the differences observed may largely depend on the duration of the disease.

SSPE and IME may well represent opposite ends of a spectrum of disease induced by measles virus persisting in the brain, and the nature and severity of immunological deficiency at the time of the initial infection may determine the latent period and rate of progress of the encephalitis. Various immunological abnormalities have been found in patients with SSPE (Addy, 1977) but proof that they were present when primary infection occurred and predisposed to the 'slow' virus infection is lacking. Our patient contracted measles when there were good reasons to suspect that cell-mediated immunity was still depressed: the exanthem appeared 3–4 weeks after cyclophosphamide treatment had been stopped because of neutropenia, and the girl received radiotherapy which has been shown to prolong drug-induced immunosuppression (Campbell *et al.*, 1973). Typical SSPE began 8 years later.

The only similar recorded case was that of Loirat *et al.* (1971); during immunosuppressive treatment for the nephrotic syndrome, this boy developed an exanthema suggestive of measles and he died 2 years later of an SSPE-like illness during which the serum measles antibody rose to a high titre. Necropsy was not performed.

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Response of neonatal hypocalcaemia to 1α -hydroxyvitamin D₃

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SUMMARY Administration of 1α -OH-D₃ to hypocalcaemic neonates (mean $\pm$ SD, serum calcium 1.50 ± 0.13 mmol/l) significantly increased serum calcium in all 24 infants within 48 hours after starting therapy (mean $\pm$ SD 1.83 ± 0.23 mmol/l). The time required to correct hypocalcaemia was significantly shorter (2.04 ± 0.56 days) in infants treated with 1α -OH-D₃, than in 24 infants treated with calcium gluconate infusions (4.12 ± 1.0 days). Treatment with 1α -OH-D₃ was effective, easy to maintain, and produced no side effects.

Decreased parathyroid hormone (PTH) secretion and/or end organ response, increased serum calcitonin concentrations, and defects in vitamin D metabolism have been implicated in the pathogenesis of neonatal hypocalcaemia (Tsang *et al.*, 1976).

$1\alpha,25$ -Dihydroxyvitamin D ($1\alpha,25(\text{OH})_2\text{D}$), the biologically active metabolite of vitamin D, which stimulates intestinal calcium transport, is synthesised by successive hydroxylation of vitamin D in the liver and kidney (DeLuca, 1976). Derangements in these metabolic pathways, and maternal vitamin D deficiency during pregnancy, may well be important factors in the pathogenesis of neonatal hypocalcaemia (Hillman and Haddad, 1975; Weisman *et al.*, 1976; Hillman *et al.*, 1977). We, therefore, investigated the effect of 1α -hydroxyvitamin D₃ (1α -OH-D₃), a readily synthesised and commercially available analogue of $1\alpha,25(\text{OH})_2\text{D}_3$, in the treatment of neonatal hypocalcaemia.

Patients and methods

48 infants (mean gestational age 33.5 ± 2.8 , $\pm$ SD

weeks; mean weight $1947 \pm 613\text{g}$, $\pm\text{SD}$) with symptomatic hypocalcaemia presenting within the first 4 days of life were studied, with the informed consent of the parents. Most infants had muscular twitchings or apnoeic episodes and a few had frank convulsions. The serum calcium of each infant averaged $<1.75\text{ mmol/l}$ ($7\text{ mg}/100\text{ ml}$). The radioassayable serum 25-hydroxyvitamin D concentrations were $>25.0\text{ nmol/l}$ ($\approx 10\text{ ng/ml}$) in all patients (mean $\pm\text{SD}$ $58.0 \pm 22.9\text{ nmol/l}$ ($23.2 \pm 9.1\text{ ng/ml}$)). All the patients received brief IV infusions of calcium gluconate to alleviate symptoms and were then divided randomly into two groups equally matched in gestational age and 1-minute Apgar score. Group 1 received 1α -OH-D₃, $0.33\text{ }\mu\text{g}$ in arachis oil orally, twice daily for 5 days. Group 2 received IV infusions of calcium, 20 mg/kg per day, as 10% calcium gluconate. Serum calcium was determined twice daily by Eppendorf flame photometer.

Results

Administration of 1α -OH-D₃ significantly increased serum calcium in each patient within 48 hours after starting treatment (Table) and there was no recurrence of the symptoms of hypocalcaemia. The mean recovery time (time required to correct hypocalcaemia) was significantly ($P < 0.01$, t test) shorter in infants treated with 1α -OH-D₃ (group 1) than in infants treated with calcium gluconate infusions (group 2). No episodes of hypercalcaemia were recorded. All infants remained normocalcaemic when 1α -OH-D₃ was stopped.

Table Data for hypocalcaemic infants before and after treatment

Group	Treatment	Calcium mmol/l (mean $\pm$ SD)		Calcium $>1.75\text{ mmol/l}$
		Before treatment	48 hours after treatment	Mean ($\pm$ SD) recovery time (days)
1	1α -OH-D ₃	1.50 ± 0.13	$1.83 \pm 0.23^*$	$2.04 \pm 0.56^{**}$
2	Calcium gluconate	1.54 ± 0.10	1.56 ± 0.28	4.12 ± 1.00

*Significantly different from group 2, $P < 0.05$; **significantly different from group 2, $P < 0.01$.

Conversion SI to traditional units: Calcium— $1\text{ mmol/l} \approx 4\text{ mg}/100\text{ ml}$.

Discussion

Renal 25-hydroxyvitamin D- 1α hydroxylase activity is influenced by a variety of factors including serum and tissue concentrations of calcium, PTH, $25(\text{OH})\text{D}$, and $1\alpha,25(\text{OH})_2\text{D}$ (DeLuca, 1976). Thus, impairment in the synthesis of $1\alpha,25(\text{OH})_2\text{D}$ may be the end result of the derangements in PTH, calcitonin,

and vitamin D metabolism, which have been implicated in the pathogenesis of neonatal hypocalcaemia (Tsang *et al.*, 1976; Weisman *et al.*, 1976). Indeed, newborn rats are unable to synthesise $1\alpha,25(\text{OH})_2\text{D}$ to detectable levels (Weisman *et al.*, 1976). The present data demonstrate the effectiveness of 1α -OH-D₃ in the treatment of neonatal hypocalcaemia and are in good agreement with those of earlier studies in which $1\alpha,25(\text{OH})_2\text{D}_3$ was evaluated for the prevention (Chan *et al.*, 1978), and treatment (Kooh *et al.*, 1976), of neonatal hypocalcaemia, and with one case report in which 1α -OH-D₃ was given to an infant with protracted hypocalcaemia (Doxiadis and Lapatsanis, 1977).

1α -OH-D₃ is converted to $1\alpha,25(\text{OH})_2\text{D}_3$ *in vivo*, a necessary step for its biological activity (DeLuca, 1976). It was suggested that the hydroxylation of vitamin D to 25-hydroxyvitamin D may be impaired in premature infants (Hillman and Haddad, 1975). In our study, however, premature infants responded to treatment with 1α -OH-D₃, indicating that 25-hydroxylation of 1α -OH-D₃ had taken place in these infants. Traditional treatment of neonatal hypocalcaemia with continuous calcium gluconate infusions is difficult to maintain and may cause severe complications (Tsang *et al.*, 1976). However, 1α -OH-D₃ treatment was easy to maintain and produced no side effects.

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