Chronic exposure to CMZ did add some protective effect. Anticholinergic effects such as decreased bowel motility and sinus tachycardia were common; however, cardiac conduction defects were rare.

The authors conclude that serum CMZ levels less than 40 mcg/ml are not predictive of toxicity, therefore management decisions should be based on the patients, clinical presentation.

Blunt Renal Trauma

The management of blunt abdominal trauma in the child has changed dramatically, especially pertaining to hepatic and splenic injuries. Renal injuries may also have improved outcome by a conservative approach avoiding the additional stresses of surgery. Bass *et al.*(3) evaluated the usage of intravenous pyelogram in the management of suspected renal injuries. The study included 333 patients. The results of IVP were compared to the eventual need for surgery, the pathology discovered by surgery or additional evaluation, and the results of the initial urinalysis. The majority of patients studied were victims of MVA-pediatrician accidents (245). The age of patients studied ranged from 6 months to 13 years. The urine was examined using Ames Multistix and results were graded from 1+ to 4+. All IVPs were read by a pediatric radiologist.

A majority of requested IVPs showed no evidence of renal injury (72%). Ninety one (27%) renal injuries identified by radiographic study were then further classified into 4 groups ranging from intrarenal contusions (Grade I) to injuries to the vascular pedicle (Grade IV). All patients who sustained major renal injuries requiring surgery demonstrated 4+ hematuria.

The authors emphasize that the reconstruction of a renal pedicle injury was advisible only if there were no associated major injuries, the diagnosis was made promptly with surgery within 8 hours, and the CT scan demonstrated an intact kidney. The contrast studies should be done on those children who have gross microscopic and macroscopic hematuria and for those with loin tenderness or a palpable loin mass. Limiting the usage of IVPs would enhance cost effectiveness in trauma care.

REFERENCES

1. Wald ER. Purulent nasal discharge. Pediatric Infect Dis J 1991, 10: 329-333.
2. Spiller HA, Krenzelok EP, Cookson E. Carbamazepine overdose: A prospective study of serum levels and toxicity. J Toxicol Clin Toxicol 1990, 28: 445-458.
3. Bass DH, Semple PL, Cywes S. Investigation and management of blunt renal injuries in children: A review of 11 years experience. Pediatr Surg 1991, 26: 196-200.

APNEA, BRADYCARDIA AND PERIODIC BREATHING: ARE THEY ALWAYS PATHOLOGICAL ?

V. Bhandari
A. Narang

With easy availability of continuous monitoring of premature babies, more and

From the Neonatal Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh 160 012.

Reprint requests: Dr. Anil Narang, Additional Professor, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh 160 012.

more babies are likely to be diagnosed apneic and bradycardiac and in the era of conflicting understanding of their relationship, there may be overzealous treatment of tiny babies with its inherent serious side effects. We aim to highlight the controversies in the present day understanding for optimal management.

Definitions

Apnea has been described as cessation of breathing for 20 seconds or more with or without associated bradycardia; many have used the duration of 2-30 second respiratory pauses as apneic episodes(1-6). However, most of the recent publications have taken a respiratory pause of greater than 10-15 seconds as diagnostic of an apneic episode(7-11).

Similarly, there is no unanimity on the definition of bradycardia and a rate of less than 80-100 beats per minute has been considered as bradycardia(2,4,5,7,8,11-13). Henderson-Smart *et al.*(9) on the other hand have described bradycardia as a drop in the heart rate by 30% below the baseline whereas Barrington and Finer(10) have suggested that a drop of 10% from the previous mean as suggestive of bradycardia.

Periodic Breathing

Periodic breathing has been defined(6) as the presence of one or more 4 seconds respiratory pauses per 20 seconds during at least 3 successive 20 second epochs (*i.e.*, 1 minute). Barrington and Finer(10) on the other hand, have defined it as "3 or more cyclical apneas of ≥3 seconds duration separated by regular respirations of less than 20 seconds". Nathanson *et al.*(13) use the term "extensive periodic breathing of >3% of the time spent in periodic breathing in a 12 hour recording" to denote an abnormal pneumogram. Rigatto and Brady(12) used a more comprehensive definition–considered breathing as periodic if (*a*) groups of respiratory movements were interrupted by intervals of apnea, with the apnea lasting not less than 3 seconds, (*b*) the ratio of the duration of breathing/duration of apnea was not more than 4, and (*c*) the period of apnea and breathing intervals, lasting for 30 seconds or less, was repeated during at least 2 minutes in a total period of 10 minutes. Chernick *et al.*(3) have called it as 'wherein periods of ventilatory efforts are regularly interrupted by periods of apnea of at least 3 or 4 seconds'.

Hodgman *et al.*(11) have used the term "as a visual pattern (on the pneumogram) of repetitive short central pauses separated by bursts of respirations". To qualify, the pauses had to be between 3 and 10 seconds duration separated by respiratory pauses lasting 20 seconds or less and the pattern had to persist for at least 30 seconds.

Thus, the definitions of apnea, bradycardia and periodic breathing are quite controversial. This is not a matter of mere semantics as the total management of these "physiological"/"pathological" states would depend upon the definition of what constitutes these clinical conditions.

Discussion

Infants who have had an episode of prolonged apnea are perceived by physicians as having experienced a life threatening event and being at risk for another. Prolonged and especially recurrent apnea can be a symptom of a wide variety of conditions ranging from sepsis to gastroesophageal reflux(1).

With the advent of continuous elec-

tronic monitors, what needs to be highlighted is that healthy preterm neonates have "respiratory pauses" of a significant duration without a fall in heart rate. Periodic breathing need not necessarily be an ominous sign heralding "pathological" apnea. Conversely, transient episodes of bradycardia have been recorded without apnea(14).

It has been postulated that apnea in preterm infants is due to reduced or absent chemoreceptor tone; however, even neonates as early as 26 to 28 weeks of gestation possess the ability to respond appropriately to altered oxygen tensions(15). Hypoxia and hypercapnia both require increased levels of ventilation. Infants who fail to respond thus may do so because of the following reasons: (*a*) central respiratory depression due to hypoxia, (*b*) mechanical limitations preventing increased respiratory work from being translated into increased ventilation; and (*c*) neurologically reduced drive to breathe. The sleep state of the infant would be expected to have the maximum impact on the neurological factors but there are conflicting reports in the literature(6,15,16).

Episodes of bradycardia occur fairly often in preterm infants. They have been reported to occur in association with apnea(4,5,7-9,11,17). Bradycardias are more common in longer episodes of apnea(4,9,17), but transient episodes of bradycardia can occur without apnea(7,8,11,14). Sixty eight per cent of the brief episodes of apnea occurred without evidence of central apnea of 15 seconds or longer(11). Smith and Milner's study(8) also stated that bradycardias can occur "not necessarily in association with apnea". Krauss *et al.*(7) opined that "it was difficult to relate the occurrence of bradycardia to apnea in terms of sleep state or gestational age. It is concluded that no simple relationship between sleep state, apnea and bradycardia exists".

Notwithstanding the above comments, it must be remembered that sufficiently prolonged episodes of cessation of respiration will lead to a bradycardic response. But, transient episodes of bradycardia may be taken to be "physiological" in an otherwise healthy preterm.

In a study(14) correlating the effects of apnea/bradycardia with the oxygen saturation (SaO_2), 1029 episodes were analyzed. Reductions in SaO_2 of upto 40% occurred with apneas of <10 seconds duration. The baseline SaO_2 measurement immediately before an apneic attack had a pronounced effect on whether bradycardia resulted during the attack. The median baseline SaO_2 was 95% in those episodes that did not result in bradycardia but only 92% in those with bradycardia ($p<0.0001$). Episodes of apnea with bradycardia had a greater reduction in SaO_2 than those without bradycardia. The authors have stated that the absence of respiratory effort is not in itself likely to be deleterious to a preterm infant.

Chernick *et al.*(3) in their study on 22 infants concluded that the commonest form of apnea, in the premature infant is the recurrent apnea associated with periodic breathing. This view has been challenged by others. Hodgman *et al.*(11) stated that 9 of 66 infants who spent more than 20% of their time in periodic breathing, none exhibited apnea of 15 to 19 seconds and only 1 had apnea of 20 seconds or longer, suggesting that periodic breathing did not predispose to apnea in healthy premature infants. This was also supported by the fact that only 1/5th of the 94 episodes of apnea (of 15 seconds or longer) occurred during periodic breathing. Barring-

ton and Finer(10) found that of 1116 significant apneic spells, only one occurred during the epoch of periodic breathing, five others occurred within 2 minutes of the end of an epoch of periodic breathing. They concluded that periodic breathing is not a precursor to significant apnea as less than 0.6% of significant apneic spells occurred within 2 minutes of periodic breathing.

Apneic spells, brief periods of bradycardia and periodic breathing may be justifiably only manifestations of an immature cardio-respiratory system–which may be "physiological" and hence not necessarily be over zealously monitored or treated. Besides the toxic effects of the drug therapy, the deleterious effects of oxygen therapy in these premature neonates have been well documented(18-20). This, however, does not detract from the "pathological" apneas which could be a harbinger of many disease states in the baby. With the increasing continuous electronic surveillance of the preterms, it is imperative to draw a line between the two–"physiological" and "pathological" conditions.

It is necessary to reiterate that the importance of apnea, bradycardia or periodic breathing lies in its risk of causing hypoxemia to the neonate. Hence, it would be more appropriate to detect hypoxia rather than noting the heart rate or duration of cessation of breathing. Based on this, the following recommendations may be useful for management of these babies.

1. "Pathological" apnea be defined with frank cyanosis and bradycardia (a heart rate <100/min).
2. It may also be defined as any duration of cessation of respiration associated with a fall of SaO_2 <82% (even in the absence of cyanosis/ bradycardia).
3. Periods of cessation of respiration and isolated episodes of bradycardia without cyanosis or fall in oxygen saturation can be defined as "physiological".
4. The ideal monitoring of an infant prone for apnea should include heart rate, apnea/respiratory rate and oxygen saturation monitoring.
5. A "physiological" apnea would warrant a closer continued monitoring while a "pathological" apnea would warrant a full septic workup; metabolic profile (blood glucose, electrolytes and renal function; arterial blood gases); cranial ultrasonography. In special circumstances, a seizure disorder or a gastro-esophageal reflux would need to be ruled out.
6. If a specific cause is delineated, therapy should be directed to the same. In the absence of such, apnea of prematurity should be treated with aminophylline.

REFERENCES

1. American Academy of Pediatrics Task Force on prolonged infant apnea. Pediatrics 1985, 76: 129-131.
2. Narang A. Definition for major neonatal illnesses as applicable at different levels of healthy care delivery system. *In:* Neonatal Nomenclature and Data Collection. Eds Singh M, Paul VK, Bhakoo ON. Vani Press, Delhi 1989, pp 27-35.
3. Chernick V, Heldrick F, Avery ME. Periodic breathing of premature infants. J Pediatr 1964, 64: 330-340.
4. Daily WJR, Klaus M, Meyer HBP. Apnea in premature infants: monitoring, incidence, heart rate changes and an effect of environmental temperature. Pediatrics 1969, 43: 510-518.

5. Valimaki I, Tarlo PA. Heart rate patterns and apnea in newborn infants. Am J Obstet Gynecol 1971, 110: 343-349.

6. Curzi-Dascalova L, Christova-Gueorguieva E. Respiratory pauses in normal prematurely born infants. Biol Neonate 1983, 44: 325-332.

7. Krauss AN, Solomon GE, Auld PAM. Sleep state, apnea and bradycardia in preterm infants. Dev Med Child Neurol 1977, 19: 160-168.

8. Smith ML, Milner AD. Bradycardia and associated respiratory changes in neonates. Arch Dis Child 1981, 56: 645-648.

9. Henderson-Smart DJ, Butcher-Puech MC, Edwards DA. Incidence and mechanism of bradycardia during apnea in preterm infants. Arch Dis Child 1986, 61: 227-232.

10. Barrington KJ, Finer NN. Periodic breathing and apnea in preterm infants. Pediatr Res 1990, 27: 118-121.

11. Hodgman JE, Gonzalez F, Hoppenbrouwers T, Cabal LA. Apnea, transient episodes of bradycardia and periodic breathing in preterm infants. Am J Dis Child 1990, 144: 54-57.

12. Rigatto H, Brady JP. Periodic breathing and apnea in preterm infants. 1. Evidence for hypoventilation possibly due to central respiratory depression. Pediatrics 1972, 50: 202-218.

13. Nathanson J, O'Donnell J, Commins MF. Cardiorespiratory patterns during alarms in infants using apnea/bradycardia monitors. Am J Dis Child 1989, 143: 476-480.

14. Upton CJ, Milner AD, Stokes GM. Apnea, bradycardia and oxygen saturation in preterm infants. Arch Dis Child 1991, 66: 381-385.

15. Krauss AN, Tori CA, Brown J, Soodalter J, Auld PAM. Oxygen chemoreceptors in low birth weight infants. Pediatr Res 1973, 7: 569-574.

16. Gabriel M, Albani M, Schulte FJ. Apnea spells and sleep states in preterm infants. Pediatrics 1976, 57: 142-147.

17. Starrs CN. Cardiovascular effects of apnea in preterm infants. Arch Dis Child 1977, 52: 534-540.

18. Kattwinkel J, Fanaroff AA, Klaus MH. Bradycardia in preterm infants. Indications and hazards of atropine therapy. Pediatrics 1976, 58: 494-499.

19. Aranda J, Grandin D, Sasyniuk BI. Pharmacologic considerations in the therapy of neonatal apnea. Pediatr Clin North Am 1981, 28: 113-133.

20. Patz A. The role of oxygen in retrolental fibroplasia. E. Mead Johnson Award Address. Pediatrics 1957, 19: 504-524.