PLATELET FUNCTION AND VALPROATE

The role of arachidonate metabolites in valproate-induced platelet dysfunction and hemorrhagic diathesis was investigated by ex vivo methods at the Albert Szent-Gyorgyi Medical University, Szeged, Hungary. Platelets isolated from patients receiving long-term valproate (VPA) therapy or carbamazepine (CBZ) as a control were labeled with C14 arachidonic acid. C14-eicosanoids were separated by thin layer chromotography and determined quatitatively by liquid scintillation. VPA, even in low concentrations, reduced the activity of the arachidonate cascade in platelets, inhibiting the synthesis of the platelet aggregator thromboxane A2. (Kis B, Szupera Z, Mezei Z et al. Valproate treatment and platelet function: the role of arachidonate metabolites. Epilepsia March 1999;40:307-310). (Reprints: Dr B Kis, Department of Pathophysiology, Albert Szent-Gyorgyi Medical University, Szeged, H-6701, Semmelweis u 1, PO Box 531, Hungary).

COMMENT. VPA may cause alterations in hemostasis and increase surgical bleeding. Thrombocytopenia and platelet dysfunction are suggested causes for the bleeding, and ex vivo experiments have demonstrated a VPA-induced inhibition of arachidonate cascade in the platelets, leading to reduced synthesis of platelet aggregators.

Phenytoin-associated thrombocytopenia is reported in a 2-year-old girl on the 11th day of therapy, with recovery 5 days after withdrawal of treatment. There were no signs of bleeding.

ANTIEPILEPTIC SKIN REACTIONS AND BRAIN TUMORS

The frequency of both severe and mild skin reactions in 289 adult patients with brain tumors treated consecutively (1988-93) with cranial radiation and AEDs was studied retrospectively by review of records at the Brigham and Women's Hospital, Boston, MA. Erythema multiforme had occurred in only one patient, whereas milder rashes occurred in 18% of exposures to AEDs, including 22% of exposures to phenytoin, compared with the expected rate of 5-10%. Most rashes (59%) occurred before the initiation of radiotherapy. An increased frequency of mild drug rashes among patients with brain tumors, especially primary tumors, is not related to radiation. The increased prevalence of erythema multiforme and Stevens-Johnson syndrome frequently reported in patients with brain tumors treated with phenytoin or carbamazepine and cranial irradiation was not confirmed. (Mamon HJ, Wen PY, Burns AC, Loeffler JS. Allergic skin reactions to anticonvulsant medications in patients receiving cranial radiation therapy. Epilepsia March 1999;40:341-344). (Reprints: Dr HJ Mamon, Department of Radiation Therapy, Joint Center for Radiation Therapy, 330 Brookline Ave, Boston, MA 02215).

COMMENT. The rare occurrence of severe skin reactions in brain tumor patients receiving AEDs and cranial radiation in this study might be explained by discontinuation of AED before starting radiation therapy or at the earliest sign of a mild rash. Previous reports of erythema multiforme in patients receiving cranial irradiation and phenytoin or carbamazepine have alerted neurosurgeons to this increased risk of severe skin reactions and prompted heightened vigilance for this hazardous complication. The increased incidence of mild AED skin reactions noted in this series of primary brain tumor patients is unexplained. Tapering of a dexamethasone treatment was not a dominant factor but may have contributed to development of skin rash. Stevens-Johnson syndrome can be life-threatening, and the prophylactic use of phenytoin or carbamazepine following