Infectious Complications Following Snakebite by Bothrops lanceolatus in Martinique: A Case Series

Dabor Resiere,1* Hossein Mehdaoui,1 Rémi Névière,2 Claude Olive,3 Mathieu Severyns,4 Adeline Beaudoin,1 Jonathan Florentin,1 Yannick Brouste,1 Rishika Banydeen,1 André Cabié,3 Bruno Mégarbane,6 José Maria Gutierrez,7 and Hatem Kallel8

1Department of Critical Care, University Hospital of Martinique, Fort-de-France, France; 2Department of Cardiology, University Hospital of Martinique, Fort-de-France, France; 3Department of Microbiology, University Hospital of Martinique, Fort-de-France, France; 4Department of Orthopedic Surgery, University Hospital of Martinique, Fort-de-France, France; 5Department of Infectious Diseases, University Hospital of Martinique, INSERM CIC 1424, Antilles University, Fort-de-France, France; 6Department of Medical and Toxicological Critical Care, Larboisière Hospital, Paris-Diderot University, INSERM UMR5114, Paris, France; 7Instituto Clodomiro Picado, Facultad de Microbiología, Universidad de Costa Rica, San José, Costa Rica; 8Intensive Care Unit, Cayenne General Hospital, Cayenne, France

Abstract. Infections secondary to snakebite occur in a number of patients and are potentially life-threatening. Bothrops lanceolatus bites in Martinique average 30 cases per year and may result in severe thrombotic and infectious complications. We aimed to investigate the infectious complications related to B. lanceolatus bite. A retrospective single-center observational study over 7 years (2011–2018) was carried out, including all patients admitted to the hospital because of B. lanceolatus bite. One hundred seventy snake-bitten patients (121 males and 49 females) were included. Thirty-nine patients (23%) presented grade 3 or 4 envenoming. Twenty patients (12%) developed wound infections. The isolated bacteria were Aeromonas hydrophila (3 cases), Morganella morganii (two cases), group A Streptococcus, and group B Streptococcus (one case each). Patients were treated empirically with third-generation cephalosporin (or amoxicillin–clavulanate), aminoglycoside, and metronidazole combinations. Outcome was favorable in all patients. The main factor significantly associated with the occurrence of infection following snakebite was the severity of envenoming (P < 0.05). Our findings clearly point toward the frequent onset of infectious complications in B. lanceolatus–bitten patients presenting with grade 3 and 4 envenoming. Thus, based on the bacteria identified in the wounds, we suggest that empiric antibiotic therapy including third-generation cephalosporin should be administered to those patients on hospital admission.

INTRODUCTION

Snakebites account for about 1.8–2.7 million envenoming and 81,000–138,000 deaths per year worldwide.1 In Martinique, about 30 cases of snakebite are recorded every year. Bothrops lanceolatus, a member of the Viperidae family, Crotalinae subfamily, is the only venomous species encountered in Martinique. Bothrops lanceolatus bite may result in severe thrombotic complications, including cerebral, pulmonary, and myocardial infarction, as well as coagulation disorders and endothelial injuries, which could be fatal or involve long-term sequelae.2–4 Thus, envenomed patients should promptly receive a specific antivenom to prevent such severe complications.

Snakebites are frequently responsible for local complications combining pain and local edema in the minutes following the bite, followed, in severe cases, by local necrosis and blistering. Wound infection may contribute to tissue necrosis, bacteremia, and even septic shock.5,6 Like in envenomings by other snakes, because data regarding the risk and outcome of infectious complications resulting from B. lanceolatus bite are poorly known, we designed this observational study to determine the incidence of wound infection in patients bitten by this species and describe the involved bacteria and the patients’ outcome.

PATIENTS AND METHODS

We conducted a retrospective single-center observational study at the University Hospital of Martinique from January 1, 2011 to September 4, 2018. In Martinique, all B. lanceolatus–bitten patients presenting with grade 3 and 4 envenoming. Thus, based on the bacteria identified in the wounds, we suggest that empiric antibiotic therapy including third-generation cephalosporin should be administered to those patients on hospital admission.

Because data regarding the risk and outcome of infectious complications resulting from B. lanceolatus bite are poorly known, we designed this observational study to determine the incidence of wound infection in patients bitten by this species and describe the involved bacteria and the patients’ outcome.

### Severity score of envenoming after Bothrops lanceolatus bite (adapted from ref. 11)

| Grade | Severity | Symptoms |
|-------|----------|----------|
| 1 | Minor | No swelling | No pain |
| 2 | Moderate | Local swelling confined to two segments of the bitten limb | Moderate pain |
| 3 | Severe | Regional edema, extension of swelling beyond two segments of the bitten limb | Persistent and resistant pain to analgesics |
| 4 | Major | Swelling spreading to the trunk | No general signs |

**Severity is defined by at least one confirmed item.**
are referred to our hospital because the BothroFav® antivenom is only available at our Emergency Department.

All patients admitted to the hospital for snakebite by B. lanceolatus during the study period were included. Patients with a history of snakebite but without medical or computer records and patients with a history of bite but without evidence of envenoming were excluded. Our database has been registered at the Commission Nationale de l’Informatique et des Libertés (registration n° 2213908 v 0.) in compliance with the French law on electronic data sources.

Data collection. Patients were selected using the medical information department database, the antivenom dispensing list, and the emergency department records. Clinical and biological data were collected from the patient medical records and the various emergency department software (Dx Care, X-plore, and cyberlab). We collected the usual demographic,

| Variables                        | Total patients (N = 170) | Infected patients (N = 20) | Noninfected patients (N = 150) | P-value |
|----------------------------------|--------------------------|---------------------------|--------------------------------|---------|
| Age (years)                      | 45 ± 18                  | 48 ± 15                   | 48 ± 18                         | 0.4     |
| Male, N (%)                      | 121 (71%)                | 15 (75%)                  | 106 (71%)                       | 0.7     |
| Hospitalization, N (%)           | 107 (63%)                | 20 (100%)                 | 87 (58%)                        | < 0.0001|
| Past medical history             |                          |                           |                                 |         |
| Snakebite, N (%)                 | 10 (6%)                  | 1 (5%)                    | 9 (6%)                          | 0.9     |
| Immunosuppression, N (%)         | 4 (2%)                   | 2 (10%)                   | 2 (1%)                          | 0.02    |
| Cardiovascular risk, N (%)       | 28 (17%)                 | 3 (15%)                   | 25 (17%)                        | 0.9     |
| Coagulopathy, N (%)              | 4 (2%)                   | 2 (10%)                   | 2 (1%)                          | 0.02    |
| Snakebite characteristics        |                          |                           |                                 |         |
| Time from envenoming to admission (hours) | 3.5 ± 4.3 | 3.7 ± 4.7 | 3.5 ± 4.3 | 0.8 |
| Snake captured, N (%)            | 45 (27%)                 | 8 (40%)                   | 37 (25%)                        | 0.1     |
| Site of the bite, N (%)          |                          |                           |                                 | 0.8     |
| Upper limb                       | 71 (42%)                 | 10 (50%)                  | 61 (41%)                        |         |
| Lower limb                       | 98 (58%)                 | 10 (50%)                  | 88 (59%)                        |         |
| Buttock                          | 1 (1%)                   | 0                         | 1 (1%)                          |         |
| Local bleeding, N (%)            | 91 (54%)                 | 11 (55%)                  | 80 (53%)                        | 0.9     |
| Local pain, N (%)                | 163 (96%)                | 19 (95%)                  | 144 (96%)                       | 0.833   |
| Envenoming grade, N (%)          |                          |                           |                                 |         |
| 1                                | 22 (13%)                 | 0                         | 22 (15%)                        | –       |
| 2                                | 109 (64%)                | 8 (40%)                   | 101 (67%)                       | –       |
| 3                                | 33 (19%)                 | 8 (40%)                   | 25 (17%)                        | –       |
| 4                                | 6 (4%)                   | 4 (20%)                   | 2 (1%)                          | –       |
| Clinical presentation and complications |                      |                           |                                 |         |
| Heart rate (beat/min)            | 80 ± 16                  | 79 ± 16                   | 80 ± 16                         | 0.9     |
| Temperature (°C)                 | 36.8 ± 0.8               | 37.1 ± 0.7                | 36.8 ± 0.5                      | 0.7     |
| Systolic arterial pressure (mmHg)| 137 ± 24                 | 128 ± 27                  | 139 ± 23                        | 0.04    |
| Diastolic arterial pressure (mmHg)| 80 ± 15                 | 75 ± 14                   | 81 ± 15                         | 0.1     |
| Mean arterial pressure (mmHg)    | 99 ± 16                  | 93 ± 17                   | 100 ± 16                        | 0.05    |
| SpO₂ (%)                         | 99 ± 2                   | 99 ± 1                    | 98 ± 2                          | 0.07    |
| Shock, N (%)                     | 3 (1.8%)                 | 3 (15%)                   | 0                               | –       |
| Consciousness impairment, N (%)  | 3 (1.8%)                 | 3 (15%)                   | 0                               | –       |
| Convulsion, N (%)                | 1 (0.6%)                 | 1 (5%)                    | 0                               | –       |
| Thrombosis, N (%)                | 1 (1%)                   | 0                         | 1 (1%)                          | –       |
| Compartmental syndrome, N (%)    | 6 (4%)                   | 5 (25%)                   | 1 (1%)                          | –       |
| Bacteremia, N (%)                | 3 (2%)                   | 3 (15%)                   | 0                               | –       |
| Laboratory parameters on admission |                      |                           |                                 |         |
| Creatine kinase (IU/L)           | 300 ± 283                | 311 ± 257                 | 298 ± 287                       | 0.9     |
| Platelet count (G/L)             | 238 ± 67                 | 213 ± 76                  | 241 ± 65                        | 0.07    |
| Prothrombin index (%)            | 96 ± 13                  | 92 ± 17                   | 97 ± 12                         | 0.09    |
| Activated partial thromboplastin time (minutes) | 31.5 ± 3.7 | 30.6 ± 3.6 | 31.6 ± 3.7 | 0.3 |
| Fibrinogen (g/L)                 | 3.0 ± 0.7                | 2.9 ± 1.0                 | 3.0 ± 0.6                       | 0.6     |
| C-reactive protein (mg/L)        | 7 ± 42                   | 31 ± 118                  | 4 ± 7                           | 0.009   |
| White blood cells (G/L)          | 7.8 ± 2.7                | 9.3 ± 3.6                 | 7.6 ± 2.4                       | 0.005   |
| Antivenom management             |                          |                           |                                 |         |
| Antivenom administration, N (%)  | 154 (91%)                | 19 (95%)                  | 135 (90%)                       | 0.5     |
| Number of vials                  | 1.7 ± 1.3                | 2.4 ± 1.5                 | 1.6 ± 1.3                       | 0.016   |
| Time from snakebite to antivenom administration (hour) | 6.0 ± 7.0 | 6.5 ± 8.9 | 5.9 ± 6.8 | 0.8 |
| Time from admission to antivenom administration (hour) | 3.2 ± 5.3 | 4.3 ± 7.5 | 3.1 ± 5.0 | 0.4 |
| Antivenom reinjection, N (%)     | 19 (12%)                 | 10 (53%)                  | 9 (7%)                          | < 0.001 |
| Empiric antibiotic administration, N (%) | 37 (22%) | 17 (85%) | 20 (13%) | – |
| Amoxicillin-clavulanate, N (%)   | 11 (6%)                  | 2 (10%)                   | 9 (6%)                          | –       |
| Third-generation cephalosporin, N (%) | 17 (10%) | 6 (30%) | 11 (7%) | – |
| Gentamycin, N (%)                | 12 (7%)                  | 4 (20%)                   | 8 (5%)                          | –       |
| Metronidazole, N (%)             | 12 (7%)                  | 5 (25%)                   | 7 (5%)                          | –       |
clinical, biological, microbiological, management, and outcome data. The signs suggestive of *B. lanceolatus* bite, the date of bite onset, the bite zone, and the time between the bite and antivenom administration (if administered) were sought. Monthly rainfall and maximal temperatures recorded in Martinique were obtained from the French national meteorological service (Météo France).

**Diagnosis and management of snakebite wound infection.** Wound infection following snakebite was defined as the presence of at least two local suggestive signs or as the presence of fever and/or chills and one local suggestive sign. Fever was defined as body temperature above 38°C measured using tympanic thermometer. Local signs suggestive of wound infection included pain, erythema, local warmth, swelling, lymphangitis, purulence, delayed healing, crepitus in soft tissues, discolored or friable granulation tissue, and wound breakdown or dehiscence, as previously listed.8,9 Because our study was retrospective, if no abnormality was mentioned in the patient record, it was assumed that no infectious complication had resulted from the snakebite.

In patients with local signs of infection, samples obtained from blood cultures, local sampling in case of purulence, and wound culture if patients had surgical debridement were sent to the bacteriology laboratory to identify the involved bacteria. Samples were subjected to Gram staining and examined for bacterial growth. They were plated on nonselective blood agar and chocolate agar and cultured at 37°C for 2–7 days, and the color and shape of the colonies were observed. Species identification was performed with API-20E and API-20NE systems (BioMérieux, Marcy L’Etoile, France). Antimicrobial susceptibilities of all isolates were determined by the disk diffusion method based on the definition of the Antibiogram Committee of the French Microbiology Society.10 The inhibition zone diameter of each drug for each isolate was determined using Student’s *t*-tests for continuous variables and Chi-squared tests for categorical variables. Correlation between variables was determined using linear regression. Data were analyzed using the Excel (2007) and SPSS program version 24. *P*-values < 0.05 were considered as significant.

**RESULTS**

During the 8-year study period, 170 patients (age: 45 ± 18 years, including seven children (4%); male-to-female gender ratio of 2.5) were referred to our hospital for snakebite management (Table 2).

**Incidence.** The number of snakebites was 21 cases per year (Figure 1A), corresponding to an incidence rate of six bites per 100,000 inhabitants per year in Martinique. Monthly distribution of snakebites showed peak incidence in June, July, and September, with an average of two bites per month (Figure 1B and C). No significant relationship between the seasonal incidence of snakebite and precipitation registered by the French national meteorological service was observed (Figure 2A), whereas the number of snakebites significantly increased when the recorded maximal temperature was above 30°C (*R*² = 0.33; Figure 2B and C).

**Presentation and post-snakebite infection onset.** On hospital admission, 39 patients (23%) presented with grade 3 or 4 envenoming. Twenty patients (12%) had clinical signs suggestive of post-snakebite infections. Bacteriological samples were positive in seven cases (35%). The isolated bacteria were *M. morganii* in two cases, *A. hydrophila* in three cases, *Streptococcus A* in one case, and *Streptococcus B* in one case. All isolated *M. morganii* and *A. hydrophila* were susceptible to third-generation cephalosporins. The main factor associated with the occurrence of infection following snakebite was the severity of the bite. Twelve patients (31%) developed infection in the severely envenomed patients versus eight (6%) in the non-severely envenomed patients (*P* < 0.0001; Figure 3).

**Management and outcome.** Seventy-nine patients (46%) were admitted to the medical ward, 25 (15%) to the intensive care unit (ICU), and three (2%) to the surgical ward, whereas 63 (37%) were discharged after management in the emergency department. Almost all patients (93%) were treated with the specific BothroFav antivenom. It is noteworthy that patients presenting infections more frequently required antivenom readministration than those without infection (53% versus 7%, *P* < 0.001; Table 2). Based on the severity of the envenoming grade and the suspicion of local infection, 37 patients received one antibiotic or a combination of antibiotics. The following antibiotics were administered empirically: third-generation cephalosporin in 17 (10%) patients, amoxicillin–clavulanate in 11 (6%) patients, gentamycin in 12 (7%) patients, and metronidazole in 12 (7%) patients.

The complications observed during hospitalization are reported in Table 3. No myocardial infarction or brain stroke occurred. No patient died. Length of hospital stay was 3 ± 5 days (6 ± 9 days in the ICU versus 3 ± 4 days in the other hospital wards, *P* = 0.01). Length of hospital stay significantly increased according to the severity grade of the snakebite (*R*² = 0.77; Figure 4) and was significantly longer in patients with infection (11 ± 10 versus 2 ± 1 days, *P* < 0.0001).
DISCUSSION

Infection following *B. lanceolatus* bite is relatively frequent (12% in our case series), and patients at highest risk are those presenting with severe envenoming (grades 3 and 4). The bacteria responsible for wound infection are those commonly isolated from the snake mouth, suggesting that the main source of contamination comes from the snake causing the bite.

Wound infection following snakebite usually accounts for 9–77% of the bitten patients, as described in several studies (Table 4).5,6,8,12–15 The large differences in the reported prevalence of secondary infections in snakebites between different studies can be related to variations in the criteria used to establish the presence of infection. A strict criterion is the laboratory isolation and identification of bacteria from the affected tissues or blood in envenomed patients. However, clinical criteria are also used to diagnose infection. In this regard, discrepancies may arise because some clinical manifestations of local infection can also be caused by the action of venom toxins in the tissue, associated with inflammation. In our study, infection was defined as the presence of two of the following local signs: pain, erythema, local warmth, swelling, lymphangitis, purulence, delayed healing, crepitus in soft tissues, discolored or friable granulation tissue, and wound breakdown or dehiscence, or alternatively, the presence of fever and/or chills and at least one of these signs.8,9 Thereafter, in patients with local signs of infection, samples were obtained from local tissues, fluids, and blood and sent to the laboratory for bacterial culture and identification. In case of sterile microbiological cultures, the diagnosis of infection was assessed according to clinical and biological parameters. Indeed, initial antibiotic therapy can result in negative...
microbiological culture, and the prevalence of patients who developed wound infection secondary to snakebite could not be calculated as only those with positive microbiological cultures.\textsuperscript{16,17} Future studies should attempt to develop a more uniform set of criteria to define infection in snakebite envenomings to harmonize parameters that would allow comparison between studies.

The main involved bacteria are \textit{A. hydrophila} (Gram-negative bacilli), recognized to cause soft tissue infections and necrotizing fasciitis.\textsuperscript{18} \textit{Aeromonas hydrophila} is generally recognized to cause soft tissue infections and necrotizing fasciitis.\textsuperscript{18}
found in sewage, freshwater, stagnant water, and feces. Other bacteria such as *M. morganii* have also been isolated in abscesses after *B. lanceolatus* bite. They are also found in the mouth and on the fangs of these vipers. Staphylococci, group D streptococci, *Clostridium*, *Escherichia coli*, and *Enterococcus faecalis*, involved in wound infection, have been also isolated from the mouth of viperid species. *Serratia marcescens* is rarely isolated from cellulitis following snakebite but may be responsible for bullous cellulitis. By contrast, *Staphylococcus aureus* is not commonly isolated from the snake mouth, suggesting that if the organism causes post-snakebite infections, it probably originates from the patient’s skin rather than having been inoculated by the snake fangs. Therefore, strict disinfection of the bite site should systematically be performed. In the snake mouth is colonized by bacteria which can be transmitted to the bitten patient through the skin injury associated with the bite. Inoculation of bacteria from the mouth, fangs, or venom of *B. lanceolatus* following a bite can cause local infection with abscess and necrotizing fasciitis in the most severe cases, as described in other cases of snakebites. Based on the most frequently isolated bacteria in the snakebite site according to the literature (Table 4), active antibiotics include third-generation cephalosporins, piperacillin–tazobactam, and ciprofloxacin. Conformingly, in one recent study, isolated Enterobacteriaeae following snakebite infection showed 69% resistance to ampicillin, 60% resistance to amoxicillin–clavulanate, and 66% resistance to second-generation cephalosporins. By contrast, bacteria were sensitive to ceftriaxone in 97% of the cases and sensitive to ciprofloxacin and aminoglycosides in 100% of the cases. *Enterococcus faecalis* showed 92% sensitivity to ampicillin and amoxicillin–clavulanate and 100% sensitivity to ciprofloxacin. A recent experimental study examining the bacteria sampled from the oral cavity of 26 *B. lanceolatus* specimens collected from various areas in Martinique supported that microbiota from *B. lanceolatus* oral cavity was polymicrobial. The most frequently isolated bacteria were *A. hydrophila* (present in 50% of the samples), *M. morganii*, *K. pneumoniae*, *Bacillus* spp., and *Enterococcus* spp. Analysis of antibiotic susceptibility revealed that 67% of the isolated bacteria were resistant to amoxicillin–clavulanate. By contrast, most of the isolated bacteria were susceptible to third-generation cephalosporins (i.e., 73% to cefotaxime and 80% to cefazidime). Similar data were also reported in the oral microbiota of snakes from Brazil and India.

Despite snake oral and fang contamination with a wide variety of pathogenic bacteria, envenoming can be seen as a process associated with relatively limited risk of bacterial infection, except in cases associated with prominent tissue damage at the site of venom injection. Antibacterial effects of snake venoms may limit the likelihood of infection. Bactericidal activity against Gram-positive and Gram-negative bacteria was attributed to various components, including L-amino acid oxidases and phospholipase A2 enzymes. However, these bactericidal effects are likely to decrease once the venom has been injected. Soft tissue infection occurs in patients suffering severe envenomings (grade 3 or 4) in which the injected venom amount is likely to be high. Therefore, it is suggested that venom-induced skin and muscle damage is favorable for bacterial colonization and constitutes the bed of infection, as has been shown in an experimental model in mice.

In the Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections, use of antimicrobial agents active against both aerobic and anaerobic bacteria, such as amoxicillin–clavulanate, is recommended in bitten patients. However, the widespread systematic antibiotic administration is questionable after snakebite. Most authors recommend antibiotics in severely bitten patients, especially when local tissue damage occurs and inflammatory signs are suggestive of infection. Interestingly, empiric amoxicillin–clavulanate use was shown to be ineffective in preventing secondary infections from *Bothrops* snakebites because of the resistance to β-lactam antibiotics in the bacterial species commonly found infecting the snakebite site. Recently, analysis of the antibiotic susceptibility of bacteria isolated from *B. lanceolatus* mouth showed 67% of strains resistant to amoxicillin–clavulanate, whereas most isolated bacteria were

---

**Table 3**

Local signs recorded in 170 infected and noninfected Bothrops lanceolatus–bitten patients.

|                      | Total patients (N = 170) | Infected patients (N = 20) | Noninfected patients (N = 150) |
|----------------------|--------------------------|---------------------------|-------------------------------|
| Increasing pain      | 28 (17%)                 | 20 (100%)                 | 8 (5%)                        |
| Absscess             | 7 (4%)                   | 7 (35%)                   | 0                             |
| Erythema             | 17 (10%)                 | 16 (80%)                  | 1 (1%)                        |
| Cellulitis           | 4 (2%)                   | 4 (20%)                   | 0                             |
| Necrosis             | 5 (3%)                   | 5 (25%)                   | 0                             |
| Necrotic fasciitis   | 1 (1%)                   | 1 (5%)                    | 0                             |
| Gangrene             | 0                        | 0                         | 0                             |

---

**Figure 3.** Prevalence of infection according to the grade of envenoming. This figure appears in color at www.ajtmh.org.

**Figure 4.** Length of hospital stay according to the grade of envenoming in 170 Bothrops lanceolatus–bitten patients.
| Reference          | Year of publication | Geographic region | Responsible snake                                      | Number of bitten patients, N | Number of infected patients, N (%) | Number of positive samples, N (%) | Number of isolated strains, N | Aerobic Gram-positive bacteria, N (%) | Aerobic Gram-negative bacteria, N (%) | Anaerobic bacteria, N (%) | No growth (% of infected patients), N (%) |
|--------------------|---------------------|-------------------|-------------------------------------------------------|-----------------------------|-----------------------------------|----------------------------------|---------------------------------|--------------------------------------|--------------------------------------|---------------------------------|------------------------------------------|
| Chen et al.        | 2011                | Taiwan            | Trimeresurus mucrosquamatus, T. stejnegeri, N. atra   | 231                         | 21 (9%)                           | 21 (100%)                        | 61                              | 14 (23%)                            | 39 (64%)                            | 8 (13%)                        | 0 (5%)                                    |
| Mao et al.         | 2016                | Taiwan            | Naja atra                                             | 112                         | 86 (77%)                          | 50 (58%)                         | 113                              | 21 (24.8%)                          | 77 (68.1%)                          | 1 (6.2%)                      | 1 (0.9%)                                  |
| Hsieh et al.       | 2017                | Taiwan            | Taiwan cobra, Bamboo viper                            | 148                         | 42 (28%)                          | 21 (50%)                         | 49                              | 11 (27%)                            | 24 (49%)                            | 1 (3%)                         | 9 (18%)                                   |
| Wagener et al.     | 2017                | South Africa      | Naja mossambica                                       | 164                         | 42 (26%)                          | 40 (65%)                         | 66                              | 31 (47%)                            | 35 (53%)                            | 11 (6%)                        | 3 (135%)                                  |
| Garg et al.        | 2009                | India             | –                                                     | –                           | –                                 | –                                | –                               | –                                    | –                                    | –                              | –                                         |
| Sachett et al.     | 2017                | Brazil            | Bothrops sp.                                          | –                           | –                                 | –                                | –                               | –                                    | –                                    | –                              | –                                         |
| Jorge et al.       | 1994                | Brazil            | Bothrops jararaca                                     | 187                         | 74 (40%)                          | 43                               | 53                              | 42 (14%)                            | 25 (47%)                            | 11 (6%)                        | 0 (68%)                                   |
| Our study          | 2019                | Martinique        | Bothrops lanceolatus                                  | –                           | 40                                | 74 (40%)                         | 7                               | 40                                  | 37 (69%)                            | 5 (25%)                        | 13 (65%)                                  |

RESIERE AND OTHERS
susceptible to third-generation cephalosporins.\(^7\) In our hospital, empiric cephalosporin (or amoxicillin–clavulanate), aminoglycoside, and metronidazole combinations are routinely used in grade 3 or 4 envenoming and in case of clinical evidence of infection. Ciprofloxacin is the antibiotic of choice in case of allergy to \(\beta\)-lactams. This antibiotic treatment strategy probably explains the low prevalence of positive cultures (only 35\%) from our patients’ samples in comparison to other reports in the literature (Table 4). However, we do not support the systematic antibiotic administration in all snake-bitten patients to reduce the risk of infection because such prophylactic use (including in non-severely envenomed patients) may have little impact on further infection but may give rise to side effects and select resistant organisms. Antibiotic administration should be considered only in patients having prominent local tissue damage and inflammation.

Our study has limitations. The diagnosis of wound infection involves repeated clinical assessment, biological dosing, and microbiological cultures. The involved bacteria were only identified in a limited number of cases having clinical evidence of infection possibly because of the difficulties of wound sampling in the emergency department and the fact that sample collection was performed after the antibiotic administration in some cases. This diagnostic approach is approved by many authors working on the diagnosis of wound infection and how to differentiate true infection from colonization.\(^8,9,16,17\) Further studies are needed to assess the sensitivity and specificity of clinical and biological parameters to assess the diagnosis of wound infection following snakebite independently of the microbiological results. In our study, anaerobic bacteria were not identified, although they are reported to be one of the responsible microorganisms causing cellulitis following snakebite. This is explained by the lack of bacteriological media for the isolation of anaerobic bacteria in our work. Our retrospective study methodology also limited further analysis. In addition, no clear indications and determined regimen of antibiotics were available, and treatment was only based on the judgment of the physicians in charge of the patients.

In conclusion, wound infection following \emph{B. lanceolatus} bite is relatively frequent in grade 3 and 4 envenomed patients. The main involved bacteria are \emph{A. hydrophila} and \emph{M. morganii}. The empirical scheme for antibiotics adapted to the bacterial ecology of \emph{B. lanceolatus} oral cavity are recommended for at least patients with grade 3 and 4 envenoming or having signs suggestive of local infection, regardless of the degree of envenoming. Our data support that the most appropriate empirical antibiotics are third-generation cephalosporins and that empirical amoxicillin–clavulanate should no longer be used in this context.

Received May 13, 2019. Accepted for publication July 12, 2019.

Acknowledgment: ANR generique Mitobothrops R. N. 2018

Authors’ addresses: Dabor Resiere, Hossein Mehdaoui, Adeline Beaudoin, Jonathan Florentin, Yannick Brouste, and Rishika Banydeen, Department of Critical Care, University Hospital of Martinique, Fort-de-France, France, E-mails: dabor.reziere@chu-martinique.fr, hossein.mehdaoui@chu-martinique.fr, adelinebeaudoin@gmail.com, jonathan.florentin@chu-martinique.fr, yannick.brouste@chu-martinique.fr, and rishika.banydeen@chu-martinique.fr. Rémi Névrière, Department of Cardiology, University Hospital of Martinique, Fort-de-France, France, E-mail: remi.nevriere@chu-martinique.fr. Claude Olive, Department of Microbiology, University Hospital of Martinique, Fort-de-France, France, E-mail: claude.olive@chu-martinique.fr. Mathieu Severyns, Department of Orthopedic Surgery, University Hospital of Martinique, Fort-de-France, France, E-mail: mathieu.severyns@chu-martinique.fr. André Cabié, Department of Infectious Diseases, University Hospital of Martinique, Antilles University, Fort-de-France, France, E-mail: andre.cabie@chu-martinique.fr. Bruno Mégarbane, Department of Medical and Toxicological Critical Care, Lariboisière Hospital, Paris-Diderot University, Paris, France, E-mail: bruno.megarbane@aphp.fr. José María Gutiérrez, Instituto Molodrom Picado, Facultad de Microbiología, Universidad de Costa Rica, San José, Costa Rica, E-mail: jose.gutierrez@ucr.ac.cr. Hatem Kallel, Intensive Care Unit, Cayenne General Hospital, Cayenne, France, E-mail: hatem.kallel@ch-cayenne.fr.

This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

REFERENCES

1. Gutiérrez JM, Calvete JJ, Habib AG, Harrison RA, Williams DJ, Warrell DA, 2017. Snakebite envenoming. Nat Rev Dis Primers 3: 17063.

2. Resiere D, Hossein M, Mégarbane B, 2018. Snake bites by \emph{Bothrops lanceolatus} in Martinique. Med Sante Trop 28: 37–43.

3. Thomas L, Chausson N, Uzan J, Kaidmar S, Vignes R, Plumelle Y, Bucher B, Smadja D, 2006. Thrombotic stroke following snake bites by the “Fer-de-Lance” \emph{Bothrops lanceolatus} in Martinique despite antivenom treatment: a report of three recent cases. Toxicon 48: 23–28.

4. Thomas L et al., 1998. Prognostic significance of clinical grading of patients envenomed by \emph{Bothrops lanceolatus} in Martinique. Trans R Soc Trop Med Hyg 92: 542–545.

5. Garg A, Sujatha S, Garg J, Acharya NS, Chandra Parija S, 2009. Wound infections secondary to snakebite. J Infect Dev Cities 3: 221–223.

6. Wagener M, Naidoo M, Aldous C, 2017. Wound infection secondary to snakebite. S Afr Med J 107: 315.

7. Résière D, Olive C, Kallel H, Cabié A, Névrière R, Mégarbane B, Gutiérrez JM, Mehdaoui H, 2018. Oral microbiota of the snake \emph{Bothrops lanceolatus} in Martinique. Int J Environ Res Public Health 15: E2122.

8. Mao YC, Liu PY, Hung DZ, Lai WC, Huang ST, Hung YM, Yang CC, 2016. Bacteriology of \emph{Naja atra} snakebite wound and its implications for antibiotic therapy. Am J Trop Med Hyg 94: 1129–1135.

9. Huang LW, Wang JD, Huang JA, Hu SY, Wang LM, Tsan YT, 2012. Wound infections secondary to snakebite in central Taiwan. J. Venom Anim Toxins Incl Trop Dis 18: 272–276.

10. Soussy CJ et al., 2000. Antibiogram committee of the French Microbiology Society. Report 2000–2001. Pathol Biol (Paris) 48: 832–871.

11. Resiere D, Mégarbane B, Valentino R, Mehdaoui H, Thomas L, 2010. \emph{Bothrops lanceolatus} bites: guidelines for severity assessment and emergent management. Toxins (Basel) 2: 163–173.

12. Chen CM, Wu KG, Chen CJ, Wang CM, 2011. Bacterial infection in association with snakebite: a 10-year experience in a Northern Taiwan medical center. J Microbiol Immunol Infect 44: 456–460.

13. Hsieh YH, Hsueh JH, Liu WC, Yang KC, Hsu KC, Lin CT, Ho YY, Chen LW, 2017. Contributing factors for complications and outcomes in patients with snakebite: experience in a medical center in southern Taiwan. Ann Plast Surg 78 (3 Suppl 2): S31–S36.

14. Jorge MT, Ribeiro LA, Da Silva MLR, Kusano EJU, de Mendonça JS, 1994. Microbiological studies of abscesses complicating \emph{Bothrops} snakebite in humans: a prospective study. Toxicon 32: 743–748.

15. Sachett JAG et al., 2017. Poor efficacy of preemptive amoxicillin clavulanate for preventing secondary infection from \emph{Bothrops}
snakebites in the Brazilian Amazon: a randomized controlled clinical trial. PLoS Negl Trop Dis 11: e0005745.

16. Ki V, Rotstein C, 2008. Bacterial skin and soft tissue infections in adults: a review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. Can J Infect Dis Med Microbiol 19: 173–184.

17. Cefalu JE, Barrier KM, Davis AH, 2017. Wound infections in critical care. Crit Care Nurs Clin North Am 29: 81–96.

18. Gold WL, Salit IE, 1993. Aeromonas hydrophila infections of skin and soft tissue: report of 11 cases and review. Clin Infect Dis 16: 69–74.

19. Jorge MT, de Mendonça JS, Ribeiro LA, da Silva ML, Kusano EJ, Cordeiro CL, 1990. Bacterial flora of the oral cavity, fangs and venom of Bothrops jararaca: possible source of infection at the local bite. Rev Inst Med Trop Sao Paulo 32: 6–10.

20. Lam KK et al., 2011. A cross-sectional survey of snake oral bacterial flora from Hong Kong, SAR, China. Emerg Med J 28: 107–114.

21. Shaikh IK, Dixit PP, Pawade BS, Potnis-Lele M, Kurhe BP, 2017. Assessment of cultivable oral bacterial flora from important venomous snakes of India and their antibiotic susceptibilities. Curr Microbiol 74: 1278–1286.

22. Al-Asmari AK, Abbassmanthiri R, Abdo Osman NM, Siddiqui Y, Al-Bannah FA, Al-Rawi AM, Al-Asmari SA, 2015. Assessment of the antimicrobial activity of few Saudi Arabian snake venoms. Open Microbiol J 9: 18–25.

23. Bustillo S, Leiva LC, Acosta O, Bal de Kier Joffé E, Gorodner JO, 2008. Antimicrobial activity of Bothrops alternatus venom from the northeast of Argentina. Rev Latinoam Microbiol 50: 79–82.

24. Hakim Md, Reza M, 2015. In vitro antibacterial activity of snake venom, Naja naja from Bangladesh. Br Biotechnol J 8: 1–5.

25. Nascimento Canhas I, Dias Heneine LG, Fraga T, Sampaio de Assis DC, Borges MH, Chartone-Souza E, Amaral Nascimento AM, 2017. Antibacterial activity of different types of snake venom from the Viperidae family against Staphylococcus aureus. Acta Scientiarum Biol Sci 39: 309–319.

26. Perumal Samy R, Gopalakrishnakone P, Thwin MM, Chow TK, Bow H, Yap EH, Thong TWJ, 2007. Antimicrobial activity of snake, scorpion and bee venoms: a comparison with purified venom phospholipase A2 enzymes. J Appl Microbiol 102: 650–659.

27. Santamaria C, Larios S, Angulo Y, Pizarro-Cerda J, Gorvel J-P, Moreno E, Lomonte B, 2005. Antimicrobial activity of myotoxic phospholipases A2 from crotilid snake venoms and synthetic peptide variants derived from their C-terminal region. Toxicon 45: 807–815.

28. Saravia-Otten P, Gutierrez JM, Arvidson S, Thelestam M, Flock JL, 2007. Increased infectivity of Staphylococcus aureus in an experimental model of snake venom-induced tissue damage. J Infect Dis 196: 748–754.

29. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJC, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC, 2014. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis 59: 147–159.