

circulating vitamin D metabolites. *Clin Endocrinol Metab* 1980; 9: 63-79.

⁷ Potter E L. *Pathology of the fetus and infant*, second edition. New York: Year Book Medical Publishers, 1961: 14.

⁸ Hillman L S, Haddad J G. Perinatal vitamin D metabolism. II. Serial 25-hydroxyvitamin D concentrations in

sera of term and premature infants. *J Pediatr* 1975; 86: 928-35.

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Neonatal tetanus—long-term residual handicaps

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SUMMARY Thirty-eight survivors of neonatal tetanus were assessed, 5 to 12 years after recovery, for neurological sequelae, physical growth, and maturation. Apart from appreciable handicaps (cerebral palsy, mental deficit, behavioural disturbances) in 4 cases, no harmful effect on physical growth or development was found. The fact that affected patients had frequent and prolonged bouts of spasms and apnoea suggests that anoxia was the main cause of brain damage.

Generalised convulsive spasms, associated with cyanosis and apnoea and consequently with brain hypoxia, are a common and severe disorder in neonatal tetanus. It is generally believed that tetanus does not leave neurological sequelae.^{1,2} This paper presents the results of a long-term follow-up study of children who survived neonatal tetanus.

Subjects and methods

By the end of the 1970s neonatal tetanus had almost disappeared in Greece.³ This study is based on 73 children (56 of them boys) who were admitted to hospital during 1966-1977 with a clinical diagnosis of tetanus. Each came from a poor family with bad living conditions, and most of them had been delivered at home without the presence of a doctor or midwife. In every case septic cutting of the cord was the cause of the tetanus.

The presence of spasms and their management, the duration of each attack and interval between attacks, the presence of cyanosis and apnoea and the duration of each were noted. Each case was treated conservatively. Spasms were controlled by diazepam alone or in combination with barbiturates generally intravenously, by phenobarbitone, intra-

muscularly or through a nasogastric tube, or by sodium phenobarbitone, intravenously, intramuscularly, or rectally. Patients were classified according to severity: 32 of them had the mild form (grade 1), 13 the moderate (grade 2), and in 28 tetanus was severe (grade 3). Treatment and classification are described in detail elsewhere.³

At least 3 years after leaving hospital each survivor was invited for evaluation. This comprised history since leaving hospital, a general examination (including an assessment of physical growth and development) and a neurological evaluation, as well as a social history, psychometric, and psychological evaluation and an electroencephalogram (EEG). The history since leaving hospital was focused especially on the detection of possible causes of neurological involvement. Hearing was evaluated by an audiologist, using audiometry if applicable. The eyes were examined by an ophthalmologist. In addition, an evaluation of the child's speech was made.

To assess intellectual functioning we used (1) the Denver development screening test, (2) the Stanford-Binet test, (3) the Wechsler intelligence scale for children, and any other tests as indicated depending on the response of the patient. For the children attending school, the results of these tests were compared with school performance and social status. Behaviour evaluation was based on information obtained from the parents as well as on the child's behaviour during the examination.

Results

There were 23 deaths, a mortality rate of 31.5%; the majority (18 of 23) had had grade 3 tetanus. Of the 50 survivors, 38 (76%) attended hospital for assessment. In addition, information was obtained for 3 other patients. One had died from pulmonary

infection at age 2½ years; his growth and development were reportedly normal. The other 2 patients, 7 and 9 years old, with normal growth and development and good progress in school, were considered normal.

The age of the 38 patients at the time of assessment ranged from 5 to 12 (mean 9.3 ± 2.1) years; 33 of them were older than 7. Eighteen of the children had had grade 1 tetanus and the remaining 20 were equally distributed between grades 2 and 3.

Significant defects were found in 4 patients. All 4 had had severe tetanus, with frequent and prolonged bouts of spasms not easily controlled by anti-convulsive drugs and often associated with intense cyanosis and episodes of apnoea. One 8-year-old boy, had severe cerebral palsy, pronounced mental deficiency, and an abnormal EEG, and required custodial care. The remaining 3 patients had depression of intelligence, with an IQ below 68, and various behavioural problems, and were unable to attend a normal school; they had passed the milestones of development with marked delay. Pregnancy in the mothers had been normal. The infants had been born normally at term with birthweight appropriate for gestational age. Their first days of life, before the onset of tetanus, had been uneventful and the history and the clinical and laboratory evaluations showed no other possible cause of subsequent brain damage (such as infection, trauma, metabolic defects). Brain dysfunction could not be related to the socioeconomic status of the patients' families. There were no known near relatives with mental retardation or neurological defects.

The remaining 34 patients were apparently unaffected by the disease in terms of permanent sequelae, and those attending school showed good performance there.

With the exception of one, physical growth was normal. The exception, a 6-year-old boy, was short but so too were both his parents. Head circumference in all cases was within the normal range, with the exception of the severely handicapped boy who had marked microcephaly. Maturity indices (genital and breast development, pubic hair) in 6 patients (4 of them boys), aged 11 or older, were normal.

Discussion

Four of our patients, about 10% of the survivors, had appreciable handicaps. This figure is much greater than the normal incidence of these handicaps in children, which is about 0.05–0.1% for cerebral palsy and 3% for mental retardation.⁴ In the absence of other obvious causes of brain damage, the defects in these children can be ascribed to the neonatal illness.

Similar observations are reported by other workers,^{5–7} mainly after 1970. Huault⁵ found significant neurological sequelae in 4 of 9 survivors of severe neonatal tetanus. Salimpour⁶ found mild mental retardation in 2 of 43 survivors, reviewed 6 months to 4 years after recovery. Significant sequelae (cerebral palsy, microcephaly, mental defect) were also found by Khoo *et al.*⁷ in 2 of 17 survivors of severe tetanus.

Neurological sequelae were also reported in adults who survived tetanus by Illis and Taylor.⁸ They followed up 25 patients and noted fits in many of them, myoclonus, decreased libido, irritability, and electroencephalographic abnormalities.

According to Illis and Taylor,⁸ sequelae of tetanus in adults can be explained, in part, by a direct effect of tetanus toxin on synapses and by their subsequent changes. While this explanation cannot be entirely discounted, the fact that all the patients with sequelae had had severe tetanus with frequent and prolonged apnoeic attacks suggests that brain damage in neonatal tetanus is due mainly to the severity of cerebral hypoxia. The increase in recent years of reports of handicaps is probably due to advances in treatment and hence to the survival of patients who would otherwise have died.

With tetanus, the evaluation of a therapeutic regimen and prognosis is based only on survival rate, without taking into consideration long-term effects.^{1,2} Our findings show that survival and subsequent handicaps should be taken into account.

References

- 1 Marshall F N. Tetanus of the newborn. *Adv Pediatr* 1968; **15**: 65–110.
- 2 Adams E B, Laurence D R, Smith J W G. *Tetanus*. Oxford: Blackwell, 1969.
- 3 Teknetzi P. Tetanus neonatorum. A clinical and biostatistic study. Thesis, Aristotelian University, Thessaloniki, 1981.
- 4 Kinsbourn M. Disorders of mental developments. In: Menkes J H, ed. *Textbook of child neurology*, second edition. Philadelphia: Lea & Febiger, 1980: 642–3.
- 5 Huault G. Tétanos du nouveau-né. Traitement par la ventilation artificielle et la curarisation prolongée. Thesis, Paris 1964.
- 6 Salimpour R. Follow-up studies in tetanus neonatorum. In: *Proceedings of the Thirteenth International Congress of Pediatrics, Vienna 1971*. Vol. VI. Vienna: Verlag Wiener Medizinischen Akademie, 1971: 402–5.
- 7 Khoo B, Lee E L, Lam K L. Neonatal tetanus treated with high dosage diazepam. *Arch Dis Child* 1978; **53**: 737–9.
- 8 Illis L S, Taylor F M. Neurological and electroencephalographic sequelae of tetanus. *Lancet* 1971; **ii**: 826–30.

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