bosis. This paper describes a model in which thrombosis is initiated by an electrical stimulus. The thrombus produced has the histological and biochemical features of human deep vein thrombosis (DVT).

The minimum stimulus necessary to induce thrombosis was first determined by passing a fixed current for timed intervals along the femoral veins of 10 rabbits. Thrombi were seen 24 hours later if the total charge passed exceeded a threshold value of 25 millicoulombes. With this small current, no endothelial changes were visible immediately after the passage of the charge on light or scanning electron microscopy. At 24 hours a mural thrombus formed, which had fully corss-linked fibrin and histological features resembling human DVT.

In the second series of experiments, the sequence of changes occurring in thrombus production was investigated in 3 groups of 18 rabbits each. After passage of the critical charge along the femoral vein in each animal, veins were removed at fixed intervals, the contralateral vein acting as a control. The veins were examined by scanning electron-microscopy (Group I), transmission electron-microscopy (Group II) and light microscopy (Group III). The earliest changes were detectable at 5 minutes and consisted of the laying down of an organised structure of criss-crossing fibrin strands with small platelet clumps at fibrin intersections. Later the fibrin structure spread towards the lumen; platelet clumps fused and a coralline thrombus was formed by 24 hours. The significance of these changes will be discussed.

M. B. Donati, E. Dolfini, A. Cavenaghi, L. Morasca and G. de Gaetano (Istituto di Ricerche Farmacologiche 'Mario Negri,' Via Eritrea, 62 – 20157 Milano, Italy): **Retraction of Thrombin-Induced Fibrin by Rhabdomyosarcoma BA 1112 Cultured Cells. (523)**

The capacity to induce fibrin retraction has been considered a specific property of platelets until recently, when Niewiarowski et al. (Proc. Soc. Exp. Biol. Med. *140*, 1199, 1972) observed fibrin retraction induced by human fibroblasts. As a part of a larger study on the interactions of cultured cells with fibrin, we have investigated the ability of the following cell lines to retract fibrin: KB (human oral epidermoid carcinoma); HeLa (human cervix carcinoma); Chang Liver (human, normal epithelium; Chang Conjunctiva (human normal epithelium); NCTC clone 929 (L) (fibroblasts from C3H/AN mice) and BA 1112 (rhabdomyosarcoma developed on WAG/Rji inbred rats). Cells were cultured in Eagle's MEM, in Hank's blanced salt solution plus 10% calf serum, removed from the flasks by trypsin treatment and resuspended at a concentration of 2×10^6/ml in Tyrode-albumin solution, containing Ca^{++} and Mg^{++}. Human citrated platelet-poor plasma was clotted in a test tube at 37° C by thrombin in the presence of either the cell suspensions or buffer. Only BA 1112 cells were able to retract fibrin; the presence of Ca^{++}, cellular integrity and random distribution in the sample were required for this activity. BA 1112 cells were able to modify the structuration of thrombin-induced fibrin as indicated by the marked increase of the maximal amplitude of thrombelastogram. BA 1112-induced fibrin retraction was inhibited by PGE_1 and by some pyrimido-pyrimidine derivatives, not by apsirin. No retraction occurred when reptilase instead of thrombin was used as the clotting agent, even if the cells were preincubated with ADP. These results suggest that BA 1112 cells have a susceptibility to thrombin similar to that of platelets; this hypothesis is interesting in view of the muscular origin of these cells.

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A. Poggi, N. Polentarutti, M. B. Donati, G. de Gaetano and S. Garattini (Istituto di Ricerche Farmacologiche 'Mario Negri,' Via Eritrea, 62 – 20157 Milano, Italy): **Fibrinogen, Platelet and Red Cell Kinetics in Mice Bearing an Experimental Tumor. (524)**

In view of the possible role of platelets and coagulation mechanisms in the growth and dissemination of solid tumors, a number of haematological parameters have been followed during development of an experimental syngeneic tumor in mice (Lewis Lung Carcinoma, 3LL). This tumor, when transplanted intramuscularly in C_{57}Bl/6 mice, grows locally and

gives spontaneous metastases to the lungs. The transplanted animals survive for about 4 weeks. Metastases are visible since the third week. A slight but constant increase in plasma fibrinogen level and a marked thrombocytopenia were observed starting during the second week after tumor implantation. No other significant changes in coagulation and fibrinolysis parameters were found. Moreover, the animals developed a marked haemolytic anaemia, possibly microangiopathic in origin. ^{125}I-fibrinogen survival was decreased of about 20% during the second week after tumor implantation and was not further reduced later on. Fibrinogen turnover was accelerated since the second week and was further increased thereafter, being more than doubled at the end of the third week. Labelled fibrinogen accumulated in the primary tumor and in the lungs; its rats of disappearance from the tumor was much slower than from lungs or blood. These data suggest the occurrence of a low-grade, localized fibrinogen consumption (intravascular coagulation ?). ^{51}Cr-platelet survival was not modified throughout the observation period, whereas platelet turnover was markedly reduced since the end of the second week, suggesting a defective platelet production. ^{51}Cr-red cell survival was drastically reduced to about 30% of controls starting from the second week, whereas labelled red cell turnover was almost doubled. The pathogenetic relevance of the observed modifications in the processes of grwoth and dissemination of 3 LL remains to be established.

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P. B. A. Kernoff, G. Fieldhouse, J. Williams and G. P. McNicol (University Department of Medicine, The General Infirmary and Regional Cytogenetics Unit, St. James's Hospital, Leeds, England): **Haemophilia in a Girl with XX/XXX Mosaicism. (525)**

Investigations performed on a 17 yr. old girl with factor VIII deficiency indicated haemophilia rather than von Willebrand's disease. She had a life-long history of defective haemostasis but was otherwise normal and had normal menstruation. There was no definite family history of a bleeding disorder. She had a low level of factor VIII clotting activity (12%) but normal factor VIII-related antigen (126%), bleeding time, ristocetin aggregation of platelets in PRP, ristocetin co-factor and platelet glass bead adhesion. There was no evidence of circulating anti-VIII. Following transfusion of cryoprecipitate there was an immediate rise and then rapid fall-off in the level of factor VIII clotting activity (50% disappearance time about 11.5 hours). Levels of antigen paralleled these changes.

Chromosomal analysis of peripheral lymphocytes showed 46XX/47XXX mosaicism. It is suggested that the clinical expression of haemophilia was due to this chromosomal abnormality, the pathophysiology of which probably included non-dysjunction of a haemophilia-carrying X chromosome.

A. Spinelli, W. Schmid and P. W. Straub (Department of Medicine, Kantonsspital, University of Zurich, CH 8091 Zurich, Switzerland): **Hemophilia B in A Girl with Deletion of a Short Arm of One X-Chromosome. (526)**

12 females with hemophilia B have been reported. One had a 45 XO-Turner syndrome, one an XX–XO mosaicism. We report the first case with deletion of a short arm of one X-chromosome.

The I-yr. girl was referred because of spontaneous hematomas and bruising. During observation a lingual hemorrhage could be stopped only with factor IX, Clinical findings were normal, development corresponding to the age. Factor IX repeatedly was $< 1\%$, PTT 81 sec (n. 40–55), the recalcification time 375 sec (n. 80–120). Other findings were normal, including factors VIII, XI, XII. Parents, 2 siblings and 8 family members of the mother were also normal.

Chromosomal analysis: deletion of one short arm of one X-chromosome. Deletion being known to suppress the activity of the entire affected chromosome, the functional result is that of the XO-Turner syndrome. The morphologically normal X-chromosome must have the hemophilia abnormality. The possibilities that the mother is a carrier or