Editorial

Birth Asphyxia, Apgar Score and Neonatal Encephalopathy

As infant mortality rates decline steadily in South Asia, largely through a fall in post-neonatal mortality, increasing attention is turning to the perinatal period(l). Many studies in this region have demonstrated birth asphyxia to be a major cause of perinatal death(2). However, the contribution of birth asphyxia to the burden of neurodisability in developing country populations is still to be accurately defined. More recently, neuro-epidemiologists have revisited the definition of birth asphyxia and suggested that future work should focus on the clinical entity of neonatal encephalopathy (NE). In this commentary we briefly review these concepts.

Birth Asphyxia

Birth asphyxia refers to an impairment of the normal exchange of respiratory gases during parturition, and the ensuing adverse effects on the fetus. It is an important cause of fresh stillbirth and early neonatal death. The condition of a newborn infant is determined by a complex interaction of maternal, placental, uterine and fetal factors extending through pregnancy to delivery. At the core of the feto-maternal unit is the process of placental exchange whereby oxygen from the maternal circulation and carbon dioxide from the fetal circulation passively diffuse across the placental membrane. The labor process imposes great strains on placental exchange. During normal uterine contractions placental exchange is abolished when the uterine pressure exceeds 10 mm Hg. Studies using infra-red spectroscopic techniques during normal labor show that many infants undergo intermittent hypoxia during the process of delivery(3). Despite this hypoxic stress most infants are born in good condition.

Apgar Score

In 1953 the anesthetist Virginia Apgar described her popular scoring system which permitted a quantitative expression of the early postnatal condition of the newborn infant(4). It *was* designed to be a guide to the need for resuscitation of newborns. An infant suffering from birth asphyxia is usually in poor condition at birth and therefore has a low Apgar score. Over time the universality and convenience of the Apgar score led many investigators to adopt it as a marker for birth asphyxia. This remains the case, and varying definitions of birth asphyxia based on Apgar scores are found in the literature. Most commonly a one minute Apgar less than or equal to three, or a five minute Apgar less than seven have been taken to indicate birth asphyxia. The International Classification of Diseases (10th revision) classifies birth asphyxia with reference to Apgar scores at one minute of age (Apgar[1] 4-7: mild/moderate birth asphyxia, Apgar[1] < 3: severe birth asphyxia)(S).

There are many causes other than birth asphyxia for a low Apgar score(6). Healthy premature infants have low Apgar scores due to their immature nervous system. Naso-pharyngeal suction, maternal drugs and anesthesia may temporarily depress the Apgar score, and other pathological processes such as sepsis may also result in poor condition at birth. There is also con-

siderable inter-observer disagreement in the allocation of Apgar scores.

Apgar scores correlate poorly with outcome, which limits their usefulness for epidemiological studies(7). In the USA, in the 1950's the Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke (NCPP) used trained independent observers to record the Apgar scores of over 50,000 newborn infants until 20 minutes after birth. Follow-up demonstrated the poor specificity of the early Apgar score for neurodevelopmental outcome. However, the extended Apgar score recorded 20 minutes after birth had much better specificity for the prediction of both early death and disability(8). It is apparent that continuing depression of the infant after the first minutes of life is more significant than responses immediately after birth.

Hypoxic Ischemic Encephalopathy

In 1976 Sarnat and Sarnat published a combined clinical and EEG study of 21 term infants who displayed evidence of fetal distress(9). They described a syndrome of neurological and electro-encephalogram (EEG) features that they labeled *neonatal encephalopthy following fetal distress.* In their original study the syndrome was divided into three stages, with severely affected infants typically progressing from grade 1 to grade 3. This scheme was later modified by Fenichel, who grouped the clinical features of what he termed *hypoxic-ischemic encephalopathy* (HIE) into three different patterns (mild, moderate and severe) *(Table 1)*(10). The asphyxiated infant was not considered to progress through the grades but rather to exhibit the characteristic features and time course (of either deterioration or resolution) consistent with **a** particular grade. Whilst the Sarnat system continues to be used by investigators in specialised centers with neonatal EEG expertise, the Fenichel approach, or minor modifications thereof, has been widely adopted in clinical studies(11-15).

Neonatal Encephalopathy

More recently the definition of HIE has

TABLE I - *Syndromic Diagnosis of Neonatal Encephalopathy*

Feature	*Grade I (mild)*	*Grade 2 (moderate)*	*Grade 3 (severe)*
Conscious level	**irritable/hyperalert**	**lethargic**	**comatose**
Tone	**either**[a] mildly abnormal (hypo/hyper)	**moderately abnormal** (hypotonic or dissociated)	**severely abnormal** (hypotonia)
Suck	**or**[b] abnormal	**poor**	**absent**
Primitive reflexes	exaggerated	**depressed**	**absent**
Seizures	**absent**	present	present
Brain stem reflexes	**normal**	**normal**	**impaired**
Respiration	tachypneic	occasional apneas	**severe apnea**

Adapted from Fenichel (10).
The features in **bold** are the main requirements for each grade.
Features not in bold may be present but are essential for syndrome assignment.
a/b: either abnormal tone or abnormal suck should accompany altered conscious level to assign grade 1.

itself been criticised(16). Most investigators have included some marker of fetal distress and /or low Apgar score in their case definition of HIE. There are two problems with this approach. In the absence of a practical method of directly measuring fetal asphyxia during the birth process- these secondary markers have problems of interpretation(17). Secondly high quality information on the condition of the fetus during labor is often lacking. In 1992 a task force set up by the World Federation of Neurology Group for the Prevention of Cerebral Palsy and Related Disorders concluded that researchers should employ a wider definition of neurobehavioural abnormality in the newborn infant - *neonatal encephalopathy of early onset* (NE)(18). NE has been described as a *'disturbance of neurological function in the earliest days of life in the term infant manifested by difficulty initiating and maintaining respiration, depression of tone and reflexes, subnormal level of consciousness and often by seizures'(16)*. It is most usefully defined and graded in a comparable manner to that described for HIE.

Differential Diagnosis of NE

The task force recognised that birth asphyxia is not the only cause of NE and recommended that 'clinical information be recorded as to possible antecedents of the encephalopathy'. Causes of neonatal encephalopathy recognized to date include: (i) perinatal hypoxia-ischemia; *(ii)* hypoglycemia; *(iii)* infection; *(iv)* severe hyperbilirubinemia; *(v)* cerebral trauma; *(vi)* intracranial hemorrhage; *(vii)* idiopathic cerebral infarction; *(viii)* inherited metabolic disorders; *(ix)* congenital neuromuscular disease; and *(x)* congenital dysmorphic syndromes. The causes of NE are likely to differ according to the population studied and the exact definition of encephalopathy employed. A recent Australian study found evidence of adverse intrapartum events in only 13 of 89 cases (15%) in a large population based study of NE in full term singleton infants(19). This series includes 15 congenital malformation syndromes. Intrapartum asphyxia as a cause of NE might be expected to be more common in developing countries because risk factors are more common, and services less accessible, but epidemiological data is required to inform perinatal intervention strategies.

Antecedent Risk Factors for NE

Interest is growing in antecedent factors which might render the developing fetal brain at increased risk of developing NE. In this model NE is conceived as a clinical outcome resulting from the interplay of multiple etiological processes. An adverse birth experience is an obvious antecedent factor, but ongoing case-control studies are evaluating the importance of maternal hemoglobin, thyroid and magnesium status, as well as cytokine activity resulting from sub-clinical uterine infection. South Asian women have a high exposure to many risk factors associated with NE. We have demonstrated a prevalence of NE in Kathmandu of 6 per 1000(20) which, although higher than in industrialized populations, demonstrates NE to be a relatively rare event. Case-control studies focusing on preventable risk factors for NE in South Asia are needed as the logical precursors to intervention studies.

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