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Parenteral Nutrition Facilitates Activation of Coagulation but Not of Fibrinolysis during Human Endotoxemia

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Venous thrombosis and bacterial infections are common complications of parenteral nutrition. To test the hypothesis that infection facilitates activation of coagulation during parenteral nutrition, healthy subjects were intravenously injected with endotoxin (2 ng/kg) after they had received either 1 week of standard parenteral nutrition (n = 7) or normal enteral feeding (n = 8). Compared with enteral feeding, parenteral nutrition was associated with a selectively enhanced activation of the coagulation system (plasma levels of thrombin-antithrombin III complexes) during endotoxemia. Activation of the fibrinolytic system (plasminogen activator activity, tissue-type plasminogen activator, plasminogen activator inhibitor type 1) proceeded similarly in both study groups. In patients receiving parenteral nutrition, one common complication (bacterial infection) may facilitate the occurrence of another common complication (venous thrombosis) by synergistic stimulation of the coagulation system.

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The study was approved by the Institutional Review Board of Cornell University Medical College and written informed consent was obtained from all subjects before enrollment in the study.

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or local irri a ion a he ca he er si c. Blood was ob ained before and 1, 1.5, 2, 3, 4, 5, 6, and 24 h af er adminis ra ion of endo oxin. Blood was also ob ained from paren erally fed volun eers before he ini a ion of paren eral nu ri ion and 3 days hereaf er. All blood samples were cen rifuged a 4°C for 20 min a 1600 g and s ored a –70°C un il assayed.

**Assays.** All assays were done in ci ra ed plasma samples. Co-agula ion ac iv ion was de ermined by measuring hrombin-an i-hrombin III (TAT) complexes (ELISA; Behringwerke, Marburg, Germany). Fibrinoly ic ac iv ion was moni ored by measuremen s of issue ype plasminogen ac iv or ( PA) by use of an ELISA, of plasminogen ac iv or inhibi or ype 1 (PAI-1) by use of an ELISA modified from an RIA, and of plasminogen ac iv or ac iv-i y by use of an amidoly ic assay. All assays have been described in de ail previously [10, 11].

**Statistical analysis.** All values are given as means ± SE. Com-parisons wi hin and be ween groups were done by analysis of variance followed by Newman-Keuls es for mul iple comparison where appropria e. P < .05 was considered a s a is cally signifi-can difference.

**Results**

Adminis ra ion of endo oxin o en erally fed subjec s resul ed in a ransien ac iv ion of he coagula ion sys em, as reflec ed by an increase in he plasma concen ra ions of TAT complexes peaking af er 4 h (34.9 ± 4.0 ng/mL, P < .001) (figure 1). Paren eral nu ri ion per se did no influence he plasma levels of TAT complexes in he week prior o endo oxin adminis ra ion (da a no shown). However, paren erally fed volun eers showed a significan ly more pronounced ac iv ion of he coagula ion sys em af er endo oxin injec ion, wi h levels of TAT complexes reaching a peak of 59.9 ± 3.8 ng/mL (P < .001 vs. en erally fed subjec s).

Injec ion of endo oxin was associa ed wi h ac iv ion of he fibrinoly ic sys em, as indica ed by increases in he plasma concen ra ions of plasminogen ac iv or ac iv-i y, PA, and PAI-1 (all P < .001 vs. baseline) (figure 2). Paren eral nu ri ion per se did no influence fibrinolysis indexes in plasma in he

![Figure 1](image1.png)

**Figure 1.** Ac iv ion of coagula ion. Mean (±SE) plasma concen-ra ions of hrombin-an i hrombin III (TAT) complexes af er in ravenous injec ion of endo oxin (2 ng/kg) a t = 0 in heal hy humans who had received n al paren eral nu ri ion (TPN, n = 7) or normal en eral feeding (EN, n = 8) in week before endo oxin adminis ra ion. *P < .05 vs. en erally fed humans by analysis of variance and Newman-Keuls es.

![Figure 2](image2.png)

**Figure 2.** Ac iv ion of fibrinolysis. Mean (±SE) plasma concen-ra ions of plasminogen ac iv or (PA) ac iv-i y, issue- ype plasminogen ac iv or ( PA), and plasminogen ac iv or inhibi or ype 1 (PAI-1) af er in ravenous injec ion of endo oxin (2 ng/kg) a t = 0 in heal hy humans who had received n al paren eral nu ri ion (TPN, n = 7) or normal en eral feeding (n = 8, EN, closed circles) in week before endo oxin adminis ra ion.
week before endotoxin administration. Further, ac ivan ion of the fibrinolytic system during endotoxia was not influenced by an ecceended paren eral nu ri ion, compared with intravenous feeding (figure 2).

Discussion

Central venous thrombosis and bact erial infec con are the mos frequent complica ons of paren eral nu ri on. We hypothesized that bact erial infec con during paren eral ns may be influenced by the model of endotoxia, leading to enhanced acute-phase protein production, activation of coagulation and fibrinolysis by endotoxin [11–13]. Al hough endotoxin during paren eral ns may influence serum indices for ac vation of the Bradykynesysmic system, these findings may have relevance for the selec on of patients with paren eral ns who are likely to benefit mos from heparin prophylaxis.

References

3. Grisone ER, Me a SK, Connors AF. Thrombosis and infec con complica ons - a model previously shown to induce ac iva ion of bo h coagulation and fibrinolysis [11–13]. Al hough paren eral ns may influence serum indices for ac vation of the Bradykynesysmic system, these findings may have relevance for the selec on of patients with paren eral ns who are likely to benefit mos from heparin prophylaxis.

We consider it unlikely that the presence of an in ravenous ca he er, ra her han a 7-day period of bowel res, caused the enhancement of endotoxin-induced coagulation and ac iva ion. Indeed, we hypothesized that the presence of paren eral ns may influence serum indices for ac vation of the Bradykynesysmic system, these findings may have relevance for the selec on of patients with paren eral ns who are likely to benefit mos from heparin prophylaxis.

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