Seizures in Infancy*

BY

MAURICE A. KIBEL

F.R.C.P.(EDIN.), D.CH.

The title I have chosen for this paper requires a little amplification. I do not wish to use the term "seizure" in the American sense as synonymous with epileptic convulsion, but rather in its broader English usage, meaning "a sudden attack, or the sudden appearance of certain signs of disease". Indeed, the main purpose of this presentation is to highlight certain seizures which are often mistaken for convulsions but which have no relation to them.

CONVULSIONS

Of the seizures we are to discuss, convulsions or fits are certainly the most significant from the clinical viewpoint, so let us consider them first.

That commonest of paediatric emergencies, the convulsing infant, is a sight which strikes terror into the heart of parents and jangles the equanimity of the physician also. The doctor knows that, provided he does not reach his patient with unseemly haste, the infant will almost certainly have recovered from his fit and be bawling lustily by the time he gets there, for the simple febrile convulsion is by far the commonest type in infancy. Yet the list of potentially serious causes of the seizure, common, unusual, or exotic, is almost endless. In fact, I will not even attempt to cover all the causes of convulsions in this paper but will consider only the most important aetiological factors in various age groups.

(a) *The Neonatal Period* (from birth to four weeks of age):

When seizures occur in this period they should always be viewed seriously and appropriate investigations implemented. The main causes are perinatal brain damage, malformations of the brain, metabolic upsets, and infection.

In a difficult labour, where anoxia has developed prenatally, fits are likely to ensue within the first 24 hours of life. The baby's condition will have been poor after delivery, and abnormal neurological signs will invariably be present - hyper-excitability, or apathy, and perhaps apnoeic attacks, absent Moro reflex, or absent sucking and swallowing reflexes. On the other hand, fits may occur *after* 24 hours as a result of brain damage sustained later by

*Presented at the R.M.A. (Midlands) Symposium Morgenster Mission: August, 1974.

intracranial haemorrhage, or repeated apnoeic spells, especially in premature or "small for dates" infants (de Souza and Milner, 1974).

Congenital malformation of the brain is a possible cause of convulsion in this early period, as in the following case:

L.T. was born normally following an uneventful pregnancy; at 24 hours of age there was a sudden attack of stiffening and cyanosis, followed by limpness and unresponsiveness for five minutes. She then recovered quickly, but several similar attacks occurred over the next three days. Lumbar puncture produced clear fluid, and detailed investigations were entirely negative. A lumbar air encephalogram at one month, however, showed an advanced degree of cortical atrophy, almost certainly due to cerebral malformation in utero. Now aged four years, she is severly retarded, and grand mal seizures are frequent. The head circumference is five cm. below the mean for the age.

Hypoglycaemia and *disorders of mineral metabolism* are important causes of fits in the neonate. Neonatal hypoglycaemia can be defined as a blood sugar below 20 mg.% in the infant of low birth weight; below 30 mg.% in full-term infants less than 72 hours of age; and below 40 mg.% in full-term infants after 72 hours. Seizures due to *transient hypoglycaemia* occur most commonly between 24 and 72 hours of age. Tremors, cyanosis, apnoea, or irregular respirations, apathy, a high-pitched cry, and reluctance to feed are symptoms which may be seen before convulsions ensue. A low birth weight for the period of gestation is a common feature. Routine monitoring of blood glucose in newborns shows that transitory hypoglycaemia can occur without symptoms, and infants of diabetic mothers seem to tolerate hypoglycaemia well. *Persistent hypoglycaemia* may indicate cerebral birth injury, septicaemia (perhaps with adrenal haemorrhage), and cold injury, not to mention a large range of specific disease entities including such disorders of carbohydrate metabolism as galactosaemia and glycogen storage disease (Forfar and Arneil, 1973).

Disorders of *mineral metabolism,* notably of calcium, phosphorus, and magnesium, are the cause of neonatal convulsions in 50 per cent. of cases in Edinburgh (Cockburn *et al.,* 1973), but other studies in the U.K. have reported hypocalcaemia as an aetiological factor in less than one per cent. of convulsions in neonates (Harris and Tizard, 1960), and the incidence is certainly low in Rhodesian neonates. The peak incidence of the first convulsion is on the sixth day of life, and it is rare in the first 48 hours or after the tenth day. A typical convulsion consists of rhythmic, focal, myoclonic jerking at the rate of one to three per second; they may be multi-focal or generalised, but true tonic and clonic grand mal fits are not seen. Between attacks the infant appears normally alert or hyper-alert, and is hypertonic and jittery with increased muscle response to stimulation and increased tendon reflexes. Specific metabolic disorders include hypocalcaemia, hypomagnesaemia, or hyperphosphataemia, and any combination of these, can occur, i.e. low calcium and magnesium with high phosphate; low calcium, normal magnesium, and high phospate; or, low calcium and magnesium with normal phosphate levels (Cockburn *et al.* 1973). Tremor of the extremities is a distinctive feature of these infants. On the other hand this tremor, sometimes referred to as juddering, is seen not uncommonly in normal full-term or pre-term infants. *Juddering* is the first of the abnormal movements in our list of non-convulsive seizures. The normal *Moro reflex,* or *startle response,* is another. Exaggerated in states of hyperexcitability from any cause in the neonate, this reflex may be a useful pointer to neurological abnormalities; yet more than once I have had a perfectly normal infant brought to me with a suspicion of convulsions when all that was present was an active Moro reflex.

(b) *One to six months.*

In this period infection assumes a significant rôle in the causation of convulsions. Meningitis is an especially common and dangerous cause.

D.G., a previously healthy male infant, developed sudden high fever, and was admitted to hospital six hours later with continuous jerking of the left limbs. He was comatose, with a rectal temperature of 41°C., and mottled cyanosis of the extremities. The fontanelle was tense. Lumbar puncture yielded purulent CSF, which grew haemophilus influenzae, Group B. The seizures were controlled with intravenous diazepam and ampicillin 300 mg/kilo/24 hours administered intravenously six hourly. He remained extremely ill for five days, but following the aspiration of large subdural hygromata on both sides, there was a rapid and sustained improvement.

(c) *Over six months.*

In the infant over six months, convulsions are a frequent problem, and generally of much less serious import than in the younger groups. They are mostly commonly precipitated by fever. Some infections, notably roseola infantum, shigellosis, and lobar pneumonia, are particularly liable to cause febrile convulsions, perhaps due to the rapidity of temperature rise in these illnesses. Certain strains of virus also seem more prone to induce febrile convulsions than others.

Recent studies of the prevalence of virus infection amongst children with febrile seizures have suggested that virus encephalopathy occurring during febrile illnesses may be a more important cause of major convulsions in young children than was previously recognised (Wallace, 1972).

Epilepsy and febrile convulsions; Much has been written on the relationship of febrile convulsions to epilepsy. According to Lennox, approximately two out of ten patients presenting with a first convulsion with fever are likely to have later epileptic attacks (Forfar and Arwell, (1973). They appear more likely to do so if febrile convulsions are recurrent. Wallace (1974) has shown a higher risk of subsequent epilepsy in infants with febrile convulsions in the following circumstances:

(a) boys with a positive family history of seizures in first degree relatives;

(b) girls, in whom the first fit occurred before 19 months;

(c) where the first is prolonged;

(d) where persisting nuerological abnormality is present.

As stated earlier, I shall make no attempt to cover systematically all the conditions which are associated with convulsions in infants. In the metabolic group, hypoglycaemia may persist beyond the neonatal period, and defects of amino acid metabolism — of which the commonest is phenylketonuria — should always be considered. Hypernatraemia (hypertonic dehydration) is a possibility in the infant with a diarrhoeal upset, generally due to the use of an over-concentrated milk formula.

Viral encephalitis, the demyelinating encephalopathies, intracranial thrombosis, and thrombophelebitis, the large but fortunately rare group of degenerative brain diseases, neurolipidoses such as Tay-Sachs disease, and the toxic encephalopathies, cannot be discussed further here. In the last-named category is included the interesting syndrome of toxic encephalopathy with fatty changes in the viscera — (Reye's Syndrome) — which appears much more prevalent in recent years, particularly in certain countries (Laxdal, *et al.*, 1969).

H.S., a plump and previously healthy male infant of six months, suddenly developed stertorous respirations. He became progressively more irritable, with threshing, maniacal movements and rapidly deepening unconsciousness over the space of three hours. On admission to hospital he was deeply comatose with decerebrate rigidity and massive enlargement of the liver. Lumbar puncture was negative, but blood sugar very low and blood ammonia raised. Treatment included intravenous glucose, corticosteroids, and peritoneal dialysis, but was quite ineffective and he died 12 hours later. At post mortem the liver and kidneys showed diffuse and extensive fatty degeneration. The brain was histologically normal.

Before leaving the subject of convulsions, let us consider their character in infancy a little further. The classical grand mal seizure, with its tonic phase, culminating in symmetrical clonic jerking may occur, but more often the attack is less typical. The infant may simply be unresponsive, the eyes staring fixedly or turned upward. The tonic component may be entirely absent, or tonicity may be limited to the trunk so that the infant stops breathing for a period and may become intensely cyanosed. Twitching can be either absent or very slight; often it is focal, involving perhaps one hand and the same side of the mouth. Later it may start in the contra-lateral limbs or become generalised. Sometimes the conscious level is not much affected and the infant will then look about or even suck a bottle while a limb jerks rhythmically in true Jacksonian style. Convulsions are, thus, frequently focal in young infants, and their localisation does not have the same significance as it would in older children or adults. On the other hand, transient or persistent postictal weakness of a limb (Todd's paralysis) *does* merit full investigation for an underlying lesion in the contralateral cerebral hemisphere.

Lightning Spasms: Lightning spasms, known also as infantile spasms, massive myoclonic jerks, salaam attacks, and various other names, usually have their onset in infancy, and only rarely commence after the age of two years. The main importance of recognising these seizures for what they are is the prognosis of the syndrome. Over 90% of affected infants are either retarded at the time of diagnosis or will be within several weeks of onset. They tend to occur in runs of several seizures many times a day. The infants have a startled look, their arms either flex or extend in abrupt fashion, and the head tends to move forward. The entire trunk may flex because of the rapidity of onset and the short duration of the individual spasm or jerk; if the child is able to stand he may be pitched to the floor with considerable force. Lightning spasms may be noticed at any time of the day, but are particularly likely to occur when the child is sleepy or just wakening. These seizures are frequently misinterpreted. The infants are thought erroneously to have colic, and attention may be directed to the intestinal tract.

This type of seizure is apparently age-specific rather than aetiology-specific. A variety of insults can contribute to the appearance of the seizures provided that the brain is young and sufficiently immature:

I.T., a male infant, appeared to be developing normally until the age of five months, when he began having sudden attacks in which the arms would shoot outwards and the head pull forward for one to two seconds. He would then look surprised or cry. Such attacks recurred every 15 to 30 seconds for ten minute periods several times a day. He showed several small patches of vitiligo on the back and limbs, and much later developed the typical adenoma sebaceum of tuberous sclerosis. His younger sister was similarly affected, and both are now severely retarded and epileptic. His mother had adenoma sebaceum but was intellectually normal and seizure free. She died of bilateral renal tumours.

C.K., a normal 16 month old female, had a pyrexial convulsion. Two months later she began having seizures in which she would suddenly throw herself backwards, the arms jerking out from the sides for two to three seconds. There would be many attacks during the day. Full investigations were negative apart from the EEG which showed a hypsarhythmic pattern. The attacks improved on ACTH and Rivotril, but speech and neuromuscular development regressed, and at two years she began showing multifocal myoclonic jerks and akinetic spells. The aetiology of this encephalopathy was not established but was presumed to be viral.

A highly characteristic electroencephalogram is often present in lightning spasms, known as hypsarhythmia. The pattern is completely disorganised, consisting of multifocal spikes irregularly alternating with high slow waves. Approximately 90% of infants with infantile spasms have hypsarhythmia at some stage of their seizure history (Friedman & Pampiglione, 1971). As children grow older infantile spasms are likely to diminish in severity and frequency and may eventually stop. The patient may be either seizure-free or subject to convulsions. Convulsions may occur while the child is still having lightning spasms.

When seizures begin within the first six months of life it is almost invariable that the brain is grossly malformed or severly damaged in prenatal, perinatal, or postnatal life. Degenerative brain disorders, such as Tay Sach's Disease, phenylketonuria, or tuberous sclerosis are often the cause. In children in whom the attacks begin later, such gross abnormalities of the brain may be absent and the condition often appears to be an encephalopathy of viral origin. In this group a minority may be restored to full normality following administration of steriods or ACTH.

Akinetic-myoclonic epilepsy (the Lennox Syndrome): This is another seizure disorder which can begin in infancy. In akinetic attacks the child will suddenly lose consciousness and posture. If sitting or standing, he tends to collapse suddenly, like a deflated balloon, in complete contrast to the violent increase in tone seen in the lightning spasm. In association with these attacks, but at other times, there are often myoclonic jerks, generally restricted to individual muscle groups, and these may be localised or range haphazardly from one part of the body to another. This syndrome is also characterised by hyperkinetic behaviour and varying degrees of intellectual retardation. The aetiology is unknown. In older children, myoclonic epilepsy may indicate the development of a progressive brain disorder, such as subacute inclusion body encephalitis.

The diazepines - especially diazepam (Valium, Dipam) and nitrazepam (Mogadon) - are the most effective anticonvulsants in the control of lightning spasms and akinetic myoclonic seizures. Hanson and Menkes (1972) have shown that the newer diazepine, clonazepam (Rivotril) is the drug of choice in these difficult seizure disorders. In a trial of clonazepam in a mixed group of epileptic children, I found this agent to lessen the number of seizures significantly in all four cases of this type. It is also remarkably effective in petit mal attacks, and can be given intravenously for the control of status epilepticus.

Petit mal, and psychomotor epilepsy, seldom, if ever, occur in the first two years of life and so will not be discussed here.

NON-CONVULSIVE SEIZURES

Neonatal Tetanus: No discussion on abnormal movements in infancy would be complete without mention of tetanus, which is so prevalent in Rhodesia. The onset of symptoms is usually three to ten days after birth; difficulty in sucking, with stiffening of the upper lip, is often the earliest symptom, and this is followed by generalised body stiffness and intermittent spasms or jerking. Varying degrees of trismus, increased tonicity of muscles, and spasms following stimulation are present. Attempts to examine the throat are thwarted by the increase in trismus which this procedure produces. These manifestations serve to differentiate tetanus from the seizures associated with disturbed calcium, magnesium and phosphate levels, and from the opisthotonic posture of *kernicterus*.

Tetanus, of course, results from infection of the moist umbilical stump to which infected

material, such as dung or mixtures of oil and charcoal, have been applied as a dressing.

Kernicterus (bilirubin encephalopathy): The clinical picture of kernicterus results from damage to the basal ganglia due to toxic levels of bilirubin. Symptoms generally come on in the first five to seven days of life and the established picture is one of spasticity and opisthotonus, hyperpyrexia, irregular breathing, pulmonary haemorrhage, and death in 50 per cent. of cases. Clonic seizures may occur. In infants who survive there is temporary improvement, followed later by a characteristic form of cerebral palsy associated with deafness.

The dyskinesias, athetosis, and chorea are not, however, seen in young infants and will not be discussed further.

Dancing Eyes, Dancing Feet: This picturesque title was applied by Dyken and Kolar in 1968 to a syndrome affecting infants and young children and characterised by shock-like involuntary muscle movements (polymyoclonia), irregular, multi-directional, spontaneous eye movements (opsoclonus), and marked truncal ataxia. The syndrome generally develops quickly in a previously healthy child. Its importance lies in the fact that in some cases neural crest tumours are discovered, and the abnormal picture disappears with removal of the tumour. Such tumours are often difficult to detect clinically, often residing in the posterior mediastinum behind the heart. The urine, however, almost always contains increased amounts of catecholamines where such a tumour is present. The majority of cases of this disorder are not, however, associated with neural crest tumours, and are presumably due to a viral encephalopathy. Where a neuroblastoma or related tumour is not found, corticosteroids or ACTH have proved of benefit in some cases.

C.W., a healthy female toddler of 18 months, had a fall and cut her forehead, but was not unconscious. One week later she was noted to be unsteady on her feet, and within a few days was unable to walk. She was happiest lying flat, and any movement appeared to induce severe dizziness. There was a symmetrical tremor of both hands. Eye movements were normal. Lumbar puncture showed normal pressure and fluid, and the diagnosis was considered to be an acute cerebellar ataxia. Later, however, irregular multi-directional eye movements, fluttering of the eyelids, and myoclonic jerking of the limbs developed. The dancing eyes, dancing feet syndrome was suggested by a Johannesburg neurologist*. Urine contained no excess of catecholamines. Two years after the onset of the disease she was still seriously handicapped by ataxia despite prolonged courses of corticosteroids and ACTH.

*Dr. M. Ronthal.

Spasmus Nutans: In contrast with the recently described disorder just mentioned, Spasmus Nutans is a classic syndrome of the older paediatric textbooks, which now appears much less common. The condition is not present at birth but develops some months afterwards. There are nystagmus, involuntary head nodding, and torticollis. The eye movements may be in any direction — vertical, horizontal, or both — characteristically the infant focuses on objects which attract his attention, by holding the head in a skewed position with the eyes deviated in the other direction. Spontaneous recovery is the rule. The relationship of this syndrome to unlit rooms, poor economic circumstances, and unsatisfactory mother/child relationships has been disproved, so that the diminishing incidence in the last two decades is difficult to explain.

Breath-holding Attacks: These common and frightening seizures occur almost exclusively in the first three years of life. They most often begin between 9-18 months, but I have seen the first signs of a breath-holding tendency on the first day of life. The infant starts to cry and then holds his breath in expiration. As he does so his back arches and his limbs extend, and there is often cyanosis. During the few seconds of unconsciousness which ensue in severe cases, there may be clonic limb movements. Respiration invariably then starts again, and the child regains consciousness immediately. Following a severe attack he may then go off to sleep for an hour or two. There are no abnormal neurological signs, and the EEG is normal. During an attack marked slowing of the heart is present, and the theory that bradycardia is responsible for the loss of consciousness, as in the Stokes-Adams attack, has been postulated by Super (1972). "Pallid" breath-holding attacks in which consciousness is lost rapidly before cyanosis develops are also seen, often in attacks initiated by falls or shocks rather than by frustration or temper. Breath-holding attacks are generally more severe when anaemia is present. They are usually precipitated by pain, anger, or frustation in rather self-willed children. Parents should be reassured and helped to lose their fear of these harmless attacks and to try to maintain firm, kindly, and constant discipline. Drug treatment is not indicated.

Masturbation is practised at all ages, but it is not generally known that it may be practised by very young infants. I am not referring to the normal manipulation of the genitals which is seen in any infant from about five months onwards.

True masturbation may be witnessed in infants of either sex of five to six months of age, and rarely younger, but is seldom recognised as such. It is practised by rubbing the thighs together, and the infant achieves this by a variety of rubbing movements — rhythmic elevation of the pelvis in the supine position, or rocking back and forth on hands and knees in the prone in older children. It may be associated with head banging. During these rhythmic activities the child's face may become flushed and sweaty. The eyes are fixed, and it is well-established that orgasm may be reached, even in infants of a few months. Local irritation, such as from vulvo-vaginitis, threadworm infestation, or napkin rash, induce the habit in some infants. (Illingworth, 1968.)

N.B., a female of 15 months, had had attacks since the age of eight months. These occurred several times during the day and were regular at night on going off to sleep. She would lie flat in her cot in the prone position, with the legs apart, and there were rhythmic downward movements of the pelvis, culminating in flushing, sweating, and a dazed look. After the episodes she would generally go off to sleep.

Epilepsy is, of course, sometimes suspected in such infants. Parents are apt to be shocked by masturbation at any time, and especially in an infant so young. Local sources of irritation should, of course, be removed, but reassurance is all that is required.

Iatrogenic Seizures: The last abnormal movement to be described is that seen in an overdose or abnormal sensitivity to phenothiazine tranquillisers. This always startling and sometimes dangerous syndrome may be ushered in by a true clonic convulsion. It is characterised particularly, however, by spasm of voluntary muscles, which may vary in severity from mild unilateral spasms of the neck muscles to a severe attack resembling tetanus, with opisthotonus, trismus, extensor spasm of the extremities, inability to swallow, and episodic involuntary shrieking. Occasionally, dangerous laryngospasm may occur.

M.M., a four month old female infant, took ill with vomiting and diarrhoea. She received an injection of chlorpromazine (dosage unknown) and two hours later developed marked head retraction. The eyes were constantly turned upwards, and the arms were extended at the elbow with the hands clenched. No specific treatment was given, and the abnormal posture disappeared after six hours.

Intravenous diphenhydramine is beneficial in severe cases.

References

Cockburn, F., Brown, J. K., Belton, N. R. and Forfar, J. O. (1973) *Arch. Dis. Child.* **48,** 99.

De Souza, S. W. and Milner, R. B. G. (1974) *Arch. Dis. Child* **49,** 351.

Dyken, P. and Kolar, O. (1968) Brain **91,** 305.

Forfar, J. O. and Arneil, G. C. (1973) Textbook of Paediatrics. (Churchill Livingstone, Edinburgh and London (1) p. 195; ibid. (2) p. 794.

Friedman, E. and Pampigliowe, G. (1971) *Brit. Med. J.* **4,** 323.

Hanson, R. A. and Menkes, J. H. (1972) *Develop. Med. Child Neurol.* **14,** 3.

Harris, R. and Tizard, J. P. M. (1960) *Journal of Paediatrics,* **57,** 501.

Illingworth, R. S. (1968) *The Normal Child* (4th edition J. & A. Churchill Ltd., London, p. 306.

Laxdal, O. E., Sinha, R. P. Merida, J., Ching Wong, L. and Stephen, J. D. (1969) *Am. J. Dis. Child.* **117,** 717.

Super, M. (1972) Paper presented at Rhodesian Medical Congress, September, 1972.

Wallace, S. J. (1972) *Arch. Dis. Child.* **47,** 171.

Wallace, S. J. (1974) *Arch. Dis. Child.* **49,** 763.