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LETTER TO THE EDITOR

ACUTE-PHASE RESPONSE IN SNAKEBITE

Sir,

I have recently read the article intitled "Search of intravascular hemolysis in patients with the cutaneous form of loxoscelism" published in the *Rev. Inst. Med. trop. S. Paulo,* 36: 149-151, 1994, by MORENA et al. [9], and I would like to make some considerations about it. The authors evaluated the haptoglobin levels in 19 patients with clinical diagnosis of cutaneous form of loxoscelism aiming to detect any presence of intravascular hemolysis. The haptoglobin level results observed in these patients showed values significantly higher than those of the control group ($p<0.0001$). In addition, some patients presented fever, leucocytosis with neutrofilia. In our Tropical Diseases Service of the School of Medicine of Botucatu - Brazil we have treated patients bitten by *Bothrops spp.* and *Crotalus durissus terrificus* with specific antivenom. This later accident is more severe than the *Bothrops* one. On the other hand, in a collaborative study with researchers from Sweden, we observed an increase of interleukin-6 (IL-6) and interleukin-8 (IL-8), but not of interleukin-1 (IL-1β) and tumor necrosis factor (TNFα), more intense in patients bitten by *Crotalus durissus terrificus* [1, 2]. An increase of IL-6 levels could explain the leucocytosis and neutrofilia observed, since this cytokine is capable of increasing adrenocorticotropic hormone and glucocorticoid secretion [4]. IL-6 is known to be an important sign for inducing the fever and the synthesis of acute-phase proteins in the liver including C-reactive protein, haptoglobin, complement factor C_3, fibrinogen and mucoproteins [5, 6, 8]. Experimentally, LOMONTE et al. [7] inoculated *Bothrops asper* venom into mice and observed an increase of IL-6 after envenomation which peaked between 3-6 hours and returned to normal values after 12 hours. IL-1β and TNFα increases were not detected. These observations are in agreement with our patients' results.

Based on these data, we have hypothesized that the snakebite envenomation closely resembles an acute trauma, inducing a typical acute-phase response [1, 2, 3]. In conclusion, our observations agree with those by MORENA et al. [9], and I would like to suggest that the acute-phase reactions frequently observed in this situation are responsible for increasing the haptoglobin levels in these patients.

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REFERENCES

1. BARRAVIERA, B. - As reações da fase aguda nos acidentes ofídicos. **In:** BARRAVIERA, B. - *Venenos animais: uma visão integrada.* Rio de Janeiro, EPUC, 1994. p. 91-96.

2. BARRAVIERA, B.; LOMONTE, B.; TARKOWSKI, A.; HANSON, L.A. & MEIRA, D.A. - Acute-phase reactions, including cytokines, in patients bitten by *Bothrops spp.* and *Crotalus durissus terrificus* in Brazil. **J. venom. Anim. Toxins,** 1995 (in press).

3. BARRAVIERA, B.; MARCONDES-MACHADO, J.; PEREIRA, P.C.M. et al. - Acute-phase reactions in patients bitten by *Bothrops* and *Crotalus* snakes. **Toxicon, 31:** 936, 1993.

4. CASTELL, J.V.; ANDUS, T.; KUNZ, D. & HEINRICH, P.C. - Interleukin-6: the major regulator of acute-phase protein synthesis in man and rat. **Ann. N. Y. Acad. Sci., 557:** 87-101, 1989.

5. KAPLAN, M.E. - Hemolytic disorders. **In:** WYNGAARDEN, J.B. & SMITH Jr., L.H. *Textbook of medicine.* Philadelphia, W.B. Saunders, 1988. p. 907-909.

6. LEWIS, E.J.; SEDGWICK, A.D. & HANAHOE, T.H.P. - *In vivo* changes in plasma acute phase protein levels in the rat induced by slow release of IL-1, IL-6 and TNF. **Mediators Inflamm., 1:** 39-44, 1992.

7. LOMONTE, B.; TARKOWSKI, A. & HANSON, L.A. - Host response to *Bothrops asper* snake venom: analysis of edema formation, inflammatory cells, and cytokine release in a mouse model. **Inflammation, 17:** 93-105, 1993.

8. MACKIEWICZ, A.; GANAPATHI, M.K.; SCHULTZ, D. et al. - Regulation of rabbit acute phase protein biosynthesis by monokines. **Biochem. J., 253:** 851-857, 1988.

9. MORENA, P.; NONOYAMA, K.; CARDOSO, J.L.C. & BARRETTO, O.C.O. - Search of intravascular hemolysis in patients with the cutaneous form of loxoscelism. **Rev. Inst. Med. trop. S. Paulo, 36:** 149-151, 1994.

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