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Guidelines for the diagnosis and differential diagnosis of snakebite envenoming of ruminants in Brazil[1]

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ABSTRACT.- Graça F.A.S., Caldas S.A., França T.N., Brust L.A., Nogueira V.A., Cecco B.S., Santos B.B.N. & Peixoto P.V. 2022. **Guidelines for the diagnosis and differential diagnosis of snakebite envenoming of ruminants in Brazil.** *Pesquisa Veterinária Brasileira 42:e07105, 2022.* Centro de Ciências e Tecnologias Agropecuárias, Universidade Estadual do Norte Fluminense Darcy Ribeiro, Av. Alberto Lamego 2000, Parque Califórnia, Campos, RJ 28013-602, Brazil. E-mail: flaviovet1968@gmail.com

In Brazil, snakebites are often cited as a cause of mortality in ruminants, but there are discrepancies in the literature regarding its actual prevalence, either by lack of diagnosis or by mistakes in the differential diagnosis. Among the factors that hinder the diagnosis are included the inconsistencies to distinguish between accidents caused by *Bothrops* and *Crotalus*, responsible for over 90% of the cases. For the diagnosis of accidents involving *Lachesis muta*, both the neurotropic and the proteolytic/hemolytic effects must be considered, similar to what is described in *Crotalus scutulatus*. This article describes the main clinical, pathological, and laboratory findings observed in envenoming by the aforementioned snakes and suggests procedures for establishing the diagnosis and differential diagnosis starting from a logical sequence, based on epidemiological evidence, clinical, laboratory, and pathological findings.

INDEX TERMS: *Bothrops*, *Crotalus*, snakebite, diagnosis, ruminants, Brazil.

RESUMO.- [**Diretrizes para o diagnóstico e diagnóstico diferencial de envenenamento por picadas de cobra em ruminantes no Brasil.**] No Brasil, acidentes ofídicos são frequentemente citados como causa de mortalidade em ruminantes, mas existem discrepâncias em relação a sua atual prevalência, seja por falta de diagnóstico ou por erros no diagnóstico diferencial. Entre os fatores que dificultam o diagnóstico estão as inconsistências para distinguir entre os acidentes causados por *Bothrops* e *Crotalus,* responsáveis por mais de 90% dos casos. Para o diagnóstico de envenenamentos por *Lachesis muta*, devem ser considerados os efeitos neurotrópico e proteolítico/hemolíticos concomitantes, a exemplo do que ocorre com algumas cascavéis norte-americanas (*Crotalus scutulatus*, entre elas). Este artigo descreve os principais achados clinicopatológicos e laboratoriais observados em casos de envenenamento pelas serpentes citadas e sugere um roteiro simplificado para o estabelecimento do diagnóstico e diagnóstico diferencial, a partir de uma sequência lógica, baseada em evidências epidemiológicas e achados clínicos, laboratoriais e patológicos.

TERMOS DE INDEXAÇÃO: *Bothrops, Crotalus*, picada de cobra, diagnóstico, ruminantes, Brasil.

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INTRODUCTION

In general, it is believed that snakebites are very frequent and cause severe economic losses for farmers in Brazil. In relatively recent studies, some authors, questioned the belief that snake envenomings are a common cause of deaths in cattle, and pointed out that these deaths attributed to snakebites may have other causes (Tokarnia & Peixoto 2006, Graça et al. 2008, Caldas et al. 2008, Aragão et al. 2010, Barbosa et al. 2011, Tokarnia et al. 2014). For example, the literature reveals several contradictions and gaps in the clinicopathological signs associated with envenoming by snakes of the genera *Bothrops* and *Crotalus*[8] (Tokarnia & Peixoto 2006). To our knowledge, no description regarding the clinicopathological aspects of envenomings caused by *Lachesis* and *Micrurus* in farm animals is available in the literature.

Regarding snakes of the *Bothrops* genus, the remarkable variation of the venom chemical composition can lead to systemic bleeding, local necrosis, hemodynamic changes, or both. It was also found that the species of the animals bitten by *Crotalus durissus* might present significant variation in the clinicopathological findings. For example, myoglobinuria is a common symptom in humans bitten by the South American rattlesnake (Jorge & Ribeiro 1992, Barraviera 1999, Seifert et al. 2022), but this sign does not seem to occur in cattle (Birgel et al. 1983, Graça et al. 2008). On the other hand, horses inoculated with *Crotalus durissus* venom develop marked local edema, which is not a characteristic observed in cattle or humans (Barraviera 1999, Paula Neto et al. 2005, Souza et al. 2011). Since there is scarce literature covering the real prevalence of snakebite in livestock, without accurate description of clinical signs, gross and microscopic findings, this study aims determining procedures and providing simplified guidelines for establishing the diagnosis and differential diagnosis of *Crotalus* and *Bothrops* snakebites in ruminants.

DISTRIBUTION OF *BOTHROPS* AND *CROTALUS* IN BRAZIL

In general, snakes of the genus *Crotalus* prefer dry rocky places, or deforestation areas, while *Bothrops* occur most often in tropical areas such as wetlands, banks of rivers, and lakes (Bastos et al. 2005, Tozetti & Martins 2008). However, there are some variations, as in the case of *Bothrops neuwied* (Valle & Brites 2008). It is important to emphasize that the snake populations are subjected to changes, according to climate and habitat conditions. It has been observed that the genus *Crotalus* has tended to disappear from states like Rio Grande do Sul. Whereas in Minas Gerais and Rio de Janeiro (RJ) States, these snakes have colonized certain areas on the banks of the Rio Preto River, and the cities of Valença, Rio das Flores and Resende (RJ) (Melgarejo 2003, Bastos et al. 2005) (Fig.1).

CHARACTERISTICS OF SNAKE VENOM

Snake venom is a complex mixture of proteins, nucleotides, and inorganic ions. These combinations confer a formidable array of toxic properties on the venom. The peptides and polypeptides are responsible for a variety of toxic properties (Chandra et al. 2020). The concentrations of the toxic components of the venom vary according to ontogenetic differences, geographic location, season, sex, diet, and age of the snake. Qualitative and quantitative differences and inoculation sites determine biological or clinical responses that diverge according to the individual affected (Furtado et al. 1991, Hudelson & Hudelson 1995, Magro et al. 2001, Zelanis et al. 2010, Saad et al. 2012, Lourenço Jr. et al. 2013).

THE CROTALIC VENOM - SOUTH AMERICAN RATTLESNAKES

The venom produced by *Crotalus durissus terrificus* contains several toxins such as crotalin, gyroxin, and convulxin (Varanda & Giannini 1999). Crotoxin, the main toxin, is responsible for progressive muscular hypotonia which culminates in animal death by respiratory paralysis. This toxin is composed of two subunits: phospholipase A_2 which has potent neurotoxic effects characterized by inhibition of acetylcholine release, and crotapotin which potentiates the action of phospholipase (Brazil 1980, Graça et al. 2008). This protein complex is also responsible for systemic selective changes in the membranes of skeletal muscle fibers of type I (slow-twitch fibers) and IIA (fast-twitch fibers). The toxins crotalin, gyroxin, and convulxin, are less relevant in cases of fatal envenoming in ruminants caused by South American *Crotalus* snakes (Varanda & Giannini 1999, Radostits et al. 2000, Salvini et al. 2001). These changes in the membranes of fibers caused coagulation necrosis of individual fibers or small groups of fibers in skeletal muscle of experimentally poisoned cattle (Graça et al. 2008).

THE BOTHROPIC VENOM

The myotoxic effect of the venom produced by snakes of the genus *Bothrops* has been linked to the action of phospholipase A_2, directly affecting the plasma membrane of muscle cells. However, it can additionally be determined by the indirect action of hemorrhagic metalloproteinases that degenerate the blood vessels, leading to tissue ischemia and eventually necrosis (Ferreira et al. 1992). The effect of phospholipase A_2 varies according to the *Bothrops* species and can trigger the release of chemical mediators such as histamine, bradykinin, eicosanoids, cytokines, and nitric oxide (Teixeira et al. 1994). The clotting activity is a response to the proteolytic action of metalloproteinases that degrade the basal membrane and activate or inhibit components of the coagulation cascade affecting the endothelial cells of the capillaries directly. The serine proteinases have coagulant activity of the thrombin type whereas the integrins block the fibrinogen receptor (Melo et al. 2004, Barbosa 2007, França & Málaque 2009).

The proteolytic action is more concentrated in the venoms of *B. atrox*, *B. erythromelas, B. jararaca,* B. *moojeni*, and *B. pradoi*. Furthermore, the phospholipase activity is low in *B. alternatus* and *B. atrox* and not frequently detected in *B. cotiara*. The necrotizing activity is predominant in the venoms of *B. neuwiedi* and *B. pradoi* while the myotoxic activity is more intense in *B. jararacussu* and *B. pradoi* (Ferreira et al. 1992). The venoms derived from the species *B. jararaca, B. moojeni,* and *B. neuwiedi* have been found to have predominantly

[8] Recently, there was an unsuccessful attempt to change the nomenclature of certain snakes of the *Bothrops* genus to *Bothropoides* and *Rhinocerophis*, and of the *Crotalus* genus to *Caudisona* (Bernarde 2011).

hemorrhagic and proteolytic action in sheep (Mandelbaum et al. 1982, Rocha & Furtado 2005, Aragão et al. 2010, Cunha & Martins 2012, Diefenbach et al. 2012). Similarly, the venom of *B. jararacussu* is characterized by causing proteolytic action and mild hemorrhagic action in sheep (Dos Santos et al. 1992, Franco 2003, Tsetlin & Hucho 2004, Aragão et al. 2010). In horses, inflammatory and hemorrhagic action has been reported in animals naturally poisoned by *B. pauloensis* (Franco 2003, Tsetlin & Hucho 2004, Pereira et al. 2010).

OCCURRENCE OF *BOTHROPS* AND *CROTALUS* SNAKEBITES IN BRAZIL

In veterinary medicine literature, there are two cases of dogs, both nonfatal, related to *Bothrops* and *Crotalus* snakebite. The first, a bothropic accident that happened in São Paulo, but the snake species was not identified and the second was envenoming by *C. durissus terrificus* (Ferreira Júnior & Barraviera 2001, Collicchio et al. 2002). There are also scientific reports on bothropic envenoming of horses in Brazil with the description of a fatal case in a foal (Raposo et al. 2000, 2001). In 2011, the envenoming of three horses was caused by a single specimen of *Bothrops pauloensis* (Chiacchio et al. 2011). In Pará, another fatal case caused by bothropic envenoming was described in an equine (Silva et al. 2011).

Based on a survey performed across Brazil, Tokarnia & Peixoto (2006) suggested that fatal snakebites in cattle are much less frequent than previously thought and their occurrence is overestimated. In Brazil, seven cases of natural envenoming by *Bothrops* snakes have been described, and from all animals bitten, only a one-day-old calf died (Menezes 1995/96). In the state of Rio Grande do Sul, only one animal died of the four cows with signs of bothropic envenoming seen at the Veterinary Hospital (Grunert 1967, Grunert & Grunert 1969). Also, in Rio Grande do Sul, in just five months, it was reported that 22 out of 123 sheep were bitten by *Bothrops neuwiedi,* and 11 died (Méndez & Riet-Correa 1995).

Tokarnia et al. (2008) reported that four sheep, housed in the same stall, were bitten by the same *B. jararaca*. Although no animal died spontaneously, one of them was euthanized for scientific reasons. Two snakebite outbreaks by *Bothrops alternatus* were reported in Santa Catarina, causing the death of 15 and 8 sheep, respectively, while grazing near rocky areas (Gabardo et al. 2010).

CLINIC AND PATHOLOGICAL FINDINGS OF SNAKEBITE ENVENOMING IN RUMINANTS

Given the difficulty of following natural cases of snakebite envenoming in ruminants, the data found in the literature largely comes from experimental envenoming in cattle and sheep (Tokarnia & Peixoto 2006). In the case of *Crotalus* envenoming in cattle, clinical signs generally appear between one and eight hours after inoculation (Lago et al. 2000). On

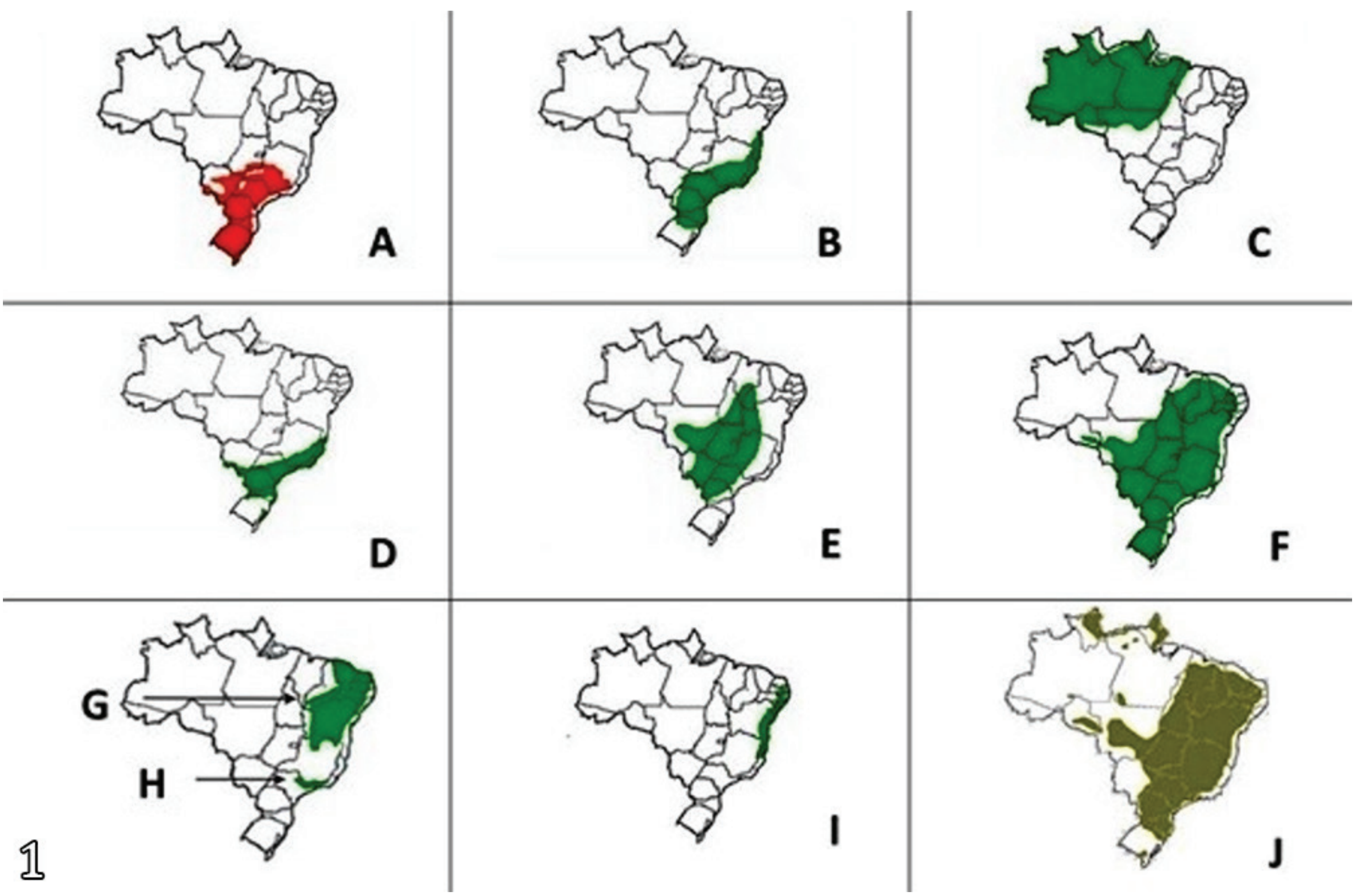


Fig.1. Geographical distribution of the most common snakes in Brazil. *Bothrops alternatus* (A). *B. jararaca* (B). *B. atrox* (C). *B. jararacuçu* (D). *B. moojeni* (E). *B. neuwiedi* (F). *B. erythromelas* (G). *B. fonsecai* (H). *B. leucurus* (I). *Crotalus durissus terrificus* (J). (Zelanis et al. 2010)

the other hand, the clinical evolution varies according to the inoculated dose and individual sensitivity, ranging from 5 to 44 hours in animals that died up to 17 days after inoculation and those that recovered (Belluomini et al. 1982, Saliba et al. 1983, Lago et al. 2000, Graça et al. 2008, Barbosa et al. 2011).

The clinical signs of bothropic envenoming start earlier and may range from seven minutes to one hour after the experimental infection. The venom of *Bothrops jararaca* induces the faster onset of signs, followed by *B. jararacuçu, B. moojeni, B. neuwiedi*, and *B. alternatus*. The clinical evolution period can vary between seven and 66 hours in animals that died and were extended for another 13 days in animals that recovered (Caldas et al. 2008, Graça et al. 2008, Aragão et al. 2010, Diefenbach et al. 2012). In experimentally poisoned sheep, the evolution period ranged between 22 hours and 13 days. Sheep injected with *Bothrops* venom showed initial signs between 16 minutes and an hour while clinical evolution lasted between seven and nine hours approximately. In one case in which a sheep was bitten by *B. jararaca*, the local swelling began immediately after the bite, but total involution of the injuries occurred within five days (Tokarnia et al. 2008).

CLINIC AND PATHOLOGICAL ASPECTS OF ENVENOMING BY *CROTALUS*

After inoculation with *C. durissus terrificus* venom, studies demonstrated that cattle showed no apparent necrosis or local injury until death (Araújo et al. 1963, Graça et al. 2008). In other study, buffalo showed increased sensitivity on the site of subcutaneous inoculation, restlessness, and frequent urination (Barbosa et al. 2011). In both cases, all animals had adipsia, but the appetite was maintained while the arrest and chewing movements were not compromised. Upon respiratory auscultation, progressive mixed dyspnea was observed, without frequency-changing (Lago et al. 2000, Graça et al. 2008).

Among nervous signs, the first change described by several authors was "dragging the hoof," followed by the decrease of response to external stimuli by reducing the approach radius and the permission to manual contact. A gradual decrease in muscle tone and drooling occurred in some cases. Later the animals came into sternal recumbency and could not rise, even when stimulated, but could still support the head and neck (Belluomini et al. 1982, Lago et al. 2000, Graça et al. 2008). There is also the description that, as the signs progressed, cattle and buffaloes had difficulty in sustaining their heads (Graça et al. 2008, Barbosa et al. 2011).

In cattle, cutaneous sensitivity was observed to be decreased in more caudal body regions. While eyeball paralysis was demonstrated by the gradual partial exposure of the sclera as the head was rotated lateral-caudal (Bicudo 1999, Graça et al. 2008) (Fig.2-3). In some cases, the animals supported the head on the ground and remained in lateral recumbency (Graça et al. 2008) (Fig.4). Mild myoclonus can also be observed. In one study, six of eight cows had markedly diminished tongue muscle tone (Fig.5), intense salivation, paddling movements, protrusion of the anal sphincter, severe paralysis of facial muscles, episodes of vocalization, and death (Graça et al. 2008). Similar clinical signs were observed in buffaloes (Belluomini et al. 1982, Lago et al. 2000, Barbosa et al. 2011).

At clinical pathological testing, bleeding time have been described to be increased up to 27 minutes in some animals, with a moderate increase in activated partial thromboplastin time (APTT) from 6 hours post-inoculation. Urine tests are usually unchanged (Lago et al. 2000, Graça et al. 2008). Upon necropsy, macroscopic changes are usually absent; however, the histological examination can indicate necrosis (hyalinization) of isolated fibers or myocytes groups in muscles (Graça et al. 2008) (Fig.6-7).

CLINIC AND PATHOLOGICAL ASPECTS OF ENVENOMING BY *BOTHROPS*

Prominent swelling at the site of venom inoculation was observed in natural and experimental cases of envenoming by *Bothrops* (Fig.8-9). Bleeding time and capillary refill time (CRT) was described to be increased, and in some cases, hematomas were observed in different parts of the body due to blood restraint caused by trauma (Caldas et al. 2008, Tokarnia et al. 2008, Aragão et al. 2010, Diefenbach et al. 2012). Bleeding may be

Fig.2-3. (**2**) Paralysis of the eyeball in cattle poisoned by *Crotalus durissus terrificus*. The partial exposure of the sclera is shown as the head is rotated in the lateral-caudal direction. (**3**) Control. (Graça et al. 2008)

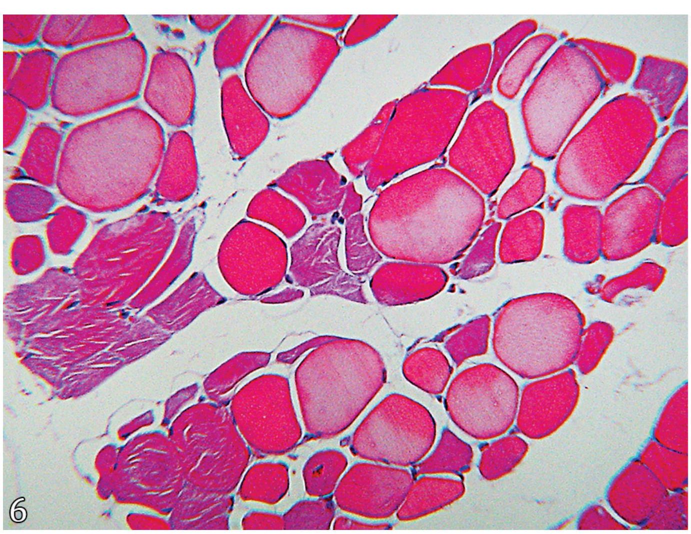
present in wounds in the early stages of healing and locals punctured by needle (Caldas et al. 2008). Animals bitten in the head can present dyspnea and restlessness whereas bites in limbs cause the animals to limp during the walk (Grunert 1967, Grunert & Grunert 1969).

In cases where sheep were bitten by *B. jararaca*, only one of four sheep, had signs indicating the exact location of the bite, marked by a small skin lesion with clotted blood (Silveira & Nishioka 1995). In the final envenoming phase of accidents involving *B. jararaca*, animals exhibited extremely pale mucous membranes, increased heart rate, mixed dyspnea, and sternal recumbency, followed by hypovolemic shock (Caldas et al. 2008). Petechiae, bruising and bleeding in the gums, epistaxis, and hematochezia were also observed (Caldas et al. 2008, Aragão et al. 2010, Diefenbach et al. 2012). In the non-lethal cases, necrosis can be observed surrounding the bite and decreased swelling, from the fifth day (Grunert 1967, Menezes 1995/96). In these cases, the hemogram results showed progressive normocytic and normochromic anemia, moderate hypofibrinogenemia, as well as a moderate decrease in total serum protein. Most animals had moderately increased levels of glucose, urea, creatine kinase (CK), and lactate dehydrogenase (LDH). Ruminants poisoned by *Bothrops* snakes showed neither visible changes nor altered laboratory analysis of urine samples (Caldas et al. 2008).

Necropsy findings consisted of extensive hematomas (*B. alternatus* and *B. jararaca*) or sero-hemorrhagic lesions (*B. jararacuçu*) in the subcutaneous region, which spread from the inoculation site to the surrounding areas, and reaching the musculature (Grunert 1967, Grunert & Grunert 1969, Menezes 1995/96, Caldas et al. 2008, Aragão et al. 2010, Diefenbach et al. 2012) (Figs.8-9 and 10). In addition, it was

Fig.4. Cattle experimentally poisoned by *Crotalus durissus terrificus*. Abnormal posture with sharp loss of muscle tone in the forelimbs and head. (Graça et al. 2008)

Fig.5. Cattle experimentally poisoned by *Crotalus durissus terrificus*. Flaccid paralysis of the tongue and mydriasis. (Graça et al. 2008)



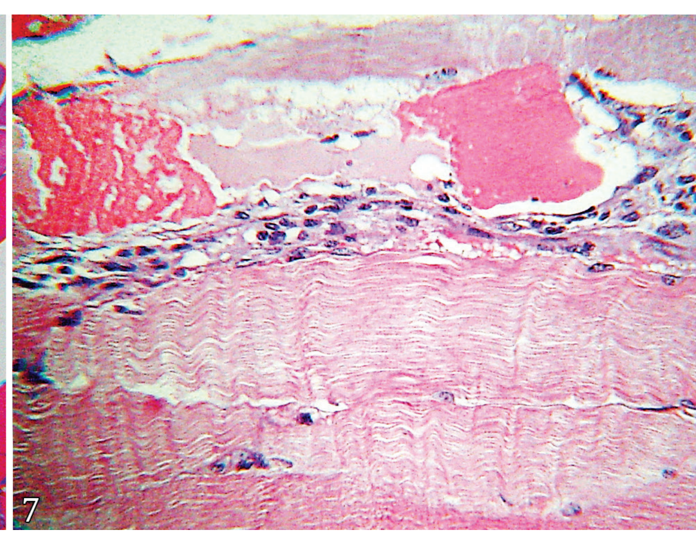


Fig.6-7. (**6**) Cattle experimentally poisoned by *Crotalus durissus terrificus*. Necrosis is characterized by intense acidophilia and hyalinization of the skeletal muscle fibers, isolated or in small groups (Biceps, SAP 30027). HE, obj.16x. (**7**) Coagulative necrosis with muscle fiber fragment accompanied by inflammatory reaction and likely satellite cell proliferation (longissimus dorsal, SAP 30.232). HE, obj.16x. (Graça et al. 2008)

described petechiae on the serosa of the rumen and omasum, abomasum mucosa, gallbladder, rectum and testicles, and bruises and suffusions in serous of the reticulum. Presence of blood (either liquid or coagulated) was observed inside the abdominal cavity, small intestine, colon, rectum, and bladder (Fig.11). The carcasses, liver, spleen, kidneys, and lungs of animals that died of hypovolemia were usually very pale. Lymph nodes might have presented blood drainage areas (Grunert 1967, Grunert & Grunert 1969, Menezes 1995/96, Caldas et al. 2008, Aragão et al. 2010). The muscle necrosis observed in cattle poisoned by *B. alternatus* venom intramuscularly was an important find. The lesion was characterized by extensive areas of myocytes with markedly eosinophilic cytoplasm, glassy, without striation, pyknotic or missing nuclei amid the bleeding areas. Additionally, some fibers showed flocculate degeneration (granulate) with the formation of eosinophilic cytoplasmic granules or masses, often vacuolated, in portions of skeletal muscle fiber. Rupture and segmental hyper contraction of fibers (fibers with "wavy" appearance) were also observed. The popliteal lymph nodes and the pelvic cavity were draining blood. Granular shock corpuscles were observed in liver sinusoids of three animals (Caldas et al. 2008).

DIAGNOSIS OF SNAKEBITE ENVENOMING IN RUMINANTS

The diagnosis of snakebite envenoming should be based on the association of epidemiology, clinical course, and clinical signs. Clinical examination should be complemented by clinical pathology tests and, in case of death, by necropsy and histopathology (Tokarnia & Peixoto 2006, Caldas et al. 2008, Graça et al. 2008). Regarding the epidemiological aspects, it should be initially checked the existence of snakes of the suspected species. Given the clinical suspicion of snakebite, it is necessary to be aware of the differences between *Crotalus* and *Bothrops* envenoming in ruminants, and the evolution of the clinical symptoms due to *Bothrops* species or the varying composition of their venom (Barraviera 1999).

The procedures for the diagnosis of snakebite envenoming might start with the history and possible evidence, as the presence of the snake at the site, bite marks on the skin, or characteristic signs such as swelling of the affected area (Lago et al. 2000, Caldas et al. 2008, Graça et al. 2008, Aragão et al. 2010, Barbosa et al. 2011, Diefenbach et al. 2012) (Fig.12).

Differentiation between bothropic and crotalic envenomings begins with the history and anamnesis, e.g., the weather and vegetation in the area may indicate which of the two species best suits the local habitat. In addition, the possibility of observing the snake next to the site should be considered, as

Fig.8-9. (**8**) Cattle experimentally poisoned by *Bothrops alternatus*. A sharp increase in volume around the right hind limb is observed from the vicinity of the inoculation site. (**9**) Necropsy revealed that the increase in volume is composed almost entirely of blood (hemorrhage). (Caldas et al. 2008)

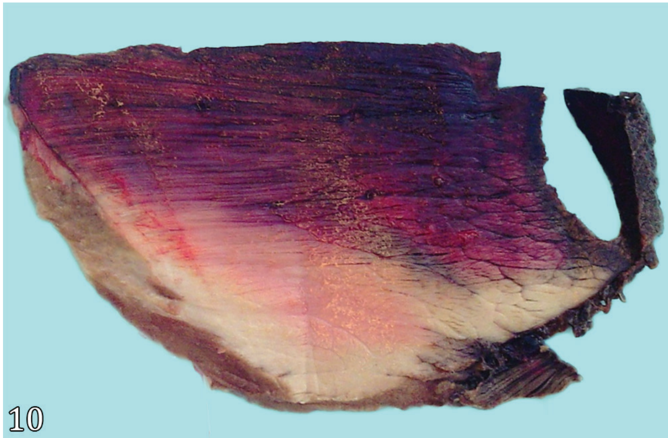


Fig.10. Cattle experimentally poisoned by *Bothrops alternatus*. Extensive bleeding in the semimembranosus muscle of the limb that was inoculated with the *Bothrops alternatus* venom intramuscularly. (Caldas et al. 2008)

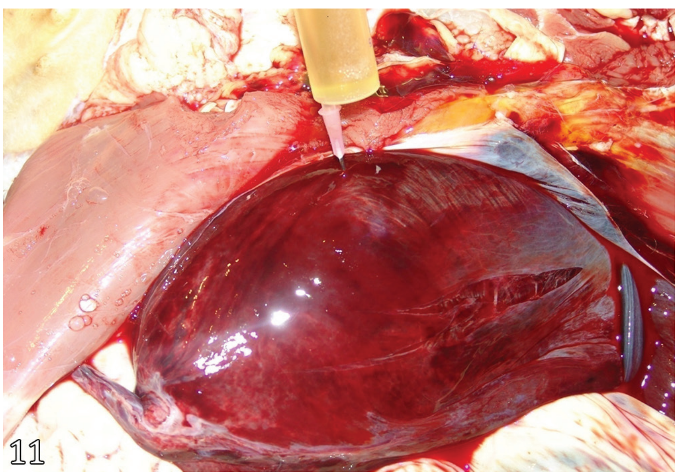
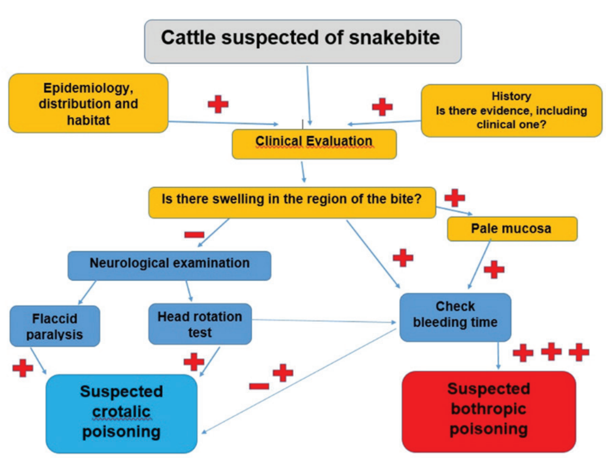


Fig.11. Cattle experimentally poisoned by *Bothrops alternatus*. Remarkable hemorrhagic trend; marked subserosal diffuse hemorrhage in the bladder. However, urine was translucent. (Caldas et al. 2008)



12

Fig.12. Flowchart detailing the procedures for the differential diagnosis of envenoming by snakes of the genera *Bothrops* and *Crotalus* in ruminants. Sharp increase (+++), slight increase (+-), negative (-), positive (+). (Dos Santos et al. 1992, Caldas et al. 2008, Graça et al. 2008, Aragão et al. 2010)

described for the cases with sheep and horses (Tokarnia et al. 2008, Chiacchio et al. 2011). Several misconceptions in the national literature might lead to misidentification. The safest recommended way to identify poisonous snakes would be to check for the loreal pit since this indicates solenoglyphous snakes. Then, the tail should be inspected to check for the presence of the rattle to differentiate between the genera *Crotalus* from *Bothrops* or for bristling scales, characteristic of the *Lachesis* genus (Sandrin et al. 2005). The presence or absence of swelling at the bite site should be checked as well. In the presence of local swelling, the bleeding time must be measured since it is greatly increased in most envenoming cases by *Bothrops*. Other findings as pale mucous membranes, tachycardia, tachypnea, bloody stools or uninterrupted bleeding can be strong clinical indications of bothropic envenoming. In the absence of local swelling and either moderately increased or normal bleeding time may indicate crotalic envenoming, among other causes. The clinical examination then should search for neurological disorders characterized by progressive muscle weakness and paralysis of the eyeball upon the head rotation test, findings that corroborate this clinical diagnosis (Caldas et al. 2008, Graça et al. 2008) (Fig.12).

The potential lethality, given the amount of poison present in the glands of *Crotalus* and *Bothrops* snakes, is well known. However, the studies of Clarke & Clarke (1969), Silveira & Nishioka (1995), Bucaretchi et al. (2002) and Melgarejo (2003) reported the relevant occurrence of the so-called dry bites, when only a portion of the poison is injected, thus rising uncertainty as to the inoculated dose. There are several reports in the literature stating that snakebites are dry bites in approximately 40% of the cases when there is no poison inoculation (Silveira & Nishioka 1995, Bucaretchi et al. 2002).

DIFFERENTIAL DIAGNOSIS OF SNAKEBITE ENVENOMING

The differential diagnosis of snake envenoming can be difficult. In veterinary, there is a tendency not to recognize poisoning outbreaks by plants and diseases such as rabies and clostridial diseases and, to attribute the death caused by such occurrences to snakebites (Tokarnia & Peixoto 2006). There is no doubt that some *Crotalus* specimen have enough venom to kill up to five adult cattle while some snakes of the *Bothrops* genus can also kill an adult bovine. This is not discussed. The question is: *how often does this occur compared to other diseases of infectious origin or poisoning by plants?*

DIFFERENTIAL DIAGNOSIS OF CROTALIC ENVENOMING

Establishing a differential diagnosis of crotalic envenoming by clinical examination is very important and depends on performing the general clinical and nervous system examinations properly. Other diseases of the central and peripheral nervous system are important in cattle. The clinical signs of *Crotalus* envenoming in cattle can be difficult to identify, with the aggravating circumstance that in many cases, evolution is rapid and, except for horses, there is no apparent macroscopic lesion. Diseases that cause neurological disorders without changing the consciousness could easily be confused with this type of poisoning, for example, acute form of botulism. Also, the signs of *Crotalus* envenoming with slower evolution can be very similar to those observed in subacute cases of botulism in cattle (Tokarnia & Peixoto 2006).

The breadth of clinical evolution of both conditions does not help their differentiation. There are other diseases with neurological signs or mobile disability that, given the rapid evolution and absence of lesions at necropsy, should be considered in the differential diagnosis, such as rabies, infection by herpesvirus 5, ketosis, puerperal hypocalcemia, plants or agents that cause muscle necrosis, or even "sudden death" caused by plants (Lago et al. 2000).

Diseases that cause muscle necrosis and myoglobinuria as poisoning by *Senna ocidentalis* and *S. obtusifolia*, excessive consumption of ionophore antibiotics and the fallen cow syndrome should be considered in the differential diagnosis (Radostits et al. 2000, Tokarnia et al. 2000, Barros 2001). The muscle necrosis observed histologically in cases of *Crotalus* envenoming in cattle is mild and does not affect the heart muscle or progress to releasing myoglobin in the urine and it cannot be observed macroscopically (Birgel et al. 1983, Graça et al. 2008).

DIFFERENTIAL DIAGNOSIS OF BOTHROPIC ENVENOMING

Envenoming by *Bothrops* causes characteristic changes in the bite site, as swelling, increased sensitivity, and can therefore be confused with several diseases, especially malignant edema, blackleg and even photosensitivity when marked by edema on the face, as in sheep and goats (Caldas et al. 2008, Aragão et al. 2010). The acute hemorrhage observed in cases of envenoming by snakes of the species *Bothrops alternatus* and *B. jararaca* should be differentiated from poisoning by warfarin (Brito et al. 2005) or acute hemorrhagic syndrome caused by the ingestion of *Pteridium arachnoideum* (Peixoto et al. 2011, Tokarnia et al. 2012). For the diagnosis of accidents involving *Lachesis muta*, both the neurotropic and the proteolytic/hemolytic effects must be considered, like what is described in *Crotalus scutulatus*.

CONCLUSIONS

Diagnosis and differential diagnosis of venomous snakebites by *Bothrops* and *Crotalus* in ruminants are quite feasible provided that the epidemiological, clinical and anatomopathological aspects are present and are taken into account.

The data set suggests that snakebite envenoming as cause of death in ruminants is not as common as previously thought and that deaths by other agents have been wrongly attributed to the snakes of these genera.

Conflict of interest statement.- The authors declare that there are no conflicts of interest.

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