## 131 Platelet Disorders in Patients with Hematopoetic and Nonhematopoetic Malignancies

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Experimental and clinical findings demonstrate that neoplastic disease is often associated with platelet disorders.

*Abnormal platelet count.* Reactive thrombocytosis occurs in solid tumors of the lung, ovary, breast, stomach and in Hogkin's disease. Autonomous thrombocytosis is present in myeloproliferative disorders such as polycythemia vera, myelofibrosis, myelosclerosis, chronic myelogenous leukemia and essential thrombocytosis. Acute leukemias and metastatic cancer are commonly associated with thrombocytopenia caused by several mechanism (production defects due to blast proliferation, bone marrow infiltration or chemotherapy; platelet destruction due to autoimmune-mediated mechanisms; isolated or combined platelet consumption).

*Abnormal platelet function.* Abnormalities in megakaryocyte and platelet morphology as seen in myeloproliferative disorders (MPD), myelodysplastic syndromes (MDS) and acute leukemias are often associated with increased $\alpha$-granular platelet secretion in vivo. In MPD a selective platelet $\delta$-granular storage pool defect is commonly observed. These platelets show defective aggregation responses in vitro. Some of these abnormalities seem to correspond to biochemical disorders such as defects in platelet receptors and/or disturbances of platelet arachidonic acid metabolism. In patients with extended infiltrations or metastases of solid tumors activation of platelets and coagulation occurs as a result of the interaction between tumor cell proliferation and the hemostatic system. However, our own data do not support findings from other laboratories reporting significantly higher plasma levels of platelet-secreted proteins and/or fibrinopeptide A in patients with progressive neoplasia than in those with limited malignancy or remission. In contrast, we observed a rather low sensitivity and specificity of platelet secretion and thrombin generation related to the extent of tumor progression (J. Cancer Res. Clin. Oncol. 111: 101, 1986).

*Chemotherapy-induced platelet dysfunction.* Thrombocytopenia is an expected complication of aggressive chemotherapy regimens. Treatment with the alkylating agent busulfan or with nitrosoureas such as BCNU, CCNU or methyl-CCNU can produce severe and prolonged thrombocytopenia due to marrow suppression. Melphalane, methotrexate, bleomycin and cytosine arabinoside are known to induce platelet aggregation defects in response to collagen and ADP. Vinca alkaloids have been shown to inhibit platelet secretion and aggregation in vitro and in vivo. However, the mechanisms by which these drugs interfere with platelet metabolism are not yet well understood.