SERUM CYTOKINE LEVELS IN MICE INJECTED WITH *TITYUS SERRULATUS* SCORPION VENOM

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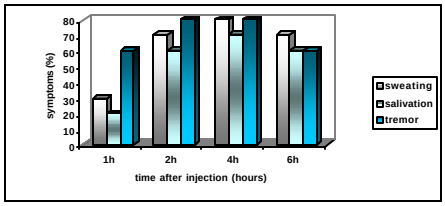
Introduction. *Tityus serrulatus* scorpion stings in Brazil are important not only because of their incidence, but also for their potential ability to induce severe, and often fatal, clinical situations, especially among children. Specific signs and symptoms directly related to the venom toxic components, patients bitten by scorpions may develop a systemic inflammatory response and the cytokines released play a major role in the pathogenesis. In order to get a better insight into cytokine network regulation in systemic envenoming IL-1, IL-6,IL-10 and IFN-γ were evaluated.

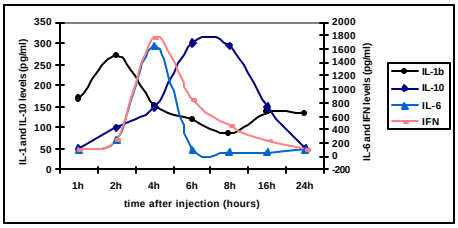
Methodology. Freezing crude venom from *T.serrulatus* was obtained from Instituto Butantan. BALB/c mice were infected intraperitoneusly (ip) route with scorpion venom and bled at different times after infection. The levels of IL-6, IL-1 and IL-10 present in sera were assayed by ELISA method. The levels of TNF and IFN-γ present in sera were used as a standard bioassay with L-929 cells.

Results and Discussion. Median lethal doses (LD_{50}) of *T.serrulatus* venom in two groups BALB/c female mice, one of them with 16-20g and other with 24g the ip route were injected with 30 and 35 μg/mice, respectively.
When mice received an ip injection of one LD_{50} of the venom, the time-course of mortality no differed between the groups. In both groups, the majority of deaths occurred within the first 4 and 6 h and presented the similar symptoms (Figure 1).

Figure 1. Symptoms observed in mice injected with TSSV.



Mice injected with saline solution had undetectable levels of the cytokines assayed in serum. To determine the cytokine production pattern *in vivo* in envenomated mice, animals were injected ip with one LD_{50} of scorpion venom. The venom induced a marked increase in IL-1α levels, with an early increase occurring within the first 2h, decaying thereafter (Figure 2). The highest levels of IL-1β after injection of scorpion venom were observed with one peak at 2 and a second one at 16 h (Figure 2). Levels IL-6 increased gradually, reaching highest values at 4 h and decreasing at later time intervals (Figure 2). The maximum peak in serum



levels of IFN-γ after injection of scorpion venom was observed 4 h after envenomation (Figure 2). The venom was able to induce an increase in serum levels of IL-10, with the highest values occurring at 6 and 8 h (Figure 2).

Figure 2. Cytokine production.

Conclusions. Changes in serum levels of cytokines were studied in BALB/c mice injected intraperitoneally with one median lethal dose (LD_{50}) of the scorpion venom of *Tityus serrulatus*, The time-course in serum cytokine levels, the venom induced prominent elevations of IL-1, IL-6, IL-10 and IFN-γ. The major correlation between cytokine released and symptoms occurred between 2 and 4 h when there was an early increase in IL-1 and IL-6. The highest IFN-γ levels were obtained at 4 h, whereas IL-10 levels reached higher values at 6 h, and this cytokine probably modulates the secretion of IFN-γ and the synthesis of acute-phase proteins.

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References.

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