

Correspondence

Sodium valproate and pregnancy

Sir,

We were presented with a baby born to a mother taking sodium valproate who wished to breast feed. There are no data on breast milk levels of sodium valproate; it is presumed from collateral evidence that some of the drug would pass across from maternal serum into the milk. Studies in animals given modest doses of sodium valproate during pregnancy (30-90 mg/kg) showed no significant teratogenic effects. When a much higher dose was used (about 600 mg/kg) there was a dose-related increase in the rate of intrauterine death and major fetal abnormalities, most of which involved the kidneys or the lower lumbar spine (Whittle, 1976).

Information on the outcome of the pregnancies where sodium valproate has been taken as the main anticonvulsant is very scanty; in most reports two or more drugs have been used or, in the case of an abnormality, the family history has suggested a strong genetic element (W. Reckitt-Labaz, 1978, personal communication).

Case 1, a 22-year-old primipara, was epileptic and changed to sodium valproate in November 1975. She was well controlled taking 1600 mg/day in divided doses. She had had irregular periods and did not realise that she was pregnant until she was about 14 weeks. She consequently booked at the hospital clinic at about 18 weeks. Her anticonvulsant drug was not changed.

She was admitted in labour at term in July 1978 and delivered a healthy boy weighing 3010 g; Apgar score was 9 at one minute, and no abnormalities were observed. The baby breast fed well and was discharged home on the 6th day, slightly under his birthweight. Mother and baby were seen at 29 days after delivery. The baby was still breast feeding well, gaining weight, and beginning to smile.

The sodium valproate level was measured in the mother's serum, as shown in the Figure. The level fell slightly at term without any change in the oral dose and then rose to the previous level by 29 days. The valproate level in the serum of the neonate was of the same order as that of the mother's at delivery, but fell to insignificant levels by 5 days and was undetectable at 29 days (Figure). The mean level of valproate in breast milk at 5 days was 50 mmol/l; it had fallen to 21 mmol/l by 29 days.

The neonatal valproate level indicates that valproate crosses the placenta freely and maternal serum levels will reflect fetal serum levels. Sodium valproate crosses through from serum into breast milk and will be found at a level between 5 and 10% of that in the mother's serum. The absorption of valproate from breast milk by the neonate appears to be insignificant. In this instance there was no evidence of any abnormality associated with the use of this drug.

It may be concluded that breast feeding while on therapeutic doses of sodium valproate is safe and will not

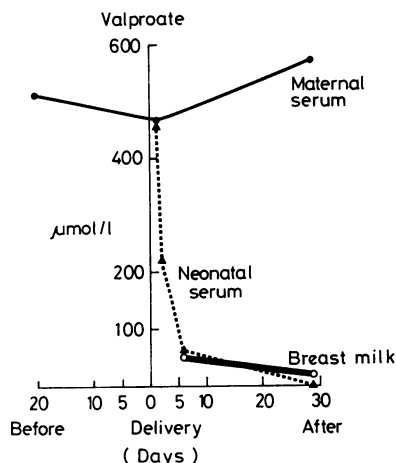


Figure Maternal serum and breast milk levels of sodium valproate, note marked fall in neonatal serum levels.

result in detectable neonatal blood levels. Nevertheless, in early pregnancy it must still be prescribed with caution until there is evidence of its safety.

Reference

Whittle, B. A. (1976). In *Proceedings of a Symposium on Clinical and Pharmacological Aspects of Sodium Valproate*, Nottingham, September 1975, p. 105. Edited by N. J. Legg. MCS Consultants: Tunbridge Wells.

F. W. ALEXANDER
Newcastle General Hospital,
Children's Department,
Westgate Road,
Newcastle upon Tyne NE4 6BE

Breast feeding and smoking

Sir,

Success at breast feeding has been related to social class (Martin, 1978) and the age at which the mother finished full-time education (Last, 1978; Martin, 1978; Pursall *et al.*, 1978). This study was aimed at determining the prevalence of breast feeding in Cambridge, after delivery and at 3 months. The influence of smoking by mothers was also examined. Smoking by the mother has been shown to have adverse effects on the fetus (Butler *et al.*, 1972) and smoking by either parent an adverse effect on the health of the infant (Leeder *et al.*, 1976), but its effects on lactation do not appear to have been investigated.

330 women delivered consecutively at the maternity hospital in Cambridge in 1978 were questioned after delivery and again at 3 months. The overall prevalence of breast feeding after delivery was 82% and at 3 months' postpartum it was 46%. Initial choice of infant feeding was influenced by social class, with 86% of women from the nonmanual classes starting by breast feeding compared with 76% of manual class women.

The Table compares the prevalence of bottle feeding from delivery, bottle feeding at 3 months by those who began by breast feeding, and breast feeding at 3 months in smokers and nonsmokers. Smokers were less likely to attempt breast feeding than nonsmokers, and this achieves statistical significance in the group overall ($\chi^2 = 6.752$, $P < 0.01$) and the manual classes ($\chi^2 = 6.389$, $P < 0.02$). Furthermore mothers who smoked and began by breast feeding were more likely to have changed to bottle feeding by 3 months than mothers who did not smoke, and this achieves statistical significance in the nonmanual classes ($\chi^2 = 3.894$, $P < 0.05$). Comparison of the mothers who began by bottle feeding with those who were breast feeding at 3 months shows that there were more smokers among the bottle feeders in the group overall ($\chi^2 = 15.494$, $P < 0.001$) and in both the nonmanual ($\chi^2 = 4.657$, $P < 0.05$) and manual classes ($\chi^2 = 5.26$, $P < 0.05$).

Table *Maternal smoking and infant feeding*

	Social class	Total	Artificial feeding		Changed to artificial feeding by 3 months		Breast feeding at 3 months	
			No.	%	No.	%	No.	%
Smokers	Nonmanual	18	5	28	6	33	7	39
	Manual	26	11	42	11	42	4	15
Non-smokers	Nonmanual	117	14	12	28	24	75	64
	Manual	69	12	17	37	54	20	29

There were, as might be expected (Capell, 1978), more (27%) smokers among the manual class mothers than among the nonmanual women (13%). The reasons for smokers being less inclined to breast feed and less likely to persist with breast feeding cannot be ascertained from this study. Smoking was not associated with any particular reason for giving up breast feeding. Nevertheless it appears that smoking by the mother is yet another factor which may influence the prevalence of breast feeding.

References

- Butler, N. R., Goldstein, H., and Ross, E. M. (1972). Cigarette smoking in pregnancy: its influence on birth weight and perinatal mortality. *British Medical Journal*, **2**, 127-130.
- Capell, P. J. (1978). Trends in cigarette smoking in the United Kingdom. *Health Trends*, **10**, 49-54.
- Last, P. (1978). Letter: Breast feeding and mother's education. *Lancet*, **2**, 896-897.
- Leeder, S. R., Corkhill, R. T., Irwig, L. M., Holland, W. W., and Colley, J. R. T. (1976). Influence of family factors on asthma and wheezing during the first five years of life.

British Journal of Preventive and Social Medicine, **30**, 213-218.

Martin, J. (1978). *Infant Feeding 1975: Attitudes and Practice in England and Wales. A Survey*. HMSO: London.

Pursall, E. W., Jepson, M. E., Smith, B. A. M., and Emery, J. L. (1978). Letter: Breast feeding and mother's education. *Lancet*, **2**, 734-735.

MARGARET J. WHICHELOW AND BARBARA E. KING
Office of the Regius Professor of Physic,
Level 5,
Addenbrooke's Hospital,
Hills Road,
Cambridge CB2 2QQ

Circulating immune complexes in mucocutaneous lymph-node syndrome (Kawasaki disease)

Sir,

The clinical features of mucocutaneous lymph-node syndrome (MLNS) are well established (Kawasaki *et al.*, 1974), but the aetiology is unknown. Fossard and Thompson (1977) described a Japanese child living in England in whom raised levels of circulating immune complexes by the platelet agglutination test were found early in the disease. Total haemolytic complement and C_4 were depressed although C_3 levels were normal.

Recently we have been able to confirm the abnormal immune complex findings in a 9-month-old Caucasian girl with MLNS. She presented with fever, rash, and stomatitis. After 3 days she became irritable and photophobic; the rash became confluent and prominent over the palms and soles. Lumbar puncture and CAT scan were normal, and she showed no response to several antibiotics (erythromycin, fucidin, flucloxacillin, or ampicillin). Two weeks after the onset of symptoms she was admitted to this hospital where she was noted to have an erythema multiforme-like rash, marked cervical lymphadenopathy, stomatitis, nonpurulent conjunctivitis, puffy feet, and tachycardia. The skin at the fingertips had started to desquamate. She was mildly anaemic and had a leucocytosis. IgE was 44 IU/ml (normal) and total haemolytic complement and C_3 levels were also normal (155 and 124% of normal human serum respectively). Immune complexes containing IgG were raised (41.5% inhibition of IgG latex agglutination (Levinsky and Soothill, 1977): normal subjects <20%). Her illness resolved without further treatment and she was well when she was discharged home on the 43rd day.

Many of the clinical features of this disorder—such as arthralgia, rash, and myocarditis with coronary artery vasculitic changes—could well be due to immune complex deposition. However, raised levels of soluble immune complexes have been described in a variety of diseases and it is difficult to decide whether they are the cause or the result of the disease. Isolation and characterisation of the complexes in patients with this disorder may help to establish the aetiology of this strange disease.