

THROMBOCYTOPENIA IN SEPTICEMIA: ? THE ROLE OF DISSEMINATED INTRAVASCULAR COAGULATION. Peter B. Neame, Jack Hirsh and Hymie L. Nossel. Hamilton General Hospital and McMaster University, Hamilton, Ontario, Canada and Columbia University College of Physicians and Surgeons, New York, U.S.A.

Thrombocytopenia is frequently seen in septicemia but its mechanism is uncertain. We have carried out detailed studies in 18 septicemic patients who had associated thrombocytopenia to determine whether this was associated with coagulation abnormalities indicative of disseminated intravascular coagulation (DIC) or whether it was more frequently an isolated event.

Tests performed as indicators of DIC included fibrinogen degradation products (FDP), protamine sulfate test (PS), T_{125} fibrinogen survival and in some patients fibrinopeptide A assay (FPA). Two distinct patterns of results emerged. In one, made up of patients with mild to moderate thrombocytopenia (platelet count 48,000-135,000 μ l), there was no evidence of DIC on the basis of FDP, PS and FPA assays. In the second group, in which there was more severe thrombocytopenia (platelet count 2,000-39,000 μ l), there was definite evidence of DIC on the basis of FDP and protamine sulfate assays. The levels of fibrinogen, Factor VIII and Factor V were significantly lower in group 2 than in group 1.

It is concluded that thrombocytopenia can occur in septicemia without evidence of associated DIC, but in those cases with severe thrombocytopenia the fall in platelet count is usually accompanied by consumption of fibrinogen.

PREVENTION OF THE GENERALIZED SHWARTZMAN REACTION BY BRADYKININ AND PROSTAGLANDINS. J.G. Latour, C. Léger-Gauthier and C. Groulx. Institut de Cardiologie de Montréal, Montreal, Quebec, Canada.

We have investigated, in the pregnant rat, the implications of Hageman factor and prekallikrein activation in the pathogenesis of the generalized Schwartzman reaction (GSR). We have found that unlike the hyperlipemic animal, the pregnant rat, which develops the GSR after a single injection of endotoxin (*S. typhosa* 0.4 mg) on day 20 of gestation, does not consume prekallikrein. Prekallikrein was estimated by measurement on TAME of the arginine esterase activity generated by kallikrein upon addition of active Hageman factor to the test plasma. Bradykinin triacetate (2 or 4 μ g/kg/min.), prostaglandin (PG) E₁ (0.3 μ g/kg/min.), PGA₁ (1.0 μ g/kg/min.) or isoproterenol (0.66 μ g/kg/min.) when given as a slow infusion over 4 hours, from the time of the endotoxin to the sacrifice of the animals, were found to prevent the GSR. On the other hand, aspirin (150 mg/kg) or propranolol (2 mg/kg) given before endotoxin enhance the incidence or severity of the GSR. Furthermore, aspirin markedly reduces the prevention generated by bradykinin infusion and to a less extent that of isoproterenol. Finally, indomethacin (7 mg/kg) given twice daily for 3 days sensitizes the male rat to the GSR, since a single injection of endotoxin triggers deposition of fibrin in the glomerular capillaries. It is concluded that bradykinin generates the release of PG's and that together they prevent, like the α -adrenergic and the D-serotonergic blocking agents and or like a β -adrenergic stimulation, the renal vasomotor reactions found necessary for the GSR. These results support the hypothesis that impairment of kinin generation may possibly account for the sensitization of the pregnant rat to the GSR.

DIFFUSE OR LOCALIZED INTRAVASCULAR COAGULATION IN SEVERE CASES OF MALARIA TROPICA: HEPARIN OR NOT? J. Vreeken and Th.M. Goote. University Hospital "Wilhelmina Gasthuis", Amsterdam, The Netherlands.

The value of additional heparin therapy in patients with malaria tropica and signs of intravascular coagulation is far from clear. Whereas at one side heparin could perhaps be of value to prevent further obstruction of the microcirculation; at the other hand heparin could add additional bleeding risk when restoration of a hemostatic defect does not occur (e.g. when there is concomitant liver damage or uremic thrombopathy). Nine non immune patients with imported malaria tropica were followed during varying period for blood platelets number, coagulation factors, circulating fibrin monomers and fibrinogen degradation products (F.D.P./f.d.p.). Three of them had severe renal damage and two signs of cerebral malaria. All patients showed initially before the 15th day of illness an episode of thrombocytopenia. None of them had signs of circulating fibrin monomers. Elevated levels of F.D.P./f.d.p. were only occasionally found and were not seen in the patients with cerebral malaria and/or severe renal damage. Low fibrinogen levels were found in only three patients (all had renal damage). There were no signs of diffuse intravascular coagulation in those patients, some of the patients showed coagulation defects attributed to liver damage. Therefore intravenous heparin was not additionally given. All patients recovered completely.