LEUKOCYTE GENERATED - RENAL DIALYSIS MEMBRANE INDUCED - PROCOAGULANT (TISSUE FACTOR) ACTIVITY
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Leukocytes are capable of generating procoagulant-tissue factor activity (Tfa) if appropriately stimulated. One such well established stimulus is bacterial lipopolysaccharide. Other stimuli of Tfa by leukocytes have been described. We have recently reported that leukocytes harvested from renal hemodialysis membranes have a significant Tfa. Experiments were done to elucidate the mechanism whereby this stimulation occurred. Sterile, pyrogen free, cuprophane membrane segments from a renal hemodialysis apparatus were incubated for 18 hours with human leukocytes, platelet rich or platelet poor heparinized plasma, tissue culture media etc., and tested for activity after removal of plasma and sonic disruption of the leukocytes. Maximum generation of Tfa required leukocytes, platelet rich plasma and membranes. When membranes were omitted significantly less Tfa was generated (110 vs 40 units $P < 0.02$). No Tfa was generated in the absence of leukocytes or plasma. The effect of membranes on plasma was also tested. Heparinized plasma shaken with membranes (or Zymosan) had the ability to stimulate leukocytes to generate Tfa, while EDTA or citrated plasma had no such stimulatory effect. These data suggest that a factor (s) in plasma is activated which induces leukocytes to generate Tfa.

PROCOAGULANT ACTIVITY OF RABBIT PERITONEAL WBC: EFFECTS OF CORTISONE AND ENDOTOXIN. A.J. Robinson, S.I. Rapaport, and S.F. Brown. Univ. of California and V.A. Hospital, San Diego, California, U.S.A.

This study tested the hypothesis that cortisone increases the procoagulant activity of WBC of rabbits injected with endotoxin. Rabbits were given either saline (control) or cortisone acetate, 25 mg daily for 5 days intramuscularly. On day 5, animals received intravenously either 1 ml of saline or of *E. coli* endotoxin, 100 μ g/kg. Peritoneal leukocytes were collected 1 hour (h) later. Two types of suspensions were prepared following intraperitoneal starch: primarily heterophils (16 h after starch), primarily macrophages (72 h after starch). Suspensions were washed, counted, and examined for clotting activity in a one-stage thromboplastin time assay. Activity was expressed in units (U) from a reference curve made with rabbit brain thromboplastin (clotting time of 1/10 dilution, 12.6 sec = 100 U). Heterophil suspensions were tested at approximately 60,000 WBC per mm^3 . After incubation in Hank's solution at 37° for 30 min they gave the following results: saline-saline, 1.8 U; cortisone-saline, 0.6 U; saline-endotoxin, 7.8 U; cortisone-endotoxin, 5.3 U. Sonicated suspensions were also tested and possessed markedly decreased activity. Incubated macrophage suspensions were tested at different concentrations: saline-saline (30,000 per mm^3) 3.1 U; cortisone-saline (15,000 per mm^3) 0.7 U; saline-endotoxin (14,000 per mm^3) 51.8 U; cortisone-endotoxin (6,000 per mm^3) 82.2 U. Sonicated macrophages from endotoxin-treated animals retained potent procoagulant activity. Thus, endotoxin induces WBC procoagulant activity primarily in macrophages rather than heterophils. Activity is greatest in macrophage suspensions from cortisone-treated animals.

LEUCOCYTE ADHERENCE TO ARTERIAL ENDOTHELIUM. H.N. Mayrovitz, M.P. Wiedeman, and R.F. Tuma. Temple University School of Medicine, Department of Physiology, Philadelphia, Pennsylvania, USA.

Adherence of leucocytes to the endothelium of microvessels is one of the initial responses seen after tissue injury. Leucocyte adherence and their occasional emmigration into adjacent tissue is considered to mark the beginning of an inflammatory process. The underlying mechanisms responsible for the initial adherence is unknown. A method of studying this problem *in vivo* is complicated by the fact that most experimental preparations to expose the microvessels for direct microscopic observation involve surgery which itself is sufficient to promote adherence. In the present studies, laser irradiation of microregions of tissue at various distances from arterioles in the intact bat wing were used to probe the time course of trauma-induced changes in leucocyte-vessel wall interaction. It was found that, for equivalent tissue injury, the time required for normally nonadherent leucocytes to begin sticking and rolling along the arterial wall was dependent on the square of the distance between tissue injury site and the vessel wall. At a fixed distance, the latency time decreased by an amount which was inverse related to the extent of tissue injury. The measured latency times, which ranged from 15 to 400 seconds, shows that the primary mechanism causing leucocyte adherence may act much more rapidly than previously thought. Calculations indicate that the measured latency times may be accounted for either by a laser released tissue substance having a diffusion coefficient of 5×10^{-7} , or possibly due to temperature elevation of the vessel wall by heat from the laser beam.