Thromboembolism has been frequently reported in cancer patients, mainly in cases with solid tumors. Besides in several animal models, fibrin deposition around the cancer and platelet aggregates appear to be involved in invasion and metastasis. This study was aimed at evaluating the extent of in vivo platelet activation and fibrin formation in several kinds of human cancer. We excluded from this study patients whose blood was sampled with difficulty as well as those having clinical evidence of thrombosis or embolism, those with thrombocytopenia, increased fibrinogen degradation products or biological pattern of disseminated intravascular coagulation. Fibrinopeptide A (fPAM) and B-thromboglobulin (fPBTH) were measured by RIA. Platelet release and fibrin formation frequently occur in cancer patients showing no sign of thrombotic process. It was found that in more than fifty percent of patients, fPAM was significantly increased above the upper reference limit. Cases with increased f-tg were less frequent. Separate increases in fPAM or fPBTH levels were often observed. fPAM remained within the reference values in almost all patients. fPBTH and f-tg were usually above 150 % of the reference mean.

We conclude that platelet release and fibrin formation frequently occur in cancer patients showing no sign of thromboembolic process. Increased level of fPAM with normal plasma f-tg level suggests that thrombin generation occurs only in the extracellular compartment, probably next to the tumoral tissues. Increased levels of plasma f-tg with normal fPAM levels may result from platelet activation by other stimuli than thrombin. It must be emphasized that normal fPAM does not exclude the presence of fibrinous circulating aggregates which cannot be dispersed by EDA. High fPAM activities may be due to the release of the von Willebrand factor from tumoral vessels.

The mechanisms of platelet activation by human tumour cells grown in vitro or freshly dissociated from tumour tissues have been investigated. MOCCL human 2-lymphoblastic cells cultured "in vitro" induced platelet aggregation through the production of ADP, as evidenced by inhibition of the effect by aspirin. The maximum of ADP production by tumour cells was reached after 1 hour and was 225 ± 10-6 M. On the contrary, platelet aggregation induced by 5637 human bladder carcinoma cells was not inhibited by aspirin, but was abolished by hirudin, indicating the important role of thrombin in this effect. Tumour cells dissociated from 3 breast carcinomas showed a very high platelet aggregating activity, which was not inhibited by hirudin or aspirin, but was abolished by iodoacetic acid, suggesting a role for a cystein-protease in platelet activation. These results confirm that platelets can be activated by tumour cells through different mechanisms; they also suggest that the methods employed to obtain the tumour cells can influence the results, probably because of the different cell populations which are present in the dissociated tumour tissues.

Information obtained with freshly dissociated cells is interesting, because this method has been used seldom so far and because it provides a more physiological approach to the study of the interactions of tumours and platelets.