1105 INFLUENCE OF ANTICOAGULANT? ANTIAGGREGANT AND ANTIFIBRINOLYTIC DRUGS ON THE WALKER-256-CARCINOSARCOMA OF RATS

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In order to find out, if there is an influence of blood coagulation factors on tumours we determined the effects of various anticoagulant drugs (Phenprocoumon, Arvin?, Acet.-salicyl.-acid) and the antifibrinolytics (EACA) on the development, metastasis formation and the rates of survival of the Walker-256-tumour. Tumorcells were the subcutaneously injected upon the back of the tail of female Whistar rats in a total number of 850. We tested the effect of Marcoumar by weekly controls of Quick's test of every single rat. 52 % of the control survived, while up to 96 % of the rats which were treated with different doses of Marcoumar survived.(n= 23 in each group). In another series only 25 % of control-animals survived, but 64 % of the rats, which were treated with EACA and with ASA, and 33 % of the rats which were treated with Arvin, survived (n= 27 in every group) The spread of the tumour in Arvin-treated rats was most invasible.The effects of clotting mechnism on the four stages in the spreding tumour are being discussed.

1106 ADRIAMYCIN (A) INDUCES A DELAYED HYPERCOAGULABLE AND PROTHROMBOTIC STATE IN RATS.

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The effects of anticancer agents on the host's haemostatic mechanism have been given limited attention so far. We have studied the early and long-term changes in haemostatic parameters of normal rats given A. Single doses of A (5-10 mg/kg b.w.), at levels active as an anticancer agent in this animal species, did not induce any acute changes in platelets, fibrinogen or fibrinolytic activity, as long as plasma drug levels were measurable. Two weeks later, however, a hypercoagulable stat developed, characterized by increased fibrinogen and F.VIII:C activity, short APTT, low total antithrombin and heparin cofactor levels and markedly depressed fibrinolytic activity (measured by euglobulin and dilute whole blood clot lysis times, plasminogen and antiplasmin amidolytic activity).These changes were dose-related and lasted at least five weeks after treatment. When the plasma antithrombin level was low,this inhibitor could be measured in the urine. A significant reduction in the occlusion time of an aortic loop was observed in A-treated rats. The occurrence of ascites, proteinuria and reduced plasma protein levels in the same animals suggests that A-induced nephrotoxicity (nephrotic syndrome?)could be involved in the pathogenesis of the hypercoagulable and prothrombotic state observed.

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1107 COAGULATION CHANGES IN EXPERIMENTAL RENAL VEIN THROMBOSIS

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Renal vein thrombosis is followed by dysfunction and degenerative alteration of the kidneys.The serious form may take a lethal course.In experimental bilateral renal vein thrombosis in rats death occurs within 4.5 hours in irreversible shock with the morphological presentation of fibrin clots.Coagulation and chemical analyses were performed in 34 animals with experimentally induced bilateral renal vein thrombosis and in 46 controls. A significant ($p < 0.05$) decrease or prolongation of fibrinogen,prothrombin time,thrombin time,reptilase time,APTT,the factors VIII and IX and a slight but not significant reduction of platelet count,factors V,IX and XII could be shown.These data exclude an early and primary occuring defibrination syndrome as cause of death.The blood loss into the kidneys and toxic substances released from the kidneys may cause refractary shock.The early,moderate impairment of the blood coagulation parameters may be the result of an activation of the kallikrein-kinin system.Finally a massive consumption coagulopathy develops and produces disseminated intravascular coagulation.

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