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Exotic venomous snakebites in Switzerland reported to the National Poisons Information Centre over 22 years

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Summary

OBJECTIVE: The private keeping of exotic venomous snakes is legally permitted in Switzerland. The aim of the present study was to characterise the epidemiological and clinical features of bites by exotic venomous snakes over a period of 22 years in Switzerland.

METHODS: We included all calls related to exotic snakebites recorded at the Swiss National Poisons Information Centre (Tox Info Suisse) from 1997 to 2018. Exclusion criteria comprised indigenous snakes, non-venomous exotic snakes such boas or pythons, clinical courses incompatible with a snakebite or calls from abroad. Follow-up information was graded according to the Poisoning Severity Score.

RESULTS: Within the study period, 1,364 calls related to snakebites were recorded at Tox Info Suisse; 148 (11%) cases were attributed to exotic venomous snakes and fulfilled the study criteria. A total of 112 (98%) of 114 patients with medical follow-up information exhibited sufficient causality between exposure and clinical effects. Only adult patients were affected. The median age was 40 years (range 16–71) and the male gender was predominant (n = 136, 92%). Viperidae were involved in 87 (78%) and Elapidae in 25 (22%) patients. Overall, the main affected body part was the hand (89 patients, 79%). In the majority of the patients the clinical course was mild (46, 41%) or moderate (40, 36%), in a lower proportion asymptomatic (6, 5%) or with severe symptoms (20, 18%). No fatalities were reported in the study period. Severe symptoms were observed after elapid bites in six patients (24%) and after viper bites in 14 patients (16%). Besides local effects, neurological disorders after elapid bites and haematological disorders after viper bites were most frequently reported. Antivenom was administered in 24% (27 patients: 18 Viperidae, 21% and 9 Elapidae, 36%; 5 patients (4%) required multiple doses), overall, with good resolution of symptoms.

CONCLUSION: Exotic snakebite is a rare occurrence in Switzerland but has led to medically relevant morbidity, sometimes requiring antivenom treatment. Over half of the envenomed patients required symptomatic or specific treatment. No fatalities or bites in children were reported.

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Introduction

The private keeping of venomous snakes is legally permitted in Switzerland. Although no definite numbers can be provided because of cantonal and not central reporting, an estimated 2000–10,000 specimens can be found in the homes of the aficionados [1], and many keepers own more than one snake. Because keepers in Switzerland are required to register their snakes, they usually know the Latin name of their pet [1]. Reptiles are reported to be the most popular exotic pets worldwide [2]. In the United States it is estimated that 1.5 to 2.0 million households own one or more pet reptiles. Snakes account for approximately 11% of the imported reptiles, with as many as 9% of those reptiles being venomous [3]. In a recent study, 1.1% of snake envenomation cases reported in the US between 2015 and 2018 concerned non-indigenous venomous snakes [4]. Another study found that one quarter of the snakebites reported in the UK between 2004 and 2010 resulted from non-indigenous snakes, but only 3% were attributed to venomous non-indigenous snakes [5]. Envenomation by exotic pets is an increasing concern in Europe, the USA and Asia, because physicians are often not used to treating patients after an exotic snakebite [3, 6–13]. In addition, the continuing worldwide antivenom shortage poses a further difficulty for specific treatment, since antivenom is the first-line therapy in patients with severe snakebites [2]. In the US Poisons Center Database 258 cases of exotic snake envenomation were reported between 2005 and 2011, involving at least 61 different exotic species [8]. Forty percent of those bites occurred in the keepers of the snakes. Another study recorded 18 non-indigenous snakebites over a period of 15 years, with symptoms ranging from mild local pain to ventilator-requiring respiratory paralysis [9]. The aim of our study was to characterise the epidemiologic and clinical features of bites by exotic venomous snakes in Switzerland over a period of 22 years.

Methods

Data collection

In Switzerland, nationwide (and complementary) consulting to the general public and doctors on poisonings and envenomation resulting from various toxins is provided by the Swiss National Poisons Information Centre, Tox Info Suisse. All calls recorded at this centre from January 1997 to December 2018 related to exotic snakebites in Switzerland were included. Basic demographic (age, sex, region) and clinical (type of caller, circumstance of exposure) data are systematically collected for all calls related to snake bites and standardised by a clinical toxicologist. For some cases there were several calls (i.e., first ambulance, then hospital, etc.), these calls were then aggregated into one case before analysis. Patients <16 years of age are toxicologically classified as children. Among patients in hospitals or medical practices for clinical care, the treating physician may provide a follow-up report. This additional information contains further details on the clinical findings, treatment course (i.e., use of antivenom), and clinical outcomes, which enables Tox Info Suisse to assess severity and causality in a standardised manner. Standards and quality measures comprise review of each case by a senior clinical toxicologist to ensure completeness and correctness of the entered data. Exceptional cases are discussed by an internal expert panel with clinical toxicologists and poison information specialists present, and discrepancies are resolved by consensus before being entered into the database. The Cantonal Ethics Commission of Zurich approved the use of National Poisons Information Centre patient data without specific informed consent of the patients due to the inherent nature of poisons centre data.

Eligibility criteria

Inclusion criteria for our retrospective study of exotic venomous snakebite were all cases with follow-up and identification of the snake by its keeper or a herpetologist. All except one snake were identified at least to the species level. Exclusion criteria were non-venomous exotic snakes such as boas and pythons, calls from countries other than Switzerland and calls from Swiss citizens bitten abroad. Follow-up was graded according to the Poison Severity Score [14] and only cases with sufficient causality (where the temporal context, clinical course, and circumstances of exposure of the bite were compatible and thus the causality was considered at least "probable") were included in the evaluation. Asymptomatic cases were those without any symptoms, minor symptoms were mostly local, moderate symptoms included extensive local and some systemic symptoms, and severe cases were potentially life-threatening with massive oedema, anaphylaxis, coagulation disorders or respiratory paralysis according to clinical toxicological classifications [14, 15].

Results

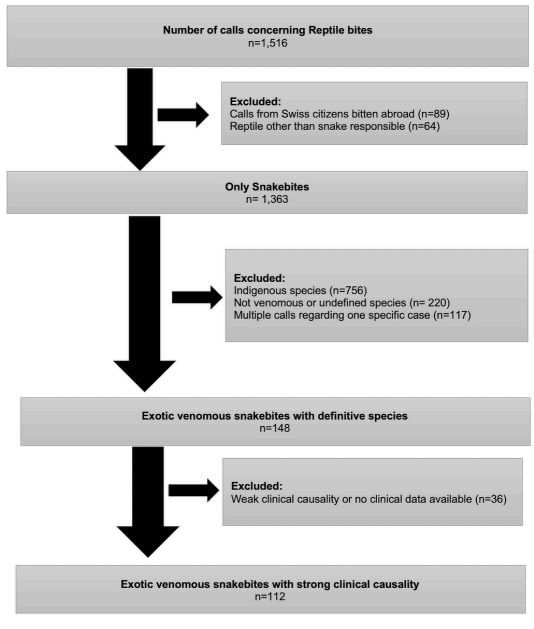
Of the 1516 calls concerning reptile-exposure at our Poison Centre, 1363 could be attributed to snakes (fig. 1); 148 (11%) concerned exotic venomous snakes and fulfilled the study criteria. Of the 114 cases with medical follow up, 112 (98%) showed sufficient causality. The quality of the follow-up in two cases did not allow for them to be graded more than "possible", so these cases had to be excluded.

Fifty-six different snake species belonging to 23 genera were responsible for these bites, 17 genera belonging to the family Viperidae and 6 to the family Elapidae. One snake was not identified beyond the genus (family Elapidae). Viperidae were involved in 87 (78%) with 30% of the bites caused by *Crotalus* sp., 11% caused by *Trimeresurus* sp. and 10% caused by *Bitis* sp.. Twenty-five patients (22%) suffered bites by Elapidae, with 56% caused *by Naja* sp., and 28% caused by *Dendroaspis* sp.. There were only adult bite victims (>16 years of age) with a median age of 40 years (range 16–71). Male gender was predominant (108 patients, 96%). Nearly all bites (97%) had happened at home or during leisure activities (table 1). Eleven percent of the patients had a past or ongoing substance abuse and 33% had been bitten on multiple occasions. Two patients had been bitten twice during the same event, but only one event resulted in severe symptoms. Thirteen patients (12%) had received antivenom on previous occasions.

Of the 112 patients included in this analysis, 89 (80%) suffered from a bite to the hand (table 2). Forty-six patients (41%) developed mild and 40 patients (36%) developed moderate symptoms, while 20 (18%) suffered a severe clinical course and 6 (5%) remained asymptomatic. Severe symptoms were observed in 6 of 25 patients (24%) after elapid bites and in 14 of 87 patients (16%) after viper bites, respectively. Overall, no fatalities were recorded, and no children were bitten.

Eighty-five patients (76%) did not receive antivenom treatment, whereas antivenom was administered to the remaining 27 patients (24%). Of the 27 patients receiving antivenom, 18 patients (21%) were bitten by vipers and 9 patients (36%) by elapids. Five patients (4%) required multiple doses, three viper and two elapid bite patients. In one case of a viper bite, less than a full dose of antivenom (1 vial instead of the prescribed 4–12 vials of CroFab (Crotalide

Figure 1: Selection of cases.



polyvalent immune fab [ovine], BTG, Pennsylvania, USA) had been administered (table 3). Anaphylactic reactions to the venom occurred in seven patients (6.3%), and mild anaphylaxis after antivenom in two patients (7.4%). Seventy-three (65%) patients did not require a hospital stay, and 27 (24%) were hospitalised for 24–48 hours. There were eight patients with severe symptoms (7%) with a hospitalisation time of >4 days (range 4–36 days).

Symptoms, treatment and outcome are detailed in table 4. Viper bites mostly resulted in local symptoms (57, 65.5%), but also caused haematological disturbances (23 patients, 26.4%) such as venom-induced consumption coagulopathy (5, 5.7%), thrombotic microangiopathy (3, 3.4%). One patient (1%) suffered from pulmonary oedema, and one (1%) from acute kidney injury. Elapid bites caused mainly local effects (14, 48%), besides neurological symptoms such as paralysis (3, 12%) requiring intubation, or paraesthesia (3, 12%), and fasciculation-induced rhabdomyolysis (1, 4%). Four patients (16%) bitten by elapids developed small local necrotic lesions, whereas only six (7%) of the patients with viper bites developed small necrotic lesions. Compartment syndrome was suspected in three cases, one after an elapid and two after viper bites. There were no haematological disturbances noted after elapid bites, and no clearly neurological symptoms after viper bites.

Table 1:
Demographics and characteristics of all patients (regardless of feedback, n = 148).

Characteristics		Patients n = 148 (>16 years)
Age	Median age (years)	39.5 (range 1671)
	16–25 years	19 (12.8)
	26–50 years	72 (48.6)
	>50 years	31 (20.9)
	Unknown	26 (17.6)
Sex	Male	136 (91.9)
	Female	6 (4.1)
	Unknown	6 (4.1)
Situation	Work	4 (2.7)
	Leisure	144 (97.3)
First caller	Ambulance	7 (4.7)
	Hospital	127 (85.8)
	Doctor, other	3 (2.0)
	General public	7 (4.7)
	Other organisations	4 (2.7)

Data are n (%) unless otherwise stated.

Table 2:
Clinical characteristics and duration of hospitalisation of patients with feedback (n = 112).

		Adults (≥16 years) n (%)
Total		112 (100)
Bite site	Arm	10 (8.9)
	Hand	89 (79.5)
	Leg	3 (2.7)
	Foot	0 (0)
	Throat	1 (0.9)
	Unknown	9 (8)
Severity	Asymptomatic	6 (5.4)
	Mild	46 (41.1)
	Moderate	40 (35.7)
	Severe	20 (17.9)
Hospitalisation	Outpatient	71 (63.4)
	0 days	2 (1.8)
	1–2 days	27 (24.1)
	3–4 days	4 (3.6)
	>4 days	8 (7.1)

Discussion

In this largest Swiss study on exotic snakebites, half of the patients required symptomatic or specific treatment for the envenomation. No children were bitten, and no fatalities were reported over the course of 22 years.

Exotic snakebite remains a rare occurrence in central European hospitals, even though there has been a documented increase in cases in some European countries [13, 16, 17]. As exotic snakebites remain rare events, physicians might not be very familiar with the clinical situation or the necessary treatment [7]. In Switzerland, there is no obligation to report animal bites, but treating physicians often contact the Poison Information Centre in order to increase the knowledge on toxicity and specific therapy [18, 19]. Our data show that there is a wide variety of different genera and species in the homes of the aficionados, which is comparable to other studies [8, 20, 21]. Distances to hospitals or medical aid are usually much shorter than in the countries of the snakes' origin, so rapid medical support thus reduces first aid times and increases the rate of survival [15, 22]. In Switzerland it is mandatory that a private person wanting to keep a venomous reptile pet provides a certificate of competence, which proves training in the husbandry of a venomous snake. Additionally, they have to provide proof of access to specific antivenom (if available) and an emergency contingency plan in case of a bite in the form of a membership of an antivenom association or a private stock. The emergency contingency plan usually contains the Latin name of the snake (as the colloquial name might be misleading [12]), with the name of the relevant antivenom and where it might be stored, information on previous bites and possible antivenom administration, allergies, and other medically relevant details. It also contains information on who would take care of the snake in the owner's absence, as well as where keys and other necessities might be stored. After an official inspection, the adult applicant is permitted to purchase the requested species. There are strict rules that are regularly enforced

Table 3:
Number of doses of antivenom in 112 patients.

	Single dose	Multiple dose	No antivenom	Incomplete dose	Total
Asymptomatic	0 (0)	0 (0)	6 (100)	0 (0)	6 (100)
Minor	2 (4.3)	0 (0)	44 (95.7)	0 (0)	46 (100)
Moderate	9 (22.5)	1 (2.5)	29 (72.5)	1 (2.5)	40 (100)
Severe	10 (50)	4 (20)	6 (30)	0 (0)	20 (100)

Data are n (%).

Table 4:
Overview of snakebites by genus/species with symptoms, treatment, and outcome.

Genus/species (total n = 112)	Symptoms	Treatment	Outcome
Vipers (n = 87)			
Agkistrodon (8)			
Agkistrodon contortrix (6)	Anaphylaxis to venom with exanthema and collapse (1/6), coagulopathy (1/6) pain and swelling (6/6), blistering (1/6), haematoma (2/6), hypertension (2/6)	Antivenom[1] (2/6), FFP (1/6), fibrinogen (1/6), antibiotics (2/6), analgesia (2/6), steroids (2/6), antihistamines (2/6), vitamin K (1/6), debridement of blister (1/6)	Resolution
Agkistrodon bilineatus (1)	Swelling, local haematoma, minimal coagulopathy	Incision of the bite site	Resolution
Agkistrodon taylori (1)	Pain, swelling	Analgesia, antibiotics	Resolution
Atheris (2)			
Atheris squamigera (2)	Local swelling (2/2), pain (1/2), bluish discolouration (1/2), tachycardia (1/2)	Analgesia (1/2), hydration (1/2)	Resolution
Bitis (9)			
Bitis arietans (2)	Anaphylactic reaction to the venom with urticaria (1/2), local pain and swelling (2/2)	Antihistamines (1/2), steroids (1/2), antibiotics (1/2), immobilisation (1/2)	Resolution
Bitis caudalis (1)	Local swelling and vomiting	Antibiotics, immobilisation	Resolution
Bitis gabonica (6)	Vasovagal shock (1/6), hypotension (1/6), pain (4/6) and swelling (5/6), small necrosis at bite site (1/6), coagulopathy (2/6), anaphylactic shock (1/6), compartment syndrome (1/6), elevation of creatine kinase (1/6)	Steroids (2/6), antihistamines (2/6), antibiotics (2/6), analgesia (2/6), antivenom[1] (1/6), FFP (1/6), fasciotomy (1/6), debridement (1/6)	Resolution (4/6), unknown course (2/6)
Bothriechis (2)			
Bothriechis schlegeli (2)	Local swelling (1/2), redness (1/2)	None	Resolution
Bothrops (3)			
Bothrops venezuelensis (1)	Massive coagulopathy, acute kidney injury, pulmonary oedema [32]	Antivenom[2], FFP, fibrinogen, oxygen, antibiotics	Resolution
Bothrops neuwiedi (2)	Fulminant infection (*Morganella morganii, Bacteroides fragilis*) (1/2)	Debridement (1/2), antibiotics (1/2)	Resolution
Calloselasma (1)			
Calloselasma rhodostoma (1)	Pain, swelling, minimal coagulopathy and thrombocytopenia	None	Resolution
Cerastes (4)			
Cerastes (4)	Massive swelling, vomiting, haematuria, coagulopathy, rhabdomyolysis, myocardial damage, brain haemorrhage [30]	Repeated antivenom[3], haemodialysis, adrenaline, antihistamines, steroids, FFP, tranexamic acid	Resolution within 20 months with no sequelae
	Swelling (3/4), pain (3/4) and blistering (1/4)	Antivenom[4] (1/4), steroids (2/4), antibiotics (2/4), analgesia (2/4), debridement (1/4), hydration (1/4)	Resolution (3/4)
Crotalus (26)			
Crotalus atrox (5)	Pain (3/5), swelling (3/5), coagulopathy (3/5), anaphylaxis to venom (1/5), hypotension (2/5), infection (1/5), tingling of the bite site (1/5), redness (1/5)	Antibiotics (3/5), antivenom[5] (3/5), elevation of the limb (1/5)	Resolution
Crotalus basiliscus (1)	Massive pain, swelling, suspected compartment syndrome, coagulopathy, rhabdomyolysis, ARDS, myocardial infarction, encephalopathy [29]	Antivenom[6], fibrinogen, factors II, VII, IX and X, fasciotomy and debridement, steroids, antihistamines, adrenaline, analgesia, oxygen, electrical resuscitation, magnesium	Bypass operation, no further information
Crotalus durissus cumanensis (1)	Pain, minimal D-dimer elevation	None	Resolution
Crotalus enyo (1)	Swelling, minimal necrosis at bite site	None	Resolution
Crotalus horridus (1)	Swelling, pain, minimal tachycardia and minor creatine kinase elevation	Analgesia, antibiotics	Resolution
Crotalus horridus (atricaudatus) (1)	Swelling, tachycardia, diarrhoea	Antibiotics	Resolution
Crotalus lepidus (5)	Pain (5/5), swelling (5/5), bluish discolouration (2/5), exanthema (2/5), bradycardia (1/5); redness (1/5), blistering (1/5), coagulopathy (1/5), anaphylaxis to venom (1/5)	Antivenom[5] (1/5), steroids (2/5), antihistamines (2/5), antibiotics (1/5), immobilisation (2/5), atropine (1/5), incision of blisters (2/5)	Resolution
Crotalus molossus molossus (1)	Pain, swelling, redness	None	Resolution
Crotalus ravus (1)	Swelling, mild pain	Disinfection, analgesia	Resolution
Crotalus stephensi (1)	Pain and swelling	Immobilisation	Resolution
Crotalus vegrandis (4)	Angioedema (1/4), pain and swelling (4/4), double vision (1/4), coagulopathy (1/4), vertigo (1/4), tachycardia (2/4)	Fibrinogen and antivenom [1, 2] (2/4), steroids (1/4), cyclocaprone (1/4), analgesia (2/4), antihistamines (1/4), adrenaline (1/4)	Resolution, redness after antivenom in one case (1/4)
Crotalus viridis viridis (1)	Swelling, pain	Antibiotics	Resolution
Crotalus (viridis) cerberus (1)	Swelling, pain, bluish discoloration	None	Resolution
Crotalus (viridis) oreganus (1)	Massive swelling, pain, thrombocytopenia, ventricular extrasystoles	None	Resolution
And unknown (1), probably *unicolor*	Massive swelling, pain, coagulopathy, rhabdomyolysis	Antivenom[7], hydration, morphine	Resolution
Echis (3)			

Echis carinatus (2)	None (2/2)	None	Resolution
Echis coloratus (1)	Severe coagulopathy	Exanthema after antivenom, otherwise resolution	
Eristicophis (2)			
Eristicophis macmahonii (2)	Local swelling (2/2), minimal coagulopathy (1/2)	Analgesia, antibiotics, immobilisation (2/2)	Resolution
Lachesis (1)			
Lachesis muta (1)	Severe coagulopathy, haematuria, shock, thrombosis of mesenteric veins	Antivenom[1], FFP, hemicolectomy	No information
Macrovipera (3)			
Macrovipera lebetina (2)	Pain (1/2), swelling (2/2), coagulopathy (2/2), moderate rhabdomyolysis (1/2), vomiting (1/2)	Antivenom[1] (2/2), FFP (1/2), antibiotics (2/2), analgesia (1/2), and hydration (2/2)	Resolution
Macrovipera schweizeri (1)	Finger swollen, painful, bluish discoloration, small necrosis	Antibiotics	Resolution
Prothobothrops (1)			
Prothobothrops cornutus (1)	Local swelling, tachycardia, hypertension, mild coagulopathy	None	Resolution
Sistrurus (5)			
Sistrurus catenatus (2)	Pain (2/2) and swelling (2/2), thrombocytopenia (1/2)	Analgesia (1/2)	Resolution
Sistrurus miliarius (3)	Pain (3/3), swelling (3/3), exanthema of the bitten limb (1/3), mild coagulopathy (1/3)	Antibiotics (1/3), Steroids (1/3)	Resolution
Trimeresurus (10)			
Trimeresurus albolabris (4)	Pain (4/4), swelling (4/4), vomiting (1/4), mild coagulopathy (1/4)	Minor incision to relieve oedema (1/4), antibiotics (1/4), hydration (1/4)	Resolution
Trimeresurus trigonocephalus (3)	Pain (2/3), swelling (2/3), mild coagulopathy (1/3)	None	Resolution
Trimeresurus stejnegeri (1)	Generalised exanthema and pruritus after the bite, swelling, minimal local necrosis	Steroids, antihistamine, antibiotics	Resolution
Trimeresurus venustus (2)	Mild local pain and swelling (2/2) [44]	Local debridement (1/2), antibiotics (1/2)	Resolution
Tropidolaemus (1)			
Tropidolaemus walgeri (1)	Mild swelling	None	Resolution
Vipera (5)			
Vipera ammodytes (3)	Pain (3/3), swelling (3/3), exanthema (1/3), angio-oedema (1/3), thrombocytopenia (1/3), anaphylactic shock (1/3), urticaria (1/3)	Antivenom[1(possibly9)] (1/3), thrombocytes (1/3), antihistamines (1/3), steroids (1/3), analgesia (1/3)	Resolution
Vipera latastei (1)	Pain and swelling, vomiting, leucocytosis, hypertension	None	Resolution
Vipera ursinii (1)	Swelling, local necrosis, generalised urticaria to the venom	Antivenom[9], antihistamine, antibiotics	Resolution
Elapids (n = 25)			
Acantophis (1)			
Acantophis sp. (1)	Local swelling and pain, urticaria, tachycardia, increased creatine kinase	Antihistamines	Resolution
Aspidelaps (1)			
Aspidelaps scutatus (1)	Local swelling	None	Resolution
Dendroaspis (7)			
Dendroaspis angusticeps-viridis hybrid (1)	Vomiting, pain, swelling, paraesthesia (tingling) of the whole body, hypokalaemia, ptosis, angio-oedema, swelling, massive pain, mild dyspnoea	Antivenom[10], analgesia, steroids, antihistamines, antibiotics, benzodiazepines	Resolution
Dendroaspis jamesoni (1)	Pain, swelling, redness of the face, dysphagia, dyspnoea, paresthaesia of the legs	Antivenom[10], steroids, antihistamines	Resolution
Dendroaspis polylepis (2)	Tachypnoea, muscle cramps, fasciculations, rhabdomyolysis (creatine kinase >16,000 U/l) [18]	Antivenom[10], steroids, antihistamines, adrenaline, hydration	Resolution
	Tingling of the lips and extremities (1/2)	None	Resolution
Dendroaspis viridis (3)	Same patient:		
	– Tingling of the lips, tachycardia, hyperventilation	None	Resolution
	– Minor tingling sensation, then massive swelling and pain with compartment syndrome	Fasciotomy, analgesia, hydration, antibiotics	Tissue defect
	– Tingling sensation of the whole body, tachycardia, dyspnoea [33]	Antivenom[10], antihistamines, steroids	Exanthema after antivenom, then delayed resolution
Hemachatus (1)			
Hemachatu haemachatus (1)	Local swelling and pain, superficial lesion	Disinfection of the wound	Resolution
Naja (14)			
Naja kaouthia (8)	Respiratory paralysis (2/8), ptosis (3/8), dysphagia (1/8), double vision (1/8), dysarthria (3/8), small necrosis (3/8), swelling (5/8), pain (4/8), vomiting and diarrhoea (3/8), somnolence (2/8), redness (2/8), leucocytosis (1/8)	Antivenom[1]*(3/8), intubation (2/8), antihistamines and steroids (4/8), adrenaline (2/8)	Deep vein thrombosis (1/8) with complete resolution
	Small necrosis, angio-oedema, apnea, cardiac arrest, and collapse (1/8) [31]	Antivenom[1]*(1/8), intubation (2/8), antibiotics (1/8), mechanical resuscitation (1/8)	Resolution
Naja melanoleuca (1)	None	None	Resolution

Naja naja (2)	Swelling (1/2), tingling sensation (1/2), small necrosis (1/2), phlegmon (1/2)	Fasciotomy (1/2), antibiotics (2/2).	Resolution
Naja nivea (1)	Swelling, pain, ptosis, hypersalivation, respiratory decompensation	Antivenom[10], intubation and ventilation, antibiotics	Resolution
Naja siamensis (2)	Small necrosis (1/2), hypertension (1/2), pain (1/2)	Debridement of necrosis (1/2), antibiotics (2/2)	Resolution
Pseudechis (1)			
Pseudechis colletti (1)	Swelling, minimal pain and bluish discoloration, hypertension, tachycardia	None	Resolution

FFP: fresh frozen plasma

[1] Antivenom not specified

[2] Antivipmyn (Instituto Bioclon, Mexico)

[3] Antirept (Pasteur Mérieux Lyon-France sérum antivenimeux, polyvalent, purifié: moyen orient – afrique du nord)

[4] Polyvalent snake antivenom, National Antivenom and Vaccine Production Centre (NAVPC), Saudi-Arabia

[5] CroFab (Crotalide polyvalent immune fab [ovine]), BTG, Pennsylvania, USA

[6] Antivipmyn Tri (Instituto Bioclon, Mexico)

[7] "Antivenin (suero antiofidico polivalente)", probably BIOL, Paraguay

[8] FAV Afrique (Sanofi-Pasteur)

[9] ViperTab, unclear which producer

[10] SAIMR polyvalent snake antivenom, SA Vaccine Producers (Pty) Ltd. (The South African Institute for Medical Research), South Africa

*Two cases are probably: Cobra Antivenin (Naja kaouthia), Queen Saovabha Memorial Institute (Thai Red Cross Society), Thailand

[n] = Previously published cases, symptoms not included in count for the other cases of the same species

(species) = old name, documented as such

and checked [23]. In this, the legal situation in Switzerland differs from other countries [24, 25].

The appropriate adherence to these rules was supported by the data of this study, as only adult patients were affected. In a US study, almost 15% were aged 17 years or less, and almost 7% were children aged 5 years or younger [20]. Also, in accordance with previous studies, the typical patient was male, as the keeping of snakes seems to be predominantly a male hobby [5, 20, 21]. It was also interesting to note that 11% of the bite victims suffered from ongoing or past substance abuse, which has been found to be a risk factor for a bite [26], and 33% had a history of at least one previous bite. Most bites occurred during activities involving the terrarium (i.e., cleaning it, changing the water) or during feeding procedures, which is reflected by the fact that the hand was the primary site of the bites. Of the four patients exposed at work, none of whom could be included in our analysis for lack of feedback, one was a 31-year-old zoo worker who got bitten by a *Naja kaouthia* and developed a small necrotic lesion, another was a 47-year-old photographer who got too close to a *Naja kaouthia* and was bitten. In a further event, a pharmaceutical industry worker had pricked herself with a syringe needle containing the venom of an *Oxyuranus scutellatus*. She had previously suffered an allergic reaction to the venom. Follow-up information was also missing in this patient. The fourth case concerned a bite by a *Bothrops neuwiedi*, where the patient remained asymptomatic suggesting a dry bite. Dry bites are snakebites without venom injection. These were suspected in all six asymptomatic patients in the present study. The incidence of asymptomatic and thus dry bites was considerably lower than in another study, although the reason for this remains unclear [21]. It is possible that asymptomatic patients would not present at medical facilities or doctors confronted with asymptomatic patients would not contact the Poison Information Centre.

Of the two cases excluded from this analysis because of insufficient follow-up and causality, one concerned a bite by a neonate *Naja nivea*, where the patient developed headache, mydriasis and subjective lockjaw. The other concerned a bite by a not further identified *Crotalus* sp, where the treating physician performed an incision at the bite site, administered cortisone and sent the patient home. Neither patient had any further follow-up that was recorded in the database, so a complete evaluation of the cases was not possible.

The symptoms experienced by the patients in our study were typical for the respective snake genus and showed a prevalence of haematotoxic symptoms in viper bites and neurotoxic symptoms in bites by elapids. There are vipers causing neurotoxic effects (i.e*., Crotalus scutulatus*) [27], and elapids causing haematotoxic or myotoxic symptoms (i.e., *Pseudechis* sp.) [28]. One patient bitten by *C. vegrandis* complained of double vision, although neurotoxicity for this snake has not previously been described. On the other hand, one patient with a *Pseudechis colletti* bite developed only local symptoms, as did another patient after a bite by an *Acanthophis* sp., so neither haematological nor myotoxic symptoms were in evidence after Australian elapid bites.

Cardiovascular symptoms have been described after bites by exotic vipers [28], but only a few of the patients in our database showed mild disturbances such as hypotension, even though there were two patients with myocardial infarctions, albeit with some delay after the bite [29, 30]. In one case, a bite by a *N. kaouthia* led to cardiac arrest [31]. Haematotoxic effects after bites by exotic vipers occurred in 26.4% of our patients and in 5 patients (5.7%) venom-induced consumption coagulopathy was diagnosed. One patient bitten by a *Bothrops venezuelensis* developed microangiopathic haemolysis, severe thrombocytopenia and disseminated intravascular coagulopathy, complicated by acute respiratory distress syndrome and acute kidney injury. He recovered with antivenom and symptomatic treatment [32]. Neurological symptoms after elapid bites manifested as fasciculations resulting in severely elevated creatine kinase in the case of a bite by a *Dendroaspis polylepis*, which is typical for this particular snake [18].

Other findings included ptosis, ophthalmoplegia, dysarthria and respiratory paralysis requiring endotracheal intubation. Extensive local necrosis, as is typical for some African and Asian *Naja* sp., was not in evidence [28], although four patients suffered small local necrotic lesions (16% of the patients with elapid bites), whereas only six (7%) of the patients with viper bites developed small necrotic lesions.

Three patients developed compartment syndrome. One after a bite by *Dendroaspis viridis* and treatment with fasciotomy was previously published as a case report [33]. Another two cases of compartment syndrome were caused by vipers, but in neither case had intracompartmental pressure been recorded. Only one of the patients had received multiple doses of antivenom [29]. The venom of some snakes can imitate compartment syndrome by causing excruciating pain and swelling. However, compartment syndrome after snakebite is not a clinical diagnosis, because the pathophysiology is different from the consequences of trauma, which primarily results from an increased pressure within the affected area. Venom-induced compartment syndrome probably involves a direct cytotoxic effect of the venom and a reduced perfusion pressure [34, 35]. Fasciotomy has been found to be only very rarely necessary after snakebite, and only if the intracompartmental pressure remains persistently elevated above 30 to 40 mm Hg over several hours, and if antivenom has been administered repeatedly [22, 35, 36]. Fasciotomy and debridement often result in worse functional results, as was also evident in the few cases of our cohort, and often requires follow-up surgical procedures [37]. In a recent review on the necessity of fasciotomy in Crotalinae envenomation, subcutaneous venom injection in dogs did not result in intracompartmental pathology and intracompartmental injection resulted in necrosis, regardless of surgical intervention [38]. So, fasciotomy as well as early debridement has to be discouraged, because muscles damaged by some snake venoms can regenerate if left in peace [12].

Symptomatic treatment of snakebite in our study included analgesia (although the use of non-steroidal antirheumatics and acetylsalicylic acid is discouraged), and antibiotics, although the use of prophylactic antibiotics has not been proven to be beneficial [15]. Other treatment included the administration of steroids and antihistamines, as well as intubation and ventilation. The administration of fresh frozen plasma in the case of haematological disorders is controversial [32]. Despite the availability of good symptomatic medical treatment, antivenom remains the first-line treatment in severe snakebites. It is indicated when systemic symptoms or massive local swelling are expected or already in evidence [12]. However, antivenom shortage has a serious impact on availability, especially in the countries of the snake's origin, but also for snake keepers [28]. In addition, cross-breeding of related snake species in order to create new hybrids with unknown venoms poses a further problem for antivenom efficacy [12, 39]. There were such cases in our analysis, i.e., a hybrid of a *D. viridis* and *angusticeps*. In some of our cases, antivenom administration was not restricted to severe cases, as some moderately envenomed patients received it (table 3). Yet, not all severely envenomed patients received antivenom, either due to unavailability or because they had refused it for fear of anaphylaxis.

Switzerland has an antivenom network in place in which eight different hospital pharmacies stock a variety of antivenoms for the registered snakes. The list of available antivenoms can be publicly accessed [40]. Antivenoms are also sent abroad in case of need in a neighbouring country [41]. In the USA and the UK, poison centres will give advice on where to procure antivenom; in other countries antivenom might be found at the zoo (which could also be of service to identify the causative specimen) [12]. Anaphylaxis after antivenom was a very rare occurrence among our patients: only two (7.4%) of the nine cases with anaphylactic reactions occurred after antivenom administration, both patients developed exanthema. Still, this is a high incidence compared with another study, where only 3.3% developed anaphylaxis [22]. Only one of these two patients had already received antivenom for a previous bite. The seven (6.3%) anaphylactic reactions caused by the venom ranged from exanthema and angio-oedema to anaphylactic shock. In a Hungarian study, anaphylactic episodes were mostly related to the venom itself, and there was even a fatal outcome due to venom anaphylaxis [42]. However, most patients had a rapid recovery following antivenom administration. In our study, only 4.3% of the patients with mild symptoms received antivenom, whereas 70% of the severe cases received the specific treatment. We observed that the percentage of patients having multiple antivenom administrations increased linearly with the severity of the symptoms.

The duration of hospitalisation was dependent on the severity of symptoms. Mild or asymptomatic cases were often treated in an outpatient setting, whereas some complicated cases required surveillance for up to 36 days [29].

The study has some limitations, as is the case with all Poison Centre data studies, which show considerable reporting bias [43]. As information is voluntarily reported, some clinical details may be incomplete or specific data may be subjectively reported by hospital physicians treating the patients. The retrospective design of the study and the lack of long-term follow-up are further limitations. Prolonged injuries, adverse effects or permanent disabilities could not be tracked. Moreover, not all bites might have been reported to the centre. Underreporting might also play a role, when owners of illegally kept snakes might be fearful of legal repercussions and fail to seek medical assistance.

Conclusion

Our study is the largest study conducted in Switzerland analysing national data on exotic snakebites, with symptoms, treatment, distribution of severity and administration of antivenom. It showed that a wide variety of different genera and species are kept in the homes of the snake enthusiasts, that their bites caused many different symptoms that were typical for the respective species, and that male gender and bites to the hand were vastly predominant. Overall, the number of annual bites by exotic snakes is low, and most patients need only symptomatic therapy to recover. Although there was a small number of asymptomatic patients with supposed dry bites, most patients developed mild or moderate envenoming. Severe envenomation with considerable morbidity occurred but showed good resolu-

tion of symptoms especially after antivenom administration.

Potential competing interests
All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

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