Clinical Toxicology (2011) **49**, 13–20

ISSN 1556-3650 print/ISSN 1556-9519 online
DOI: 10.3109/15563650.2010.550049

informa
healthcare

REVIEW

Clinical picture of envenoming with the Meadow Viper (*Vipera* (*Acridophaga*) *ursinii*)

LÁSZLÓ KRECSÁK[1], GÁBOR ZACHER[2], and TAMÁS MALINA[3]

[1]*Department of Systematic Zoology and Ecology, Eötvös Loránd University, Budapest 1117, Hungary*
[2]*Department of Emergency Medicine and Clinical Toxicology, Péterfy Sándor Street Hospital, Budapest, Hungary*
[3]*Medical Department, Lilly Hungary Ltd., Budapest 1075, Hungary*

Objective. The vipers in the *Vipera* (*Acridophaga*) *ursinii* complex are small-sized insectivorous snakes found in parts of central and southern Europe. Subspecies include *Vipera ursinii ursinii*, *Vipera ursinii moldavica*, *Vipera ursinii macrops*, *Vipera ursinii rakosiensis*, and *Vipera ursinii graeca* and are commonly known as the meadow vipers. These are the least known European *Vipera* from a clinical point of view. *Methods*. We identified cases of *V. ursinii* envenomations through three methods, including literature search in PubMed, ISI web of Knowldge, JSTOR, Biological Abstracts, Zoological Record, using the various combination of the following terms: snakebite, envenoming, bite, venom, ursinii, meadow viper, steppe viper (in English, French, Italian, Hungarian, Croatian, Serbian, Romanian), review of paper-based medical case records of hospitals in Hungary (four) and Romania (one) covering the 1970–July 2010 period, and personal communications of professional and amateur herpetologists studying *V. ursinii* and snake-handlers bitten by these snakes. *Results*. We identified 64 cases from subspecies: *V. u. ursinii* (14), *V. u. moldavica* (8), *V. u. macrops* (5), and *V. u. rakosiensis* (37). Forty-five bites were collected from the literature, 5 from hospitals, 10 cases were communicated by seven herpetologists and four cases by two snake keepers. Bites were mostly asymptomatic. Forty-five envenomings (70%) resulted in mild and moderate local symptoms, involving pain with low-intensity, pruritus, numbness, swelling with or without erythema and/or local hematoma. Bullae (n = 3, 5%), mild superficial necrosis (n = 4, 6%), cellulitis (n = 1, 2%), and moderately extended edema (n = 8, 13%) of the bitten extremity rarely develop. Massive limb edema was recorded in eight (13%) cases. The most common systemic symptoms were dizziness caused by transient hypotension and tachycardia. Gastrointestinal disorders (i.e. nausea, vomiting) were rare (n = 2, 3%) compared to other *Vipera*, and probably triggered only by anxiety. Symptomatic and supportive therapy was applied in the relatively severe envenomings and antivenom therapy in six cases. Complete recovery ranged from 12 h to 2 weeks. Moderate and severe envenomings required significantly longer recovery. Application of first aid was associated with significantly longer recovery times. Neither the age (i.e. juvenile or adult) of the culprit specimen, nor the anatomical location of the bite determined the severity of symptoms. *Conclusion*. Professional and amateur herpetologists, and snake keepers are mainly at risk. Most *V. ursinii* bites do not require first aid or medical intervention, since only local symptoms develop and resolve spontaneously. The rare hospitalized cases require symptomatic and supportive treatment only. Antivenom therapy is not indicated.

Keywords Snakebite; Envenoming; Limited swelling

Introduction

The small-sized insectivorous meadow vipers of the *Vipera* (*Acridophaga*) *ursinii* complex are the most threatened snake species in Europe,[1] with a relict post-glacial distribution, occurring as a series of small isolated populations in limited areas of southern and central Europe.[1,2] At present five subspecies are recognized: *Vipera ursinii ursinii* in SE France and C Italy; *Vipera ursinii macrops* in alpine areas of Croatia, Bosnia-Herzegovina, Serbia, Montenegro, Former Yugoslavian Republic of Macedonia and N Albania; *Vipera ursinii graeca* in S Albania and N Greece; *Vipera ursinii rakosiensis* in C and NW Hungary and C Romania, and *Vipera ursinii moldavica* in E Romania (Moldavia and the Danube-delta) (Fig. 1, Supplementary Fig. 9).[1–3]

The clinical and toxicological reports on envenomings by *V. ursinii* are the scarcest among the Palaearctic *Vipera*. Literature reports have dealt with individual cases, or discussed a single subspecies only.[4–7] These vipers generally exhibit a calm and diffident behavior, being reclusive and reluctant to bite, mostly hissing only when handled or touched,[1,6] which decreases the risk of a potential bite. Furthermore, their fangs are the shortest among the European *Vipera* (i.e. *V. u. macrops*: 2–2.5 mm;

Received 22 September 2010; accepted 17 December 2010.

Address correspondence to László Krecsák, Department of Systematic Zoology and Ecology, Eötvös Loránd University, Pázmány P. s 1/C, Budapest 1117, Hungary.
E-mail: lkrecsak@gmail.com

Fig. 1. Distribution of the *Vipera* (*Acridophaga*) *ursinii* in Europe.

V. u. rakosiensis: max 3 mm; *Vipera berus*: 4–6 mm; *Vipera ammodytes*: 8–12 mm),[8,9] consequently they cannot penetrate footwear or trousers. The general opinion and experience is that these taxa are of no medical significance, and their bites result in minor and local symptoms only.[10] Specific antivenom is not manufactured against their venom, only certain equine-derived polyvalent antivenoms, which are paraspecific for *V. ursinii* venom, are claimed to be suitable for therapeutic use (i.e. Antiviperine Sera®, National Center of Infectious and Parasitic Diseases, Sofia, Bulgaria; the European Viper Venom Antiserum®, Imunoloski Zavod, Rockefellerova, Zagreb, Croatia; Siero Antiofidico tetravalente Sclavo®, Instituto Sieroterapico Vaccinogeno Toscano ''Sclavo'', Sienna, Italy, although not available in holding centres).[11] Historical reports[12,13] documented the partial suitability of certain, presently not manufactured, antivenoms (i.e. Serum ER, Institute Pasteur, Paris, France; Serum gegen die Biss europäischer Vipern, Staatliches Serotherapeutisches Institut, Vienna, Austria; Ammodytes-Serum, Behringwerke, Marburg, Germany) against *V. u. rakosiensis*.

Contradictory speculations exist about the potency and toxicity of *V. ursinii* venom, either being considered weak, capable of causing mild local symptoms only,[1,5,6,10] or potent and capable of causing severe symptoms, and fatality in all age groups.[8,12] The venom of *V. u. ursinii* was reported to basically affect the cellular elements of the blood and slightly destroying the tissues.[1,14] Hemorrhagic activity, without myotoxic properties of the *V. u. ursinii* venom have been documented by *in vitro* studies,[15] and historical reports mention *V. u. rakosiensis* as having predominantly hemolytic and antihemostatic activities.[16] The venom glands of *V. u. ursinii* have the genes for Ammodytin I1B and I2D, two forms of phospholipase A_2 with indirect effects on hemolysis and capillary permeability.[17,18]

Our aim was to gather all the available information concerning envenomings by *V. ursinii* in Europe and analyze the reported local and systemic symptoms in humans.

Methods

Our clinical data are based on: (i) records from the literature, collected by searching PubMed, ISI web of Knowldge, JSTOR, Biological Abstracts, Zoological Record, using various combinations of the following terms: snakebite, envenoming, bite, venom, ursinii, meadow viper, steppe viper (in English, French, Italian, Hungarian, Croatian, Serbian, Romanian); (ii) paper based medical case records covering the 1970-July 2010 period, from the Emergency and Clinical Toxicology Wards of four Hungarian hospitals (i.e. Péterfi Sándor street Hospital, Budapest; Semmelweis Medical University, Budapest; Kecskemét County Hospital, Kecskemét and Municipal Hospital of Kiskunfélegyháza, Kiskunfélegyháza) and one Romanian hospital (Centre for Emergency Medicine, Braşov); (iii) personal communications of professional and amateur herpetologists (hereinafter herpetologists) and snake keepers bitten by these snakes. We have interviewed all herpetologists presently involved in *V. ursinii* research. Additionally employees of national parks within the Hungarian distribution range of *V. u. rakosiensis* and locals were interviewed. Members of the Hungarian meadow vipers conservation project (LIFE07 NAT/H/000322) provided further assistance by interviewing locals during public forums held in settlements located in the vicinity of viper habitats.

V. ursinii is the single native venomous snake in the areas from which our data come. Data were recorded on patient demography, activity at the time of accident, anatomical location of the bite, signs and symptoms with laboratory findings, first aid methods, and hospital treatment (e.g. administered antivenom, supportive- and ancillary treatment).

Envenomings were clustered into four severity groups by cumulating the symptoms in each case: (1) Minor local symptoms only, (2) Minor local symptoms with transient and mild systemic symptoms, (3) Moderate to severe local symptoms without systemic symptoms, (4) Moderate to severe local symptoms with systemic symptoms. Statistical analysis was performed using the grouped data.

Data analysis was performed using the SPSS 17.0 for Windows (SPSS Inc.) software, by means of the Kruskal–Wallis test and Mann–Whitney *U* test.

Results

Demographic data and severity of envenomings

Data of 64 envenomings were reviewed: 14 by *V. u. ursinii*, eight by *V. u. moldavica*, five by *V. u. macrops*, and 37 by *V. u. rakosiensis*. Forty-five bites were collected from the literature, five from hospitals, 10 cases were communicated by seven herpetologists and four cases by two snake keepers. Accidents were significantly more common during the summer months (June, July, August) (n = 27; 42%) than autumn (September, October, November) or spring (March, April, May) (n = 12 in both seasons; 19%) (13 cases unavailable data). The earliest incident occurred in April, the

latest in November. Only 11 victims (17%) were laymen, all others were amateur keepers, or professionals. Most patients were males (n = 59; 92%), only five (8%) were female. Age of the victims ranged from 6 to 61 years, and only three victims (5%) were children (aged below 16) (8 cases age unavailable). The location of the bites was as follows: 44 on the fingers (69%), 2 on the palm (3%), 7 on the hand (11%), one on the forearm (2%), 3 on the ankle (5%), 2 on the dorsum of the foot (3%), and 2 on the shin (3%) (three cases not documented). The distribution of the anatomical location of the bites in the four severity groups is itemized in Table 1. The comparison of anatomical location of the bites and the severity of the envenomings (grouped symptoms) revealed no significant difference between the groups (Kruskal–Wallis test; $\chi^2 = 7.930$, d.f. = 4, $p = 0.094$) (20 cases unavailable data). The severity of the envenoming was not influenced neither by the number of fangs that penetrated the extremity (Mann–Whitney *U* test; $z = -0.864$, $p = 0.419$) (8 cases unavailable data), nor by approximate age (i.e. juvenile or adult) of the culprit specimen (Mann–Whitney *U* test; $z = -0.762$, $p = 0.501$) (10 cases unavailable data). Similar results were obtained in the comparison of anatomical location of the bites, the number of fangs that penetrated the extremity, the approximate age of the culprit specimen and the severity of the envenomings, when the data collected from the historical literature, and the personal communications from non-professional sources were removed from the dataset analyzed (results of these analyses not shown).

Pre-hospital and hospital treatment

Thirty-five victims (55%) received first aid (including medicines) soon after the bite, as follows: pressure dressing (n = 3); local incision (n = 8); immediate squeezing of the wound after the bite or after local incision (n = 19); wound washing with $KMnO_4$ (n = 2) or H_2O_2 (n = 2); use of venom extractor (n = 3); suction with mouth (n = 5); local injection with LMW heparin (i.e. Lovenox® – enoxaparine and Calciparine® – heparin calcium, n = 3; Soludécadron® – dexamethasone i.m, n = 1; non-steroidal anti-inflammatory, Voltaren® – diclophenac, n = 3) (Table 2). Only nine patients (14%) required ambulance transport and treatment in Hungarian (eight) and Romanian (one) hospitals. Five hospitalized victims received supportive treatment only, and antibiotics, antihistamines, and intravenous fluid, and corticosteroids being in addition occasionally administrated. Although, the incidents and degree of envenomation did not warrant antivenom therapy, it was administered six times in cases of *V. u. rakosiensis* envenomings (Table 2): four times administered by a physician (European Viper Venom Antiserum in two cases 5 ml, once 2 × 10 ml; Serum ER once 10 ml) and twice self-administered by the victims (one ampoule of unknown antivenom). Four patients had received antivenom previously, three after bites by *V. ammodytes*, and one after a *V. berus* bite. Skin or conjunctival sensitivity tests were not performed in any of these cases. Late hypersensitivity reactions to antivenom that developed in two patients were general urticaria that lasted for 2 and 4 days, respectively.[19]

Complete recovery ranged from 12 h to 2 weeks (Table 2). Patients who received some kind of first aid recovered in a significantly longer time (days) than those who did not (Mann–Whitney *U* test; $z = -2.340$, $p = 0.018$) (20 cases unavailable data). Recovery time was 3.9 days (min. 0.5 day, max. 14 days) in patients who did not receive first aid, and 5.1 days (min. 0.5 day, max. 14 days) in those who did. The difference in severity between the groups (i.e. first aid, no first aid) was not significant (Mann–Whitney *U* test; $z = -1.075$, $p = 0.295$).

The Kruskal–Wallis test revealed a significant difference ($\chi^2 = 9.585$, d.f. = 3, $p = 0.022$) in the comparison of the envenomings grouped in severity classes and the recovery time (days). The data collected from the historical literature, and the personal communications from non-professional sources did not bias the above results, as shown by the analyses when these data were removed from the dataset and, which provided similar results (results of these analyses not showed).

Table 1. Anatomical location of the bites in the four severity groups.

	Number				
	I	II	III	IV	SUM
Finger	30	2	11	1	44
Palm	1		1		2
Hand	5		2		7
Forearm				1	1
Ankle	2			1	3
Dorsum of foot	1			1	2
Shin	1			1	2

I, Minor local symptoms only; II, Minor local symptoms with transient and mild systemic symptoms; III, Moderate to severe local symptoms without systemic symptoms; IV, Moderate to severe local symptoms with systemic symptoms.

Clinical features of the envenomings by different **V. ursinii** *subspecies in Europe*

Vipera ursinii ursinii

We have reviewed 14 accidents from France, reported in the literature.[5,6,20] All incidents occurred in the snake's natural habitat and involved all but one male, adult ''snake-handlers'', bitten during studying/photographing the snakes. Symptoms are itemized in Table 3, and shown in Supplementary Fig. 1. We should emphasize a case in which conjunctival edema developed 2 h post-bite on the left lower eyelid of a patient, which was attributed by the authors[6] to direct contact with the blood that pressed out from the fang marks. Although several victims were sensitive to snake venoms due to previous bites, systemic manifestations were not common.[6] All symptoms generally resolved within 1–2 days, although in four cases local pain

Table 2. Clinical profile of *V. ursinii* envenomings on European patients.

	Number (%)				
	Vuu	Vumo	Vum	Vur	Total
First aid and medication	6 (43)	1 (13)	3 (60)	25 (68)	35 (55)
Antivenom administration				6 (16)	6 (9)
Median time from bite to antivenom therapy				2 h 36 min (n = 5)	NA
Minor local symptoms only	12 (86)	5 (63)	3 (60)	23 (62)	43 (67)
Recovery time (days) in the above severity group: mean (min.-max)	4 (0.5–10)	2 (1–7)	2 (1–3)	4 (2–7)	3 (0.5–10)
Minor local symptoms with transient and mild systemic symptoms		1 (13)		1 (3)	2 (3)
Recovery time (days) in the above severity group: mean (min.-max)		7 (NA)		0.5 (NA)	4 (0.5–7)
Moderate to severe local symptoms without systemic symptoms	1 (7)	2 (25)	1 (20)	10 (27)	14 (22)
Recovery time (days) in the above severity group: mean (min.-max)	10 (NA)	11 (7–14)	2 (NA)	7 (3–10)	7 (2–14)
Moderate to severe local symptoms with systemic symptoms	1 (7)		1 (20)	3* (8)	5 (8)
Recovery time (days) in the above severity group: mean (min.-max)	3 (NA)		14 (NA)	NA	9 (3–14)

Vuu, *V. u. ursinii* (n = 14); Vumo, *V. u. moldavica* (n = 8); Vum, *V. u. macrops* (n = 5); Vur, *V. u. rakosiensis* (n = 37); Total (n = 64); NA, not applicable.
*all victims deceased.

Table 3. Different local and systemic symptoms on patients envenomated by *V. ursinii*.

	Number (%)				
	Vuu	Vumo	Vum	Vur	Total
Local symptoms					
Prolonged bleeding from fang marks	1 (7)	2 (25)	1 (20)	15 (41)	19 (30)
Painless	7 (50)	1 (13)		6 (16)	14 (22)
Weak and moderate pain	4 (29)	7 (88)	4 (80)	28 (76)	43 (67)
Sharp pain	3 (21)		1 (20)	3 (8)	7 (11)
Pruritus		3 (38)	2 (40)	4 (11)	9 (14)
Numbness	5 (36)		1 (20)	4 (11)	10 (16)
Local swelling	8 (57)	4 (50)	1 (20)	16 (43)	29 (45)
Edema involving half of the bitten limb	6 (43)	2 (25)	2 (40)	13 (37)	23 (36)
Edema of the whole extremity		1 (13)	2 (40)	5 (14)	8 (13)
Local erythema and/or hemorrhage	7 (50)	5 (63)	2 (40)	22 (59)	36 (56)
Bullae		1 (13)		2 (5)	3 (5)
Superficial necrosis		1 (13)		3 (8)	4 (6)
Local arthralgia	1 (7)			8 (22)	9 (14)
Regional lymphopathy	3 (21)	1 (13)		9 (24)	13 (20)
Systemic symptoms					
Chloropsia			1 (20)		1 (2)
Breathing difficulties	1 (7)		1 (20)		2 (3)
Blurred vision		1 (13)			1 (2)
Auditory disturbances			1 (20)		1 (2)
Gastrointestinal symptoms		1 (13)	1 (20)		2 (3)
Hypotension		2 (25)	1 (20)	3 (8)	6 (9)
Tachycardia	1 (7)	2 (25)	1 (20)	3 (8)	7 (11)
Dizziness			1 (20)	3 (8)	6 (9)
Headache		1 (13)			1 (2)
Shock				3 (8)	3 (5)

Vuu, *V. u. ursinii* (n = 14); Vumo, *V. u. moldavica* (n = 8); Vum, *V. u. macrops* (n = 5); Vur, *V. u. rakosiensis* (n = 37); Total (n = 64).

and numbness persisted until day 7 (n = 1) and day 10 (n = 3). Recovery times of incidents of different severity are summarized in Table 2.

Vipera ursinii rakosiensis

Data on 37 envenomings were analyzed as follows: four incidents from Austria,[21–23] two caused by captive specimens in Germany,[19] 30 cases from Hungary (22 from the literature;[7,8,24–27] and eight new cases), and one unpublished case from 2007 from Transylvania (Romania). Twenty-six accidental bites occurred in a natural setting, nine in private homes, one at a university, and one in a museum. Only five bites occurred accidentally, the victims being bitten after they stepped on a specimen, or during agricultural work; all other incidents befell during some snake related activity (i.e. study, photographing, feeding). Signs and symptoms are listed in Table 3, and depicted in Supplementary Fig. 2–6. Systemic symptoms were rare even among cases exhibiting massive limb edema. The lone exception was a child who had dizziness and general weakness described in a report published in 1908.[21] Complete recovery ranged from one-half day to 10 days.

Only three fatalities caused by *V. u. rakosiensis* are known, all from Hungary. Detailed descriptions were not available in any of the cases, and the autopsy reports are lost (if ever issued), therefore a follow-up was impossible. The following supplementary data are available on these cases. *Case 1*: Adult male bitten by a viper on his ankle during ditch digging in 1908 in Hanság (NW Hungary) (only *V. u. rakosiensis* occurs in this area).[8] The bitten limb was edematous, tense and extensive suffusion was additionally observed.[8] The accident occurred at approximately 9:00 a.m. and the victim expired the next morning.[8] *Case 2*: Adult male bitten on the shin at Lébény in Hanság (NW Hungary) in 1911.[8] Only progressive edema of the entire limb was recorded and death supervened within 24 h.[8] *Case 3*: Street reported,[26] without further details, based on personal communication by M. Janisch, that a 6-year-old child died in Hungary. We could only find out that this accident happened in the late 1950s, in the area of Kiskunság (C Hungary). The exact geographical location is unknown. The boy was bitten on the dorsum of foot by an adult snake and died after 4 days.

Vipera ursinii moldavica

In 1937, Băcescu[28] reported that local pain and throbbing typically followed the bite of vipers in the Danube delta. We have collected data on eight bites, six incidents in nature and two caused by captive specimens. All bites occurred during snake handling, and affected upper extremities. Symptoms are itemized in Table 3, and shown in Supplementary Fig. 7. Complete recovery took from 1 to 14 days (Table 2).

One case worth highlighting: victim 21-year-old, healthy male with a history of two *V. u. moldavica* envenomings, bitten with two fangs in the distal phalanx of the left thumb during snake handling in the Danube-delta. No first aid was applied. Local pain immediately emerged, and dizziness appeared and lasted for 1.5 h. The wound was not bleeding. Blurriness was noted by the patient and his eyes were sanguineous. The normal vision recommenced only after 1 h. Erythemic freckles developed over the entire body surface, which resolved after 24 h, while the extensive edema diminished after 7 days. The patient complained of gout and tenderness of axial lymph nodes for 14 days. Bullae extended on the interphalangeal joint of the thumb, and the necrotized tissue was surgically removed in the hospital on day 14.

Vipera ursinii macrops

Data on five accidents were analyzed, four from Bosnia and Herzegovina (three from the literature[4,29–31] and an unpublished incident from Korita), and an additional new case from the Korab Mountains (Albania). All accidents happened in nature, during snake handling, and affected the upper extremity of adults. Symptoms are summarized in Table 3, and shown in Supplementary Fig. 8. Recovery took from 1 to 14 days (Table 2).

One case should be detailed: adult male victim, bitten on Lebršnik Mountain (Bosnia and Herzegovina) in 1913.[4,30] The snake bit with two fangs the index finger and weak pain emerged within a few minutes. Hematoma and numbness developed locally, the latter in both hands. The bitten hand was livid, and the whole extremity became tense and tender. Within 3–4 min shivering, intensive dizziness with auditory disturbances (tinnitus) developed. The envenoming progressed, increased heart rate and breathing difficulties with general weakness manifested. The patient described the weakness as paralysis-like but he was conscious. The patient developed profused nausea with vomiting and abdominal cramps, and experienced a remarkable symptom, binocular chloropsia (saw everything in green[4,30]). The edema extended to the whole arm within 3 h. Systemic symptoms gradually disappeared within 20 h while the edema resolved completely on day 14.

Laboratory findings

Laboratory analysis data were available for three *V. u. rakosiensis* envenomings only, and no large deviations were reported. A slightly elevated CPK (193 U/l; normal 38–174 U/l) and bilirubin (23 μmol/l; normal range 2–17 μmol/l), reduced lymphocytes (0.21; normal range 0.25–0.33), and increased leukocyte count (18.6 G/l; normal 4.5–11 G/l) were reported.

Discussion

Meadow vipers are medically less significant than other European *Vipera* sp., since the majority of envenomings generally display mild and negligible local symptoms only, which spontaneously resolve, without any medical treatment in 48–72 h. Mostly herpetologists are victims of *V. ursinii* bites, while laymen encounter these snakes very rarely due to the restricted distribution and sedentary life-style of meadow vipers.

Characteristic local symptoms in *V. ursinii* envenomings include pain and swelling, the latter centered at the fang marks only. The initial bite-induced pain is negligible, while

the secondary edema-induced pain is more severe but lower compared to *V. berus* envenomings. Hemorrhage and/or redness of the skin often stagnate locally. The tenderness and pain of the regional lymph nodes is occasionally associated with the early phase of *V. ursinii* envenomings. Numbness, bullae and necrosis development around the fang marks was rare, the latter always being superficial and of milder severity compared to that caused by other *Vipera* sp. (e.g. *V. ammodytes*).[32] The use of some form of venom extractor and local incision may have contributed to the development of local necrosis. Massive edema involving the entire extremity is rare in *V. ursinii* envenomings, and has been reported in *V. u. rakosiensis* envenomings only,[8,24,33] and its development appears to not be associated with systemic symptoms.

Contradictory statements have been published pertaining to meadow vipers' venom, being either considered the weakest,[1,34] or as dangerous to humans as that of other European *Vipera*.[8] Our findings corroborate the first view as envenomings rarely caused systemic toxicity. This may be associated with these viper's diet (almost exclusively orthoptera)[1,2,6] and their venom yield, which is the lowest within *Vipera* sp. (1–4 mg in dry weight).[1,35] Nevertheless, mild and transient systemic symptoms (mainly hypotension with dizziness) may occasionally occur, and their decrudescence often befell spontaneously within 20–24 h. Recurrent systemic symptoms could not be documented. Arrhythmias are not characteristic to *V. ursinii* envenomings but sinus tachycardia may occasionally develop. Tachycardia was recorded in the literature as well[6] in a case inflicted by *V. u. ursinii* and was attributed to anxiety and high fever (40°C). Opposite to envenomings by other *Vipera*, based on our data further systemic symptoms do not occur. Nausea with/without vomiting, perspiration, breathing difficulties, and paleness were additionally reported in the literature,[21,30] however, these symptoms were triggered by psychological distress, that often concomitantly appears in snake-bitten patients.[36] Typical anaphylactoid symptoms (e.g. laryngeal edema, bronchoconstriction) that may manifest in other viper envenomings (i.e. *V. berus*),[37] did not occur, not even in hypersensitive persons, with allergic background or a history of snakebites.

The presence of venom neurotoxins in certain *V. ursinii* populations was suggested in the literature but without further proof,[34,38] and symptoms (i.e. wheezing, breathing difficulties, and paresis of the bitten limb) were incorrectly defined as neurotoxic in *V. u. macrops* envenomings.[21,30] Paresthesia was also documented[39,40] in *V. u. ursinii* envenomings, which is considered to be a neurotoxin-induced symptom in other viperid species (e.g. *V. aspis*, *V. ammodytes*).[17,41] The genes of a PLA_2 with neurotoxic activity (i.e. Vaspin), are presumed to be present in all European *Vipera* [18] although this has not been proven with *V. ursinii* yet. The genome composition of *V. u. ursinii* (Vaucluse, SE France) contains the genes of Vaspin isoforms but they were not detected in the venom gland.[17] The transient binocular chloropsia reported in a *V. u. macrops* bite,[30] is an unusual symptom that has never been recorded yet in *Vipera* envenomings, although the historical report may be biased. This abnormality may have peripheral neurological origin as well, being documented in other poisonings (e.g. consumption of *Digitalis purpurea* leaf), in which ocular neurotoxicity can also develop.[42,43] In the present case, its development was likely connected to the patient's expressed psychological reactions (anxiety, panic), which may easily enrich and augment the manifestation and severity of the early clinical features of envenoming.[36] We deem that the blurriness following a bite of *V. u. moldavica* was rather caused by a capillary and/or cornea damage, although blurred vision may develop in neurotoxic snakebites.[44]

In symptomatic patients envenomed by *V. ursinii* 8–12 h of monitoring is likely sufficient, since the development of severe symptoms are rarely delayed, and recurrent and long-term consequences have not been reported. Therefore, the required use of antivenom therapy is highly improbable. Only symptomatic treatment may be required. Corticosteroid therapy should not be applied, as already recommended,[45] because of the infrequent manifestation of extensive edema and complete lack of severe anaphylactoid manifestations. The administration of non-sedating antihistamines and calcium may be beneficial, while the administration of analgesics may rarely be needed only, since the edema-induced pain is of low intensity. Antiemetics may very rarely be needed.

Fatality caused by *V. ursinii* envenoming is very rare. The authenticity of the fatal cases reviewed cannot be critically evaluated based on limited available records and documentation. If the victims were hospitalized, their death was probably the result of the inadequate therapy and malpractice in snakebites in Hungary, which in the early 1900s included several, today contra-indicated, directly harmful and injurious therapeutic methods. Nowadays, as a result of the advances in snakebite treatment and medical care the probability of a fatal *V. ursinii* envenoming is remote.

Conclusions

The risk of a *V. ursinii* bite for layman is minimal based on the small number of bites over a long period of time, which clearly reflects the rarity of these taxa in the wild. The infrequent envenomings can additionally be attributed to the non-aggressive behavior and secretive lifestyle of the snake. Herpetologists are frequently the victims of envenomings, and incidents occur because of carelessness during snake handling. Envenomings are characterized by transient, mild systemic symptoms, which require symptomatic and supportive treatment only, with antivenom therapy not indicated because of the lack of significant systemic toxicity, and the majority of local complications being minor. In certain cases (mainly in *V. u. rakosiensis* envenomings and occasionally in *V. u. modavica*) local swelling may progress to massive limb edema but systemic symptoms can basically not be expected. The peculiarity of the *ursinii* species group is unique within the Palaearctic *Vipera*. Today, fatality caused by *V. ursinii* envenoming can be excluded. Neither

the size of the culprit specimen nor the location of the bite was associated with the severity of symptoms.

Acknowledgments

We thank the hospitals, researchers and snake-keepers, who provided data on their accidents, and Dr. Oscar Arribas (Barcelona, Spain), Tamás Péchy (Budapest, Hungary), Bálint Halpern (Budapest, Hungary), AB, and Nikola Rahme (Budapest, Hungary) for the photographs. Special thanks to Alexander Westerström (Stockholm, Sweden) for providing photographs and data on *V. u. macrops* envenomings and for translating Swedish materials. Bálint Halpern (Budapest, Hungary) is acknowledged for drawing the map, and Tamás Tóth (Budapest, Hungary) for providing certain historical references. Prof. Dr. Deitrich Mebs (University of Frankfurt, Germany) and Prof. Dr. David A. Warrell (University of Oxford, UK) are acknowledged for their useful comments and critics.

References

1. Dely OG, Joger U. Vipera (Pelias) ursinii Bonaparte, 1835–Wiesenotter. In: Joger U, Stümpel N, eds. Handbuch der Reptilien und Amphibien Europas, 3/IIB Schlangen (Serpentes) III Viperidae. Wiesbaden: Aula Verlag; 2005. pp. 374–414.
2. Nilson G, Andrén C. The Meadow and Steppe Vipers of Europe and Asia – The Vipera (Acridophaga) ursinii complex. Acta Zool Acad Sci Hung 2001; 47:87–267.
3. Krecsák L, Zamfirescu Şt. Vipera (Acridophaga) ursinii in Romania: historical and present distribution. North-West J Zool 2008; 4:339–359.
4. Bolkay StJ, Ćurčić V. O našim zmijama otrovnicama. Glasn zemalj Mus Bosni Herceg 1920; 32:155–206.
5. Orsini P, de Haro L, Arribas OJ, Baron JP, Ferrières R, Labeyrie A, Mossot M. Envenomation par vipère d'Orsini: 8 observations. Presse Med 1998; 27:1277–1278.
6. Orsini P, Arriba O, Baron J-P, Cheylan M, Cluchier A, Ferrière R, et al. Envenimations par la Vipère d'Orsini *Vipera ursinii* (Bonaparte, 1835). Bull Soc Herp Fr 2007; 124:49–62.
7. Malina T, Krecsák L, Korsós Z, Takács Z. Snakebites in Hungary – epidemiological and clinical aspects over the past 36 years. Toxicon 2008; 51:943–951.
8. Méhely L. A hazai viperákról. Term Tud Közlöny 1912; 44:1–48.
9. Biella HJ. Die Sandotter Vipera ammodytes. Wittenberg Lutherstadt: A. Ziemsen Verlag; 1983.
10. de Haro L, Glaizal M, Tichadou L, Blanc-Brisset I, Hayek-Lanthois M. Asp Viper (Vipera aspis) envenomation: Experience of the Marseille Poison Centre from 1996–2008. Toxins 2009; 1:100–112.
11. Chippaux J-P, Goyffon M. Production and use of snake antivenin. In: Tu AT, ed. Handbook of Natural Toxins: 5. Reptile venoms and toxins. New York: Marcel Dekker; 1991. pp. 529–555.
12. Otto R. Untersuchungen über die Toxine europäischer Vipereinen. Z Hyg Infekt-Kr 1929; 110:82–92.
13. Schlossberger H, Bieling R, Demnitz A. Untersuchungen über Antitoxine gegen Schlangengifte und die Herstellung eines Heilserums gegen die Gifte der europäischen und mediterranen Ottern. In: Bieling R, Demnitz A, Schaumann O, Schlossberger H, v Schuckman W, Schwarz E, eds. Die europäischen und mediterranen Ottern und ihre Gifte. Grundlagen zur Darstellung eines wirksamen Schlangenserums. Behringwerk-Mitteilungen. Marburg-Lahn: Selbstverlag der Behringwerke Marburg-Lahn; 1936. pp. 111–158.
14. Saint Girons H, Detrait J. Étude électrophorétique des venins de Viperinae (Serpentes) du genre Vipera: variations des proteinogrammes et implications phylogénetiques. Bull Soc zool Fr 1992; 117:399–412.
15. Mebs D, Langelüddeke T. European viper venoms: haemorrhagic and myotoxic activities. Toxicon 1992; 30:1303–1306.
16. Reuss FAT. Observations on four species of European Toxicophidia. C R 12 Congr Int Zool – Lisabonne 1937; 1787–1804.
17. Ferquel E, Haro de L, Jan V, Guillemin I, Jourdain S, Teynié A, et al. Reappraisal of Vipera aspis venom neurotoxicity. PLoS ONE 2007; 11:1–18.
18. Jan VM., Guillemin, I., Robbe-Vincent, A., Choumet, V. Phospholipase A2 diversity and polymorphism in European viper venoms: Paradoxical molecular evolution in Viperinae. Toxicon 2007; 50:1140–1161.
19. Schottler WHA. Notes on the venom of *Vipera ursinii* (Bonaparte). Bull Antiven Inst Am 1932; 5:80–81.
20. Arribas OJ. Un diseño atípico en *Vipera ursinii* y datos sobre los efectos de su mordedura. Bol Asoc Herpetol Esp 1997; 8:30–31.
21. Knauer F. Die Ursinishe Viper (*Vipera ursinii* Bonaparte). Natur und Haus, Berlin 1908; 16:338–341.
22. Werner F. A harmless viper (*Vipera ursinii* Bonaparte). Bull Antiven Inst Am 1929; 3:77–79.
23. Psenner H. Die Vipern Großdeutschlands. Ein Buch vom Leben und Treiben unserer heimischen Giftschlangen. Braunschweig: Gustav Wenzel & Sohn; 1939.
24. Prochnov J. Kígyómarás esete. Eljárás mérgezett sebeknél-marásoknál. Gyógyászat 1887; 40:499–499.
25. Bókai Á. Gyakorlatilag fontosabb mérgezések. Belgyógyászat Kézikönyve. Budapest: Dobrovszky és Franke kiadása; 1896.
26. Street D. The reptiles of Northern and Central Europe. London: B.T. Batsford; 1979.
27. Takács Z, Janisch M, Korsós Z. Contribution to the epidemiological and clinical aspects of snake bites in Hungary. Toxicon 1987; 25:376.
28. Băcescu M. Cîteva interesante date herpetologice pentru fauna Romîniei şi unele propuneri de rezervaţii naturale în legătură cu ele. Rev Ştiinţ ''V. Adamachi'' 1937; 23:122–128.
29. Gugler W. Herpetologische Skizzen aus Südistrien, Dalmatien, Montenegro und der Herzegovina. Bl Aqu Terr Kd 1903; 10:132–134, 11:143–46.
30. Fejérváry G. A Vipera macrops Méh. biológiájához. A Természet 1915; 11:145–147.
31. Westrin LG. Innan mörket. Snoken 2003; 33:3–20.
32. Marinov I, Atanasov VN, Stankova E, Duhalov D, Petrova S, Hubenova A. Severe coagulopathy after Vipera ammodytes ammodytes snakebite in Bulgaria: a case report. Toxicon 2010; 56:1066–1069.
33. Péchy T. The Hungarian meadow viper (*Vipera ursinii rakosiensis*, Méhely, 1893). In: Halpern B, ed. Studies on the conservation of the Hungarian meadow viper. Budapest: Duna-Ipoly Nemzeti Park Igazgatóság; 2007. pp. 23–29.
34. Kramer E. Variation, Sexualdimorphismus, Wachstum und Taxionomie von *Vipera ursinii* (Bonaparte, 1835) und Vipera kaznakovi Nikolskij, 1909. Rev Suisse Zool 1961; 68:627–725.
35. Ernst CH, Zug GR. Snakes in question: The Smithsonian answer book. Washington DC: Smithsonian Institution Press; 1996.
36. White J. Poisonous and venomous animals–The physician's view. In: Meier J, White J, eds. Handbook of clinical toxicology of animal venoms and poisons. Boca Raton, FL: CRC Press; 1995. pp 9–26.
37. Warrell DA. Treatment of bites by adders and exotic venomous snakes. BMJ 2005; 331:1244–1247.
38. Reuss T. Über eine neurotoxische Otterngruppe Europas, Mesocoronis 1927, und über ihre Stellung unter den Solenoglyphen der Welt. Glasn zemalj Mus Bosni Herceg 1930; 42:57–114.
39. Bowquier JJ, Guibert J, Dupont CL, Umdenstock R. Les piqûres de Vipère chez l'enfant. Etude de 43 cas. Arch Fr Pediatr 1974; 31:285.
40. Persson H. Clinical toxicology of snakebite in Europe. In: Meier J., White J. eds. Handbook of clinical toxicology of animal venoms and poisons. Boca Raton, FL: CRC Press; 1995. pp. 413–432.
41. Logonder U, Križaj I, Edward GR, Harris JB. Neurotoxicity of Ammodytoxin A in the envenoming bites of Vipera ammodytes ammodytes. J Neuropathol Exp Neurol 2008; 10:1011–1019.

42. Pinckers A, Cruysberg JRM, Liem TA. Chromatopsia. Documenta Ophthalmologica 1989; 72:385–390.
43. Lin C-C, Yang C-C, Phua D-H, Deng J-F, Lu L-H. An outbreak of Foxglove Leaf poisoning. J Chin Med Assoc 2010; 2:97–100.
44. Warrell DA. Injuries, envenoming, poisoning, and allergic reactions caused by animals. In: Warrell DA, Cox TM, Firth JD, Benz EJ, eds. The oxford textbook of medicine, 4th ed. Oxford: Oxford University Press; 2003. pp 923–951.
45. de Haro L, Jouglard J. Dictionnaire de l'été 1997: Morsure de vipère en France métropolitaine. Morsure et p piqûresd'arthropodes terrestres en France métropolitaine. Rev Prat Méd Gén 1997; 11:35–40.

Supplementary material available online

Figures showing the symptoms of envenoming with the Meadow Viper (*Vipera* (*Acridophaga*) *ursinii*)

Supplementary material for <*L. Krecsák et al.*>. <Clinical picture of envenoming with the Meadow Viper (***Vipera (Acridophaga) ursinii***)>, <Clinical Toxicology>, <2010>

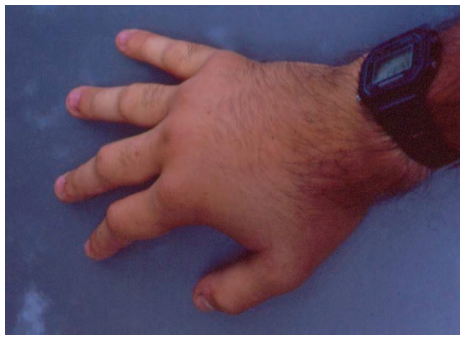

Figure 1. Edema involving the whole hand and the fingers, 3 h after a *V. u. ursinii* bite on the right thumb. (Photograph by Dr. Oscar Arribas)

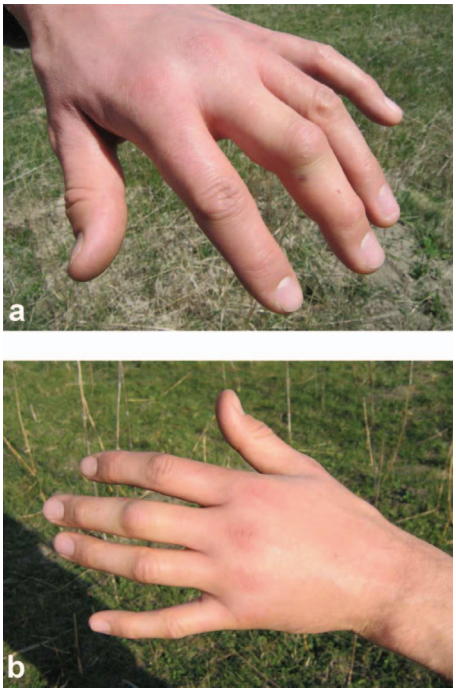

Figure 2. Local signs of a *V. u. rakosiensis* bite in Transylvania (Romania): a) local swelling and local hemorrhage on the left middle finger 1h post-bite; b) edema extended on the left hand 5h hours post-bite. (Photographs by Bálint Halpern.)

Figure 3. Moderate edema of the foot with dual fang marks following a *V.u. rakosiensis* bite in Hungary. (Photograph by Dr. Gábor Zacher.)

Figure 4. Mild erythema on the shin following a *V.u. rakosiensis* bite in Hungary. (Photograph by Bálint Halpern.)

Figure 5. Local minor erythema around the fang marks with local swelling of the ankle following a *V.u. rakosiensis* bite in Hungary. (Photograph by Dr. Gábor Zacher.)

Figure 6. Edema and local hematoma following a *V.u. rakosiensis* bite in Hungary. (Photograph by Tamás Péchy.)

Figure 7. Bullae, seven days after a bite of *V.u. moldavica* from the Danube-delta on the distal phalange of the left thumb. (Photograph by AB.)

Figure 8. Puncture of fang marks of *V.u. macrops* on the left ring finger after the resolving of local swelling (22 h post bite) (Photograph by Alexander Westerström.)

Figure 9. Hungarian meadow viper (*Vipera ursinii rakosiensis*) from Hungary. (Photograph by Rahme Nikola.)