Comments to NO in Trauma

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I would like to make some comments on nitrite/nitrate production in baboons. We think that the nitrite/nitrate production is dependent on the concentration of endotoxin in blood, which can either be translocated during hemorrhagic shock or released as a result of live *Escherichia coli* infusions. Therefore we established two different animal models in baboons. In the acute trauma model a decrease in the flow of the superior mesenteric artery occurs during the hypotensive period. Acidosis of the gut wall could be demonstrated via indirect tonometric methods. The low gut pH improves during the resuscitation period. With this model we could clearly show the translocation of bacteria during traumatic shock in nonhuman primates. The translocation is accompanied by endotoxemia in this model. In addition, we developed a subchronic model over 72 h to simulate the posttraumatic course in patients. During this 72 h period hemodynamic and respiratory parameters were monitored regularly and blood samples taken.

In this model we addressed the question of whether hypovolemic-traumatic shock with bacterial translocation induces nitrate formation.

During NO formation cyclohydrodolase 1 is important; it produces biopterin upon stimulation by LPS and cytokines. We measured both biopterin and neopterin, which is a coproduct of the activation of the tetrahydrobiopterin production. Biopterin is a cofactor of NO synthase (Fig. 1). During hypovolemic-traumatic shock endotoxemia with a maximal concentration of between 200 and 600 pg/ml developed. Neopterin increased only by a

![Fig. 1](image-url)
small amount during the first 24 h and decreased until the end of the experiment (probably due to dilution). Biopterin and nitrate are almost normal during the hypovolemic period and after retransfusion. Therefore we conclude that trauma and a small amount of translocated endotoxin is not sufficient to induce nitrate formation. During the hypotensive period we performed the norepinephrine test to test vascular reactivity. After 4 h of hypoperfusion as well as after reinfusion the norepinephrine test was normal.

In addition to our trauma model we tried to detect nitrate formation in the chronic septic model in baboons. This model consists of an infusion of live *E. coli* 1 - 2 × 10⁹/kg over 2 h. After 4 h the animals were transferred back into the cage and observed for an additional 72 h with regular measurements of respiratory and hemodynamic parameters (similar to the trauma model). In these animals, in which a much higher endotoxin concentration is achieved (nanogram compared to picogram levels in traumatic shock), an *E. coli* dose-dependent formation of pteridines and nitrates was found. After 24 h there was a significantly increased concentration of neopterin and also of biopterin. Parallel to the increased neopterin and biopterin levels, nitrates were significantly elevated at 8 h and 24 h after (Fig. 2) *E. coli* sepsis induction. From these observations we draw the conclusion that nitric oxide formation depends on the concentration of endotoxin in nonhuman primates.

**Discussion**

Traber:
Where does the baboon sit in relationship to what cells make nitric oxide? Do their macrophages and smooth muscles make nitric oxide like a rat or more like the human in which the cells do not make nitric oxide?