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0353 INCREASED SENSITIVITY TO ENDOTOXIN INDUCED DISSEMINATED INTRAVASCULAR COAGULATION (DIC) IN VITAMIN E-DEFICIENT RABBITS

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DIC in rabbits was induced by i.v. injection of E. coli endotoxin (e) (50µg/kg). The levels of fibrinogen (F) and FDP, fibrin monomer (FM), PTT, white blood cells and platelet counts were determined before and 3 hours after e injection. Fibrin (f) deposited in organs was calculated by counting the radioactivity of ^{125}I-F introduced i.v. beforehand. Pretreatment of rabbits, maintained on laboratory chow, with dl-α-tocopheryl acetate (vit. E) (40mg/kg/day i.m. for 3 days) did not protect the animals against DIC induced with 2 doses of e 24 hours apart, and only slightly reduced amount of f deposited in organs. On the other hand, rabbits maintained on a vit. E-deficient diet were found to be extremely sensitive to e. Single doses of e caused 100% mortality within 24 hours, as compared to 100% survival in a group fed the same diet containing vit. E. Laboratory findings (F depletion, presence of FM, increased FDP and prolonged PTT) and increased f deposition in organs (kidneys, lung, liver and spleen) indicated activation of intravascular coagulation by a single dose of e in vit. E-deficient rabbits. It is possible that normal levels of vit. E protect against cell injury by e and thus prevent a release of procoagulants into the blood stream.

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0354 PLATELET AND FIBRINOGEN PRODUCTION: EFFECT OF LIPID A AND LIPOSOMES

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Previous studies have demonstrated that endotoxin administered in a single intravenous dose produced increased platelet and fibrinogen production. To determine if the lipid moiety of the endotoxin was implicated, we studied the effect of intact endotoxin (E. coli 026:B6), lipid A, lipid A incorporated into liposomes, and lipid A solubilized in triethylamine (TEA) on platelet and fibrinogen production in male New Zealand rabbits. Animals received these preparations by single intravenous 1 h infusions of 1.0, 5.0, 10.0, 25.0, or 50.0 µg/kg body weight. Selenomethionine-^{75}Se was injected 18 h after infusion, and the percentages of incorporation into platelet and fibrinogen were used to measure thrombopoiesis and fibrinogen synthesis. All 4 types of infusions increased both platelet production and fibrinogen synthesis and a dose-response relationship was observed; however, the threshold dose for stimulation varied with the type of material infused. More lipid A (by weight) was required to stimulate either platelets or fibrinogen than any of the other materials infused. When incorporated into liposomes or solubilized with TEA, lipid A produced a response similar to that produced by intact endotoxin. These data suggest that the lipid A moiety itself can stimulate platelet and fibrinogen production.

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0355 THE EFFECT OF HIRUDIN ON THE GENERALIZED SHWARTZMAN REACTION (GSR) IN RABBITS

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The inhibitory effect by hirudin on the course of the GSR induced by two spaced injections of endotoxin (E.coli) 24 hours apart was investigated in two groups of six animals: I: endotoxin only. II. endotoxin with hirudin, which was infused (1000 ATU/kg/h) for a period of 6 hrs after the 2 endotoxin injection (EI). Fibrinogen, soluble fibrin monomer complexes (SFMC), AT III, platelet- and leukocyte counts were determined and pathological studies performed. Fibrinogen in II remained significantly elevated over the whole experiment, while in I the fibrinogen decreased significantly after the 2.EI. SFMC was significantly increased in I from 3.2% before the 1.EI to 10.7% before the 2.EI, and to 16.7% 6 hrs after the 2.EI. SFMC of II increased from 3.0% before the 1.EI to 10.5% before the 2.EI and stayed unaltered during hirudin infusion. The decrease of AT III and platelets was significantly smaller in II than in I. The decrease of leukocytes was similar in I and II. The findings indicate, that the hematological consequences of GSR can be corrected by infusion of hirudin while the dysfunction of the kidneys can be improved only slightly