

# Regional distribution of endothelin-1 and endothelin converting enzyme-1 in porcine endotoxemia.

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## Abstract

Endothelin-1 (ET-1) levels are markedly increased in sepsis. Since ET-1 is primarily transcriptionally regulated, there should be a corresponding increase in pre-pro-endothelin-1 (ppET-1). Our objective was to determine whether ppET-1 is increased in pigs with a low systemic vascular resistance. We also examined the distribution of ET-1 and the regulation of endothelin-converting enzyme 1 (ECE-1), the rate limiting enzyme in ET-1 production. We anesthetized and ventilated 16 pigs. We measured arterial, pulmonary, and central venous pressures, as well as cardiac output. ET-1 was measured by radioimmunoassay in plasma and in multiple tissues. We infused 20 microg/kg of endotoxin over 2 h and then sacrificed the animals. ppET-1 and ECE-1 mRNA were assessed by Northern analysis. We performed immunohistochemistry for the assessment of tissue ET-1 and ECE-1. The systemic vascular resistance rose at 30 min, but fell by 120 min. Plasma ET-1 more than doubled by 2 h. However, there was no change in the concentration of ET-1 in any tissue except in the pulmonary artery. By immunohistochemistry, there was also no change in ET-1 in aorta, vena cava, heart, lung, liver, and kidney. Distribution of ECE-1 followed that of ET-1 on immunohistochemistry. There was a significant increase in ppET-1 mRNA in liver, kidney papillae, and vena cava, and a tendency for an increase in other tissues. This was paralleled by an increase in ECE-1 mRNA. In conclusion, the amount of ECE-1 mRNA and protein parallel those of ET-1. Endotoxemia is associated with a marked increase in plasma ET-1 and an increase in ppET-1 and ECE-1 mRNA in multiple tissues; however, there was no significant change in tissue ET-1 except in the pulmonary artery. The rise in plasma levels without a change in tissue levels suggests a greater release into the vasculature in sepsis than under normal conditions.