

A STUDY OF SYMPTOMATIC BIRTH ASPHYXIA -
ITS IMMEDIATE MANIFESTATIONS AND LONG TERM SIGNIFICANCE

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ABSTRACT

Despite improvement in healthcare during pregnancy and childbirth, intrapartum asphyxia remains a substantial problem. Mild degrees are common, producing signs of fetal distress during labour and temporary depression of vital function at birth, but, in the absence of neonatal sequelae, are generally benign without longer term implications. More severe degrees of intrapartum asphyxia may be followed by disturbances of function in many body systems, most notably the central nervous system; a situation referred to as symptomatic birth asphyxia. Although such disturbances are often transient, there is a risk of permanent neurological handicap in some cases. Acute, neonatal, neurological consequences of intrapartum asphyxia have long been recognised, but, in the literature, differences remain of the detailed neurological findings described, of the interpretation of their immediate significance and of the prognostic significance attributed to such neonatal findings. To look at these aspects, a prospective study of symptomatic birth asphyxia has been conducted.

Fifty, mainly mature, infants were identified in the early hours of life by their fulfillment of preselected criteria of symptomatic birth asphyxia. Their general characteristics, antenatal and intrapartum factors, birth condition and the abnormalities of performance and behaviour which the infants displayed are reported. The infants' status over the early neonatal period, carefully assessed by repeated neurological examinations, appropriate investigation, and physiological recording of electroencephalograph, polygraph, and sucking and respiratory patterns, is described and illustrated. The majority of the children have been the subject of regular assessments to primary school age to determine their outcome.

Three infants died in the first days of life and a fourth, who was severely brain damaged, in later infancy. Five children have significant handicap, seven mild degrees of neurological or developmental /

mental abnormality, while the remaining thirty-four children are considered normal. A number of neonatal events and findings correlated well with outcome. Indicators of condition at birth, the occurrence of apnoeic episodes, prolonged gasping respirations, a phase of apathy, tonic seizures, prolonged depression of feeding reflexes, hypothermia, and certain patterns of neurological abnormality - persistent hypotonia, marked extensor hypertonus with preceding and succeeding hypotonic phases, bulbar palsy and ophthalmoplegia, all bore a highly significant relationship to poor outcome. Of these, the abnormalities of muscle tone and ophthalmoplegia correlated strongly with outcome; the consideration of additional, significant risk factors did not add to their predictive value.

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CHAPTER I

INTRODUCTION

BIRTH ASPHYXIA, REVIEW OF THE LITERATURE

The potential hazards of childbirth, both to the mother and the infant, have been recognised since earliest times. It was in the more recent past however that the association between birth asphyxia and survival with subsequent handicap was made, the first clear accounts in the English medical literature being those of Little, 1843, 1853, and 1862, (Ingram, 1964). Prior to this, it would seem that a major asphyxial insult to the fetus in labour was thought to result in stillbirth, early neonatal death or otherwise in the child surviving intact; those children exposed to such an insult, who subsequently developed cerebral palsy, were thought to have suffered this as a result of unrelated problems in early childhood - fits, infections, teething, etc. (Little 1862). The writings of Little therefore are a landmark in the understanding of this subject and are distinguished for their clear, clinical observation and sound interpretation.

"Nearly twenty years ago, in a course of lectures published in the "Lancet" and more fully in a "Treatise on Deformities" published in 1853, I showed that premature birth, difficult labours, mechanical injuries during parturition to head and neck, where life had been saved, convulsions following the act of birth, were apt to be succeeded by a determinate affection of the limbs of the child, which I designated spastic rigidity of the limbs of newborn children, spastic rigidity from asphyxia neonatorum, and assimilated it to the trismus nascentium and the universal spastic rigidity sometimes produced at later periods of existence."

"The forms of abnormal parturition which I have observed to precede certain mental and physical derangements of the infant consisted of difficult labours, i.e. unnatural presentations, tedious labours from rigidity of maternal passages or apertures, instrumental labours, labours in which turning was had recourse to, breech presentations, premature labours, and cases in which the umbilical cord had been entangled around the infant's neck or had fallen down before the head."

Little, 1862.

The improvements that have been achieved in healthcare in pregnancy and childbirth have allowed new standards and aims to be adopted. It is only half a century since the prime concern had to be for the survival of the mother in childbirth. In the Simpson Memorial Maternity Pavilion, Edinburgh, in 1934, there was a total maternal mortality rate of 16/1,000, 38 mothers dying; the well-being of the infant must of course have been of secondary importance. In the same year, the total perinatal mortality rate for the hospital was 143/1,000 births, and, for infants born after the 38th week, 90/1,000. Having secured the safety and well-being of the mother in childbirth, it has become possible to focus more attention on the well-being of the child during pregnancy, delivery, and the early days of life, (Ounsted, 1982), and with improved methods both of ascertaining fetal condition and of intervention to expedite delivery when necessary, without endangering the mother, many intrapartum problems can now be recognised and the threat to the child avoided. Perinatal mortality has fallen dramatically. The impact of conditions such as birth trauma, birth asphyxia, prematurity and infection has been reduced substantially, but nevertheless these continue to produce mortality and short and long term morbidity. (Forfar, 1978).

The 1958 Perinatal Mortality Survey found a national perinatal mortality rate of 33/1,000 births, (Butler, 1963). This had fallen to 24/1,000 in the 1970 British Births Survey (Chamberlain, 1975); 54% of stillbirths and 17% of deaths in the first week were thought to be due to intrauterine anoxia. This second figure did not include the contribution that anoxia made to mortality from other problems such as the complications of prematurity. Despite improvements, there is clearly no room for complacency, (Lancet, 1976). Birth asphyxia remains a substantial problem, an ever present threat, not only to life but to the quality of life of the survivors.

Morbidity in the newborn period and in the longer term gives a clearer indication of the importance and frequency of intrapartum asphyxia than do mortality statistics. Brown et al, 1974, found that symptomatic /

symptomatic neonatal asphyxia, the clinically manifest disturbance which may follow perinatal asphyxia, occurred in almost 6/1,000 liveborn infants, 91% due to ante- or intra-partum asphyxia and only 9% to post-partum causes. Cerebral palsy, the major longterm sequel of birth asphyxia, is generally considered to have an incidence of about 2.5/1,000 livebirths, although figures have varied from 0.6-5.9/1,000 livebirths, (Hagberg, 1975; Woods, 1976; Brown, 1982). The majority of cases arise from problems in the perinatal period; Brown and Dykes, 1977, considered that perinatal causes were nine times more frequent than postnatal, while Brown, 1982, found that 65% of cerebral palsy was due to perinatal abnormality.

Mild degrees of intrapartum asphyxia are common and are little more than an exaggeration of the physiological degree of hypoxaemia and hypercapnia that occurs during normal labour and stimulates the onset of respiration at birth. James *et al*, 1958, felt from their studies of the acid-base status of the human infant at birth that "varying degrees of asphyxia occur during all forms of delivery".

Much work has been done in the study of various aspects of intrapartum asphyxia to elucidate the pathogenesis of and the pathophysiological responses to an anoxic-ischaemic episode, to identify pregnancies which may be at particular risk, and to detect and evaluate early signs of fetal compromise during pregnancy and especially in labour. The condition of the infant immediately after birth has received much attention, perhaps disproportionately more than the condition of the child over the early neonatal period. These main areas will be reviewed briefly.

Pathogenesis and Pathophysiological Responses

Theories of pathogenesis of perinatal asphyxial brain damage are based /

based largely on the retrospective study of clinical and neuropathological findings in patients dying at varying times after a perinatal insult. In those dying in the acute stage, there may be no gross pathological abnormality or brain-softening, oedema and haemorrhage may be found, while in those dying months or years later there may be cerebral atrophy, hemiatrophy, ulegyria, status marmoratus, hydrocephalus, porencephaly or cystic leucomalacia, (Malamud, 1964; Myers 1972; Brown, 1976). Clearly, apparently similar asphyxial insults can produce widely differing results. Experimentally induced brain damage in laboratory animals has also been used to draw parallels with the human situation.

The complete pathogenesis of perinatal brain damage is not fully understood. Different patterns of damage are found in the preterm and mature infants' brains. The main susceptible areas in the term infant's brain are the brain stem centres, areas of cerebral cortex, deep white matter structures, thalamus, basal ganglia and cerebellum. In most cases, some evidence of an intrapartum insult will be apparent, but specific information about its precise effect - hypoxaemia, hypotension leading to ischaemia, or some combination of these, is not generally available. For this reason, the comprehensive term, hypoxic-ischaemic encephalopathy, has found some favour, (Volpe, 1975; Sarnat, 1976; Fenichel, 1980). The precise timing, duration and severity of the insult are not usually known either. Similarly, the relative importance of trauma to the fetal head by acute or more prolonged compression, perhaps followed by rapid decompression at delivery, is difficult to assess in the individual case, although the major degrees of head injury during birth seen in the past are now rare, (McGregor, 1960; Brown, 1974).

The concept of selective vulnerability of certain areas of brain to damage from asphyxia allows some insight into the pathological patterns found. The brain of the mature newborn may be relatively resistant to pure hypoxaemia, (Brown, 1976), and it is certainly common clinical experience that newborn infants with cyanotic congenital heart /

heart disease tolerate marked degrees of hypoxaemia well, in the absence of hypotension and tissue ischaemia. Areas of brain that have the highest oxygen uptake, (Kety, 1963), are most vulnerable to asphyxia; for example, the brain stem which is functionally well developed at term with well formed dendritic connections, (Grossman, 1971), appears to be more sensitive to oxygen lack than the cerebral hemispheres where dendritic connections have yet to form.

Systemic hypotension producing ischaemia, tissue hypoxia, glucose depletion and intracellular acidosis may be an important mechanism, the resulting pattern of damage depending on the relative metabolic activity of areas of brain and on the distribution of haemodynamic disturbance produced. Areas at the periphery of the field of supply of the major cerebral arteries, and of the arteries penetrating into cerebral substance from the exterior in and from the centre out, are vulnerable, resulting in watershed zone lesions, (Brierley, 1971), areas of infarction in cerebral cortex and deep white matter, cystic leucomalacia.

These mechanisms help to explain how a generalised insult such as asphyxia can produce localised damage. Much of the symptomatology of neonatal hypoxaemic-ischaemic encephalopathy is due to the vulnerability of the brain stem of the term infant, (Brown, 1976a), although there is debate about the anatomical level of some of the neurological disturbance seen, (Volpe, 1977).

Improved techniques for the study of acute dynamic disturbances secondary to an asphyxial insult in the newborn infant and in experimental animals have added to the understanding of pathogenesis. Methods have been developed to study disturbances of cerebral blood flow, (Cross, 1976; Cooke, 1979; Lou, 1977, 1979). Cerebral blood flow, C.B.F., is normally carefully protected so that it remains stable within a physiological range of blood pressures - the concept of autoregulation of C.B.F. first postulated by Sherrington. In studies of newborn infants with respiratory distress and varying degrees of birth asphyxia, Lou et al, 1977, 1979, have demonstrated that cerebral blood /

blood flow is low in association with systemic hypotension in these situations, autoregulation having been lost. Lou et al, 1979, concluded that, "as hypotension is the rule during the first few hours after birth in moderate or severely distressed newborn infants, low C.B.F. must be considered a frequent complication of asphyxia" and stressed the importance of measuring and maintaining blood pressure, of giving glucose, and of the vigorous treatment of fits, which increase oxygen consumption. Loss of autoregulation can also give rise to excessive C.B.F. at normal or increased levels of blood pressure, (Lou, 1979 + 1979a). These dynamic changes go some way to explaining some of the patterns of damage seen, such as cortical infarction, periventricular leucomalacia, and possibly also areas of haemorrhage as a result of hypertension, (Lou, 1979a; Volpe, 1979; Milligan, 1980). Although in such circumstances, loss of autoregulation is generally accepted, it is not universally held. Bejar et al argue that pressure passive C.B.F. need not indicate an intrinsic disturbance of autoregulatory mechanisms, but may be an inherent part of the relatively low blood pressures found in the human newborn, (Bejar, 1982; Volpe, 1982).

Cerebral oedema is a further important, common, acute complication of an hypoxic-ischaemic insult, having the potential to produce more severe brain damage than the primary insult alone, (Stark, 1972). Cellular and interstitial oedema may result from disturbance of the normal function of cerebral vascular endothelial cells in a number of ways. Rappoport, 1976, describes how the normally tight endothelial cell junctions may be stretched or disrupted, while Goldstein, 1979, suggests that lack of supply of oxygen and various oxidative fuels may disturb the metabolic function of the endothelial cells resulting in fluid and electrolyte shifts and abnormal pinocytotic transport of proteins through the cells.

Recognition of cerebral oedema in the newborn unfortunately may be difficult and although there has been some progress in the development of objective methods of measurement of intracranial pressure, (Wealthall, 1974; Robinson, 1977), there are as yet no satisfactory, non /

non-invasive methods available for general use in the nursery.

Animal models, especially full term, newborn Rhesus monkeys, have been used to help elaborate the pathogenesis of perinatal asphyxia in the newborn nervous system, firstly in producing a model of acute, total asphyxia, similar to the clinical problem of complete compression of the prolapsed umbilical cord. In this type of experimental asphyxia, damage is confined to the brain stem nuclei, thalamus, basal ganglia and spinal cord, while brain swelling, cortical necrosis and fits do not tend to occur, (Brann, 1977). The animal model which, many workers feel, more closely resembles the human situation in the insult delivered and the pattern of brain damage inflicted is that of prolonged partial asphyxia, (Myers, 1972; Adamson, 1973; Brann, 1975), the monkey developing seizures after 12-18 hours and, in those sacrificed in the first four days, cerebral oedema, cortical necrosis and damage to the basal ganglia. However, as Dobbing, 1974, points out, caution must be exercised in extrapolating conclusions from experimental evidence in animals to man, especially because of a difference in the stage of brain development relative to the time of birth. It is apparent that in the human infant a few weeks difference in gestational age can greatly affect the pattern of brain damage resulting from similar insults.

On the basis of human and animal data, Brann and Dykes, 1977, have suggested the following sequence of events in the pathogenesis of most perinatal hypoxic-ischaemic brain damage in the full term infant:

- intrauterine asphyxia
- redistribution of organ flow
- oxygen debt to brain cells
- impaired autoregulation of cerebral blood flow
- intracellular swelling
- focal ischaemia
- generalised brain swelling
- increased intracranial pressure
- cerebral necrosis
- atrophic /

atrophic cortical sclerosis.

It can be seen that an asphyxial insult, because of the train of secondary haemodynamic and homeostatic disturbances which may be set in motion, can produce differing results, that at the time of birth the insult must not be regarded as a fait accompli and the infant left to his fate, good or bad, as certainly has happened with the "cerebral baby" in the past. There is considerable scope for appropriate observation and management to reduce the risks of longterm damage.

Identification of Intrapartum Asphyxia

Many obstetric factors have been shown to have some relationship to the risk of occurrence of fetal asphyxia. For example, Larks and Larks, 1972, in a study of 4,600 deliveries found 29 perinatal factors that correlated significantly with Apgar score and identified 19 prenatally known factors which were of value in predicting Apgar score. These factors ranged from aspects of the mother's health, her parity, previous stillbirths and hypertension to evidence of fetal compromise in labour, such as the passage of meconium and abnormalities of fetal E.C.G. and heart rate. MacDonald *et al*, 1980, in a review of 38,405 deliveries over a five year period, found that asphyxia, defined simply as the need for resuscitation with I.P.P.V. for more than 1 minute at birth, occurred in 1.2% of the population, 9% of those less than 36 weeks gestation and 0.5% of those at term. At term, asphyxia was more common in infants of black, unmarried, diabetic or toxæmic mothers and infants who were growth retarded, or delivered by breech. They concluded that at every gestation asphyxia increased the risk of dying - by two fold at 27 to 28 weeks gestation, and by a hundred fold at greater than 36 weeks gestation.

From such findings, the concept of the high risk pregnancy has evolved and has been widely accepted in obstetric practice. In a study of /

study of 600 high risk pregnancies, i.e. those with a maternal medical, obstetric or fetal complication, or a variety of problems in labour, Low et al, 1975, 1975a, 1975b, found an eight fold increase in incidence of fetal asphyxia, defined as an umbilical arterial buffer base level of less than 36.1 mEq/l., -2 S.D., at birth, in the high risk groups compared to the normal obstetric population. All obstetric, medical or gestational complications studied were associated with an increased risk of fetal asphyxia, but some factors were of particular significance, fetal asphyxia occurring in 50% of breech deliveries, 33% of prematures, 25% of pregnancies complicated by toxæmia and 22% by antepartum haemorrhage.

By the use of scoring systems to identify pregnancies at increased risk, available facilities can be used more effectively. Boddy et al, 1976, in a "Systematic Approach to Perinatal Care" describe a prenatal care programme, the assessment of risk and a plan of management through pregnancy. Using such a scheme, these workers in a community based project in a housing area of Edinburgh have demonstrated that perinatal mortality and some aspects of morbidity can be substantially reduced, (McKee, 1982).

It would be reassuring if, following the identification of high risk pregnancies, intrapartum asphyxia could then be avoided by close monitoring of fetal condition in labour by electronic techniques and appropriate management of the course of labour; however, this is not invariably possible. Some causes of intrapartum asphyxia, for example placental haemorrhage or umbilical cord problems, are difficult to anticipate and may occur acutely with little or no warning. Further, despite the widespread use of cardiotochographic fetal monitoring in the assessment of fetal condition, its value is not fully established and sufficient equipment for monitoring of all high risk cases is not always available, (Gillmer, 1979).

Certain fetal heart rate patterns have been shown to have an association with other indicators of intrapartum asphyxia such as fetal /

fetal acidosis and Apgar score, (Hon, 1963; Wood, 1967; Beard, 1971). Beard et al, 1971, in a study of changes in fetal heart rate and pH occurring in 279 high risk labours, found that when decelerations in fetal heart rate were accompanied by baseline tachycardia, loss of beat to beat variation, or were deep or delayed after uterine contractions, fetal acidosis suggestive of fetal asphyxia was common, while in the absence of such patterns the incidence of fetal acidosis was low.

Asphyxia results in tissue oxygen debt either by hypotension producing tissue ischaemia or by hypoxaemia. Identification of tissue oxygen debt is based upon the resultant hyperlactataemia which leads to a metabolic acidosis, decreased buffer base and, in turn, a decrease of pH, (Low, 1975).

Reviewing methods for the detection of fetal asphyxia in labour, Beard, 1974, concluded that, "Continuous recording of fetal heart rate, F.H.R., and fetal pH estimation provide a reliable system for monitoring the condition of the fetus in labour. If the F.H.R. record remains normal, it can safely be assumed that the fetus is in good condition. Interpretation of abnormalities on the trace is sometimes difficult, and it is only possible to determine with certainty whether the fetus is asphyxiated or not by estimating the fetal pH. Experience to date suggests that the selection of high risk patients for monitoring only partially solves the problem of intrapartum stillbirth and that only by monitoring all patients will intrapartum asphyxial stillbirth be eliminated".

Clinical studies of fetal heart rate monitoring have not however clearly established its value. A number of workers have compared the outcome of high risk, monitored labours with either low risk labours observed by traditional auscultatory methods, (Paul, 1974; Tutera, 1975) or with the outcome of their practice in the years preceding the general use of fetal heart rate recording, (Lee, 1976; Edington, 1975, Johnstone 1978; Ingemarsson, 1981), and have demonstrated a lower fetal mortality rate in the monitored groups. Such studies are subject to some criticism /

criticism, (Renou, 1976; Neutra, 1978; Johnstone, 1978), some being retrospective, not comparing similar populations over the same period, or being influenced by changes in practice in addition to fetal heart rate monitoring. The main differences found in these studies did not reach statistical significance, but the use of more sensitive indicators of the outcome of labour than fetal wastage might reveal more definite differences.

Neutra et al, 1978, in a large retrospective study of almost 16,000 liveborn infants to assess the effect of electronic fetal monitoring, adjusted for differences in inherent risk, changes in mortality rate and rates of monitoring during the years of the study, and concluded that there was a 1.4 times higher neonatal death rate in unmonitored infants than in those monitored. These workers devised a numerical scoring system for risk and found that in the highest risk group 109 lives might be saved per thousand babies monitored, while in the lowest risk group, i.e. babies at term with no risk factors, there was no indication of benefit from monitoring.

To date, there have been few controlled trials comparing fetal heart rate monitoring with traditional auscultatory means of assessment. Renou et al, 1976, in a study of 350 high risk pregnancies found a lower incidence of neonatal neurological abnormalities and better cord blood gas values in the monitored group, but no significant difference in Apgar scores. In a larger study, Haverkamp et al, 1979, found no significant difference in cord gases, Apgar scores, neonatal morbidity or mortality in monitored and traditionally observed labours. Differences between studies might relate in part to differences in labour management and action taken when abnormalities were detected on fetal monitoring. Auscultation of fetal heart rate has been shown to be subject to error especially at extremely high and low rates, precisely when it is most important to be accurate, (Check, 1979), and even when fetal scalp pH measurements are used as an adjunct when auscultated heart rates are abnormal, intrapartum asphyxia will be partly unrecognised (Beard, 1974).

Check, 1979, summarises the conclusions of the National Institute of Health Conference on antenatal diagnosis concerning the place of electronic fetal monitoring (E.F.M.) thus:

"E.F.M. should not be regarded as a diagnostic test but a screening test because of the large number of false positive findings. The use of fetal scalp pH determination should be encouraged as an adjunct to heart rate monitoring. Prospective and retrospective analyses show no apparent effect of E.F.M. on perinatal mortality and morbidity in low risk patients. As the risk increases, there emerges a trend suggesting a beneficial effect of E.F.M.; therefore, in high risk patients, E.F.M. should be strongly considered."

Condition of the Infant at Birth

Birth is only an event, albeit a vitally important one, in the life of the child which has its beginning at conception. It is not surprising that the condition of the child immediately after birth, when he or she is first fully revealed, has been the focus of great attention. Condition at birth relates to many factors, particularly those that have been operative immediately before, in labour, and it has been clearly demonstrated that adverse effects such as intrapartum asphyxia can produce depression of function vital when the infant becomes separated from the mother.

Since the Apgar scoring system was devised in 1953, it deservedly has achieved widespread use as a simple, effective method of summarising the infant's condition in the first minutes of life and of identifying some of those in need of attention and surveillance in the early neonatal period. Partly through its use, medical attention has been drawn to the infant born in poor condition and methods and standards of resuscitation employed have improved. This change may have modified the significance of the Apgar score in some cases, especially where, by prompt, effective resuscitation, prolonged postpartum asphyxia and prolonged low Apgar scores might otherwise have occurred, (Sykes, 1982).

The relationship of low Apgar scores to intrapartum asphyxia, as indicated /

indicated by fetal acidosis, has been studied by James et al, 1958, and Low et al, 1973a. The former found that infants with low 1 minute scores, 0-4, tended to show a marked reduction in buffer base in umbilical cord blood at birth, indicative of more prolonged asphyxia, while severe degrees of hypoxaemia at birth were not necessarily associated with central depression and, indeed, hypoxaemia or an acute respiratory acidosis could result in a vigorous rather than a depressed infant. In severe anoxia, breathing took the form of gasps. Low et al, 1975a, also demonstrated an association between low Apgar scores and fetal acidosis, 56% of infants, judged to have suffered intrapartum asphyxia with umbilical arterial buffer base levels more than 2 S.D. below the mean for a control group, having a 1 minute Apgar score of 7 or less and 15% 7 or less at 5 minutes. However, 44% had good Apgar scores. The correlation was better with more severe degrees of fetal acidosis, 80% of those with a significant lactic acidosis, having 1 minute scores of less than 7. Nevertheless, it can be seen that normal Apgar scores do not exclude intrapartum asphyxia, as indicated by fetal acidosis, even of severe degree. Low et al, 1975, also make the important point that the shift of the oxyhaemoglobin dissociation curve as a result of low pH in asphyxia, although producing a small decrease in oxygen tension, results in a marked decrease of oxygen saturation and content, the oxygen saturation in their asphyxia group being just 50% that in the normal group during the last 2 hours of labour.

Numerous studies have shown a good correlation, especially in preterm infants, between Apgar scores and mortality, particularly death in the first 2 days after birth, (Schachter, 1959; Apgar 1962; Drage, 1964, 1966, 1966a; Richards, 1968). An association also exists between low Apgar scores, especially at 5, 10 or more minutes, and long term morbidity, (Drage, 1966; Nelson, 1979, 1981; Finer, 1981); this association is again stronger in the low birth weight group. However, Thomson et al, 1977, in their study of 31 surviving children, who had a 1 minute score of 0 or 5 minute score of less than 4, found that 29 (93%) had no serious neurological or mental handicap and neither /

neither a score of 0 at 1 minute or the numerical value of very low 5 minute scores, 0-3, had predictive value. More recently, Nelson and Ellenberg, 1981, reporting results of Apgar scores in 49,000 infants from the Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke, found that low Apgar scores were risk factors for cerebral palsy, but 55% of children with later cerebral palsy had Apgar scores of 7 to 10 at 1 minute, and 73% scored 7 to 10 at 5 minutes. This is partly an indication that some cases of cerebral palsy are due of course to causes other than intrapartum asphyxia, but suggests also that not all cases of cerebral palsy due to intrapartum asphyxia have low Apgar scores. Further, of 99 children with prolonged Apgar scores of 0-3 at 10, 15, or 20 minutes, who survived, only 12 had later cerebral palsy.

Due to changes in management of the depressed infant at birth, there is some evidence that the significance of the Apgar score may have been modified. Sykes et al, 1982, reporting the results of cord blood gas analyses of 1039 of 1210 consecutive deliveries, found that of those with a severe acidosis, i.e. umbilical arterial base deficit greater than 12 mmol./l. or pH less than 7.11, greater than 2 S.D., 73% had a 1 minute score of 7 or more, and 86% a 5 minute score of 7 or more. These authors suggest that since, "the Apgar score does not usually reflect the degree of acidosis at delivery, its value as an index for asphyxial assessment must be questioned."

A common cause of poor condition at birth is the central nervous system depressant effect of drugs, such as opiate analgesics, general anaesthetic agents and sedatives such as benzodiazepines, given to the mother during labour. With appropriate management this situation has an entirely different significance to depression from intrapartum asphyxia, although not uncommonly such drugs may complicate the depressant effects of intrapartum asphyxia and as James, 1958, points out inhalational anaesthesia given to mother may augment the metabolic depression from intrapartum asphyxia. Unless the contribution of drugs is taken into account /

account, any prognostic significance of the Apgar score is seriously diluted and studies using the occurrence of low Apgar scores as the sole indicator of intrapartum asphyxia invalidated.

Apgar herself was realistic in her appraisal of the predictive value of the scoring system:

"While we believe the score is useful, it has many limitations. It is no substitute for a careful physical examination or serial observations over the first few hours of life. Nor will it predict neonatal death or survival of individual infants. Indeed few signs in medicine give that definite an answer. This objection in no way detracts from the value in estimating the probability of survival or death in groups of infants."

Apgar and James, 1962.

Neonatal Manifestations of Intrapartum Asphyxia

"Perhaps in no other neonatal disease is careful clinical assessment so critical and, unfortunately, so frequently overlooked."

Volpe, 1977.

It is generally accepted that where significant intrapartum asphyxia has occurred, this will be clinically detectable in the early neonatal period by changes in the behaviour and neurological responses of the infant. Where there have been maternal, obstetric and intrapartum risk factors, but no sign of such disturbances in the infant in the neonatal period, it can be concluded that the risk of intrapartum asphyxia has not materialised to any significant degree. Similarly, when the infant has been depressed at birth with low Apgar scores, has required resuscitation, but has demonstrated no abnormality in the newborn period, there is no real cause for anxiety over the child's long term progress in this context, (Brown, 1976a).

Little, 1862, noted many of the important neonatal manifestations, albeit /

albeit in a florid degree, in his summaries of 63 cases:

"Stupor for 4 or 5 days after birth or alternatively crying or convulsed. Unable to suck until 5 days old."

"Apparently born perfect, but slept unusually during 14 days, did not cry for 3 weeks, and then not as another child."

"Child black (deeply cyanosed), supposed to be dead; restored with difficulty. Did not cry for half an hour. Head out of shape; long and high."

"Labour 32 hours, at full period. Delivery by forceps; did not rally for 3 hours; convulsed during first fortnight. Did not suck until a month old; deglutition very difficult. Convulsion of hands was so considerable as to require padding of the palms."

"Gasping breathing for 2 hours."

A variety of clinical disturbances have been recognised in the term infant as occurring after significant intrapartum asphyxia. Those stemming from the central nervous system fall into 2 main categories. Firstly, the overt disturbances of behaviour and performance, which will be apparent to those caring for the child. Brown, 1974, 1976a, has described these and studied their significance. He identified 7 main "symptoms": feeding depression, persistent vomiting, apnoeic or cyanotic episodes, fits, apathy, cerebral cry, and hypothermia. Others such as irritability and jitteriness could be added to this list. Secondly, by careful neurological assessment, signs and responses that deviate from the expected for gestation can be elicited.

It must of course be remembered that a hypoxic-ischaemic insult not only represents a stress to the central nervous system, but can produce effects on every body system, and indeed protective mechanisms come into play to reduce the risk of C.N.S. effects at the expense of other systems. The result may be impairment or failure of renal function, (Crispin, 1972; Dauber, 1976), myocardial damage or dynamic cardiovascular disturbances, such as persistent fetal circulation, (Burnard /

(Burnard, 1961; Rowe, 1978; Lees, 1980), necrotising enterocolitis, gastric stress ulcers, disseminated intravascular coagulation, metabolic disturbances such as dilutional hyponatraemia, hypocalcaemia, hypoglycaemia, and pulmonary complications such as meconium aspiration syndrome or pulmonary haemorrhage, (Sexson, 1976; Fitzhardinge, 1977).

The most common disturbances, however, are manifestations of central nervous system disorder and it is one aim of the present study to examine these more closely. Close observation of neurological performance is of great importance. Volpe, 1977, states that in this situation it is "imperative to perform a detailed neurological examination", and that "the greatest amount of most significant data is derived from careful observation of the infant." The value of this approach may be in 4 main areas.

Firstly, although major disturbances will be apparent, the child with symptomatic birth asphyxia may remain undetected until 24 or 48 hours after birth when an overt disturbance such as a fit or apnoeic episode occurs; time has been lost since careful assessment in the first hours of life would probably have revealed earlier abnormality. By earlier awareness of the problem, measures for closer supervision of the infant's clinical and biochemical state and appropriate management can be instituted. Prechtel, 1967, performed detailed neurological assessments of 1,515 newborns and reported that all the infants with "obvious" neurological signs - facial palsy, bulging fontanelle, deviation of eye position, absence of suck, Moro or grasp reflexes, or severe hypotonia, showed in addition a variety of other abnormalities on neurological assessment, while "a very large number of babies with no classical, neurological signs obtained the same neurological scores as those with classical signs." He concluded that "examination merely for gross pathological signs will result in the omission of a considerable amount of neurological abnormality which is prognostically ominous."

Secondly, by detailing the neonatal neurological manifestations and /

and observing changes in them, one might hope to be aware at an earlier time of secondary complications such as fits of various forms, raised intracranial pressure, problems with respiratory control, etc., which might put the asphyxiated infant at further hazard.

Thirdly, although this is an area which has been the subject of several studies, there remain some differences in the accounts of neurological manifestations and, particularly, the changing patterns observed over the early days of life, and in the interpretation of these findings. It is desirable to document clearly the different patterns of neurological dysfunction which may follow intrapartum asphyxia, perhaps particularly since therapeutic measures, such as high dose barbiturate administration and hyperventilation with or without the use of muscle relaxants, which will modify or suppress their expression, are being more commonly used.

Finally, patterns of neurological abnormality may be recognised which, by comparison with findings at longterm follow up of the children, may have some favourable or adverse prognostic significance. There is uncertainty about the prognostic value of abnormal neurological signs exhibited by the neonate. Craig, 1950, reporting the outcome for a large series of infants with cerebral irritation, mainly from birth trauma and intracranial haemorrhage, felt that a poor cry, tense fontanelle, hypertonicity, apathy, abnormal respiration, irritability, poor sucking and fits were the significant neonatal abnormalities. In 1973, Natelson and Sayers in their report of the outcome for a group of infants suffering severe head injury during birth, reached similar conclusions, finding that apathy, pallor, absent Moro reflex, respiratory abnormality, poor sucking, third nerve palsy and a bulging fontanelle were signs of a poor prognosis.

Amiel-Tison, 1969, in a prospective study of cerebral damage in 41 term infants from birth trauma or asphyxia, found it difficult to recognise /

recognise patterns of neurological abnormality in these infants - "except for status epilepticus, we did not notice any definite clinical profile during the initial phase, the manifesting signs varying greatly from day to day rendering a clinical classification impossible." She felt, however, that fits, irritability, abnormal muscle tone, abnormal reflexes and eye signs, decreased conscious level, abnormal respiration and signs of raised intracranial pressure were the most significant neonatal signs.

The changeable nature of neurological signs in the early newborn period following intrapartum asphyxia or trauma, stressed by Amiel-Tison, is much less apparent in the designation of constellations of abnormal neonatal signs, (Precht1, 1965, 1967), as syndromes - hyperexcitability syndrome, apathy syndrome, and hemisyndrome. However, Precht1, 1967, has demonstrated the prognostic significance of this classification, 67, 59 and 73% of cases respectively, showing continuing neurological abnormality when examined at 2-4 years and at 8 years. De Souza and Milner, 1974, using the same classification also found an association between apathy and hyperexcitability syndromes and later neurological abnormalities, but to a much smaller degree. These workers concluded that among the many clinical findings in abnormal infants, apnoeic attacks, absent Moro reflex, absent sucking and swallowing were particularly significant.

Amiel-Tison writing in 1973 and with Minkowski et al, 1977, felt able to discern patterns out of the changing neurological manifestations in the early newborn period and describes 3 groups of infants by the severity and duration of their neonatal neurological abnormality. These groups carry some prognostic significance.

Other workers have selected particular aspects of neurological function as being useful indicators of prognosis; muscle tone (James, 1973; Brown, 1974, 1976a), conscious level, (Sarnat, 1976), frequency of seizures (Monod, 1972; Volpe, 1975), persistently abnormal electroencephalogram, (Sarnat, 1976).

Aims of the Study

The main aims of the present study are as follows:

1. Identification of a large group of newborn infants, who had suffered a significant degree of intrapartum asphyxia.
2. By careful assessment of the infants in the early neonatal period by repeated neurological examinations and recording of abnormalities demonstrated, to document in detail neonatal manifestations of intrapartum asphyxia.
3. Detailed study of important aspects of the infants' disturbance of function; physiological recording of sucking, respiratory and polygraphic/electroencephalographic activities.
4. Long term follow up of the group with periodic neuro-developmental assessments to allow correlates to be drawn between perinatal factors and subsequent outcome.

Diagnosis of Significant Intrapartum Asphyxia

The criteria used for selection of the study group are described in Chapter II. However, it is appropriate to discuss here how the diagnosis of significant, intrapartum asphyxia may be made and justified.

Reference to the large numbers of studies performed of various aspects of birth asphyxia reveals wide variation in the criteria used in selection of cases. This alone makes it difficult to draw comparison between studies.

Condition of the infant at birth has commonly been used as convenient /

convenient and reproducible evidence of intrapartum asphyxia. Ucko, 1965, extracted information from the labour ward nurses' report of the infant's condition at birth. Hall, 1980, and Lou, 1979, relied on Apgar scores alone as an indication of birth asphyxia and Thomson et al, 1977, selected 1 minute Apgar scores of 0 or 5 minute scores of less than 4 as indicating severe birth asphyxia. A combination of low Apgar scores and the giving of resuscitation has been used, (Dweck, 1974; Walsh, 1982). De Souza et al, 1981, selected a low birth score, i.e. modified Apgar score, of 0 or 1 at 1 minute and the need for intensive resuscitation for at least 10 minutes before spontaneous respirations were established, as indicative of severe birth asphyxia, while Scott, 1976, chose apparent stillbirth and failure to establish respiration within 20 minutes of birth as indicating this.

Such evidence has limitations as discussed earlier. While many infants, who have been subject to a significant intrapartum asphyxial stress, will be in poor condition at birth, this evidence alone is insufficiently specific, there being other common causes of low Apgar scores. Nor does it relate well to the degree of asphyxial stress, many infants with very low Apgar scores showing no subsequent disturbance. It is also known that fetal asphyxia can occur without depression at birth, (Sykes, 1982).

Similarly, it has not proved possible to rely solely on intrapartum evidence of fetal asphyxia such as abnormal fetal heart rate patterns or fetal acidosis, since although such findings are valuable clinical warnings to the obstetrician, they do not necessarily indicate that a significant intrapartum stress has been sustained, and indeed the majority of infants should, with appropriate management, emerge unscathed from such circumstances.

The best evidence that can be collected of significant intrapartum asphyxia is firstly, from intrapartum events and birth condition, that the /

the infant has been exposed to such a stress, and secondly that it has in fact been of a degree sufficient to produce disturbance in the neonatal period, and therefore significant. Evidence of this type had been used in a number of studies, e.g. Brown et al 1974; De Souza et al, 1978; Finer et al, 1981, Fitzhardinge et al, 1981, and is the approach adopted in the present work.

CHAPTER II

MATERIALS and METHODS

Selection of Cases of Significant Intrapartum Asphyxia

Newborn infants were included in the study when they fulfilled each of 4 criteria:-

1. One or more of the following problems of performance or behaviour in the early neonatal period:
 - feeding depression
 - persistent vomiting
 - apnoeic episodes
 - cyanotic episodes
 - irritability
 - cerebral cry
 - apathy
 - fits
 - hypothermia.
2. Abnormality on neurological assessment.
3. Evidence from the pregnancy, labour, or immediate post-delivery period to suggest that the abnormalities, in 1 and 2 above, were due to intrapartum asphyxia.
4. Absence of any other factor likely to be the principal cause of the observed abnormality.

These four criteria will be considered in more detail.

1. The abnormalities in performance or behaviour were defined as follows:-

Feeding /

Feeding depression - absence or underactivity of the feeding reflexes necessitating a period of nasogastric tube feeding of at least 24 hours.

Persistent vomiting - recurrent, frequent vomiting over the first days of life with exclusion of other causes.

Apnoeic episodes - periods of respiratory cessation with associated colour change and bradycardia requiring stimulation or active resuscitation.

Cyanotic episodes - cyanotic spells occurring spontaneously, or with feeding or handling, or in association with fits or apnoea but not due to a primary respiratory or cardiac cause.

Irritability - a state of increased excitability, with resentfulness of handling, persistent crying, sleeplessness, and jitteriness.

Cerebral cry - an abnormal sounding, high pitched, shrieking cry, spontaneously or with handling, usually associated with irritability.

Apathy - a decreased level of alertness, with reduced or absent response to stimulation and decreased or absent spontaneous movement.

Fits - fits occurring in the first days of life where other causes such as infection or primary metabolic disturbance were excluded.

Hypothermia - poor temperature regulation with falls of rectal temperature below 35.5°C., but not including falls immediately following resuscitation at birth.

2. Abnormality on neurological assessment.

This /

This was defined as being any definite abnormality of central nervous system function, such as disturbance of muscle tone or reflex response appropriate to the gestational age of the infant, cranial nerve palsy, weakness, athetosis, or asymmetry of tone, power or posture, except where these abnormalities were due to some other primary cause. Peripheral nervous system abnormalities, e.g. lower motor neurone facial palsy, Erb's palsy, per se, did not qualify.

3. Evidence from the pregnancy, labour, or immediate post-delivery period to suggest that abnormalities in 1 and 2 were due to intrapartum asphyxia.

In clinical practice, it is often difficult to be certain that intrapartum asphyxia has occurred, except where there has been an acute, overt stress, such as cord prolapse, placental separation and haemorrhage, tonic uterine contractions or eclampsia. This difficulty is apparent in the widely differing criteria, taken as indicative of intrapartum asphyxia, in various studies in the past, ranging simply from low Apgar scores or the need for a period of assisted ventilation at birth to firmer evidence of fetal compromise during labour with depression of vital functions at birth.

An aim of the present study was to identify patterns of behaviour and neurological dysfunction in the infant with symptomatic asphyxia and, to this end, a wide range of severity of asphyxial stress was considered necessary. Naturally, the evidence for an asphyxial insult is often less substantial when the insult has been covert and less severe, and the resulting abnormalities at birth and during the neonatal period may deviate less from the accepted norm.

For the purposes of this study, therefore, in addition to the acute, overt stresses already referred to, other evidence has been accepted; signs of fetal distress by cardiotochography or traditional methods, complicated labour and delivery, where labour has /

has been short or prolonged, complicated by malpresentation, disproportion or obstruction, signs of more prolonged stress, intra-uterine growth retardation, placental insufficiency, pre-eclamptic toxæmia, and also depression of vital, central and cardio-respiratory function at birth.

4. Absence of any other factor likely to be the principal cause of the observed abnormality.

None of the features described in 1 and 2, are specific in their relationship to intrapartum asphyxia, and each can be produced by a variety of other causes. It would be unrealistic to exclude each case where other primary factors, in addition to intrapartum asphyxia, were operative, such as maternal drugs or birth trauma, as this would no longer be representative of clinical practice, these additional factors commonly accompanying intrapartum asphyxia. However, in each case selected, intrapartum asphyxia was judged to be the principal cause of the observed abnormalities, although other factors coincidental, related, or secondary to the asphyxial stress, could contribute to the clinical state.

Method of Selection

Over a 23 month period from February 1976 to December 1977, a large number of newborn infants were seen and examined in the special care nursery and postnatal wards of the Simpson Memorial Maternity Pavilion, Edinburgh, by the author. Infants were referred by the paediatric medical and nursing staffs, because of difficulties during labour and delivery, poor condition at birth, or problems with behaviour and performance.

Most infants were seen in the early hours of life; the majority during their first 12 hours, although some presented with their first apparent problem later than this. After consideration of the presenting /

presenting problems, of the information available about the pregnancy, labour and condition at birth, and of the findings on general and neurological examination, a decision was taken as to whether the 4 admission criteria were fulfilled. In a small number of cases, this decision was deferred until re-examination of the infant, usually some hours later.

Following inclusion in the study, the parents were interviewed to give them information about their child's condition, to ask permission for observations and recordings, and to make initial contact with them. In each case, there was further discussion with the parents during their child's stay in hospital, often on several occasions, and the research health visitor, attached to the study, introduced.

General physical examination

A careful general examination was made of each infant. Particular note was taken of the infant's growth and proportions, as assessed by appearance and the centile positions of weight, crown-heel length, and occipito-frontal circumference on a Gairdner and Pearson chart, (Gairdner, 1971), of the infant's temperature and that of the incubator, and of the presence of any apparent congenital abnormality. Heart rate, blood pressure in the right arm was recorded using a trans-cutaneous doppler (Parks Electronics Lab.), and 3 cm. sphygmomanometer cuff, the presence of cyanosis or need for oxygen therapy, respiratory distress, respiratory rate and rhythm, the presence of periodic breathing or apnoeic episodes, and the auscultatory findings in the chest were all noted.

Gestational age was assessed by external features (Appendix II): the stage of development of lanugo, sole creases, breast tissue, ear cartilage and the quality of hair and appearance of the genitalia, whether the labia minora were prominent or enclosed by the labia majora /

majora, or the degree of rugosity of the scrotum in the male.

Neurological examination

Each child was submitted to a detailed neurological examination prior to admission to the study. This was then repeated daily for the first 4 days and more frequently in the seriously ill infants, showing rapidly changing signs. Daily examinations continued when there were persisting abnormalities, and otherwise were at twice weekly intervals. Each infant was re-examined before discharge from hospital.

The neurological examination was based on that described by Brown (unpublished scheme; Brown, 1974a). The detailed plan, which was followed, is shown in Appendix I. Findings were recorded on proforma, illustrated in Appendix II.

A description of the neurological examination follows. This will be considered in several parts:-

State of arousal.

Examination of the head.

Cranial nerves.

Phasic and primitive reflexes.

Tone and posture.

Movement and muscle power.

Hemisynndrome.

Neurological assessment of gestational age.

State of arousal.- As many neurological findings are dependent on the state of arousal of the infant, the examination began with an assessment of this. Changes in state are normally found over a period of time, and in relationship to feeds and to disturbance from handling. Such /

Such changes in state during the examination and, conversely, the lack of variability of state in some infants, were noted. Where possible, infants were seen midway between feeds and the time since the last feed noted.

State of arousal was graded as follows:-

Apathetic - little or no spontaneous movement or response to stimulation.

Hypoalert - reduced spontaneous movement, slow and decreased response to stimulation, similar to the state of the recently fed, soporific infant.

Normally alert - the state of alertness of the wakeful, but content, term infant.

Hyperalert - increased arousal, as in the infant stimulated by hunger, thirst, hypoglycaemia, hypocalcaemia, etc., with agitation, increased spontaneous movement, brisk reflex responses, and often sleeplessness.

Cranial nerves.- The cranial nerves were examined systematically as outlined in Appendix I. External ocular movements, III, IV, VI nerves were tested for forms of ophthalmoplegia, by inspection for loss of upward conjugate gaze in the sunset sign, and, for strabismus by using the doll's eye and rotation test responses. Pupil size and reaction to light, blinking in response to light and head turning towards a soft, diffuse light were indicative of some visual response. After the first days of life, fixation on a face or bright object and nystagmus were useful signs of visual fixation.

Facial /

Facial sensation and movement, V and VII nerves, were examined by eliciting the corneal, rooting and cardinal point reflexes, the glabella tap response, and by inspection for asymmetry of the mouth, naso-labial folds and palpebral fissures. Eighth nerve auditory function was difficult to assess, being very state dependent; blinking or startling to a sharp sound, and, quietening and head turning to soft voicing, close to the infant's head, were taken as evidence of some acoustic response. Labyrinthine function of the VIII nerve was assessed in the labyrinthine rotation test with the infant held in the air at 30° and spun round.

IX, X, XII nerve functions were examined by eliciting sucking on a blind teat or finger and, where appropriate, by the infant's competence at nutritive sucking, swallowing, and co-ordination of swallowing and respiration. As described later, in some infants sucking patterns were studied in more detail using a pressure recording system to show frequency of sucks and duration of sucking bursts. Bulbar function was tested also by the cough and gag responses. The tongue was inspected for shape and fasciculation and head position, head turning and active and passive range of head movement noted, unless there were doubts about cervical spine stability.

Phasic and primitive reflexes.-

Phasic reflexes.- The integrity of the phasic, muscle stretch reflexes and the balance between facilitation and inhibition in the extrapyramidal system were assessed by the presence and activity of several phasic, or tendon, reflexes. The biceps, knee, ankle, toe and jaw jerks were routinely tested, the response being graded as +, ++, +++. Facilitation was considered to be present when the reflex responses were brisk and there was sustained clonus of the jaw, ankles, hamstrings, or thigh adductors, and was often accompanied by "jitteriness", with spontaneous limb and jaw clonus, which could be terminated by changing the infant's position, thus distinguishing these /

these movements from those of a clonic fit.

Primitive reflexes.- These will be considered under 5 groupings:

1. Extension reflexes. These are reflex responses which are most active when the balance between flexor and extensor tone is in favour of extensor tone. They are, therefore, usually inactive or absent in the normal, well-flexed, term infant, while the presence of strong extension reflexes forms part of the picture of extensor hypertonus in some neurologically deviant, term infants.

Reflexes elicited were the asymmetrical tonic neck reflex (A.T.N.R.), the truncal reflexes - Perez and trunk incurvation, the Moro response, and the crossed extensor reflex; this last can be grouped also with the progression reflexes. The Moro response was not sought when there was any doubt about the stability of the cervical spine, for example following delivery complicated by shoulder dystocia or where there was an Erb's palsy. The degree of reflex response was noted; whether, for example, the Moro response produced full arm abduction, extension and hand opening along with extension of the legs with return to a flexed, adducted limb posture, whether the A.T.N.R. involved legs as well as arms and whether this reflex, and the two truncal reflexes, were obligatory, the infant being held in the reflex position for as long as the stimulus - the position of the head, or thumb pressure on the infant's back or loin - continued to be applied.

The snout reflex, obtained by finger pressure on the infant's nose, was used to reveal, or heighten, underlying extensor hypertonus, the normal infant responding by free, struggling movements of the limbs, while the infant with extensor hypertonus showing forced arm extension, pronation and fisting, leg extension with dorsiflexion of the great toes, and head and back arching. The presence of Babinski response either spontaneously, on handling, on being held in suspension under the arms, or during the snout or perineal pressure responses /

responses, again is a feature of extensor hypertonus.

Asymmetry of any of these reflexes occurs in reflex hemisyndromes as well as in peripheral palsies and in pseudoparesis, secondary to a painful lesion, fracture or osteitis, in a limb.

2. Progression reflexes are those responses in which the infant demonstrates movements resembling those of later, voluntary locomotion. The walking, limb placement of arm and leg, cliff edge and cycling reflexes were tested in those infants who readily could be moved. In others, restricted by equipment or when minimal handling was desirable, the crossed extensor reflex and Bauer reflex were used to elicit similar responses in the legs. All this group of reflexes are variable, being present or absent in the same infant over a short period of time, and are highly state dependent. They are more active when there is extensor hypertonus, and may be absent or difficult to elicit in the infant who is hypoalert or apathetic and hypotonic, and also in the infant with very strong flexor tone, flexor hypertonus.

3. Cutaneous reflexes consist of the contraction of a muscle group in response to stimulation of the overlying or segmentally related skin, a dermatome to myotome response, (Brown, 1974a). They, therefore, depend on intact sensation and the spinal reflex arc. Palmar grasp and the traction response, the converse - hand opening on stroking the dorsum of the hand, plantar grasp, and the abdominal and anal reflexes were all tested.

4. Cranial nerve reflexes. These have been discussed in the description of cranial nerve testing.

The most important reflexes of this group are the feeding reflexes and the associated bulbar reflexes, which protect the pharynx and upper airways. The term bulbar palsy was used when there was absence /

absence of normal sucking activity, and the gag and cough reflexes.

Some infants show a pattern of reversion to more primitive reflex responses, not normally seen in the mature newborn, with lip pursing, rejection of the teat by the tongue, gagging, retching and vomiting. This pattern, with absence of the normal ingestion reflexes, tends to be found in highly irritable infants and may follow compressional head injury and subarachnoid haemorrhage, (Brown, 1974a).

5. Nociceptive spinal reflexes.- These are reflex responses to a painful stimulus produced through a spinal reflex arc under some higher centre control. The flexor withdrawal reflex, consisting of flexion of the leg when a painful stimulus is applied to the sole of the foot, can be useful in showing loss of higher level inhibition of spinal reflex activity in the severely neurologically abnormal infant with spinal cord trauma or severe higher centre depression, the reflex being grossly exaggerated resulting in alternating flexion and extension of the leg about the stimulus, (Ivan, 1973).

Tone and posture.- Abnormalities of muscle tone are common and important in neonatal paediatrics. In symptomatic birth asphyxia, muscle tone is almost invariably disturbed to a greater or lesser extent over a variable period of time, (James, 1973; Brown, 1974, 1976a). The appraisal of tone forms a central part of the neurological assessment and allows patterns of changing muscle tone and neurological status to be recognised.

Muscle tone can be evaluated in several, complementary ways: by observation of the predominant posture that the infant assumes, by changing the infant's orientation in space and observing the effects of gravity on head, body and limb position, by testing the resistance to passive movement and observing the strength of recoil of the limb to its original position following passive movement and, finally, by measurement /

measurement of the passive range of movement at any joint being dependent on the balance of extensor and flexor tone about that joint. As already mentioned, the testing of primitive reflexes, especially the extension reflexes, can give additional information about the predominant type of muscle tone.

By these means, several variations of muscle tone can be recognised in the newborn infant: normal flexion appropriate to the gestation of the infant, increased tone - either flexor or extensor hypertonus, decreased tone - hypotonia, where there is a generalised reduction in muscle tone, or regression of muscle tone to a pattern similar to that of a less mature infant, there being a greater reduction in tone in the arms than legs.

These patterns of muscle tone are more fully described in Chapter VIII.

Tone was assessed at each examination by these methods. The drawing of simple "matchstick" diagrams of the infant's posture, lying supine, prone, held in vertical and ventral suspension, sitting and standing, was found a useful method of recording.

Movement and muscle power.- The presence of any deformity such as asymmetry of head, face or general body position, talipes, instability of the hips and of any clear preference for lying with the head turned to one side rather than the other were recorded. Limb muscles were palpated to give some impression of bulk, wasting and quality, whether firm or soft. Fasciculation or a direct myotactic response, the muscle contracting on being stimulated by tapping over it, suggesting denervation, was noted and some assessment of muscle power made.

Spontaneous movement was described as absent, reduced, normal, increased or continuous and the distribution noted, whether all four limbs were equally involved or not. Abnormal movements, such as tremor or athetosis, with sinuous hand movements, mouthing and tongue /

tongue activity, were recorded.

Hemisynndrome.- The term hemisynndrome, applied to the young infant, is used where there is any unilateral abnormality of neurological findings. When neonates are examined frequently, transient asymmetries are not uncommonly found and are described here as hemisyndromes when present on at least two consecutive occasions.

Hemisyndromes can consist of asymmetry of muscle tone, increased or decreased, producing asymmetry of posture, recoil, passive range of movement, etc., asymmetry of reflex activity, most commonly of extension reflexes, or asymmetry of muscle power, a paretic hemisynndrome.

Detection and description of such asymmetries is, of course, by the methods of assessment of posture, tone, reflex activity, and power already described. At times, it can be impossible to say which is the abnormal side, purely that an asymmetry exists.

Neurological assessment of gestational age.- As illustrated in Appendix II, various neurological features: reaction to light, head turning, activity of reflex response such as the A.T.N.R., grasp, crossed extensor, walk, suck, root, and Moro reflexes, and an assessment of muscle tone, were considered together to give an apparent neurological stage of gestational development. In the infant with abnormal neurological features, this, of course, does not equate with true gestational age, as indicated by dates and by external features, but is useful, allowing a comparison of the degree of regression of neurological function, which such an infant shows at intervals over the early days of life, to be made.

After /

After each neurological examination, the findings were summarised, classed as "normal" or "abnormal", and changes since the previous examination detailed. In addition, at the time of admission to the study, each infant's clinical state, taking into account such factors as shock, acidosis, respiratory difficulty and abnormality on neurological assessment, was classified as "fair" or "poor".

Other recorded information

In addition to details of the infant's family, social situation, parents' occupations, family and maternal medical history, details of mother's previous obstetric history and health during the presenting pregnancy were recorded. Detailed information about the antepartum and intrapartum periods was noted; the presence of particular problems such as hypertension or pre-eclamptic toxæmia, poor weight gain, low urinary oestriols or antepartum haemorrhage was recorded along with any treatment given. Progress in labour, whether spontaneous or induced in onset, duration of first and second stages of labour, and any evidence of fetal compromise, either traditional signs of fetal distress or abnormalities on cardiotochographic recordings, were noted. The result of blood gas analyses of fetal scalp samples or samples from the umbilical vessels at birth were recorded along with details of drugs, such as analgesics and uterine stimulants given to the mother during labour, their times and dosages, and of epidural or general anaesthesia.

The presentation and mode of delivery of the infant, and indications for any obstetric intervention in the birth were detailed, and a simple assessment of the appropriateness of obstetric management, from a retrospective, paediatric view-point made.

After birth, the infant's initial condition, Apgar scores at 1 and 5 minutes, the times to onset of spontaneous respiration and to the /

the establishment of regular, independent respirations, along with details of initial resuscitation, were noted. Subsequent medical treatment in the early neonatal period, support given, drugs administered, and details of fluid balance were recorded.

Details were also recorded of the occurrence of problems, other than those directly under study, such as respiratory distress, jaundice or infection.

Physiological recordings

In addition to the routine observations of vital signs, such as temperature, heart rate, respiratory rate, e.c.g., and apnoea monitoring, periods of physiological recordings of various functions were performed. Two separate recording systems were used.

1. A 6 channel recorder, Devices MX6, with heat sensitive paper was linked to other equipment as follows:-

(a) Suck recording. A pressure transducer, Elcomatic EM750, connected to a Cardiac Recorders' pressure amplifier, type 152, and oscilloscope monitor, type 141, was used to record pressure waveforms from a blind, water filled teat placed in the infant's mouth at least two hours after a feed. When there was no spontaneous sucking on the teat, this was encouraged by rhythmical movement in the infant's mouth.

(b) Respiratory recording. An Air Shields' apnoea alarm, attached to the infant's chest by 2 electrode jelly-filled, chest leads, measured changes in impedance across the thorax with respiration and other movement, giving a recording of respiratory waveform.

(c) Electrocardiogram and beat-to-beat heart rate were recorded using Cardiac Recorders' E.C.G. module, type 142D, and monitor, type 141 /

141, connected to the infant by 3 disposable, E.C.G. chest leads.

(d) Arterial systolic and diastolic blood pressure were measured through an umbilical arterial catheter, positioned with its distal end in the abdominal aorta at the level of the third lumbar vertebra, connected through a C.F.S. Intraflo Continuous Flush System to a physiological pressure transducer, Century Technology Model CP-01, and Cardiac Recorders' arterial pressure module, type 143, and monitor, Type 141. The system was calibrated using a water column.

(e) Arterial pO_2 was continuously recorded through a 5 F.G. Searle umbilical arterial catheter, with oxygen electrode at its distal tip, and Searle pO_2 monitor and recording interface, the catheter being placed as in (d) above.

Arterial pressure and arterial pO_2 recordings were made when the opportunity arose, the insertion of an umbilical arterial catheter being undertaken only when there was a clinical indication, (Figure 2,1).

2. An 8 channel E.E.G. recorder, Officine Galileo Model E8A, was used to make polygraphic recordings of electroencephalogram, electro-oculogram, electromyogram, electrocardiogram, and respiration.

Silver cup electrodes filled with saline gel were fixed to the scalp with collodion over the right and left parietal regions and vertex (E.E.G.), were taped lateral to each eye (E.O.G.), under the chin to record movement, sucking and background muscle activity (submental E.M.G.), and to each wrist (E.C.G.). Respiration, as indicated by nasal airflow detected by a simple 2 wire thermistor taped in front of one nostril, was also recorded.

The same instrument was used for standard recordings of E.E.G., where these were indicated - in infants who had had fits, shown asymmetries or severe abnormalities of neurological function. The principal montage used is shown below, (Figure 2, 2).

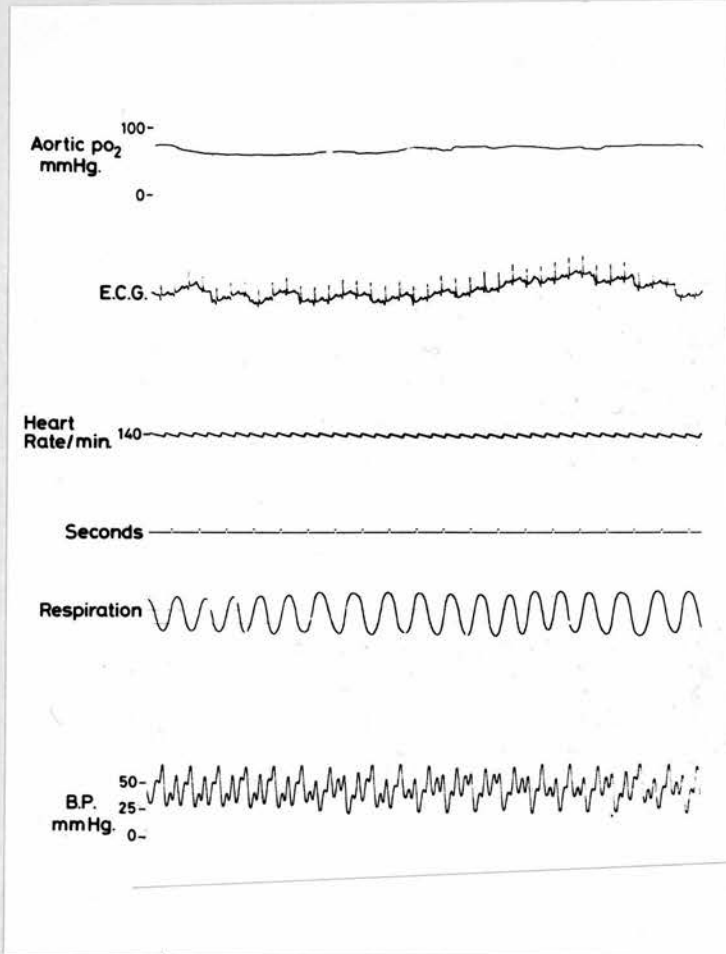
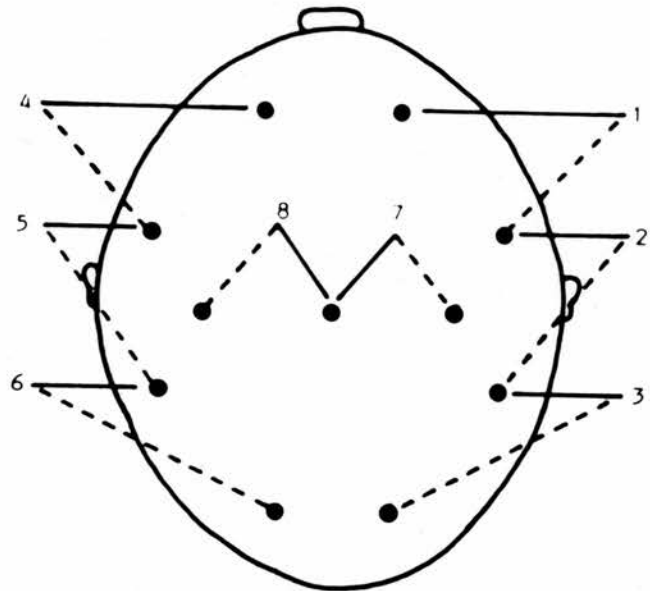


Figure 2,1

Example of a normal recording: E.C.G.,
heart rate, respiration, arterial pO_2
and arterial blood pressure



Electrode placement for electroencephalography in the newborn.

Figure 2,2

The first recording system was used by the author, the second by an E.E.G. technician experienced in work with neonates. With careful attention to technique, especially in setting up the recording systems, good recordings could be obtained. The systems shared two main drawbacks, common to clinical recordings especially when these have to be made in the nursery rather than a specially prepared room. Electrical interference from other equipment, such as incubators and infusion pumps, was a common problem. It could be reduced by careful fixation of skin electrodes, by careful positioning of power cables and leads, and by identifying and eliminating the source of interference when it did occur. Artefacts on the recordings, mainly due to infant movements, emphasised the importance of careful handling of the infant, of recording when he settled, if possible after a feed, and of careful observation of the infant during recordings so that the true cause of disturbance of tracings could be recognised and misinterpretation avoided.

Biochemical Measurements

Routine biochemical analyses of plasma were performed by the clinical chemistry laboratory of the Edinburgh Royal Infirmary, using automated micro-sample equipment, S.M.A.C. Values of plasma urea, sodium, potassium, bicarbonate, calcium, phosphate and magnesium were obtained regularly, the frequency being determined by clinical indication rather than a predetermined regimen. All infants had these measurements made at least daily over the early days of life. Plasma and urine osmolalities were determined by the author using an osmometer, Wide Range Model 3W, Advanced Instruments Inc.

Cerebrospinal fluid was obtained by lumbar puncture, again when there were clinical grounds for this investigation. The fluid was examined microscopically, cultured bacteriologically, and protein and glucose content measured by the clinical chemistry laboratory. Spectrophotometric /

Spectrophotometric examination was performed to detect haemoglobin breakdown products when the fluid was bloodstained or xanthochromic by the biochemistry laboratory, Department of Child Life and Health, University of Edinburgh.

Coagulation screening of venous blood, consisting of platelet count, prothrombin time, partial thromboplastin time, fibrinogen and fibrin degradation product levels, was performed by the Regional Blood Transfusion Service Laboratory, Edinburgh Royal Infirmary.

Follow up assessments

Following the discharge of the infant from hospital, each family was visited at home by the research health visitor prior to the first follow up examination at the age of six weeks. As a minimum, follow up assessments were at six weeks, 4 months, 1 year and yearly thereafter until school age. Many children were seen more frequently, especially in their first year, when there was a medical indication for more frequent hospital review or because of parental anxiety. Between these visits, the families generally were visited at home by the research health visitor, who recorded her appraisal of the home, of the child's progress and behaviour, and of parental attitudes towards and anxieties for their child.

Follow up assessments were conducted by the author in the maternity hospital. At each assessment, a full history of the child's progress, illnesses, behaviour and problems was taken, height, weight, and occipito-frontal circumference measured, and a detailed physical, neurological and developmental assessment made. Following each visit, the general practitioner was informed of the child's progress. As the children reach the age of 4½ years, psychometric assessment consisting of the Stanford-Binet Test, Form L-M, W.P.P.S.I. Geometric Designs and the Goodenough-Harris Drawing test were performed by a senior /

senior educational psychologist, who also made an appraisal of the child's personality and temperament, and asked the mother for her recollections of the child's behaviour during infancy.

Analysis of data

Information was extracted from the study case records (Appendix II). As these had not been designed for computer analysis of data, a further step to code the data into a suitable form was necessary subsequently, as illustrated in Appendix III. The coded information was transferred then to coding forms. Computer analysis was performed by the Medical Computing and Statistics Unit, Edinburgh University Medical School.

Much of the data lent itself to analysis by simple methods, the study group being divided into subgroups by the presence or absence of individual findings and occurrences and comparison of the final outcome for the subgroups made, as expressed in 5 outcome categories or simply as "normal" or "abnormal".

1. The chi-square test was applied to 2 x 2, 2 x 3, and 2 x 5 Contingency tables with 1, 2, and 4 degrees of freedom. Differences were taken as significant, $p < 0.05$, when $X^2 > 3.84$, 5.99 or 9.49 respectively, and highly significant, $p < 0.01$, when $X^2 > 6.63$, 9.21, or 13.28 respectively.

2. When individual frequencies were 5 or less, Fisher's exact probability test was employed.

3. Kendall rank correlation was used as a measure of significant association of ordinal variables, such as parity, socio-economic grouping, birth weight centile positions, Apgar scores, etc., and outcome categories.

4. /

4. Where the study group was divisible into 2 subgroups by the presence or absence of a factor, Wilcoxon's rank sum test was employed to determine whether outcome was significantly different for the subgroups.

5. Where division of the total groups was into several unordered subgroups, e.g. by differing forms of umbilical cord problem, modes of delivery, or patterns of muscle tone, the Kruskal-Wallis test was applied to determine whether outcome was significantly different for individual subgroups.

Finally, the factors which had shown a highly significant relationship to outcome were analysed further to see which could contribute most information as predictors of outcome, by serial exclusion of those factors not adding information to those that remained. The method used was the proportional odds model, (McCullagh, 1980).

CHAPTER III

OUTCOME - INITIAL DESCRIPTION OF FINDINGS

AT FOLLOW-UP

A brief account of the outcome for the children forming the study group will be given at this stage to allow reference to quality of outcome to be made in the subsequent consideration of antenatal, natal and neonatal events and findings. Outcome is described in more detail in Chapter XI.

Of the 50 infants selected, 3 died in the early neonatal period, cases 22, 33 and 35, at 25, 48 and 16 hours respectively. A fourth infant, case 34, who was severely brain damaged, died at 16 months. All of the 46 survivors have been seen for follow-up examination and the majority, 43 children, have been kept under review until 4-6 years of age.

Three children were lost to follow-up when they left the area or the country, cases 7, 25, and 27, last seen aged 14 months, 6 months and 8 months. Cases 7 and 27 showed no abnormality when last seen and have been assumed to be normal. Case 25, who has left the country, was grossly handicapped with microcephaly and spastic quadriplegia when last seen at six months.

The quality of outcome for the 47 infants, who survived the neonatal period, has been graded according to the scheme suggested by Rutter et al, 1970.

Category 1: No abnormal neurological findings.

Category 2: Neurological findings of slight or doubtful significance.

Category /

Category 3: Definite disorder, but producing little or no physical handicap.

Category 4: Definite and obviously handicapping disorder.

This classification has the advantage that it has been used in previous studies of birth asphyxia and allows some parallels, therefore, to be drawn, but has shortcomings in that the distinction between Categories 2 and 3 is imprecise, and the place of other forms of handicap, rather than purely physical limitations, such as epilepsy, learning disorder and mental retardation, is not apparently included. For the purpose of this study, Category 2 has been taken as definite neurological abnormality but of no practical importance to the individual; Category 3 has been interpreted as meaning definite physical, neurological handicap, causing some impairment of function but consistent with a generally normal childhood and education. This category also includes milder degrees of mental impairment, consistent with normal schooling, but where the child is clearly of poorer intelligence than expected for that family. Children allocated to Category 4 have clearly apparent, physical, neurological handicap, with or without mental handicap, of a severity to interfere with many normal activities of childhood.

Those children who died in the neonatal period will be referred to as Category 5.

Table 3,1
Outcome for 13 children with neurological
abnormality

The findings on follow-up of the 13 children with varying degrees of neurological abnormality are shown in Table 3,1. Of those with obvious significant handicap, Category 4, case 34 died at 16 months, cases 9 and 12 will be starting at normal school but will require special /

Table 3,1

	Case No.	Neurological Abnormality
Category 2	23	Hypotonia, delayed early motor + speech development, normal outcome.
	28	Slow early development, speech delay, very poor social background.
	40	Minimal left hemiparesis, no functional importance.
Category 3	3	Definite mild left hemiparesis, minimal functional importance.
	14	Definite mild right hemiparesis, minimal functional importance.
	18	Slow early development, mild truncal ataxia, slow speech, IQ 70
	36	Right Erb's palsy, mild right hemiparesis, good general development.
Category 4	9	Moderate ataxic diplegia, normal intelligence.
	12	Moderate ataxic diplegia, IQ 80 - equal to that of twin.
	25	Microcephaly, spastic quadriplegia, fits.
	34	Microcephaly, spastic quadriplegia, intractable fits, bulbar palsy, died 16 months
	44	Dyskinetic cerebral palsy, microcephaly, severe global retardation.
	49	Severe hypotonia, dyskinetic, markedly physically and mentally retarded.

Outcome for 13 children with neurological abnormality

special help, cases 44 and 49 are in longstay hospitals for handicapped children, and case 25 lives abroad and no further details of her are available. Case 49 is complicated in that the mother is of subnormal intelligence and a younger sibling of this child, without perinatal or other acquired insult, is mentally handicapped.

CHAPTER IV

GENERAL CHARACTERISTICS OF THE STUDY GROUP

Over a 23 month period from February 1976 to December 1977, 50 infants were seen, who satisfied the selection criteria and they form the study group. 47 infants were inborn; 3 were transferred from other hospitals in the early hours of life. During this period, there were 7,922 liveborn infants in the hospital, giving an inclusion rate of 5.9/1,000 liveborn.

No infant, following selection, was subsequently excluded.

Time of inclusion

The times of inclusion in the study are shown in Figure 4,1. All but one of the infants were included in the first 24 hours of life. The exception presented at the age of 48 hours with fits and other abnormalities of behaviour. Mean age at inclusion was 9.5 hours, S.D. \pm 8.4; 25 infants were selected in the first 8 hours of life, and 38 by the age of 12 hours.

There was a tendency for infants with more severe intrapartum problems, marked depression at birth and marked neurological abnormality, to come to the author's attention earlier and be included in the study earlier. Thus many infants, whose behaviour, neurological status and early neonatal course were most deranged, were observed from shortly after birth, allowing accurate observation of their changing state to be made throughout the early days of life.

Where an infant was included in the study rather later, use has been made of the examination findings made by other members of the paediatric medical staff.

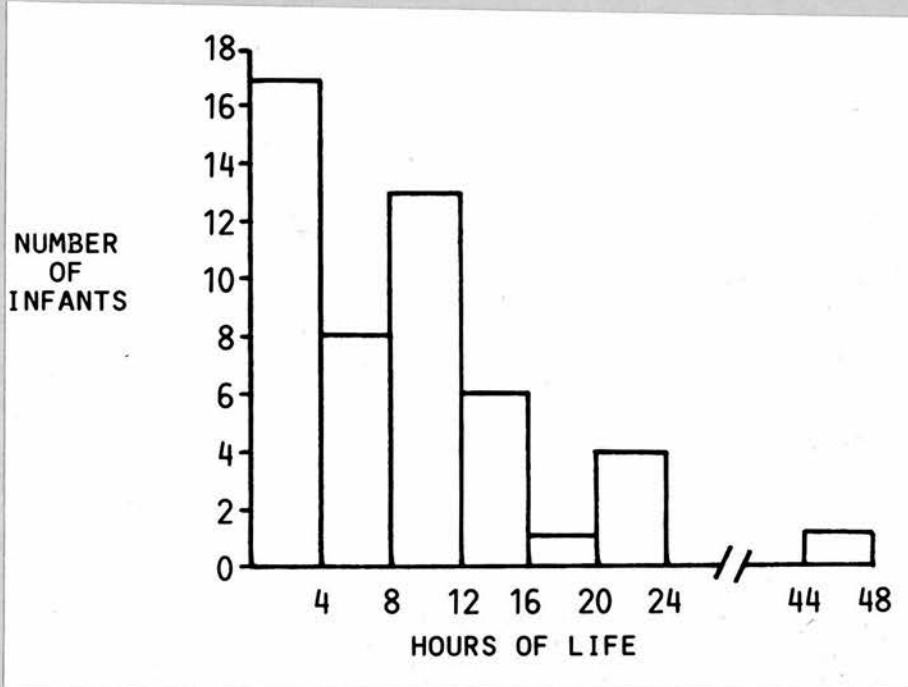


Figure 4,1
Time of inclusion in the study

Sex, gestational age, and birth size

The group consisted of 32 males and 18 females, a not surprising, but not statistically significant, male predominance. In birth asphyxia, as with some other important neonatal problems, the male infant is more commonly involved, (Huntingford, 1963; Ucko, 1965; Chamberlain, 1975). The outcome for male children, however, was better, 7 of the 32 males as compared to 9 of the 18 females being allocated to outcome categories 2-5; this difference is not, however, statistically significant, $X^2 = 2.39$. Four infants were the second of twins, 8% as compared to the expected 1.1% in the general population.

The majority were born at term, 37-41 weeks gestation. Gestational age, by assessment, ranged from 32 to 42 weeks, but only 5 infants were less than 37 weeks and 1 less than 35 weeks, while 2 infants were greater than 41 weeks gestation; neither was markedly postmature. Mean gestation age was 39.1 weeks, S.D. 1.9.

In this population, therefore, intrapartum asphyxia in association with significant postmaturity was not a problem, unquestionably a result of induction policies for pregnancies continuing much beyond term. Premature infants are also poorly represented in the study group, not because the premature are not susceptible to intrapartum asphyxia, but because the selection criteria used tended to select infants showing the abnormalities of performance, behaviour and neurological state more commonly associated with more mature infants, while the markedly premature infant is likely to have an increased liability to develop problems already commonly associated with prematurity, such as the idiopathic respiratory distress syndrome, (Robertson, 1977; Bowes, 1977).

The birthweights of the group ranged from 1.8 Kg. to 5.3 Kg., with a mean of 3.34 Kg., S.D. 0.62. From the data prepared by Gairdner and Pearson, 1971, 3 infants had birthweights below the 10th centile /



centile for gestational age, but none were markedly light. Of the larger infants, 4 had birthweights above the 90th centile; a further 6 had an occipito-frontal circumference greater than the 90th centile on the third day of life, 4 of these infants were proportionately large, having length measurements above the 90th centile also. Three showed marked moulding of the head.

Interestingly, the study group does not contain a greater percentage of either inappropriately grown, small for date infants, or unduly large infants than the general population. Both these groups might be expected to be represented in larger numbers, the small for dates infants because of placental insufficiency leading to an acute stress in labour, and the larger infants because of their greater liability to malpresentation, cephalopelvic disproportion, prolonged labour and dystocia in the second stage.

Maternal age and parity

The mothers' ages ranged from 17 to 43 years, but only 5 were less than 20 years, and 6 more than 30 years old. The mean maternal age was 25.1 years, S.D. 4.6.

Thirty-four mothers were primiparous. Of the 16 parous, 7 mothers had one previous child, 7 had 2 previous children and 2 had 3 children. Five mothers had had a single spontaneous or therapeutic abortion, and 1 mother 2 spontaneous abortions. No mother had had a stillborn child, but 2 had lost children in the neonatal period - 28 week twins, and an infant with spina bifida and hydrocephalus.

Time of birth

The time of birth has also been examined, since arguably birth during night hours, 21.00 - 09.00, or at weekends, night, because of reduced /

reduced staffing levels at these times, carry some increased risk for the infant during delivery or during the immediate hours of life, (Hendry, 1981). No significant difference was found for outcome during general working hours and these times.

Socio-economic group

The socio-economic grouping of the study families and the general population using the maternity hospital, on the basis of the father's occupation, are shown in Table 4,1. The distributions are very similar and the study group is representative of the class structure of the hospital population.

Table 4,1

Socio-economic group

	1	2	3	4	5
Study Group %	10	16	44	18	12
Hospital Population %	7	21	46	17	9

Socio-economic group distribution of study group
and maternity hospital population

All but one of the mothers were married at the time of delivery of their child; 1 was single and 3 separated from their husbands.

Relationship of general characteristics to outcome

No statistically significant association was found between these general /

general features of the study group and subsequent outcome, with the exception of the time of inclusion in the study and the parity of the mothers. Where inclusion was within the first 8 hours of life, there was a higher risk of subsequent allocation to outcome categories 2 - 5, $\chi^2 = 4.50$ $p < 0.05$, and when only categories 4 and 5 are considered, this association is highly significant, $p < 0.001$, exact probability test. This is a readily understandable association since infants were more likely to be seen early and included early in the study following a major incident during labour and delivery, or more severe problems at birth and in the early hours of life, and therefore, at higher risk or poorer outcome.

There is a highly significant association, $p < 0.005$, Kendall rank correlation, between parity and outcome. 63% of the infants of parous mothers, as opposed to 18% of primiparous, were allocated to outcome categories 2 - 5. A similar relationship is found when only outcome categories 4 and 5 are compared to the rest with a more favourable outcome, $p < 0.005$. It is commonly stated that birth asphyxia is commoner in the infants of primiparous mothers (Chamberlain, 1975), but no reference has been found to a higher risk of handicap in asphyxiated infants of multiparous mothers.

Male infants although more numerous had, in general, a better long term outcome, 22% of males compared to 50% of females being allocated to outcome categories 2 - 5. This is not statistically significant, $\chi^2 = 1.47$, and when only categories 4 and 5, significant handicap or neonatal death, are considered, the sexes are similarly represented, 22% females and 19% males. Finer et al, 1981, in their study of hypoxic-ischaemic encephalopathy found that although males were more commonly involved, there was a significantly higher incidence of severe handicap or death in females.

CHAPTER V

PRENATAL AND NATAL FACTORS

Maternal health and pregnancy related problems

The health of most mothers during their pregnancy was good, 28 of the 50 having a completely uneventful pregnancy to the time of labour. In Table 5,1 are listed problems with general health in pregnancy and in Table 5,2 problems more particularly related to pregnancy.

Table 5,1

Case No.	Maternal health problems in pregnancy
2	Epileptic, phenytoin throughout pregnancy, no fits.
7	Urinary infections, renal calculus removed at 22/52 gestation.
19	Road traffic accident, 16/52 gestation, no serious injury.
23	Thrombocytopenia, treated with steroids in late pregnancy.
34	Pleurisy at 38/52 gestation.
43	Recurrent urinary infections.

Table 5,2

Case No.	Obstetric problems - before labour
7,35	Recurrent threatened abortion.
2,5,22,26, 30,36,47,50)Mild or moderate pre-éclamptic)toxaemia
1	Severe pre-eclampsia
15,46	Eclampsia
3,14,30,41	Antepartum haemorrhage
12,32,41	Polyhydramnios, case 12 with twins
32	Hypotensive episode 5 days before delivery, secondary to ritodrine.
47	Anaemia.

Toxaemia was the commonest complication of pregnancy, but, of the 9 cases of pre-eclampsia, in no case was delivery considered necessary before 38 weeks gestation. Two of these were twin pregnancies. Both mothers with eclampsia presented with problems only at term. One had a single fit in a small district hospital, was treated with diazepam infusion and diamorphine and delivered by forceps by the obstetric "flying squad". The other case of eclampsia had several fits at home and during transfer to hospital, was treated with diazepam infusion and delivered by caesarean section.

Four mothers had antepartum haemorrhage. In 3, this did not appear to be severe and occurred some weeks before delivery. One was due to placenta praevia and was delivered by caesarean section at 36 weeks gestation. The fourth mother, also with placenta praevia, presented with severe haemorrhage at term and was delivered by emergency caesarean section. The child had suffered major blood loss.

Problems in labour

All the deliveries, except two (cases 24 and 42), had evidence of some complication. Eight of the mothers were either not in labour or labour had not been fully established at the time of delivery by caesarean section; details of these are summarised in Table 5,3.

Table 5,3

8 cases delivered by caesarean section before
labour established

Eighteen labours were surgically induced by artificial rupture of the membranes; 13 of these were stimulated by oxytocics or extra-amniotic prostaglandin. A further 8 labours, with a spontaneous onset, were similarly enhanced.

Traditionally /

Table 5,3

Case No.	Delivery problems
3	Placenta praevia, A.P.H. at 29 + 36 wks, L.U.S.C.S. at 36 wks.
5	Elective L.U.S.C.S. at term, twin II hyper-extended in utero, difficult delivery.
9	Emergency L.U.S.C.S., cord prolapse after spontaneous membrane rupture.
14	Emergency L.U.S.C.S., severe A.P.H., placenta praevia.
32	Oblique lie, fetal distress before labour established, emergency L.U.S.C.S.
35	Previous classical section, ruptured uterus at 32 wks, emergency delivery.
43	Emergency L.U.S.C.S., cord prolapse after spontaneous membrane rupture.
47	Hypotension during Elective L.U.S.C.S., epidural anaesthesia, breech presentation.

8 cases delivered by caesarean section before labour established

Traditionally complications of labour can be grouped as follows:

- placenta and cord disorders.
- faults of "the powers", uterine activity.
- faults of "the passage", such as pelvic contraction.
- faults of "the passenger", fetal factors.

In practice, it is difficult to allocate each case to such categories. More than one factor may be operative, the mechanism of the dystocia may not be apparent, or fetal distress may occur without clear cause. Consequently, the difficulties in delivery which occurred in the study group will be described under the following headings:

1. Cord and placental disorders.
2. Duration of labour, brief and prolonged.
3. Malpresentation.
4. Fetal distress.
5. Method of delivery.

1. Cord and placental disorders

The umbilical cord is not commonly found round the infant's neck at birth; in the study group, this occurred in 5 cases (Nos. 1, 2, 7, 8, and 34). All except Case 8 had shown signs of fetal distress during labour; the cord position may or may not have contributed to this. Paradoxically, Case 8, despite the absence of fetal distress, undoubtedly had a significant cord problem, the infant having marked engorgement and petechial haemorrhages over the face and head, and subconjunctival and retinal haemorrhages (Figure 5,1). In addition to the interference to venous return from the head caused by neck compression, the placento-fetal circulation may be compromised resulting in an anoxic-ischaemic episode.



Figure 5,1

Facial suffusion, petechial haemorrhage and
subconjunctival haemorrhage from the umbilical cord
being tight round the neck, (Case 8)

No cases of knotted cord occurred, but in 3 instances there was prolapse of the umbilical cord. In two, Cases 9 and 43, this followed spontaneous rupture of the membranes in hospital and delivery was achieved promptly by caesarean section. The third case, Case 22, suffered cord prolapse after the delivery of the first twin; there was loss of the fetal heart beat during internal version and breech extraction.

Placental haemorrhage complicated 4 pregnancies. In Cases 30 and 41, this occurred some weeks before delivery at term. Cases 3 and 14 had a major degree of placenta praevia, producing haemorrhage at 29 and 36 weeks in Case 3 and presenting with severe blood loss at term in Case 14. Both were delivered by emergency caesarean section; Case 14 had suffered severe intrapartum blood loss and required vigorous resuscitation, and transfusion at birth.

The condition and weight of the placenta, and the ratio of placental weight:infant weight, were recorded. Seven placentae showed areas of infarction or extensive calcification; however, only in one case was this associated with significant intrauterine, fetal growth retardation, with a birthweight less than the 10th centile for gestation.

Placental weight ranged from 350-1000 gms., mean 606 gms. S.D. 137.8, and the ratio of placental weight:infant weight from 0.11-0.28, when only infants over 37 weeks gestation were considered.

2. Duration of labour, brief and prolonged

(a) Total duration.

The total duration of labour, first and second stages, or the time from /

from onset of labour to surgical delivery, ranged from 1 hr. 38 mins. to 23 hrs. in 41 cases. Eight mothers were delivered before labour was established; one presented to hospital in the second stage and was uncertain when labour had started. The mean duration of labour in the remaining 41 cases was 11.1 hours, S.D. 5.25.

Total labour duration was 3 hours or less in 4 cases. Details are given in Table 5,4.

Table 5,4

Case No.	Duration 1st stage	Duration 2nd stage	Labour stimulation	Fetal Distress	Delivery
25	2 hours	50 mins	+, tonic	Bradycardia, F.H. lost.	Undiagnosed twins Breech extraction
34	2½ hours	25 mins	+	Bradycardia	R.O.T., forceps rotation.
44	1½ hours	5 mins	-	Bradycardia	Spontaneous vertex
50	3 hours	3 mins	+, tonic	Late deceleration, fetal acidosis	Spontaneous vertex

Details of labour of 3 hours or less duration

Labour continuing for 18 to 24 hours occurred in 4 cases, numbers 6, 10, 37, 41. The main factor in each appeared to be unappreciated, cephalopelvic disproportion. Three had had stimulation of uterine activity; in two, the response was excessive. All showed evidence of fetal distress, three were delivered by forceps assisted vertex, one by spontaneous vertex, and all 4 infants had excessive moulding of the head. No labour lasted more than 24 hours.

(b) Duration of second stage of labour

Thirty-three/

Thirty-three labours had a second stage, 30 of which ended by vaginal delivery and 3 by caesarean section after delay in this stage. Two other infants were delivered vaginally, but at the onset of the second stage, by forceps. A breakdown of the duration of second stage of labour is shown in Table 5,5.

Table 5,5

Duration of second stage	Number of cases
< 10 mins	7
11 - 30 mins	5
31 - 60 mins	12
> 60 mins	9

Duration of second stage of labour

The duration ranged from 3 to 160 minutes, mean 48.9 mins., S.D. 38.2.

Two cases, 8 and 50, had very brief second stages, 5 and 3 minutes respectively, Case 8 being a parous mother with stimulation of uterine activity by oxytocin, and Case 50 having tonic uterine contractions following extra-amniotic prostaglandin. Case 11, a breech presentation, also had a rapid delivery with poorly controlled descent of the head, but a second stage of 38 minutes.

Prolonged second stage of labour was common, being greater than 30 minutes in 64% of those who had a second stage. Details of 9 cases with a second stage greater than 60 minutes are given in Table 5,6. In most, there had been clear signs of fetal distress during the first stage of labour, the problem becoming more apparent when failure to progress in second stage ensued. Cephalopelvic disproportion is an important factor in this group, all the infants having moderate or severe degrees of moulding, and all but one having a birth weight greater than the mean birth weight, 3.34 kg., for the group as a whole.

3. Malpresentation

Details of 11 cases with malpresentation, the duration of labour, method of delivery and occurrence of fetal distress, are shown in Table 5,7.

Table 5, 7

Presentation	Case No.	Duration of Labour		Fetal Distress	Delivery
		1st Stage hours	2nd stage minutes		
<u>Breech</u>	5	-	-	-	El.L.U.S.C.S., 2nd twin, hyper- extended head.
	11	7	38	-	Vaginal delivery, rapid descent of head
	20	10	19	Tachycardia	Vaginal delivery
	47	-	-	-	El.L.U.S.C.S., Maternal hypo- tension
<u>Occipito- transverse</u>	4	14	54	Bradycardia	Rotation with Keilland's forceps.
	7	9	10	Late deceleration, Bradycardia	ditto
	34	2½	25	Bradycardia	ditto
	36	5	90	Late deceleration, Bradycardia	ditto
<u>Occipito- posterior</u>	17	15	48	Meconium, Bradycardia.	Forceps delivery face to pubis.
	26	8	30	Tachycardia Bradycardia	Rotation with Keilland's forceps
<u>Oblique Lie</u>	32	-	-	Tachycardia Bradycardia	Em. L.U.S.C.S.

Details of 11 cases with malpresentation

There were 4 breech presentations, one a second twin. Two were delivered vaginally with forceps to the head. In addition, Cases 22 and 25 were emergency deliveries by internal rotation, and breech extraction under general anaesthesia.

Apart from the two cases delivered by elective caesarean section, all but one of this group showed signs of fetal distress and went on to surgical delivery.

4. Fetal distress

Fetal distress in labour, as evidenced by the detection of fetal heart rate abnormalities, tachycardia greater than 160/min., bradycardia less than 120/min., type I dips or early decelerations in heart rate, type II dips or late decelerations, and loss of beat to beat variations, occurred in 37 cases. Passage of meconium in utero occurred in 12 cases, but in 2, where there was no other evidence of fetal distress, this has not been considered significant. Further evidence of fetal distress by the finding of significant acidosis, $\text{pH} < 7.25$, on fetal scalp blood sampling or from umbilical arterial blood at delivery, was obtained on only 8 cases, the number of pH estimations done being small. pH measurements ranged from 6.89 to 7.24. Of these 8 cases, 7 also had fetal heart rate abnormalities. The remaining case had been delivered by caesarean section, during which the mother became hypotensive; cord blood pH was 7.13.

These findings are summarised in Table 5,8.

Table /

Table 5,8

Abnormality detected	Number of cases
Early decelerations	9
Late decelerations	9
Tachycardia $>160/\text{min.}$	16
Bradycardia $<120/\text{min.}$	20
Loss of beat to beat variation	2
Fetal acidosis $\text{pH} < 7.25$	8
Meconium staining with heart rate abnormality	10

Evidence of fetal distress in 37 cases

Twenty-seven labours were monitored by cardiotochography, either by an external ultrasound transducer attached to the mother's abdomen, or by a unipolar electrode screw attached to the fetal scalp or presenting breech. All of these showed abnormal heart rate tracings. 54% of the study group, as compared to 42% of total labours in the hospital over the same period, were monitored in this way. The incidence of abnormal recordings in the total population was approximately 20%, (Boddy, 1977). In 10 labours, fetal tachycardia or bradycardia was detected by traditional fetal heart auscultation.

Consideration of the 23 cases not monitored by cardiotochography shows that in 11 cases monitoring would not have been feasible for the following reasons:-

- delivery by emergency caesarean section without preceding labour or opportunity for monitoring,
- elective caesarean section,
- laboured in peripheral hospital without monitoring facilities.

- /

- admitted to hospital in second stage.

Details of the remaining 12 cases are shown in Table 5,9.

Table 5,9

Case No.	Pregnancy Problem	Labour Problem	Fetal Distress	1st stage hours	2nd stage mins	Delivery
4	-	O.T., prolonged 2nd stage	Bradycardia	14	54	Keilland's Forceps
8	-	Cord tight round neck, suffused.	-	4	5	Vertex
11	-	Breech, rapid delivery of head	-	7	38	Breech
20	-	36/52 gestation, breech.	-	10	19	Breech
21	-	C.P.D., prolonged 2nd stage	Tachycardia	11	80	Keilland's Forceps
24	Poor fetal growth	No apparent problem	-	13	30	Vertex
37	-	Prolonged labour	Tachycardia	19	48	Forceps assisted
38	-	Delay in 2nd stage	Meconium at birth	8	80	Forceps assisted
39	-	Delay in 2nd stage	-	9	50	Vertex
41	APH, 36/52 hydramnios	Delay in 2nd stage	Meconium	9	70	Forceps assisted
42	-	Apparently normal labour	-	7	7	Vertex
48	-	Delay in 2nd stage, failed forceps	Tachycardia + bradycardia	4	150	Emergency caesarean section

Details of 12 cases not monitored by Cardiotocography

It can be seen that in all but two of these the pregnancies were uncomplicated. Two were breech presentations; both delivered vaginally. In several cases, there was no apparent problem in labour until difficulty was encountered at delivery and it may be that more detailed observation of the fetal state in labour in these cases, and, indeed, in those where traditional signs of fetal distress were found, might have provided earlier warning of fetal difficulty. Meconium staining of the liquor throughout labour occurred in one of these twelve cases, and, in a second, meconium was aspirated from the infant's trachea at resuscitation; in neither of these had there been fetal heart rate abnormalities detected by auscultation.

Thirteen of the study group did not have evidence of fetal distress; however, there was a complicated birth in all but two of these. Four infants were delivered by emergency caesarean section, for antepartum haemorrhage, eclampsia, failed forceps delivery or cord prolapse. In two instances, there were difficulties during an elective caesarean section - maternal hypotension and delayed delivery of the second twin. Delay in the second stage of labour occurred in 3 cases and 2 of these were delivered instrumentally. One labour had a brief second stage and the cord was tightly round the infant's neck causing compression, while a breech delivery ended with poorly controlled descent of the head. In the remaining 2 cases, no problem was detected during labour or delivery, although one infant had grown poorly in utero. Details of these 13 cases are listed in Table 5, 10.

Table /

Table 5,10

Case No.	Summary of labour and delivery
3	Placenta praevia, A.P.H., L.U.S.C.S. at 36 weeks gestation for premature labour.
5	Second twin, hyperextended posture, delayed delivery at elective L.U.S.C.S.
8	Brief second stage, cord tight round neck.
11	Vaginal breech delivery, rapid delivery of head.
15	Eclampsia, emergency forceps delivery.
24	Intrauterine growth retardation, no apparent problem during delivery, premature, 35 weeks.
30	Failed forceps in peripheral hospital, emergency L.U.S.C.S.
38	Prolonged second stage.
39	Prolonged second stage.
41	Long first and second stages.
42	Normal pregnancy, labour and delivery.
43	Cord prolapse, emergency caesarean section.
47	Hypotension during elective caesarean section.

13 cases where fetal distress not demonstrated

5. Method of Delivery

The mode of delivery in the 50 study cases is listed below:-

Spontaneous vertex	13 cases	26%
Keilland's forceps (with rotation 5 cases)	10 cases)	
)	
)	
Haig Ferguson forceps	5 cases)	38%
)	forceps
Breech with forceps to the head (breech extraction 2 cases)	4 cases)	
)	
Elective caesarean section	3 cases)	36%
)	caesarean
Emergency caesarean section	15 cases)	section.

Over the same period, 22% of the total hospital deliveries were forceps assisted, and 14% were by caesarean section. There were 3 failed forceps deliveries in the group compared with a total of only 8 for the whole study period.

Eighteen labours were surgically induced in onset and delivered as follows:-

spontaneous vertex	4 cases
forceps assisted	7 cases
caesarean section	7 cases.

The mode of delivery of this group, therefore, is similar to the study group as a whole.

Summary of obstetric problems

In summary, the main problems occurring in late pregnancy and labour were these:-

Toxaemia	pre-eclampsia	9 cases
	eclampsia	2 "
Antepartum haemorrhage		4 "
Cord problems	prolapse	3 "
	round the neck	5 "
Maternal hypotension		2 "
Ruptured uterus		1 "
Brief labour (i.e. total 3 hrs, or 2nd stage < 5 mins)		5 "
Prolonged labour (i.e. total > 18 hours, or 2nd stage > 60 mins)		12 "
Malpresentation		11 "
Cephalo-pelvic disproportion		12 "
Undiagnosed twins		1 "
Fetal distress		37 "
Surgical delivery		37 "

Some /

Some of the difficulties that occurred were unforeseeable, and unavoidable. Others might have been recognised, or recognised earlier, and appropriate action taken. With the advantage of hindsight, it is easy for the paediatrician to be wise and to be critical of obstetric management. Nevertheless, many adverse intrapartum events are avoidable, or, with earlier recognition, the situation may be saved without irreparable harm. It is, therefore, important to learn from such experience.

At the time of admission of the infants to the study, a simple evaluation of obstetric management, from a paediatric viewpoint, was made into three categories by whether there had been apparent signs of particular concern about progress in labour and the wellbeing of the fetus, and whether any action had been taken to remedy the problem or expedite delivery. In addition, where action was taken, a subdivision by whether or not the action appeared well timed and appropriate was made, Table 5,11.

Table 5,11

Category 1 - no concern	9 cases
Category 2 - concern - no action	8 cases
Category 3 - concern and action	<u>33 cases</u>
(a) appropriate action	21 cases
(b) delayed or inappropriate action	12 "

Evaluation of obstetric management

Antepartum and intrapartum factors and long term outcome

Antepartum and intrapartum factors were examined for possible relationships with the outcome for the infants. Little association was found. The presence of the following was not significantly correlated with outcome:-

a clinical placental or cord problem, toxæmia, placental infarcts /

infarcts, placental weight to infant birth weight ratio, antepartum haemorrhage, a significant clinical problem in labour, total duration of labour, duration of second stage of labour, spontaneous or induced onset of labour, medical stimulation of labour, excessive uterine activity, maternal opiates during labour, cardiotochographic monitoring, passage of meconium in utero, early decelerations, late decelerations in fetal heart rate, tachycardia, malpresentation, method of delivery.

The detection of fetal distress by traditional auscultatory, or cardiotochographic means was significantly associated with a complicated outcome, $p < 0.05$, while the occurrence of fetal bradycardia showed a highly significant correlation with poor outcome, $p < 0.01$, Wilcoxon's rank sum test, being a finding in all but one of the nine infants who died or survived with handicap, outcome categories 4 and 5.

"Acute" or "prolonged" stress

Following the animal work of Myers, 1972, suggesting that two distinct, pathological patterns of brain damage can result from different types of asphyxial insult, prolonged partial asphyxia leading in the fetal monkey to brain swelling, damage to the basal ganglia and sometimes areas of cortical softening, and acute total asphyxia tending to cause lesions in the brain stem alone without brain swelling or cerebral hemisphere involvement, Scott 1976, in her study of severe birth asphyxia found that "prolonged" stress was associated with death from asphyxia, or survival with cerebral palsy more commonly than "acute" stress. In clinical practice, however, it is difficult and, indeed, without detailed monitoring of the labour and the fetus, somewhat arbitrary to classify insults as "acute" or "prolonged" stresses.

The /

The study group has been divided on a similar basis to that used by Scott, 1976.

Acute stress: severe antepartum haemorrhage, cord prolapse, eclampsia, maternal hypotension, acute obstructed labour e.g. shoulder dystocia, second twin delay, gross fetal distress i.e. severe bradycardia with severe acidosis, or loss of fetal heart rate, tonic uterine contractions.

Prolonged Stress: previous antepartum haemorrhage, pre-eclamptic toxæmia, chronic placental change, intrauterine growth retardation, prolonged first stage of labour, non-dramatic fetal distress, malpresentation without acute obstruction or other factors in acute category.

Table 5,12 shows the distribution of 48 infants by type of stress and by outcome category.

Table 5,12

Outcome Category	Acute Stress	Prolonged Stress	Acute + Prolonged
1	13	18	1
2	-	3	-
3	3	1	-
4	5	1	-
5	2	-	1

"Acute" or "prolonged" stress in 48 infants and outcome

Two infants have not been included as they could not readily be classified in this way. Using these criteria for division into "acute" and "prolonged" stress, there is, in fact, a significant association between acute stress and neonatal death, or survival with significant handicap, $p < 0.05$, Kruskal-Wallis test.

CHAPTER VI

CONDITION AT BIRTH

The majority of infants showed depression of vital function at birth and required resuscitation.

Apgar scores

The distribution of Apgar scores at 1 and 5 minutes in the group is shown in Figure 6,1, and Tables 6,1 and 6,2, subdivided by outcome category; the mean Apgar score for each category is also given.

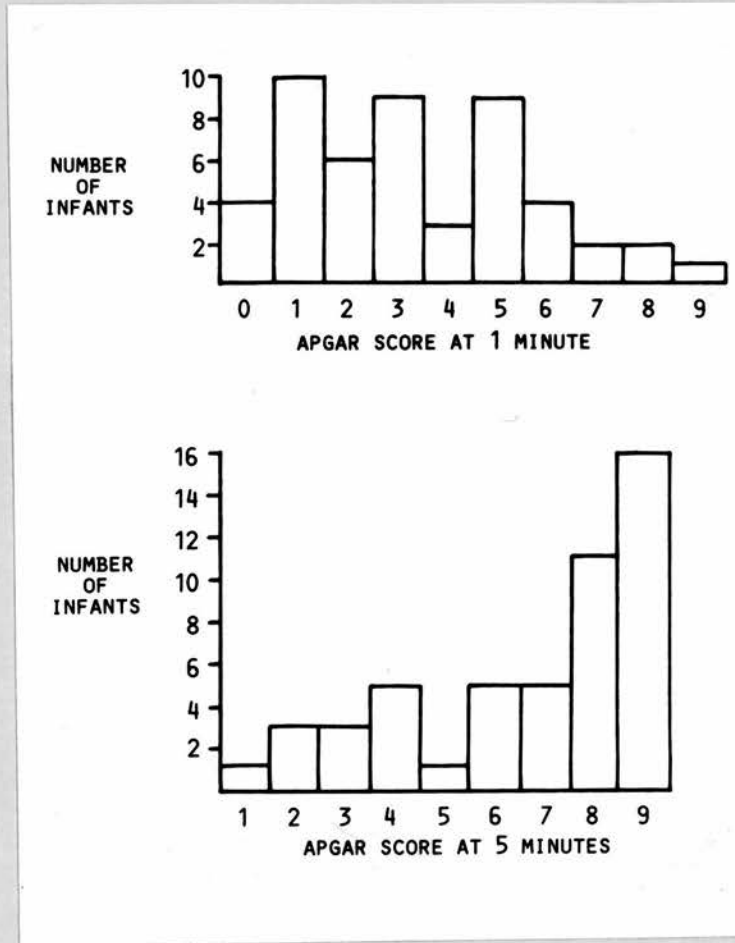
Table 6, 1
1 minute Apgar score

	0	1	2	3	4	5	6	≥ 7	mean	
Outcome Category	1	1	5	5	7	3	5	2	5	3.8
	2	-	-	-	-	-	2	1	-	5.3
	3	1	1	-	1	-	1	1	-	3.0
	4	-	4	-	1	-	1	-	-	2.2
	5	2	-	1	-	-	-	-	-	0.8
Total	4	10	6	9	3	9	4	5		

Crosstabulation of 1 minute Apgar score by outcome category

Table /

Figure 6, 1



Distribution of Apgar scores
at 1 and 5 minutes

Table 6,2
5 minute Apgar score

	1	2	3	4	5	6	>7	mean
Outcome	1	1	2	3	-	2	25	7.3
Category	2	-	-	-	-	-	3	8.3
	3	1	1	-	-	-	3	5.6
	4	1	-	1	1	2	1	6.0
	5	1	-	1	-	1	-	3.3
Total	1	3	3	5	1	5	32	

Crosstabulation of 5 minute Apgar score by outcome category

Mean Apgar score at 1 minute was 3.4, S.D. 2.3, and at 5 minutes 6.8, S.D. 2.3. 58% of the group had a very low 1 minute score of 3 or less, while only 10% had a good score of 7 or more. By 5 minutes of age, all the infants had improved scores, to varying degrees; 26% still had a low 5 minute score of 5 or less, but 64% a score of 7 or more, while 32% had achieved a score of 9 by that time.

There is a significant relationship between Apgar scores and outcome; considering all the outcome categories, this is significant, $p < 0.05$, 1 minute scores, and highly significant, $p < 0.01$, for 5 minute scores, while if only categories 2-5 are considered, the relationship is highly significant, $p < 0.01$, for both 1 and 5 minute scores, Kendall rank correlation. It is important to recall, however, that these infants have been selected on evidence of intrapartum asphyxia, abnormal neonatal behaviour and neurological state, not solely on the basis of poor Apgar scores. A number of infants with fairly good scores had an unfavourable outcome.

Looking at the total population of infants delivered in the hospital over the 2 year period, which includes the 23 months of the study, Table 6,3, 4.8% of infants had a 1 minute Apgar score of 3 or less and 1.35% a score of 0 or 1, while only 1.74% still had a low score of 5 or less at 5 minutes. If only mature infants, 37 weeks gestation or more, are considered, these percentages fall slightly.

Table 6,3

Apgar Score	2 year Hospital Population		Study Group	
	All gestations	≥ 37 wks gestation	All gestations	≥ 37 wks gestation
1 min. ≤ 3	392 4.8%	289 3.8%	29 58%	26 52%
1 min. 0 or 1	110 1.4%	68 0.9%	14 28%	12 24%
5 min. ≤ 5	142 1.7%	81 1.1%	13 26%	12 24%

Apgar scores in total population and study group

It can be inferred that over the study period, of all the infants of 37 weeks gestation or more, 9.4% with a 1 minute score of 3 or less, 18.4% of those with a score of 0 or 1, and 15.5% of those with a 5 minute score of 5 or less were considered to have developed neonatal, symptomatic asphyxia and were, therefore, included in the study. A large number of infants, therefore, with very low Apgar scores, even 0 or 1 at 1 minute, did not develop neonatal problems.

Spontaneous respiration

The times taken to the onset of respiration and to the establishment of regular, independent respirations, broken down by outcome category are shown in Tables 6,4 and 6,5.

Table /

Table 6,4

		Time to spontaneous respiration - minutes				
		< 2	2-5	6-10	11-30	> 30
Outcome Category	1	27	6	1	-	-
	2	3	-	-	-	-
	3	2	1	-	1	-
	4	2	1	3	-	-
	5	-	-	1	-	2
Total		34	8	5	1	2

Time to onset of spontaneous respiration by outcome category

Table 6,5

		Time to regular, independent respirations - minutes			
		0-3	6-10	11-30	> 30
Outcome Category	1	22	10	2	-
	2	3	-	-	-
	3	2	1	1	-
	4	1	-	4	1
	5	-	-	-	3
Total		28	11	7	4

Time to regular, independent respirations by outcome category

There is a correlation between these times and outcome. Infants who took longer than 2 minutes or 5 minutes to initiate spontaneous respiration are significantly more likely to belong to an abnormal, outcome category: $x^2 = 4.83$, $p < 0.05$, and $x^2 = 10.66$, $p < 0.01$, respectively /

respectively. When those in outcome categories 4 and 5 are compared with the remainder, there is a highly significant difference in time to onset of spontaneous respiration, $p < 0.005$, Exact probability test.

A similar relationship is shown with time to establishment of regular, independent respirations. If this is greater than 5 minutes or 10 minutes, there is a significant increase in the risk of poor outcome, $\chi^2 = 11.18$, $p < 0.05$, and $\chi^2 = 17.41$, $p < 0.01$, respectively, 2 x 5 contingency tables. When those in category 4 and 5 are compared to the remainder, there is a highly significant increase in time to regular, independent respirations, $p < 0.005$, Exact probability test. Again it should be recalled that these infants were selected on the basis of various other abnormalities, not purely delay in initiating or establishing respiration at birth.

Assisted ventilation and resuscitation

Thirty-six infants, 72% compared to 4% of the total hospital births, were given a period of assisted ventilation by endotracheal tube immediately after birth. The duration of ventilation ranged from 2 to 60 minutes. In addition, one infant was ventilated continuously until the time of death at 16 hours, having failed to establish adequate, regular respiration. Excluding this infant, the mean time of ventilation was 10.7 mins., S.D. 12.5. Duration of ventilation at birth by outcome category is shown in Figure 6,2. All 9 infants in outcome categories 4 and 5 required ventilatory assistance at birth and in 5 of these this was prolonged, greater than 20 minutes. When ventilation was given for more than 10 minutes, there was a highly significant risk, $p < 0.01$, of subsequent allocation to an abnormal outcome group, Exact probability test.

Dextrose, 5 ml. 10%, and sodium bicarbonate, 5 ml. 5%, were given shortly after birth into the umbilical vein to 37 infants, including

33 of the 36 infants who had a period of assisted ventilation. Fifteen infants, whose mothers had been given opiate analgesia within 4 hours of delivery, were given nalorphine intravenously at birth.

Apparent stillbirth

Eight infants were apparently stillborn, there being no signs of life at birth. Details of these cases are given in Table 6,6.

Table 6,6

Case No.	Labour and Delivery	Apgar 1+5 min	Heart Reestrart mins.	Spont. resps. mins.	Regular Resps. mins.	Outcome Category
14	Pl.praevia, severe fetal haemorrhage, EM.L.U.S.C.S, no F.H.	1+3	1	5	6	3
22	2nd twin, prolapsed cord, breech extraction, no F.H.	0+4	2	50	60	5
25	Undiagnosed 2nd twin, breech extraction after oxytocin, no F.H.	1+5	1	6	60	4
26	R.O.P., prolonged labour, rapid KFRD after no F.H.	1+4	1	1	5	1
27	Admitted 2nd stage, shoulder dystocia	0+4	2	5	10	1
34	R.O.T., cord round neck, bradycardia-no F.H., KFRD	1+2	1	8	30	4
35	Ruptured uterus, 32/52 previous classical section, no F.H.	0+1	5	60	not est.	5
36	Large infant, R.O.T. KFRD, shoulder dystocia	0+2	3	16	30	3

Details of 8 cases of apparent stillbirth

Four of these infants responded rapidly to external cardiac massage and ventilation, having a 1 minute Apgar score of 1, indicating some return of heart activity. It can be seen that all these deliveries were complicated by obstetric emergency situations, predictable or unpredictable. The fetal heart was undetectable in 6 of these cases shortly before delivery, but it is not possible to know the complete duration of cardiac arrest. Heart activity had returned in all 8 infants by 5 minutes of age. Two of the 3 neonatal deaths belong to this group; Case 34 died at 16 months. Of the 5 long term survivors only 1, Case 25, is seriously handicapped. This small group of extreme, acute birth asphyxia, therefore, has tended either to die from severe brain damage, or to survive reasonably, or completely, intact. Not unexpectedly, there is a significant association between apparent stillbirth and outcome, $p < 0.01$, Wilcoxon's rank sum test.

Summary

It can be seen, therefore, that there is a correlation between subsequent outcome and the condition of the infant immediately after birth, as indicated by Apgar scores, time to the onset of respiration and absence of signs of life at birth, in this group of infants who went on to show abnormalities of behaviour, performance and neurological function in the neonatal period. However, as low Apgar scores and a need for resuscitation at birth are common occurrences, most commonly followed by an uneventful, early neonatal course and uncomplicated outcome, such information by itself is of limited prognostic significance for the individual child. This will be discussed more fully later, Chapter XII.

CHAPTER VII

ABNORMALITIES OF PERFORMANCE AND BEHAVIOUR

As described in Chapter II, the occurrence of various abnormalities of behaviour and performance in the first days of life was taken as one criterion for selection to the study group. These can be regarded as the "symptoms" of neonatal, symptomatic asphyxia, (Brown, 1974), the deviations from normal that the nurse, doctor or mother caring for the infant would observe. The frequency of occurrence of these 9 abnormalities, broken down by outcome category, is shown in Table 7,1.

Table 7, 1

Outcome Category

Also shown are the percentages of infants in Category 1, 2 + 3, 4 + 5, who demonstrated each abnormality, grouped in this way because of the similarities between the paired outcome categories. The mean number of abnormalities in each outcome category is also shown in Table 7,1, and the actual number in Figure 7, 1. There is an increased likelihood of unfavourable outcome, the greater the number of abnormalities exhibited; this is highly significant, $p < 0.01$, Kendall rank correlation.

The individual abnormalities will now be described and discussed.

Individual abnormalities

Feeding depression.- Depression of feeding reflexes, necessitating a period of naso-gastric tube feeding or intravenous fluids for at least 24 hours, was very common, occurring in 80% of the study group.

Examination /

Table 7, 1

Outcome Category

Abnormality	No. of Infants	1	2	3	4	5	% Category 1	% Categories 2 + 3	% Categories 4 + 5
Feeding depression	40	26	2	3	6	3	76	71	100
Persistent vomiting	5	4	1	-	-	-	12	14	0
Hypothermia	5	1	1	-	3	-	3	14	33
Apnoeic episodes	11	4	2	-	2	3	12	28	56
Cyanotic episodes	16	9	2	-	2	3	26	28	56
Irritability	39	28	1	3	6	1	82	57	78
Cerebral cry	18	12	1	2	3	-	35	43	33
Apathy	26	11	3	3	6	3	32	86	100
Fits	18	8	2	3	3	2	24	71	56
Total No. Infants	50	34	3	4	6	3			
Total No. abnormalities	178	103	15	14	31	15			
Mean No. abnormalities	3.6	3.0	5.0	3.5	5.2	5.0			

Abnormalities of performance and behaviour
by outcome category

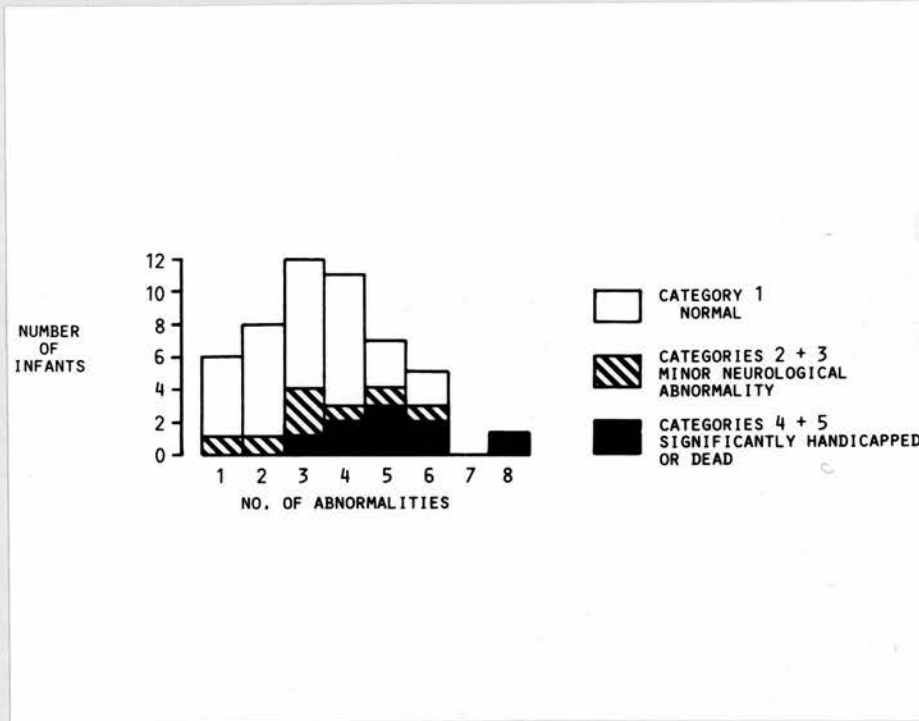


Figure 7, 1

Distribution of number of abnormalities of performance and behaviour by outcome category groups.

Examination of these infants produced a variety of findings: 12 had a complete bulbar palsy with absence, not only of feeding reflexes, but of the reflex protection of the pharynx and upper airway, there being loss of gag, cough, and swallow reflexes and some tendency to pool saliva in the mouth and pharynx. As a result, one infant developed an orthostatic pneumonia, despite regular oral and pharyngeal suction and chest physiotherapy. Other infants showed an isolated loss of feeding activity or inadequate sucking or sucking/swallowing/respiratory co-ordination to allow safe, oral feeding initially.

In addition to temporary depression of sucking, reversion to the primitive pattern of active, rejection reflexes - head turning away from a stimulus to root, lip pursing, tongue pushing, gagging, retching and vomiting, was seen in some infants, usually associated with irritability and some evidence of compressional head injury.

As described in Chapter I, sucking activity was studied by recording pressure waveforms from a blind, water-filled teat placed in the infant's mouth at least 2 hours after a feed. When there was no spontaneous sucking at the teat, this was encouraged by rhythmical movement of the teat in the infant's mouth. Examples of pressure tracings are shown, Figures 7,2 - 7,6. In many infants, there was no sucking activity demonstrated initially; sucking activity recovered over a wide range of times over the first days of life. Recovery was heralded in some by the presence of mouthing movements and then occasional single sucks, going on to short sucking bursts. Finally, when oral feeding had been established, normal sucking activity with long bursts, 15-20 sucks, was seen. The rate of sucking varied between 1.2 and 1.7 sucks/second, the rate increasing usually as the sucking bursts became longer.

In contrast to depression of sucking activity, increased activity with prolonged, almost continuous, sucking was seen in some hyperalert, irritable infants. This occurred in a variety of situations - in association /

association with compressional head injury, hypocalcaemia, and also shortly after birth in hyperalert infants with a metabolic acidosis, Figure 7,7.

The occurrence of feeding depression did not carry any prognostic significance, the frequency being similar in those who did and did not show subsequent abnormality on follow up, 85% and 76% respectively. All the infants in Category 4, significant handicap, required tube feeding. The absence of feeding depression was found only in infants later allocated to outcome categories 1, 2, and 3, but this is not significantly related to a good outcome, $\chi^2 = 2.8$.

When the length of time over which tube feeding was required is considered, a different pattern is seen, Figure 7, 8. With increasing duration of tube feeding, there is an increased risk of unfavourable outcome; this is highly significant, $p < 0.001$, Kendall rank correlation.

Persistent vomiting

Persistent vomiting in the early days of life can be the result of many different mechanisms. In the context of birth asphyxia, it was noted in 5 infants of the study group. Other causes of vomiting such as surgical conditions, infection, metabolic disorder were excluded by clinical examination and appropriate investigation. Each of these infants showed similar features with irritability and facilitation of the rejection, feeding reflexes. Two showed evidence of subarachnoid haemorrhage with blood in the cerebrospinal fluid and 3 had marked moulding of the head, suggesting compressional head injury.

None of these infants had any significant problem on follow up assessment.

Hypothermia /

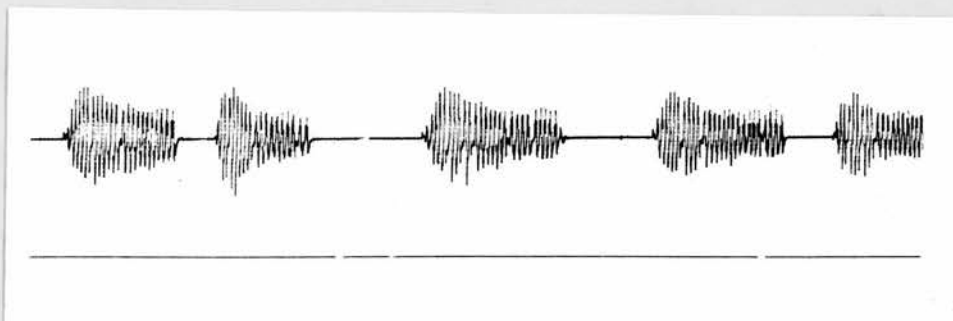


Figure 7, 2

Normal sucking pattern of a term infant at 3 days.

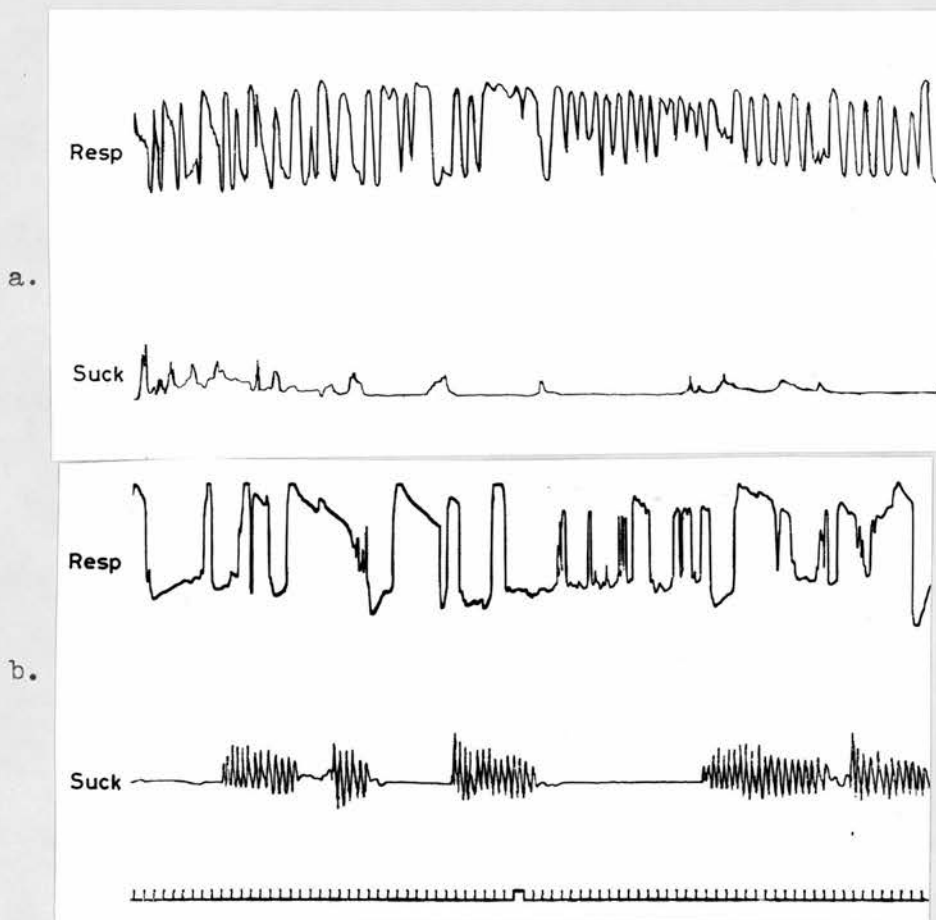


Figure 7, 3

Sucking patterns following intrapartum asphyxia, (Case 28)
(a) at 12 hours, (b) at 48 hours showing recovery

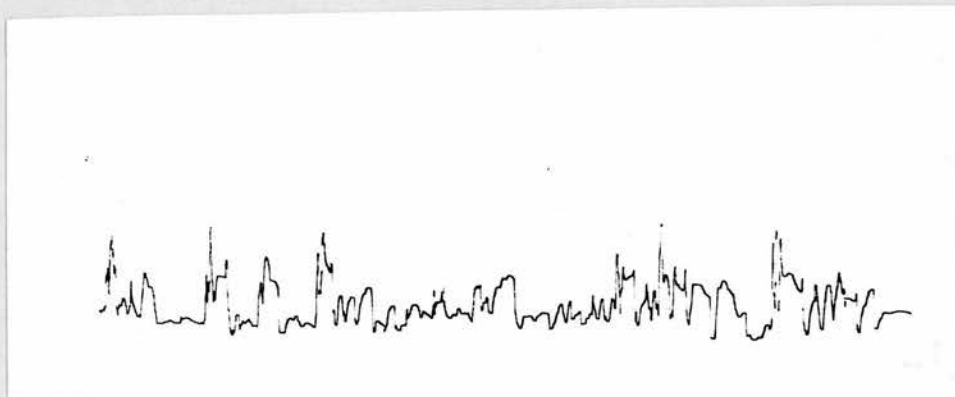


Figure 7, 4

Mouthing activity prior to the recovery of sucking -
Case 27 at 10 hours of age.

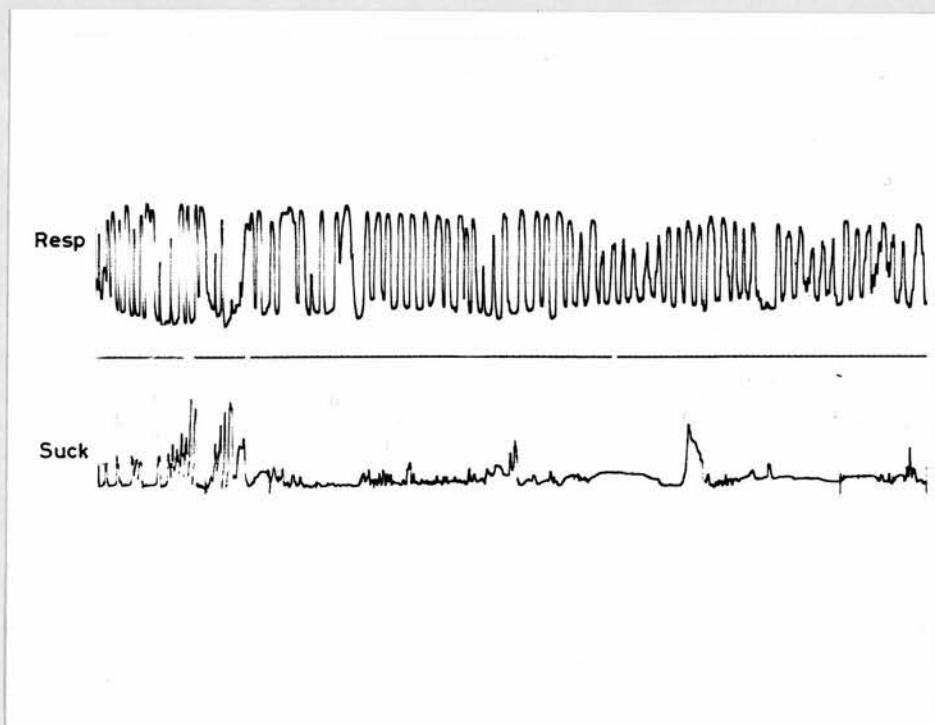


Figure 7, 5

Mouthing activity with short sucking bursts at a
frequency of 1.3 sucks/sec. - Case 32 at 24 hours of age.



Figure 7, 6

Persisting abnormal sucking activity, with short bursts
at a slow rate: (a) at 6 days 1.2/sec.
(b) at 14 days 1.5/sec
(Case 25)

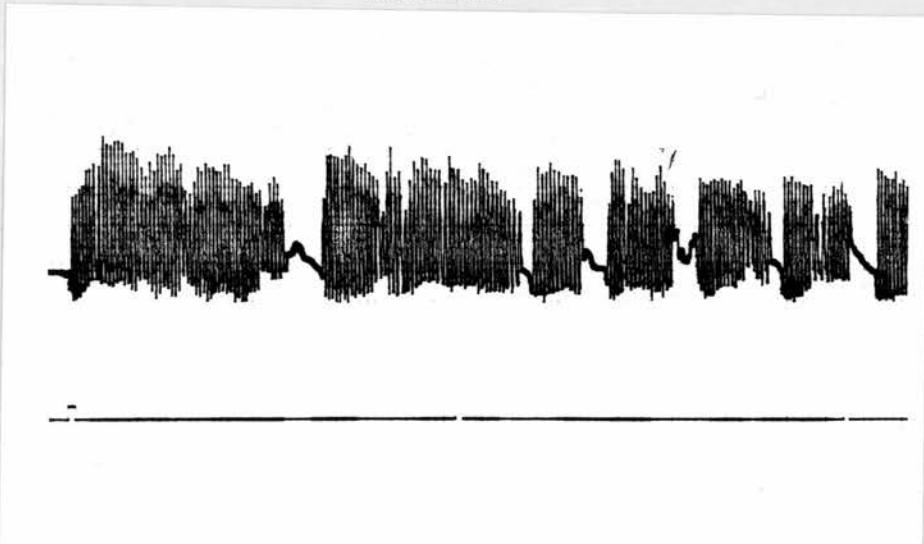


Figure 7, 7

Almost continuous sucking in an irritable
hyperalert infant, (Case 26).

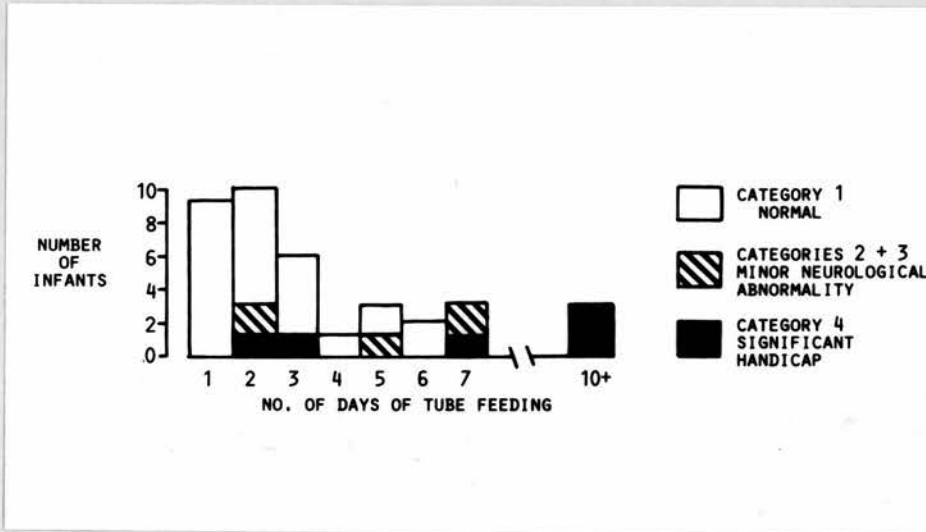


Figure 7, 8

Duration of nasogastric tube feeding and subsequent outcome category groups

Hypothermia

A fall in rectal temperature to less than 35.5°C, not including its occurrence following resuscitation at birth, was also an infrequent problem, occurring in only 5 cases. This low figure is in part due to the careful attention given to controlling the temperature environment of infants with birth asphyxia. Marked temperature lability was seen in 3 infants, Cases 25, 34, 44, all of whom showed other features of loss of homeostasis and gross neurological abnormality. In addition, all were given anticonvulsants and in 2 these were a combination of drugs including diazepam, which may have contributed to poor temperature control. Figure 7,9 shows rectal temperature recordings from Case 44 and demonstrates what amounts to poikilothermia, with failure of the normal thermal autoregulation of a mature, newborn infant.

The occurrence of hypothermia was significantly related to unfavourable outcome, $p < 0.01$, Exact probability test.

Apnoeic episodes and cyanotic episodes

Periods of apnoea were a problem in 11 infants in the study. This was in association with hypoglycaemia in Case 12 at 6 hours of age. Apart from one other instance of a single apnoeic episode, these were recurrent. Most responded to simple stimulation and oxygen, but 3 infants were artificially ventilated because of apnoea, Cases 24, 33 and 35, this last infant having failed to initiate regular respiration from the time of birth. Cases 33 and 35 died at 48 hours and 16 hours.

The third neonatal death, Case 22, who died at 25 hours, had established regular respiration at one hour following prolonged resuscitation. Recording of respiration, by measurement of impedance across /

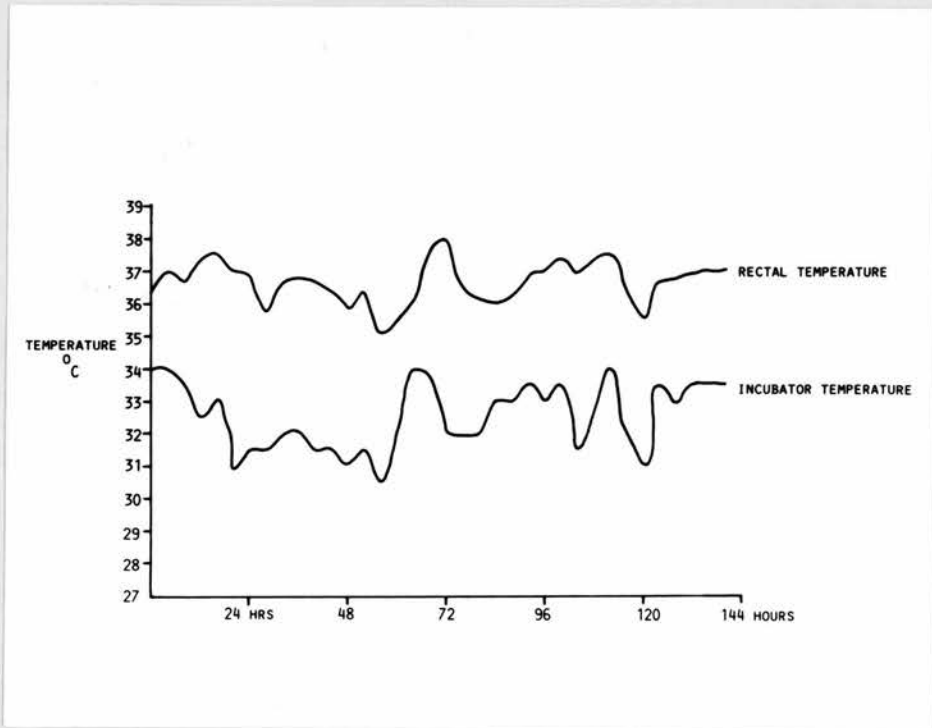


Figure 7, 9

Loss of temperature homeostasis in a severely asphyxiated infant (Case 34)

across the chest, showed an abnormal pattern (Figure 7,10), with very regular respirations punctuated by fairly regular gasps. Figure 7,11, from the same child, shows a sequence of respiratory tracings, compressed in time, each strip representing 18 minutes. Tracing (a) shows regular gasps followed by brief apnoea, similar to Figure 7,10. In (b) and (c), there are prolonged apnoeic periods usually following a gasp, the gasping continuing fairly regularly. Regular respiration has ceased and only gasping remains in the terminal tracing (d). These recordings suggest that respiration in this infant may have been driven by two brain stem oscillators, stimulating chest movement at widely different frequencies. Further, it can be implied that the slower gasping activity may have produced interference with the more frequent, regular respiration, resulting in periods of apnoea, tracings (a) and (c).

Gasping, apart from its not uncommon occurrence for a brief period immediately after birth, was noted in 7 infants in the early hours of life. The rate of gasping varied from about 5/minute to once every 1-2 minutes, Figures 7,12, and 7,13. It is clearly a most abnormal respiratory pattern and was strongly associated with a poor outcome, 2 of the infants dying and 4 surviving with significant handicap. This relationship is highly significant, $p < 0.0001$, Exact probability test. Figure 7,13, in addition to slow gasps, shows an unusual rhythmicity of respiratory excursion.

Case 24, a 35 week gestation, light for dates infant, delivered apparently uneventfully, developed frequent apnoeic episodes over the first hours of life, Figure 7,12. Mother had had pethidine 4 hours before delivery. The infant had low Apgar scores, required resuscitation and was given an opiate antagonist. A further dose of this did not affect the apnoeic episodes. These became more frequent, prolonged and resulted in hypoxaemia, Figures 7,14 and 7,15. Artificial ventilation was given for 24 hours from 16 hours of age. He also showed neurological abnormalities with extensor hypertonus and /

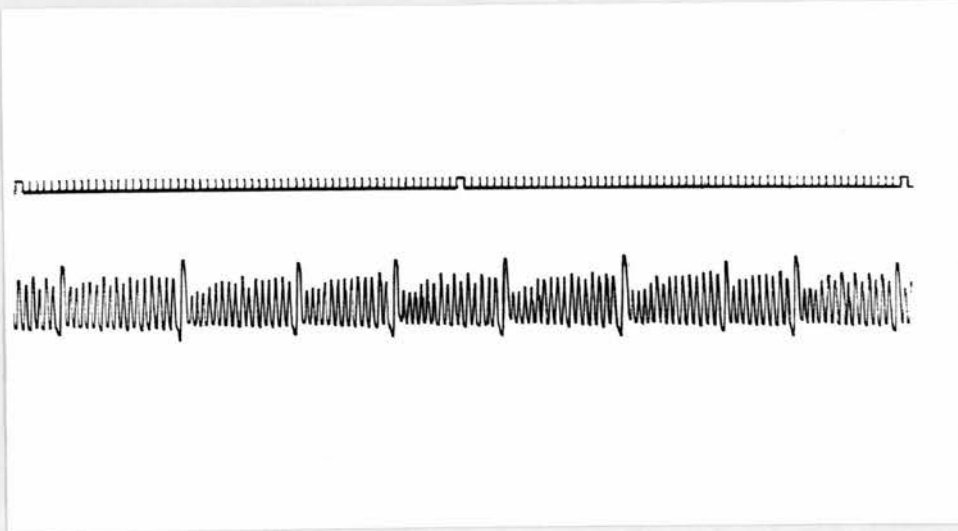


Figure 7,10

Regular respiratory rhythm with fairly regular gasps,
(Case 22); child died at 25 hours

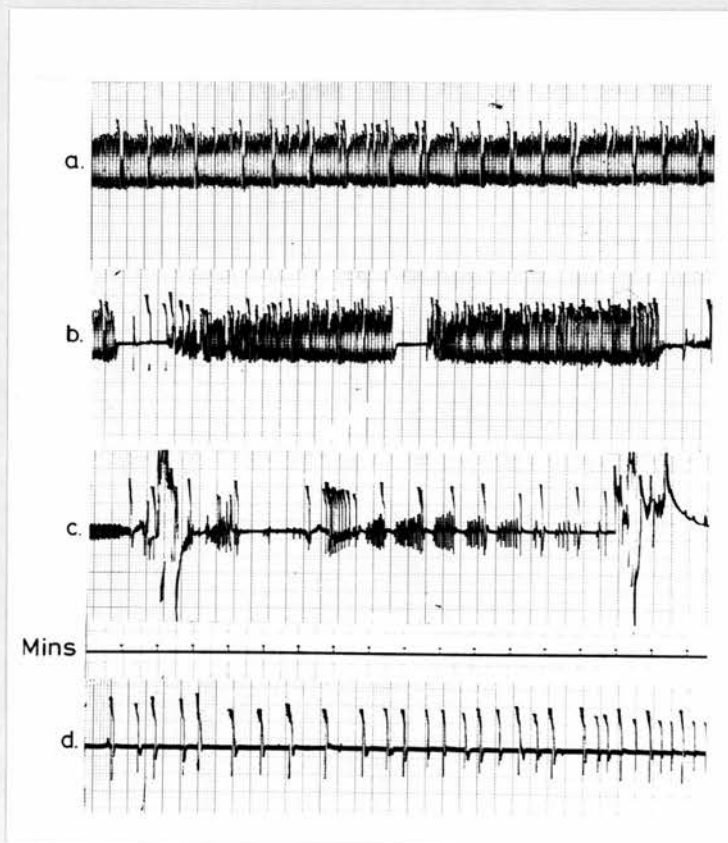


Figure 7,11

Compressed respiratory recordings also from Case 22, samples from several hours: (a) regular respiration with regular gasping, (b)+ (c) gasping with increasing periods of apnoea. (d) Terminal gasping with loss of regular respiratory rhythm.

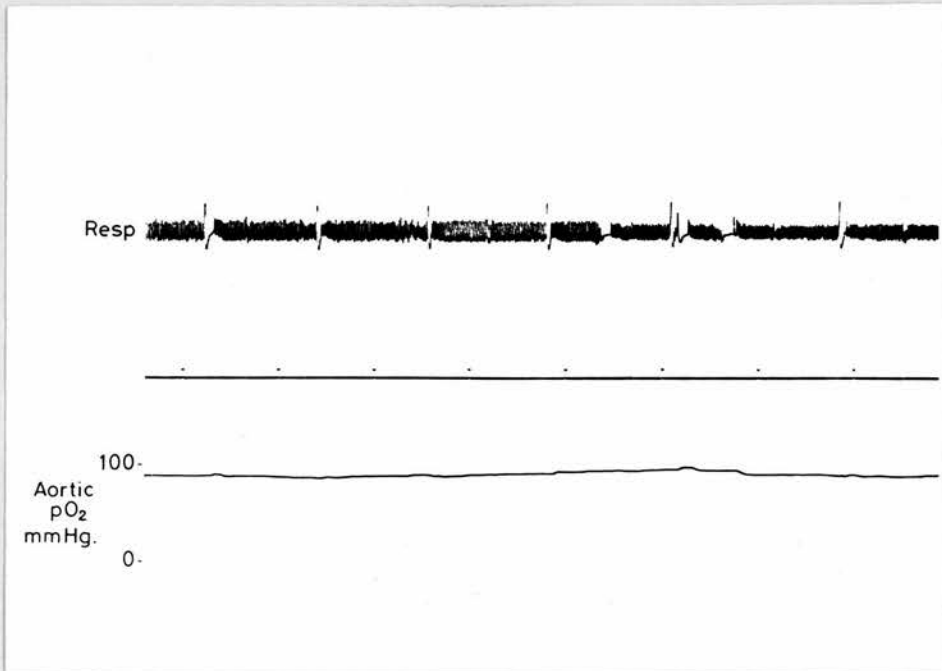


Figure 7,12

Gasping and short periods of apnoea without secondary hypoxaemia, (Case 24)

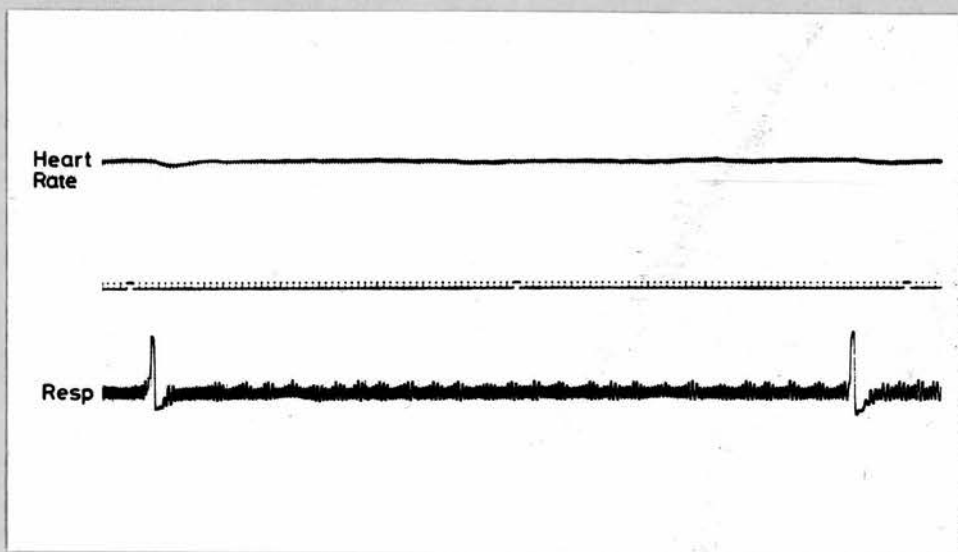


Figure 7,13
Gasping and regular variation in respiratory excursion (Case 25).

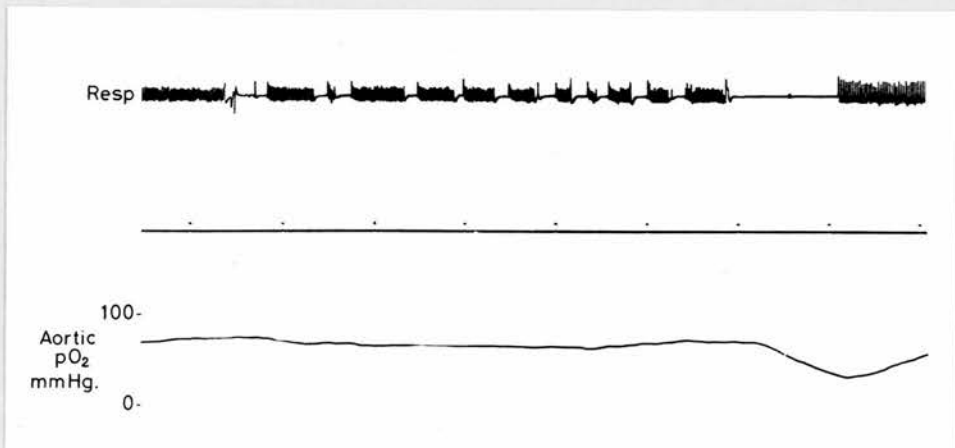


Figure 7,14

Recurrent apnoeic episodes starting and terminating with deeper gasps. Hypoxaemia secondary to more prolonged apnoea, responding to the start of assisted ventilation, (Case 24)

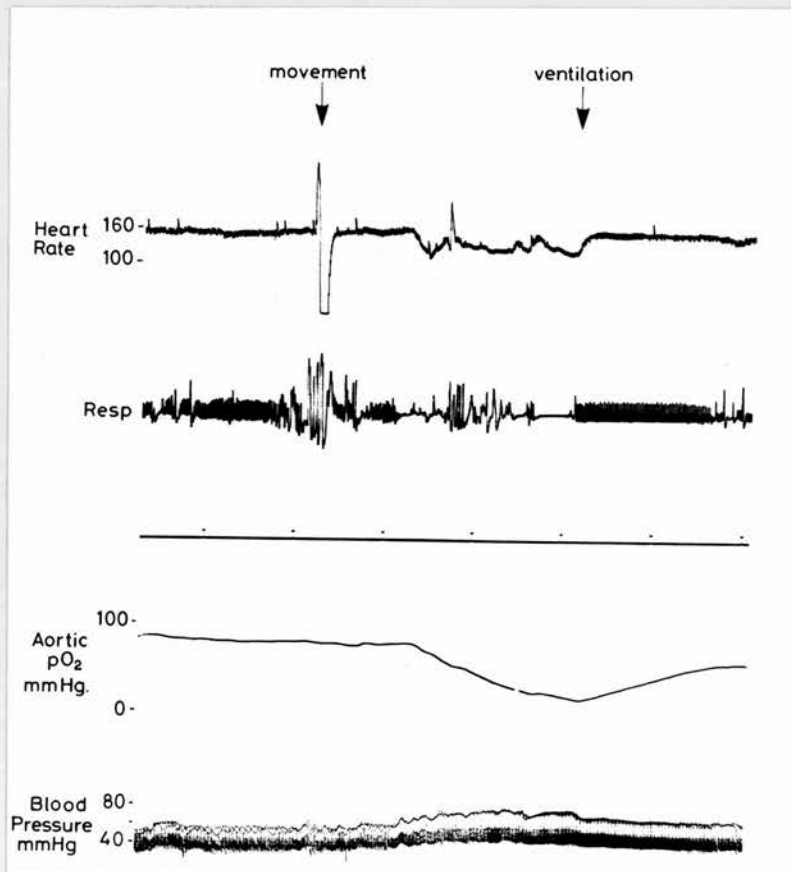


Figure 7,15

Case 24.- apnoeic episodes with secondary hypoxaemia and compensatory blood pressure elevation, when assisted ventilation stopped.

and a transient left hemiparesis. E.E.G. was abnormal (Figures 10,10 and 10,11, Chapter X). His subsequent progress has been uneventful.

Five infants, Cases 25, 28, 39, 40 and 50, had repeated apnoeic episodes solely or partly in association with fits. These were tonic in Case 25, brain stem in Case 28, generalised clonic in Case 39, and , in Cases 40 and 50, were focal clonic fits with other brain stem features such as chewing, sucking and paddling arm movements.

The occurrence of apnoeic episodes was significantly correlated with a poor outcome, $p < 0.01$, Wilcoxon's rank sum test.

Cyanotic episodes, single or repeated, were noted in 16 cases. In all of these, there was associated apnoea. In 3 cases, 1, 41 and 47, cyanosis occurred spontaneously and during feeding. One of these infants aspirated milk into the chest with subsequent radiological changes. There was no significant relationship between cyanotic episodes and outcome.

Irritability

This was a common finding, noted in 39 infants, 78%. Five of these also showed persistent vomiting, 17 demonstrated cerebral cry and 13 of the 18 infants, who had fits, were irritable at some stage. Of the 20 infants, who developed a phase of extensor hypertonus, 18 were irritable, while 12 of the 15 infants who were considered to have evidence of intrapartum, compressional head injury, with excessive moulding of the head, were also irritable. Blood staining of the cerebrospinal fluid was found in 7 infants, of whom 4 showed irritability.

The /

The degree of irritability varied, from occurring only when the infant was disturbed, to being present continuously in the hyperalert, sleepless infant, Figure 7,16. Infants in this latter situation were given sedation with triclofos.

There was no relationship between the occurrence of irritability and either favourable or unfavourable outcome; although irritability was a little commoner in infants subsequently allocated to Category 1, 82% as opposed to 69% of the remainder. The absence of irritability at any stage in the infant with severe neurological abnormality in the newborn period, however, is part of the picture of marked central nervous system depression, obtundation, inactivity and profound hypotonicity.

Cerebral cry

An abnormally high pitched, shrieking cry was shown by 18 infants. This carried no prognostic significance. It is common in the child with compressional head injury, 6 of 15 cases, and in the phase of hyperexcitability and extensor hypertonus following an asphyxial insult, 8 of 20 cases. Of the 7 infants found to have blood in the cerebrospinal fluid, 3 had a cerebral cry and, as stated above, cerebral cry and irritability occurred together in 17 infants.

Apathy

Apathy, usually as a transient phase in association with hypotonicity, absent or much reduced response to stimulation, inactivity, depression of feeding and other reflexes such as the walk reflex and Moro response, was a feature of the early neonatal course of 26 infants, 52% of the study group. Seventeen of these infants also demonstrated the converse state, usually following the period of apathy, with irritability, hyperexcitability, sleeplessness and active primitive reflexes.

A /

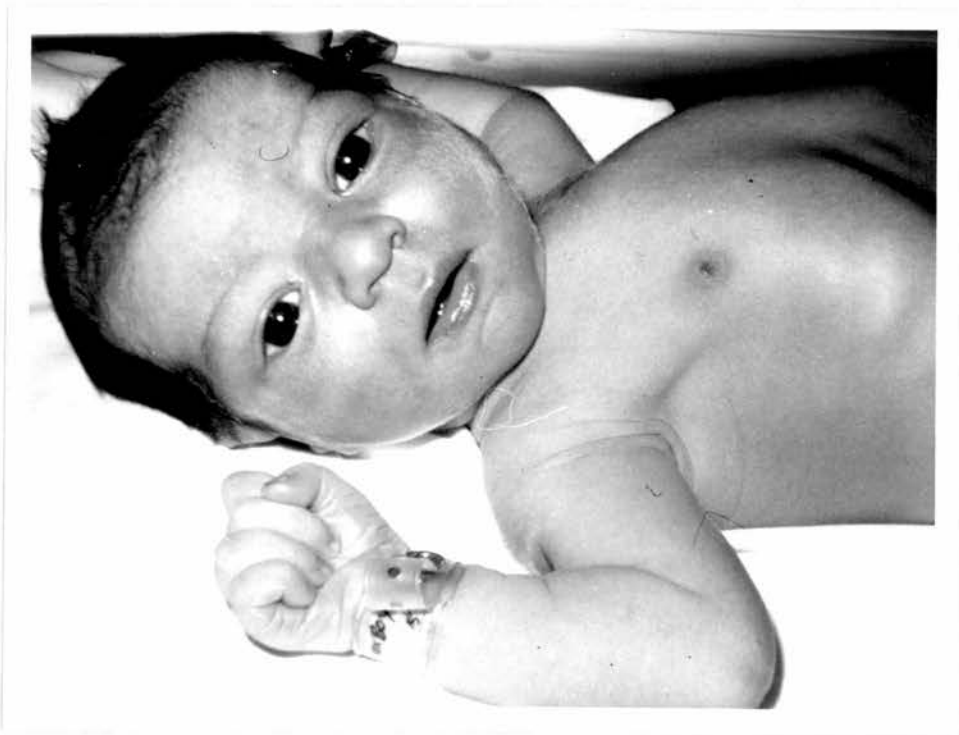


Figure 7, 16

Wide eyed, hyperalert, sleepless infant.

A second phase of apathy and hypotonia followed in 5 of these 17 infants. This will be discussed more fully later in the consideration of patterns of muscle tone (Chapter VIII).

The level of responsiveness varied, 13 infants being rousable but with a much diminished response to stimulation and 13 infants being apparently unconscious with no spontaneous movement and no response to stimulation. Feeding depression was a universal feature of these 26 infants; 10 also had apnoeic episodes, while 12 manifested fits.

Drugs may have played some part in their reduced responsiveness. Opiate analgesics had been given to 9 of their mothers in the 4 hours before birth, but each infant had been given an opiate antagonist at birth. All of the 12 infants of this group, who fitted, were given anticonvulsant drugs, including phenobarbitone, 10 infants, and intermittent diazepam, 5 infants, and, while this is clearly an important factor, as indeed are the fits themselves, 11 of these infants were noted to be apathetic prior to the onset of fits and the introduction of anticonvulsant therapy.

It is difficult to make a meaningful assessment of conscious level in the newborn infant, but, as previously described, a grading of state of arousal is a clinically practical and important part of the general and neurological appraisal of the infant. Apathy is a clearly recognisable and important disturbance of the normal, neonatal state of arousal and, in this study, its occurrence correlates with a complicated outcome to a highly significant degree, $p < 0.001$, Wilcoxon's rank sum test. No child who died or is significantly handicapped failed to show an apathetic phase, while apathy was also a feature of 6 of the 7 children who have subsequently shown less marked neurological abnormality, outcome categories 2 and 3.

The degree of depression of responsiveness is also significant; those /

those infants who appeared unconscious, 7 of the 9 who died, or are significantly handicapped, and 4 of the 7 children of outcome categories 2 and 3, being at greater risk of subsequent abnormality than those who were apathetic but rousable, $p < 0.001$, Wilcoxon's rank sum test.

Exhibition of both apathetic and irritable phases did not carry different prognostic significance from apathy alone. However, when those 22 infants, who demonstrated irritability, but not apathy, are considered, this statistically is a feature associated with favourable outcome, $p < 0.0005$, when this group is compared to the remainder of the study group, and $p < 0.001$, when comparison is made with those 17 infants showing both irritability and apathy, Exact probability test.

Fits

Fits of various clinical types occurred in about one third of the group, 18 cases. These were tonic in 6 infants, clonic in 7, while both tonic and clonic convulsions were demonstrated by 4 infants. A single infant was recognised as having brain stem seizures alone, consisting of deviation of the eyes, spontaneous sucking bursts and facial twitchings; however, similar brain stem features were common accompaniments of both tonic and clonic convulsions.

The age of onset of fits was largely restricted to the first 48 hours of life, 16 of the 18 infants, 89%, having fitted by that time. Indeed, the majority, 66%, had their first fit within 12 hours of birth, Figure 7,17. Three infants fitted within the first hour of life; one of these, most unusually, only minutes after birth.

The occurrence of fits, per se, was not strongly related to a poor outcome, reaching significance at a $p < 0.05$ level, $\chi^2 = 5.58$, Table 7,1.

Tonic /

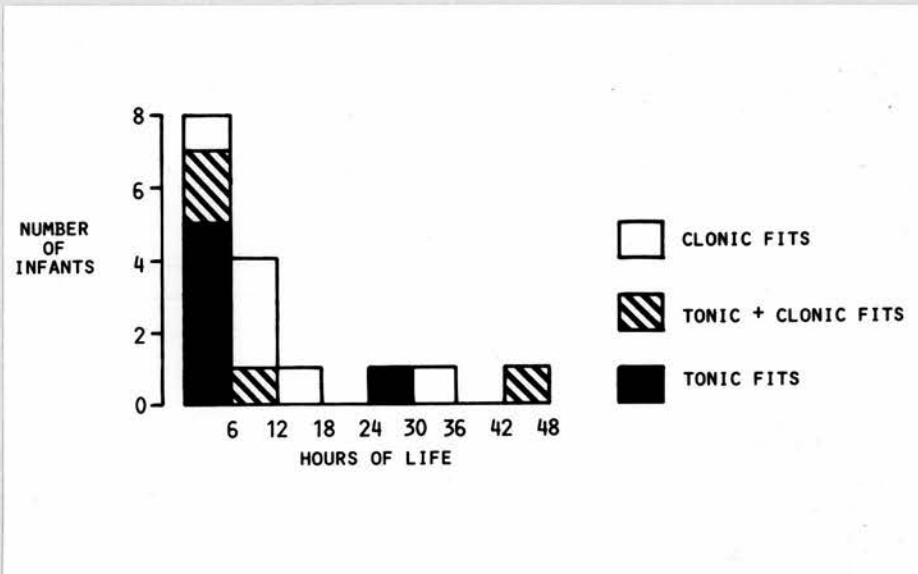


Figure 7,17

Age of onset of fits and type of seizure

Tonic fits, Figure 7,18, with tonic extensor posturing into decerebrate, Moro, asymmetrical tonic neck reflex or adersive positions, usually with accompanying apnoea, were associated with poor outcome in half of the cases, 5 of the 10 infants dying in the neonatal period, or surviving with significant handicap, Figure 7,19. In contrast, no child with clonic fits alone died or is significantly handicapped. This difference is significant, $p < 0.05$. When those infants with tonic fits are compared to the 40 infants without such fits, the relationship of tonic fits to neonatal death or significant handicap is highly significant, $p < 0.01$, Exact probability test.

There is a tendency for tonic fits to have an early onset, Figure 7.17; of the 10 infants who showed such fits, 7 had begun in the first 12 hours of life. As a result, there is some relationship between an early onset of fits and poor outcome, $p < 0.05$, Kendall rank correlation.

Clonic fits were generalised (Cases 11, 36, 39, 44), focal (Cases 5, 13, 29, 40, 50), or multifocal (Cases 34, 37), although these clinical patterns did not always agree with electroencephalogram findings (see below). Signs of a hemisyndrome were present in 3 of these infants (Cases 13, 34, 50), but none has demonstrated asymmetry subsequently. Case 40, who had frequent left, focal, clonic fits over the first 60 hours of life, has developed a mild left hemiparesis of no functional significance; electroencephalogram and echoencephalogram were normal in the neonatal period.

The number of fits observed varied widely, Figure 7,10, from a single episode in 3 infants to numerous fits in 7. There was some tendency for tonic fits to be more frequent and more resistant to suppression by anticonvulsant therapy. With increasing number of fits, there is an increased risk of unfavourable outcome, Figure 7,21; when more than 10 fits, this is significant, $p < 0.05$, Exact probability test.

These /

(a)



Figure 7, 18

(b)



(c)



(d)



Figure 7,18

Postures adopted in tonic seizures
(a) decerebrate, (b) Moro, (c) asymmetrical
tonic neck reflex, (d) adersive.

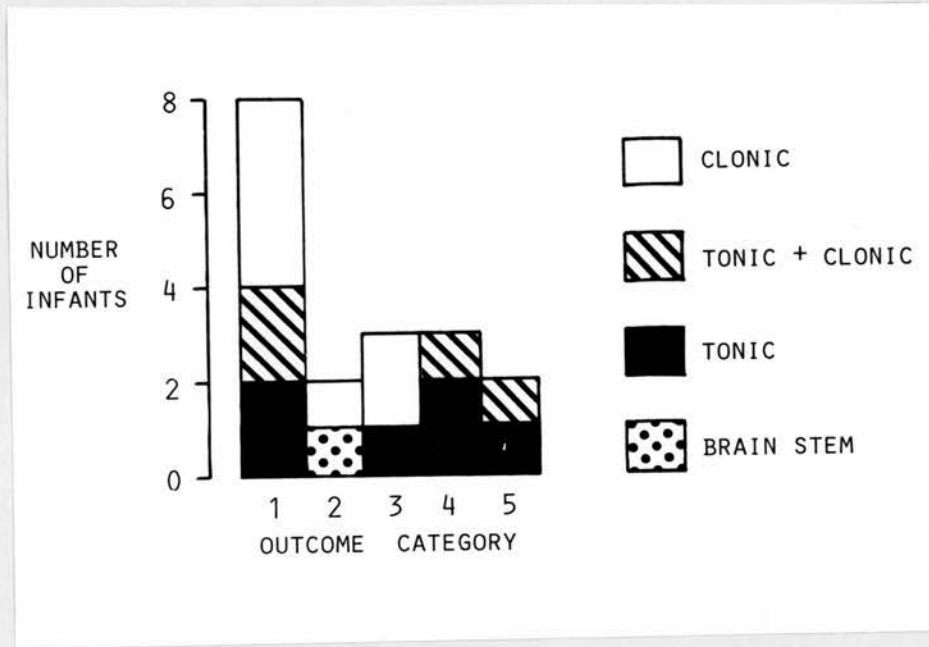


Figure 7,19
Type of fit, and outcome category

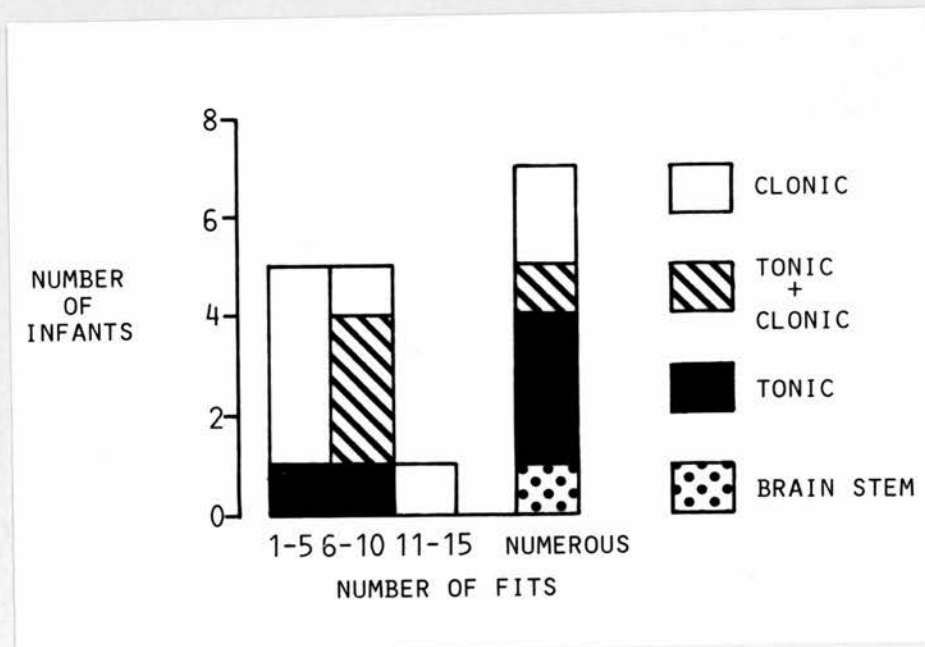


Figure 7,20
Number of fits by clinical type.

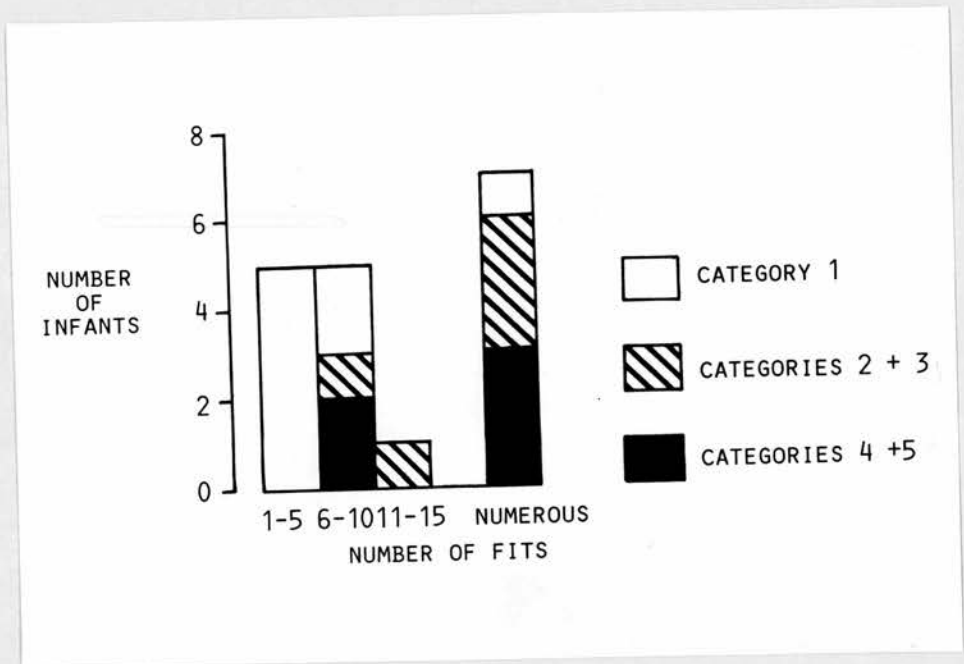


Figure 7, 21

The relationship between number of neonatal fits and outcome.

These associations do not necessarily indicate that neurological damage resulted from a particular type of fit or frequent fits, although this is, of course, an important risk. It may be that the infant who has suffered a severe anoxic-ischaemic insult is more prone to fits that are tonic, frequent and refractory to treatment, but this does not reduce the importance of appropriate, well regulated, anticonvulsant therapy and of attention to the many aspects of homeostasis which are readily disturbed and may compromise the infant's condition further.

Figure 7,22 illustrates the profound changes that can occur during a tonic fit, with marked elevation of blood pressure, impairment of lung expansion, despite artificial ventilation, and hypoxaemia.

Disturbances of biochemical homeostasis are common and important, (Chapter IX), and may increase the likelihood of fits occurring. Eight infants were found to be hypocalcaemic, plasma calcium less than 1.85 mmol/l, at the time of a convulsion and this was corrected by infusion of calcium gluconate. All the infants had repeated blood glucose estimations, and only 1 was found to be hypoglycaemic in association with a fit.

Electroencephalographic findings in those who had fits

Each of the 18 infants who fitted had at least one E.E.G recording. These showed a wide variety of features, ranging from normal E.E.G. patterns (Figure 7,23) to gross generalised disturbance, (Figure 7,24).

Between these extremes, focal or multifocal, rhythmical, electroconvulsive discharges were common temporary findings. These were not necessarily accompanied by clinical manifestations of a fit during the recording. Multiple foci or a focus that appeared to move during the course of a recording were seen., (Figure 7, 25a, b, c).

Rates /

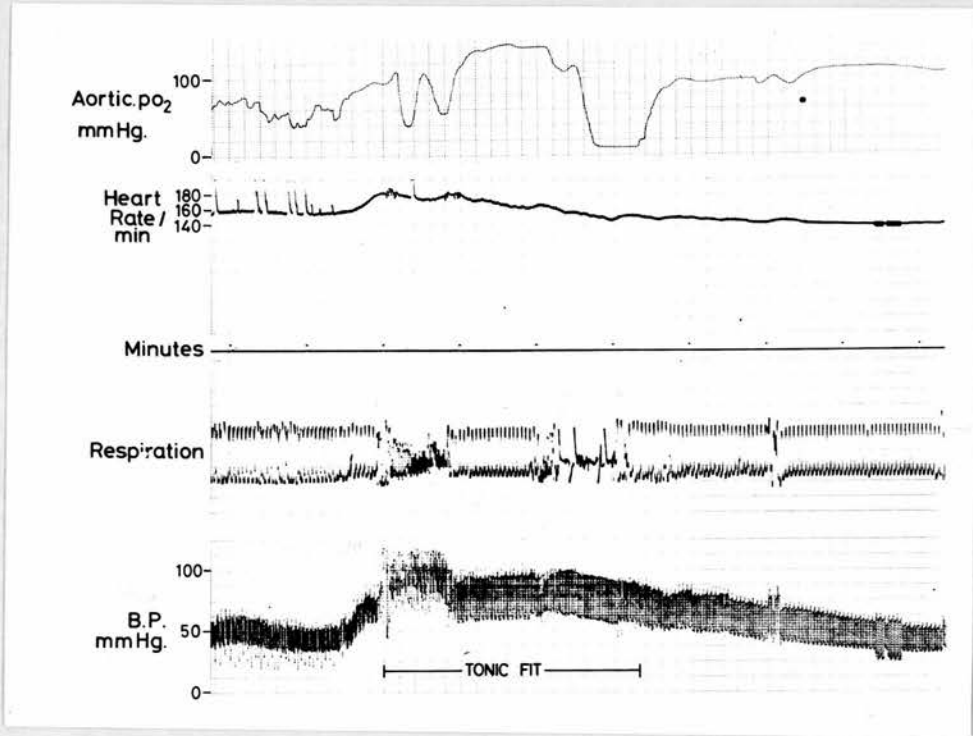
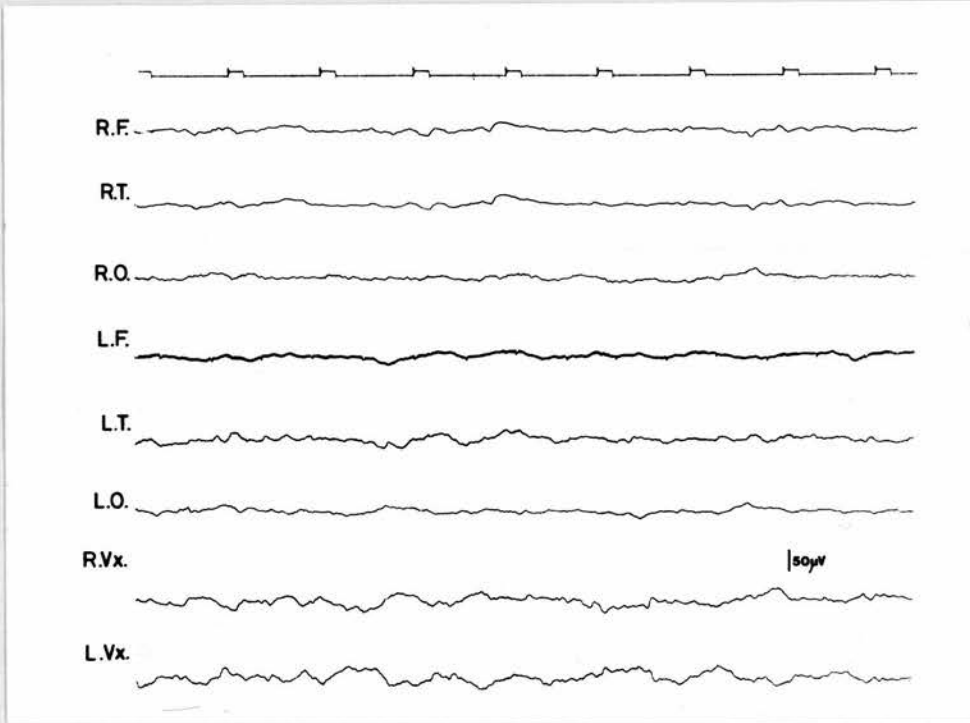


Figure 7, 22

Changes in arterial po₂, heart rate, chest excursion and arterial blood pressure during a tonic fit. Assisted ventilation throughout record. (Case 33)

(a)



(b)

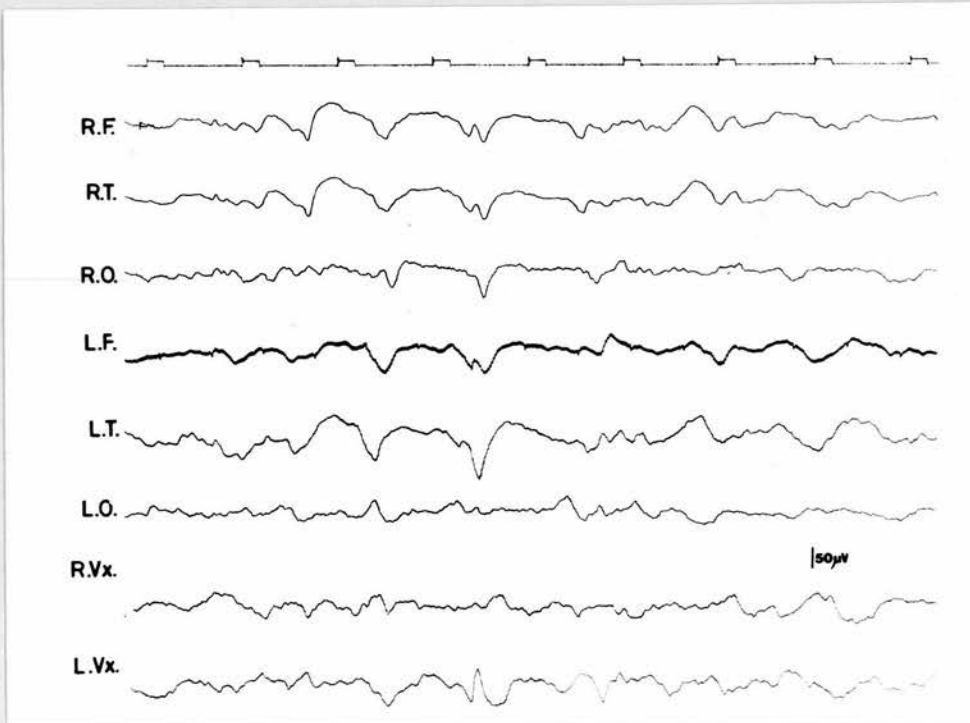


Figure 7, 23

E.E.G. recording from Case 13, at 2 days of age. Infant had tonic seizure, but was subsequently normal. (a) normal in wakefulness; (b) drowsy, increased slow activity, normal.

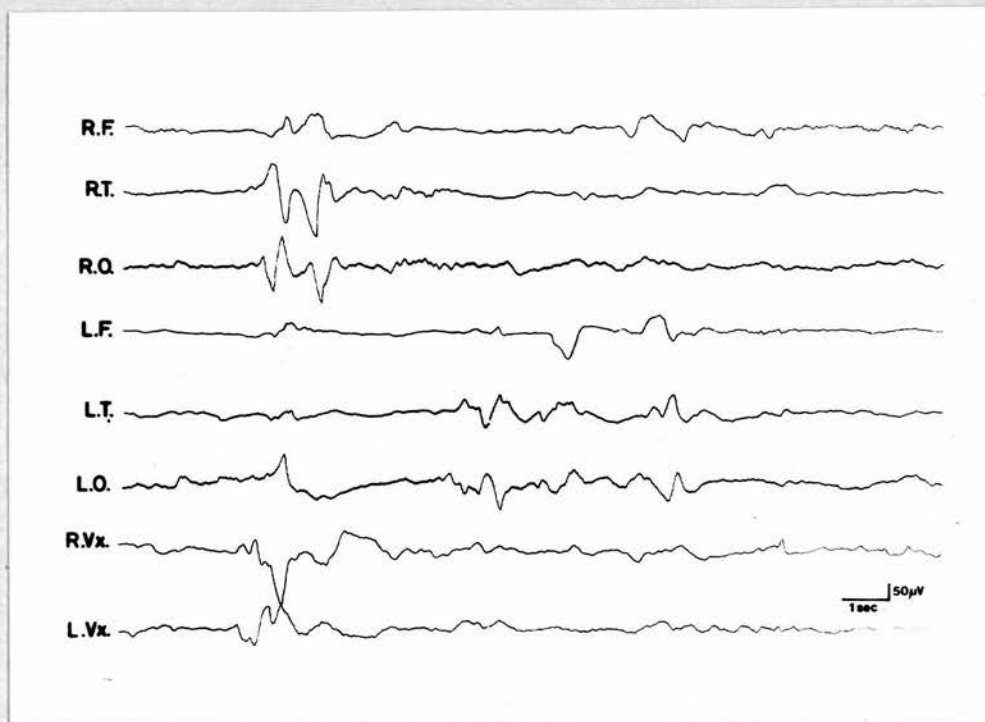


Figure 7, 24

Case 44. Tonic and clonic seizures. Subsequently severely handicapped. E.E.G. - grossly abnormal with slow epileptic discharges, lack of symmetry, and low voltage background.

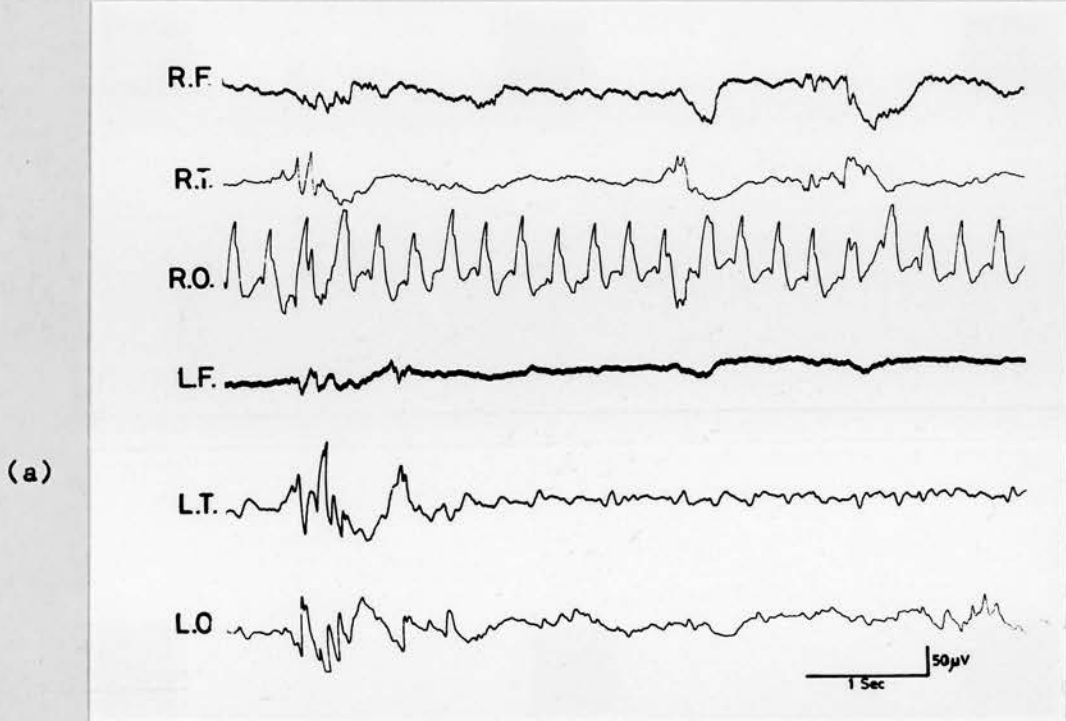
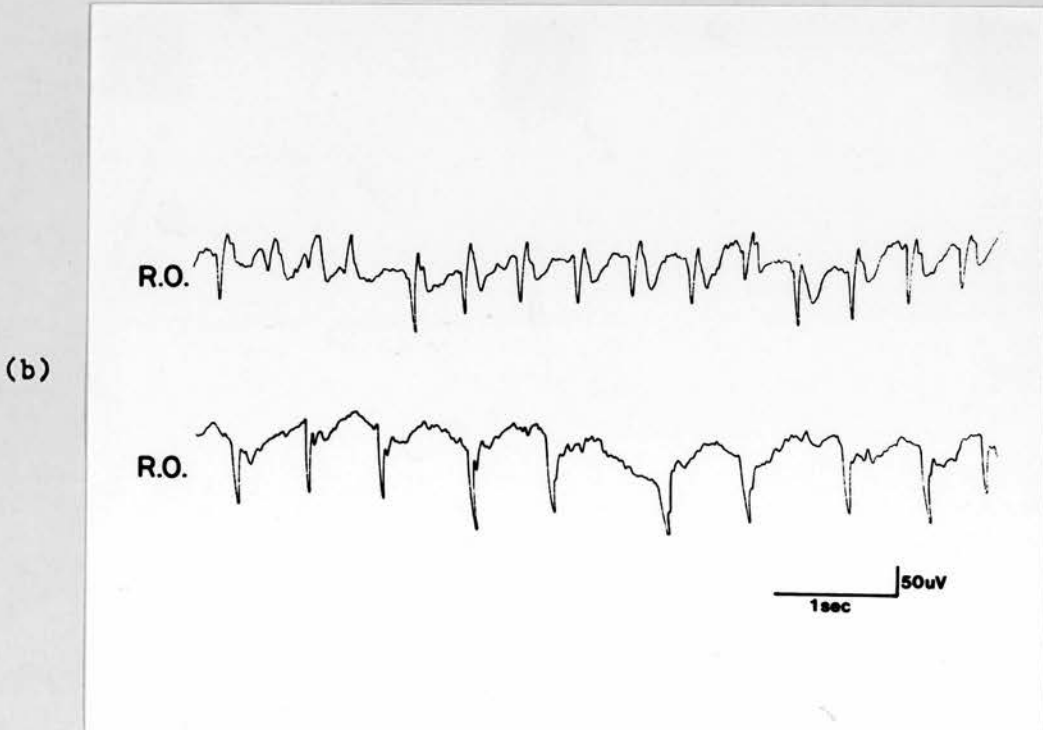


Figure 7,25



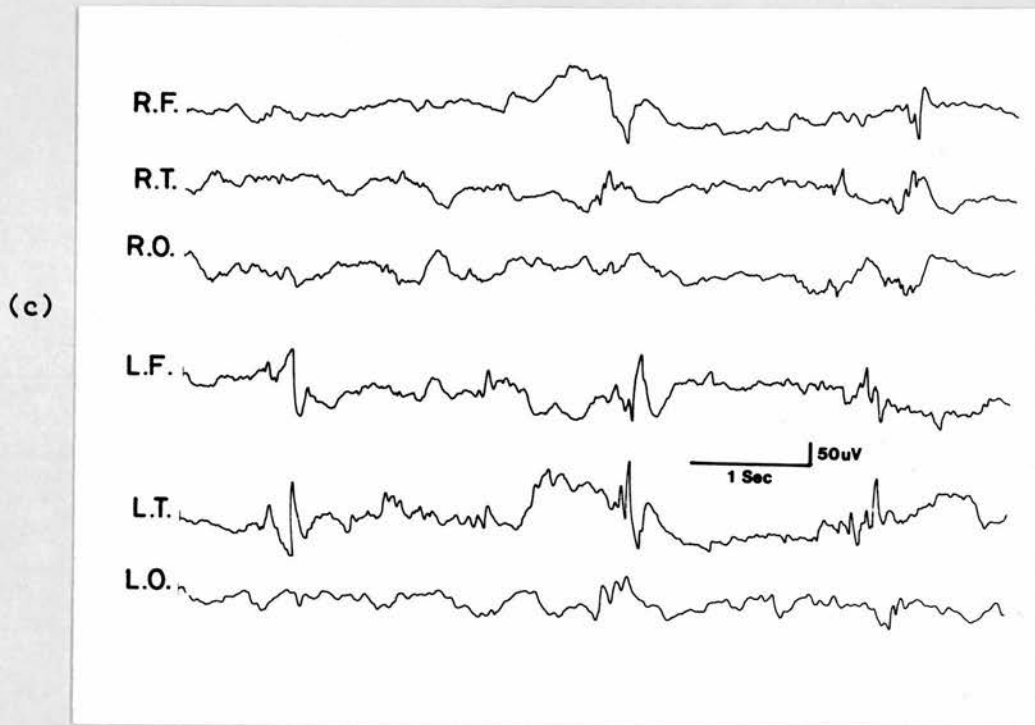


Figure 7,25

- Case 50. - Numerous, mainly right sided fits, developed a right hemisyndrome.
- (a) left posterior focus with propagation to right posterior, discharging at 4/second.
 - (b) right posterior discharge at 3/sec, changing to 1/sec.
 - (c) shift of focus to left temporal area.

Rates of discharge of epileptic foci varied from infant to infant and in the individual infant with time. Rhythmical discharges varied from 4/sec. to once every 2 seconds (Figures 7,25; 7.26; 7.27). The appearance of the spike discharge depended partly on electrode placement relative to the focus (Figure 7,26).

Repetitive, single spike discharges were found less frequently and occurred with or without the propagation of a more rapid, rhythmical charge. No child was recorded during a tonic convulsion.

Within single recording periods, usually 1-2 hours, marked variability of E.E.G. appearance was seen in some children, (Figures 7,25; 7,28). Figure 7,28 illustrates a sequence from one infant who had brain stem fits, (Case 28). They show unusual episodic sleep activity for a term baby with delta waves, a right-sided electroconvulsive focus, a period of disorganised, slow wave activity and, finally, the effect of drugs in changing the E.E.G. tracing and complicating interpretation.

Fits in the total maternity hospital population.- To put the problem of convulsions from intrapartum asphyxia in perspective, over the 23 months of the initial part of the study, 55 infants born in the maternity hospital had at least one fit, an incidence of 6.9/1000 liveborn. Seventeen of these infants belong to the study group. Twenty-six infants were found to have primary, uncomplicated, hypocalcaemic/hypomagnesaemic convulsions, while the remaining 12 resulted from a miscellany of developmental, antenatal, neonatal or undefined causes. Details of these infants are given in Table 7, 2.

Table 7, 2

Causes of neonatal convulsions in 55 infants
over a 23 month period.

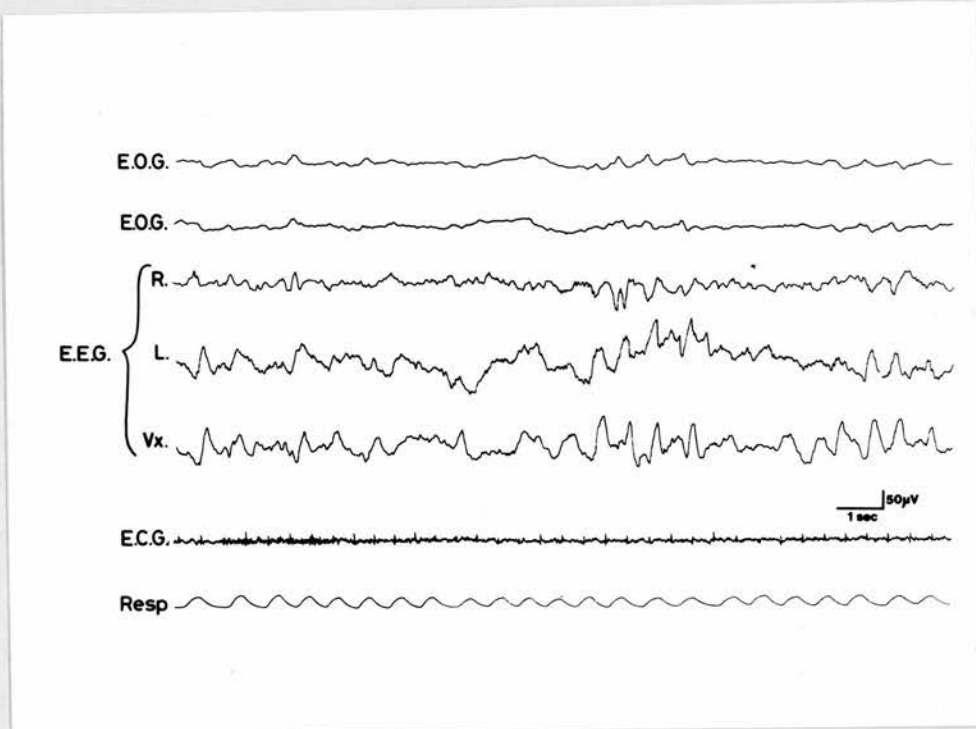


Figure 7,26

Case 29 - Single right sided clonic fit. E.E.G. - run of slow, 1/sec. discharge, electrode placement not over focus.

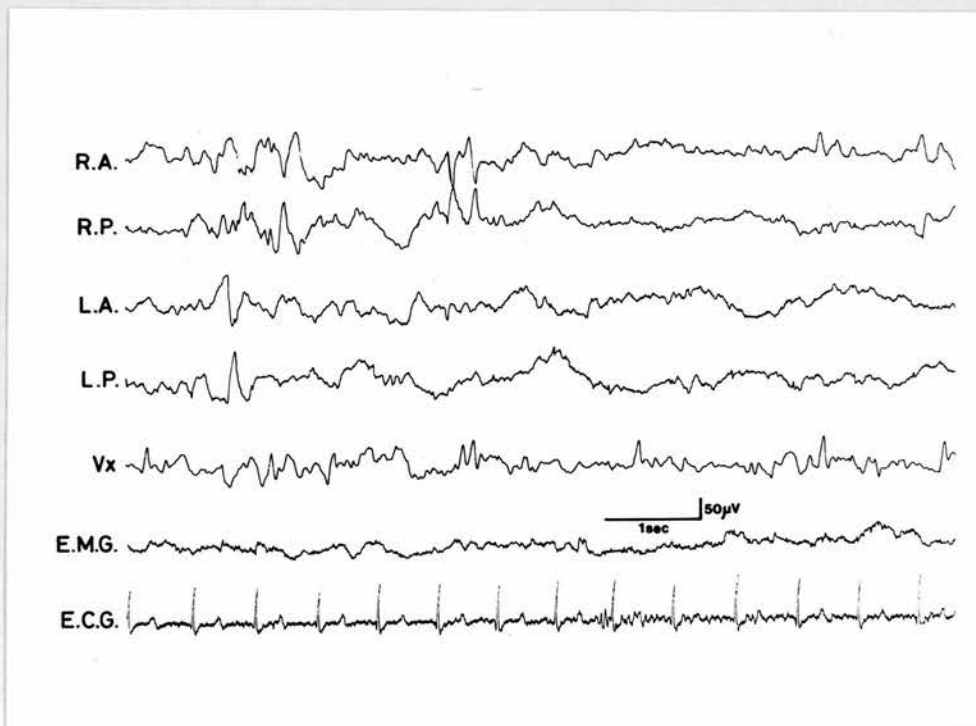
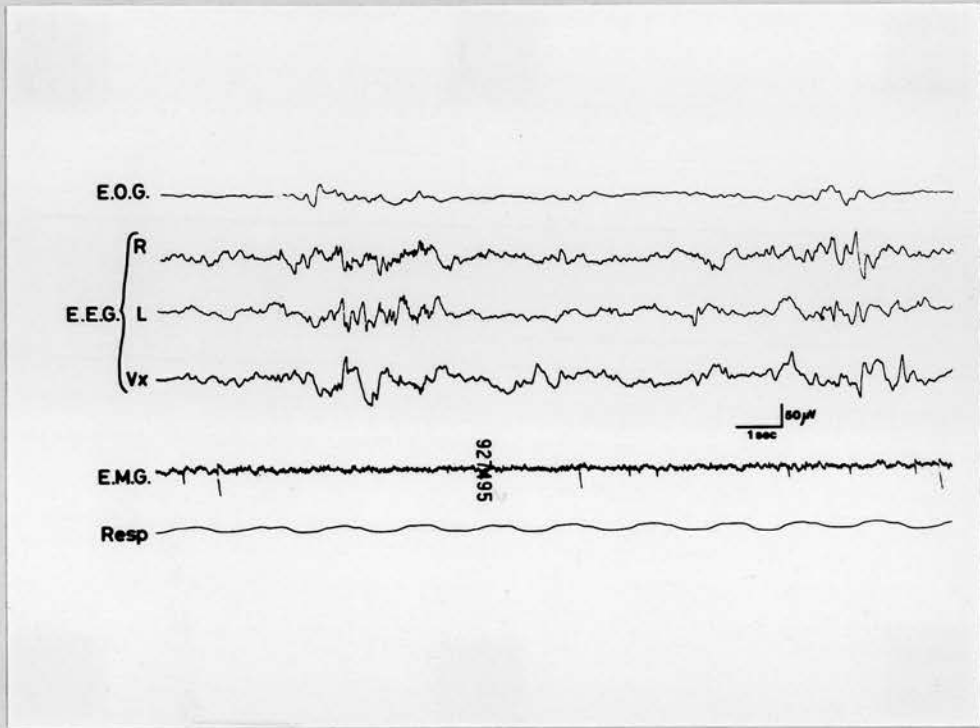


Figure 7,27

Case 37 - numerous multifocal, clonic seizures. E.E.G. - during right sided fit, focus near vertex, 2 second discharges.

(a)



(b)

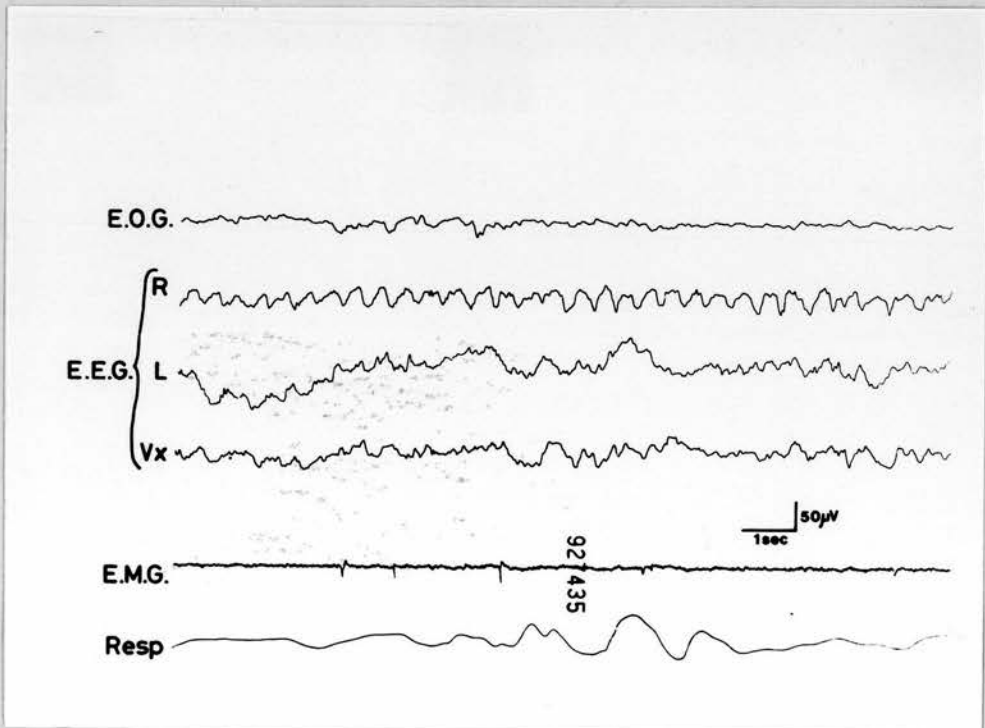


Figure 7, 28 /

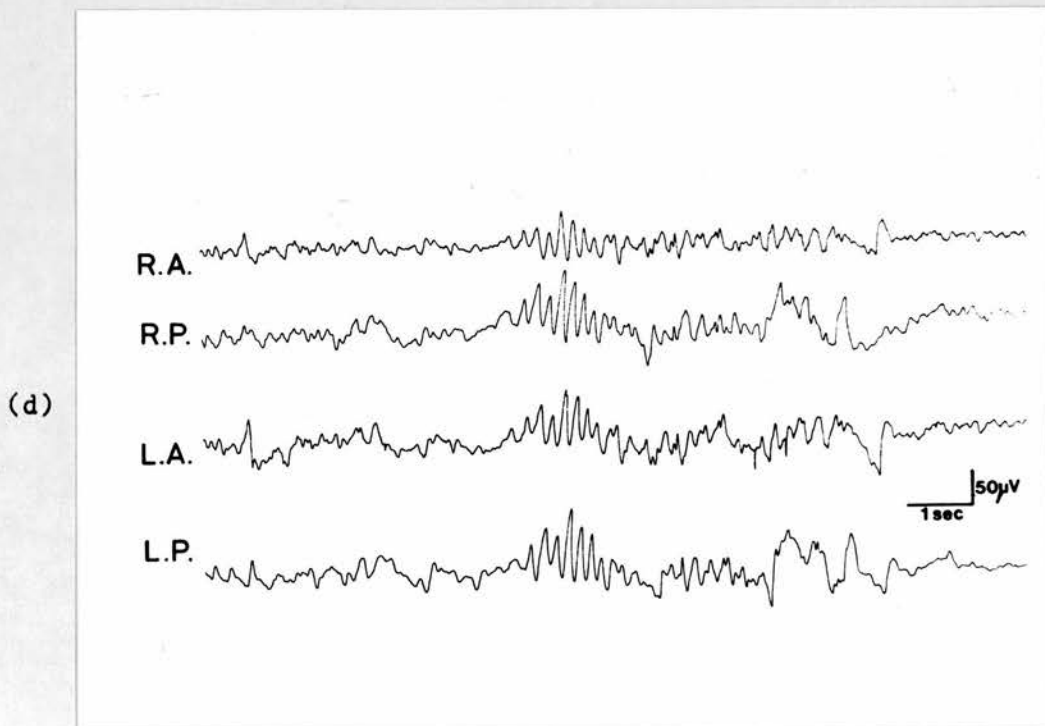
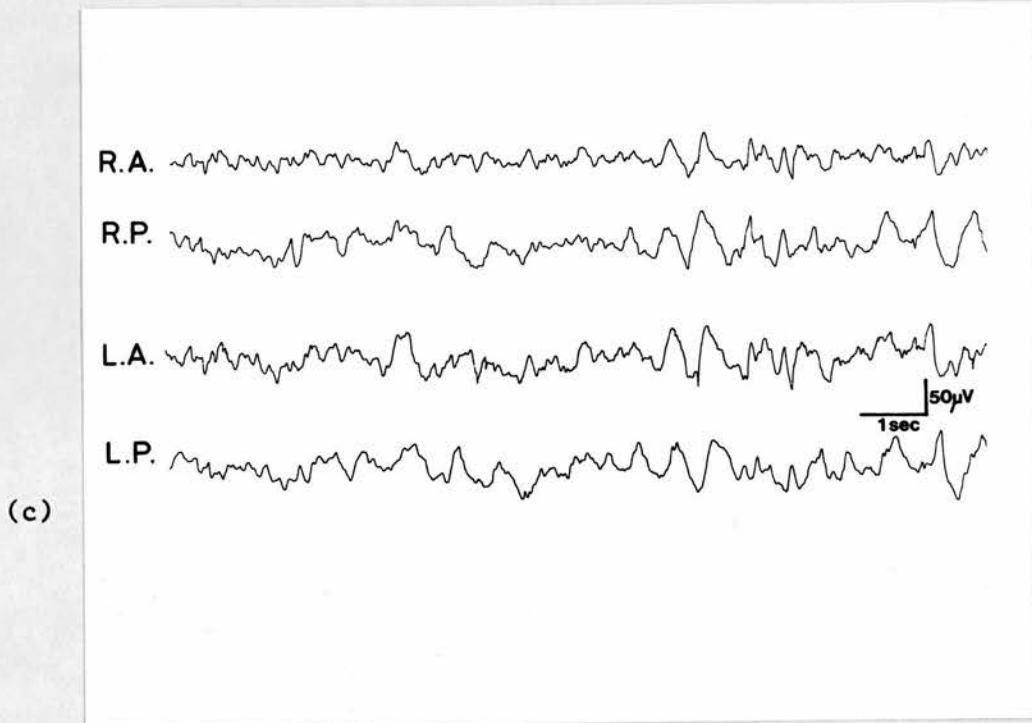


Figure 7,28

Case 28, 41 weeks gestation - brain stem fits: sucking bursts, eye deviation, facial twitching, and left hemisyndrome. Samples from 2 hr. E.E.G. - (a) episodic sleep activity with delta activity, "premature ripples", (b) right sided focus discharging at 2/sec., (c) disorganised, fast and slow activity, (d) increased fast activity with bursts of 5/sec. spike activity, following intravenous diazepam.

Table 7, 2

17 infants	intrapartum asphyxia.
26 infants	primary uncomplicated hypocalcaemia/hypomagnesaemia.
12 infants	miscellaneous causes:
	1 - Leigh's encephalopathy.
	1 - intracranial haemorrhage.
	1 - multiple congenital abnormalities including choanal atresia.
	1 - neurolipidosis, type unclassified.
	1 - Coxsackie myocarditis.
	1 - maternal opiate withdrawal.
	1 - encephalocoele and meningitis.
	1 - extreme prematurity, intraventricular haemorrhage.
	2 - neonatal asphyxia, prematurity, persistent fetal circulation.
	2 - "idiopathic".

Causes of neonatal convulsions in 55 infants
over a 23 month period.

The age of onset of fits in these three groups is shown in Figure 7,29, and follows the expected pattern, the intrapartum asphyxia group having fits starting mainly in the first two days of life, the hypocalcaemic/hypomagnesaemic group when several days old, while age of onset of fits in the miscellaneous group was scattered, (Brown, 1972).

At the time of this study, approximately half of the infants were breast fed while in hospital. The artificially fed infants were given a relatively unmodified milk with a high phosphate content. All of the infants with primary hypocalcaemic/hypomagnesaemic fits were mature and bottle fed, all had clonic fits, usually multifocal, and the majority, 73%, were born in the four Spring months, March - June. None of these infants are known to have subsequent problems, but they have not been the subject of prolonged follow up, although many were seen again at the age of one year. With the introduction of modified, low solute, milk feeds and an increase in breast feeding, hypocalcaemia and hypomagnesaemia without complicating factors have almost disappeared as a primary cause of neonatal fits. If this group is excluded from the figures from 1976 and 1977, the incidence of convulsions from intrapartum asphyxia and miscellaneous causes was 3.7/1,000 liveborn for this maternity hospital population.

The outcome for the miscellaneous group was dependent, of course, on the underlying problem. Four died in the neonatal period or later infancy, and 3 have survived with significant problems. The outcome for this mixed group is similar to, but rather poorer than, the intrapartum asphyxia group, where 3 of the 17 infants died and 2 have survived with significant handicap. The difference does not reach statistical significance, $p = 0.09$, Exact probability test. The miscellaneous group mainly showed focal or multifocal clonic convulsions and in half of the group fits were numerous and difficult to control.

Summary /

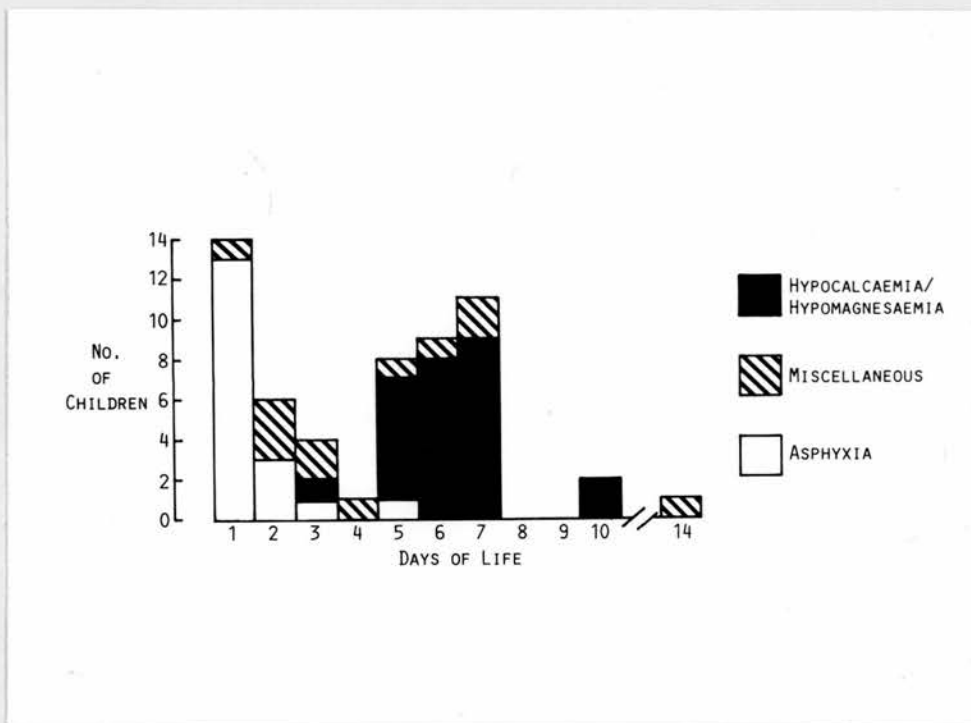


Figure 7,29

Fits in the total hospital population over 2 years.
Age of onset by cause of fits.

Summary

Of the 9 abnormalities of performance and behaviour selected, all but hypothermia and persistent vomiting, were found quite commonly in the study group. The number of abnormalities demonstrated by the infants correlated with the risk of an unfavourable outcome.

Of the individual abnormalities, the following were most strongly associated with the risk of a complicated outcome:

hypothermia	$p < 0.01$
apnoeic episodes	$p < 0.01$
apathy	$p < 0.001$
tonic fits	$p < 0.01$

The occurrence of prolonged gasping respirations, the degree of depression of responsiveness and the duration of feeding depression also bore a highly significant relationship with outcome, while irritability without apathy at any stage was a favourable prognostic feature.

Patterns of sucking activity and respiratory waveform seen on physiological recordings of some of the infants, and electroencephalographic findings in those infants who had fits are illustrated and described.

CHAPTER VIII

NEUROLOGICAL ABNORMALITIES

Patterns of muscle tone

In the early neonatal period, several patterns of changing muscle tone were recognised in the study group. These are represented in Figure 8,1. All but 3 infants showed a clear deviation from the flexor tone expected for their gestational age. By far the commonest initial disturbance of tone was hypotonia, 76%, usually as a transient phase, followed by a change to extensor hypertonus or to flexor tone. In a small number, hypotonia was persistent, i.e. lasting more than 7 days, while in other infants a later phase of hypotonia, which will be referred to as "late hypotonia", followed an extensor phase. Extensor hypertonus was present in a small number of infants as the first pattern demonstrated in the early hours of life. Seven infants were flexed at this stage. This flexor tone was maintained in 3, the remainder developing a phase of extensor hypertonus before regaining flexion.

Hypotonia

Hypotonia of varying degrees was a common finding. Two main patterns of differing severity were recognised. In the first, there was a mild or moderate reduction in tone, producing a picture of regression of tone and posture resembling that of a less mature infant, the reduction in flexor and adductor tone being more marked in the arms than legs, (Figures 8,2, and 8.3.). Secondly, a more severe loss of tone resulted in generalised hypotonicity, (Figure 8,4).

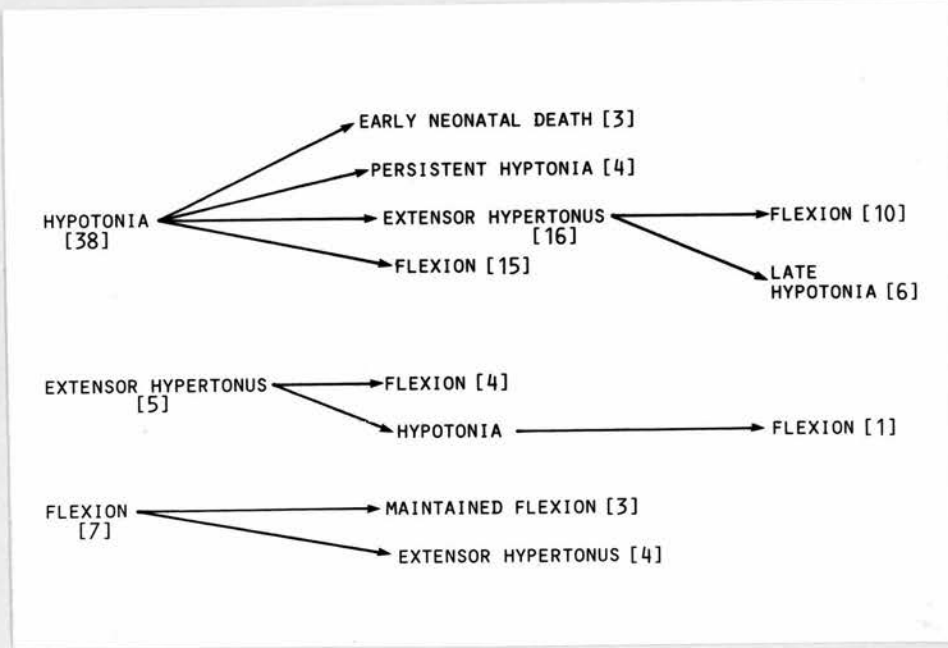


Figure 8, 1

Patterns of muscle tone in the early neonatal period -numbers in brackets represent the number of infants showing each phase.



Figure 8, 2

Regression of postural tone, loss of flexion and adduction in arms, and adduction in the legs. Term infant, also has a facial weakness (Case 26).



Figure 8, 3

Regression of postural tone, loss of adduction in arms and legs, 41 weeks gestation, (Case 28).



Figure 8,4

Severe generalised hypotonia, (Case 34).

A reduction in muscle tone was invariably associated with a reduced state of alertness, varying from the hypoalert, sleepy, but rousable infant to the infant who was completely apathetic, unconscious and unrousable. There was noted to be a direct relationship between the degree of hypotonicity and reduction of alertness.

By and large, the infants with more profound hypotonicity and apathy either changed rapidly to a phase of marked extensor hypertonus and irritability, or remained hypotonic for a prolonged period. The infants with lesser degrees of hypotonicity, with a pattern of regression of tone, tended to recover flexor and adductor tone gradually over the first days of life. These patterns will be discussed fully later.

In addition to hypotonia, the infants showed depression of other aspects of central nervous system function, again generally varying in severity in parallel with the degree of hypotonia. With mild hypotonia, absence of feeding reflexes might be the only other feature, while the profoundly hypotonic infant might show complete absence of bulbar reflexes, ophthalmoplegia, and absence of the Moro, walk, and grasp reflexes.

Three-quarters of the study group showed an initial hypotonia, lasting from 1 hour to 5 days with a mean duration of 42 hours. In four infants, there was a more persistent hypotonia lasting for more than 7 days.

Extensor hypertonus

Fifty per cent of the infants demonstrated a phase of extensor hypertonus, most commonly following a short lived, hypotonic phase. Their resting posture was one of loss of flexion and increase of extension of the limbs, often more markedly in the legs. The extended posture /

posture became more apparent when the infants were handled and became irritable and agitated, Figure 8,5. In some, there was a clear increase in truncal extensor tone, the infant lying with head and back extended, with head retraction or even opisthotonus in the most severe cases, Figure 8,6. The increased extensor tone also produced abnormal posture when the infants were placed in prone lie, ventral suspension, sitting or when pulled to sit, Figure 8,7a, b, c.

The extensor reflexes were increased in their activity. The asymmetrical tonic neck reflex was prominent, and, in some infants, obligatory, determining their resting posture, Figure 8,8a. The trunk reflexes, Perez reflex and the trunk incurvation reflex, were also active and often obligatory, the infant being fixed in the reflex response position for as long as the stimulus was applied, Figure 8,8b.

Some infants, however, with marked irritability, had reduced reflex activity as part of their picture of intense hyperexcitability, the Moro and walk reflexes in particular being absent.

The application of firm finger pressure to the nose or pubis, the snout and perineal reflexes, heightened the degree of extensor posturing, the arms being thrown forward in forced extension, the hands pronating, and, in the more pronounced responses, the legs also extending with dorsiflexion of the great toes, Figure 8,9. These reflex responses were useful in revealing the predominant pattern of tone in infants with lesser degrees of abnormality.

During the phase of extensor hypertonus, some infants were otherwise neurologically intact with normal cranial reflexes, full eye movements, feeding reflexes and bulbar responses, while others showed deep depression of these functions.



Figure 8,5

Irritable, hyperalert infant with moderate extensor hypertonus, (Case 30)

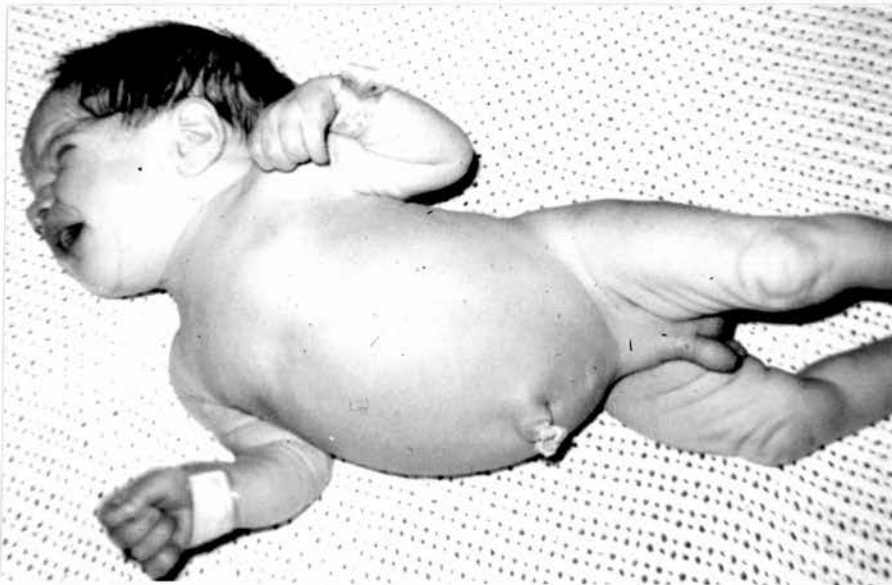


Figure 8,6

Extensor hypertonus, head retraction and back arching, (Case 20).

(a)



(b)



(c)



Figure 8,7

Extensor hypertonus: (a) prone lie,
(b) ventral suspension, (c) pull to sit. (Case 21)



(a)



(b)

Figure 8,8

Extensor reflexes: (a) asymmetrical tonic neck reflex
(b) trunk incurvation reflex

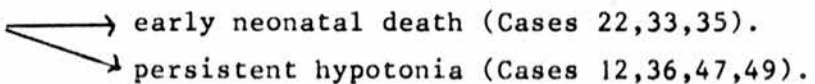


Figure 8,9

Positive snout reflex - obligatory arm extension,
pronation, and fisting. (Case 20)

The eight variations of muscle tone pattern, shown in figure 8,1 can be reduced to 5 main patterns as shown in Figure 8,10. The 2 progression of tone starting with extensor hypertonus will be considered with the 2 which have a phase of hypotonia preceding the development of extensor hypertonus, patterns 2 + 3, Figure 8,1, since it is felt that the individual members of these two pairs of tone patterns are similar; the difference may be simply in the timing of the asphyxial insult relative to the time of birth, so that some of these infants may have progressed already through the hypotonic phase to extensor hypertonus by the time of birth. The two small groups of infants who showed flexion initially will also be considered together.

Pattern 1

Hypotonia 

The 3 infants who died in the early neonatal period had suffered severe asphyxial insults: cord prolapse following birth of the first twin, ruptured uterus, marked signs of fetal distress with severe fetal acidosis, pH 6.9. Two were apparently stillborn, there being no sign of life at birth, and the third had very low Apgar scores. All showed gross neurological abnormality from birth. Following an initial period of flaccidity and lack of any response, signs of peripheral nervous, spinal, and brain stem abnormality became apparent. One infant, Case 33, developed clear signs of release of spinal activity producing a pattern of partial flexion, Figure 8,11, due to spinal flexor activity being revealed by loss of higher centre inhibition. The other 2 infants showed muscle fasciculation, myotactic responses - the muscle contracting in response to tapping over it, exaggerated phasic reflexes and sustained clonus, both spontaneous and readily induced, in the limbs, especially the thigh adductors, and the jaw, Figure 8,12. These infants showed grossly exaggerated flexor withdrawal reflexes in the limbs.

Ophthalmoplegia /

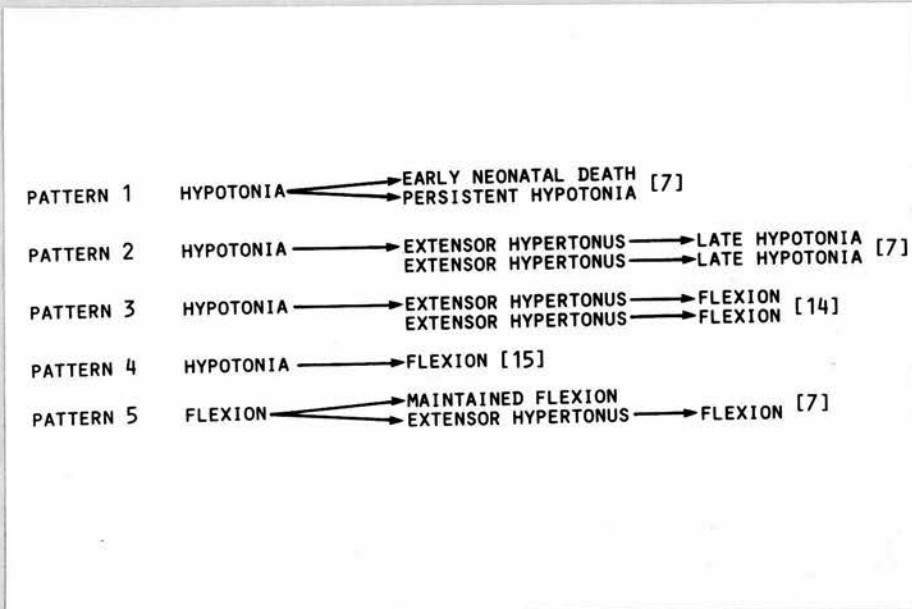


Figure 8,10

5 main patterns of muscle tone - numbers in brackets represent the number of infants in each group

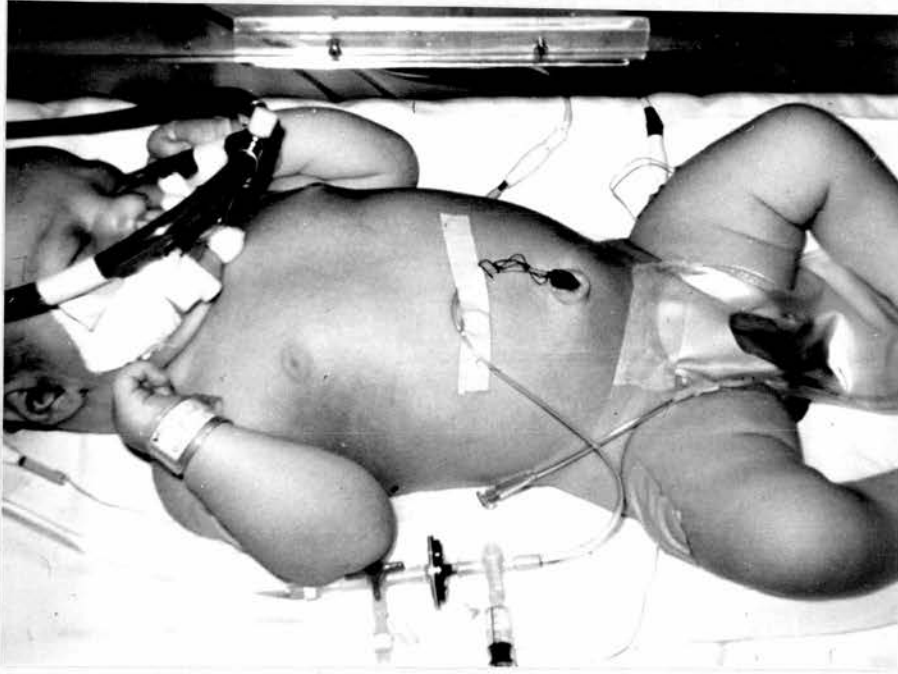


Figure 8,11

Release of spinal flexion; absence of brain stem reflexes;
assisted ventilation for recurrent apnoea; died at 48 hours,
(Case 33).

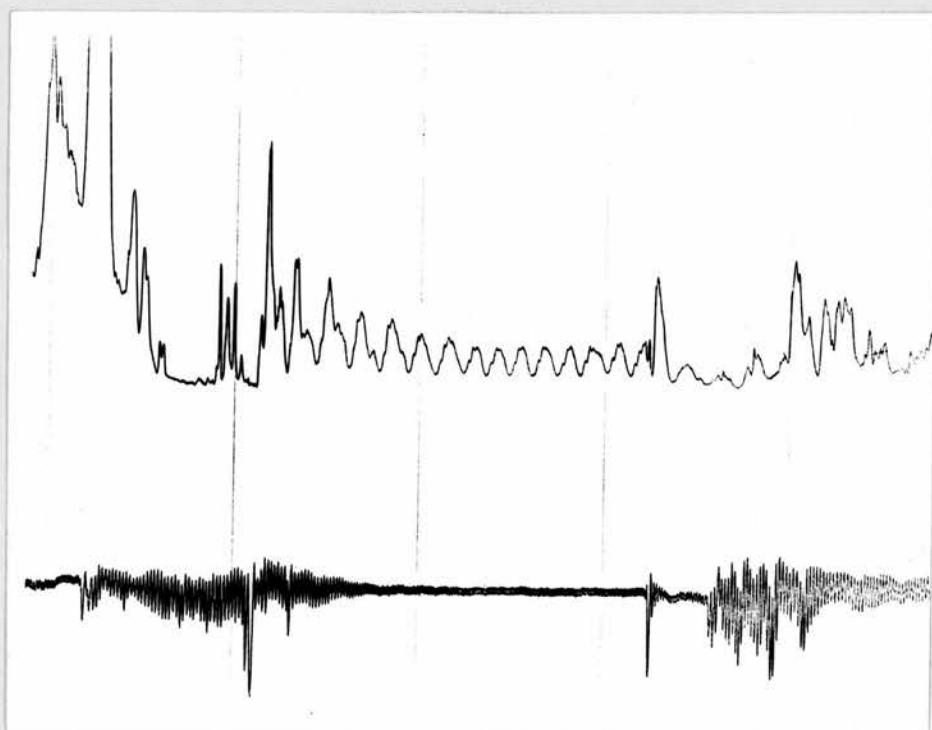


Figure 8,12

Spontaneous jaw clonus. Upper trace respiration.
Lower trace pressure recording from water filled teat in mouth.
Time divisions - 6 seconds. (Case 9).

Ophthalmoplegia, bulbar palsy, and absence of the primitive reflexes were present in all 3 infants. One infant, Case 33, had fits. These were tonic and recurrent from 5 to 36 hours of age.

An acute, severe stress during labour was a feature also of the 4 infants with persistent hypotonia. In Case 47, the mother had become hypotensive during Caesarean section, and in the others there were clear signs of fetal distress, with late decelerations and baseline bradycardia in 2 and meconium staining of the liquor and a severe fetal acidosis in the third. In addition in Case 36, the second stage of labour was obstructed and prolonged due to fetal size, birth weight 5.3 Kg., and there was both severe asphyxia and birth trauma, with compressional head injury, an Erb's palsy and fractured humerus on one side, and a brachial plexus palsy on the other. This infant had no heart beat at birth and was given external cardiac massage and artificial ventilation for 30 minutes. He was profoundly hypotonic initially, while the other 3 infants showed less severe degrees of hypotonia, amounting to marked regression of tone. Case 36, unlike the other 3 infants, showed signs of spinal release, perhaps due to cervical trauma, with very brisk leg reflexes and marked flexor withdrawal. This infant differed in other respects also, having fits, generalised clonic convulsions from 36 to 48 hours, and showing a bulbar palsy and ophthalmoplegia.

All four infants were apathetic with depression of feeding reflexes, Table 8,1. Muscle tone gradually improved but each still showed significant hypotonia at 10 days of age. Their outcome has been mixed. Cases 12 and 49 have significant handicap, outcome category 4: ataxic diplegia with normal intelligence and dyskinetic cerebral palsy with mental handicap. This second child showed clear athetoid features in the early neonatal period with typical hand movements and posturing and mouthings, (Figure 8,13 a, and b). Case 36 has made good progress, but has a persistent Erb's palsy and a minimal hemiparesis on the same side.

(a)



(b)

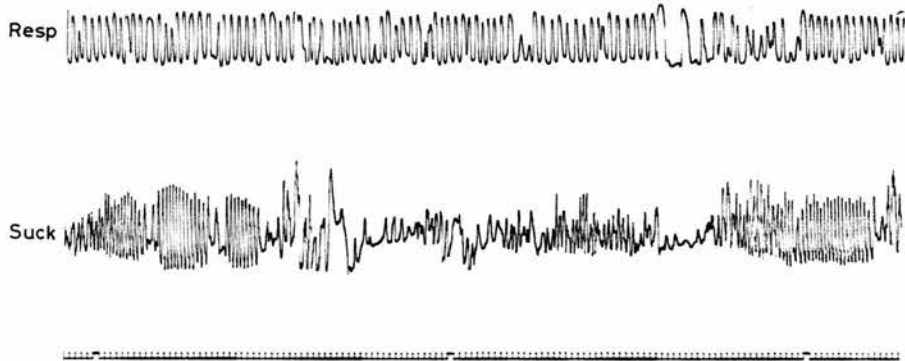


Figure 8,13

Case 49 - athetoid features.

- (a) typical hand posturing and movements
- (b) excessive mouthing activity on sucking record.

Table 8, 1

Abnormality	Pattern 1 7 infants	Pattern 2 7 infants	Pattern 3 14 infants	Pattern 4 15 infants	Pattern 5 7 infants	Total No.of infants
Feeding depression	7	7	12	10	4	40
Persistent vomiting	-	1	2	1	1	5
Hypothermia	-	4	-	-	1	5
Apnoeic episodes	4	2	2	2	1	11
Cyanotic episodes	5	2	5	3	1	16
Irritability	3	7	12	11	6	39
Cerebral cry	1	4	5	5	3	18
Apathy	7	7	4	7	1	26
Fits	2	7	7	1	1	18
Total abnormalities	29	41	49	40	19	178
Mean number	4.1	5.9	3.5	2.7	2.7	3.56

Distribution of abnormalities of behaviour and performance
in 5 tone pattern groups.

Pattern 2

Hypotonia → extensor hypertonus → late hypotonia (Cases 9, 13,
14, 25, 34, 44).
extensor hypertonus → late hypotonia (Case 28).

These 7 infants had a similar early course. In 4 cases, there had been an acute, major, asphyxial insult: cord prolapse, severe antepartum haemorrhage with maternal and fetal blood loss, undiagnosed second twin - oxytocin given before delivery, very rapid labour and delivery with fetal bradycardia. The remaining labours were complicated by clear signs of fetal distress.

Three infants were apparently stillborn. The remainder had very low Apgar scores. In the 6 with initial hypotonia, this was profound: they were flaccid and unresponsive, but each showed a rapid transition to severe extensor hypertonus between 1 and 4 hours of age, Table 8,2. They demonstrated hyperexcitability and central nervous system disinhibition with obligatory reflex responses. Each of these infants fitted, all having tonic fits, 3 with clonic fits in addition, the onset usually accompanying the development of extensor hypertonus. They were treated with phenytoin and phenobarbitone, with intermittent diazepam intravenously to terminate individual prolonged fits. In 4, the fits were frequent and refractory to treatment, Table 8,2. The age of cessation of fits was more variable, 24 to 48 hours in 5 infants, while Case 9 had occasional fits until the age of 5 days. With the exception of this last infant, fits had ceased before the second hypotonic phase began.

Table 8, 2

Tone Pattern 2 - details of 7 infants

These 6 infants also showed evidence of central hyperventilation during /

Table 8, 2

Fits

Case No.	Ext. Hyper-tonus. Onset, hrs	Age Onset	Number	Age Cessation	Treatment	Dexamethasone	Late Hypotonia Onset	Ophthalmoplegia	Bulbar Palsy	N.G. Feeds Stop, days	Outcome Category
9	5	5 hr	10	5 days	Phenytoin, phenobarb.	+	48 hrs	-	+	15	4
13	1	1 hr	8	30 hrs	Phenytoin, phenobarb.+ diazepam.	+	6 days	-	-	6	1
14	1	1 hr	Numerous	36 hrs	Phenytoin + diazepam.	+	7 days	-	-	7	3
25	1	2 hr	Numerous	36 hrs	Phenytoin, phenobarb.+ diazepam	+	36 hrs	+	+	7	4
34	2	2 hr	Numerous	72 hrs	Phenytoin, phenobarb.+ diazepam.	+	70 hrs	+	+	16	4
44	3	10hr	9	24 hrs	Phenytoin,+ diazepam.	+	48 hrs	+	+	13	4
28	Birth	5dys	Numerous	6 days	Phenytoin + diazepam	-	48 hrs	-	-	2	2

Tone Pattern 2 - details of 7 infants

during part or all of the phase of extensor hypertonus with tachypnoea, without dyspnoea, and lowering of arterial or capillary blood $p\text{CO}_2$, generally to between 3 and 4.5 kPa. Two infants demonstrated profuse sweating at this stage.

The seventh infant, Case 28, showed initially a regressed pattern of posture at rest, but on handling demonstrated extensor posturing and a marked increase in extensor reflexes. She manifested brain stem fits at 5 days of age, at a time when she had become hypotonic and the extensor hypertonus had settled.

In the other 6 cases, the phase of extensor hypertonus ended between 48 hours and 7 days of age. Severe hypotonia and much diminished responsiveness followed in 5 infants, while Case 13 showed only mild hypotonia at 6 days. The hypotonia gradually improved but each was considered neurologically abnormal at the time of discharge from hospital, 15-35 days old.

The 6 infants with initial hypotonia were given dexamethasone, 2 mgs. Q.I.D., intravenously on a prophylactic basis, starting within the first 2 hours of life, as they were considered at risk of developing cerebral oedema. Brain swelling, as a cause of extensor hypertonus and signs of decerebration, cannot be excluded in this group, but there were no other clinical signs to suggest it and steps had been taken from an early stage to reduce the risk of its occurrence. Fluid intake was carefully restricted and plasma electrolyte and osmolality levels measured frequently. No infant developed major salt and fluid imbalance, the lowest plasma sodium level being 127 mmols./l. and plasma osmolality, 277 mosmols./l. Case 9 was given mannitol intravenously when extensor hypertonus, cycling and fits developed, but without improvement.

Early hypocalcaemia was a finding in 5 of the 7 infants, plasma calcium less than 1.85 mmols./l., arising between 1 and 3 days of age, at /

at a time when 2 were in the late hypotonic phase and 3 were showing extensor hypertonus.

Feeding depression, apathy, irritability and fits were common to all 7 infants. Four also showed poor thermoregulation with drops of rectal temperature below 35.5°C , Table 8,1. During the late hypotonic phase, signs of depression of brain stem function and autonomic nervous system imbalance were common, 4 infants having a bulbar palsy and requiring more prolonged naso-gastric feeding, 3 infants an ophthalmoplegia, 3 infants having episodes of bradycardia down to 80 beats/minute and 2 infants episodes of apnoea. Retention of urine, controlled by regular bladder expression, was also common.

The phase of late hypotonia is felt to be an inherent result of a major asphyxial insult to the brain, but clearly other factors also are involved. Drug treatment with anticonvulsants may well have contributed to the picture of central nervous system depression. At that time, facilities were not available for frequent measurement of blood levels of drugs in small infants, but periodic levels were ascertained and did not suggest that drug accumulation was important.

Other neurological features were observed. Case 13 showed athetosis at the sixth day of life and this infant and 3 others, Cases 25, 28, and 34, demonstrated transient hemisyndromes.

The outcome for this group has been poor. Two children, Cases 25 and 34, developed severe, quadriplegic cerebral palsy with microcephaly and fits; one of these died at 16 months. Two others have been allocated to outcome category 4, an ataxic diplegia of moderate severity but normal intelligence, and a severe, dyskinetic cerebral palsy with microcephaly, Cases 9 and 44. Case 4, outcome category 3, has a mild right hemiparesis of no functional importance and Case 28, outcome category 2, had slow early development and speech delay. Only 1 child, Case 13, is entirely normal; he showed a lesser degree of late hypotonia /

hypotonia than the others, and has been considered neurologically normal since the age of 4 weeks.

Pattern 3

Hypotonia → extensor hypertonus → flexion (Cases 5,8,11,15, 19, 20,21,31,40, 50).
extensor hypertonus → flexion (Cases 31,37,41,42).

This group consists of 14 infants who showed generally similar features, Tables 8,3, and 8,1. The commonest labour problem was fetal distress, often with a prolonged delivery, although 2 infants clearly had had a severe, acute stress: prostaglandin induced, tonic contractions with marked late deceleration of fetal heart rate and fetal acidosis, and eclampsia. No infant had cardiac arrest at birth; 3 were ventilated for between 10 and 20 minutes.

Table 8,3

Tone Pattern 3 - details of 14 infants

In the 10 infants with an initial hypotonic phase, this was a pattern of regression rather than profound reduction of tone. There was accompanying apathy in 4, and, although all but 2 infants required tube feeding for feeding depression, this was for relatively short periods, 1 to 6 days, return of feeding activity coinciding with the change from hypotonia to extensor hypertonus in some infants. Three infants had a bulbar palsy over their first 24 hours. None showed an ophthalmoplegia or signs of release of spinal activity.

The initial phase of hypotonia ended with the transition to extensor hypertonus between 1 hour and 5 days, with 2 to 3 days being a common time, generally rather later than in Pattern 2,, Table 8,2.

The /

Table 8, 3

Fits

Case No.	Labour Problem	Apgar 1+5 mins.	Extensor Hypertonus Onset	Age Onset	Number	Age Cessation	Treatment	Dexamethasone	Extensor Hypertonus Cessation	Outcome Category
5	Hyperextended twin, difficult delivery.	6+8	5 days	48 hr	8	8 dys	Phenytoin, phenobarb.	-	21 days	1
8	Cord round neck, rapid delivery.	3+9	3 days	-	-	-	-	-	5 days	1
11	Breech, rapid descent of head.	7+9	2 days	12 hr	3	18 hr	Phenobarb.	+	5 days	1
15	Eclampsia	1+2	2 days	-	-	-	-	+	5 days	1
19	Prolonged F.D.	3+8	12 hrs	-	-	-	-	-	2 days	1
20	Breech delivery	8+9	6 hrs	-	-	-	-	+	6 days	1
21	C.P.D., F.D., 2nd stage delay.	6+9	1 hr	-	-	-	-	+	5 days	1
32	F.D., oblique lie, L.U.S.C.S.	2+6	2 days	-	-	-	-	-	4 days	1
40	F.D., 2nd stage delay	6+7	2 days	14 hr	Numerous	60 hr	Phenytoin, phenobarb. diazepam.	+	4 days	2
50	Tonic contractions, F.D., acidosis.	4+8	6 hrs	7 hr	Numerous	48 hr	Phenytoin, phenobarb. diazepam.	+	3 days	1
31	F.D.	3+9	birth	3 min	1	-	-	-	2 days	1
37	F.D., 2nd stage delay	3+8	birth	60 hr	13	4 dys	Phenytoin, phenobarb. diazepam.	-	4 days	1
41	Prolonged labour, meconium.	9+9	birth	-	-	-	-	-	3 days	1
42	No apparent problem	1+6	birth	30 hr	3	30 hr	Phenytoin	+	3 days	1

Tone Pattern 3 - details of 14 infants

(F.D. = fetal distress: C.P.D. = cephalo-pelvic disproportion)

The extensor hypertonus in most of these infants, including the 4 who showed hypertonus from the outset, also was less severe than in Pattern 2. The infants were irritable, 12 of 14, showed extensor posturing at rest, increasing on handling, and an increase in extensor reflexes. Change from extensor hypertonus to flexor tone occurred between 2 and 6 days in all but one infant, where this was delayed until 21 days. This infant, Case 5, had been lying in an abnormal, hyperextended posture in utero and, not surprisingly, this persisted for some time after birth, Figure 8, 14a and b. Case 31 developed flexor hypertonus, with a tightly flexed and adducted posture, strong flexor recoil and reduced joint angles on passive movement, after extensor hypertonus had settled at 2 days, lasting until 4 days of age.

Fits occurred in 7 of this group. Four had focal or generalised clonic fits, one had a single tonic fit shortly after birth, 1 infant had 3 brief, tonic fits at a time when he was hypocalcaemic, and 1 infant in addition to focal clonic fits had several tonic fits. The tonic fits occurred during the extensor hypertonus phase, whereas in those with clonic fits alone, these occurred during the preceding phase of hypotonia in 3. Further details of these fits are given in Table 8,3.

In contrast to Tone Pattern 2, where hyperventilation was found in all the infants during the phase of extensor hypertonus, a low capillary pCO_2 , less than 4.5 KPa, was uncommon in Pattern 3, being found in 2 of the 14 infants. Hyponatraemia, plasma sodium less than 130 mmols./l., was found in 5 infants, with a lowest level of 123 mmols./l. Hypocalcaemia, plasma calcium less than 1.85 mmols./l., was found in 8 infants and in 6 occurred during the phase of extensor hypertonus and may have contributed to the clinical findings.

Two infants, Cases 15 and 50, demonstrated a hemisyndrome, Case 50, in association with frequent focal fits, Figures 7,25, and 8,15. Neither child has any residual asymmetry.

The ↗

(a)



(b)



Figure 8,14

Second twin, breech presentation, hyperextended neck, (Case 5)
(a) Xray - in utero position; (b) position when trunk held vertical.



Figure 8, 15

Hemisyndrome with asymmetrical snout reflex,
(Case 50)

The outcome for all this group has been favourable, none having significant handicap. Only 1 child, Case 40, has abnormal neurological findings, a minimal left hemiparesis of no functional importance, outcome category 2.

Pattern 4

Hypotonia —————> flexion. (Cases 1, 2, 4, 6, 7, 10, 16, 18, 23, 26, 27, 39, 43, 46, 48).

This group of 15 infants had fewer, and less severe, neonatal problems than the preceding three groups. There had been a variety of labour problems, but only 3 clearly major and acute: eclampsia with several fits, cord prolapse, shoulder dystocia with loss of fetal heart rate. Of the remaining 12 cases, in 11 there were signs of fetal distress, while in one there had been no apparent problem until the second stage of labour, which was prolonged. In two, there was evidence of placental insufficiency and in 4 malpresentation, occipito-transverse and occipito-posterior positions. Total duration of labour was greater than 18 hours in 2 cases and second stage was prolonged, greater than 60 minutes in 3 cases and 50 minutes in 1 case.

Apgar scores at 1 minute were 3 or less in 10 of the 15, but only 3 had 5 minute scores of 5 or less. Two infants had no heart rate at birth, Cases 26 and 27, but responded quickly to resuscitation, 5 minute scores being 4 and independent respirations being established by 5 and 10 minutes respectively.

Hypotonia, in all but 2 cases, consisted of mild or moderate regression. Cases 27 and 43, shoulder dystocia with loss of fetal heart rate and prolapse of the cord, had generalised loss of tone. The duration of this initial phase ranged from 2 hours to 5 days, with 2 to 4 days being common, 11 of 15 cases. This is similar to Pattern 3. Tone gradually recovered to appropriate flexion, but 1 infant, Case / . .

Case 27, showed flexor hypertonus from 2 to 40 hours. Apathy was an early feature of 7, while 11 infants became irritable as tone improved. Feeding depression was common, 10 infants, but duration of tube feeding short, 1 to 3 days, feeding activity again recovering in parallel with improvement in tone and level of alertness. Only 1 infant showed a bulbar palsy, over the first 24 hours. There were no other neurological features apart from asymmetries: 3 infants having a transient hemisyndrome, 2 a facial palsy, and 2 an Erb's palsy. One infant, Case 39, had a single generalised, clonic fit at 7 hours. Four infants were given dexamethasone, but none developed clinical evidence of brain swelling.

This group were all fit for discharge home at an early date, 6 to 12 days. All were considered normal at that time, apart from Erb's palsy in 2, which settled over the early weeks. Thirteen children have been allocated to outcome category 1, Case 23 to category 2 with slow early motor and speech development in association with hypotonia, and Case 18 to category 3, slow early development, mild truncal ataxia and low I.Q., 70.

Pattern 5

Flexion → maintained flexion (Cases 3, 38, 45).
 → extensor hypertonus → flexion (Cases 17, 24, 29, 30).

An initial pattern of flexor tone was found in 7 cases. None are thought to have had a severe, asphyxial episode, Table 8,4. Case 3 had had an antepartum haemorrhage, but was in good condition at birth. In 5, there was evidence of a problem during labour: fetal distress, passage of meconium, fetal acidosis, prolonged second stage. Case 17 also had evidence of a compressional head injury.

Initial /

Initial condition at birth was good, only Case 30 having very low Apgar scores. Six infants were irritable initially, and 4 showed depression of feeding activity, but required tube feeding for a short period, 1 to 5 days. None had a bulbar palsy.

Table 8, 4

Case No.	Labour Problem	Apgar	Pattern of Muscle Tone and Time of Changes	Outcome Category
3	A.P.H., L.U.S.C.S.	5+8	Normal flexion, left hemi-syndrome.	3
38	Meconium, prolonged second stage	5+9	Flexor hypertonus - 48 hours- normal flexion	1
45	F.D., fetal acidosis	3+8	Flexor hypertonus - 24 hours- normal flexion.	1
17	C.P.D., F.D., compressional head injury.	3+9	Flexor hypertonus - 36 hours - extensor hypertonus - 5 days - flexion	1
24	35/52, I.U.G.R., no apparent labour problem.	5+7	Approp. flexion - 48 hours- extensor hypertonus - 14 days - flexion.	1
29	F.D., fetal acidosis	8+9	Flexion - 24 hours - extensor hypertonus - 4 days - flexion.	1
30	Failed forceps, prolonged second stage	1+3	Flexor hypertonus - 72 hours - extensor hypertonus - 11 days - flexion	1

Tone Pattern 5 - details of 7 infants.

Muscle tone was normal flexion throughout in 1 infant, Case 3, apart from a mild left hemisyndrome and this is the only child with abnormality at follow up, a mild left hemoparesis, outcome category 3. Four infants initially showed flexor hypertonus: two of these gained normal flexor tone at 24 and 48 hours, while two developed extensor hypertonus at 36 and 72 hours. The extensor hypertonus, shown by 4 infants in all, was mild and not associated with fits. One infant, Case 29, had a single clonic convulsion at 4 hours with hypoglycaemia.

Hyponatraemia /

Hyponatraemia occurred in 3, Cases 17, 24, 29, but was never less than 128 mmols/l., while hypocalcaemia, plasma calcium less than 1.8 mmols/l., was found in Cases 17 and 24 at a time when they were both showing extensor hypotonus. Case 24 had frequent apnoeic episodes over the first hours of life, was ventilated from 16 hours for 24 hours, and, although the problem was well controlled, hypoxaemia at this time may have contributed to the subsequent neonatal abnormalities, extensor hypertonus and transient left hemisyndrome, in this child. This infant and Case 17 were treated with dexamethasone.

All this group were discharged home from hospital at an early date, 9 - 14 days, except Case 38, who developed a urinary infection and septicaemia; all were considered normal at the time of discharge.

Relationship of tone pattern to outcome

The major changes of muscle tone and other neurological features occurring in the early neonatal period in the study group have been described. There is a strong association between patterns of muscle tone and outcome, Figure 8,16. This is highly significant, $p < 0.001$, Kruskal-Wallis test. It can be seen that all the significantly handicapped children, outcome category 4, belong to patterns 1 or 2, while those with minimal, neurological abnormalities, categories 2 and 3, emanate from all 5 tone patterns. The occurrence of bulbar palsy, or ophthalmoplegia also shows a highly significant relationship to a poor outcome, $p < 0.001$, Wilcoxon's rank sum test, while hemisyndrome or athetosis do not carry any such significance. Bulbar palsy, ophthalmoplegia and the disturbance of performance and behaviour, which show a relationship to outcome, Chapter VII, are, of course, much commoner in infants of tone patterns 1 and 2, Table 8,5, and help to form aggregates of clinical abnormalities by which infants can be identified as being at greatest hazard.

Table /

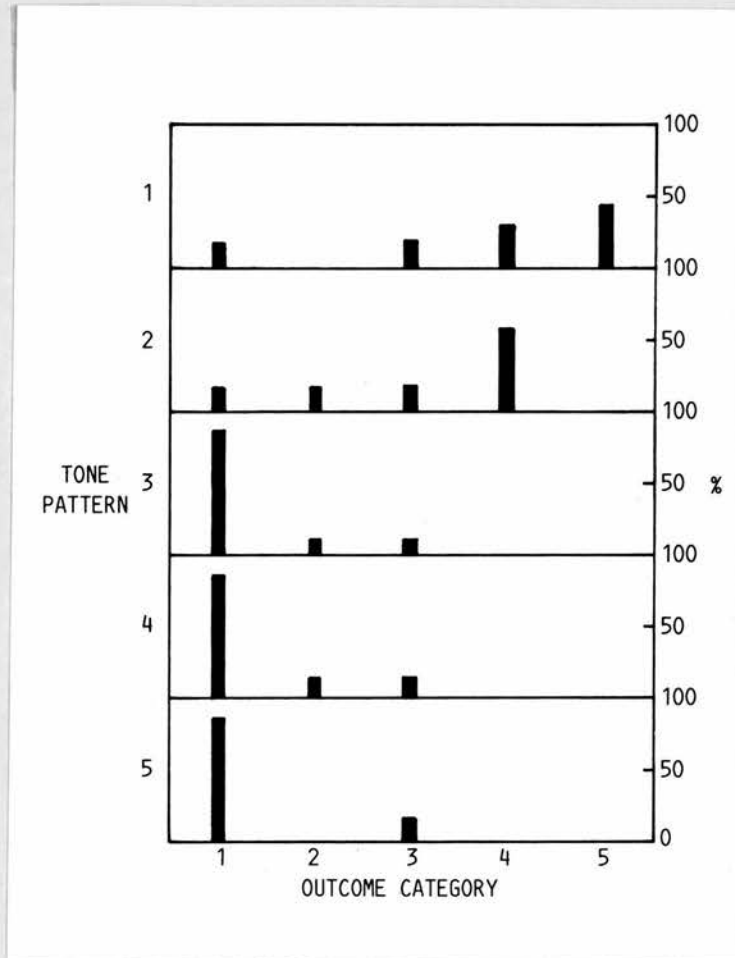


Figure 8,16

Outcome category distribution percentages
in 5 tone pattern groups.

Table 8,5

Tone Pattern	Total No. Infants	Hypo-thermia	Apnoea	Apathy	Unconsciousness	Tonic Fits	Bulbar Palsy	Ophthalmoplegia
1	7	-	4 (57)	7 (100)	4 (57)	1 (14)	4 (57)	4 (57)
2	7	4 (57)	2 (28)	7 (100)	5 (71)	6 (86)	4 (57)	3 (43)
3	14	-	2 (14)	4 (28)	3 (21)	3 (21)	3 (21)	-
4	15	-	2 (13)	7 (47)	1 (7)	-	1 (7)	-
5	7	1 (14)	1 (14)	1 (14)	-	-	-	1 (14)

Occurrence of abnormalities of performance, behaviour and neurological function in 5 tone patterns. Numbers in brackets represent percentages.

The tone patterns described are distinct and can be recognised readily by careful, repeated, neurological assessment. Patterns 2 and 3 show some similarities but differ in a variety of ways: initial hypotonia, when it occurred was more severe in pattern 2, extensor hypertonus was more florid, and these two phases were accompanied more commonly by other abnormalities, bulbar palsy, ophthalmoplegia, tonic fits, poor temperature regularion, apathy and unconsciousness, in pattern 2 than pattern 3. The persistence of abnormal muscle tone, late hypotonia, is a further important distinction.

Late hypotonia

Late hypotonia, arbitrarily taken as persistence of hypotonia more than 7 days after birth, by definition was seen in all surviving infants of tone pattern 1 and those of tone pattern 2, 11 infants. The hypotonia was of varying degrees, but in most was severe at the start of this /

this period, Figure 8,4. Four infants, Cases 13, 28, 36, 47, showed a steady recovery to normal muscle tone between 10 and 28 days and subsequently they made good progress. None is significantly handicapped. The remainder, Cases 9, 12, 14, 25, 34, 44, 49, showed continuing abnormality of muscle tone, the hypotonia gradually improving to a pattern of regression, Figure 8,17 a, b. All, but Case 14, have a significant handicap, outcome category 4. The progress made by the infants with late hypotonia is described in Chapter XI.



(a)

(b)

Figure 8, 17

Case 25, late hypotonia, age 14 days.
Subsequently severely handicapped.

CHAPTER IX

OTHER COMPLICATIONS IN THE EARLY NEONATAL PERIOD

A variety of problems, in addition to those already described, were seen in the study group, either as a direct consequence of intrapartum asphyxia or apparently as coincidental events.

Hypoglycaemia

This was an infrequent problem, probably as a result of the routine policies employed: many infants were given intravenous dextrose at resuscitation, and fluid and calorie intake was ensured by naso-gastric or intravenous fluids in the early hours of life. "Dextrostix" measurements of blood glucose were performed on admission to the nursery and thereafter at 3 hourly intervals; when low results were obtained, formal biochemical measurement of blood glucose was performed.

Four infants had a single episode of hypoglycaemia, blood glucose less than 25 mg.% - 1.1 mmols/l. Each occurred between 4 and 8 hours of age. Two were symptomatic - an apnoeic episode, and a focal, clonic fit. The other two infants showed marked neurological abnormality before hypoglycaemia occurred and no clinical change could be attributed to its occurrence. All were treated with intravenous glucose and hypoglycaemia did not recur.

Hypocalcaemia

Hypocalcaemia, plasma calcium less than 1.85 mmol/l, was detected in 22 infants. The age of detection was as follows:

days /

days of age:	1	2	3	4
number of infants:	5	9	7	1

Plasma calcium levels ranged widely; the lowest recorded was 0.97 mmols/l. but most were between 1.4 and 1.85 mmol/l. All were treated with calcium gluconate either added to intravenous fluids, 8 ml. 10%/100 ml. fluid, or to milk feeds, 5 ml 10% calcium gluconate/60 ml. feed. Despite this treatment, 8 infants remained hypocalcaemic for 3-4 days until the 4th - 6th day of life; 7 of these were also hyperphosphataemic, phosphate greater than 2.9 mmol/l., while the remaining infant was premature, 35 weeks gestation. In three of these infants with hyperphosphataemia, there was evidence of acute renal failure. Hyperphosphataemia was found also in 2 infants with more transient hypocalcaemia.

Other neonatal factors may have contributed to the occurrence of hypocalcaemia. The administration of sodium bicarbonate at resuscitation and of dexamethasone over the first days of life were commoner in the hypocalcaemic infants, 82% and 73% respectively as compared to 68% and 25% of those who were not hypocalcaemic. However, in addition to any hypocalcaemic tendency that these agents might encourage, their use, of course, related to poor clinical state.

It is difficult in this group to know the contribution hypocalcaemia made to the clinical state of the infants. Eight infants were found to be hypocalcaemic in association with fits, but, in 6 of these, fits had started before hypocalcaemia developed. Two infants, each with clonic fits, were found to be hypocalcaemic at the time of onset of fits at 36 and 60 hours of age. Hypocalcaemia was found during different neurological states and presumably may have contributed to irritability and extensor hypertonus in some infants.

Hypomagnesaemia, plasma magnesium less than 0.5 mmol/l., was not found in any infant, but magnesium levels were measured less frequently and regularly than plasma calcium.

No association was found between the occurrence of hypocalcaemia and outcome.

Hyponatraemia

Hyponatraemia, plasma sodium 130 mmols/l. or less, was found in 14 infants. In none was this severe. The lowest recorded level was 123 mmol./l., but all other measurements were between 127 and 130 mmol/l. The age of first occurrence of hyponatraemia was as follows:-

Days of age:	1	2	3	4	5	7
Number of infants:	3	2	5	2	1	1

Seven of these infants also had low plasma osmolality, less than 280 mosmols/l., with a range of 255-278 mosmols/l. In 11 of the 14 infants, hyponatraemia was found on one occasion only, while the remaining 3 infants showed mild hyponatraemia for 2, 3, or 4 consecutive days.

Most of the study group were given a restricted fluid intake, starting at 50 ml/Kg./24 hours in the first day, gradually increasing depending on their plasma urea, sodium and osmolality levels. All but 3 of the infants who showed hyponatraemia had been managed in this way, while, in these 3, fluid intake was reduced when hyponatraemia occurred. The absence of more severe hyponatraemia in the study group reflects this policy.

In some infants, repeated measurements of plasma and urine osmolality and plasma sodium demonstrated clearly that hyponatraemia was due to inappropriate water retention and the excretion of concentrated urine, Figure 9,1.

This policy of fluid restriction, when applied from the start in anticipation of inappropriate fluid retention, was not without complication, some infants developing mildly elevated plasma sodium, osmolality and /

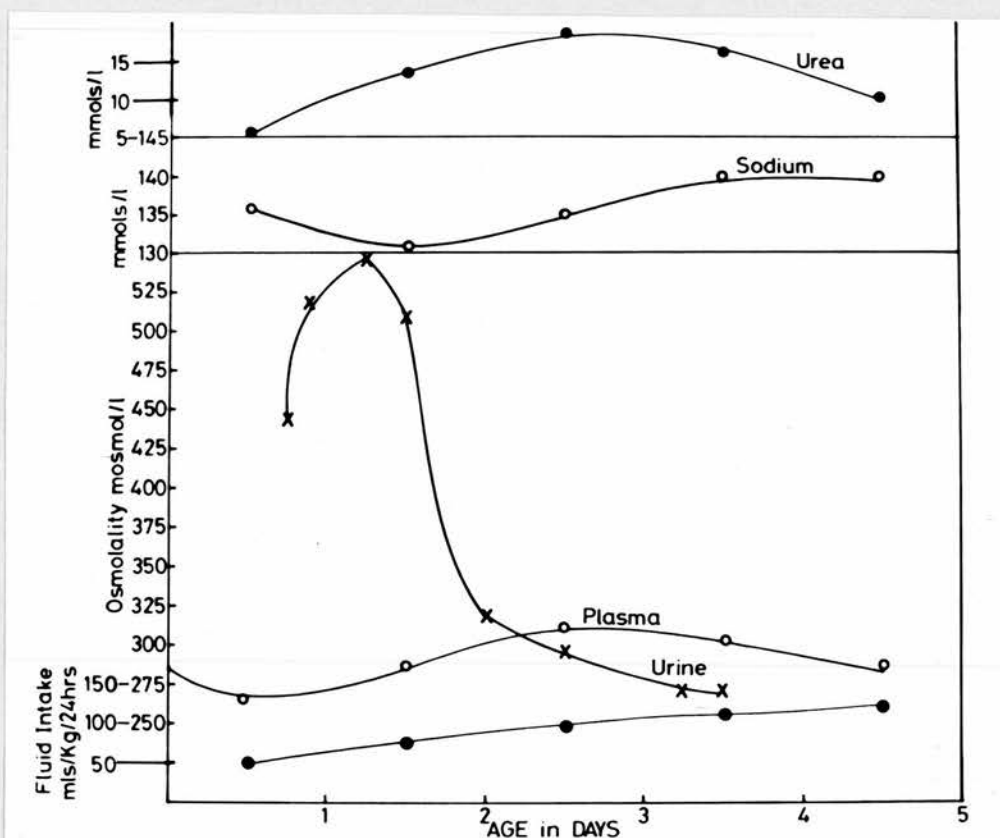


Figure 9. 1

Inappropriate water retention, dilutional hyponatraemia - plasma urea, sodium and osmolality, urinary osmolality and fluid intake. (Case 15)

and urea levels when fluid restriction had been too strict and they, presumably, did not have inappropriate A.D.H. Secretion, Figure 9, 2.

The occurrence of hyponatraemia did not show any significant relationship to outcome.

Acute renal failure

Acute renal failure in the first days of life can be difficult to recognise and must be distinguished from the moderate rise in blood urea and low urinary output seen as a result of fluid restriction. Renal failure was diagnosed when there was a combination of uraemia, fluid retention, and severe oliguria with the passage of very small volumes of unconcentrated urine. This occurred in 3 infants, Cases 14, 34, and 36, all of whom had suffered severe intrapartum asphyxia - blood loss from antepartum haemorrhage, marked fetal bradycardia with absent heart rate at birth, obstructed second stage of labour from disproportion with shoulder dystocia. The biochemical findings in one of these infants, Case 14, are shown in Figure 9, 3.

In these 3 infants, severe oliguria was the earliest sign, only a few millimetres of unconcentrated urine being passed over the first 24 hours. Red blood cells and casts were seen on urine microscopy and, in one infant, renal tubular cells. Blood urea rose steadily over the first days reaching a peak between 2 and 4 days, maximum levels 19.6, 22.4, 29.5 mmols/l. Hyponatraemia was not a problem at this stage, sodium levels remaining in the normal range over the first 3 days. Hyperkalaemia, maximum plasma potassium levels 5.3, 6.0, 6.2 mmols/l., occurred in each infant, as did hypocalcaemia, lowest plasma calcium levels 1.44, 1.54, 0.97 mmols/l., and hyperphosphataemia, maximum plasma phosphate levels 3.6, 3.78, 3.9 mmols/l. Plasma osmolality for each varied over the first week within the range, 283-321 mosmols/l. Two infants had clinically enlarged kidneys. Each infant showed some weight gain above birth weight over the first days /

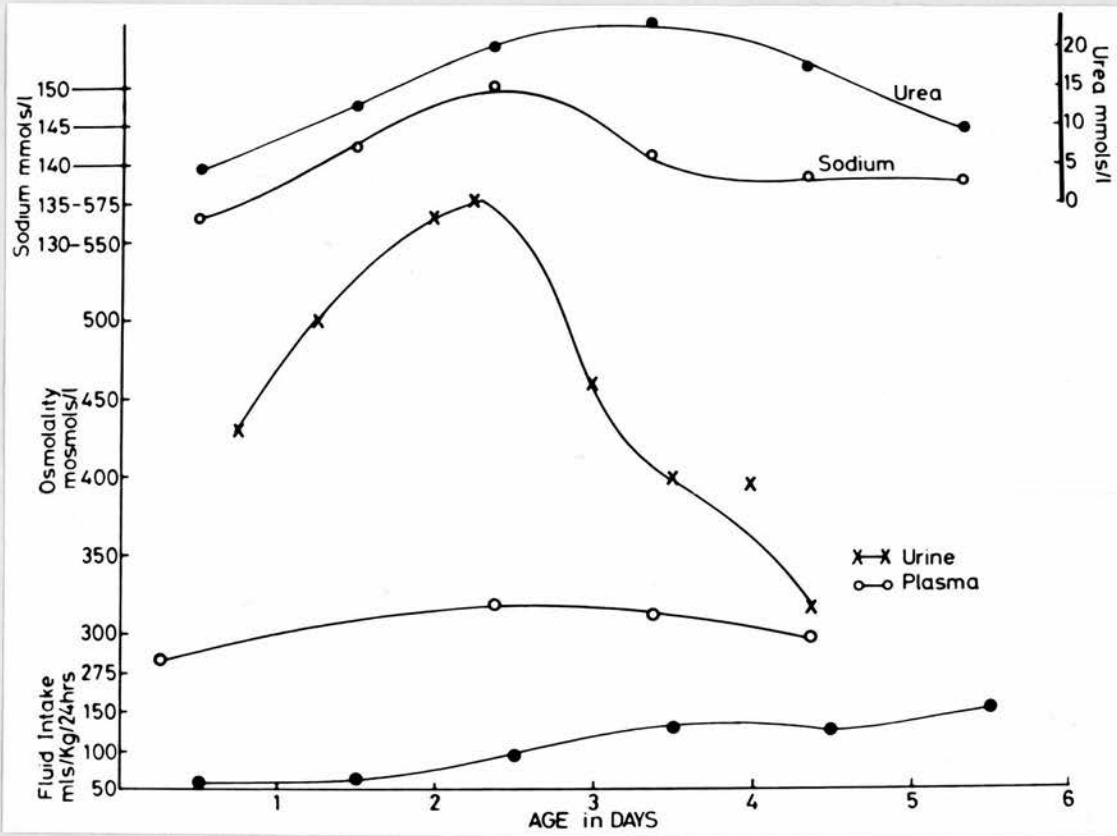


Figure 9, 2

Fluid restriction leading to a hypernatraemic/
hyperosmolar state in the absence of inappropriate
A.D.H. secretion. (Case 26)

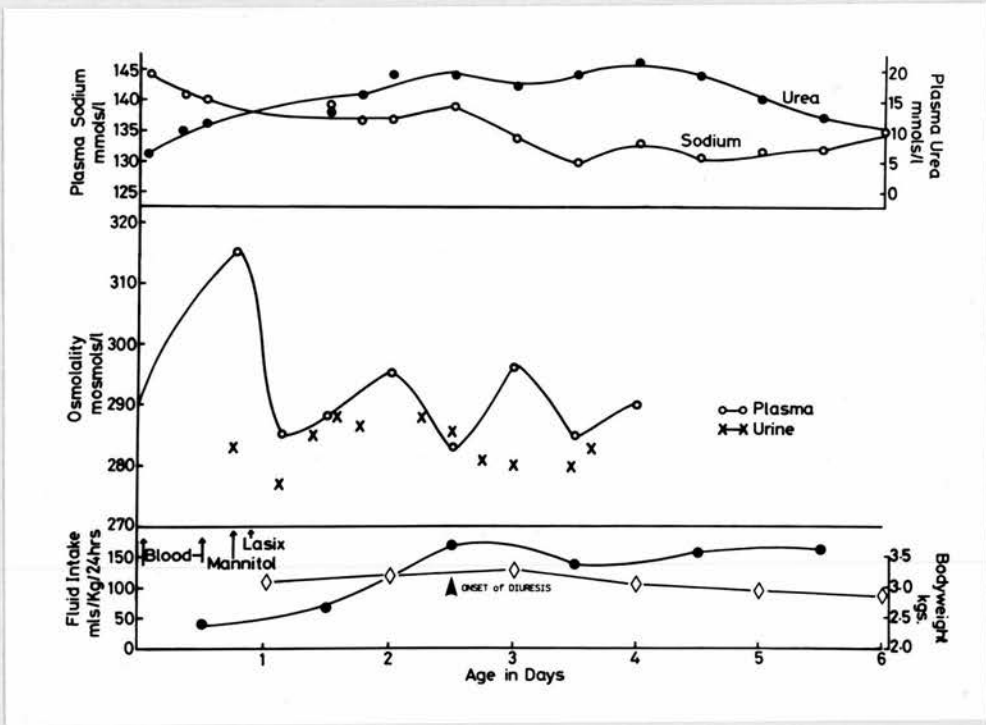


Figure 9, 3

Acute renal failure, secondary to severe intrapartum asphyxia. (Case 14).

days of life despite careful regulation of fluid intake. There was no response in urine output to frusemide or mannitol. One infant became oedematous at 48 hours of age.

The diuretic phase started between the third and fifth days and was met by increased fluid intake. At this stage, there was some tendency to hyponatraemia, plasma sodium levels falling to 130, 127, and 133 mmols/l., in the three cases.

The two long term survivors, Cases 14 and 36, have shown no impairment of renal function after the neonatal period.

Birth trauma

With improved obstetric management of complicated labours, major birth trauma has become uncommon, but degrees of compressional head injury resulting from cephalo-pelvic disproportion, or malpresentation leading to prolonged labour, remain common accompaniments of birth asphyxia, Figure 9,4. No child, felt to have suffered from compressional head injury alone, has been included in the study group, but this form of injury was considered to be a factor in 13 infants, each showing pronounced moulding of the head, and some, caput, bruising of the scalp, and cephalhaematoma. The neonatal problems which this group of 13 infants demonstrated - disturbances of behaviour and performance, such as irritability, cerebral cry, fits, patterns of disturbed muscle tone, disturbance of biochemical homeostasis and their eventual outcome, were very similar to those shown by the remainder of the study group, substantiating the initial impression that both birth asphyxia and birth trauma had occurred in these infants.

One infant, Case 11, born by breech delivery with poorly controlled descent of the head, suffered an acute compression/decompression head injury. This infant, and two of the 13 infants mentioned above, had evidence /

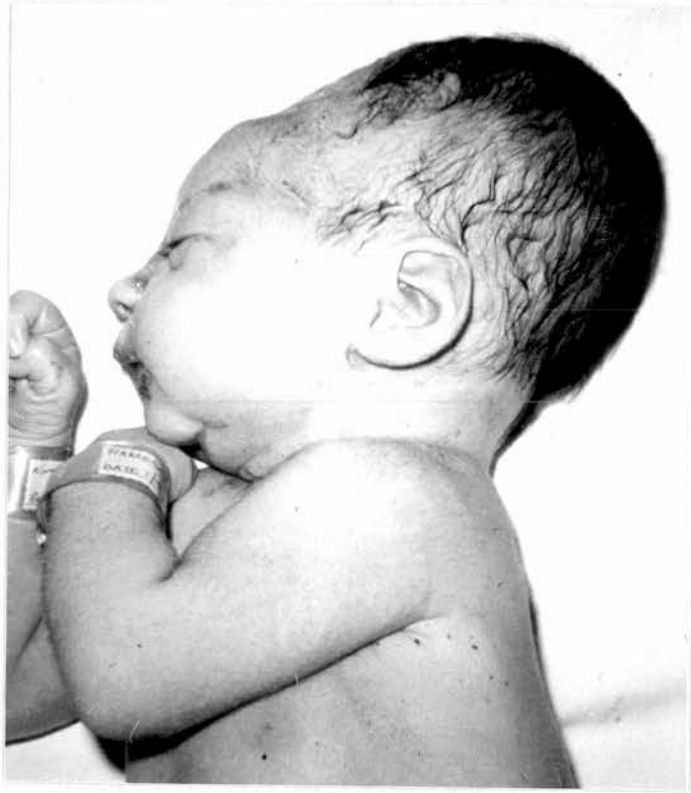


Figure 9, 4

Compressional head injury, excessive degree
of moulding. (Case 17)

evidence of subarachnoid haemorrhage with blood staining of the cerebro-spinal fluid. In all, 7 of the 24 infants who had lumbar puncture performed had blood stained cerebro-spinal fluid, but this appeared slight except in 2 cases, 11 and 36. A-scan echoencephalography was performed on all these infants, but failed to show any midline shift.

Erb's palsy was found in 3 infants, Cases 10, 27, 36, one following a forceps rotational delivery, while the other 2 deliveries were complicated by shoulder dystocia. As previously described, Case 36, a 5.3 Kg. infant, suffered major trauma during an obstructed second stage with head injury, facial nerve weakness, Erb's palsy and contralateral brachial plexus palsy and fractured humerus. This infant's injuries resolved early with the exception of the brachial plexus injury, which has improved to an Erb's palsy.

Lower motor neurone facial palsy was seen in 8 infants, 5 forceps deliveries and 3 spontaneous vertex deliveries. All resolved quickly. One of these infants also suffered trauma to the middle ear, the forceps blade impinging anterior to the mastoid process with resultant rupture of the tympanic membrane; this healed rapidly and hearing is normal.

Following a difficult birth, the possibility of cervical spine injury must be considered. In 2 infants in particular, Cases 13 and 36, there was anxiety about the stability of the cervical spine following shoulder dystocia. Each infant was handled with appropriate caution, but fortunately subsequent investigation proved negative.

Respiratory problems

Disturbances of central control of respiration - apnoeic episodes, gasping and other abnormal respiratory rhythms, such as central tachypnoea, have been described earlier, (Chapter VII). Pulmonary problems were /

were infrequent. Three infants, Cases 33, 38 and 46, following passage of meconium in utero, showed clinical and radiological evidence of meconium aspiration, but of mild degree. Cases 39 and 47 were felt to have transient tachypnoea of the newborn, while this second infant developed further respiratory difficulty at the age of 48 hours, having aspirated milk into the chest. A further infant, Case 9, while in the phase of late hypotonia with profound depression of conscious level, developed an orthostatic pneumonia, despite regular suction of secretions and physiotherapy. This child subsequently showed mild stridor from laryngomalacia over the first year of life.

Cardiac problems

Sinus bradycardia due to depression of the cardiac regulating centre, in association with other manifestations of brain stem function depression, has been described earlier, (Chapter VIII). One infant, Case 34, showed evidence of hypoxic damage to the myocardium, developing cardiomegaly, Figure 9,5, with biventricular failure, pulmonary oedema, liver enlargement, metabolic acidosis, peripheral oedema and poor perfusion at the age of 3 days. Electrocardiogram showed only right ventricular hypertrophy and echocardiography subsequently was normal. Cardiac function recovered following diuretic therapy and heart size returned to normal.

Adrenal Haemorrhage

Case 34 was further complicated by the appearance of a mass in the left paraumbilical area at the age of 4 days. Ultrasound scan suggested that this was adrenal haemorrhage, rather than a renal mass due to renal vein thrombosis, and this was later confirmed by the radiological finding of adrenal calcification later in infancy, Figure 9, 6 a and b.

Coagulopathy /

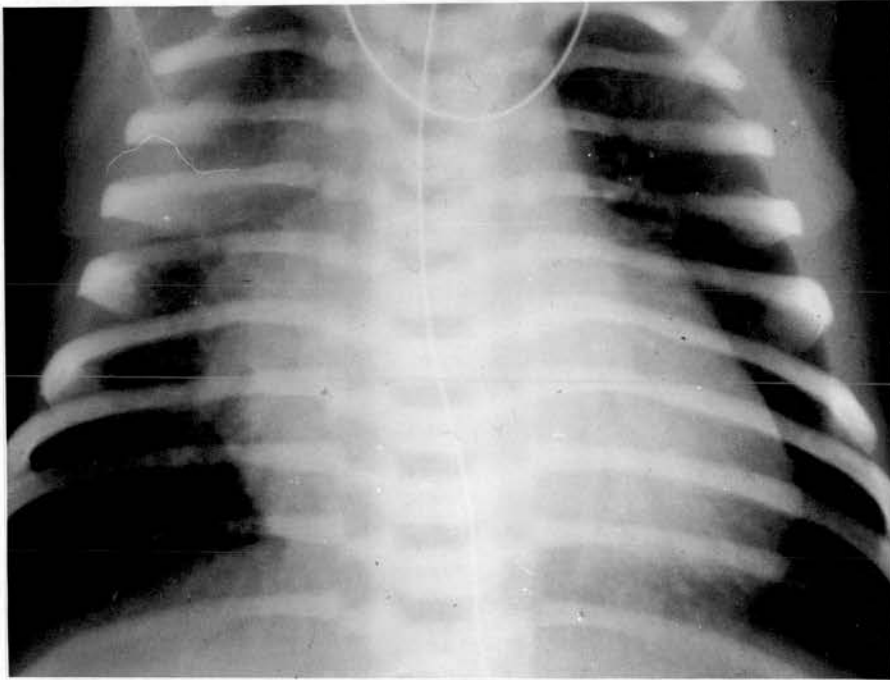
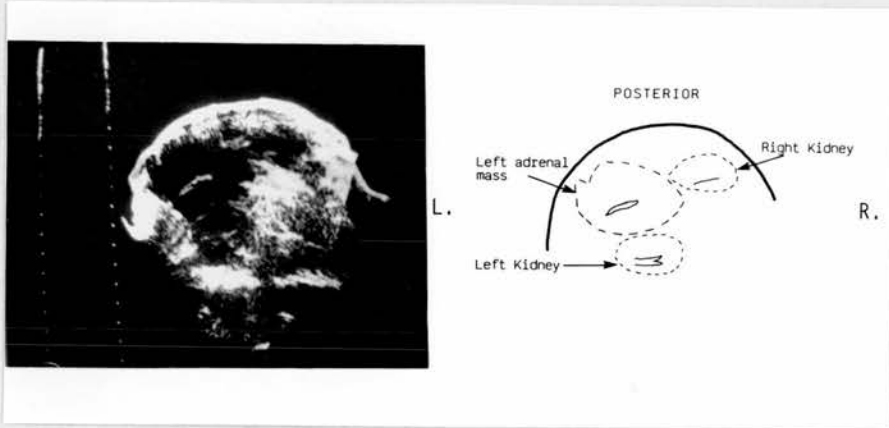


Figure 9,5

Case 34: Cardiomegaly and pulmonary oedema
secondary to severe intrapartum asphyxia.

(a)



(b)

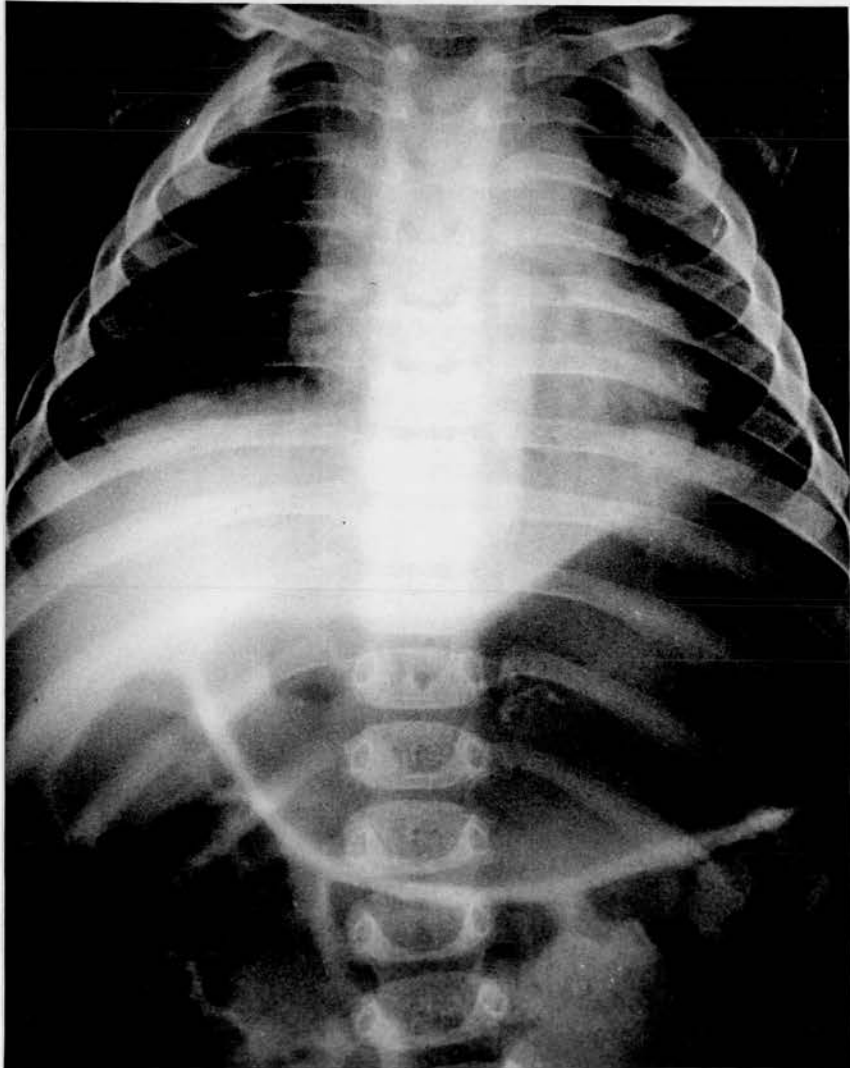


Figure 9, 6

Case 34: (a) left adrenal haemorrhage, ultrasound scan appearances at 5 days.

(b) left adrenal calcification, abdominal X-ray at 9 months.

Coagulopathy

Coagulation studies were not performed routinely in the study group. Nineteen infants had at least one coagulation screen performed, consisting of the measurement of prothrombin and partial thromboplastin times, platelet count, and fibrinogen and fibrin degradation product levels. These were performed on clinical grounds because of anxiety about poor general condition, bruising or bleeding. Four infants showed abnormal results; Case 27 had isolated low fibrinogen level, while Cases 22, 33, and 35, all of whom died in the early neonatal period following severe intrapartum asphyxia, developed disseminated intravascular coagulation.

Neonatal problems unrelated to birth asphyxia

Significant jaundice, indirect bilirubin level greater than 170 $\mu\text{mols/l.}$, occurred in 9 infants. In none was this severe, the highest indirect bilirubin achieved being 277 $\mu\text{mols/l.}$ Five infants were treated with phototherapy.

Major infection was a complication of the early neonatal period in 3 infants. Case 5 developed some signs of meningitis at 7 days of age with 780 white blood cells/cu.mm. and reduced glucose and elevated protein in the cerebro-spinal fluid, but without any positive bacterial or viral findings. Treatment was given with intrathecal and intravenous antibiotics. A further infant, Case 6, developed severe bacterial meningitis due to *Listeria monocytogenes* at the age of 10 days, 3 days after discharge from the neonatal nursery. Following major complications, with cardiac arrest and fits, this child has made uneventful, normal progress. Case 38 developed *E. coli* mastitis, urinary tract infection and septicaemia at 7 days and responded well to antibiotic therapy.

None of the study group was found to have any congenital malformation.

CHAPTER X

ELECTROENCEPHALOGRAPHIC AND POLYGRAPHIC FINDINGS

The value of E.E.G. recordings in the newborn infant with symptomatic birth asphyxia and with fits has been the subject of much debate; the place of E.E.G. abnormalities as predictors of long term outcome is controversial, (Harris, 1960; Torres, 1968; Monod, 1972; Sarnat, 1976).

Using the recording systems described in Chapter II, 41 infants had at least one polygraphic or E.E.G. recording. For practical reasons, it was not possible to perform the recordings at a set age, but each was performed as early as possible after the infant's admission to the study, usually in the first 3 days of life. Where the initial recording showed abnormality, or the infant demonstrated continuing abnormal neurological features, further recordings were made. Each infant who fitted had at least one E.E.G. recording; the findings have been described earlier, Chapter VII.

Of the 9 infants of the group, who did not have a recording made, 7 were born during the early part of the study before an E.E.G technician was available, while the remaining 2 infants died before a recording was performed.

The recording period was from 1 to 2 hours. One aim was to demonstrate E.E.G. patterns during different states, quiet wakefulness, active sleep and quiet sleep. During the recordings, observations of conscious level, movements, eye movements and changes of position were noted.

As described earlier, the recordings were made in the special care nursery and electrical interference from other equipment was commonly encountered /

encountered. Continued awareness of artefactual features from this and from infant movements was necessary. Polygraphic recordings were particularly valuable in allowing ready recognition of the nature of artefacts on the tracings. Sudden movements, such as a startle response during active sleep, sucking activity, and, in low amplitude E.E.G. recordings, E.C.G. or respiratory activity might be confused with epileptic bursts, (Figures 10,1; 10,2; 10,3; 10,4).

Sleep states with their described classical, clinical and polygraphic features were clearly displayed on some records. During quiet wakefulness, low amplitude rhythms were seen with variable eye movements and fairly regular respiration, (Figures 7, 23a; 10,5). In active, or stage I, sleep in the mature infant, the E.E.G. shows continuous, low amplitude, mixed frequencies with eye movements on a background of continuous E.M.G. activity, (Figure 10,6).

The establishment of quiet, or stage II, sleep is indicated by a pattern of bursts of higher amplitude activity on a low amplitude continuous background, episodic sleep activity or tracé alternant, with no eye movements, regular heart rate and respirations, and a featureless E.M.G. background activity, (Figure 10,7).

The term infant is expected to spend some 50% of sleep time in active sleep and 40% in quiet sleep, the remainder being occupied by indeterminate sleep where the features recorded do not fulfil the criteria for active or quiet sleep, representing, at times, transition between the two main sleep states, (Fenichel, 1980).

In practice, however, it proved difficult in many infants to demonstrate quiet sleep. This was not surprising in those who were irritable, unsettled and hyperactive, settled to sleep with difficulty and slept for brief periods. In addition to these infants, others also failed to show quiet sleep despite being recorded during prolonged periods of undisturbed sleep. Failure of organisation of sleep states with /

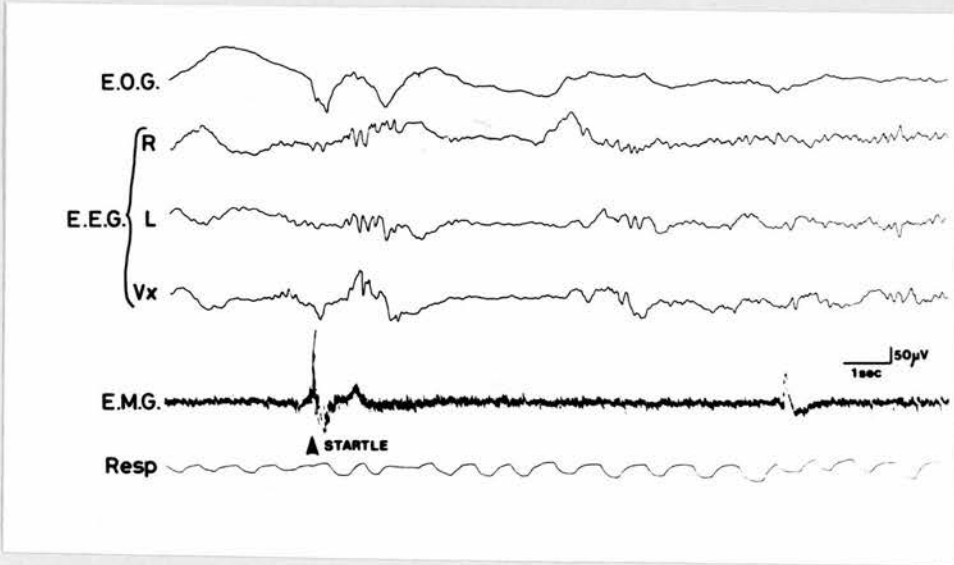


Figure 10, 1
Polygraphic recording - startle activity
shown on E.M.G. and E.E.G. (Case 27)

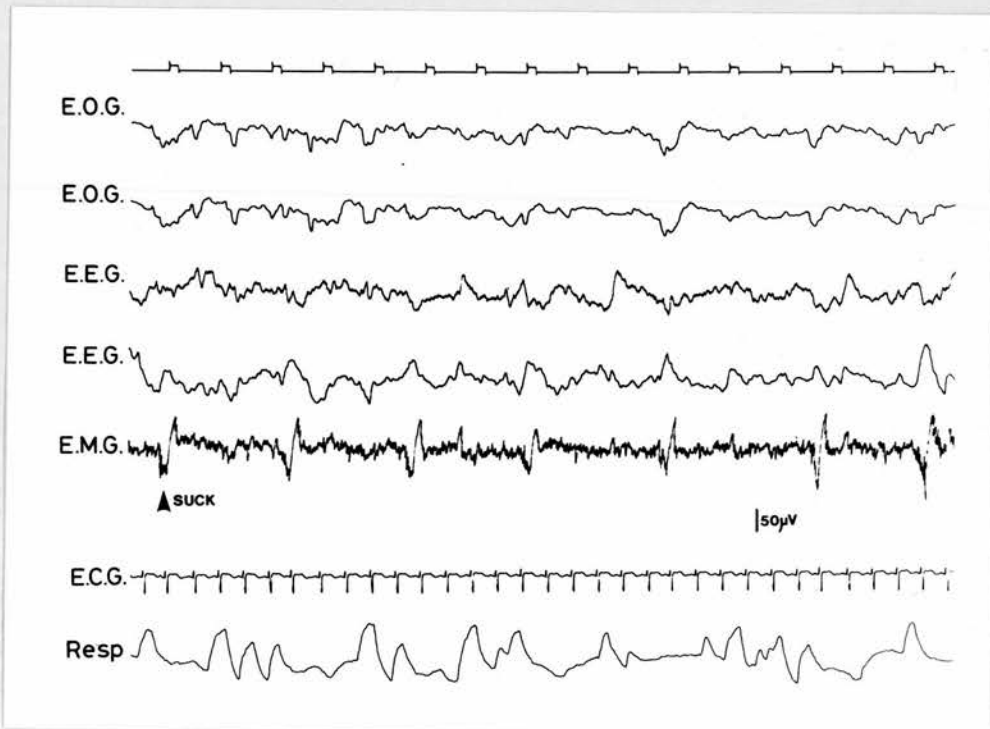


Figure 10, 2
Polygraphic recording - sucking activity on submental
E.M.G., suck artefact on E.E.G. (Case 13)

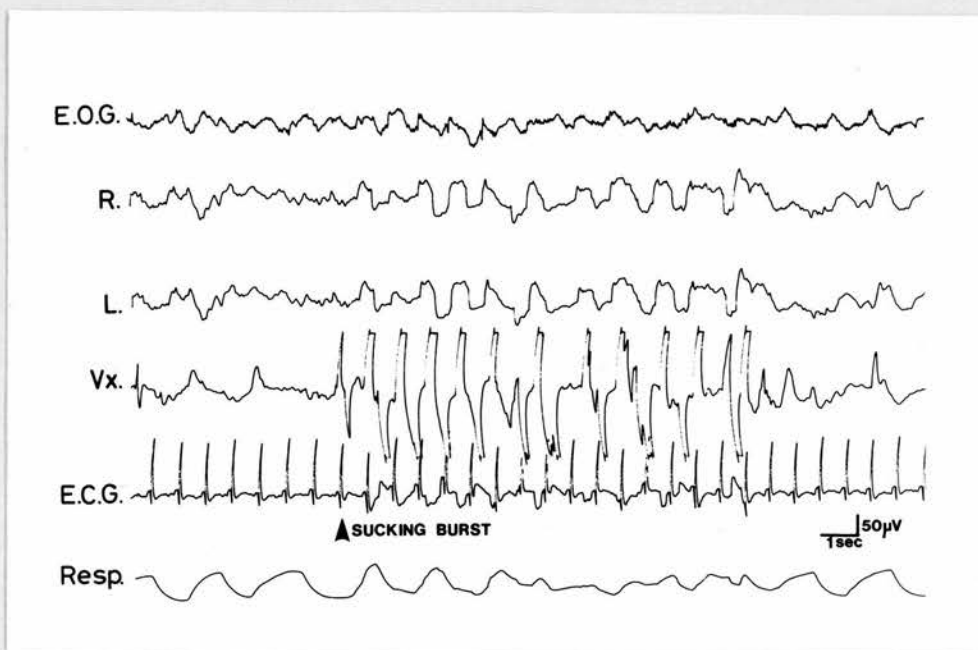


Figure 10, 3

Polygraphic recording, without E.M.G. lead
Sucking burst producing E.E.G. artefact. (Case 47)

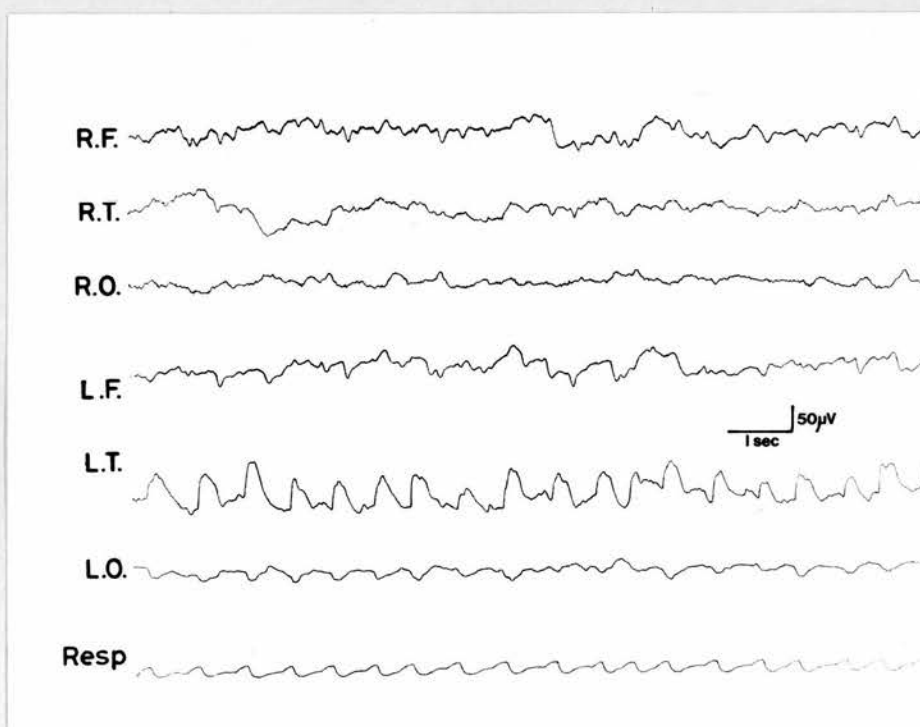


Figure 10, 4

E.E.G. with respiratory lead. Respiratory artefact
superimposed on abnormal, low amplitude E.E.G. (Case 34)

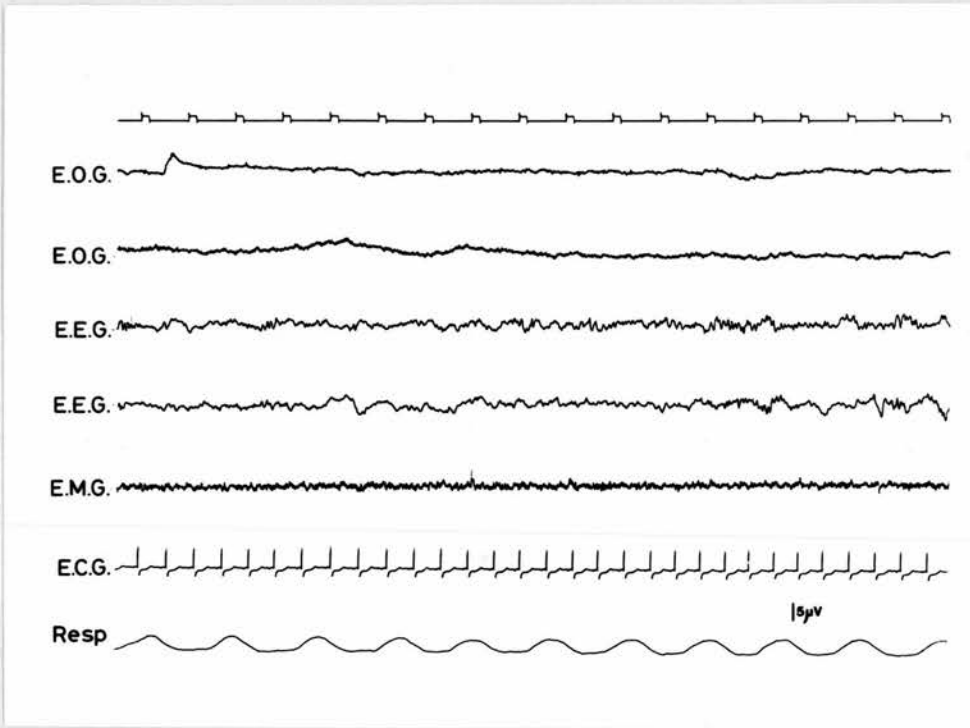


Figure 10, 5

Polygraphic recording, infant awake and quiet.
Low amplitude E.E.G., regular respirations, no
eye movements. (Case 45)

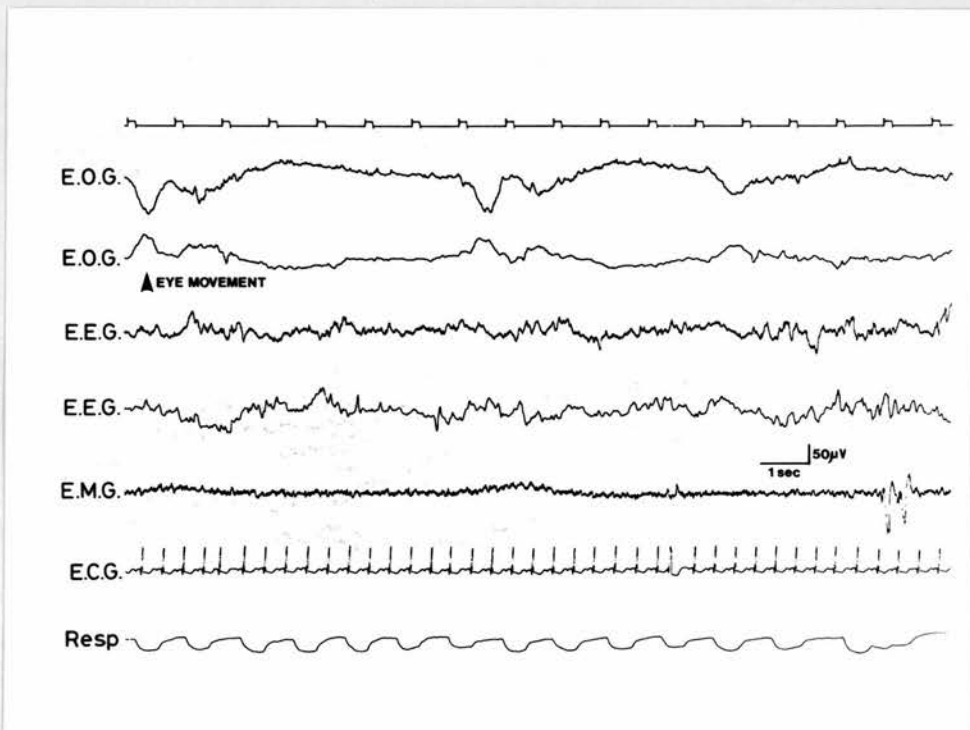


Figure 10, 6

Polygraphic recording, active sleep. Eye movements,
low amplitude, mixed E.E.G. activity, some respiratory irregularity
and some movement on low level E.M.G. background. (Case 46)

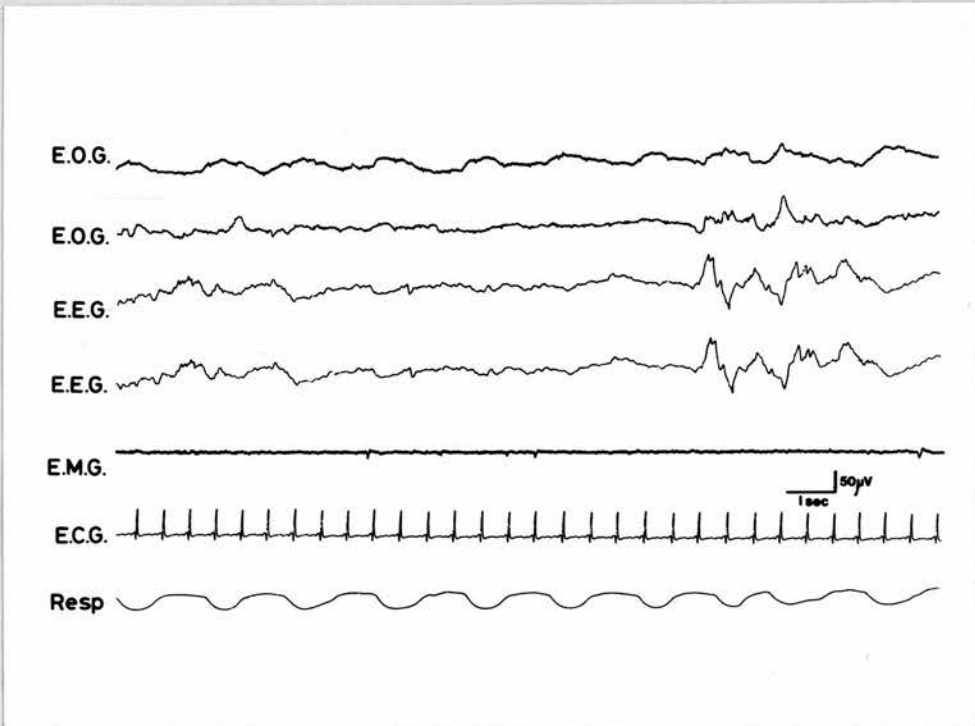


Figure 10, 7

Polygraphic recording, quiet sleep. Episodic sleep activity, no eye movements, regular respirations and E.C.G, low level E.M.G. (Case 46)

with their typical features was also seen, (Figures 10,8; 10,9), and the impression was formed that some infants seemed unable at this early stage to exhibit fully organised, sleep states, but without serial E.E.G. recordings and detailed analysis of time spent in definable sleep states, this remains only a preliminary impression.

Other abnormalities of sleep patterns occurred; Case 24, a 35 weeks gestation infant, who developed major apnoeic episodes over the early hours of life for which a period of assisted ventilation was required, showed lack of variability of E.E.G. patterns as the age of 18 hours, (Figure 10,10), with a continuing burst suppression pattern with superimposed delta activity, unaltered by stimulation of the infant, over a period of two hours. This may represent regression of E.E.G. activity to that usual for a more immature infant. In a second recording 23 hours later, (Figure 10,11), burst suppression had been replaced by abnormal, continuous slow waves with superimposed delta waves.

Figure 7,28, Case 28, also shows episodic sleep activity with delta waves, or premature ripples, a pattern typical of the premature infant rather than the infant at term.

Episodic sleep activity with excessive sharp waves was seen between 4 and 6 days of age in a number of infants at a time when their neurological state was improving, (Figure 10,12).

The E.E.G. findings in those infants who had fits has been described in Chapter VII. Apart from electroconvulsive foci, other asymmetries were seen. These appeared minor and of doubtful significance and were without clinical correlates, (Figures 10,13; and 10,14).

Severe, generalised E.E.G. abnormalities were uncommon. Following major asphyxial insults, 2 infants with gross neurological abnormalities showed marked reduction in E.E.G. amplitude. In Case 33, this amounted to /

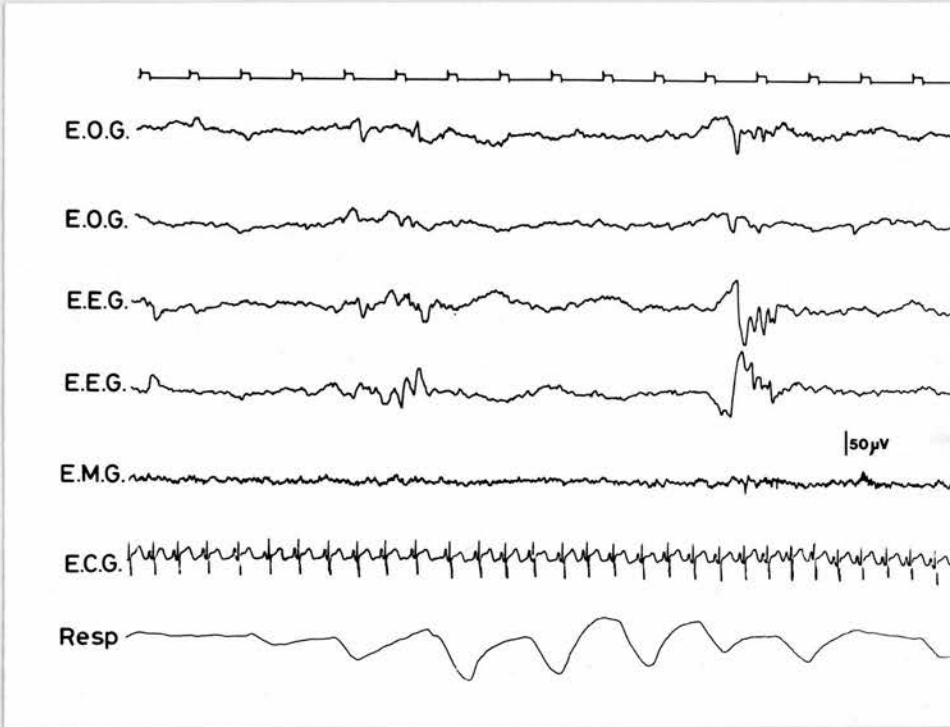


Figure 10, 8

Episodic sleep activity, but with irregular respirations. Inactive E.M.G, no eye movements. (Case 12).

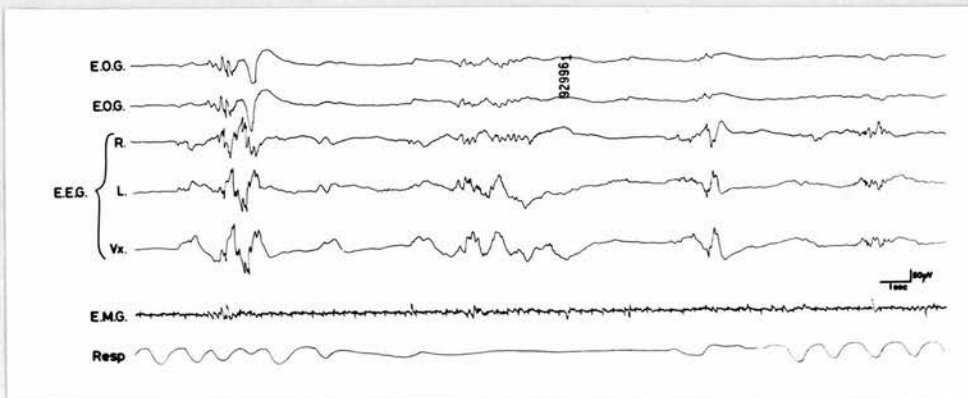


Figure 10, 9

Episodic sleep activity with periodic respirations (Case 43)

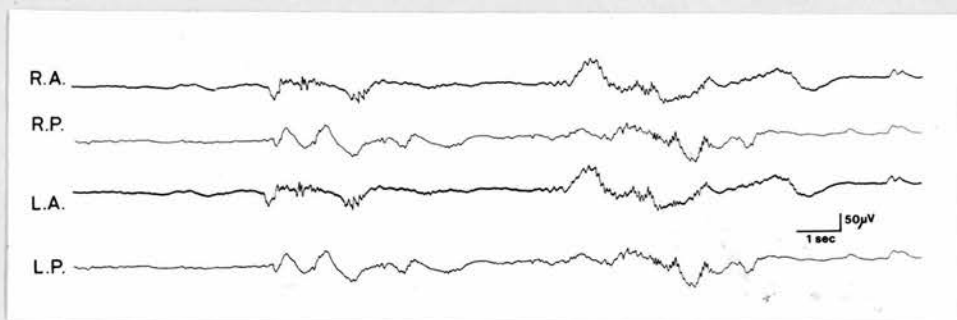


Figure 10,10

Case 24, 35 weeks gestation. Burst suppression E.E.G. which continued throughout 2 hour record at 18 hours of age.

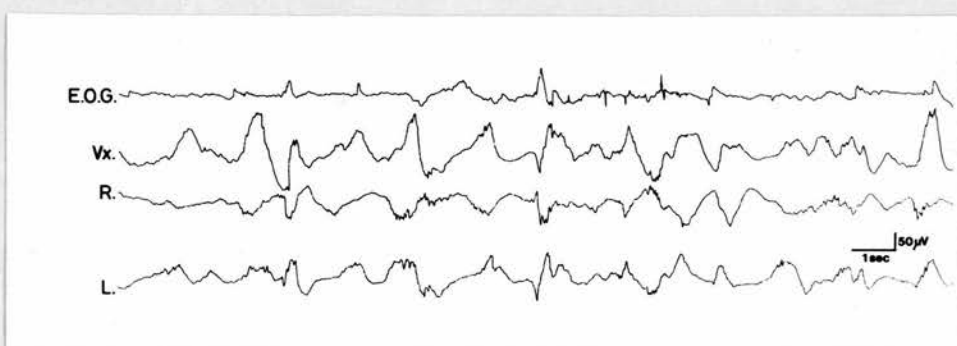


Figure 10,11

Case 24, same infant as Figure 10,10. E.E.G. at 41 hours, abnormal, continuous slow waves with superimposed delta activity.

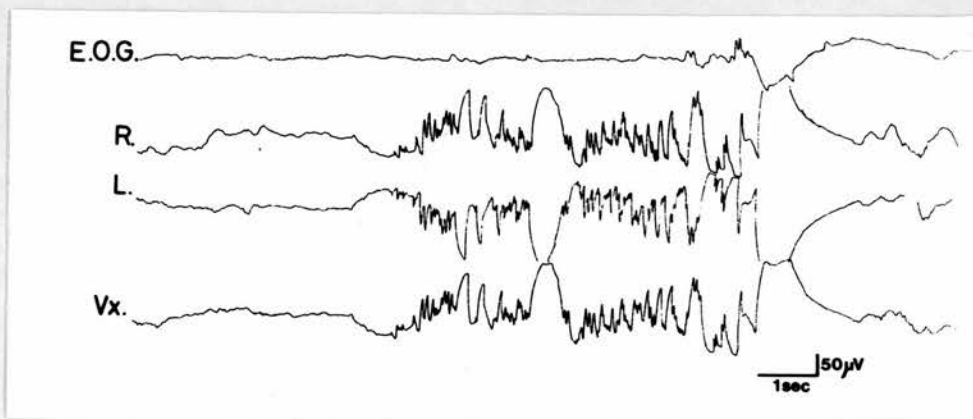


Figure 10,12

Episodic sleep activity with excessive sharp waves, low amplitude periods of suppression. (Case 28, at 6 days).

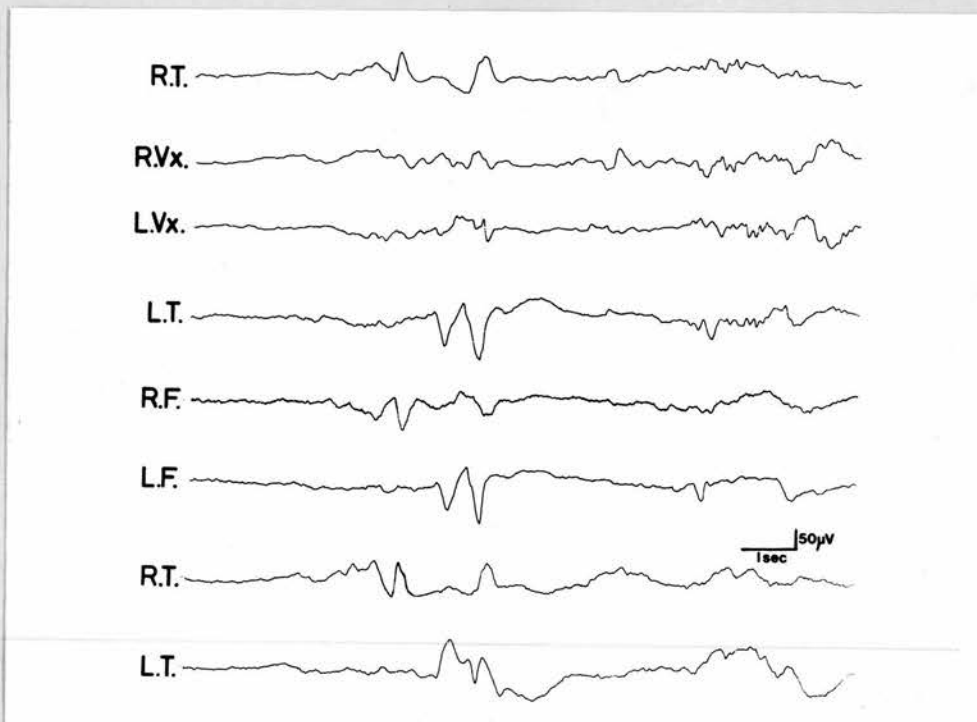


Figure 10, 13
Left temporal spike activity. (Case 5).

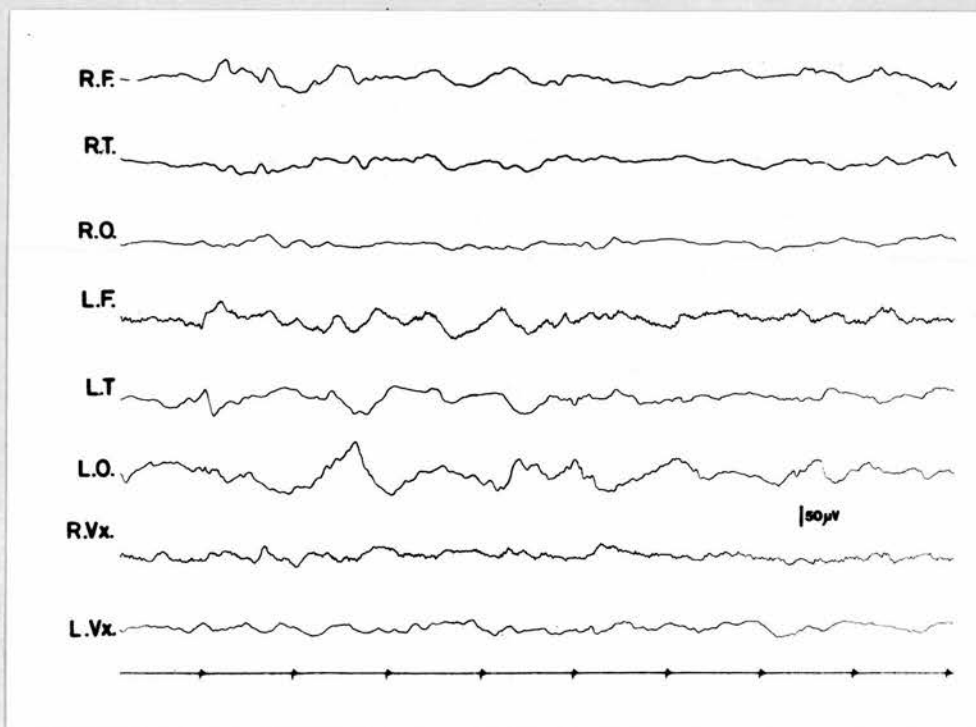


Figure 10, 14
Mild asymmetry - decreased amplitude right
temporal and occipital areas. (Case 38)

to E.E.G. silence, (Figure 10,15), and very low voltage activity in Case 34, (Figure 10,16). A later recording from this second infant at 16 days,(Figure 10,17), showed continuing low amplitude and this infant went on to develop a severe spastic quadriplegia, myoclonic seizures with a diffusely abnormal E.E.G.

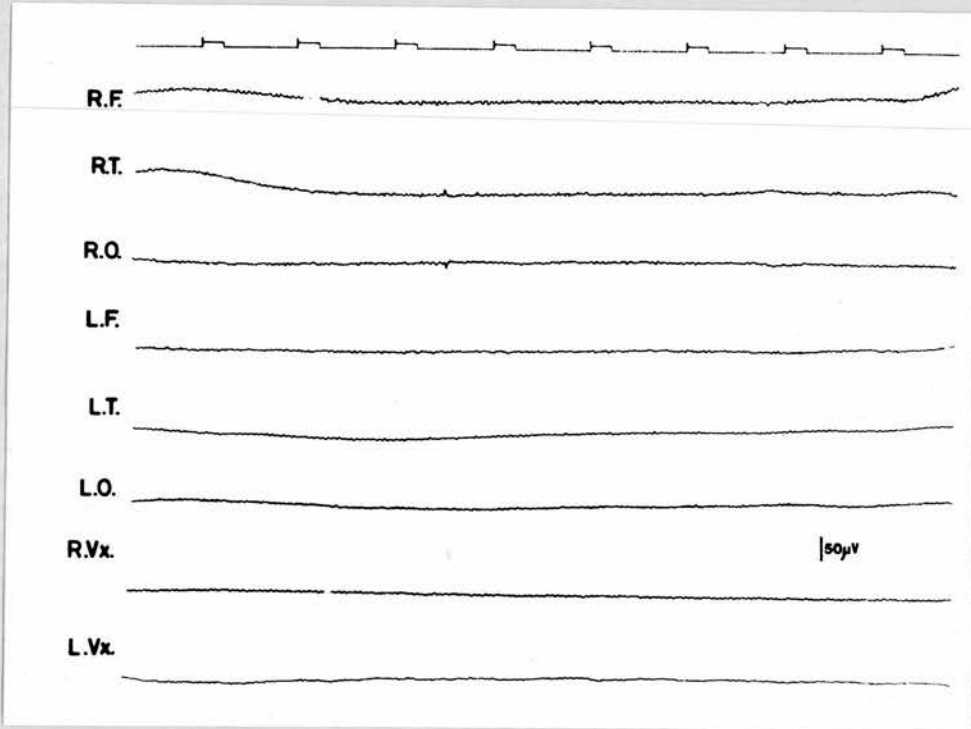


Figure 10,15

Case 33, at 36 hours, isoelectric E.E.G.
- child died at 48 hours.

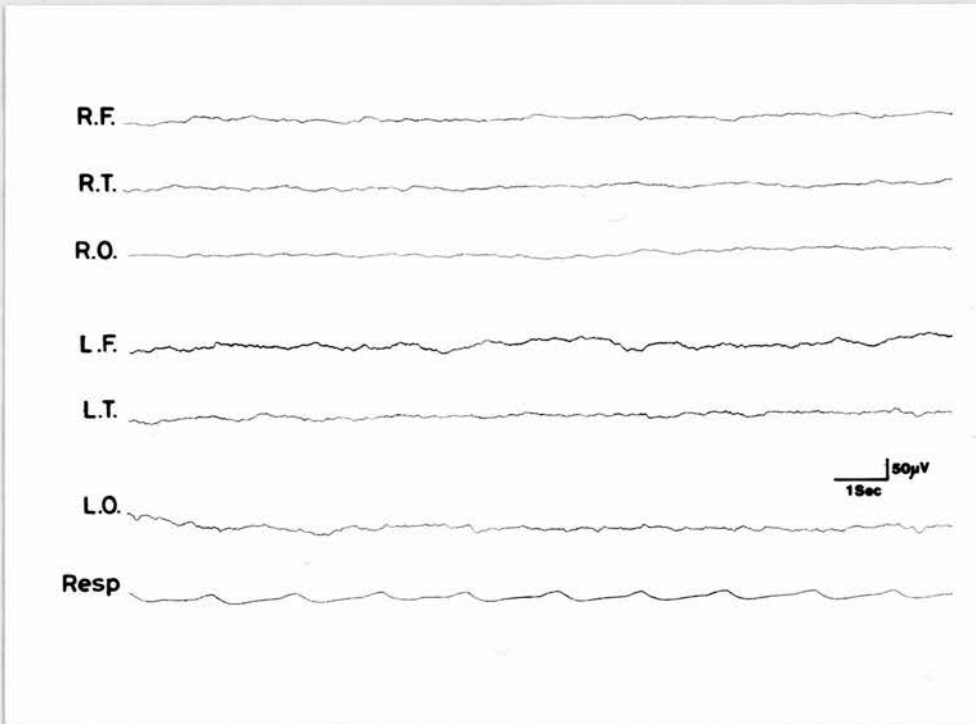


Figure 10,16

Case 34 - Very low voltage E.E.G. activity, 3 days old. Child developed spastic quadriplegia, died at 16 months

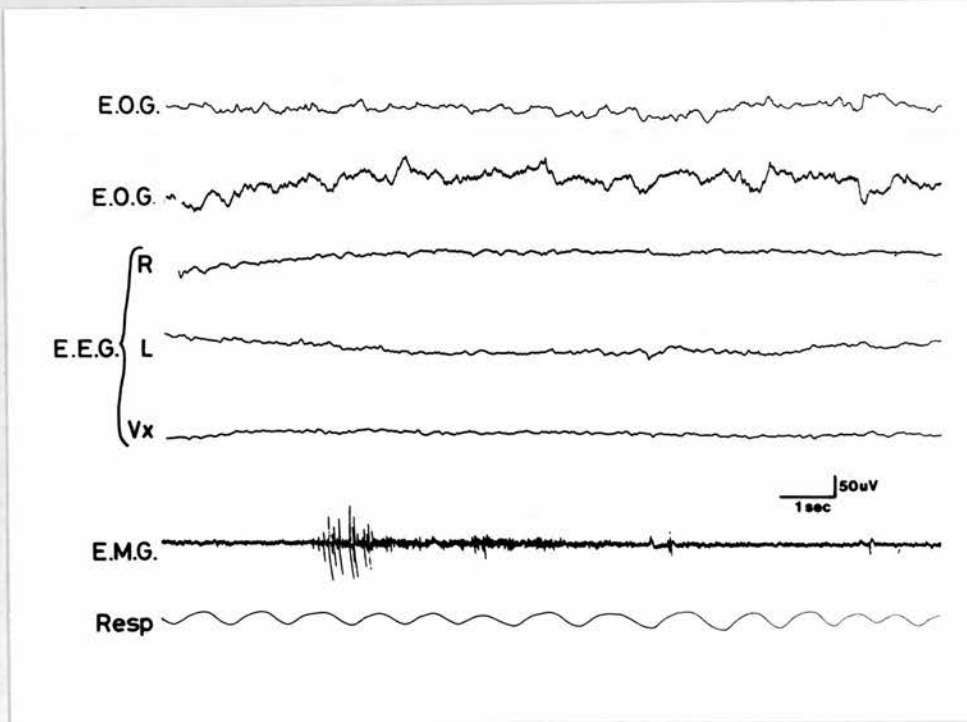


Figure 10,17

Case 34 - at 16 days old. E.E.G. remains low amplitude; active movements and sucking activity.

CHAPTER XI

PROGRESS OF THE STUDY GROUP CHILDREN
AFTER THE EARLY NEONATAL PERIOD

A brief account of the main findings at follow up has been given in Chapter III. The different aspects of the children's course over early childhood will now be described in more detail. Case summaries of all the children of outcome categories 2-5 and of others selected to illustrate points of interest are given at the end of this chapter.

Time of discharge from hospital

Forty-seven infants survived the neonatal period. Discharge home from hospital ranged from 6 to 35 days, mean age 12.8, S.D. 6.8; 70% of the infants were discharged home by 14 days of age. In general, the time of discharge reflected the severity and duration of neonatal problems from birth asphyxia, delay in discharge being due to continuing abnormalities of neurological state and performance such as failure to establish adequate oral feeding. There is a strong relationship between late discharge and subsequent abnormality, $p < 0.001$, Kendall rank correlation. Sixty-six per cent of those discharged home after 14 days, compared to 14% on or before the 14th day, were allocated subsequently to outcome categories 2, 3, or 4. If 3 infants discharged late because of reasons other than sequelae of birth asphyxia, i.e. meningitis, septicaemia/urinary tract infection, prematurity, are excluded, then 89% of these discharged home after 14 days were allocated subsequently to outcome categories 2, 3, or 4.

State /

State at time of discharge home and relationship to later findings

At the time of discharge, 14 of the 47 infants were considered to show abnormality of neurological findings or of performance. Details of these infants and their subsequent progress are summarised in Table 11,1. Five of the 14 later showed no abnormality, outcome category 1, and the age of their first, entirely satisfactory examination is also given. The 9 remaining infants showed persistent abnormalities, with the exception of one child, Case 28, whose progress in the first months of life was satisfactory, but whose later development has been mildly delayed in each area. Her home background is poor, her parents are of low ability, and these subcultural factors and her inherent potential are certainly important aspects of her slow development.

Four of the 33 children considered satisfactory at the time of discharge have shown abnormalities later; details are given in Table 11,2. Two have developed signs of a mild left hemiparesis of little or no functional significance and two have shown slow development in all areas, one with a satisfactory outcome and the other of low intelligence.

Each child with major physical or mental handicap has shown continuing abnormality from the neonatal period and at each stage of follow up, while mild developmental delay or mild asymmetries in some cases were not revealed till towards 1 year of age.

Late hypotonia

As noted in Chapter VIII, late hypotonia, i.e. hypotonia persisting more than 7 days after birth, was a finding in 11 infants. Over the ensuing weeks, the hypotonia improved to a pattern of appropriate tone in 4 cases, changed to a degree of extensor tone in excess of that expected /

Table 11,1

Case Number	Age at Discharge Days	Abnormalities at Discharge	Subsequent Findings
9	20	Hypotonia, bulbar incoordination	Slow motor development, mild ataxic diplegia
12	19	Hypotonia, lethargy.	Ditto.
13	17	Mild hypotonia, right hemi-syndrome	Normal at 4 weeks and subsequently
14	20	Mild hypotonia	Right hemiparesis from 4 months.
15	9	Mild left hemisyndrome	Normal at 4 months and subsequently.
20	14	Increased extensor tone and posture	Normal at 6 weeks and subsequently.
25	15	Hypotonia, underactive, mild asymmetry	Spastic quadriplegia, microcephaly.
28	15	Regression of muscle tone	Mild global developmental delay.
34	35	Slow feeding, lethargy, hypotonia	Spastic quadriplegia, bulbar palsy, died 16 months.
36	28	Brachial plexus palsy, Erb's palsy.	Persistent Erb's palsy, mild ipsilateral hemiparesis.
44	17	Slow feeding, underactive, hypotonia.	Severe dyskinetic cerebral palsy, retardation.
47	10	Mild regression of tone	Normal at 3 weeks and subsequently.
49	12	Hypotonia, athetosis.	Hypotonia, mentally retarded.
50	13	Mild right hemisyndrome	Normal at 3 weeks and subsequently.

Details of 14 infants who showed abnormalities at the time of discharge from hospital

Table 11,2

Case Number	Abnormalities demonstrated	Age at detection	Outcome category
3	Mild left hemiparesis, leg mainly affected	8 months	3
18	Global developmental delay, truncal ataxia	9 months	3
23	Delayed early development, hypotonia	12 months	2
40	Mild left hemiparesis	11 months	2

4 children considered satisfactory at discharge from hospital with subsequent problems.

expected for age - extensor dystonia, 4 cases, or the hypotonia persisted, 3 cases. Continuing hypotonia, Cases 14, 34, 49, was invariably associated with significant long term abnormality. Change to extensor dystonia, Cases 9, 12, 25, 44, was followed in each by signs of cerebral palsy of different forms - ataxic or spastic diplegia, or dyskinetic cerebral palsy, while the 4 infants who gained muscle tone appropriate to age fared better, there being no significant long term morbidity, Cases 13, 28, 36, 47.

Extensor dystonia

Extensor dystonia, an exaggeration of the physiological increase in extensor tone seen mainly between 6 weeks and 4 months of age, not uncommonly occurs in infants born prematurely and some of those who have had intrapartum and neonatal difficulties. Eleven infants of the study group, including the 4 referred to above with preceding late hypotonia, showed a phase of extensor dystonia. These 4 infants have been allocated to outcome category 4, while all the 7 infants without preceding late hypotonia have had an entirely satisfactory outcome, outcome category 1. There is a highly significant difference in outcome in those with and without late hypotonia preceding extensor dystonia, $p < 0.005$, Exact probability test.

Fits after the neonatal period

Of the 18 children who had neonatal fits, 5 have subsequently had fits, Cases 6, 25, 34, 39, and 50. Neonatal fits were secondary to intrapartum asphyxia in all but Case 6, who had fits in association with listeria meningitis at 10 days. Cases 25 and 34, both of whom suffered severe brain damage with spastic quadriplegia, had frequent myoclonic seizures in infancy. Cases 6 and 50 have had what appear to be febrile convulsions in association with intercurrent infections, but /

but it is too early to know whether they may be truly epileptic. E.E.G. recordings are normal. A further child, Case 39, who had a single clonic fit as a newborn, has had several reflex anoxic seizures following painful experiences. Her E.E.G. is also normal. No other children have had fits.

Behaviour disturbance in infancy and early childhood

(a) Infancy

Difficulties with aspects of their child's behaviour were reported by the parents of 15 children. In the first months of life, difficult infant behaviour poses a common and taxing problem for parents. Without a control group, it is not possible to estimate how far the study group children differ from the norm in this respect. Complaints that the infant was unsettled, demanding of attention, crying excessively, suffering from "colic", and sleeping poorly by day and night were common difficulties in management experienced at home. In 5 infants, this occurred in association with extensor dystonia and the parents observed that their child would thrust his legs into extension, while hyperextending the head and back, when upset. If such behaviour is related to continuing brain dysfunction then a relationship with subsequent neurological impairment might be expected and indeed a significant association exists between the occurrence of behaviour disturbance in infancy and subsequent abnormality in the study group, $p < 0.01$, Wilcoxon's rank sum test.

Demanding infant behaviour imposes considerable stresses on the parents. However, behaviour disturbance in the infant may be a manifestation of parental anxiety and stress, as well as a cause of it, and indicate some temporary failure of the relationship between the parents and their child. Following problems during birth and the early neonatal period, many parents would experience continuing anxiety about /

about their child, especially over the early months of life until there were clearer indications of their child's progress. This might be the case particularly in the first experience of parenthood, and, while 3 of the 8 children who displayed unsettled behaviour and subsequent abnormality were first children, 6 of the 7 children, who proved entirely normal later, were the first children of the family. This difference is not statistically different.

It would seem probable that behaviour disturbance in infancy in this group is due to a combination of the effects of the preceding stresses both on the child's brain and on the parents' level of anxiety.

(b) Early childhood

After the first year of life, behaviour problems remained common. Ten children showed a pattern of difficult, negativistic behaviour, being readily upset, prone to temper tantrums, stubbornness, poor cooperation with their parents, and other attention seeking devices. Sleep disturbance, either difficulty in settling in the evening, or waking during the night, was also common in this group and, in addition, was an isolated complaint made by parents of 3 other children. Seven of the 15 children, who had shown behaviour disturbance as infants, continued to present problems to their parents over the first years of childhood; four of these children have shown neurological abnormalities at follow up, but only 2 have significant abnormalities. None of the 8 children without preceding difficulties in infancy belong to outcome categories 2, 3, or 4. There is no statistically significant relationship between this later form of behaviour disturbance and the outcome for the children, suggesting that factors other than direct effects of intrapartum asphyxia were more important. It was apparent in some families that there were other reasons for the child's behaviour pattern. One child became overactive, restless, distractible and difficult from 2 to 3 years old following the birth of twin sisters. Other /

Other stresses, such as breakdown of two marriages, the problems of a single mother, unrealistic expectations of parents for their child, inconsistent or unrealistic approaches to child rearing and discipline were clearly related to the child's behaviour pattern.

Long term morbidity

Morbidity in the study group has been summarised in Table 2,1. Outcome categories 2 and 3 are often referred to as minimal brain damage. Six infants have been allocated to outcome category 4, significant handicap, and one of these children died at sixteen months. Two children, Cases 9 and 12, have minor disability consistent with essentially normal schooling and life with small limitations. The remaining three children, Cases 25, 44, and 49, survive with gross physical and mental handicap. There is some doubt as to the cause of this in Case 49, since, although there is good evidence of an intrapartum asphyxial insult and symptomatic neonatal asphyxia, the mother is mentally handicapped and a younger sibling of this child is backward, but to a much lesser degree. It may be that hereditary factors in this child are more important than intrapartum asphyxia.

Secular trend

It is felt that full identification of cases of symptomatic asphyxia, as defined by the admission criteria, was achieved over the initial 23 month period of case selection, 1976-77, and that comparison can, therefore, be drawn with figures from the maternity hospital for previous years, Table 11,3.

Table /

Table 11,3

	1968-1971	1972-1975	1976-1977
Definite handicap	1.6	0.4	0.5
Minimal brain damage	1.0	0.7	0.8
Total morbidity	2.6	1.1	1.3
Death	1.3	0.6	0.5

Mortality and long term morbidity from symptomatic, intrapartum asphyxia per 1,000 inborn, liveborn infants

Case histories

Case summaries follow of all infants allocated to abnormal outcome categories, i.e. 2-5; in addition, summaries are given of several other children to illustrate points of interest.

Case 3: tone pattern 5, outcome category 3.

Following episodes of antepartum haemorrhage at 17 and 29 weeks gestation from placenta praevia, this infant was delivered by Caesarean section when labour began prematurely at 36 weeks gestation. Brief resuscitation was needed at birth; Apgar scores were 5 at 1 minute, and 8 at 5 minutes. This infant was found to have a mild left hemisindrome, but otherwise normal flexor tone appropriate to gestation. She was tube fed for 48 hours because of depression of feeding reflexes and was treated with phototherapy for moderate jaundice, maximum indirect bilirubin, 233 μ mol./l. There was no disturbance of general, or biochemical homeostasis. Her condition was satisfactory at discharge from hospital and at early follow up. At 8 months, a mild left hemiparesis became apparent, mainly affecting the leg with a cavo-varus foot position, mild erythrocyanosis and asymmetrical phasic reflexes. Her parents /

parents expressed some difficulty with her unsettled behaviour in the first six months of life and mother, in retrospect, feels that she had difficulty in relating warmly to the child at that stage. Subsequently, there has been little limitation of function, her general progress is good and assessment has shown her to be of average abilities with mild developmental delay in visuo-motor skills.

Case 5: tone pattern 3, outcome category 1.

This infant was the second of twins. Pregnancy was complicated by mild pre-eclamptic toxæmia. X-ray before delivery had shown the infant lying with hyperextension of the head, Figure 8,14. Elective Caesarean section was performed at 38 weeks gestation and some difficulty was experienced in delivering the second twin. Condition at birth was good and no resuscitation was required. He was noted to have odd facial features, upper limb hypotonia and extension of the head. Behaviour became abnormal at 48 hours with a cyanotic attack and several multifocal clonic convulsions, mainly right-sided. There was generalised hypotonia, but no depression of brain stem function or disturbance of biochemical homeostasis. Lumbar puncture was clear. At the age of 5 days, behaviour became increasingly abnormal with marked head retraction and back arching. E.E.G. showed no abnormality. Despite treatment with phenytoin, the infant had a tonic fit followed by a further series of clonic fits at 7 days old. Repeat lumbar puncture showed an elevated C.S.F. white cell count, 780 cells/cu. mm., glucose 0.6 mmol./l., and protein 8.8. gms./l., but without organisms seen or grown on culture. Treatment was given with chloramphenicol and with gentamycin, intravenously and intrathecally; the C.S.F. changes resolved satisfactorily. The child fed well throughout and a variety of other investigations were negative. At the time of discharge home at 35 days, there was still marked head retraction and poor head control when pulled to sit or put in the sitting position. This gradually improved over the following months, but the child was noted to sleep with head retraction until the age of 3 years. Subsequent progress has /

has been entirely satisfactory and similar to that of the twin; intelligence is above average with no weaknesses.

Case 6: tone pattern 4, outcome category 1.

This is the first child of a young mother, who had been well during pregnancy. There had been a transverse lie until 37 weeks gestation. Labour was induced by rupture of the membranes at 41 weeks gestation, and enhanced initially by extra-amniotic prostaglandin and then oxytocin infusion. An epidural anaesthetic was given. First stage of labour was prolonged at 17½ hours with long standing signs of fetal distress: early decelerations going on to late decelerations in fetal heart rate 2 hours before delivery. Second stage of labour was 55 minutes. Apgar scores were 2 at 1 minute and 7 at 5 minutes, there being a good response to endotracheal intubation and I.P.P.V. and intravenous sodium bicarbonate and dextrose. The infant showed marked moulding of the head and was initially hypoalert with regression of muscle tone and irritability on handling. Tube feeding was given and muscle tone and activity recovered to appropriate flexion over the first 48 hours. Biochemical homeostasis was not disturbed and the infant was discharged home at 6 days, behaving satisfactorily. At 10 days, he was re-admitted to hospital with meningitis caused by listeria monocytogenes, having become acutely ill; he suffered tonic fits and respiratory and cardiac arrest shortly after admission to hospital. Treatment with antibiotics, intravenously and intrathecally, and hydrocortisone was given; assisted ventilation was required for 15 hours. He responded well and returned home at one month old. Subsequent progress has been good. At the age of 3 years, he had 2 separate episodes of grand mal convulsion with febrile illnesses. E.E.G. was normal and following a period of anticonvulsant prophylaxis, he has had no further fits. Intelligence is low average with mild visuo-spatial motor incoordination.

Case /

Case 9: tone pattern 2, outcome category 4.

After an uneventful pregnancy, the membranes ruptured spontaneously at term in hospital and the umbilical cord prolapsed. Delivery was achieved rapidly by Caesarean section, but condition at birth was poor, Apgar scores 1 and 4 at 1 and 5 minutes. Endotracheal intubation and I.P.P.V. and external cardiac massage were performed, and intravenous sodium bicarbonate and dextrose given. Gasping respirations started at 7 minutes and regular respirations at 17 minutes. Initially, in the nursery, the child was flaccid and apathetic with gasping respirations. Tonic extensor convulsions started at 5 hours and the infant changed to become agitated, very irritable with marked extensor hypertonus, cycling and "doggy paddling" movements. Treatment with phenytoin, phenobarbitone and dexamethosone was given and fluid intake restricted. Intravenous mannitol, 7 ml./Kg.20% solution, was given without apparent effect. Plasma biochemistry and coagulation screen were normal. Cerebro-spinal fluid was clear, but with an elevated creatine kinase level of 4.0 i.u./l. (range 0.7 - 2.0 i.u./l). By the third day, the infant had become hypotonic and apathetic with depression of bulbar reflexes but retention of eye movements. Anticonvulsant blood levels were satisfactory. Despite regular oral suction, physiotherapy and withdrawal of gastric feeding, the tendency towards pooling of pharyngeal secretions led to an orthostatic pneumonia. She remained apathetic, with episodes of bradycardia to 80 beats/minute, but gradually improved over the next 10 days. Oral feeding was established by 15 days. Plasma biochemistry was carefully monitored and remained normal apart from mild hyponatraemia, plasma sodium 130 mmols./l. and plasma osmolality 278 mosmols./l., at 7 days. Following mild late hypotonia, she showed mild extensor dystonia, maximal at 4 months. Feeding was satisfactory, but there were some signs of continuing bulbar incoordination over the early months of life with pooling of saliva, dribbling, gurgling and two episodes of chest infection. Barium swallow X-ray and other investigations were normal. Early motor development was mildly delayed and there were clear signs of an ataxic diplegia towards the end of the first year. She walked independently at /



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at 18 months and gait at 6 years is mildly incoordinate and broadly based, legs are hypotonic and plantar responses extensor. Manipulation is mildly clumsy, intelligence low average and she attends normal school with some extra help.

Case 12: tone pattern 1, outcome category 4

This infant is the second of twins diagnosed at 32 weeks gestation. Parents had married during the pregnancy. The pregnancy was uneventful apart from hydramnios and threatened premature labour at 35 weeks gestation. Delivery was by emergency Caesarean section at 36 weeks because of fetal distress in labour, the first twin showing bradycardia and late decelerations of heart rate. Twin I was in good condition at birth and has had no subsequent difficulties. Twin II was depressed at birth; Apgar scores 1 at 1 minute, 6 at 5 minutes. Endotracheal intubation and I.P.P.V. were given for 5 minutes along with intravenous sodium bicarbonate and dextrose. There was gasping in addition to regular respirations over the first hour. Blood gas analysis, shortly after birth, showed a severe metabolic acidosis. Initially, the infant was hypotonic and hypoalert with depressed feeding reflexes, but irritable with a cerebral cry on handling. At 7 hours, there was an apnoeic episode related to hypoglycaemia. She remained hypotonic with regression of posture and tone, depression of feeding reflexes, but without a bulbar palsy or ophthalmoplegia. Tube feeding was continued for 5 days. She was discharged home at 19 days, feeding satisfactorily but still hypotonic in comparison to the twin. Early behaviour was unsettled with crying and irritability especially in the evenings and at night. Her mother initially was anxious and depressed, in need of continual support. The child developed mild extensor dystonia and motor development was delayed with signs of ataxic diplegia. She sat unsupported at 10 months, moved about by rolling at 1 year and later crawled and "walked" on her knees. After a long period of walking with support, she walked independently at 3 years. She remains ataxic, with a clumsy, broad based gait, is unable to stand on one leg or /

or jump, but has little disability for most activities. Manipulation is poorly coordinated but effective. Assessment at 4½ years has shown an I.Q. of 80, similar to the twin brother, and relatively poor visuo-motor function. She attends normal school with extra help.

Case 13: tone pattern 2, outcome category 1

After an uncomplicated pregnancy, there was spontaneous onset of labour at 39 weeks gestation; delivery was by spontaneous vertex. Pethidine had been given 90 minutes before birth, early decelerations in fetal heart rate were detected 1 hour before birth, and there was some difficulty with shoulder dystocia during the second stage of labour, although this stage lasted only 10 minutes. Resuscitation was given with I.P.P.V. and intravenous bicarbonate, dextrose, and lethidrone. Apgar scores were 2 at 1 minute, 3 at 5 minutes, and 6 at 10 minutes. Over the first hour, the infant was tachypnoeic, pale with poor peripheral circulation, but a systolic blood pressure of 80 mm.Hg. Conscious level and muscle tone were reduced. Blood gas analysis showed a mixed respiratory and metabolic acidosis. Muscle tone quickly increased and by one hour of age there was marked extensor hypertonus and the onset of tonic extensor fits, cycling movements and spontaneous sucking bursts. Blood gas analysis then showed evidence of central hyperventilation with reduced capillary pCO_2 levels. Treatment with intravenous diazepam, dexamethasone, phenobarbitone and phenytoin was given and fluid intake restricted. Coagulation screen and lumbar puncture were normal and E.E.G's at 18 hours and 4 days showed no abnormality. Plasma biochemistry was satisfactory apart from mild hypocalcaemia at 24 hours of age. This child showed depression of feeding reflexes, without a full bulbar palsy or ophthalmoplegia, and was tube fed until 6 days old; in addition, there was a mild right hemisyndrome which persisted until 1 month old. Extensor hypertonus gradually gave way to mild hypotonia by 6 days of age and this and the mild hemisyndrome were persisting at the time of discharge at 17 days; assessment at 4 weeks, however, was satisfactory.

Behaviour /

Behaviour in infancy and early childhood has presented no problems and general progress has been good. At 4½ years, assessment showed low average abilities with no specific weaknesses, in keeping with expectations for the family.

Case 14: tone pattern 2, outcome category 3

The pregnancy was uneventful until a type I placenta praevia became revealed in labour at term with a large intrapartum haemorrhage. The fetal heart rate slowed and became undetectable. Following emergency Caesarean section, the infant was pale, flaccid and pulseless. Endotracheal intubation, I.P.P.V. and external cardiac massage were performed and a slow heart rate returned within one minute. Dextrose and sodium bicarbonate were given intravenously and spontaneous respirations started at 7 minutes. 100 ml. blood was transfused over the first hours of life. Blood gas analysis showed a severe metabolic acidosis, which was then corrected. Neurological state changed from severe hypotonicity and unresponsiveness, to extensor hypertonus with tonic extensor fits, cycling movements, fisting and bursts of spontaneous sucking by one hour of age. There was evidence of central hyperventilation. Dexamethasone, diazepam, and phenytoin were given and fluid intake restricted. Coagulation screen was normal. Acute renal failure became apparent over the first 24 hours of life with severe oliguria, fluid retention, rising blood urea and passage of urine containing blood, protein and renal tubular cells, Figure 9,3. There was no response of urine output to mannitol or frusemide. Diuresis started on the third day and was met by increased fluid intake. Blood urea rose to a maximum of 21.5 mmols./l. Mild hyponatraemia, plasma sodium 130 mmols./l., was found between days 2 and 4 with associated hyperphosphataemia. Renal function has shown full recovery at later assessment. Late hypotonia started at 7 days, initially accompanied by episodes of mild bradycardia. Mild hypotonia persisted at the time of discharge at 20 days and this continued over the first 3 months. Asymmetry of the Moro reflex was noted at this time/

time and by 4 months there were early signs of a right hemiparesis. This has proved mild; right hand function is poorly coordinated, but over all there is no manipulative disability and no functional impairment of the leg. Her general progress has been excellent and she attends normal school.

Case 18: tone pattern 4, outcome category 3

Because of mild pre-eclamptic toxæmia, labour was induced at 38 weeks gestation and delivery was by Keilland's forceps. There was fetal tachycardia for 3 hours before birth and second stage of labour was prolonged at 55 minutes. Apgar scores were 6 at 1 minute and 8 at 5 minutes; no resuscitation was required. The head was very moulded. Initially, the child was apathetic and hypotonic, showing regression of posture to a 34 week gestation level, but with normal feeding activity. Dexamethasone was given over the first four days and fluid intake restricted. Muscle tone returned progressively and by 48 hours the child was appropriately flexed, but irritable. Plasma electrolyte levels remained normal apart from early hypocalcaemia, plasma calcium 1.56 mmols./l., from days 3 to 5. It was felt that this child had suffered a degree of acute compressional head injury and intrapartum asphyxia. Progress over the first months was satisfactory, but by 6 months the parents were concerned that the child was too contented, placid, disinterested and showing little voluntary manipulation. He sat unsupported at 9 months, and walked independently at 21 months. Speech development has been more delayed. He shows signs of a mild truncal ataxia, but, more significantly, global developmental delay and will require special education. His parents have experienced great difficulty in accepting the child's problem, have responded by keen efforts to stimulate and encourage him, but have met with disappointment, frustration and behaviour disturbance in the form of temper outbursts, aggression towards them and anti-social, attention seeking devices.

Case /

Case 22: tone pattern 1, neonatal death

This infant was the second of twins. Pregnancy had been complicated by mild hypertension and, following the spontaneous onset of labour at 38 weeks gestation, the umbilical cord of this infant prolapsed after birth of the first twin. Delivery was effected by breech extraction under general anaesthesia. Fetal heart activity was undetectable and the child lifeless at birth. Following resuscitation with external cardiac massage and I.P.P.V., heart activity returned at two minutes, but spontaneous respirations were not established until 50 minutes - some 10 minutes after resuscitative efforts had ceased. After a period of complete flaccidity, the child showed gross neurological abnormality with signs of decerebration, bulbar palsy, ophthalmoplegia and peripheral nervous system excitability with exaggerated flexor withdrawal responses, spontaneous clonus, increased tendon reflexes and also myotactic responses. Respiration was regular with superimposed gasping and, later, periods of apnoea, Figures 7,10, 7,11. There was then loss of neurological activity, major apnoeic periods and death at 25 hours of age. At post mortem examination, there was brain softening, some dilatation of the heart, haemorrhages in the gastric mucosa, and interstitial and intra-alveolar pulmonary haemorrhage.

Case 23: tone pattern 4, outcome category 2

This infant's mother was given prednisolone in late pregnancy for idiopathic thrombocytopenic purpura; pregnancy was otherwise straightforward. Delivery was by spontaneous vertex after labour had been induced at 42 weeks gestation. There was no sign of fetal distress by traditional means during labour, but second stage was prolonged at 70 minutes. Condition at birth was fair, Apgar scores 5 and 9 at 1 and 5 minutes, the infant responding to I.P.P.V. by bag and mask. There was moderate moulding of the head, mild regression of muscle tone and a transient left facial weakness. Normal flexor tone was gained by 36 hours, there was no feeding depression and biochemical homeostasis was /

was undisturbed. Condition was satisfactory at discharge home at 7 days, but subsequently she has shown mild motor delay in association with hypotonicity, most markedly of the legs. She sat unsupported at 8 months and walked independently at 19 months, having achieved mobility earlier by rolling and by shuffling on her bottom, and latterly cruising. Speech therapy has been arranged for developmental speech delay. Assessment at 4½ years has shown her to be of low average abilities with no specific weaknesses; this is in keeping with her family expectations.

Case 25: tone pattern 2, outcome category 4

The pregnancy was uncomplicated and delivery was planned for a G.P. unit. The first twin had been delivered and oxytocin given to the mother before the presence of twins was recognised. Delivery of the second twin was by breech extraction under general anaesthesia some 30 minutes later. The fetal heart beat had become undetectable; the child was lifeless at birth, but responded to resuscitation with Apgar scores of 1 at 1 minute and 5 at 5 minutes. Over the first hour, there was gasping in addition to regular respirations and by two hours the infant had changed from being profoundly hypotonic, unresponsive with bulbar palsy and ophthalmoplegia, to a state of disinhibition with screeching, agitation, extensor hypertonus with tonic fits, consisting of limb extension, head retraction, and back arching, and very strong reflex responses - flexor withdrawal, rooting, sucking, and asymmetrical tonic neck reflexes. Phasic reflexes were exaggerated and ankle, hamstring and jaw clonus easily elicited and sustained. Blood gas analysis indicated central hyperventilation. Despite vigorous anticonvulsant therapy with diazepam, phenobarbitone and phenytoin, there were numerous tonic fits until 36 hours of age. At this time, the infant changed to hypotonia, unconsciousness with little response to stimulation, and ophthalmoplegia with no bulbar reflexes. Phenytoin and barbiturate levels at 48 hours were not excessive. She remained drowsy over the first ten days, tone gradually improving /

improving and oral feeding was introduced at 8 days. Plasma electrolytes, with the exception of calcium remained normal; hypocalcaemia was found between day 2 and day 5. Fluid intake was carefully regulated and dexamethasone given over the first 4 days. At the time of discharge at 14 days, feeding was satisfactory and there was regression of tone to a 35 weeks gestation level. The family moved to another part of the country and by the age of six months, when they returned to South America, the child was showing signs of a spastic quadriplegia, microcephaly and myoclonic seizures.

Case 28: tone pattern 2, outcome category 2.

This is the first child of a young, single mother, who had been well during the pregnancy apart from proteinuria with normal blood pressure in the last weeks. Labour began spontaneously at 42 weeks gestation. First stage lasted 10 hours; there was fetal tachycardia during a prolonged second stage of 160 minutes. Delivery by Keilland's forceps was unsuccessful and Caesarean section was performed. Condition at birth was fair; Apgar scores were 5 at 1 minute and 9 at 5 minutes. The child had 2 cyanotic episodes spontaneously in the first hours of life and, on examination, showed marked moulding of the head, regression of posture at rest, but extensor hypertonus on handling. There were increased extensor reflexes and positive snout and perineal reflexes, but otherwise she was neurologically intact. She was irritable over the first 48 hours, with persistent vomiting over the first day, changing to mild hypotonia with regression of muscle tone at 48 hours. On the fifth day, she demonstrated brain stem fits and unstable neurological features with inconsistent asymmetries and episodes of eye deviation, facial twitchings and sucking bursts. There was apathy and some depression of feeding activity. Echoencephalogram was midline, and subdural taps and lumbar puncture negative. Plasma biochemistry was normal apart from mild hypocalcaemia, plasma calcium 1.82 mmols./l. E.E.G. demonstrated variability and abnormal features, illustrated in Chapter VII (Figure 7,28), with unusual episodic sleep activity /

activity for a mature infant, a right sided, electroconvulsive focus and a period of disorganised slow wave activity. The fits were controlled with diazepam and phenytoin. At the time of discharge at 15 days, there was persisting late hypotonia. Early development was satisfactory, but, from 6 months, there has been mild delay in all areas. This child is from a very poor, family background, and it may be that her slow progress largely reflects this.

Case 33: tone pattern 1, neonatal death

This infant was born after an uncomplicated pregnancy by emergency Caesarean section at 41 weeks gestation, there having been signs of severe fetal distress with meconium-stained liquor for some hours in the first stage of labour going on to late decelerations in fetal heart rate and severe fetal acidosis, pH 6.9, shortly before delivery. Condition at birth was poor, assisted ventilation was given for the first five minutes and again at 30 minutes, for 45 minutes, because of the recurrence of apnoea and bradycardia. Blood gas analysis showed a severe metabolic acidosis. Chest X-ray appearance was in keeping with meconium aspiration. Initially, the child was flaccid, unresponsive with absent reflex responses. By 3 hours of age, there were signs of release of spinal activity, producing a partially flexed posture, (Figure 8, 11), absence of brain stem responses with ophthalmoplegia, upward deviation of the eyes, and bulbar palsy. At 5 hours, she started to have tonic extensor fits with apnoea and cyanosis; these were resistant to treatment with phenytoin, phenobarbitone and paraldehyde and further ventilatory support was required. Hyponatraemia, plasma sodium 128 mmols./l., was found from 6 hours and coagulation studies were abnormal, with reduced fibrinogen level, prolonged partial thromboplastin and prothrombin times and, subsequently, elevated fibrin degradation products. There was partial correction following cryoprecipitate infusion. General condition continued to deteriorate with flaccidity, unresponsiveness and absent brain stem responses and the child died at 48 hours. Post mortem examination showed brain stem /

stem softening, pulmonary, renal and gastric haemorrhages, areas of hepatic infarction and focal renal tubular necrosis.

Case 34: tone pattern 2, outcome category 4.

This infant was delivered by Keilland's forceps with rotation because of occipito-transverse position with fetal bradycardia, labour having been induced at 41 weeks gestation and stimulated with oxytocin. First stage of labour lasted 2½ hours, second stage 25 minutes. The cord was round the infant's neck and no heart beat was present at birth. With external cardiac massage and assisted ventilation, heart action had returned by 1 minute and gasping respirations commenced at 8 minutes, although adequate spontaneous respirations were not established until 30 minutes. Apgar scores were 1, 2 and 5 at 1, 5 and 10 minutes respectively. By 2 hours, initial flaccidity had changed to extensor hypertonus with marked irritability, obligatory asymmetrical tonic neck reflexes, spontaneous Babinski responses, ankle and jaw clonus, and absent doll's eye and bulbar reflexes. There were numerous fits, tonic convulsions and, later, multifocal clonic fits with a right hemisindrome. Blood gas analysis showed severe metabolic acidosis. Phenobarbitone, phenytoin and diazepam were given to control fits, fluid intake controlled and dexamethasone administered. Plasma biochemistry, coagulation studies, and echo-encephalogram were satisfactory. Cerebro-spinal fluid was grossly clear, but lactate and creatine kinase levels were elevated. On the third day, there was major deterioration with tachypnoea, tachycardia, poor peripheral perfusion, decreased spontaneous movement with extensor hypertonus and further tonic fits. There was recurrence of severe metabolic acidosis with low pCO_2 . Chest X-ray suggested pulmonary oedema with cardiomegaly, (Figure 9, 5). Subdural taps were negative. There was some improvement following frusemide, correction of the acidosis, maintenance of paO_2 and antibiotic therapy, but the infant went on to develop hepatomegaly, signs of acute renal failure with uraemia, oliguria, haematuria and proteinuria, and also a left loin/

loin mass, subsequently demonstrated to be due to adrenal haemorrhage, (Figure 9,5). Metabolic acidosis recurred and investigations of possible organic acidaemias, or other primary metabolic disease were negative. An exchange transfusion was performed on day 4 with some improvement of the metabolic disturbances. Neurological state changed to severe hypotonia with persisting bulbar palsy and ophthalmoplegia and this only improved very slowly. By day 7, there was some return of spontaneous movement, weak gag and suck reflexes, eye movements, and primitive reflex responses. Some oral feeding was introduced by day 12 and naso-gastric feeds stopped by day 16. E.E.G. recording at day 3 showed very low amplitude activity, (Figure 10,16), and this persisted at day 16, (Figure 10,17). Neurological state remained abnormal at the time of discharge home, 35 days, although until 3 months of age this was not gross - hypotonia, slow feeding, reduced responsiveness. Thereafter, there were increasingly clear signs of major problems with disturbed behaviour - irritability, inconsolability, sleep disturbance, feeding difficulty, slow head growth, hypotonia, persistence of primitive reflexes and minimal awareness. E.E.G. was disorganised and grossly epileptic and there were myoclonic seizures from 10 months of age. The child died at 16 months secondary to aspiration of feed and respiratory infection. Post mortem examination was not performed.

Case 35: tone pattern 1, neonatal death

A previous child had been delivered by classical Caesarean section. In this pregnancy, there were threatened abortions at 19 and 24 weeks and, while the mother was in hospital for rest at 32 weeks gestation, she developed acute abdominal pains and hypotension. The fetal heart was undetectable and, at laparotomy, rupture of the uterus was found with the infant lying free in the peritoneal cavity. The baby was apparently stillborn, but after 5 minutes of resuscitation with external cardiac massage, I.P.P.V., and intravenous dextrose and bicarbonate, heart activity restarted. She was transferred to the nursery /

nursery, having assisted ventilation. There was a severe mixed metabolic and respiratory acidosis. Neurological state remained grossly abnormal with ophthalmoplegia - eyes central, immobile with unreactive pupils, no bulbar responses, only gasping respiration, severe generalised hypotonia with marked spontaneous clonus of all limbs, brisk phasic reflexes and myotactic responses. There was fibrillation of the tongue. Blood pressure, from an arterial catheter in the abdominal aorta, was 60/35, falling later to 40/20. Coagulation studies were abnormal with prolonged prothrombin and partial thromboplastin times, elevated fibrin degradation products, but normal platelet numbers. Regular respirations were not established and the child died at 16 hours. Post mortem examination findings were unremarkable, showing only lung congestion and hyaline membrane disease.

Case 36: tone pattern 1, outcome category 3

This infant was the result of the second pregnancy of a 32 year old, 4 ft. 11 inch mother, whose first child had been delivered by forceps-assisted vertex, weighing 3.53 Kg. Father is 6 feet in height. Labour was induced in this pregnancy at 39 weeks gestation because of mild pre-eclamptic toxæmia and mother given an epidural anaesthetic. Following a first stage of 5 hours, delivery was attempted by Keilland's forceps with rotation for an occipito-transverse position complicated by late decelerations in fetal heart rate and baseline bradycardia. Second stage of labour, duration 90 minutes, was complicated by shoulder dystocia and delivery was achieved after great difficulty and fracture of the humerus. At birth, the infant was pale, pulseless and flaccid. In response to external cardiac massage and I.P.P.V., the apex beat became detectable at 5 minutes and gasping respirations started at 15 minutes. Apgar scores were 0 at 1 minute, 2 at 5 minutes, and 4 at 10 minutes. Regular, adequate respirations were established at 30 minutes. Birth weight was 5.3 Kg., length 60 cm., O.F.C. 38 cm. Initially, there was profound hypotonia, which slowly improved over the first /

first 3 hours. The head was very moulded and bruised; there was a right brachial plexus palsy, fractured left humerus and Erb's palsy, and a mild right facial weakness. X-ray of the cervical spine was normal, but as a precaution the neck was immobilised. At 12 hours of age, there were signs of spinal release with very brisk leg reflexes and exaggerated flexor withdrawal. Muscle tone remained decreased, with a bulbar palsy and ophthalmoplegia over the first 48 hours. At 36 hours, there were several clonic fits affecting the left arm, leg, and face. There was acute renal failure with oliguria; blood urea rose steadily to a maximum of 29.5 mmols./l., followed by a diuresis at 5 days. From 2-6 days, there was marked hypocalcaemia and hyperphosphataemia; other plasma electrolytes remained normal. E.E.G. showed no abnormality. Muscle tone and spontaneous activity slowly improved and oral feeding had started by 6 days. At the time of discharge at 4 weeks, general behaviour was satisfactory, the left Erb's palsy had improved, but the right arm remained flaccid apart from some distal flexion. Right deltoid electromyography showed fibrillation with no action potentials, indicating complete denervation.

This boy has made excellent progress. His brachial plexus palsy improved to a persistent Erb's palsy, with which he learned to cope ably. He shows signs also of a minimal right hemiparesis of no functional importance. General abilities are good, intelligence above average with no specific weaknesses.

Case 40: tone pattern 3, outcome category 2

This infant was born in a peripheral maternity unit, following an uneventful pregnancy, by induced labour at 41 weeks gestation. First stage of labour was 5½ hours; fetal bradycardia to 80 beats/minute was noted during a second stage of 55 minutes. Delivery was by spontaneous vertex. Apgar scores were 6 at 1 minute and 7 at 5 minutes. At 14 hours, there was a left sided, clonic fit with cyanosis. There was no metabolic disturbance. Following further similar fits, diazepam /

diazepam, phenobarbitone and dexamethasone were given and the child was transferred to the regional intensive care nursery at 24 hours. The infant showed reduction in flexor tone with some increase in extension; there were full eye movements, weak bulbar responses, and no asymmetry. Echoencephalogram and lumbar puncture were satisfactory. Several apnoeic and cyanotic episodes occurred without clinical evidence of fits, but later there were further left sided clonic fits with cycling movements, upturning of the eyes and apnoea. Phenytoin and phenobarbitone were continued, dexamethasone given, and fluid intake restricted. E.E.G. showed no abnormality. There was no response to pyridoxine and investigations of a possible primary metabolic disturbance were negative. Plasma electrolytes and glucose remained normal. Fits ceased by 60 hours. The infant remained lethargic over the first 5 days, and the mild extensor hypertonus gave way to appropriate flexor tone. He was discharged home at 13 days. Subsequent progress has been good; there is a mild left hemiparesis, which is causing no significant impairment of manipulative function.

Case 44: tone pattern 2, outcome category 4

This is the second child of a teenage mother, who had been well throughout pregnancy. Birth was shortly after admission to hospital, following a rapid labour with strong uterine contractions: first stage 2 hours, second stage 8 minutes. A brief period of fetal heart rate recording showed bradycardia and spontaneous delivery occurred before forceps could be applied. Condition at birth was poor; gasping respirations started at 1 minute, but regular respirations were not established until 25 minutes. I.P.P.V., intravenous sodium bicarbonate and dextrose were given. Apgar scores were 3 at 1 minute, and 6 at 5 minutes. Blood gas analysis at 30 minutes showed a marked metabolic acidosis. Severe hypotonia and unresponsiveness changed rapidly to the converse state by 3 hours of age, with extensor hypertonus on the least disturbance, with agitation, cerebral cry, obligatory asymmetrical tonic neck reflexes, dictating arm and leg postures, disinhibited /

disinhibited root, suck and gag reflexes, and central hyperventilation with a low paCO_2 . There were also periods of bradycardia to 90 beats/minute. Fluid intake was restricted and dexamethasone given. There were several fits from 10 hours of age, both generalised clonic and tonic with extension of the limbs and trunk. Phenytoin and diazepam were administered. Plasma biochemical homeostasis remained undisturbed, but E.E.G. was abnormal with epileptic discharges, lack of synchrony and low amplitude background, (Figure 7,24). At 48 hours, neurological state had changed to depression of function with no spontaneous movement, generalised hypotonia, loss of eye movements, bulbar responses and primitive reflexes, and continuing episodes of bradycardia. There was slow improvement from this state; by 5 days, tone had risen to a 34 weeks gestation level and eye movements and bulbar reflexes had returned. At the time of discharge home at 17 days, there was still regression of tone and slow bottle feeding. By 4 weeks of age, there were clear signs of continuing problems; feeding remained slow, behaviour irritable and unsettled, handling difficult, and extensor dystonia apparent. Progress has been poor. Dyskinetic movements have been a feature since 4 months of age. Primitive reflexes, such as the grasp, stepping, Moro, and the truncal reflexes have persisted. This child has a dyskinetic cerebral palsy, poor somatic growth, microcephaly and mental retardation.

Case 49: tone pattern 1, outcome category 4

This is the first child of parents of low intelligence; mother is educationally subnormal. Apart from vomiting, she had been well during pregnancy. After spontaneous onset of labour at 41 weeks gestation, there were signs of fetal distress, passage of meconium, severe fetal acidosis - pH 7.07, but no fetal heart rate abnormality on cardiotocho-graphy. Delivery was by spontaneous vertex and condition of the infant at birth was fair with Apgar scores of 5 and 9 at 1 and 5 minutes. Acidosis was confirmed on cord blood analysis, and was corrected with sodium bicarbonate and intravenous dextrose also given. There was some abnormality /

abnormality of behaviour, the infant having a wide-eyed staring look, regression of tone and posture to a 34 weeks' gestation level, and marked athetoid movements of the upper limbs and mouth. There was mild irritability. Feeding was satisfactory. Hyponatraemia, plasma sodium 128 mmols./l., was found at 24 hours. Hypotonia and athetosis continued, but early neonatal course was otherwise uneventful. With support to the parents, the child went home at 12 days, but had several admissions to hospital over the next months with intercurrent upsets. He remained markedly hypotonic. Athetoid movements continued over the first 6 months, and, partly as a result of being slept lying on one side, he developed moderate plagiocephaly, chest asymmetry and asymmetry of the asymmetrical tonic neck reflexes at about 4 months old. His further progress has been poor. He is mentally retarded, with generalised hypotonicity and joint laxity, but has achieved competence in basic everyday activities: independent mobility, feeding, toileting. The child is at present in long term foster care.

Case 50: tone pattern 3, outcome category 1

Because of mild hypertension, labour was induced at term and stimulated with extra-amniotic prostaglandin; however, there was greatly increased uterine contractility, signs of fetal distress with major late decelerations in heart rate and a severe acidosis on scalp blood gas estimation. The first stage of labour lasted 3 hours, the second 3 minutes. Delivery was by spontaneous vertex, while arrangements were being made for surgical intervention. Apgar scores were 4 at 1, and 8 at 5 minutes. I.P.P.V., intravenous dextrose and sodium bicarbonate were given. Following a short period of hypotonia and apathy, there was a change to irritability and extensor hypertonus at 6 hours. Hypoglycaemia occurred at 4 hours and was corrected by dextrose infusion. At 7 hours, when normoglycaemic, the infant had a brief tonic fit with cyanosis, apnoea and bradycardia. Until the age of 48 hours, there were many clonic fits affecting the right side, with chewing and eye movements, which proved refractory to anticonvulsant therapy with phenytoin /

phenytoin, phenobarbitone and diazepam. E.E.G. demonstrated a left posterior epileptic focus, (Figure 7,25). Echoencephalogram and lumbar puncture were satisfactory. Fluid intake was regulated and dexamethasone given. There was mild hypocalcaemia, plasma calcium 1.74 mmols./l. on day 2, and a mild hyponatraemia, plasma sodium 129 mmols./l., on day 3. A deep, postictal, right hemisyndrome persisted until the time of discharge at 13 days, but this and the E.E.G. focus had resolved by 3 weeks of age. Subsequent progress has been good without any focal abnormality. Intelligence is average with no specific weaknesses, but he has required speech therapy for developmental speech delay. At the age of 4 years, he had a single grand mal convulsion in association with tonsillitis; a further E.E.G. showed no abnormality.

CHAPTER XII

DISCUSSION

Despite improvements in perinatal care, birth asphyxia remains the commonest cause of neurological abnormality in the infant and a major cause of stillbirth, neonatal death and survival with handicap, (Volpe, 1975; Sarnat, 1976). Much attention has been given to this problem, both in clinical practice and in the medical literature, yet fundamental difficulties remain in several areas in the consideration of birth asphyxia.

Of prime importance are, of course, methods of prevention. Although this is largely beyond the scope of the present work, some comment can be made from the experience which has been gained.

Secondly, there is the problem of recognition of intrapartum asphyxia. The obstetrician and midwife, from the relatively limited information obtainable about fetal condition in labour, hope to detect early signs of fetal distress and by appropriate management avoid significant asphyxia. Some aspects of the detection of fetal asphyxia have been discussed in Chapter I, and will not be reconsidered now. Recognition by the neonatal paediatrician of the infant who is at risk of developing, or has developed neonatal sequelae of intrapartum asphyxia, implies failure of methods of prevention or early detection and modification since it is apparent that with ideal supervision and management most cases of intrapartum asphyxia could be avoided. In reaching a diagnosis of neonatal symptomatic asphyxia, the paediatrician must be aware of the range of disturbances from subtle to gross that may present. However, since the repertoire of the newborn infant is limited in the disturbances displayed and the signs which can be elicited, these lack specificity in their relationship to their causation, (Graziani, 1977). It is clearly important to give active consideration to other causes of neonatal encephalopathy. By careful study /

study of the neonatal manifestations of significant intrapartum asphyxia, patterns can be recognised, both in the aggregations of abnormalities which occur and in the changes which unfold over the early neonatal period, which together with information of the pregnancy and intrapartum course, carry much greater weight in diagnosis than a number of isolated findings.

Thirdly, apart from diagnostic considerations, what value do the neonatal findings in symptomatic birth asphyxia have in making an assessment of the infant's condition, in indicating when secondary complications are occurring, and in prognostication? Following from this, when can the neonate or older infant confidently be said to have sustained continuing damage or to have escaped unscathed, and what are the best indications of this?

Lastly, what are the important aspects of management in the neonatal period of the infant who has been subject to a hypoxic-ischaemic stress during birth? While techniques of resuscitation have improved with time and are now fairly standard, it is only more recently that the observation and management of the infant with symptomatic asphyxia has become more active and the scope for intervention, although still limited, has expanded. It was not an objective of the present study to consider the management of the infant, but this is clearly an important aspect of the problem and some observations will be made.

Prevention of intrapartum asphyxia

Birth asphyxia is largely a preventable condition, as can be appreciated from clinical experience and consideration of the cases described here. As discussed in Chapter I, efforts in prevention can be aimed at two major areas. Firstly, the identification of adverse factors in the social, maternal, medical and obstetric background /

background is necessary for the direction of policies for improvement, for deployment of resources for care and for planning for the individual pregnancy, (Larks, 1972; Low, 1975a; MacDonald, 1980). A system of risk scoring can be used, and updated as the pregnancy proceeds, to identify those pregnancies where closer surveillance and perhaps active management, such as induction of labour or elective surgical delivery, are indicated, (Boddy, 1976; Neutra, 1978).

Secondly, close monitoring of fetal condition in labour, especially in higher risk situations, with cardiotocography, complimented by fetal scalp blood pH measurements, will allow earlier recognition of fetal difficulty in many instances, but this must, of course, be followed by appropriate, well timed action when problems are detected, (Beard, 1971, 1974; Neutra, 1978; Check, 1979).

Despite the 30 per cent improvement in perinatal mortality, which was achieved in Britain between 1958 and 1970, (Butler, 1963; Chamberlain, 1975), it was clear from the 1970 British Births Survey that many deficiencies in perinatal care remained, (Lancet, 1976). For example, the perinatal mortality rate for social class I was 7.5/1,000, while that for classes IV and V 3½ times greater at 26.8/1,000, evidence of the combined deleterious effect of various aspects of social circumstances, attitudes, habits and medical care related to social class. Postpartum asphyxia complicated intrapartum asphyxia in a sizeable number of infants, there being a delay of at least 1 minute in the onset of respiration in 22.9% of babies and of more than 3 minutes in 4.7%; 53% of all first week deaths belonged to this second group. Of the infants delayed more than 3 minutes in the onset of respiration, 87% were born in consultant units and only 37% of these were intubated at birth.

The 1970 British Births Survey brought to attention major shortcomings in antenatal, intrapartum and neonatal care and prompted the formation of a number of working parties. A joint working party of the /

the National Medical Consultative Committee was formed in 1976 under Professor James Walker to estimate the need for maternity and neonatal services in Scotland. Its report in 1980, although showing improvement since 1970, voiced concern over several areas: unacceptably high perinatal mortality rate and low birth weight incidence, varying standards of care in different areas and inadequate paediatric staffing levels in neonatal units. It stressed the value of early and good antenatal care and of ensuring that the at-risk mother or infant is delivered in a hospital with matching facilities.

From the present study, a number of shortcomings in labour management can be discerned: labours where cephalo-pelvic disproportion was not recognised, where electronic fetal heart rate monitoring was not employed and might have given earlier indication of fetal difficulty, labours where such monitoring techniques were used but action was delayed or not taken on the findings. The additional information which fetal scalp pH measurement would have given in assessing fetal condition was commonly not sought.

Discussion of problems by obstetricians and paediatricians informally and in perinatal mortality and morbidity meetings is of considerable importance in improving standards of perinatal care. The establishment of confidential enquiries into causes of perinatal death as a permanent feature of health service monitoring was recommended by the Joint Working Committee on Standards of Perinatal Care in Scotland, (Walker, 1980).

Pharoah, 1982, reports the findings of a confidential enquiry by obstetric and paediatric assessors into perinatal deaths in the Mersey Region. In 59% of 309 perinatal deaths, there were between 1 and 4 avoidable factors, while in those of normal birthweight, i.e. greater than 2.5 Kg., 74% had avoidable factors. These factors were obstetric in 35%, paediatric in 13%, and maternal/social in 29% of perinatal deaths. The commonest obstetric factors were failure to diagnose /

diagnose intrauterine growth retardation although reason existed which should have prompted a high index of suspicion, failure to take appropriate action when significant maternal weight loss or inadequate weight gain occurred, general practitioner booking of high risk pregnancies, inappropriate level of care in hospital, i.e. by junior medical staff when consultant staff should have been involved, and inappropriate response to abnormalities detected on fetal heart rate monitoring. Inadequate resuscitation at birth and inadequate provision of respiratory support, particularly for low birth weight babies, were the two important avoidable, paediatric factors identified, and failure to attend for antenatal care, lack of support for the mother and failure to comply with medical advice the important maternal/social factors.

Studies such as the Edinburgh Sighthill Project of community based antenatal care, (McKee, 1982), have clearly demonstrated that meticulous application of well established practices in antenatal and intrapartum care can substantially reduce perinatal mortality and some aspects of perinatal morbidity by planned antenatal assessment, following pre-determined policies, efficient use of the antenatal care team, and active encouragement of reluctant mothers to attend. This was achieved with little or no increased expenditure. Increased spending, however, is needed to improve levels of equipment in antenatal clinics and labour wards for fetal monitoring, (Gillmer, 1979), and to improve staffing levels especially in newborn nurseries, (B.P.A./R.C.O.G. Liaison Committee, 1978; Dunn, 1979; Walker, 1980).

Recognition and diagnosis of neonatal symptomatic asphyxia

As in other areas of medical practice, a high level of awareness and suspicion in assessment of the newborn is the important starting point for recognition and diagnosis of clinical conditions, followed by systematic elicitation of the history and a detailed physical examination /

examination, complimented by planned investigation. It is perhaps tempting in neonatal medicine to undervalue the importance of information from the history and careful examination in favour of investigative and laboratory data. It must be recognised, however, that although such information may be less specific in its diagnostic significance than in older patients, this is an indication for greater care in the collection and scrutiny of such evidence, proceeding then to appropriate investigation. These two aspects of assessment should be, of course, complimentary.

In the ideal situation, symptomatic birth asphyxia will be confidently diagnosed from a sequence of events and findings, starting perhaps in pregnancy with signs of placental insufficiency, poor fetal growth, maternal hypertension or antepartum haemorrhage, followed by well documented evidence of fetal distress in labour with fetal heart rate changes and a significant metabolic acidosis, and continuing problems with the baby - depression of vital function at birth and abnormalities of performance, behaviour and neurological function in the early days of life. However, such complete evidence may not be available. The pregnancy may have been uncomplicated. Little or no sign of fetal distress may have been detected in labour although this is dependent partly on how closely fetal condition has been observed. Similarly, some infants with other substantial evidence of significant birth asphyxia have normal Apgar scores, (Low, 1975b; Sykes, 1982). Conversely, signs of fetal distress or depression at birth do not necessarily indicate significant asphyxia; they are common, often not associated with subsequent abnormality, and may result from other adverse factors - intrauterine infection, drugs administered to mother, underlying fetal abnormality, etc. Diagnosis then is based on evaluation of the available evidence and recognition of patterns of neonatal abnormality, consistent with symptomatic birth asphyxia, together with methodical consideration of other possible causes and appropriate investigation.

The /

The term "birth asphyxia" is commonly used loosely in clinical practice; infants with low Apgar scores are often said to be "asphyxiated at birth". Such terminology is best avoided as birth condition is the result of a variety of factors in addition to intrapartum asphyxia. It may also be misleading, suggesting that depression at birth is the important element, while its main significance is as an indicator of preceding problems, since, with efficient resuscitation, postpartum asphyxia should be avoidable in all but the most severely depressed infants.

Unless newborn infants are carefully assessed by experienced staff, milder degrees of symptomatic asphyxia may go unrecognised, or recognition may be delayed until some frank abnormality, such as a fit occurs, (Brann, 1977). Prechtl, 1967, stressed the value of detailed neurological assessment as otherwise many infants with no gross pathological signs, but with a considerable amount of neurological abnormality on careful examination, which was prognostically ominous, would be missed.

A particularly difficult diagnostic predicament is presented when fetal abnormalities predispose to intrapartum asphyxia by reducing the ability of the fetus to cope with the stresses of labour. The resulting fetal distress and neonatal abnormalities may then be interpreted as being due to primary intrapartum asphyxia and the underlying problem go unrecognised. A number of writers have drawn attention to this situation, (Freud, 1897; Ingram, 1964; Illingworth, 1979). A number of infants during the study period presented difficulty in this way; with two infants in particular, suffering from coxackie myocarditis and neurolipidosis, the nature of the underlying problem only slowly became apparent, but the atypical patterns of neurological abnormality shown along with other features avoided confusion with primary intrapartum asphyxia.

The following list compiled from experience over a number of years, while not intended to be exhaustive, illustrates some of the conditions, which /

which may be confused with symptomatic birth asphyxia:

Infection - encephalitis, acute or chronic,
intrauterine meningitis,
viral myocarditis

Renal/Hepatic failure.

Primary metabolic disease - proprionic acidaemia
galactosaemia
maple syrup urine disease
Leigh's encephalopathy.

Myopathy - dystrophia myotonica
Prader-Willi syndrome
myasthenia gravis

Drug depression/withdrawal.

Spinal cord trauma.

Degenerative encephalopathies - acute infantile Gaucher's
disease.

Zellweger's Syndrome
(Burt and Brown, 1980).

The early significance of neonatal events and findings in neonatal
symptomatic asphyxia.

Neurological findings

"Considerable and frequently decisive information can be elicited from a detailed and standardised neonatal evaluation by an experienced clinician or investigator who is aware of the limitations of clinical assessments".

Graziani and Korberly, 1977.

Neurological /

Neurological assessment of the infant is a useful clinical tool, but it is important to realise its limitations. The first problem encountered is in distinguishing mildly abnormal findings from variation within the normal range. Detailed studies of infant behaviour and neurological performance have demonstrated the inherent variability of the neonate, both within the population and in the individual infant with time, (Andre-Thomas, 1960; Precht1, 1964; Brazelton, 1973). The considerable variability in normal neonatal behaviour due to the influences of gestational maturity, state of arousal, and other aspects of the infant's physiological condition and environmental influences - temperature, noise, posture and prior handling, complicates the clinical interpretation of neurological findings, (Brown, 1974a; Graziani, 1977). An experienced clinician takes these factors into account in his appraisal of the infant's condition, but it is difficult to define precisely criteria that allow separation of the range of normality from mild abnormality and, indeed, there is some overlap between these.

Variability in neurological findings in the neonate over a period of time due to changes in state and other influences is expected. Lack of variability or the persistence of minor deviations, such as mild hypotonicity or asymmetry of tone, reflexes, or posture on repeated examinations, suggests abnormality, (Brown, 1974a). Serial assessments are therefore of considerable value in determining the significance of minor neurological findings.

The relatively objective clinical methods of neurological assessment, such as the schemes developed by Andre-Thomas, Precht1, and Brazelton, and, that used in the present study, by Brown, (Appendix I), form useful guides for a comprehensive examination, but pose problems in the interpretation of findings. For example, Touwen et al, 1977, using the systems of examination of Precht1, 1964 and 1977, found that 25 of 100 unselected, full term infants examined, showed "deviant" signs, this surprisingly large number illustrating the variability of the neonatal population.

Abnormal neurological behaviour is non-specific, generally not localising in neuroanatomical terms, and related to acuteness of the damage to the nervous system as well as to its severity. Many congenital and chronic causes of brain injury, although resulting in severe sequelae in later childhood, are not associated with neonatal neurological abnormality, while infants with severe neurological dysfunction from an acute cause, such as intrapartum asphyxia, may recover if the insult has been insufficient to produce permanent damage to the brain structure. In addition, because of the acute nature of the insult, the clinical condition at birth is not a steady state; the abnormalities shown are likely to change over the early neonatal period as recovery takes place, secondary complications ensue or as a reflection of the changing expression of continued damage to the developing brain, (Amiel-Tison, 1969; Volpe, 1977). This is well illustrated by many of the cases in the present study.

Neurological assessment of the ill newborn infant is limited also by practical considerations. Access to the child may be restricted by attachment to monitoring equipment, intravenous lines and ventilatory support apparatus. Treatment already given may modify the neurological responses assessed and greatly complicate interpretation. Anticonvulsant drugs, particularly those with a pronounced C.N.S. depressant effect, are commonly used, and here plasma levels can be helpful in judging the contribution of therapy to the clinical picture.

The behaviour and responses observed during the neurological examination that can be carried out in the nursery depend largely upon the maturation and functional integrity of subcortical neuroanatomical structures, especially the brain stem, (Brown, 1976a; Graziani, 1977). Although the brain stem was previously considered to be relatively resistant to hypoxic-ischaemic damage, (Adams, 1966; Gilles, 1969), it has been recognised more recently that pathological evidence of brain stem damage is characteristic of hypoxic-ischaemic encephalopathy, (Brierley, 1973; Leech, 1977). The latter workers found ischaemic cell /

cell change, neuronal loss and reticular formation gliosis in the brain stem and thalamus of infants dying from a perinatal asphyxial episode. There is considerably less understanding, however, of the neuropathological basis of the clinical features in the neonatal period than of the neurological sequelae of asphyxia in later infancy and childhood. Volpe, 1977, reviewing current thinking of correlates between neonatal neurological and neuropathological features, summarised his understanding of the situation thus:

Neuropathology	Topography	Neurological features in the neonatal period
Selective neuronal necrosis	Cerebral and cerebellar cortex; thalamus; brain stem nuclei	Stupor, coma; hypotonia; oculomotor disturbances; disturbed sucking, swallowing, tongue movements
Status marmoratus	Caudate, putamen, globus pallidus, thalamus	Unknown
Parasagittal cerebral necrosis	Cerebral cortex and sub-cortical white matter in parasagittal ("watershed") areas	Hip-shoulder weakness
Periventricular leukomalacia	Periventricular white matter	Lower limb weakness
Intraventricular haemorrhage	Periventricular, intracerebral haemorrhage with rupture into ventricular system	Coma; decerebrate posturing; generalised tonic seizure; respiratory arrest; fixed pupils and eyes; flaccid quadriplegia

Brown, 1976b, postulated that many aspects of brain stem function might be controlled by groups of oscillators, firing stimuli in a rhythmical fashion, to produce their peripheral effects: rhythmical activities such as sucking and respiration, the more complex rhythms of electroencephalogram, and maintenance of tonic activity such as muscle tone through the γ efferents and vascular tone through the autonomic nervous system. Disturbance of these systems of control could then, in a general way, explain some of the acute manifestations of /

of hypoxic-ischaemic encephalopathy: depression of sucking activity with abnormally short sucking bursts and slow rates of sucking during recovery, the respiratory dysrhythmias observed - hyperventilation, gasping, periodical respiration and apnoeic episodes, abnormalities of muscle tone, bradycardia and hypotension, disturbances of conscious level, sleep state and E.E.G. rhythms. Brown's suggestions are summarised below:

Physiological	Pathological
1. Respiratory rhythms	Apnoea, periodic respiration
2. γ facilitation	Hypotonia
3. Sucking rhythm	Feeding depression
4. Sleep rhythms	No sleep, abnormal sleep E.E.G
5. E.E.G. rhythms	Low voltage, abnormal patterns
6. Vasomotor tone	Hypotension
7. Stepping, cycling, "doggy paddling"	Lack of spontaneous movement.
8. Reticular "arousal" of cortex.	Apathy, unconsciousness, hyperexcitability.

Examples of physiological and pathological brain stem centre oscillator function - Brown, 1976.

Disturbance of the normal balance between facilitatory and inhibitory pathways of modulation of brain stem centre function was further postulated by Brown, 1976b, as an explanation of some aspects of neurological dysfunction observed. He suggested that function could be lost, could be exaggerated or released from normal control by recovery of facilitatory before inhibitory pathways, or could be depressed by continued imbalance. Thus in the early hours of life, after a severe asphyxial insult, there is loss of function - profound hypotonia, apathy or unconsciousness, absent reflex activity, followed in some cases by a degree of recovery with facilitation but loss of inhibition, resulting in a picture of disinhibition with extensor hypertonus /

hypertonus, irritability, hyperexcitability, sleeplessness, exaggerated or obligatory reflex responses and other release phenomena, such as fits. These are the changes described in tone patterns 2 and 3, Chapter VIII. Lack of recovery to this extent at this early stage, i.e. tone pattern 1 - persistent hypotonia, depressed state of arousal and reflex response, would as expected be of more sinister prognostic significance, (Brown, 1974).

Subsequent loss of extensor hypertonus, hyperreflexia, etc., with instatement of normal flexor tone and responses, as in tone pattern 3, may represent recovery of the inhibitory mechanisms and return to inhibitory/facilitatory balance.

The mechanisms of late hypotonia, the second phase of depression of neurological function seen in tone pattern 2, are more difficult to explain and may be multifactorial. In this group of infants, the early manifestations were more florid with profound initial hypotonia, severe extensor hypertonus with a higher incidence of other abnormalities - tonic fits, bulbar palsy, ophthalmoplegia, and the progression to late hypotonia rather than recovery of flexor tone would seem to be inherent in the more abnormal clinical course shown by these babies and an indication of continuing abnormality.

It could be argued that the phase of extensor hypertonus and disinhibition is a manifestation of raised intracranial pressure from cerebral oedema, producing pressure effects on the midbrain and a pattern of decerebration from release of lower brain stem extensor activity. As noted, there were no other clinical signs of brain swelling and steps had been taken shortly after birth to reduce the risk of its occurrence - fluid intake was carefully controlled and dexamethasone given. It is apparent, however, that other clinical features of brain swelling are insensitive and may be absent and since extensor hypertonus was very early in onset, between 1 and 4 hours after birth, such treatment may, therefore, have been ineffectual. Intravenous mannitol, however, /

however, also produced no clinical improvement. The findings of hyperventilation with low blood $p\text{CO}_2$ levels in all the infants of tone pattern 2 may also support the presence of cerebral oedema, representing a physiological attempt to reduce intracranial pressure through vasoconstriction. Alternatively, central hyperventilation could simply be another aspect of neurological excitation and loss of inhibitory control. Without satisfactory means of measuring intracranial pressure, and ideally cerebral blood flow, in this situation, the clinical diagnosis of cerebral oedema and interpretation of extensor hypertonus is empirical.

Although, of course, similar, there are differences in the various accounts of the clinical events in neonatal symptomatic asphyxia. Few workers have clearly described the changing patterns that occur over the first days after birth. The classification by Prechtl, 1965, of the main patterns of abnormality into hyper-excitability syndrome, apathy syndrome and hemisyndrome, which was then adopted by other workers, (De Souza, 1974), does not give emphasis to this point, while by contrast, Amiel-Tison, 1969, considered the clinical state too changeable in the first days to allow a clinical classification to be made.

Brown, 1974, reported the neurological findings of 94 infants with perinatal asphyxia and gave a clear description of their changing state over the early newborn period, categorising the abnormalities shown on the basis of the state of muscle tone. Other neurological abnormalities correlated with muscle tone, as did the occurrence and severity of subsequent handicap.

In an excellent account of severe hypoxic-ischaemic encephalopathy in a group of 21 neonates, Sarnat, 1976, identified 3 clinical stages, based largely on conscious level. Stage 1, lasting less than 24 hours and entered by a third of the infants, was characterised by hyperalertness, uninhibited Moro and stretch reflexes, and signs of sympathetic nervous system activation - mydriasis, tachycardia, alertness. The E.E.G. was interpreted as showing normal wakefulness. No clear /

clear description is given of the predominant pattern of muscle tone at this time, and strangely fits were not observed at this stage. Stage 2 was shown by all the infants and in two-thirds from birth. It had a mean duration of 4.7 days and was characterised by obtundation, hypotonia, strong distal flexion with fisting with the thumb adducted, and by multifocal seizures. Sarnat describes generalised sympathetic effects at this time - constricted pupils, bradycardia, copious pharyngeal secretions and increased gastrointestinal peristaltic activity. A periodic pattern of E.E.G. activity was found in Stage 2, consisting of polymorphic sharp and slow waves of 50 to 200 μ V bursts for 1 to 3 seconds alternating with low amplitude delta and theta waves for 3 to 6 seconds. At times, "premature ripples" of 16-20 Hz were superimposed on both phases.

Those 6 infants who entered Stage 3, showed further depression of C.N.S. activity with stupor, flaccidity, depression of brain stem and autonomic functions. Decerebrate posturing only occurred in this stage, precipitated by non-specific stimuli. Corneal and gag reflexes were absent; in some, temperature regulation was lost and others were given ventilatory assistance because of shallow, ataxic breathing with apnoeic periods. The E.E.G. showed further depression of the periodic pattern, going on to become totally isopotential. Fits were uncommon in this stage.

Writing in 1977, Volpe also gives a detailed description of the neonatal manifestations of severe asphyxia, breaking down the main clinical features over the first days of life by time periods. This is summarised below:

Birth - 12 hours

Deep stupor
Periodic breathing
Intact pupillary responses
Intact oculomotor reflexes
Hypotonia, minimal movement
Seizures.

12 - 24 hours

Less stuporous
More seizures
Apnoeic spells
Jitteriness
Weakness
 Hip-shoulder (full term)
 Lower limbs (pre term)

24 - 72 hours

More stuporous
Respiratory arrest
Brain stem oculomotor abnormalities
Possible catastrophic deterioration in premature infants
 from intraventricular haemorrhage

72 hours and later

Persistent, though diminishing, stupor
Disturbed sucking, swallowing, gag, tongue movements
Hypotonia much commoner than hypertonia.

Volpe, 1977.

The account given by Sarnat is of particular interest for the attention it gives to changes in conscious level and associated E.E.G patterns, and the manifestations of autonomic nervous system disturbance discerned. Neither Volpe nor Sarnat record a phase of extensor hypertonus with other signs of neurological excitation, although this has been widely reported elsewhere, as well as in the present work, (Precht1, 1965; Amiel-Tison, 1969, 1973; Brown, 1974; De Souza, 1974, 1978; Finer, 1981). However, Sarnat does note other features of neurological disinhibition in infants of Stage 1, and both writers mention episodes of decerebrate posturing in association with stupor and /

and profound hypotonia. Comparison of different accounts of the clinical, investigative and outcome findings in neonatal symptomatic asphyxia is greatly hindered by the varied criteria adopted for selection of cases, and, therefore, varied nature and degree of the disturbances shown, (Scheiner, 1980).

The description of neonatal hypoxic-ischaemic encephalopathy based on muscle tone patterns employed here and in the work of Brown, 1974, 1976a, has certain advantages. To be of practical value in the nursery such a description must allow clear distinction of differing neurological states by the recognition of features and signs by paediatricians of varied experience in neonatal neurological assessment. The predominant pattern of muscle tone can be quite readily and reliably ascertained and, with the other neurological features, used to form a more complete clinical assessment.

Early significance of neonatal manifestations of symptomatic asphyxia

The immediate significance of some aspects of abnormalities found on neurological assessment has been discussed. The importance of many of the disturbances of behaviour and performance described, in assessment and management in the neonatal period, is apparent. Of particular importance are those disorders which are common, such as feeding depression, or carry more serious acute implications for the infant - fits, apnoeic episodes.

Feeding depression

Of practical importance in the nursing care of the infant are the problems encountered with depression of the feeding and bulbar protective reflexes. Feeding depression is, of course, very common in neonatal practice, as a non-specific sign of a wide variety of disturbances. It is common in symptomatic asphyxia, 80% in the present study being tube fed /

fed for at least 24 hours, and 32% for 4 days or more. In addition, those with bulbar palsy are at risk of cyanotic episodes or aspiration of pharyngeal secretions, gastric contents, or milk if they are inadvisably encouraged to feed orally. Pooling of secretions in the pharynx was interpreted as due to failure of normal clearance in those with bulbar palsy, but increased salivation from sympathetic overactivity may have been a contributory factor, (Sarnat, 1976).

Surprisingly little work has been done on sucking activity and sucking/swallowing/respiratory coordination, either in normal infants or those with problems. Gryboski, 1965, 1969, identified 2 patterns of suck/swallow activity in premature infants, after an initial phase of mouthing. Firstly an "immature" pattern of short sucking bursts at a rate of 1 - 1.5 sucks/second, increasing to longer bursts of around 30 sucks at a rate of 2/second with increasing weight and maturity. This second "mature" pattern was attained in about 5 days in infants of 2.1 - 2.5 Kg. birthweight, but was delayed until 2 - 4 weeks when the birthweight was 1.8 - 1.9 Kg. Cowett, 1978, reported retardation of maturation of suck pattern at term in prematurely born infants who had had severe early problems.

Gryboski, 1965, 1975, and Kron, 1963, found that full term infants typically show a transient "immature sucking pattern" during their first feeding attempts with short bursts of 3 to 5 sucks, increasing to a "mature" pattern with bursts of 10 to 30 sucks by 24 to 48 hours of age. Over this transition period, non-nutritive sucking rates increase from 1 to 1.5 - 2 sucks/second, the nutritive sucking rate being approximately 1/second.

The findings reported here of non-nutritive sucking activity in some of those infants who showed feeding depression, therefore, appear to represent an exaggeration of the changes normally occurring in mature infants over the first 24-48 hours of life, and have some similarity to the maturation of function shown by premature infants, absence

absence or depression of sucking activity being followed by mouthings, sucking in short bursts at a slow rate, and delayed achievement of a mature sucking pattern.

It is apparent in health that an infant's feeding behaviour is dependent not only on the interval elapsed since last fed, but on a number of other physiological alerting forces that determine the state of arousal, the alert or irritable infant often being willing to suck even when recently fed. Feeding patterns observed in infants following an intrapartum asphyxial insult, in addition to being dependent on intact brain stem mechanisms, reflect the level of arousal, the balance between facilitatory pathways in the brain stem particularly the reticular formation. Thus infants, during the phase of C.N.S. excitation and hypertonus, will often root and suck vigorously and spontaneously without stimulation, while the return of sucking activity in the phase of hypotonia and C.N.S. depression, in tone patterns 1 and 2, is an early sign of improving neurological status.

There is scope for further work in this area in the study of nutritive feeding activity and the coordination of sucking, swallowing and respiration in the asphyxiated infant during the recovery phase.

Respiratory control and asphyxia

"Reflection on the nature of a delay of only a few moments in the substitution of pulmonary for the ceased placental respiration would lead to the apprehension that even the want of a few breathings, if not fatal to the economy, may imprint a lasting injury on it".

Little, 1862.

Much attention has rightly been given to the mechanisms of the onset of respiration at birth and to the problems of the infant who does not rapidly institute independent respiration. There are two widely held /

held theories invoked to explain the onset of respiration, (Purves, 1974). Firstly that the change from the relative sensory deprivation of the intrauterine environment to the sensory bombardment of birth and the extrauterine world, relayed through peripheral receptors, stimulates the central respiratory neurones activating respiratory movement. Secondly, Barcroft, 1937, from his work on sheep fetuses, suggested that respiration was actively inhibited in the mature fetus in utero and in some way this inhibition was lifted at the time of birth.

The work on breathing movements in fetal sheep, (Dawes, 1970, 1972), and later, with the development of ultrasound techniques, on breathing movements in the human fetus, (Boddy, 1972, 1975), have helped to give new insights into the development of respiratory control. Fetal breathing movements can generally be detected by 13-14 weeks gestation in the human. Until the last few weeks of gestation, they are very irregular in character and have been shown to be of two types: rapid, irregular movements present during rapid eye movement sleep and episodes of slow, 1-4/minute, relatively deep, respiratory efforts or gasps. After 36 weeks gestation, breathing movements are regular in many fetuses and present for a greater proportion of the time, although this incidence falls near the onset of labour. The proportion also shows diurnal variation, is lowered by maternal fasting and hypoglycaemia, and increased by administration of glucose to the mother, (Boddy, 1975). Breathing movements continue during normal labour, but in the presence of fetal asphyxia, as indicated by a reduction in scalp pH and pO_2 and late decelerations in fetal heart rate, there is a cessation of normal, regular, respiratory movements and the appearance of gasping. Maternal hyperventilation and hypocapnia also produce a reduction in fetal breathing, but without gasping.

The factors that stimulate the onset of respiration at birth have long been argued, but, as it is apparent that breathing movements have been well rehearsed by the fetus, the questions that now arise are why some /

some infants fail to continue breathing movements after birth and what produces the change from episodic movement antenatally to the normal regular pattern after birth? Clearly, birth entails major sensory stimulation of the infant and radically alters both the mechanical and chemical status of the respiratory system. The large differences in blood gas values normally maintained in the fetus and the normal neonate have prompted the assumption that some resetting either of the chemoreceptors in the medulla and aortic and carotid bodies or of the central response of the respiratory centre to blood gas levels must occur at birth. In support of this theory is the finding that the normal, maintained, respiratory response to hypoxia is gradually achieved over the first weeks of life. This may relate to increased blood flow through the carotid bodies, secondary to increased sympathetic activity, (Purves, 1966). There is increased sympathetic nervous system activity at birth and increased levels of circulating adrenaline, especially if the fetus has been stressed, (Cheek, 1963).

There are two separate components to the regulation of respiration. One is automatic, persisting in sleep and all but the deepest levels of anaesthesia, and is largely concerned with subserving the metabolic requirements of the body and acid base homeostasis, while the second component may be regarded as behavioural, comprising respiratory responses to cortical stimuli, sensory stimuli, and emotional inputs, (Purves, 1974). There is evidence that they are served by different pathways and, therefore, likely to be affected separately in disease, (Plum, 1970), although both systems appear to respond similarly to a variety of stimuli and to the level of arousal. A close relationship is thought to exist between the reticular formation and respiratory neurones, hence the association between levels of arousal and respiratory activity and changes in respiratory pattern with sleep state.

The respiratory control mechanisms are clearly highly sensitive to varying degrees of asphyxia. James, 1958, considered that a mild degree of asphyxia was a normal finding in all births and formed part of the /

the process of respiratory stimulation at birth. He also found that acute asphyxia, indicated by a respiratory acidosis without a metabolic component, was associated with vigorous respiratory activity at birth, while prolonged asphyxia - a metabolic acidosis superimposed on a respiratory acidosis, was likely to result in respiratory depression at birth with initial, gasping respirations or, if more severe, complete respiratory depression and apnoea. The respiratory responses of the neonate and the breathing movements of the fetus are therefore similar - the fetus responding to hypercapnia by increased movements and to degrees of asphyxia by gasping, loss of regular movements and apnoea, (Boddy, 1975).

As described, Chapter VII, in the first days of life following a significant intrapartum asphyxial insult, a number of forms of disturbed respiratory control may occur. Central hyperventilation found in infants showing extensor hypertonus, tone pattern 2, as discussed earlier, might represent a response to cerebral oedema, an attempt to reduce intracranial pressure through vasoconstriction, or may be a further example of the neurological excitation or arousal which is shown in infants in this state. Sarnat, 1976, also considered from his observations of hypoxic-ischaemic encephalopathy that central neurogenic hyperventilation and other forms of respiratory dysrhythmia were common, while Volpe, 1976, states that apnoeic spells occur in 50% of asphyxiated babies.

The precise mechanism of the disturbance of respiratory control which results in periodic breathing, or apnoeic episodes, is not well understood, (Rigatto, 1982). Clearly, the respiratory centre is unable to maintain regular, rhythmical discharges. Observing that periodic breathing in immature infants was most evident in transitional sleep, an intermediate sleep state with characteristics of both active and quiet sleep, Wealthall, 1976, suggested that in sleep there were two independent systems of respiratory rate control, normally locked to active or to quiet sleep, and that periodic respiration in transitional sleep /

sleep might be the result of interference between these two controlling systems. He drew an analogy with the "beating" phenomenon produced by the interaction of two musical frequencies.

As indicated in Chapter VII, the abnormalities of respiratory rhythm recorded in Case 22, Figure 7,20, suggest a similar possibility - apnoeic episodes following gasps due to interference between respiratory centre oscillators, one producing a regular and the other a gasping rhythm.

The occurrence of gasping is not uncommon in the first minutes of life, and, indeed, the first respiratory efforts often have a gasping quality. Cross, 1970, described a gasp reflex in the human newborn infant in response to inflation of the lungs, similar to the paradoxical reflex first observed by Head, 1889, in rabbits in response to lung inflation. This latter reflex has been considered important in triggering a strong inspiratory effort when compression of the thorax is removed by the act of birth. Dawes, 1968, described 3 phases of gasping in mechanically asphyxiated, rhesus monkeys: the first as an immediate response to respiratory obstruction, the second followed a brief period of primary apnoea and preceded secondary or terminal apnoea, while the third occurred in response to resuscitation, but sometime after heart rate and blood pressure had risen. Gupta and Tizard, 1967, in a study of the sequence of events in neonatal apnoea in the human, made the assumption that if resuscitative measures led to a gasp or regular respiration before an improvement in colour, the infant had been in the stage of primary apnoea, while improvement in colour before the onset of gasping would suggest terminal apnoea, as they anticipated that a rise in arterial po_2 would be necessary before spontaneous respiration could be initiated. James *et al*, 1958, found, however, that initial respiratory gasps could occur in some infants in the absence of measurable arterial oxygen.

Gasping persisting after the resuscitation period has received little /

little attention. It can be observed in all ages as an agonal respiratory pattern, and, indeed, two of the 7 infants who showed prolonged gasping died in the first day of life. Four of the remaining 5 infants, survived with significant handicap, suggesting that this respiratory pattern is often indicative of major neurological dysfunction, which may be persistent. North and Jennett, 1974, describe gasping along with other abnormal respiratory patterns in 60% of 227 patients in a neurosurgical unit in association with a variety of intracranial pathology, particularly medullary and pontine lesions and raised intracranial pressure. Tachypnoea was significantly related to poor outcome and carried a high mortality when combined with hyperventilation sufficient to lower the arterial $p\text{CO}_2$ below 30 mm.Hg., (3.4 k Pa).

Neonatal fits in symptomatic asphyxia - early significance

Neonatal fits are generally clear, well documented events. The brain of the infant around term has a lowered threshold to convulsions and will fit in response to a wide variety of insults. Perinatal asphyxia is the most common cause of fits at this time, accounting for 30-65% of neonatal convulsions in most reported series, (McInery, 1969; Volpe, 1973; Eriksson, 1979).

Figures for the incidence of neonatal fits vary both by time and place of study, reflecting trends with time and differences related to population and standards of perinatal care, (Dennis, 1978). Burke, 1954, reported an incidence of 5.4/1,000 deliveries in Sheffield, the majority being due to birth asphyxia. In some later reports, the over all incidence had increased, partly from an increase in simple metabolic fits from uncomplicated hypocalcaemia/hypomagnesaemia: Brown, 1972, reported an incidence of 14/1,000 livebirths from Edinburgh, Keen, 1973, 12.2/1,000 livebirths from Manchester. Dennis, 1978, recorded an incidence of only 4.2/1,000 livebirths from the Oxford area between 1970 and 1972. Figures for fits secondary to intrapartum asphyxia are not given in this last study, but the incidence of fits from all types of problems, including perinatal, but excluding the the /

the uncomplicated metabolic group, was 3.6/1,000. The equivalent figures are 6.1/1,000 from Edinburgh, (Brown, 1972), and 7.3/1,000 from Manchester, (Keen, 1973). During the period of the present study, the total incidence of neonatal fits was 6.9/1,000 livebirths for the maternity hospital population, of which 2.1/1,000 were considered secondary to intrapartum asphyxia. If the uncomplicated hypocalcaemia/hypomagnesaemia group are excluded, then the incidence is 3.7/1,000, very similar to the Oxford experience of some years earlier.

Dennis, 1978, 1982, suggests that the comparatively good Oxford figures are a reflection of high standards of obstetric and perinatal care and the "high biological quality" of the Oxford population and proposes that the frequency of neonatal fits that start in the first 48 hours of life could be useful as an epidemiological index of the quality of perinatal care.

Eriksson, 1979, reported a remarkably low incidence of neonatal fits of 1.5/1,000 full term births from an area of Sweden between 1970 and 1976; the rate for fits secondary to perinatal asphyxia was 0.75/1,000 full term births. She draws a comparison with the incidence of neonatal fits from Gothenburg, Sweden, 1960 - 1962, of 3.7/1,000 term babies, a trend approximately in parallel with improving perinatal mortality rates - 13.5/1,000 as opposed to 23.8/1,000 for the earlier time period.

There are some difficulties, however, in such comparisons from different studies. Methods of reporting vary in the length of the time period after birth considered, in including all gestations or only those born at term, in the aetiological classifications used and probably in the criteria employed for the diagnosis of fits. For example, Sarnat, 1976, describes episodes of tonic extensor posturing that many would regard as tonic seizures, while Volpe, 1977, interprets a wide variety of neonatal behaviour manifestations as "subtle seizures", otherwise termed brain stem or fragmentary seizures, and reports /

reports that subtle seizures occur in virtually all infants with hypoxic/ischaemic encephalopathy, who show frank fits. These are differences of interpretation and terminology, but illustrate the pitfalls of comparison of reported series of neonatal seizures.

The occurrence of fits in neonatal symptomatic asphyxia is generally regarded as an indicator of poor prognosis, (Volpe, 1977a; Eriksson, 1979). This will be discussed in more detail shortly, but what is the immediate significance of fits occurring in this situation?

As can be seen from the data presented, fits secondary to intrapartum asphyxia tend to occur early, often in the early hours of life, as the infant shows recovery from the initial phase of hypotonia and depressed neurological activity, at a time when other signs of neurological excitation - irritability, hyperalertness, hyperreflexia, extensor hypertonus, are becoming apparent. The fits have a tendency to increase over the first 24 hours, to be frequent and only slowly responsive to treatment. Status epilepticus may occur (Amiel-Tison, 1969; Volpe, 1977). It is important to consider the dynamic disturbances that may occur in association with fits, especially if they are prolonged or recurrent, and which may be of immediate and long term significance for the infant. Brain metabolism increases greatly during seizures, producing higher requirements for cerebral blood flow, oxygen and energy supply. There is an increased rate of energy-dependent ion pumping, which is accompanied by a fall in brain concentrations of A.T.P. and phosphocreatine, (Plum, 1974). The rise of A.D.P. stimulates glycolysis, accelerates production of pyruvate and results in a tissue acidosis from accumulation of lactate. This has the beneficial effect of producing localised vasodilatation, but, if severe, can disrupt the metabolic processes. Seizures are often associated with an elevation of blood pressure, as illustrated in Case 33, Chapter VII, although this has not been well documented in newborn infants; this contributes to an increase in cerebral blood flow and oxygen and substrate supply, (Volpe, 1977a; Lou, 1979a). In experimental /

experimental animals, however, despite these compensatory factors, neonatal fits are accompanied by marked falls in brain glucose concentrations, (Wasterlain, 1975).

Other aspects of homeostatic disturbance associated with seizures may interfere with compensatory mechanisms. At a time when metabolic activity is high in brain and muscle, ventilation may be inadequate, especially in a tonic seizure. Raised intracranial pressure occurs during various types of childhood fits, at times to levels that could impair cerebral blood flow and the pressure elevation may be maintained for some time after the cessation of the clinical fit, (Minns, 1978). Post-convulsive brain swelling may occur, (Brown, 1976a). These factors may combine to produce a further hypoxic-ischaemic insult to the already insulted brain.

The long term significance of neonatal manifestations of intrapartum asphyxia

There has long been a quest for meaningful indicators of prognosis following significant intrapartum asphyxia. Attention has been focussed on a variety of antenatal, intrapartum, birth and neonatal factors in a large number of studies. Although many relationships with outcome have been described, which are of epidemiological value in prediction of risk for groups of children, the assessment of risk for the individual child remains much more difficult and controversial.

Two main approaches have been adopted in the design of clinical studies into this problem. Firstly, large populations of children, unselected for risk, are examined periodically from birth to an age when outcome can accurately be ascertained and correlations with early factors drawn. Since the number of children with handicap from perinatal problems is relatively small, a large population must be surveyed, by a number of different observers. In addition to interobserver variation, difficulty may arise in determining the cause of subsequent abnormalities, whether due to intrapartum factors, or to prenatal or postnatal pathology. In /

In recent years, only one large study of this type has been undertaken, the Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke, (N.C.P.P.).

Secondly, as in the present study, smaller groups of children, selected for risk and diagnosed as having sustained a significant intrapartum asphyxial insult by the fulfillment of preselected criteria, are assessed at intervals to determine their outcome and to identify correlates with perinatal factors. This method also has shortcomings, but many are common to both approaches. Scheiner, 1980, attributed discrepancies in the outcome reported for studies of this type to major inconsistencies in: the definition of asphyxia employed, the composition of groups by gestational age and birth weight, the methods of assessing and defining morbidity, methods of treatment used, experience of the observers, methods of data collection and measures of parent interaction and socio-economic status of the family. It is clearly necessary to consider these variations in method when appraising the conclusions reached. Many of these points have been discussed in the course of this thesis.

The N.C.P.P. was a very ambitious project and its findings are worthy of consideration. Of almost 54,000 infants selected before birth, approximately 40,000 were examined in the neonatal period, at 1 year and 7 years; in addition, almost 32,000 of these were seen at 4 months of age. The results are published in a series of papers by Nelson and Ellenberg, 1979 and 1981, and Ellenberg and Nelson, 1981. Although Apgar scores were risk factors for cerebral palsy, 55% of children with later cerebral palsy had Apgar scores of 7 to 10 at 1 minute, and 73% 7 to 10 at 5 minutes, partly an indication that not all cerebral palsy is due to intrapartum asphyxia, but also of the relative insensitivity of the score as a predictor of morbidity. The relationship of Apgar scores and long term handicap, of course, improves when low late scores are considered: of those infants of normal birth weight and scores of 0-3 at 10, 15, and 20 minutes, 17%, 36%, and 57% respectively of the survivors developed cerebral palsy. Low late scores /

scores, however, are of limited value as an indicator of long term prognosis since with prompt, effective resuscitation the numbers of infants in this situation should be very small, and from Nelson and Ellenberg's figures, 43% of this group will not survive the first year. Unfavourable outcome is due presumably to the combined effects of the primary intrapartum insult and secondary neonatal asphyxia engrafted on to it. As it has been shown that significant intrapartum asphyxia can occur without low Apgar scores and that low scores are not invariably the result of intrapartum asphyxia, (Low, 1975; Sykes, 1982), it seems unwise to take low Apgar scores alone as a prognostic index. Thomson *et al*, 1977, in a study of 31 children who survived after very low Apgar scores, concluded that abnormal neonatal behaviour and time taken to sustained regular respirations, and not the numerical value of the score, were the only positive discriminating factors for the occurrence of serious handicap.

The "symptoms" of neonatal symptomatic asphyxia

Nelson and Ellenberg, 1979, reporting from the N.C.P.P. on the relationship between neonatal signs and cerebral palsy, observed an increased risk of cerebral palsy of 10 to 33 fold in surviving children with any one of the following neonatal characteristics: diminished activity or diminished cry lasting more than one day, thermal instability, need for nasogastric tube feeding, hypotonia or hypertonia, single or multiple apnoeic episodes. Neonatal fits or an Apgar score of 0-3 at 10 minutes or later, carried a risk of more than 50 fold, while an "overall impression" of neurological abnormality during the early neonatal course was associated with a 99 fold increase in cerebral palsy in surviving children.

It will be recalled that 9 abnormalities of performance and behaviour were selected as a criterion of significant intrapartum asphyxia for inclusion in the study group. As might be anticipated, an association was /

was found between the number of these abnormalities demonstrated by each infant and subsequent outcome; each child who died, or is significantly handicapped showed at least 3 of these disturbances. Brown, 1974, reported a similar relationship. The occurrence of feeding depression, irritability, or cerebral cry, however, bore no relationship to outcome, although when the duration of feeding depression was considered, a highly significant association became apparent, while the finding of irritability without a phase of apathy was a favourable, prognostic feature. Further, three of the symptoms - hypothermia, apnoeic episodes, and apathy, showed a highly significant correlation with poor outcome. The infrequency of occurrence of hypothermia perhaps limits its value as a prognostic indicator, but in most instances its finding in this situation is indicative of severe brain stem depression. Sarnat and Sarnat, 1976, observed loss of temperature homeostasis in infants with the most severe degree of encephalopathy, designated stage 3, associated with a poor prognosis.

Problems of respiratory control, such as apnoeic episodes, gasping, hyperventilation and hypoventilation are clearly evidence of major disturbance of vital function when they occur in the asphyxiated, term infant. Apart from their immediate importance, not surprisingly they are indicative of a major degree of encephalopathy and associated with a significant risk of adverse outcome. Gasping continuing beyond the period of resuscitation after birth is of sinister significance, all but one of the infants who showed this, dying or surviving with handicap. Indeed, in some cases, gasping is evidence of the terminal nature of the infant's condition.

Fits complicating the neonatal course following intrapartum asphyxia have generally been regarded as an indicator of poor prognosis, (Amiel-Tison, 1969; Brann, 1977; Nelson, 1979; MacDonald, 1980). McInery and Schubert, 1969, in a review of the prognosis of neonatal seizures found that when these were due to perinatal causes, 25% died, 50% were subsequently abnormal, and only 25% normal. In the experience of Keen /

Keen and Lee, 1973, two thirds of neonates with fits secondary to cerebral haemorrhage or birth asphyxia died or survived with handicap, while Eriksson and Zetterstrom, 1979, found that after post asphyxic fits, 16% died and 29% were abnormal at 1 year - 42% if those with subsequent fits were included.

In the present study, the occurrence of fits was related to poor outcome to a significant degree, $p < 0.05$, although the outcome for these children compares favourably with the experience of others: 28% died or survived with significant handicap, while the remaining 72% were normal or showed no significant abnormality. However, the numbers are relatively small. In this group, the association with outcome appears to be due to the poor outcome for those with tonic fits, half of the infants with tonic fits dying or surviving with handicap, while no infant with clonic fits alone had an adverse outcome. Tonic fits are consistently reported as sinister in their relationship to outcome.

Knauss and Marshall, 1977, found that at least 50% of infants with tonic fits died, regardless of gestational age. Brown, 1972, concluded that tonic fits almost invariably indicated underlying brain damage rather than a simple metabolic aetiology, and, largely because of the prognostic significance of tonic fits, Rose and Lombroso, 1970, found that seizure type, rather than neonatal neurological abnormality, correlated better with outcome. Some infants with tonic fits go on to develop infantile spasms and a hypsarrhythmic E.E.G., (Volpe, 1973). In addition, fits that are very early in onset, are severe, and recur frequently are associated with poor prognosis, (Amiel-Tison, 1969; Volpe, 1979a).

Dennis, 1982, and Volpe, 1977a, reviewed the literature and demonstrated some improvement in the outcome of neonatal seizures. Prior to 1969, 40% died on average, while between 1969 and 1972, 15% died and the handicap rate remained about 35%, (Volpe, 1977a). Dennis found a similar trend /

trend over the years from 1945 to 1977, while in the Simpson Memorial Maternity Pavilion, Edinburgh, from 1968 to 1977, not only did the incidence of fits from perinatal asphyxia fall, but mortality and morbidity both improved, (Brown and Burt, unpublished data).

Dennis, 1982, states: "Overall, the impression is that neonatal seizures are powerful predictors of the risk of subsequent death or handicap". However, too great a reliance should not be placed on any single aspect of abnormal behaviour or function.

Neonatal neurological abnormality

Neonatal neurological abnormality has been found to be of useful prognostic significance. Precht1, 1969, demonstrated "a high positive correlation between non-optimal obstetric condition and neurological abnormality" in the newborn, which, in turn correlated well with subsequent neurological abnormality. Bierman-van Eendenburg et al, 1981, examined a group of 80 children at 18 months, who had been identified from an unselected group of 1,507 neonates as showing neonatal neurological abnormality using Precht1's neurological examination techniques. They found that neonatal neurological abnormality was a sensitive means of selecting newborn infants in special need of attention, but, since the rate of false positive results was high, 82% of the children subsequently being found normal, this indicated transient neonatal morbidity in the majority. This suggests that the occurrence of neonatal neurological abnormality, per se, is not sufficiently discriminating to be of great prognostic value.

More detailed study of neonatal neurological abnormality following intrapartum asphyxia has shown that particular forms and patterns of disturbed function correlate well with outcome. Abnormalities of muscle tone, conscious level, electroencephalogram, and the duration of disturbances in the neonatal period and beyond, have received particular attention.

Muscle /

Muscle tone.- The present study has demonstrated a highly significant relationship between the occurrence of bulbar palsy, ophthalmoplegia and of certain patterns of muscle tone and subsequent neurological abnormality. Allocation of infants to tone pattern groups 1 or 2, i.e. persistent hypotonia or initial hypotonia - extensor hypertonus - late hypotonia, carried a high risk of death or subsequent significant handicap. Brown et al, 1974, reported similar findings: infants with persistent hypotonia were likely to die, (43%), or survive with handicap, (22%). while those who progressed from hypotonia to a phase of extensor hypertonus were less likely to die, (18%), but had a substantial risk of survival with handicap, (45%). De Souza and Richards, 1978, after an attempt to identify antenatal, natal or post-natal conditions that would predict the occurrence of definite neurological abnormality in later childhood, concluded that only the form of neurological status in the newborn period was of any predictive value and that extensor hypertonus following an initial hypotonic, apathetic phase carried the worst prognosis.

The assessment of muscle tone is a central, essential part of the neonatal neurological examination and can be readily and reliably ascertained. The value of muscle tone changes in symptomatic asphyxia is well summarised by Brann and Dykes, 1977:

"The loss of tone in the infant is one of the first components of the Apgar score to disappear in the severely asphyxiated infant. It is the last of the components to return. For this reason, it is one of the best indicators of the severity of the intrauterine insult. If tone returns to normal within one or two hours, the infant has a good chance of surviving with an intact nervous system. However, if the infant remains significantly hypotonic after the first four or five days of life, there is an increased chance that the child will not survive the neonatal period, or will survive with severe cerebral damage. If hypotonia is replaced with marked hypertonia and increased activity during the first 24 hours, the chance of survival markedly increases, but there is an increased incidence of cerebral damage".

Conscious /

Conscious level.- The degree of depression of conscious level forms the basis of the division of neonatal neurological abnormality in hypoxic-ischaemic encephalopathy into clinical stages as described by Sarnat and Sarnat, 1976. Infants who entered stage 3, i.e. stupor, flaccidity, intermittent decerebration, depression of brain stem and autonomic functions, had a poor prognosis, as did those who showed the features of stage 2 for 5 days or more, i.e. obtundation, hypotonia, strong distal flexion, fisting with the thumb adducted, and multifocal seizures. Finer et al, 1981, using Sarnat's method of staging, reported similar results; none of the infants who showed only stage 1 encephalopathy, i.e. hyperalertness, hyperreflexia, sympathetic effects and a normal E.E.G., died or had significant handicap, while all those who entered stage 3 developed moderate or severe handicap, or died.

Similar conclusions can be drawn from the present study. The state of arousal of the infants was considered, rather than conscious level. The finding of apathy correlated strongly with subsequent handicap, while irritability and hyperalertness, without an apathetic phase, bore a highly significant relationship to a favourable outcome.

Time relationships

The importance of the changing patterns of neurological abnormality with time, seen in the neonate following intrapartum asphyxia, has been stressed earlier. The duration of neurological abnormality in the young infant is another useful indicator of prognosis. Clearly, some infants destined to have severe handicap will show persistent abnormality from the time of birth, but, as Amiel-Tison, 1969 and 1973, described, the time of return to apparent neurological normality in other infants bears a relationship to outcome. She divided term infants into three groups by the severity and duration of their neurological findings. Group 1 infants had intact consciousness and reflex responses and achieved /

achieved normality before 7 days of age; all but one infant remained normal at follow up. Infants in group 2 showed alteration of consciousness and reflexes, sometimes with convulsions, the duration of abnormality exceeding 7 days; 25-30% had moderate long term sequelae. The third group showed severe, persistent, neurological abnormality, after status epilepticus; most of these became severely handicapped.

Scott, 1976, in a study of the outcome of very severely asphyxiated infants, who were either apparent stillbirths or failed to establish spontaneous respirations within 20 minutes of birth, found that no child who later developed cerebral palsy was at any stage considered neurologically normal. The infants in this study, however, were not given a systematic neurological examination in the neonatal period by one person, their neurological status being ascertained retrospectively from the casenotes. At follow up, children were classed either as normal or cerebral palsied; minor neurological abnormalities were not described.

In the present study, 4 of the 33 children considered neurologically normal at the time of discharge from hospital have shown abnormalities subsequently; two have a mild hemiparesis and two slow development. Each child with major physical or mental handicap was found at each stage of follow up assessment to have continuing abnormality. Mild developmental delay or mild asymmetries commonly do not become apparent until later in infancy.

Thus the question of prediction of outcome can also be approached from a more positive angle - the prediction of normality rather than abnormality. The return to apparent neurological normality in the neonatal period, and its timing, are useful positive indications, (Amiel-Tison, 1969). Dennis, 1978, in her study of neonatal convulsions, found that all of the infants regarded as definitely normal at the time of discharge home, subsequently proved this judgement correct /

correct, an accuracy of forecasting not found in the present work. She reported also that the grading "definitely abnormal" at the time of discharge was a reliable prediction, and that subsequent assessments in the first year of life were of less predictive value for the individual child than this early grading. Of the 14 children in the present study, considered abnormal to any degree on leaving hospital, 5 showed no persistent abnormality, neurological status becoming normal between 3 weeks and 4 months of age.

Electroencephalographic findings

The predictive value of electroencephalographic findings in the neonate has been the subject of dispute. A number of workers have concluded that E.E.G. abnormalities are of little or no prognostic significance. Harris and Tizard, 1960, in a study of the E.E.G.'s of 41 infants with neonatal convulsions, considered that E.E.G. abnormalities, with the possible exception of unilateral or bilateral inter-seizure abnormalities, did not appear to bear any definite relationship to eventual outcome. Torres and Blaw, 1968, and Brown, 1976a, came to the same conclusion, but Tibbles and Pritchard, 1965, in a study of neonatal convulsions found that 70% of those with a normal E.E.G. developed normally, while 64% with an abnormal E.E.G. died, or had significant neurological sequelae. Monod et al, 1972, analysed the E.E.G. findings in 270 neonates, with miscellaneous but unspecified clinical problems, and concluded that a normal E.E.G. was of highly favourable, prognostic significance while various E.E.G. abnormalities - inactive, paroxysmal, low voltage, absence of lability, and persistent absence of occipital activity - were of grave prognostic import.

The electroencephalographic patterns associated with 3 clinical stages of hypoxic-ischaemic encephalopathy have been described by Sarnat and Sarnat, 1976. Infants in stage 1 showed normal E.E.G. activity, in stage 2 a periodic pattern, which improved to continuous /

continuous activity before clinical signs improved, while in Stage 3 there was depression of the periodic pattern and further voltage depression, becoming isopotential in some infants. The following neonatal E.E.G. abnormalities appeared to be associated with a poor prognosis: a totally isopotential record at any time, a periodic pattern with an isopotential phase between bursts of activity that occurred less than every 6 seconds, a periodic pattern in wakefulness persisting for 7 days or more, and recovery from a periodic pattern to abnormal, low amplitude, slow activity. Sarnat and Sarnat recommend that at least 2 E.E.G. recordings be made during the first week in asphyxiated infants, on the second and sixth days, during sleep and wakefulness and state that, "The time course of the composite clinical and E.E.G. changes provides a more sound basis for prognosis than do isolated symptoms and signs, the presence of seizures, or E.E.G. changes alone".

Holmes et al , 1982, in a retrospective study of E.E.G.'s of 38 infants with some evidence of intrapartum asphyxia, report similar findings, but claim a greater predictive value for E.E.G. abnormalities. Normal and maturationally delayed E.E.G.'s were associated with normal outcome, while low voltage, inactive and burst suppression E.E.G.'s were highly correlated with severe neurological sequelae. They concluded that, "A single E.E.G. done early in the course of asphyxia neonatorum is a more sensitive predictor of outcome than the neurological examination". It is apparent, however, that single observations of electroencephalographic patterns, as with most forms of clinical observation, can be misleading. Robertson, 1969, demonstrated that the newborn E.E.G. is altered temporarily by hypoxaemia, during attempts to wean off assisted ventilation, and, from the present study, it has been shown that E.E.G. appearances can vary considerably between recordings on consecutive days and also over the course of single, prolonged records.

The /

The study of evoked electroencephalographic responses may give useful information about neurological function following asphyxia. Hrbek et al, 1977, described disturbances of visual and somatosensory evoked responses in 57 newborn infants, with low Apgar scores, particularly visual responses, (85%), and devised a scoring system based on the alteration observed; this correlated with the degree of asphyxia as indicated by Apgar score. They also stressed the importance of repeated observations.

In summary, a number of factors, which are useful indicators of the neonatal neurological status of the asphyxiated infant, bear a strong relationship to subsequent neurological status and, from a consideration of these, it is possible to make a meaningful assessment of risk for the individual child. Relationships with outcome are not, of course, absolute and indicate probabilities; such predictive information must be regarded with caution, but nevertheless is of value in the clinical management, future planning and discussion of the individual child.

It would be unwise to place great reliance on any single factor. Patterns of abnormal neurological function, however, are composites built from a number of findings on neurological assessment of the infant. Consideration of the highly significant risk factors identified in the present study by a proportional hazards model of analysis, (McCullagh, 1980), where outcome is taken as the response variable and predictors which do not add further information are omitted in a stepwise fashion, has shown that the occurrence of tone patterns 1 and 2, as opposed to 3, 4, and 5, and of ophthalmoplegia, give the strongest correlation with outcome, rather than a more complex scoring of risk factors.

Early /

Early management of neonatal symptomatic asphyxia

An account will be given of the observation, investigation and treatment of infants who present with evidence of neonatal symptomatic asphyxia. Prompt and vigorous resuscitation will, of course, be necessary in many instances at birth. Recognition of abnormal behaviour and performance and abnormal neurological state on repeated assessments are central to the appraisal of the neonate in this situation and have been described and discussed earlier.

Observations of clinical state

Vital signs.- The routine observations made of any ill infant are of particular relevance here; much can be learnt from their careful recording and interpretation. As minimal disturbance of the infant is desirable, full use should be made of monitoring equipment to allow frequent or continuous observations to be made. Heart rate and rhythm, blood pressure, respiratory rate and abnormalities of rhythm, and rectal temperature should be recorded. An E.C.G. monitor will allow recognition of arrhythmias; bradycardias are common during phases of depressed conscious level, apnoeic episodes and fits. The possibility of other cardiovascular effects of asphyxia should be considered: persistent fetal circulation presenting with cyanosis in high ambient oxygen concentrations, tachypnoea and perhaps signs of persistence of the ductus arteriosus, and ischaemic myocardial damage with evidence of cardiac dilatation and low output cardiac failure. There is still some tendency to overlook blood pressure measurement in young infants, but with the availability of automatic devices, such as the Dinamap, Critikon Inc., blood pressure can be readily, accurately and non-invasively determined. An apnoea alarm will indicate periods of respiratory cessation and may give some indication of respiratory pattern. In the most severely affected infants, temperature regulation may be impaired; rectal and environmental temperature should be carefully recorded /

recorded and the latter controlled within narrow limits.

Infant weight and fluid balance.- Accurate weighing is essential and should be done at least daily, although this may present practical problems when the infant is in poor condition and perhaps attached to ventilator equipment. Weighings are generally still possible, and give valuable indication of fluid balance. The volume and nature of fluids given intravenously or nasogastrically must be carefully regulated and recorded. Urine output should be measured, although this again may be difficult especially in female infants, and the urine examined for the presence of blood, protein, and glucose and microscopically for renal cells and casts.

Laboratory analyses

A full blood count should be performed shortly after birth and at intervals thereafter to identify blood loss from antepartum, or intrapartum haemorrhage, and polycythaemia secondary to chronic placental insufficiency or, in those born outside hospital, to delayed cord clamping. In infants who have suffered a major degree of asphyxia, or birth injury, or in whom there is clinical suspicion of a haemorrhagic tendency, a coagulation screen is indicated. The full blood count may show reduced platelet numbers and the presence of red cell fragments. The findings of a coagulopathy secondary to intrapartum asphyxia suggests major tissue damage with release of thromoplastin, (Turner, 1976).

Determinations of acid-base state by capillary blood gas measurement should be made shortly after birth and at intervals subsequently. Measurement of umbilical arterial blood gas values from an isolated segment of cord at birth gives useful information about the severity of the intrapartum insult and is a guide for correction of acidosis. Initially, /

Initially, a mixed respiratory and metabolic acidosis is common, while later in the infant's course other disturbances may be found: the presence of hypocapnia from central hyperventilation in the irritable, hypertonic infant raises the possibility of increased intracranial pressure, while hypoventilation may occur in the centrally depressed infant, spontaneously, or as a result of the depressant effect of drugs. Associated cardiorespiratory problems, such as meconium aspiration, transient tachypnoea, and persistent fetal circulation will necessitate the control of oxygen therapy, ideally by continuous measurements of inspired oxygen and transcutaneous pO_2 , with intermittent arterial sampling.

Plasma urea, creatinine and electrolyte levels should be assayed regularly, at least once a day and more often when disturbances are found, to control the effects of treatment. Disturbances of sodium, potassium and calcium are common and varying degrees of temporary renal impairment will be found. Frequent blood glucose estimations are important and by use of capillary stick tests, hypoglycaemia can be quickly detected and treated, but it is good practice to confirm its occurrence by formal biochemical measurement. Urinary and plasma osmolality measurements are useful, particularly when inappropriate A.D.H. secretion or acute renal failure occurs.

Disturbances of these biochemical values are widely recognised, should be sought routinely and, in some instances by forethought in management, can be avoided. Biochemical evidence of hepatic disturbance is less well documented. Hume, 1983, found elevated alanine aminotransferase, A.L.T., levels in approximately 50% of term infants with severe symptomatic asphyxia. Hyperammonaemia, probably due to the combined effects of protein breakdown and hepatic damage secondary to ischaemia, has been described, (Goldberg, 1979). Goldberg *et al* suggested that hyperthermia, hypertension, exaggerated sinus arrhythmia and neurological features such as coma, seizures and longterm neurological /

neurological dysfunction might result from hyperammonaemia.

Various enzymes in cerebrospinal fluid, plasma and urine have been shown to be elevated following significant intrapartum asphyxia, to give some indication of tissue damage and, in some instances, to correlate with subsequent outcome. In C.S.F. elevated lactate dehydrogenase, L.D.H., and hydroxybutyrate dehydrogenase, H.B.D., levels have been found to bear a relation to psychomotor development at 1 year, (Dalens, 1981). In blood, the brain specific fraction of creatine kinase, CK-BB isoenzyme, is elevated after severe asphyxia and correlates with neurological outcome, (Becker, 1978; Cuestas, 1980; Walsh, 1982). Determination of these enzymes may be useful in assessing the severity of tissue damage in the neonate and has some prognostic value. Raised levels of C.S.F. lactate are found following an asphyxial insult and also give some indication of the severity of cerebral hypoxia, (Svenningsen, 1972; Mathew, 1980).

Investigative procedures

A number of other investigative techniques are of value in the assessment of the acute and subsequent condition of infants following a hypoxic-ischaemic episode. The role of the electroencephalogram has been discussed earlier and, provided the expertise is available for good recordings and for their interpretation in this situation, it may contribute useful information; evoked E.E.G. responses may also prove useful in early assessment and prognostication, (Hrbek, 1977). With the improvement in technical specification and particularly the advent of portable, real-time equipment, ultrasound echoencephalography has established a place in the recognition of cerebral oedema - by decreased ventricular size, and of intracerebral, subependymal and intraventricular haemorrhages, (Pape, 1979; Levene, 1981), although its ability to distinguish ischaemic brain tissue is uncertain, (D'Souza, 1983).

Computed /

Computed tomography is useful in the diagnosis of intracranial haemorrhage and cerebral oedema, (Chiswick, 1977), but in many hospitals there will be practical problems in access to scanning equipment for ill newborn infants. Again, there is doubt as to whether ischaemic changes such as periventricular leukomalacia can be reliably recognised, (Flodmark, 1980). It has an established role in the assessment of severely asphyxiated infants following the acute neonatal stage, (Fitzhardinge, 1981).

There remains a great need for practicable, non-invasive methods of dynamic measurement of both intracranial pressure and cerebral blood flow; these would allow a much greater understanding of the pathophysiological responses in the central nervous system in hypoxic-ischaemic encephalopathy, and would be invaluable in the rationalisation and regulation of treatment. A number of non-invasive methods of intracranial pressure measurement have been devised based on anterior fontanelle tension using an aplanation transducer, (Wealthall, 1974; Robinson, 1977), or a fibre-optic light system to detect movements of a pressure sensitive membrane placed over the fontanelle, (Vidyasagar, 1977). Measurements from such systems have shown good correlation with direct pressure recordings, although both methods can give spuriously high values due to excessive force of application, (Philip, 1982); Salmon, 1977, feels, however, that the aplanation transducer method is not affected by the tension of the fontanelle membrane, but by the force transmitted across the membrane, and, therefore, gives a direct indication of intracranial pressure.

It is difficult to find an accurate method of estimating cerebral blood flow in the newborn, even by invasive methods. Injection techniques may distort blood flow, (Lou, 1977, 1979; Philip, 1982). An estimate of cerebral blood flow can be made indirectly by deriving cerebral perfusion pressure, from mean arterial blood pressure and intracranial pressure, by Doppler ultrasound measurement of anterior cerebral artery pulsatility, (Bada, 1979), and by jugular venous occlusion /

occlusion plethysmography using a mercury-in-rubber strain gauge placed around the head, (Cross, 1976; Cooke, 1979), although all these methods carry a significant margin of error.

Treatment and management in the early neonatal period

Fluid and electrolyte balance

Fluid intake must be carefully controlled. Initially, 50 ml./Kg./24 hours can be given and the volume adjusted subsequently on the basis of body weight changes, urine output, plasma urea, creatinine, electrolyte and osmolality values. If there is evidence of inappropriate A.D.H. secretion, or of oliguria or anuria, continued fluid restriction will be necessary for some days. Hyperkalaemia, if marked, can be corrected by small intramuscular doses of insulin with intravenous dextrose infusion along with rectally administered calcium resonium. Hypotension in the early hours of life may be treated by plasma volume expansion with blood or plasma.

Cerebral oedema

This is a major complication of an asphyxial insult. It is a common finding in those infants who die in the first days of life, but as discussed earlier, its occurrence is clinically difficult to ascertain and methods of assessing intracranial pressure are limited. Dexamethasone has proven effective in other situations in preventing brain swelling if given sufficiently early, (Long, 1966; De Souza, 1973). Its mode of action is uncertain, but it is thought to prevent the development of abnormal vascular permeability. In the present study, infants considered to have sustained a severe asphyxial insult were given dexamethasone, 2 mg. Q.I.D., intravenously, from the first hours of life. Early administration is important, its effect being slow in onset, up to 10-12 hours, (Svenningsen, 1982); if there is suspicion of /

of established brain swelling, mannitol, 7 ml./Kg. 20% solution, should be given by I.V. infusion over 15 minutes. Regulation of fluid intake is also important.

Convulsions

Difficulty is not uncommonly experienced in achieving rapid control of fits secondary to intrapartum asphyxia, (Amiel-Tison, 1969; Volpe, 1977); frequently recurring seizures may occur over the first 3-4 days of life. Phenobarbitone has been, and remains, the mainstay of anti-convulsant treatment in this situation, given intravenously or intramuscularly initially in a dose of 8 mg./Kg./24 hours. Phenytoin also has a place, and in some instances its lack of profound C.N.S. depressant effects is an advantage - dose 5 mg./Kg. stat. by slow I.V. injection, followed by 7 mg./Kg./24 hours intravenously or orally. Diazepam, 0.2 mg./Kg. by slow I.V. injection or as rectal gel, is valuable in terminating individual fits, but has a short duration of action and can produce profound respiratory depression. Paraldehyde, 0.3 ml./Kg. by deep intramuscular injection is often effective in controlling fits where other methods have failed and can be repeated 4-8 hourly as necessary. Diazepam infusion is impracticable in the newborn because of the volume of fluid necessary to maintain the drug in solution. Lignocaine infusion has been used for refractory convulsions, mainly in Scandinavia. Anticonvulsant blood levels should be assayed regularly to allow control of therapy, particularly with the changing pharmacokinetics of barbiturate and phenytoin handling in the neonate, (Boreus, 1978; Loughnan, 1977).

Barbiturates and cerebral ischaemia

Barbiturates have been shown to have a number of properties which are potentially of value in hypoxic-ischaemia encephalopathy. Their anticonvulsant /

anticonvulsant, and sedative effects are of long established value. A reduction in cerebral metabolic rate for oxygen and a parallel diminution of cerebral blood flow, to less than 50% of normal, have been demonstrated in animals and man, (Pierce, 1962; Nilsson, 1975). These actions, together with an effect in reducing cerebral oedema and, therefore, cerebral hypertension in experimental animals and in some circumstances in man, (Clasen, 1974; Shaywitz, 1908), have raised hopes of some protective effect of barbiturates following cerebral ischaemia, (Steer, 1982).

High dose phenobarbitone treatment may have a place in the management of neonatal symptomatic asphyxia, but has yet to be fully evaluated. Svenningsen et al, 1982, conducted a trial of intensive treatment of severe birth asphyxia using a combination of measures, notably high dose phenobarbitone coupled in most cases with assisted ventilation to produce a degree of hypocapnia; this treatment was instituted shortly after birth. They report an improved survival and lowered morbidity in this group compared to less vigorously treated controls and to severely asphyxiated infants from previous years. The place of such management, however, is not fully established; there are a number of attendant hazards in addition to depression of vital function and suppression of useful neurological indicators of the infant's condition.

Cerebral blood flow autoregulation is thought to be impaired in hypoxic-ischaemic encephalopathy and to be pressure passive, (Lou, 1979). Hypertension and even normal blood pressure values may result in cerebral haemorrhage, (Lou, 1979a), and hypotension in further ischaemic damage. Phenobarbitone in large doses will result in, or may aggravate pre-existing cardiorespiratory depression, producing hypotension, hypoventilation, hypercapnia and cerebral ischaemia. The balance of effects is delicately poised. If treatment with high dose barbiturates and hyperventilation is used, it should be employed only when its effects can be regulated through an appropriately intensive level of physiological monitoring - continuous blood pressure, intracranial pressure, blood gas and ideally cerebral blood flow measurements.

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Without /

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ABBREVIATIONS

Abbreviations have been avoided, as far as possible. Their use has largely been confined to tables and proforma, when brevity was necessary.

Ab.	abortion
Abd.	abduction
art.	artery
A.P.H.	ante partum haemorrhage
A.T.N.R.	Asymmetrical tonic neck reflex
B.W.	birth weight
cap.	capillary
C.B.F.	cerebral blood flow
C.H.I	compressional head injury
C.P.D.	cephalo-pelvic disproportion
C.S.F.	cerebro-spinal fluid
Cv.	civil
D.O.B.	date of birth
E.C.G.	electrocardiograph
E.E.G.	electroencephalograph
E.M.G.	electromyograph
E.O.G.	electro-oculograph
E.T.	endotracheal tube
ext.	extension.
F.D.	fetal distress
F.H.	fetal heart
H.F.F.D.	Haig Ferguson forceps delivery
I.P.P.V.	Intermittent positive pressure ventilation
I.U.G.R.	intrauterine growth retardation
K.F.R.D.	Keilland's forceps rotational delivery
L.B.	live born
L.C.	live child
L.U.S.C.S.	/

L.U.S.C.S.	lower uterine segment caesarean section - el. elective em. emergency
N.A.	not applicable
N.F.B.M.	no fetal breathing movements
N.G.	naso gastric tube feeding
N.K.	not known
O.F.C.	occipito-frontal circumference.
O.P.	occipito-posterior presentation
O.T.	occipito-transverse presentation
pCO ₂	partial pressure carbon dioxide
pO ₂	partial pressure oxygen
prim	primiparous
P.T.T.	partial thromboplastin time
R.D.S.	idiopathic respiratory distress syndrome
res.	resistance
R.O.P.	right occipito-posterior presentation
R.O.T.	right occipito-transverse presentation
S.B.	stillbirth
S.M.M.P.	Simpson Memorial Maternity Pavilion, Edinburgh.
S.V.D.	spontaneous vertex delivery.
W.F.D.	Wrigley's forceps delivery.
W.P.P.S.I.	Wechsler pre-school and primary scale of intelligence
Wt.	weight
X.ext.	crossed extensor reflex

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Appendix I

NEONATAL NEUROLOGICAL EXAMINATION

(Dr J.K. Brown, Neurology Service, Edinburgh)

Name _____ Unit No. _____ Ward _____ Date _____

Reason for Referral _____

HISTORY _____

GESTATIONAL AGE

Dates _____ Dubowitz _____

Ultrasound, etc. _____

SMMP score _____

STATE OF AROUSAL

Apathetic / hypoalerted /normoalerted / hyperalerted

Change of state _____ volatile / stable / unchangeable

Sleep / wake cycles normal / abnormal _____

Clinical sleep states _____

EEG sleep states _____

Medication _____

Blood level at time of examination _____

HOMEOSTASIS

Respiration spontaneous / assisted / apnoeic attacks / cyanotic attacks

Blood gases pH _____ pCO₂ _____ pO₂ _____ HCO₃ _____ B.D. _____

Description of apnoeic attacks _____

Respiratory rate _____ pattern _____

Temperature _____ incubator yes / no _____

Lowest temperature recorded _____ stable yes / no

Autonomic Stability

Heart rate _____

Blood pressure _____

Osmolality _____

GENERAL FEATURES

Congenital malformations _____

Drugs to mother influencing examination _____

Metabolic Factors Influencing Examination

Glucose _____ Calcium _____

Magnesium _____ Bilirubin _____

Other _____

HEAD

Swelling _____ Caput _____ Bruising _____

Cephalhaematoma _____ Sutures splayed / normal / riding

Ant. fontanelle size _____ cms Tension _____ Pulsation present/absent

Shape (oxy, scapho, plagio) _____ Fracture _____

F.C. _____ Posterior fontanelle open / closed

Transillumination _____ Percussion note _____

Scalp veins normal / distended Sub-conj. haemorrhage present / absent

Intracranial bruit present / absent

CRANIAL NERVES

Head turn to light - / + Optokinetic nystagmus - / +
 Optical blink - / + / ++ Follow red ring - / + / ++ Focus - / +

Fundi

Pupils	Shape	round / irregular / oval
	Reaction light	nil / sluggish / normal / hippus
	Size	pinpoint / normal / dilated
Sunset sign	nil / transient / constant	
Nystagmus	nil / transient / constant	
Strabismus	nil / transient / constant	
Ptoisis	nil / transient / constant	
Doll's eye	(R) - / + (L) - / +	
Facial sensation	rooting	- + ++
	lip reflex	- + ++
	cardinal points	- + ++
	corneal reflex	- + ++
Facial movements	palpebral fissures	symmetrical / asymmetrical
	nasolabial creases	symmetrical / asymmetrical
	mouth	symmetrical / asymmetrical
	glabella tap	- + ++
	Chvostek's sign	- + ++
Eighth auditory	acoustic blink	- + ++
	quieten to voice	- + ++
Eighth labyrinthine	rotation test	
(1) head free	to right	- + ++
	to left	- + ++
(2) eyes with head held	to right	- + ++
	to left	- + ++
Bulbar muscles	sucking rate	- + ++ +++
	grouping sucks	- + ++ +++
	stripping	- + ++ +++
	cough reflex	- +
	gag reflex	- +
	swallow/respiration control	- + ++
	feeds breast / bottle / tube / parenteral	
	nasal regurgitation	- / +
Fasciculation tongue	- / +	
Torticollis		

REFLEXESPhasic Reflexes

(1) Biceps jerk	-	+	++	+++
(2) Knee jerk	-	+	++	+++
(3) Ankle jerk	-	+	++	+++
(4) Toe jerk	-	+	++	+++
(5) Jaw jerk	-	+	++	+++
(6) Hamstrings	-	+	++	+++
(7) Jaw clonus	-	+	++	+++
(8) Ankle clonus	-	+	++	+++
(9) Hamstring clonus	-	+	++	+++
(10) Tremor	-	+	++	+++
	coarse	/	fine	Approximate frequency _____ sec.

Cutaneous Phasic Reflexes

(1) Anal reflex	-	+	++ (spread to toes + / -)
(2) Abdominal reflexes	-	+	
(3) Dermatome to myotome flexion and adduction arms (axilla)			_____
			abdomen _____
			leg adductors _____
(4) Palmar grasp	-	+	++ (traction - / + / ++)
(5) Plantar grasp	-	+	++

Progression Reflexes

(1) Walking	-	+	++	+++
(2) Stepping	-	+	++	+++
(3) Hand placing	-	+	++	+++
(4) Cycling	-	+	++	+++
(5) Crawling	-	+	++	+++
(6) Cliff edge	-	+	++	+++
(7) Bauer	-	+	++	+++

Extension Reflexes

- (1) A.T.N.R. present / absent / arm / leg / obligatory
- (2) Trunk incurvation trunk inc. _____
 ext. leg _____
 abd. leg _____
 ext. arm, turn head _____
- (3) Perez - + ++ +++
- (4) Moro abduction - +
 extension - +
 adduction - +
 flexion - +
 legs involved yes / no _____
 threshold high / low
 tremor yes / no
 method head drop / cot bang / body drop
- (5) hand open stimulating dorsum - +
- (6) crossed extension flex / extend / adduct / fan
- (7) snout reflex present / absent
- (8) spontaneous Babinski - +
 snout / suspension / squeeze calf / perineal pressure

Feeding Reflexes

- (1) rooting latent / rapid / very wide trigger zone / neg. response
- (2) cardinal points / lip purse - + ++ +++
- (3) suck / reject - + ++ +++
- (4) swallow / gag - + ++ +++
- (5) vomit - +

Nociceptive Spinal Reflexes

- (1) flexor withdrawal reflex legs - + ++ Y
 arms - + ++ Y
- (2) Babinski response present / absent
- (3) mass flexion reflex - perineal present / absent

MOVEMENT

Deformity present / absent (type) _____

Hips normal / abnormal

Talipes present / absent (type) _____

Muscle palpation firm / normal / flabby

Muscle power normal / abnormal

Muscle	M.R.C. grade 0 - 5

Wasting _____

Fasciculation _____

Type of Movement

Spontaneous movements arm / both arms / leg / both legs / arms and legs
 none / reduced / normal / increased / continuous

Effect of arousal _____

Athetoid movements absent / present / gross

Myoclonus / startles absent / present / gross

Facial movements absent / present / gross

Tremor absent / present / gross

Gross trunk movements absent / present / gross

Head turning absent / present / gross

Stretches absent / present / gross

Convulsive or release movements _____

Hemisindrome

Reflex _____

Tone _____

Power _____

Spontaneous movements _____

Clonus _____

MUSCLE TONE

	normal	/	hypotonic	/	decerebrate	/	regressed	/	premature
Head Control	pull to sit		-		+		++		
	prone suspension		-		+		++		
	sitting			on chest	/	off chest			
Adduction	arms		-		+		++		
	legs		-		+		++		
	Moro		-		+		++		
	crossed extension		-		+				
Arms	flexed	/	extended						
	recoil		nil	/	slight	/	good	/	Y
	scarf		nil	/	slight	/	good	/	Y
	wrist angle								
	traction		present	/	absent	/	Y		
Legs	flexed	/	extended						
	recoil		nil	/	slight	/	good	/	Y
	heel to ear		nil	/	slight resistance	/	good resistance	/	
	popliteal angle		180	/	120	/	90	/	60 / Y
	tendo achilles to tibia		20	/	40	/	90	/	Y
Righting	legs	/	trunk	/	head				
Extensor Tone			inhibited	/	increased				
	neck retraction		absent	/	present				
	opisthotonus		absent	/	present				
	legs extended		nil	/	on stimulation	/	constant	/	obligatory
	arms extended		-	/	+				
	dog paddling		-	/	+				
	claw hand		-	/	+				

POSTURE

Supine

Prone Suspension

Prone Lie

Vertical Suspension

BEHAVIOUR

Cry _____

Consolability _____

Cuddliness _____

Habituation to light _____

 bell _____

 pinprick _____

Response to smell or taste _____

 hunger _____

SENSATION

Sensory level (pinprick) _____ Triple response _____

SUMMARY

normal / abnormal / suspect

Appendix II

Study No.: _____

Intrauterine Asphyxia

Mother: Mat. No.:..... Age:....

Address:.....

G.P.:.....

Cv State: M / S / W / D / C.

Mother: Previous occupation Father: Age Occupation

Medical F.H.:.....

Maternal P.H.:

Parity L.B.; L.C.;S.B.;Ab

Obstetric History

Date	Place	Gestation	Delivery	B.W.	Outcome

Infant Name: Sex:..... Unit No...... D.o.B:...
Gestation by dates Birth Wt.:
Gestation by assessment Discharge Wt.....

Delivery

Summary of problems:

Treatment at discharge:

Date of Discharge: Date of 1st Follow up:.....

Antenatal History:

1st Trimester

.....

2nd Trimester

.....

3rd Trimester

.....

Home background

Mother: temperament stable / excitable / understanding

past psychiatric illness +/- ;.....

post partum depression +/- 2^o to problems with
infant +/-

Prognosis given to parents while child in hospital

.....

.....

Parents reactions to neonatal problems:

.....

.....

Parents reactions to problems at home:

.....

.....

Ability to cope with problems: good / fair / poor

Home conditions: good / fair / poor

Mothering ability - normal child good / fair / poor

child with problems good / fair / poor

Father's involvement with family: good / fair / poor

Summary of meetings with family:

- 1.....
-
-
- 2.....
-
-
- 3.....
-
-
- 4.....

Study No.:

Intrauterine Asphyxia

Name:..... Sex:.... D.o.B.:..... Unit No:

Reason for Inclusion

Base deficit	+ / -
Scalp pH	+ / -
Gasping	+ / -
Symptomatic asphyxia	+ / - specify.....
Control	+ / -

Antepartum details

Disturbance of maternal circulation + / - specify

Disorders of placenta:

insufficiency: low oestriols + / - centile, time

poor intrauterine growth + / -

marked placental infarction + / -

transplacental haemorrhage + / -

placenta praevia + / - type

placental separation - abruption + / -

E.C.V. + / -

Twins + / -

short cord + / -

placental weight gm.

pre-eclampsia + / - mild / moderate / severe

Disorders of cord:

prolapse + / -

tightly round neck + / -

Disorders of uterus

Tonic contractions + / -

syntocinon + / - max. rate

Maternal Drugs

Analgesia

anaesthesia: general /epidural / none.

other

Foetal Breathing + / - NFBM / mixed / gasping / other
time

Intrapartum details:

prolonged labour + / - 1st stage 2nd stage.....
foetal distress + / - monitored + / -
meconium staining + / -
tachycardia + / - specify, time and duration
bradycardia + / -
type I dips + / -
type II dips + / -
variable decelerations + / -
scalp gases pH + / - lowest
base deficit + / -
cord gases + / - Normal / Abnormal
pH / pO / pCO₂ / Base Def. /
lactate / pyruvate + / - Normal / Abnormal

Delivery

Spontaneous / Induced
SVD / WFD / HFFD / KFRD / Ventouse
Breech - spontaneous / assisted
L.U.S.C.S. - elective / emergency

Indications for intervention:

Obstetric opinion of foetus

no concern / concern + no intervention / concern + intervention

Immediate Postnatal Period

Apgar 1 minute 5 minutes

Time to spontaneous respirations minutes

Time to regular independent respirations minutes

Resuscitation - nil

IPPV mask time

IPPV E.T. time

dextrose + / - dose

bicarbonate + / - dose

lethidrone + / - dose

Gases + / - cap./art. pH pCO₂..... pO₂..... Base deficit

Paediatric opinion of condition good / fair / poor

Neonatal Period

Birth weight kg. centile <10 / 10-90 / > 90

length cm. centile <10 / 10-90 / > 90

O.F.C. cm. centile < 10 / 10-90 / > 90

gestation by dates ext neuro

Neonatal Problems

Feeding Breast / Bottle poor well

tube + / - duration

persistent vomiting + / - specify

hypothermia + / - incubator +/-

apnoeic episodes + / - specify

cyanotic episodes + / - specify

convulsions + / - type, age, no.

irritability + / - specify

cerebral cry + / - specify

apathy + / - specify

jaundice, 170 umols/l + / - levelumols/l...

meconium aspiration + / - mild/moderate/severe

R.D.S. + / - mild/moderate/severe, poorest gases.

.....

.....

significant infection + / - specify.....

other problems + / -

hypoglycaemia + / - lowest level mmols/l, time,
duration, Px.....

hypocalcaemia + / - lowest levelmmols/l.....

hypomagnesaemia + / - lowest levelmmols/l

hyponatraemia + / - time, level

hyposmolality + / - time, level

coagulation defect +./ - platelets <100, 100 +/- time
prothrombin > 28 secs +/- time
P.T.T. > 100 secs. +/- time
fibrinogen <100 mg% +/- time

treatment

Neurological Examination

State of Arousal:

apathetic / hypoalert / normoalert / hyperalert

Time from last feed:

General Examination:

Congenital Abnormalities:

Heart rate/min. B.P.(Doppler) nn Hg. site, state ..

..... Resp. Rate/minute Rhythm

Temperature°C incubator + / -

General Examination

Nails	Short	Terminal	Long
Lanugo	to 36 weeks	37 - 38 weeks	Term
Sole creases	Ant.Trans.creases	Ant. 2/3 not heel	Sole covered with vert. and trans.
Breast nodule diam.	2.0 mm	4.0 mm	7.0 mm
Hair	Fine and fuzzy	Fine and fuzzy	Coarse and silky
Ear Lobe	Pliable	Some cartilage	Stiffened
Scrotum	Small few rugae	None lateral	Extensive rugae testes in sac

NEUROLOGICAL ASSESSMENT

Pupillary reaction (29 - 31 appears) Present /Absent
 Head turn to light (32 - 36 appears) Present /Absent
 Glabella (32 - 34 appears) Present /Absent
 Neck righting (34 - 37 appears) Present/Absent
 Head turning (prone 30 weeks) Present /Absent
 Trunk incurvation (28 weeks). Active 34 weak term (use thumb nail)

REFLEX CHANGES

A.T.N.R.	28 weeks	32 weeks	34 weeks	37 weeks	Term
A.T.N.R.	+	++	++	+	
Grasp	+	++	lift bed.	flex arms and neck	
X ext.	Withdraw	Extend	fan	flex ext fan and adduct	
Walk	Nil	c.support	same	on toes	flat feet
Suck	Weak	strong	synchronous with swallow		
Root	Latency ++	rapid	Full		
<u>Tone</u> Posture	Arms and legs ext.	legs flexed at hip and knee	Arms flexed as well		
Recoil	Nil	Slight legs	Good legs	Slight arms	Good arms
Scarf	No res.	No res.	Slight	Just past midline	To midline
Heel to ear	No res.	Slight	Difficult	Impossible.....	
Dorsiflexion	40°		40°	20°	To tibia
Popliteal Angle	180	150	120	90	90
Righting	Nil	Nil	Leg	Trunk	Head
Adduction	None		More legs Arms Knee jerk X ext		

Age

SKULL:
.....

CRANIAL NERVES:
.....

PRIMITIVE REFLEXES

Progression	Present / Absent
Feeding	Present / Absent
Extensor Reflexes	Present / Absent
Flexor Withdrawal	Present / Absent
Grasp	Present / Absent
Anal	Present / Absent
Babinski	Present / Absent

PHASIC REFLEXES

Biceps Jerk	-	+	++	+++	
Knee Jerk	-	+	++	+++	
Ankle Jerk	-	+	++	+++	
Toe Jerk	-	+	++	+++	
Tremor	Present	Absent	Central	Peripheral
Clonus	Ankle	Jaw	Hamstring	Other	

MUSCLE TONE

Normal flex / Regressed / Hypotonic / Ext hypertonic

Power (paresis)

Deformity

Spontaneous movement

Hemisynndrome Present Absent

Hips Normal Subluxated Dislocated Clicking
Abduction legs extended

Wasting Athetoid Movement

Posture

Summary

Normal	Abnormal
.....

2

INFANT:

Sex: Male 1 Female 2		34
Assessed gestational age		36
Birth weight		39
10th centile 1 10th-90th 2 90th 3		40
Singleton 1 Twin 2		41
Virtual stillbirth: yes 1 No 2		42
Time to spontaneous respirations mins (immed 88) ...		44
Time to regular independent respirations mins. (Immed. 88) (not established 99)		46
Ventilation: Yes 1 No 2		47
duration mins. N/A 99 Prolonged 88.....		49
Apgar 1 minute		51
5 minutes		53
Opiate antagonist: Yes 1 No 2		54
Paediatric evidence of C.H.I. Yes 1 No 2		55
Initial condition: Poor 1 Fair 2		56
Loss of consciousness: Yes 1 No 2		57
Gasping: Yes 1 No 2		58
<u>Symptoms</u>		
Feeding depression.....		59
Vomiting		60
Hypothermia		61
Apnoea		62
Cyanosis		63
Irritability		64
Cerebral cry		65
Apathy		66
Fits		67
(Yes 1 No 2)		
No. of Symptoms		68
Jitteriness: Yes 1 No 2		69
Fits age of onset hrs. (99 not applicable) ..		71
No. fits: 88 numerous 99 Not applicable		73
Type: tonic 1 clonic 2 both 3 brain stem 4 not applicable 9 ...		74
Duration of fits hrs. (999 not applicable) (001 thr. of less)		77

3.

MUSCLE TONE

Persistent hypotonia 1 Hypotonia-Ext. Hypert-hypot 2..	<input type="checkbox"/>	78
Hypotonia-Ext.Hypert-Flex. 3 Hypotonia-Flexion 4		
Flexion 5		
Late hypotonia >7 days: Yes 1 No 2 n/a 9	<input type="checkbox"/>	79
Age at end of early hypotonia hrs. (999 n/a)	<input type="checkbox"/>	82
Age at end of ext. hypertonia days (99 n/a)	<input type="checkbox"/>	84
Age at end of late hypotonia days (99 n/a 88 persistent)	<input type="checkbox"/>	86
Age at gaining normal flexor tone days	<input type="checkbox"/>	88
(99 dead/ 88 didn't/ 77 always flexed)		

OTHER NEUROLOGY

Hemisynndrome: Yes 1 No 2	<input type="checkbox"/>	89
Bulbar palsy: Yes 1 No 2	<input type="checkbox"/>	90
Ophthalmoplegia: Yes 1 No 2	<input type="checkbox"/>	91
Athetoid: Yes 1 No 2	<input type="checkbox"/>	92
Spinal release: Yes 1 No 2	<input type="checkbox"/>	93

BIOCHEMISTRY

Hyponatremia: Yes 1 No 2 n/k 9	<input type="checkbox"/>	94
age 1st detected days (n/a 9)	<input type="checkbox"/>	95
Hypocalcaemia: Yes 1 No 2 n/k 9	<input type="checkbox"/>	96
age 1st detected days (n/a 9)	<input type="checkbox"/>	97
Hypoglycaemia: Yes 1 No 2	<input type="checkbox"/>	98
Plasma Osmolality <280-1 280-300 - 2 >300 - 3		
n/k 9 High and low 4	<input type="checkbox"/>	99
E.E.G.: Normal 1 abnormal 2 doubtful 3 n/k 9	<input type="checkbox"/>	100
Time to stopping N.G. feeds days N/a 99	<input type="checkbox"/>	102
Age at discharge days: (dead 99)	<input type="checkbox"/>	104
Early behaviour disturbance: Yes 1 No 2 n/a 9	<input type="checkbox"/>	105
Extensor dystonia: Yes 1 No 2 n/a 9	<input type="checkbox"/>	106
Outcome category: 1, 2, 3, 4, 5 neonatal death		
6 late death	<input type="checkbox"/>	107