristic for minimal or moderate envenomation. The grading proposed by Audebert in 1992 [1], now universally adopted, permits a clear distinction between moderate and severe envenomation, the only clinical situation that has to be treated. The grading correlates well with the dosage of venom (ELISA) in the blood [1,3], of whose practical usefulness we have no experience. Often patients pass from grade 1 to grade 2, and, rarely, with delay to grade 3; hospital admission for surveillance is therefore indicated.

The clinical presentation of severe envenomation (grade 3), rarely discussed in the literature, is varied, as exemplified by our three most impressive cases. Three forms can be distinguished, due to different pathophysiological mechanisms: 1) shock, general symptoms and extensive oedema, due to the direct effect of venom proteins (case 1); 2) anaphylactic shock, due to a second bite, with disseminated coagulopathy and massive haemorrhage (case 2), 3) envenomation complicated by allergic manifestations (asthma, laryngeal or facial oedema, etc.) as illustrated by case 3.

Allergic symptoms are seldom after viper bite, especially in patients known for hypersensitivity to hymenoptera. Reimers et al. have demonstrated in 8 patients specific IgE against venom of snake and hymenoptera [27].

Blood abnormalities were rare in our patients. Anaemia was mainly due to blood loss in the swollen limb and we found no signs of haemolysis in any patient. Thrombocytopenia [21, 29] is of two types: 1) benign, often present at the admission, reversible, probably due to aggregation of platelets by venom proteins; 2) severe, accompanying disseminated coagulopathy, with abnormal values of PT, PTT and fibrinogen (case 3).

Other complications of snakebite due to coagulation disorder (thromboses, infarcts, haemorrhages, etc.) are reported in the literature, but mostly from Asia (20), America [5, 9, 32] and Africa. To be mentioned is also the renal insufficiency, found only in one patient here (case 1), and totally reversible.

In our series, we did not observe any signs of neurotoxicity. Are the neurological problems (ocular paralysis, dysphonia, etc.), encountered in rare cases of severe envenomation in Italy [4, 24, 26] and in France [8, 35], due to a different venom composition?

The treatment of patients after snakebite has been controversial for decades [7-9,18]. The benign natural history of the great majority of bites by European vipers has accounted in the past for many treatments, sometimes bizarre, whether in the field or in hospital. Today the attitude is simple and clear: screen for and treat only severe envenomation. As demonstrated in this series, this condition is rare, but potentially fatal.

No first aid measures, including tourniquet and suction, have been shown to be useful [6, 8, 9]. In rare situations, when no medical assistance is available, suction can be attempted, without harm, but without scientific evidence. As with all other authors, we recommend immobilisation of the limb (also not proven), rest and transport as soon as possible to a primary care institution.

All patients must be observed for 3 hours, even those with grade 0, because evolution with delay to higher grade is always possible [6, 12]. For grades 1 and 2, hospital admission is generally considered preferable. Children deserve special attention [15, 17], for at least 24 hours, because typical signs are sometimes lacking, the evolution erratic and, as exemplified by the 2 year-old boy in our study, potentially fatal.

Simple observation is usually adequate for mild and moderate envenomation (grade 1 and 2). Analgesics are sometimes given. Administration of antibiotics to prevent infection, frequently mentioned in the literature but rarely applied to our population, is not evidence-based. Corticosteroids and adrenaline are very useful in cases with allergic reactions (asthma, Quincke's oedema, etc.). Even in patients with a swollen limb, heparin has no proven efficacy, except in the very rare cases (0 in our study) of true thrombophlebitis [5].

In case of severe envenomation (grade 3), patients should be admitted to an intensive care unit and immediately treated with intravenous fluids (sometimes abundant), and with antivenom [7–9, 22, 23, 25]. "Serum antivenins" had a bad reputation in the past, because they caused many complications and several deaths from anaphylaxis especially in cases of repeated administration. In Switzerland, as opposed to Italy [24], use of antivenom was strongly advised against, except in desperate situations. This therapeutic attitude has changed in 1995 after the dramatic story of our first case. Viperfav® and Viperatab®, containing purified F(ab)2 fragments from equine serum immunised with venom of three European vipers (aspis, berus and ammodytes) is now available in our

hospitals. This antivenom preparation must be administered intravenously, in a hospital emergency room with experience in resuscitation (shock is theoretically possible because of the equine provenance). Sometimes, repeated injections are necessary. Skin testing is recommended, but has no proven predictive value [7]. Antivenom is indicated in all cases of grade 3, and in some cases of grade 2 with persistent hypotension, impending coagulopathy, or severe thrombocytopenia [8]. These recommendations are similar to the "criteria of Stockholm" defined by Persson et al. [23]. In our series, antivenom therapy, although rarely used, was very well tolerated. To our knowledge, there is no mention in the literature of adverse reactions with this type of antivenom, an expensive but life-saving preparation [7, 8, 22].

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Correspondance: Dr Jacques Petite Médecin-chef Service de Médecine Hôpital Régional CH-1920 Martigny j.petite@mycable.ch

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