INTERLEUKIN-6 AND PHOSPHOLIPASE A2 IN SEPSIS

To the Editor:

We read with interest the report of Hack et al who found increased plasma levels of interleukin-6 (IL-6) in sepsis and in septic shock. They reported that IL-6 levels were higher in septic patients who subsequently died as compared with survivors, and concluded that IL-6 may be an important mediator of inflammation and shock. The report of Hack et al assumes additional significance in its context of the relationship of cytokines to the activity of phospholipase A2 (PLA2) in sepsis and septic shock. It has become quite clear that cytokines, including IL-1 and tumor necrosis factor (TNF), exert at least part of their proinflammatory activity through the activation of PLA2 and subsequent generation of platelet activating factor and active metabolites of arachidonic acid. We have investigated the role of PLA2 in experimental and clinical sepsis and septic shock.1-3 Plasma PLA2 activity in endotoxin-induced shock in rabbits correlated with the fall in mean arterial blood pressure. Infusion of exogenous PLA2 into normal rabbits reproduced the hemodynamic and clinical picture of endotoxin shock.4 In humans, circulating PLA2 levels were markedly elevated in gram-negative septic shock and correlated significantly \((P < .001)\) with the magnitude and duration of circulatory collapse.1 Experimental endotoxiaemia in human volunteers induced a transient rise in TNF, followed 2 hours later by increased serum PLA2 activity, persisting for 24 to 48 hours postendotoxin.5 Circulating PLA2 from septic shock serum was a calcium-dependent, nonpancreatic enzyme, very similar if not identical to that discovered and identified in the synovial fluid in inflammatory arthritis.6 It seems that IL-6 is joining the family of cytokines that play an important role in initiating and regulating systemic inflammatory responses, as do IL-1 and TNF, acting through activation of PLA2. We are presently exploring this possibility.

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