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Prognostic factors for amputation in the case of envenoming by snakes of the *Bothrops* genus (Viperidae)

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The prognostic factors for amputation following envenoming by snakes of the *Bothrops* genus were identified from the medical records of 3139 patients. Each of these patients had been bitten by *Bothrops* sp. and treated in the Hospital Vital Brazil, in São Paulo, Brazil, between 1981 and 1990. The 21 (0.67%) of the patients who had undergone amputation were compared with the 3118 who had not, with respect to the characteristics of the accident, the snake, the victim, the local and systemic manifestations of the envenoming and the treatment. There was an association between amputation and the month of the accident, the time of day when the accident happened, the length of the attacking snake, the anatomical region bitten, systemic bleeding and renal failure. Patients bitten in the fingers, during the cooler months, between 00.00 and 12.00 hours and/or by snakes >60 cm in length, who developed blisters and abscesses at the site of the bite, systemic bleeding and/or renal failure underwent amputation more frequently than the others ($P<0.05$ for each).

Snakes belonging to the 31 species of the *Bothrops* genus (family Viperidae) are mainly distributed throughout South America (Campbell and Lamar, 1989). They are responsible for most of the poisonous snake bites in Brazil, causing $>16\,000$ cases and about 80 fatalities per year (Anon., 1988). Many of those bitten suffer considerable tissue damage and this may necessitate amputation of all or part of an affected limb (Ribeiro and Jorge, 1990; Milani *et al.*, 1997).

Nearly nine decades ago, Vital Brazil discussed the possible prognostic factors for the development of snake envenoming (Brazil, 1911). Although the prognostic factors for the death of patients and for the local manifestations of the envenoming have since been explored (Amaral, 1930; Fonseca, 1949; Rosenfeld, 1991; Anon., 1993), much of the information on which these studies were based was unreliable. The subject of the present study, the prognostic factors for amputation due to the bite of a Brazilian snake, had not been scientifically evaluated previously.

SUBJECTS AND METHODS

The medical records of 3139 subjects who had been bitten by snakes of the *Bothrops* genus were evaluated. Each of these had been treated for the bite in the Hospital Vital Brazil (HVB) in São Paulo, Brazil, between 1981 and 1990. Those who had undergone an amputation as a result of the bite were compared with those who had not, in terms of: the year, month and time of day when they were bitten; their sex and age; the type and length of the snake involved; the anatomical region bitten; the time lapse between the accident and arrival at the hospital; the presence of pain, oedema, ecchymosis, blisters and/or abscesses at or near the site of the bite; the presence

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TABLE 1
Seasonal distribution of bites by snakes of the Bothrops *genus, recorded as cases at the Hospital Vital Brazil, São Paulo, Brazil, between 1981 and 1990*

Month	*No. of cases and (% of those):*		*No. and (%) of all cases*
	Undergoing amputation	*Not undergoing amputation*	
January	4 (19)	397 (12.7)	401 (12.8)
February	0 (0)	319 (10.2)	319 (10.2)
March	2 (10)	437 (14.0)	439 (14.0)
April	0 (0)	354 (11.4)	354 (11.3)
May	4 (19)	143 (4.6)	147 (4.7)
June	3 (14)	77 (2.5)	80 (2.5)
July	1 (5)	73 (2.3)	74 (2.4)
August	1 (5)	93 (3.0)	94 (3.0)
September	0 (0)	115 (3.7)	115 (3.7)
October	1 (5)	267 (8.6)	268 (8.5)
November	1 (5)	412 (13.2)	413 (13.2)
December	4 (19)	431 (13.8)	435 (13.9)
All	21 (100)	3118 (100)	3139 (100)

or absence of systemic bleeding and/or renal insufficiency; alterations in blood coagulation; the use of a tourniquet; the number of ampoules of antivenom injected; and death rate. The comparisons were made using χ^2 test or exact Fisher tests, as appropriate. A difference giving a *P*-value of < 0.05 was considered significant.

RESULTS

Only 21 (0.67%) of the 3139 patients who were studied underwent an amputation, each losing at least one finger (13 cases), at least one toe (three cases), a forearm (two cases), a leg (two cases), or an ankle (one case).

The ratio of amputation cases to non-amputation cases was significantly higher during the months in which there were fewer snake-bite accidents (May–September) than at other times of the year (Table 1). Amputations were also significantly more frequent among those patients who were bitten between midnight and 06.00 hours than in the other patients (Table 2).

Amputation rates were similar for the two

TABLE 2
Distribution of bites by snakes of the Bothrops *genus according to the time of day, recorded from snakebite cases at the Hospital Vital Brazil, São Paulo, Brazil, between 1981 and 1990*

*Time** *(hours)*	*No. of cases (and % of those):*		*No. and (%) of all cases*
	Undergoing amputation	*Not undergoing amputation*	
06.00–12.00	9 (45)	968 (31.2)	977 (31.3)
12.00–18.00	7 (35)	1468 (47.3)	1475 (47.2)
18.00–00.00	2 (10)	628 (20.2)	630 (20.2)
00.00–06.00	2 (10)	41 (1.3)	43 (1.4)
Any	20 (100)	3105 (100)	3125 (100)

* Information on the time of the bite was not available for 14 (0.45%) of the cases seen, including one amputation case.

TABLE 3
Cases of Bothrops *snake bite recorded at the Hospital Vital Brazil, São Paulo, Brazil, between 1981 and 1990, separated according to the ages of those bitten*

Victim's age (years)	*No. of cases and (% of those):*		
	Undergoing amputation	*Not undergoing amputation*	*No. and (%) of cases*
0–< 10	2 (10)	390 (12.5)	392 (12.5)
10–< 20	2 (10)	816 (26.2)	818 (26.1)
20–< 30	6 (29)	566 (18.2)	572 (18.2)
30–< 40	5 (24)	456 (14.6)	461 (14.7)
40–< 50	1 (5)	378 (12.1)	379 (12.1)
50–< 60	3 (14)	283 (9.1)	286 (9.1)
≥ 60	2 (10)	229 (7.3)	231 (7.4)
Any	21 (100)	3118 (100)	3139 (100)

sexes, with two out of the 765 women and 19 out of the 2375 men undergoing amputation ($P > 0.05$). There was also no association between the age of the victim and the occurrence of amputation ($P > 0.05$; Table 3). Although it was not possible to establish an association between the species of the snake causing the bite and the occurrence of amputation, the species was only identified in 1383 cases and all but 38 of these cases had been bitten by *Bothrops jararaca*.

There was a reference to the approximate size of the snake in 1346 of the cases. Although there were seven (1.15%) cases of amputation among the 611 patients bitten by snakes ≥ 40 cm in length, there were no amputations among the 735 patients bitten by shorter snakes ($P < 0.05$). An association between the occurrence of amputation and bites by snakes longer than 60 cm could also be observed among the 801 cases for which information about the exact size of the snake was available ($P < 0.05$; Table 4).There was also an association between bites on the fingers and the occurrence of amputation ($P < 0.05$; Table 5). Those who presented at the HVB within 12 h of the bite were no less (or more) likely to have undergone subsequent amputation than those who presented later ($P > 0.05$; Table 6). It was not possible to obtain information about the exact time between the bite and the beginning of the serum therapy. However, data on the time between presentation at the HVB and the beginning of serum therapy

TABLE 4
Lengths of the snakes which caused the cases of Bothrops *snake bite seen at the Hospital Vital Brazil, São Paulo, Brazil, between 1981 and 1990*

Snake length (cm)*	*No. of cases and (% of those):*		
	Undergoing amputation	*Not undergoing amputation*	*No. and (%) of all cases*
< 40	0 (0)	410 (51.5)	410 (51.2)
40–< 60	0 (0)	100 (12.6)	100 (12.5)
60–< 80	1 (20)	75 (9.4)	76 (9.5)
80–< 100	1 (20)	115 (14.4)	116 (14.5)
≥ 100	3 (60)	96 (12.1)	99 (12.4)
Any	5 (100)	796 (100)	801 (100)

* The exact size of the snake was unknown for 2338 (74.5%) of the 3139 cases investigated, including 11 cases of amputation.

TABLE 5
Anatomical sites bitten by snakes of the Bothrops *genus, as recorded from cases seen at the Hospital Vital Brazil, São Paulo, Brazil, between 1981 and 1990*

	No. of cases and (% of those):		
*Site of bite**	*Undergoing amputation*	*Not undergoing amputation*	*No. and (%) of all cases*
Foot	0 (0)	1156 (37.1)	1156 (36.9)
Finger	13 (62)	419 (13.4)	432 (13.8)
Leg	2 (10)	416 (13.3)	418 (13.3)
Ankle	1 (5)	388 (12.4)	389 (12.4)
Toe	3 (14)	332 (10.6)	335 (10.7)
Hand	0 (0)	237 (7.6)	237 (7.6)
Forearm	2 (10)	73 (2.3)	75 (2.4)
Thigh or knee	0 (0)	45 (1.4)	45 (1.4)
Arm	0 (0)	22 (0.7)	22 (0.7)
Head	0 (0)	17 (0.5)	17 (0.5)
Trunk	0 (0)	11 (0.4)	11 (0.4)
Any	21 (100)	3118 (100)	3137 (100)

* No relevant information was available for two (0.1%) of the 3139 cases investigated.

TABLE 6
The times taken by cases of Bothrops *snake bite to receive medical attention, recorded at the Hospital Vital Brazil, São Paulo, Brazil, between 1981 and 1990*

	No. of cases and (% of those):		
*Time post-bite** *(h)*	*Undergoing amputation*	*Not undergoing amputation*	*No. and (%) of all cases*
0–<1	3 (14)	176 (5.6)	179 (5.7)
1–<3	6 (29)	1371 (44.0)	1377 (43.9)
3–<6	6 (29)	887 (28.5)	893 (28.5)
6–<12	1 (5)	287 (9.2)	288 (9.2)
≥12	5 (24)	395 (12.7)	400 (12.8)
Any	21 (100)	3118 (100)	3137 (100)

* There was no relevant information for two (0.1%) of the cases investigated.

were available for 1096 cases, nine of whom underwent amputation. There was no apparent association between the length of the presentation–serum period and amputation, although most cases (89% of those who had amputations and 78.0% of the others) received serum within 1 h of their presentation at the HVB.

The occurrence of amputation was related to the presence of blisters and abscesses at or near the bite site, to the presence of systemic bleeding, and to the occurrence of renal insufficiency ($P < 0.05$ for each) but not to the presence of ecchymosis (Table 7).

Five (0.40%) of the 1261 patients with normal coagulation times and 13 (0.75%) of the 1730 patients with abnormal coagulation suffered amputations ($P > 0.05$; Table 7). Amputations were also performed on eight (0.67%) of the 1199 patients on whom

TABLE 7
Local and systemic manifestations and the evolution of Bothrops *envenoming, recorded from cases at the Hospital Vital Brazil, São Paulo, Brazil, between 1981 and 1990*

Sign or outcome	*No. of cases and (% of those):*		P
	Undergoing amputation	*Not undergoing amputation*	
Pain	21 (100)	2980 (95.6)	0.387
Oedema	21 (100)	2973 (95.3)	0.369
Blister	15 (71)	420 (13.5)	0.000
Necrosis	19 (90)	499 (16.0)	0.000
Abscess	9 (43)	338 (10.8)	0.000
Ecchymosis	15 (71)	1747 (56.0)	0.231
Systemic bleeding	9 (43)	376 (12.1)	0.000
Renal failure	2 (10)	47 (1.5)	0.041
Death	1 (5)	8 (0.3)	0.059

TABLE 8
The doses of antivenom administered to cases of Bothrops *snake bite at the Hospital Vital Brazil, São Paulo, Brazil, between 1981 and 1990*

*Dose** *(ampoules)*	*No. of cases and (% of those):*		*No. and (%) of all cases*
	Undergoing amputation	*Not undergoing amputation*	
0–4	3 (17)	984 (31.7)	987 (31.6)
5–9	11 (61)	1317 (42.4)	1328 (42.5)
>9	4 (22)	439 (14.1)	443 (14.2)
Any	18 (100)	3105 (100)	3125 (100)

* No relevant information was available for 14 (0.5%) of the cases investigated, including three cases of amputation.

tourniquets had been used and 13 (0.67%) of the 1927 on whom tourniquets had not been used ($P > 0.05$). There was no apparent association between the doses of serum given to the patients and the occurrence of amputation ($P > 0.05$; Table 8).

Of the 3139 patients investigated, only 138 (4.40%) did not suffer pain, only 145 (4.62%) did not present oedema and only nine (0.29%) died. The relatively small numbers of such cases made it difficult to establish if pain and oedema were prognostic factors for amputation or whether amputees were more likely to die as a result of the snake bite than the other cases.

DISCUSSION

It is unclear why snakebite cases in the cooler months of the year are more likely to undergo amputation than cases at other times. Snakes travel less during the colder months (Sazima, 1988), probably catch fewer prey (Ribeiro and Jorge, 1990), presumably accumulate more venom between bites, and are therefore able to deliver more venom during bites, resulting in more serious cases of envenoming among those bitten (though less cases of snakebite; Ribeiro and Jorge, 1990) than at other times of the year. Specimens of *B. jararaca* longer than 40 cm are known to be more likely to cause

tissue destruction than shorter specimens, again, presumably, because of differences in the amount of venom injected (Ribeiro and Jorge, 1990; Puorto *et al.*, 1996).

It is also unclear why those bitten in the early hours of the morning should be at particularly high risk of needing an amputation. Bites by large *B. jararaca*, which are generally responsible for most amputations, seem to be distributed evenly throughout the day and night (Ribeiro and Jorge, 1990). In Malaysia there seems to be a similar association between the time of the day when individuals are bitten by *Naja naja* and the seriousness of the envenoming, although in this case day-time bites tend to be more damaging than those at night (Reid, 1964).

Children and the elderly are generally considered to suffer more as a result of snake bite, especially in terms of systemic manifestations and death, than young adults (Parrish, 1963; Brian and Vince, 1987; Lebrão *et al.*, 1995). In the present study, however, the likelihood of amputation following the bite of a *Bothrops* sp. was similar for each age-group.

In general, envenomings by large specimens of *B. jararaca* (i.e. those >40 cm in length) and *B. jararacussu* (>50 cm) are more severe than those by smaller specimens, and the larger species, such as *B. jararacussu* (which may reach 2200 cm in length), cause more serious envenomings than the smaller species, such as *B. jararaca* (which only grows to 1600 cm in length) (Campbell and Lamar, 1989; Ribeiro and Jorge, 1990; Puorto *et al.*, 1996; Milani *et al.*, 1997). The difference does not only relate to the quantity of venom injected, as the venom from *B. jararaca* which are longer than 40 cm has higher proteolytic activity, and therefore a greater capacity for causing necrosis, than that of smaller snakes of this species (Rosenfeld *et al.*, 1959; Kamiguti and Cardoso, 1989). A positive association between the size of the biting *N. naja* and the occurrence of necrosis in the affected anatomical region was reported by Reid (1964), in Malaysia. In envenomings by *Echis carinatus*, however, there appears to be no association between the intensity of the oedema observed and the length of the snake (Warrell *et al.*, 1977).

It is not surprising that bites on the finger lead to more amputations than bites elsewhere on the body. Bites on the hand involve all the tissues (skin, nerves, vessels, sinews, ligaments, bones and joints) and the envenoming provokes immediate oedema and vessel constriction, leading to gangrene and the necessity of amputation (Snyder *et al.*, 1972).

The time period between bite and treatment could not be not related to the occurrence of amputation, either in the present study or in a previous investigation carried out in Minas Gerais, Brazil (Nishioka and Silveira, 1992). The effectiveness of heterologous serum for the treatment of the local manifestations of the bite (Reid *et al.*, 1963; Sellehewa *et al.*, 1995) is therefore put in doubt. Heterologous serum appeared to have little therapeutic effect on the local manifestations of the envenoming. The results of a clinical trial, which compared the effectiveness of giving two ampoules/light case and four ampoules/moderate case with that of giving twice as many ampoules to similar cases, indicated that doubling the dose of serum had no effect on the incidence of local complications (Jorge *et al.*, 1995).

Blisters result from the tissue destruction caused by the venom, and abscesses appear because of the multiplication of the bacteria, principally from the snake's mouth, infecting the tissue injured by the venom (Jorge *et al.*, 1995). As blisters and abscesses are both therefore related to the tissue destruction which is the principal factor leading to amputation, the association between theses signs and amputation is to be expected.

The apparent lack of an association between abnormally long blood-coagulation times and the likelihood of amputation is interesting. In general, the venom of small, immature snakes tends to have lower proteolytic activity but higher anticoagulant activity than the venom of the larger, adult snakes (Rosenfeld *et al.*, 1959; Kamiguti and Cardoso, 1989). The bites of small *B. jararaca* (<40 cm) are therefore unlikely to cause necrosis (Ribeiro and Jorge, 1989) and, consequently, amputation,

but are likely to increase blood-coagulation times.

As in the present study, the results of studies on envenomings caused by cobras in Malaysia (Reid, 1964) and by *Bothrops* in Minas Gerais, Brazil (Nishioka and Silveira, 1992) show no association between the use of tourniquets and the occurrence of complications. Such an association, however, was indicated by the results of studies carried out in Israel (Efrati and Reif, 1953) and in São Paulo, Brazil (Ribeiro and Jorge, 1989).

In conclusion, there appears to be a definite association between amputation and the month in which the bite occurred, the time of day when the case was bitten, the length of the attacking snake, the anatomical region bitten, the presence of blisters and abscesses at or near the site of the bite, systemic bleeding, and renal failure.

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