Case 1

A 25-year-old woman, II para, in whom epilepsy had been diagnosed in 1972, had taken SV since March 1977. Throughout the pregnancy her dosage was SV 1350 mg/day and phenytoin 450 mg/day divided in 3 doses.

In spite of therapeutic serum concentrations of these two drugs, she had had several major convulsions during early pregnancy. Delivery took place at term, the healthy boy (weight 3440 g, Apgar score 9/10) did not show any abnormalities; growth and development during the first year of life were normal as was the EEG.

Case 2

A 24-year-old woman, III para, who had suffered from epilepsy since 1968, was started on SV in January 1978 (4 months before conception). During pregnancy she was well controlled taking SV 1200 mg/day, phenytoin 400 mg/day, carbamazepine 600 mg/day, and clonazepam 1 mg/day. A healthy girl, weighing 4000 g was born at term. The Apgar score was 9/9, the initial EEG and development during the first 2 months were normal.

The serum level of SV was measured in the mothers at delivery and in the neonates at birth and repeatedly postnatally. At birth, SV levels were 220 and 110 $\mu\text{mol/l}$ in the neonates, and 200 and 210 $\mu\text{mol/l}$ in the mothers, but fell to insignificant concentrations by 5 days and were undetectable at 9 days (Figure).

The plasma concentration of glycine rose markedly during the first postnatal day, the highest levels being 665 and 605 $\mu\text{mol/l}$. These values differed very significantly from controls (Figure).

From these 2 case histories it is concluded that the use of SV in the last trimester of pregnancy induces a transient secondary hyperglycinaemia in the neonatal period, although the plasma glycine concentrations are clearly lower than in nonketotic hyperglycinaemia or organic acidemia associated with hyperglycinaemia (Tanaka, 1975; von Wendt *et al.*, 1978). As these infants show normal psychomotor development, it is evident that this moderate rise of glycine concentration does not impair

Figure Glycine (upper part) and sodium valproate (lower part) in plasma and serum respectively in 2 newborn babies during the first 5 postnatal days. Normal range of postnatal glycine levels in plasma (mean $\pm$ SD, $n = 10$) is shown by shaded area.

the development of the CNS. However, it should be borne in mind that treatment with SV during pregnancy can cause a false-positive finding in metabolic screening for aminoacidaemias in newborn babies.

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S. SIMILÄ, L. VON WENDT, A.-L. HARTIKAINEN-SORRI,
P. KÄÄPÄ, AND A.-L. SAUKKONEN
Departments of Paediatrics, and
Gynaecology and Obstetrics,
University of Oulu,
90220 Oulu 22, Finland

Neutropenia during sodium valproate treatment

Sir,

Thrombocytopenia is a well-known side effect of sodium valproate (dipropylacetic acid) treatment (Winfield *et al.*, 1976; Raworth and Birchall, 1978; Sandler *et al.*, 1978). As far as we know, neutropenia has not been documented during valproate medication. Recently we treated a 3-month-old boy with sodium valproate (40 mg/kg per day) because of postanoxaemic convulsions. No other drugs were given. Total blood neutrophils decreased steadily from pretreatment values between 3.5 and $5.4 \times 10^9/l$ to a value as low as $0.460 \times 10^9/l$ during the next 2 months. Valproate was stopped and total neutrophil count promptly increased to $2.0 \times 10^9/l$ within 14 days and to pretreatment values within a few weeks. Thrombocytes remained within normal limits. Erythrocyte count did not change. Because of the fragile condition of the infant a bone marrow puncture was not performed. Antibodies against thrombocytes have been shown in valproate-induced thrombocytopenia (Sandler *et al.*, 1978); in our patient immunofluorescence studies at the time of the lowest neutrophil count failed to demonstrate antibodies against granulocytes. Thrombocytopenia, and now neutropenia, as well as hyperglycinaemia (Jaeken *et al.*, 1977; Kamoun *et al.*, 1977), normal glycinorrachia (Jaeken *et al.*, 1977), and ketonuria (Simon and Penry,

1975), all reported in association with sodium valproate medication, are classical findings in ketotic hyperglycinaemia (Scriver and Rosenberg, 1973). This suggests that sodium valproate can induce a biochemical syndrome similar to that of the ketotic hyperglycinaemias.

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J. JAEKEN, C. VAN GOETHEM, P. CASAER,
H. DEVLIEGER, AND E. EGGERMONT
*Department of Paediatrics,
University of Leuven,
3000 Leuven, Belgium*

M. PILET
*Blood Transfusion Centre,
Laboratory of Immunohaematology,
3000 Leuven, Belgium*