CHANGES OF CYTOKINE ACTIVITIES AND OTHER PARAMETERS IN EXPERIMENTALLY INDUCED ENDOTOXIN SHOCK IN DOGS

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In order to study the role of cytokines in endotoxin shock, plasma tumor necrosis factor (TNF), interleukin (IL)–1 and IL–6–like activities, together with physiologic and hemodynamic responses were measured in dogs before and after intravenous administration of lipopolysaccharide (LPS) purified from *Escherichia coli* at a dose of 500 μg per kilogram of body weight (LPS group) and an equivalent volume of physiologic saline (control group). The following results were obtained.

1. Blood endotoxin concentration increased markedly at 15 minutes after LPS administration, and remained at a high level until 24 hours. The LPS group showed a slight but insignificant increase in rectal temperature as compared with the control group throughout the study period.
2. In the LPS group, white blood cell count decreased markedly at 15 minutes, remained low untill 6 hours, and finally increased significantly at 24 hours. The red blood cell count, hemoglobin concentration and hematocrit value increased significantly at 30 minutes, and this increase persisted for 24 hours. The parameters of blood coagulation did not demonstrate significant changes except for a marked increase in the fibrinogen concentration at 24 hours.
3. The LPS group had transient, marked decreases in cardiac output, cardiac index and mean arterial pressure at 15 minutes, but they returned to the baseline levels by 24 hours. There were no significant changes in mean pulmonary arterial pressure and heart rate.
4. In the LPS group, TNF-like activity increased at 30 minutes after treatment, while IL–1–like activity did so between 30 and 60 minutes. The former reached the maximal levels at 2 hours and the latter at 1.5 hours. Both activities were then hardly detectable at 6 to 24 hours. IL–6–like activity was elevated at 1 hour, peaked at 1.5 hours, and remained at high levels until 24 hours.

These data suggested that the initial host response to endotoxin is attributable to the release of TNF, followed by IL–1 release, which consequently stimulates the synthesis and release of IL–6.