

# Presence of nitrotyrosine with minimal inducible nitric oxide synthase induction in lipopolysaccharide-treated pigs.

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### **Abstract**

The production of large amounts of nitric oxide (NO) by the inducible form of nitric oxide synthase (iNOS) and the subsequent production of peroxynitrite (OONO-) are believed to be major factors in the hemodynamic abnormalities of sepsis. This finding is based on data from rats and mice but has not been established in other species. Therefore, we examined the role of iNOS in lipopolysaccharide (LPS)-treated pigs, which have a hemodynamic pattern with sepsis that is more similar to humans than rats. Pigs were anesthetized, ventilated, and given LPS (n = 12), 20 microg/kg over 2 h, or saline (n = 7). They were killed after 2 (n = 8 LPS, 7 control) or 4 h (4 LPS). We measured cardiac output (CO), mean arterial (Part), and pulmonary and central venous pressures. We evaluated NO production by measuring expired NO, and plasma nitrate/nitrite concentration, NOS activity (in lung tissue), and iNOS protein by Western analysis, and immunohistochemistry (lung and liver), as well as iNOS mRNA by Northern analysis (liver and lung). We also measured nitrotyrosine as evidence of OONO- production by slot blot, Western analysis, and immunohistochemistry. By 2 h, Part fell and CO did not change so that systemic vascular resistance decreased from 21.5+/-2.9 to 12.7+/-3.1 mmHg x L(-1) x min (P < 0.05) and remained at 11.3+/-1.7 mmHg x L(-1) x min in the animals observed for 4 h. Plasma nitrate/nitrite, expired NO, and NOS activity did not change. We found no iNOS in tissues by Western analysis with 5 different antibodies but detected a small amount of iNOS by immunohistochemistry in inflammatory cells and small vessels. There was a small increase in iNOS mRNA in liver and lung. Despite the minimal increase in iNOS, nitrotyrosine was increased in small vessels and in inflammatory cells. In conclusion, caution should be used when extrapolating the septic response in rodents to other species, for the pattern of iNOS induction is very different.