The Turkish Journal of Pediatrics 33:253-266, 1991

FAILURE TO BREATHE AT BIRTH: CAUSES AND ASSESSMENT*

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SUMMARY: Roberton NRC. (Rosie Maternity Hospital, Cambridge, United Kingdom). Failure to breathe at birth: causes and assessment. Turk J Pediatr 33: 253-266, 1991.

A frequent misconception is that delayed onset of respiration is the result of intrapartum asphyxia. However, many factors other than asphyxia can delay the onset of respiration after delivery. To understand the effect of asphyxia on both the fetus and the neonate, and in particular in delaying the onset of spontaneous respiration, it is convenient to consider chronic partial asphyxia and acute asphyxia separately. In this article, the values of the Apgar score and cord blood pH were also evaluated. *Key words: resuscitation, asphyxia, newborn, Apgar score, cord blood pH.*

One of the most important reasons for women delivering in hospital is that if the baby is not breathing within two or three minutes of delivery a physician (usually a pediatrician) or a midwife will be present who can rapidly and efficiently resuscitate the baby. If necessary, this will be carried out by intubation and positive pressure ventilation.

Reports spread over twenty years are very consistent in reporting that about one neonate in fifty requires active resuscitation in the labor ward. Gupta and Tizard[1] found that 5.7 percent of all deliveries were apneic at one minute of age, and that a quarter of these needed intubation in the labor ward. More recently, Milner and Vyas[2] reported that 2.1 percent of all newborn babies required intubation and intermittent positive pressure ventilation (IPPV) in the labor ward.

For those responsible for this resuscitation it is crucial to recognize that there are many causes for a baby failing to breathe immediately after delivery (Table I). For these reasons, it is both inappropriate and dangerous to assume that failure to breathe by two or three minutes of age is always due to asphyxia, and to follow this misdiagnosis with blind therapy using bicarbonate or albumin.

CAUSES OF FAILURE TO BREATHE AT BIRTH (Table I)

Acute asphyxia

Although this is often thought of as the principal cause of failure to breathe after delivery, this is not so, and it is probably responsible for neonatal apnea only if the

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TABLE I: Factors Other Than Asphyxia which May Delay the Onset of Respiration After Delivery

1. Drugs - depressing the CNS
2. Trauma - especially to the CNS
3. Prematurity - in particular surfactant deficient, stiff lungs.
4. Sepsis, especially Group B Streptococci
5. Muscle weakness - due to prematurity or primary muscle disease
6. Anemia
7. Congenital malformations - obstructing the airway or preventing lung expansion.
   - neurological, impairing respiratory control.

fetus has suffered some acute episode such as an antepartum hemorrhage or cord prolapse.

Nevertheless, the animal model for acute asphyxia has been of enormous value in explaining the physiology of asphyxia, and in providing the theoretical basis for the management of resuscitation[3]. Acute *postnatal* asphyxia induced in newborn animals by delivering them in good condition by cesarean section and then preventing them from breathing by immediately sealing their heads in a bag of saline follows a very characteristic pattern (Fig. 1). After a few shallow "breaths" which, by the nature of the experiment cannot result in any gas exchange, the animal stops "breathing". This early period of apnea, so called primary apnea may last for up to 10 minutes. However, after 1-2 minutes in primary apnea, the animal usually starts to gasp. The gasps occur with increasing frequency and vigor but then decrease in frequency and vigor until the animal literally reaches the last gasp. The heart rate falls rapidly after the onset of asphyxia, plateaus or may rise slightly in primary apnea and early in the phase of gasping, then begins to slow. Cardiac activity continues for 10 minutes or more after the last gasp. The period between the last gasp and cardiac arrest is known as secondary or terminal apnea. The changes in blood pressure parallel those in heart rate.

By the end of terminal apnea the $PaCO_2$ may exceed 100 mmHg and the PaO_2 is zero. Throughout the asphyxial episode the baby's pH falls from normal (pH 7.30, H^+ 50 nmol/L) to a pH < 6.5 ($H^+ > 300$ nmol/L). The relevance of these data to human perinatal care is that the response of a human baby immediately after delivery will depend on his pH. If his pH is > 7.25 ($H^+ < 55$ nmol/L) when delivered, he may be transiently apneic in primary apnea, but in the absence of other pathology (Table I) regular respiration will soon start. If he is in the phase of gasping, he will also rapidly settle into a pattern of regular respiration. If his pH has

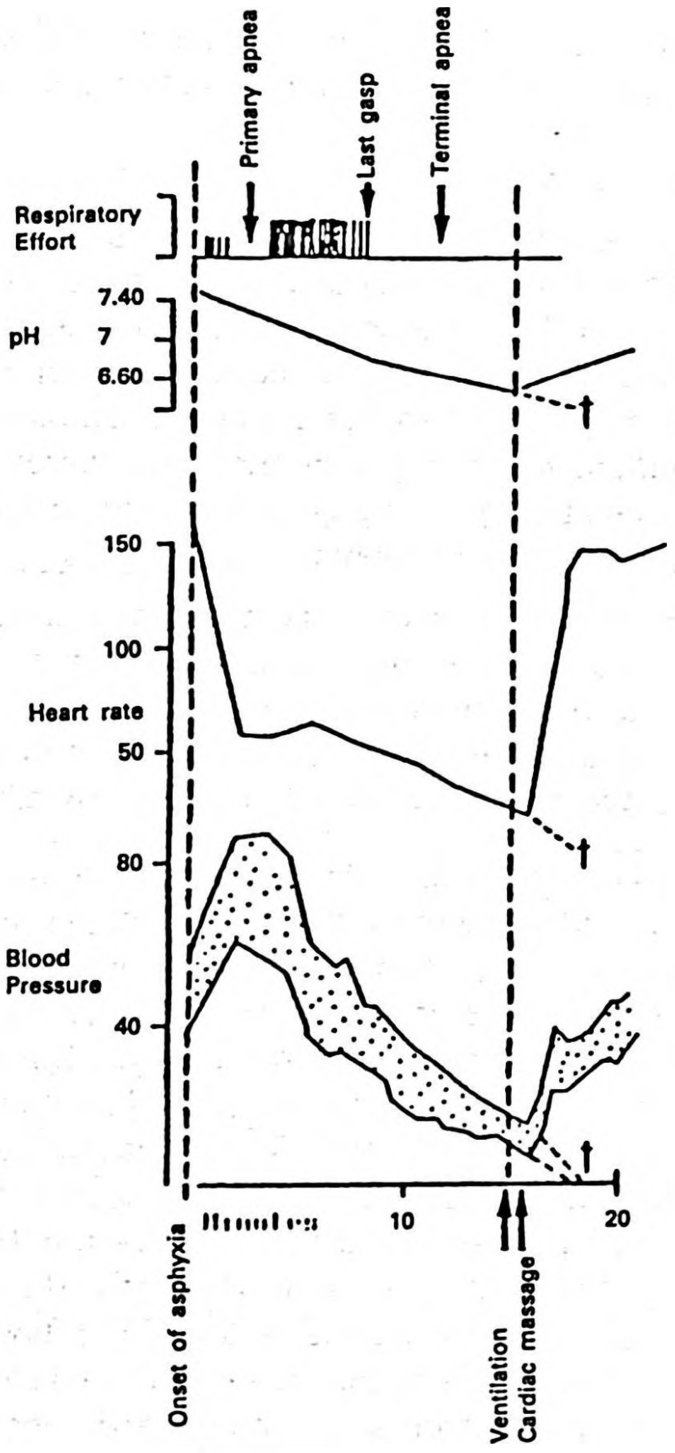

Fig. 1. Physiological changes during asphyxia and resuscitation of a newborn animal[42].

fallen to 7-7.10 (H^+ 80-100 nmol/L) he may still breathe adequately, but, particularly if there is some other complication such as heavy sedation or prematurity (see below), the primary apnea may be prolonged[4,5] or the gasping efforts may be too weak to establish alveolar ventilation. Still more severe intrapartum asphyxia will result in the delivery of an infant with a pH < 7.00 (H^+ > 100 nmol/L) who is more likely to be limp, bradycardic and in terminal apnea. A

baby born in terminal apnea will stay apneic irrespective of what therapies are given unless he is actively resuscitated by intubation and IPPV.

Chronic partial asphyxia

If asphyxia is responsible for apnea after delivery, it is very likely that this has followed events which lead to the gradual development of fetal hypoxemia and chronic partial asphyxia. This can occur before or during labor. For example, some hours or even days before delivery, a fetus may suffer a hypoxic/asphyxial insult which is not severe enough to kill him, but can cause neurological damage[6,7]. As he has not suffered *intrapartum asphyxia* he may well, therefore, show no signs of respiratory depression at birth, have a good Apgar score and establish regular breathing without any apparent problems.

Chronic partial asphyxia in labor is more common and corresponds to animal experiments in which pregnant monkeys were given an excess of halothane for periods of 4-6 hours to make them hypotensive, and their fetuses therefore became hypoxemic and acidemic. The monkeys were then delivered and their babies suffered widespread cortical, mid-brain and cerebellar damage[8].

The human counterpart of this will occur in situations such as the growth retarded fetus who already has reduced umbilical blood flow[9] which falls even further during the normal uterine contractions of labor, during recurrent episodes of umbilical cord occlusions due to entanglement round a fetal part, or compression of the cord between the presenting part and the pelvis. During these episodes, the fetal blood pressure will be sustained initially usually with a normal heart rate, though a bradycardia occasionally develops. The cardiac output is diverted to the placenta, adrenals, brain and myocardium[10-12]. The fetal PO_2 and pH fall, and energy is produced by anerobic metabolism. Since the PCO_2 also rises, a combined metabolic and respiratory acidemia develops. These changes resolve rapidly if normal utero-placental function is restored[13]. If, however, the adverse episodes are long lasting or recurrent, then the circulation will eventually fail, and the brain and heart will become ischemic and possibly permanently damaged[11,12].

If episodes of partial asphyxia have been relatively transient the fetus will not be seriously affected if delivered promptly, although his respiration may be depressed and he may be acidemic with a poor Apgar score; he will respond quickly to resuscitation and be normal thereafter.

Sequelae are likely to occur, however, if severe or prolonged chronic partial asphyxia has occurred[8]. The baby will then be born in poor condition, and will be apneic with a low Apgar score. If cord blood gas analysis is carried out he will have a marked metabolic, and in some cases respiratory acidemia with a pH < 7.00 (H^+

> 100 nmol/L). How much brain damage he has suffered can only be assessed, however, by his clinical condition in the next 12-24 hours and whether or not he develops hypoxic ischemic encephalopathy (HIE).

The fact that prenatal asphyxia can evolve in different ways has important clinical and medico-legal implications, of which the most important are:

1. Most babies who have signs of fetal distress, a low Apgar score or acidemia on cord blood gas analyses are normal in the neonatal period and on follow-up.
2. Intrauterine problems, days or weeks before labor can cause severe long-term neurological defects, yet the baby may show few, if any, neurological abnormalities in the neonatal period.
3. In the absence of clinically apparent HIE in the neonatal period, it is highly unlikely that intrapartum events were responsible for neurological sequelae.
4. Even where an "obvious" severe intrapartum asphyxial event such as a difficult breech extraction is followed by clinical HIE, it is difficult to know whether long-term neurological sequelae were solely the result of the intrapartum event, or were contributed to by neurological damage which had antedated labor by days or weeks. Making such a value judgement is even more difficult where the evidence of intrapartum asphyxia was just changes in the fetal heart rate pattern, or a fetal pH in the 7.0-7.20 range, both of which are normally associated with a good prognosis (Group 1 above).

Pre-existing neurological disease

It is crucial to remember that babies with abnormal brains or muscles may not breathe when delivered. There may be a congenital central nervous system (CNS) abnormality[14] (Table II) or severe acquired brain damage antedating delivery at any

TABLE II: Neurological Causes of Persisting Hypoventilation and Failure to Respond to Resuscitation[14]

Structural CNS malformations
Severe antenatal brain damage
Fractured cervical spine with cord damage
Dystrophia myotonica
Congenital myopathies
Werdnig-Hoffman disease
Brain tumor
Degenerative brain disorders
Ondine's curse (central hypoventilation syndrome).

stage during embryonic or fetal life. There may be primary muscle disease such as dystrophia myotonica or a congenital muscular dystrophy. In all these situations, although, the baby has not suffered any intrapartum asphyxia and will have normal blood gases when born, postnatal apnea may be complete and prolonged unless adequate resuscitation by IPPV is started promptly.

Depression of the respiratory center

Pharmacological

Virtually all the drugs which are used as analgesics, sedatives or general anesthetics during labor can cross the placenta, and depress the neonate's respiration[15]. The drugs are much more likely to cause postnatal apnea in premature babies or in those who have also suffered some degree of intrapartum asphyxia[4]. Only if the level of drug in the baby's plasma is very high, will this cause respiratory depression in an otherwise completely normal term baby. If, however, respiration is absent, as in animal experiments of acute asphyxia, there will be prolongation of primary apnea, and unless artificial ventilation is established, the neonate will become progressively hypoxemic and acidemic with all that that entails.

Hypocapnia

Maternal $PaCO_2$ may fall in women using one of the breathing techniques associated with "natural" childbirth, or in those over-using inhaled analgesics such as Entonox^R. Hyperventilation may be involuntary during general anesthesia. Since fetal $PaCO_2$ is in equilibrium with that of the mother, this may result in a baby being born with a $PaCO_2$ less than 30 mmHg in which case he will lack the CO_2 drive to ventilation, and may remain apneic until his $PaCO_2$ rises sufficiently to stimulate the respiratory center[16]. Maternal hypocapnia may also reduce placental blood flow, and thereby cause fetal hypoxemia and acidemia[17].

Trauma

It is difficult to separate the effects of fetal trauma from those of asphyxia. Tentorial tears, often with co-existing subdural hemorrhages used to be found in infants who had been difficult forceps rotations or traumatic breech extractions, in whom traumatic distortion of the fetal skull was combined with severe asphyxia. Precisely what causes the apnea in such babies after delivery, the asphyxia, the intracranial hemorrhage or the trauma is speculative. However, endorphin levels are higher in the cord blood of infants exposed to the physical stresses of vaginal delivery[18] and these substances can depress neonatal ventilation[19].

A rare traumatic cause of delayed onset of respiration at birth is injury, or trans-section of the cervical spinal cord. Depending on the level of the injury both the intercostal muscles and the diaphragm will be paralyzed, and apnea will result.

This type of injury seems to be virtually limited to babies who are extended breech presentations[20].

Prematurity

The Apgar score is low in premature babies[21] (Fig. 2) and active resuscitation is frequently required (Table III). However, the low score is not a sign of asphyxia and correlates much better with gestation[21-24] (Fig. 2). Goldenberg et al[22] did, however, show that preterm neonates with a low pH are more likely to have a low Apgar score. It is also clear, that whatever the cause of the low Apgar score in preterm babies, the score is a good marker of the high risk neonate who is more likely to die[25,26].

TABLE III: Percentage of Infants Requiring Positive Pressure Ventilation for Resuscitation[25]

Gestation	Number of Births	Requiring IPPV (%)
< 28	173	49
29 - 32	288	18
33 - 34	415	8
35 - 36	1340	2
37 - 38	5895	0.7
> 39	24,726	0.4

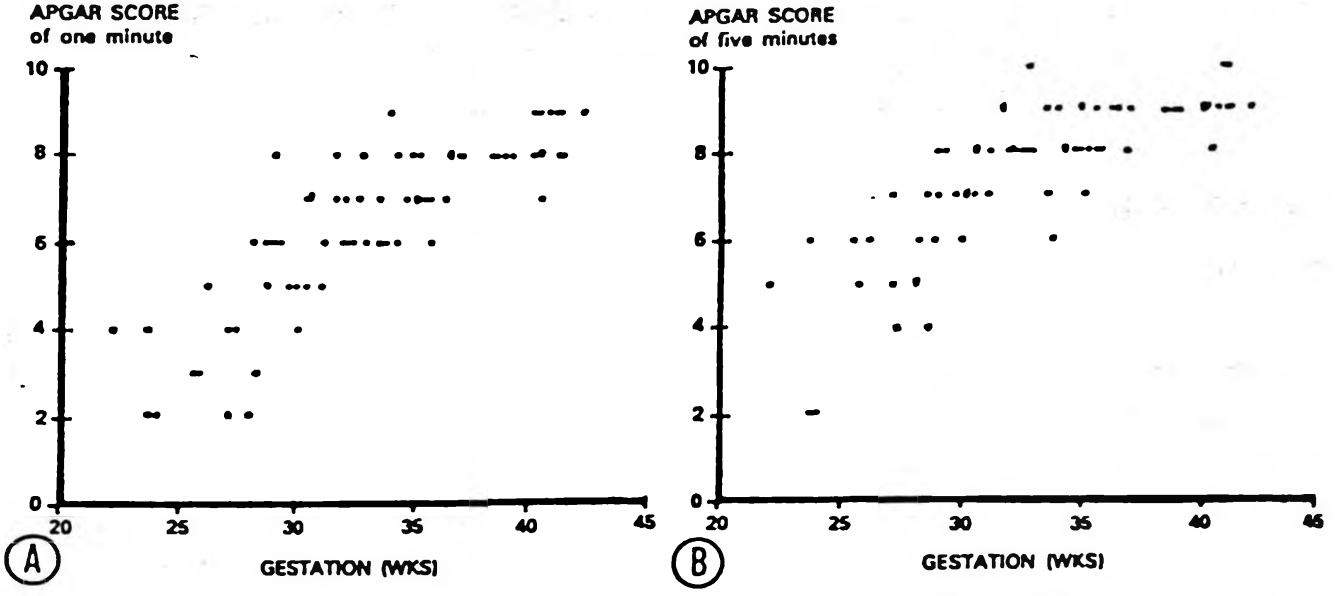

Fig. 2. Scattergram of 1 minute (A), and 5 minutes (B) Apgar scores plotted against gestation[21].

Anemia

The severely anemic neonate is often in heart failure. He lacks hemoglobin to carry oxygen to the tissues, and is therefore, more susceptible to asphyxia. Without hemoglobin, he lacks one of the body's major buffers, and may therefore, be more acidemic[27]. Severely anemic neonates may, therefore, be in very poor condition at delivery, and not only breathe inadequately, but also respond poorly to resuscitation. Although severe asphyxia causes pallor in its own right, anemia must always be excluded in a pale infant responding poorly to resuscitation. Of the two likely causes of severe anemia at birth, rhesus incompatibility and fetal hemorrhage, the former is usually expected. Unexpected severe anemia is, therefore, usually due to fetal hemorrhage, and needs prompt transfusion.

Sepsis

Babies suffering from severe intrapartum infection, both preterm and at term, classically due to Listeria[28] or Group B streptococci[29,30] can be born with very poor Apgar scores. They are critically ill at the time of birth with hypotension, acidemia and a septicemia, but may not actually be asphyxiated[30]. Although the outlook for these babies is grave, the condition must be diagnosed and vigorous anti-infection therapy commenced in addition to treating their apnea.

Congenital malformations

Malformations, in particular those affecting the lungs and airway can cause major problems at resuscitation. The babies are not usually asphyxiated, and their one minute Apgar may be reasonable, but they may then become hypoxic and acidemic with a poor color, hyptonia and inadequate respiration. Characteristically, therefore, these babies start with a reasonable Apgar score of say 6 or 7, but this actually deteriorates during the next 5-10 minutes. Typical examples are babies with diaphragmatic hernia, or one of the other causes of pulmonary hypoplasia.

Assessing the apneic baby

History

Hopefully the person responsible for the resuscitation will have ascertained whether there is a history of any of the above problems. In particular, he must know about:

1. Gestation
2. Evidence of perinatal infection.
   a) Maternal pyrexia
   b) evidence of maternal genital infection
   c) positive cultures of high vaginal swabs

3. Perinatal drug use.
   a) Sedation
   b) Analgesia including — parenteral opiates
      — inhaled agents
      — general anesthesia
   c) Other drugs likely to decrease respiration
      — anticonvulsants
      — psychotropics
4. Blood loss per vaginam which could have been fetal
   — abruptio/placenta previa
   — vasa previa
   — twin-twin transfusion
5. Known episodes of trauma which may or may not induce asphyxia
   a) difficult/failed forceps
   b) breech extraction
6. Recognized antecedents of genuine asphyxia
   a) changes in fetal heart rate pattern
   b) meconium staining
   c) fetal acid-base measurement.

With this as a historical background, the attendant should then be able to use the Apgar score and any other available data to plan his management of the baby in the next 10 minutes.

Clinical examination

Taking the Apgar score does in fact make the physician examine the baby. In addition to assessing the factors relevant to the Apgar score, other relevant factors to look for during the very rapid initial clinical assessment include:

1. Meconium staining
   — may mean asphyxia
   — may cause problems with resuscitation.
2. Dysmorphic features
   — in particular those that would suggest the pulmonary hypoplasia of Potter's syndrome or other conditions with a small chest - e.g., short limbed dwarfism.
3. Evidence for congenital malformations that would compromise resuscitation e.g., hydrops, or the scaphoid abdomen of diaphragmatic hernia.
4. Evidence of infection
   — smell: purulent liquor, skin rash

5. Evidence of hemorrhage
   — recent: poor pulse volume, marked pallor of mucus membranes
   — chronic hepatosplenomegaly, edema
6. Evidence of early neonatal lung disease
   — marked dyspnea, if any respiratory efforts present
   — stiff lungs difficult to inflate by IPPV.

Apgar score

The traditional way of assessing the newborn is to use the Apgar score devised by Virginia Apgar[31] in 1953 which grades five clinical features with scores of 0-2 at 1 minute of age (Table IV). In recent years, there has been a tendency to belittle the Apgar score because it is a poor index of asphyxia i.e. hypoxemia and acidemia (Table V)[32,33] and has little prognostic value[34,35]. This view is completely unjustifiable, since it takes a blinkered view of its purpose. If a baby has a poor Apgar score, he has a problem[36]. It could be any of the problems listed in Table I, but which ever one is present, the sooner it is diagnosed and managed appropriately, the better. The components of the score do not carry equivalent physiological weight. Heart rate and respiration are clearly more important than reflex responsiveness. It is for this reason that a narrative description of the baby's condition at birth and his response to resuscitation must be recorded in the notes. Never just say that a baby has an Apgar score of 5 at 1 minute: accurately describe his condition. For instance, "at 1 minute he was apneic. had blue hands and feet, a heart rate of 90 and normal tone: he grimaced when sucked out", or "at 1 minute the infant was pale with a heart rate of 120 and gasped twice, but he was limp and cried when sucked out". In both these situations, the Apgar score is 5 but they have very different clinical and physiological implications. In addition to

TABLE IV: Apgar Score

	Score		
Clinical feature	0	1	2
Heart rate	0	< 100	> 100
Respiration	Absent	Gasping or irregular	Regular or crying lustily
Muscle tone	Limp	Diminished, or normal with no movements	Normal with active movements
Response to pharyngeal catheter	Nil	Grimace	Cough
Color of trunk	White	Blue	Pink

TABLE V: Mean pH Base Deficit of Infant With Different Apgar Scores[32]

	1 min Apgar score								
	1	2	3	4	5	6	7	8	9
No of infants	5	12	17	11	22	30	62	147	589
pH mean	7.17	7.12	7.10	7.22	7.18	7.17	7.19	7.20	7.21
SD	0.5	0.13	0.13	0.10	0.08	0.09	0.08	0.07	0.08
BD (mEq/L)	10.6	11.8	11.5	7.8	9.6	10.6	8.8	8.4	7.9
Mean SD	4.0	5.9	6.3	5.5	4.3	3.2	4.1	3.7	3.6

BD = base deficit
SD = standard deviation

taking the Apgar score at 1 minute of age, it is traditional to record the scores at 5, 10, 15 and 20 minutes of age. This adds little to the narrative account in the notes of the baby's response, but improvement in the Apgar score from 0-20 minutes is an internationally understood and accepted shorthand for describing the success, or otherwise of the resuscitative effort, and the 15 and 20 minute scores show some correlation with subsequent neurological development[37].

Cord blood analysis

This is the only other piece of data which can be available in the labor ward to help one diagnose the cause of a baby's failure to breathe. It is the most satisfactory way of assessing whether or not asphyxia rather than one of the other conditions listed in Table I is present [38]. Ideally, therefore, at all deliveries, a blood gas should be measured on a sample drawn from the umbilical artery in a section of the umbilical cord double clamped immediately after delivery[39]. Since low Apgar scores are not often due to asphyxia, it is not surprising that there is a poor relationship between Apgar score and pH[32,40]. Two percent of babies with normal Apgar scores have a pH < 7.10 ($H^+ > 80$ nmol/L) and most babies with a pH < 7.10 ($H^+ > 80$ nmol/L) will have normal Apgar scores. However, if both the Apgar score and the pH are abnormal, and no other problems are detected (Table I), it strongly suggests that there was recent asphyxia[38,40,41]. However, it is only when umbilical artery pH values are < 7.00 ($H^+ > 100$ nmol/L) that low Apgar scores are common, or are still reduced at 5 minutes of age[40] (Fig. 3). However, even this degree of acidemia is a poor marker of subsequent neurological damage[35].

On the basis of the clinical history, the clinical examination, the Apgar score and the cord blood gas analysis, it is therefore usually possible to arrive at an accurate

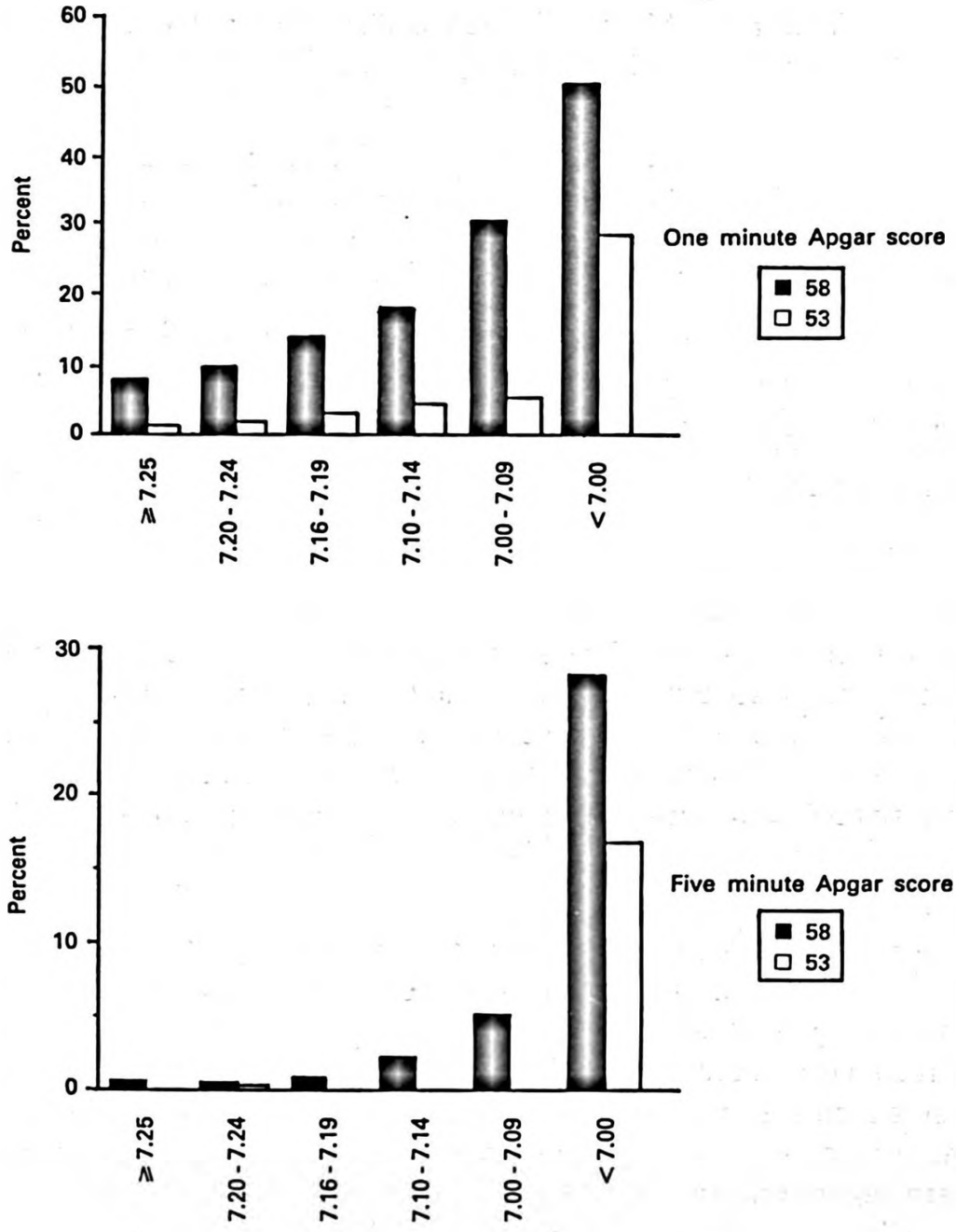

Fig. 3. Relationship between umbilical artery pH levels and Apgar scores at 1 (top) and 5 (bottom) minutes[40].

diagnosis within 5-10 minutes of age of the cause of a baby being apneic immediately after delivery and being slow in responding to resuscitation. Once this diagnosis has been established, the appropiate treatment can then be given.

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