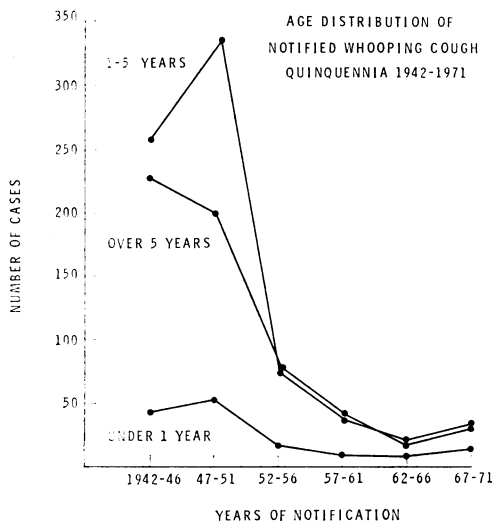

Fig 2

tion in the first year of life is causal or coincidental, the true incidence of reactions resulting from whooping-cough vaccination remains uncertain. There is indeed an urgent need for the better reporting of possible adverse reactions following all immunization and vaccination procedures. A local reporting and investigation scheme might with advantage be based on the new Regional or Area Health Authorities.

The recent investigation undertaken by the Public Health Laboratory Service (Final Report 1973) showed that much of the pertussis vaccine in use for five or six years before 1968 was not very effective. However, with increased potency, the incorporation of the prevalent 1:3 type of organism, and the addition of an adjuvant, whooping-cough vaccines are once again considered to be reasonably good protective agents. A scheme for monitoring these vaccines is now in operation. It is reassuring that there has been a very low incidence of whooping-cough in England and Wales during the last two years. (Only 3 cases were notified in Oxford in each of the years 1971 and 1972.) Every effort should be made to produce a more effective vaccine, as the present vaccines, even at best, are unlikely to eliminate whooping-cough. Whooping-cough vaccination has, however, greatly reduced the incidence of the disease and there has been an even greater fall in mortality and morbidity, although antibiotics aimed at secondary infection must, of course, also be given credit in this respect. Because whooping-cough continues to be a serious disease of very young children, it is considered that the present balance of risks is in favour of a continuation of routine whooping-cough vaccination.

Table 1

Whooping-cough cases in the Slade Hospital, Oxford, 1942–71

Years	*No. of cases*	*No. of deaths*	*Approximate population served*
1942–46	282	8	125 000
1947–51	207	10	
1952–56	117	3	500 000
1957–61	52	0	
1962–66	63	1	
1967–71	74	0	750 000

REFERENCE
Public Health Laboratory Service
(1973) *British Medical Journal* i, 259

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Biochemical Fits in the Newborn

Convulsions in the newborn infant are often associated with biochemical disturbances. Association does not necessarily imply causation and the role of biochemical disturbance is not always clear. In some instances it is secondary to a more fundamental pathological disturbance – e.g. the lowering of the cerebrospinal fluid sugar in meningitis – while in others it appears to be the primary cause of the convulsion.

The biochemical disturbance in a convulsing infant may be a deficiency of a specific substance on the one hand or an excess on the other. Examples of the former are deficiencies of calcium, magnesium, glucose, and pyridoxine, and of the latter excesses of phosphorus, bile, sodium and amino acids. These biochemical disturbances may be interlinked.

This presentation discusses disturbances of the minerals, calcium, phosphorus and magnesium, along with disturbances of glucose.

Normal Values

In the normal newborn infant the serum calcium concentration in cord blood is approximately 2 mg/100 ml above the maternal concentration. Over the next four days it falls to about 8 mg/100 ml. The serum phosphorus concentration in cord blood is also about 2 mg/100 ml above the maternal concentration but rises over the next few days to about 6–7 mg/100 ml, falling slowly thereafter. The serum magnesium concentration in cord blood is about 0.5 mg/100 ml higher than the maternal concentration and falls to about 1.8 mg/100 ml by the fourth day. The glucose concentration in cord blood is about 20 mg/100 ml lower than the maternal concentration at

delivery, falls over the first twenty-four to forty-eight hours and then rises to about 50–60 mg/100 ml by the fourth day.

Certain Factors Causing Biochemical Disturbance in the Newborn Infant

Studies at the Simpson Memorial Maternity Pavilion of the Royal Infirmary of Edinburgh of preterm infants delivered at different periods of gestation have shown the serum calcium concentration to rise steadily until the twenty-seventh to thirty-first week, reaching a mean concentration of 12.2 mg/100 ml at that time and then falling to a mean concentration of 10.9 mg/100 ml at term. Plasma phosphorus follows a similar rising pattern until the twenty-seventh to thirty-sixth week, reaching a mean concentration of 8.1 mg/100 ml and falling to a mean concentration of 4.9 mg/100 ml at term. Mean plasma magnesium concentration reaches 2.6 mg/100 ml at twenty-two to twenty-six weeks and falls to 1.9 mg/100 ml at term. Compared with singletons of like birth weight, calcium and glucose concentrations are significantly lower in twins, at least until the fourth day of life. Conditions associated with 'placental insufficiency' such as severe pre-eclampsia or prolonged gestation with low birth weight, result in significant lowering of the serum calcium and blood glucose concentrations in the infant over the first four days. In infants who are light for gestational age, serum magnesium concentrations are lower than in infants of similar weight but appropriate for gestational age. Feeding with cow's milk results in a raised plasma phosphorus concentration with lowered serum calcium and magnesium concentrations.

Clinical and Biochemical Observations on Infants Convulsing in the Neonatal Period

A study has been made over a two-year period of 142 newborn infants suffering from convulsions in the Simpson Memorial Maternity Pavilion. On the basis of criteria already published (Brown *et al.* 1972), 80 infants were considered to be suffering primarily from brain damage and 62 from metabolic disturbance. Seventy-seven per cent of fits associated with brain damage occurred during the first three days of life and 81% of convulsions considered metabolic occurred after the third day.

Significant hypocalcæmia was seen in 31%, significant hypoglycæmia in 36% and significant hypomagnesæmia in 7% of infants with convulsions and brain damage. Significant hyperphosphatæmia was seen in 10% of such infants. Seventy-one per cent of the brain-damaged convulsing infants showed biochemical disturbance involving one or more of these elements. Of the infants suffering metabolic convulsions, 57% showed significant hypocalcæmia, 35% significant hypomagnesæmia and 15% significant hypoglycæmia. Significant hyperphosphatæmia was seen in 21%. Eighty-three per cent of infants with metabolic convulsions showed significant disturbance of one or more of these elements.

Biochemical disturbance per se did not determine the neurological picture. The hypocalcæmia and hypoglycæmia seen commonly in the brain-damaged convulsing group were associated with clinical disturbances such as apnœa, the need for resuscitation and for tube feeding, apathy, diminished reflexes, hypotonia, cranial palsies, persisting neurological sequelæ and intellectual impairment. The hypocalcæmia, hypomagnesæmia and hypoglycæmia of the convulsions due primarily to metabolic disturbance were associated with muscular hypertonus involving particularly the extensor muscles, tetany, spreading of the cranial sutures, sun-setting of the eyes, a hyper-alert state and absence of long-term neurological sequelæ or intellectual impairment.

Electroencephalography showed that in 69% of infants with convulsions due to brain damage and 56% with convulsions due to primary metabolic disturbance there were abnormalities in the tracing. Repeat encephalographic examination several weeks or months later showed that in the brain-damaged group the same proportion of infants (66%) showed abnormal tracings, while in the metabolic group only 8% showed a persisting abnormality.

Twenty-two per cent of infants in the brain-damaged group continued to have convulsions after the neonatal period and up to the end of the first year while the corresponding figure for the metabolic group was 2.5%.

Conclusions

In neonatal convulsions disturbance of calcium, phosphorus, magnesium and glucose metabolism occurs in 80% of cases, including those who convulse because of structural brain damage. Where disturbance of calcium, phosphorus, magnesium and glucose is concerned, the differentiation of convulsions due primarily to structural brain damage from those due primarily to metabolic disturbance can only be made on clinical not biochemical grounds. In brain-damaged infants, convulsions are likely to occur within the first three days and the findings of apathy, hypotonia and diminished reflexes are the reverse of what would be expected with the hypocalcæmia and hypomagnesæmia which are so often present. In convulsions due to primary metabolic disturbance the neurological findings normally associated with hypocalcæmia and hypomagnesæmia are evident. Factors such as prematurity which are associated with higher calcium and magnesium concentrations may offset factors likely to depress

calcium and magnesium concentrations but may aggravate hypoglycæmia. Factors such as pre-eclamptic toxæmia, twins, and cow's milk feeding may cause or aggravate biochemical disturbance. The clinical effects associated with biochemical disturbances depend usually on the interplay of a number of pathological factors, biochemical and otherwise, and can be greatly modified according to the nature of these factors and their relationship with each other.

REFERENCE
Brown J K, Cockburn F & Forfar J O (1972) *Lancet* i, 135–139

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Non-epileptic Episodic Disorders in Young Children

A common question is 'Fits or breath-holding attacks?' A careful history usually gives the answer but occasionally the distinction is difficult.

Breath-holding attacks of the cyanotic type: The clinical description is familiar: the patient is an infant or pre-school child, occasionally even an infant of a few weeks of age; he takes one or more inspirations, holds his breath, becomes cyanosed and briefly loses consciousness. He often goes into a slightly opisthotonic position with elbows straight and forearms slightly pronated by his side with eyes turned upward. He may even pass urine and sleep after the episode and in my view it is quite unjustifiable to label the child as having had an epileptic seizure, on such evidence. Rarely, a breath-holding attack may terminate in the clonic movements of a true major seizure. Presumably in such children the epileptic threshold is relatively low and the amount of cerebral hypoxia sustained in the breath-holding is sufficient to exceed it. In my experience of these rare cases, the prognosis is no worse than in the usual case of breath-holding attacks.

The most important feature of the history in making the distinction between breath-holding attacks and epileptic seizures is that the former are always precipitated by a physical or emotional hurt, while the seizure arises spontaneously except in the very rare reflex epilepsies. The age of unsteadiness when a child is learning to walk is particularly liable to physical hurt. In some children a blow on the temporal or occipital regions is especialy provocative. The frustration produced by an older sibling stealing a toy or the mealtime battles of the food refusal stage are familiar precipitants.

The prognosis is good and follow-up studies (Lombroso & Lerman 1967) have confirmed that there are no serious sequelæ, but there are several unanswered questions. Why do they occur in certain children and in certain families? Have they any survival value like the true seizures of Chance's mice? (Chance described mice who, when confronted by a predator, convulsed and lay as if dead in postictal stupor.) Also, how does the doctor persuade the parents not to over-protect the child and compound his manipulation of the situation?

Syncope of infancy: In contrast to breath-holding attacks, syncope of infancy is rare. I have records of 4 personal cases. The infant goes pale and quiet, limp, sweating, unconscious and may vomit. Sheldon (1952) gave a graphic description of this disorder in 4 patients.

One of my patients was a doctor's infant; at the age of 3 months she had her first of 4 attacks; all occurred in the bath – she would splash for thirty to sixty seconds, then become quiet and pale and would vomit, then she became completely limp and unconscious. She looked dead but recovered after one minute. After the first attack the daily bath was made cooler but 3 more occurred over a few weeks. Bathing was therefore stopped and she had no more episodes. At 1 year of age baths were reintroduced without incident. Now she is a normal child of 5 years. In Sheldon's and my other cases the attacks were similar but the circumstances varied and the only common feature which is suggested to me is fright, although even this is not entirely convincing. A new taste during the introduction of solid food, a sudden but not severe blow on the head, putting in the bath, or removal from the bath, are various preceding factors described. Reflex epilepsy is an unlikely diagnosis – the features are those of syncope and the precipitating factors are usually varied. Are these attacks vagal asystole or true syncope? Resting ECGs and EEGs are normal and there is nothing to suggest a biochemical cause. It is not paroxysmal tachycardia. The prognosis seems to be uniformly good but one wonders uneasily if an occasional infant cot death might be due to this.

Benign paroxysmal vertigo: Excellent descriptions of this condition were given by Still (1938) and by Basser (1964); Koenigsberger *et al.* (1970) and Chutorian (1972). Sudden attacks of falling, swaying or cessation of movement makes most practitioners diagnose epilepsy, and vertigo is hardly considered; yet if he is asked, the child's own description should make the diagnosis clear: 'the walls go round' 'the ceiling falls in', 'I am falling', or as one of my patients said 'I keep drunking'. The parents' account also points to sudden vertigo: 'he screams out and clutches me or the chair', 'he lies down with his head on the floor and will only move if his head remains in contact with the floor'. Consciousness is not lost and the episode lasts less than thirty seconds,