Available online at http://www.ijcrls.com

International Journal of Current Research in Life Sciences
Vol. 07, No. 05, pp.2052-2056, May, 2018

ISSN: 2319-9490

RESEARCH ARTICLE

LONOMIC ACCIDENT AND ALLERGIC REACTION TO ANTI-LONOMIC SERUM; CASE REPORT AND LITERATURE REVIEW

[1]Nicolas Santoyo Sarmiento, *[2]Daniel Martin Arsanios, [3]Elias Quintero Muñoz and [4]Catalina Santoyo Sarmiento

[1]Bosque UniversityPhysician, Villavicencio Departamental Hospital, Colombia
[2]Sabana University Physician, Colsubsidio Health Medical Center, Colombia
[3]Sabana University Physician
[4]Cooperativa de Colombia of Villavicencio University, Colombia

Received 26th March, 2018; Accepted 20th April, 2018; Published 18th May, 2018

ABSTRACT

A 80-year-old male patient with a clinical picture of macroscopic hematuria, subsequent contact with the family of the Saturniidae family, on admission is documented by prolonged coagulation times, consumption of fibrinogen and elevation of azotees. It was managed with antilonomic serum and is a problem of reaction and allergic reaction required management with corticosteroids, plasma transfusion and tranexamic acid. In this case report, a review of the literature on poison literature, pathophysiology and treatment measures is carried out.

Key words: Lonomic accident; Coagulation; Anti-lonomic serum.

Citation: Nicolas Santoyo Sarmiento, Daniel Martin Arsanios, Elias Quintero Muñoz and Catalina Santoyo Sarmiento, 2018. "Lonomic accident and allergic reaction to anti-lonomic serum; case report and literature review" *International Journal of Current Research in Life Sciences*, 7, (05), 2052-2056.

INTRODUCTION

Lonomic accident, the accident caused by contact with caterpillars or worms of the genus Lonomia. During the last years, accidents in humans caused by contact with caterpillars of the genus Lonomia have been reported. Since 1967 lonomic accidents have been reported by in different countries of South America, taking importance for the production of a hemorrhagic picture that becomes fatal. The caterpillars of the genus Lonomia are light greenish brown and reach a length of up to 6 or 7 centimeters, they have spines that are distributed throughout the body and that break when they come into contact with the skin penetrating it, which favors the entry of the poison, which produces malaise, headache and nausea and between 2 and 72 hours later produces ecchymosis, gingival bleeding, epistaxis, vaginal bleeding, hematuria, gastrointestinal bleeding and intracranial hemorrhage, prolongation of coagulation times and fibrinogen decrease with normal platelet numbers.

Case Report

An 80-year-old male patient from Puerto Gaitán (Meta-Colombia), with no relevant medical history, who presents a clinical course of 4 days of evolution, consisting of pain in the left flank and macroscopic hematuria subsequent to contact with poisonous caterpillar. On admission, the patient is hemodynamically stable, with pain on palpation of the left flank, without signs of peritoneal irritation without any other positive finding. Paraclinics with prothrombine time (PT) that does not clot at 3 minutes, partial thromboplastin time (PTT) 37.3s control 25 s, fibrinogen 92.5 mg / dl, hemoglobin 15.1 gr / dl, hematocrit 44.7% platelets 194,000 ul, uroanalysis with 200 erythrocytes / ul and red blood cells> 25 x field, BUN: 22.7 mg / dl, creatinine 1.08 mg / dl. Anti-lonomical serum (ALS) was administered, with subsequent presentation of acute respiratory distress syndrome secondary to the administration of serum. It is transferred to intensive care unit, with significantly improved with corticosteroid and furosemide administration, did not require intubation. Two days after this event, the patient presented improvement in respiratory parameters, absence of hematuria, normalization of coagulation times and reduction of azote levels.

Poison components

Poison composition: The majority of the caterpillar venom is made up of protease inhibitors, serine protease, lipocalcionas, metalloprotease, lectins and phospholipases, among others (Maggi *et al.,* 2015).

***Corresponding author:* Daniel Martin Arsanios,**
Sabana University Physician, Colsubsidio Health Medical Center, Colombia.

The venom of the caterpillar has a protein that was called calcium activating protease that converts prothrombin into thrombin (Lopap), it´s a protein with a mass of 69 kDa in its natural form and has a serine-like protease activity activated by calcium ions (Fritzen *et al.,* 2005 and Pinto *et al.,* 2008). Consumption coagulopathy, with an onset of intravascular coagulation and thrombosis in the postcapillary vessels, has been associated with the action of Lopap that has been observed in a study with rats when said protein is administered (Maggi *et al.,* 2015; Reis *et al.,* 1999; Fritzen *et al.,* 2005 and Pinto *et al.,* 2008). It has been shown that Lopap is dose-dependent and capable of producing active thrombin, and according to its dose, calcium ions act as activity enhancers. In a study, Fritzen showed that Lopap increased the production of nitric oxide and other proinflammatory mediators such as prostacyclin 1, interleukin-6, interleukin-8, tumor necrosis factor - alpha, however, it was not able to modulate the expression of the mediators involved in the coagulation and fibrinolysis system or to induce the release of von Willebrand factor or its synthesis by the endothelial cells and neither the modulation of the tissue factor and the cellular plasminogen activator (Reis *et al.,* 1999; Fritzen *et al.,* 2005; Ávila *et al.,* 2013 and Nascimento-Silva *et al.,* 2012).

In an Alvarez / Flores study, they identified a protein named stuart-factor activator (Losac), which acts on the activation of factor X (Pinto *et al.,* 2008). This protein triggers the release of nitric oxide and stimulates the growth and inhibition of endothelial cell death. Additionally, Campos and Dias da Silva identified phospholipase A2 activity and its activity depends on the presence of a substrate of phospholipids and calcium ions; this enzyme showed a hemolytic activity (Maggi *et al.,* 2015; Nascimento-Silva *et al.,* 2012 and Medeiros *et al.,* 2014). Berger in his work found a mechanism of calcium-dependent venom that involves arachidonic acid metabolites of the cyclooxygenase pathway and the activation of phosphodiesterase 3A and thus generates platelet aggregation. Additionally, lonofibrase has been described, which is a 35 kDa enzyme that involves a rapid and selective degradation of alpha fibrinogen chains and with less beta efficiency, and has the capacity to cut fibrin and plasmin (Maggi *et al.,* 2015).

Inflammatory response

In a study carried out by Nascimento-Silva and collaborators with rats (Nascimento-Silva *et al.,* 2012), it was found that the inflammatory response is activated by direct injury at the endothelial level initially generating activation of the kallikrein-kinin system causing edema, pain and the initial clinical symptoms, the release of prostaglandins, the hypotensive and nociceptive effect. The expression of tumor necrosis factor alpha and nitric oxide release, favored by the release of proinflammatory molecules such as interleukin-8, ICAM-1 and E-selectin (Pinto *et al.,* 2008; Nascimento-Silva *et al.,* 2012; Barrios *et al.,* 2012 and Taylor *et al.,* 2016). On the other hand, interleukin-6 was implicated in the immune response mediated by ICAM-3 and CCL2 that encodes the monocyte chemoattractant protein (Pinto *et al.,* 2008). It was also documented that the activation of endothelial cells after exposure of the poison to non-hemorrhagic doses generated a significant initial vasodilation that increased the expression of adhesion molecules and endothelial interactions with circulating leukocytes with postcapillary venules (Nascimento-Silva *et al.,* 2012). The venom activates the expression of proinflammatory adhesion molecules E-Selectin and VCAM-1 and the induction of leukocyte adhesion and extravasation to the adjacent inflammatory tissue (Fritzen *et al.,* 2005; Nascimento-Silva *et al.,* 2012 and Medeiros *et al.,* 2014). The increase of the vascular permeability generated by the inflammation requires a reorganization of the cytoskeleton necessary for the formation of the cellular gap junctions, likewise the reorganization of the actin is an important component of the inflammatory response and this reorganization given by the venom facilitates the formation of stress fibers that requires anchoring to focal adhesion, such as focal kinase adhesion and signaling proteins (Nascimento-Silva *et al.,* 2012). Focal kinase activation generates an increase in phosphorylation and its subsequent association with actin (Nascimento-Silva *et al.,* 2012).

Vascular injury is associated with greater expression in adhesion molecules, growth factors, cytokines and inducible enzymes by endothelial cells (Fritzen *et al.,* 2005 and Nascimento-Silva *et al.,* 2012). These enzymes not only contribute to the appearance of the reaction through the synthesis of proinflammatory molecules but also to the resolution of the inflammatory response. The appearance of inducible enzymes in endothelial cells is controlled by the activation of NF-kB that is followed by increased expression of COX2, HO-1 (Hemoxygenase-1) and iNOS (nitric oxide synthase), as well as the induction of endothelial cells for the formation of metalloprotein from the tissue matrix (Nascimento-Silva *et al.,* 2012 and Medeiros *et al.,* 2014).

Pathophysiology

There are many physiopathological mechanisms that are carried out after the lonomic accident, in vivo study has been difficult, so most studies have been conducted in rats or rabbits and it has been shown that many of the manifestations will depend of the dose received from the poison. Within the alterations in the lonomic accident we can find alterations related with consumption coagulopathy, secondary fibrinolysis, procoagulant activity and anticoagulant simultaneously, thus generating pulmonary hemorrhage, cerebral hemorrhage, renal failure, among others (Nascimento-Silva *et al.,* 2012).

Coagulation and platelet alterations

It has been shown that there is plasma reduction of fibrinogen and factor XII and increase in the products of fibrinogen degradation (Pinto *et al.,* 2010). During the poisoning there is an expression of tissue factor increasing the activity of thrombin, plasmin and urokinase which indicates an activation of coagulation and urokinase during fibrinolysis (Fritzen *et al.,* 2005 and Pinto *et al.,* 2010). Platelet aggregation was evidenced 6 hours after exposure with the venom and produces an alteration and inhibition of ADP and collagen, additionally the increase in nitric oxide increased which decreases platelet aggregation (Maggi *et al.,* 2015; Fritzen *et al.,* 2005; Barrios et al., 2012 and Pinto *et al.,* 2010). Additionally, it was found that fibrin and fibrinogen degradation products are involved in platelet hypoaggregation since they bind to the GP Ib-IIIa receptor and prevent normal aggregation (Fritzen *et al.,* 2005 and Pinto *et al.,* 2010). The active principles of the venom generate an initial activation of prothrombin and factor X that generate significant amounts of intravascular thrombin that leads to the activation of the coagulation system and the consumption of fibrinogen and other coagulation factors, the olyntic fibrin enzymes degrade both fibrinogen and fibrin

contributing to the reduction of fibrinogen levels and the incoagulability of blood. In addition, olyntic enzymes also participate in the generation of FfDP that are probably involved in the disturbance of platelet aggregation (Pinto *et al.,* 2010). Fritzen, conducted a study with a protein from the caterpillar venom extract and showed that it produced an increase in the release of molecules that regulate vascular tone, inhibiting platelet activation and chemotaxis through the direct effect on endothelial cells (Maggi *et al.,* 2015; Fritzen *et al.,* 2005 and Nascimento-Silva *et al.,* 2012).

Intravascular hemolysis

In studies with rats it was documented that caterpillar venom has a cytolytic effect on erythrocytes, causing intravascular hemolysis and anemia (Maggi *et al.,* 2015; Fritzen *et al.,* 2005; Barrios et al., 2012 and Pinto *et al.,* 2010), initially a reduction of erythrocytes and increase of circulating hemoglobin was documented during the first 6 hours. 24 hours after poisoning, there was a decrease in hemoglobin and haptoglobin and an increase in LDH and unconjugated bilirubin, and in the peripheral blood smear general polychromatography and erythrocyte swelling were found (Maggi *et al.,* 2015; Fritzen *et al.,* 2005 and Pinto *et al.,* 2010). Such hemolytic activity is granted a phospholipase A2 or lonomiatoxin present in the venom, generating a protein degradation of the erythrocyte cell membrane. Hemolytic activity may also be due to microthrombotic deposits in the vasculature as seen in thrombotic microangiopathy (Maggi *et al.,* 2015; Pinto *et al.,* 2008 and Pinto *et al.,* 2010).

Inflammation and vascular disorders.

The contact with the poison of the caterpillar generates pain, burning sensation, edema and erythema. This type of reactions has been found in animal studies that are mediated by prostaglandins, together with other mediators such as bradykinin that could contribute to the general painful nociceptive effect (Pinto *et al.,* 2010). Additionally, an activation was found in the Kallikreina / kinina system (SKK) through the activation of prekallikrein in the plasma and in this sense the SKK seems to be the main responsible of the edema (Maggi *et al.,* 2015; Nascimento-Silva *et al.,* 2012 and Pinto *et al.,* 2010). The venom of the caterpillar has local and systemic effects including the ability to modulate vascular system properties, including hypotension and followed by intracerebral hemorrhage (Medeiros *et al.,* 2014 and Pinto *et al.,* 2010). Studies in animals have found alterations in vascular tone and in the structure of the vessel wall, which is related to intracerebral hemorrhages due to damage to the blood-brain barrier, generating an increase in permeability due to an alteration in the diameter of the vessel secondary to the action of proinflammatory molecules. Also the presence of vacuoles and the generated vasogenic edema could generate hemorrhage in the central nervous system (Nascimento-Silva *et al.,* 2012 and Pinto *et al.,* 2010). The hypotensive effect is related to the SKK, since in studies with rats after administration of aprotinin (SKK inhibitor) the hypotensive effect is completely resolved (Maggi *et al.,* 2015 and Pinto *et al.,* 2010). In conclusion, it is not possible to detail a single toxin that is involved in the systemic and vascular effects, since the procoagulant activity of the venom generates vascular alterations, for which reason the poisoning syndrome is the result of a synergistic action of the compounds (Pinto *et al.,* 2010). The activation of the Kallikreina-kinina system has been described in the action of the poison. A kinin release of all Kininogens is generated, which can be activated by low molecular weight kininogens or by the action of prekallikrein and in this way a decrease in pressure, edema and the aforementioned effects of venom can be seen (Maggi *et al.,* 2015).

Hemorrhagic syndrome

The hemorrhagic syndrome develops after contact with caterpillars and is characterized by low levels of fibrinogen, plasminogen, factor V and factor VIII (Maggi *et al.,* 2015). During the investigations, a serine protease called Lonomin V was identified as responsible for the inactivation of factor XIII from different origins with proteolytic activity on fibrin, fibrinogen and factor XIII (Maggi *et al.,* 2015 and Barrios *et al.,* 2012). The characteristic hemorrhagic syndrome is caused by consumption coagulopathy, which can progress to hypotension (together with the other factors already mentioned), edema, erythema and intravascular hemolysis (Maggi *et al.,* 2015). Among the initial findings is blood coagulation followed by depletion of fibrinogen that was attributed to the presence of factor X and prothrombin activators and coagulation factor II in the venom, and subsequently there is an activation in fibrinolytic activity (Maggi *et al.,* 2015 and Pinto *et al.,* 2008). Additionally, an association of the inflammatory response is found after the activation of TNF-alpha and fibrinogen since this cytosine causes the release of plasminogen activators from the endothelial cells with the subsequent formation of plasmin. In addition, TNF-alpha activates neutrophils that release elastase and both plasmin and elastase degrade fibrinogen (Barrios *et al.,* 2012).

Alterations in gene expression

An alteration in gene expression has been evidenced in different types of cells including fibroblasts, and also an alteration in positive regulation in proinflammatory mediators such as IL-8, IL-6, CCL2, CXCL1 and cyclooxygenase 2, who are quimoatractive of monocytes, neutrophils, basophils and T cells in the endothelial cells of small blood vessels (Fritzen *et al.,* 2005; Nascimento-Silva *et al.,* 2012 and Pinto *et al.,* 2010). Additionally, there is a gene expression in favor of the soluble receptor urokinase plasminogen activator (gene expression favored by TNF-a) that can contribute to the activation of the indirect fibrinolytic system, this activation generates proteolytic activity and may be responsible for the proteolytic activity of fibrin, the extracellular matrix, activating metalloproteases of the matrix, which facilitates cell migration and tissue remodeling; in addition, it could inactivate the coagulation factors V and VIII (Fritzen *et al.,* 2005; Pinto *et al.,* 2008; Taylor *et al.,* 2016 and Pinto *et al.,* 2010). In some studies, an increase in the expression of tissue factor phospholipase was found in the poisoned cells, and it was evidenced that the tissue factor has a procoagulant activity that is not completely neutralized with serum (Pinto *et al.,* 2010).

Transcriptome of the Oblique Lonomy

Four important families of proteins in the venom that could be related to the symptomatology have been identified (Pinto *et al.,* 2010). 1. The serine proteases are the most relevant family associated with activities similar to coagulation factors so they participate in the generation of thrombin by the activation of factor X and prothrombin and in the activation of the

fibrinolytic system contributing to the degradation of fibrinogen and as a result, hemorrhage (Fritzen *et al.,* 2005 and Pinto *et al.,* 2010). 2. Phospholipases are another group that alter hemostasis and effectively affect blood coagulation and platelet aggregation. Phospholipases directly modulate platelet aggregation and destabilize coagulation complexes by phospholipid degradation. 3. Group C lectins have also been found another type of venom, such as snakes, so there is a close relationship between the physiopathological findings related to the hemorrhagic disorder presented. Finally, the serine protease inhibitors, that generate an inhibition in the coagulation factors. These findings and characteristics have been found thanks to the transcriptomic analysis, however, the way in which the proteins of the poison act are still not exactly known (Pinto *et al.,* 2010).

Diagnosis

The diagnosis of lonomiasis is clinical and is based on the presence of coagulopathy or systemic hemorrhage in a previously healthy patient who has had contact with the worms 48 hours before the manifestations, is clearly clinical and must be included in the history (Ávila *et al.,* 2013 and Santos *et al.,* 2017).

Severity of the event

The Ministry of Health of Brazil established 3 degrees of severity:

- Mild: The cases only shows local manifestations (coagulation times altered or not) (Ávila *et al.,* 2013 and Santos *et al.,* 2017 and Sano-Martins *et al.,* 2017).
- Moderate: Local manifestations, bleeding in the skin, membranes, mucous membranes and mild coagulopathy (prolonged coagulation time) (Maggi *et al.,* 2015; Ávila *et al.,* 2013 and Santos *et al.,* 2017 and Sano-Martins *et al.,* 2017).
- Severe: Previously named symptoms associated with visceral or potentially fatal bleeding (acute renal failure (ARF), intracerebral, alveolar or peritoneal hemorrhages) (Maggi *et al.,* 2015; Ávila *et al.,* 2013 and Santos *et al.,* 2017 and Sano-Martins *et al.,* 2017).

Treatment

The treatment of choice for the lonomic accident is the administration of antilonomic serum (SAL), since its development in 1996 in Brazil (Da Silva *et al.,* 1996), since it is able to neutralize the poison and normalize the coagulation times by means of F (ab ') antibodies (Ávila *et al.,* 2013 ; Medeiros *et al.,* 2014; Pinto *et al.,* 2010 and Berger *et al.,* 2013). A dose of 10 ml is sufficient for the treatment of a conventional poisoning, studies have shown that a higher dose does not impact the outcomes or the presence of complications, therefore, it is not indicated (Caovilla and José Guardão Barros, 2004). Conventional management, prior to the development of SALT, was the use of antifibrinolytic drugs epsilon-aminocaproic acid (EACA) at an initial dose of 30 mg / kg intravenously followed by 15 mg / kg every 4 hours (main recommendation) or tranexamic acid 15 g / d (oral or intravenous). Where clinical improvement was seen in the clinical manifestations of bleeding (Ávila *et al.,* 2013 and Medeiros *et al.,* 2014). But the study done by Gonçalves et al, in 2007; who compared the effectiveness, in animals, of the use of SAL or EACA, the combination of both or the use of saline solution without any other medication; where there is improvement in coagulation and fibrinogen times regardless of the time of administration, without significant difference with the group treated with the combination of EACA and SAL, on the other hand the group treated with EACA or saline did not show improvements in the mentioned parameters previously independent of the time of administration, it can even increase mortality (Gonçalves *et al.,* 2007). It is recommended the use of purified human fibrinogen in those whose fibrinogen values are below 100 g / L, at a dose of 2-4 U / day, evaluating paraclinical parameters. On the other hand, the use of whole blood or fresh frozen plasma is not recommended since there has been a significant increase in mortality, in the case of anemia the use of red blood cells is more advisable (Arocha-Piñango and Guerrero, 2003 and Coll-Sangrona Arocha-Piñango, 1998).

Bibliography

Arocha-Piñango, CL. and Guerrero, B. 2003. Síndrome hemorrágico producido por contacto con orugas. Estudios clínicos y experimentales. *Revisión. Invest Clin*., 44(2):155–63.

Ávila, A., Moreno, A., Garzón, A. and Gomez, A. 2013. Accidente lonómico Lonomiasis. *Acta médica Colomb*., 38:95–100.

Barrios, M., Taylor, P., Rodríguez-Acosta, A., Sánchez, EE., Arocha-Piñango, CL., Gil, A. *et al.* 2012. A mouse model to study the alterations in haemostatic and inflammatory parameters induced by Lonomia achelous caterpillar haemolymph. *Toxicon.,* Apr;59(5):547–54.

Berger, M., Beys-da-Silva, WO., Santi, L., de Oliveira. IM., Jorge, PM., Henriques, JAÔP. *et al*. 2013. Acute Lonomia obliqua caterpillar envenomation-induced physiopathological alterations in rats: Evidence of new toxic venom activities and the efficacy of serum therapy to counteract systemic tissue damage. *Toxicon*., 74:179–92.

Caovilla, JJ. and José Guardão Barros, E. 2004. Efficacy of two different doses of antilonomic serum in the resolution of hemorrhagic syndrome resulting from envenoming by Lonomia obliqua caterpillars: A randomized controlled trial. *Toxicon.,* 43(7):811–8.

Coll-Sangrona, E. and Arocha-Piñango, CL. 1998. Fibrinolytic action on fresh human clots of whole body extracts and two semipurified fractions from Lonomia achelous caterpillar. *Brazilian J Med Biol Res.,* 31(6):779–84.

Da Silva, WD., Rocha Campos, ACM., Gonçalves, LRC., Sousa-E-Silva, MCC., G. Higashi, H. K., Yamagushi, I. *et al.* 1996. Development Of An Antivenom Against Toxins Of Lonomia Obliqua Caterpillars. *Toxicon*., 34(9):1045–9.

Fritzen, M,, Flores, MPA., Reis, CV. and Chudzinski-Tavassi, AM. 2005. A prothrombin activator (Lopap) modulating inflammation, coagulation and cell survival mechanisms. *Biochem Biophys Res Commun*., Jul;333(2):517–23.

Gonçalves, LRC., Sousa-e-Silva, MCC., Tomy, SC. and Sano-Martins, IS. 2007. Efficacy of serum therapy on the treatment of rats experimentally envenomed by bristle extract of the caterpillar Lonomia obliqua: Comparison with epsilon-aminocaproic acid therapy. *Toxicon*., 50(3):349–56.

Maggi, S., Faulhaber, GAM., Maggi, S. and Faulhaber, GAM. 2015. Lonomia obliqua Walker (Lepidoptera: Saturniidae): hemostasis implications. *Rev Assoc Med Bras.,* Jun;61(3):263–8.

Medeiros, DNM., Torres, HCC. and Troster, EJ. 2014.

Accident involving a 2-year-old child and Lonomia obliqua venom: clinical and coagulation abnormalities. *Rev Bras Hematol Hemoter,* 36(6):445–7.

Nascimento-Silva, V., Rodrigues da Silva, G., Moraes, JA., Cyrino, FZ., Seabra, SH., Bouskela, E, *et al.* 2012. A pro-inflammatory profile of endothelial cell in Lonomia obliqua envenomation. *Toxicon*, Jul;60(1):50–60.

Pinto, AFM., Berger, M., Reck, J., Terra, RMS. and Guimarães, JA. 2010. Lonomia obliqua venom: In vivo effects and molecular aspects associated with the hemorrhagic syndrome. *Toxicon,* 56(7):1103–12.

Pinto, AFM., Dragulev, B., Guimarães, JA. and Fox, JW. 2008. Novel perspectives on the pathogenesis of Lonomia obliqua caterpillar envenomation based on assessment of host response by gene expression analysis. *Toxicon*., May;51(6):1119–28.

Reis, C.V., Kelen, EM., Farskym, SH., Portaro, FC., Sampaio, CA., Fernandes, BL. *et al.* 1999. A Ca++ activated serine protease (LOPAP) could be responsible for the haemorrhagic syndrome caused by the caterpillar Lonomia obliqua. L obliqua Prothrombin Activator Protease. *Lancet,* (London, England). Jun;353(9168):1942.

Sano-Martins, IS., Duarte, AC., Guerrero, B., Moraes, RHP., Barros, EJG. and Arocha-Piñango, CL. 2017. Hemostatic disorders induced by skin contact with Lonomia obliqua (Lepidoptera, Saturniidae) caterpillars. *Rev Inst Med Trop Sao Paulo.,* Apr;59:e24.

Santos, JHA., Oliveira, SS., Alves, EC., Mendonça-da-Silva, I., Sachett, JAG., Tavares, A. *et al*. 2017. Severe Hemorrhagic Syndrome After Lonomia Caterpillar Envenomation in the Western Brazilian Amazon: How Many More Cases Are There? *Wilderness Environ Med*. Mar;28(1):46–50.

Taylor, P., Salazar, E., Barrios, M., Salazar, AM., Abad, M-J, Urdanibia, I., *et al.* 2016. Role of the inflammatory response in the hemorrhagic syndrome induced by the hemolymph of the caterpillar Lonomia achelous. *Toxicon*., Oct;121:77–85.

****