

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Occurrence and Mechanisms of Sudden Oxygen Desaturation in Infants Who Sleep Face Down

Aloka L. Patel, Dorota Paluszynska, Kathleen A. Harris and Bradley T. Thach

Pediatrics 2003;111:e328-e332

DOI: 10.1542/peds.111.4.e328

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://www.pediatrics.org/cgi/content/full/111/4/e328>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2003 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



Occurrence and Mechanisms of Sudden Oxygen Desaturation in Infants Who Sleep Face Down

Aloka L. Patel, MD; Dorota Paluszynska, MD; Kathleen A. Harris; and Bradley T. Thach, MD

ABSTRACT. *Objective.* Infants who sleep prone and face down on soft bedding are particularly vulnerable for sudden infant death syndrome. It has been suggested that 1 mechanism of death in this situation involves rebreathing of expired air. Many infants tolerate rebreathing while lying prone face down for long periods with stable saturations. Others occasionally have rapid desaturations and may require intervention to terminate rebreathing. The present study had 3 objectives: 1) to determine the frequency of rapid desaturations in a large group of healthy infants, 2) to elucidate the mechanism of these desaturations, and 3) to determine the timing of these events during periods of rebreathing.

Methods. We studied respiratory tracings and videotapes of 56 healthy 1- to 6-month-old infants who were sleeping face down and rebreathing on soft bedding in our laboratory. We compared the frequency of desaturations during rebreathing and nonbreathing periods. We measured respiratory frequency and apnea occurrence before desaturation and nonbreathing control episodes. We also measured minute ventilation during steady state before desaturation and just before desaturation.

Results. There were 25 desaturation episodes in infants while rebreathing, occurring in 11 (19.6%) of the 56 infants. Episodes were significantly more frequent during rebreathing than during nonbreathing periods. Three desaturation episodes reached <85%; 2 required intervention to terminate rebreathing. The respiratory frequency was not different between nonbreathing control and desaturation episodes. Brief apneas were significantly more frequent preceding desaturation than control episodes (44% vs 4%). Just before episodes, there was a transient decrease in minute volume despite increasing inspired carbon dioxide in 3 episodes. There was evidence of partial or complete pharyngeal airway obstruction in 3 episodes. Thirty-six percent of all episodes were immediately preceded by behavioral arousal.

Conclusions. Rebreathing in prone sleeping infants is associated with an increased frequency of episodic desaturations. Desaturation may result from respiratory pattern changes such as brief apneas often associated with evidence of behavioral arousal or failure to increase ventilation in the face of rising inspired carbon dioxide, also associated with behavioral arousal. *Pediatrics* 2003;111:e328–e332. URL: <http://www.pediatrics.org/cgi/content/full/111/4/e328>; SIDS, desaturation, prone.

From the St Louis Children's Hospital and the Edward Mallinckrodt Department of Pediatrics, Washington University School of Medicine, St Louis, Missouri.

Received for publication Jun 26, 2002; accepted Oct 21, 2002.

Reprint requests to (B.T.T.) Washington University, Department of Pediatrics, 660 S Euclid, Campus Box 8208, St Louis, MO 63110. E-mail: thach@kids.wustl.edu

PEDIATRICS (ISSN 0031 4005). Copyright © 2003 by the American Academy of Pediatrics.

ABBREVIATIONS. SIDS, sudden infant death syndrome; CNS, central nervous system; CO₂, carbon dioxide; O₂, oxygen; ECG, electrocardiogram; V_T, tidal volume; SAT, saturation.

Sudden infant death syndrome (SIDS) is the third leading cause of death in infants after congenital anomalies and prematurity or low birth weight.¹ Prone sleep is a known risk factor for SIDS, and face-down prone sleep increases this risk further.² Despite the American Academy of Pediatrics' recommendation of supine sleep position for infants,³ 20% of infants in the United States continue to be placed prone for sleep.⁴ Although the majority of rebreathing infants reach steady state with regard to ventilation and oxygenation, even with documented airway obstruction,⁵ a few infants have been noted to rapidly desaturate, occasionally requiring rescue.^{6,7} It has also been shown that infants usually arouse in response to hypercarbia, such as in a rebreathing environment.⁸ We sought to determine the frequency of failure to arouse and escape from the face-down position during periods of rapid desaturation in a large group of healthy infants. Because the mechanism of sudden desaturation while rebreathing is unclear, this was also studied. Desaturation may be associated with changes in respiratory pattern or airway obstruction, but there has been no documentation of this. Desaturation in a rebreathing environment is of special concern because central nervous system (CNS) depression occurs at saturations <50%, and this could prevent the infant's escape from the asphyxiating environment.⁹

Anecdotal accounts of infants dying while face down indicate that death may occur relatively rapidly. In contrast, animal models of rebreathing indicate that death occurs after a longer period of time.¹⁰ Therefore, we sought to establish the onset of rapid desaturation after assuming the face-down position, as this could be the immediate precursor to death.

METHODS

Participants

We studied 56 healthy infants from the St Louis community (mean age: 103 days; range: 40–180), all of whom were healthy at the time of the study. Four of these were premature and were studied at a mean post conceptional age of 339 days (range: 292–377); 2 additional infant's sibling had died of SIDS. The remaining infants had no history of significant medical problems. Of the 56, 11 (6 boys, 5 girls) experienced significant episodes of desaturations during the study (mean age at study: 73 days; range: 19–120). These infants formed the primary group for study of desaturations. The study was approved by the Washington Uni-

versity Human Studies Committee, and informed consent was obtained from the parents.

Sleeping Environment and Monitoring

The infants were studied while sleeping face down on soft bedding in a plastic crib during natural sleep after a meal. The mean duration of study during sleep was 50 minutes (range: 29–68); a mean of 36 minutes (range: 16–55) was spent face down and rebreathing. The bedding consisted of a corrugated foam pad covered by a polyester-filled comforter folded double (thickness of doubled comforter: 3 cm). A shallow depression (12.5 × 12.5 cm at surface, 4.5 cm deep) was cut into the foam mattress lying directly beneath the infant's head to create an environment with high rebreathing potential similar to the partially filled air mattress covered by a comforter described by Kemp et al.^{7,11} Breath-by-breath carbon dioxide (CO₂) was measured via an 8F Silastic catheter with 2 small holes that was attached to the upper lip, under the nares. The catheter was connected to an infrared photometer CO₂ analyzer (Ohmeda 5200, Madison, WI) at a low sampling rate (150 mL/min; response time: <200 ms). Before each study, the CO₂ analyzer was calibrated with standard gas mixtures. A separate nasal catheter, also positioned in front of the nares, was attached to a differential pressure transducer, comparing pressure at the narial opening with room pressure.⁸ Although there was no change in head position, the resistance to flow produced by the bedding was constant; thus, the narial pressure was proportional to flow. This relationship has been demonstrated to be linear over a range of 0 to 8 L/min,⁸ allowing us to measure relative changes in nasal airflow. The flow signal was integrated to give relative tidal volume. The infant's heart rate electrocardiogram (ECG), respiratory rate (Resptrace), and oxygen (O₂) saturation (Nellcor N-100C, Hayward, CA) were monitored. All output data were continuously recorded on a polygraph (Beckman R611). The infant and polygraph tracing were recorded with an infrared video camera (Videonics, Campbell, CA) so as to allow correlation between infant behaviors and physiologic recordings on analysis at a later date. After the infant fell asleep, baseline data were obtained. Approximately 10% of infants turned face down spontaneously. If not, then he or she was turned prone and the head was positioned face down. Rebreathing was detected by an elevation in the inspired CO₂ level $\geq 1\%$.

Desaturation Occurrence and Timing During Rebreathing

Desaturation episodes were defined as those with a decrease of $\geq 3\%$ dropping to a level of ≤ 93 occurring over 20 to 30 seconds. The 93% value is equal to 3 standard errors of the mean below the mean for sleeping infants 2 to 4 months of age.¹² We excluded desaturations that were instantaneous with desaturation $\geq 30\%$ or desaturations in which movement artifact was detected by insta-

bility in the pulse tracing and/or the ECG tracing to eliminate artifactual desaturations. We evaluated 25 desaturations with a stable pulse signal or a single spike in the pulse signal. To confirm the validity of this approach, we evaluated the change in saturation associated with this pattern during nonrebreathing periods. It was not associated with any change in saturation during nonrebreathing periods. In 6 of the 25 desaturation episodes that were studied, the pulse signal was not recorded, in which case we relied on presence or absence of movement artifacts in the ECG because movement artifacts in the ECG were invariably present when the pulse trace reflected infant movements.

Desaturation episodes were classified as occurring during rebreathing periods (inspired CO₂ $\geq 1\%$) or during nonrebreathing periods (inspired CO₂ undetectable). We calculated the duration (in minutes) of rebreathing and nonrebreathing periods for each infant. We then calculated for each infant the frequency of desaturation episodes per rebreathing and nonrebreathing periods. The timing of onset of desaturations after the infants assumed a face down position was noted.

Respiratory Parameters: Rebreathing Desaturation Episodes Versus Nonrebreathing Control

The number of desaturations was determined for each infant during control and rebreathing periods. We then randomly selected nonrebreathing control periods with no desaturations for each infant by a random sampling procedure based on that described by Huntsberger and Leaverton.¹³ Each page of the tracings represented 30-second epochs of the study. We used a random-number generator to select a page (www.randomizer.org). If the selected page met control criteria, then we selected that page. If not, then another number was drawn until a nonrebreathing page without desaturation was selected. The beginning of the page was used as the control period. This entire method was repeated for each desaturation for each infant using this method. We established 25 controls, 1 for each desaturation. We also evaluated the respiratory pattern 10 seconds before the onset of the desaturation and control periods, comparing respiratory frequency and occurrence of brief apneas (Fig 1A).

Change in Minute Ventilation During Rebreathing Before and Immediately Before Desaturation Episodes

We calculated the relative change in minute ventilation by measuring respiratory frequency and tidal volume (V_T) by the height of the integrated flow signal or the height of the Resptrace sum signal during 2 time periods: 1) the 8 seconds before the onset of the desaturation through to the desaturation nadir (to account for the 5- to 7-second averaging time of the pulse oximeter) and 2) the previous 8 seconds to the aforementioned time period if the infant's saturations were stable at that point (Fig 1B). If the satu-

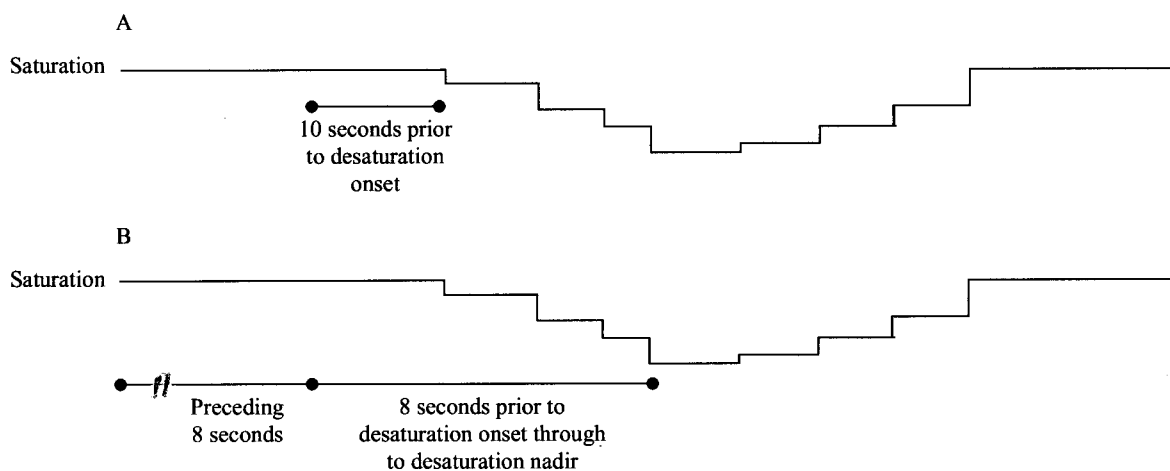


Fig 1. Methods used in analysis of behaviors and respiratory parameters. A, Respiratory pattern was evaluated 10 seconds before desaturation onset in both desaturation and control periods. B, Average minute ventilation was calculated during the 8 seconds before onset through to desaturation nadir. This was compared with average minute ventilation during the preceding 8 seconds. These time periods were selected to take into account the 5- to 7-second averaging time of the pulse oximeter.

rations were not stable, then we evaluated 8-second intervals sequentially preceding the interval until a stable time period was found. Both measures of V_T were used in the infants, but the same measure was used for each desaturation and preceding interval to allow for a measure of relative change in minute ventilation. Average minute ventilation was calculated by averaging V_T over the number of breaths counted multiplied by the frequency. This procedure was done in 17 of 25 desaturations in which V_T could be calculated for both time periods by the same method. In addition, we measured average end-inspiration CO_2 during both time periods.

Cause of Desaturation

We reviewed the polygraph tracings and videotapes of the infants to evaluate for a correlation in ventilatory patterns or behavioral features 10 seconds before the onset of desaturation. Arousal was defined as evidence of vocalization and/or body movements.

Data Analysis

Statistical analyses were performed using the Wilcoxon rank test and the paired Student *t* test. Results are reported as mean \pm standard error of the mean. Results were considered significant at $P < .05$.

RESULTS

Desaturation Occurrence and Timing During Rebreathing

Eleven (19.6%) of the 56 infants we studied experienced 25 episodes of desaturations with a mean of 2.3 spells per infant (range: 1–7; Fig 2). Spells did not occur in the SIDS siblings or any of the preterm infants. There was no apparent correlation of gender or age of the infant and occurrence of spells. Desaturations occurred more frequently during rebreathing than during nonbreathing periods (0.07 ± 0.02 vs 0 episodes/min, rebreathing and nonbreathing, respectively; $P < .01$). Eight desaturation episodes reached $\leq 90\%$. Three additional desaturations occurring in 3 infants reached $\leq 85\%$. Onset of desaturation was variable but often occurred within as short a time as 1 to 3 minutes after infants assumed the face-down position.

Respiratory Parameters: Rebreathing Desaturation Episodes Versus Nonbreathing Control

Respiratory frequency was not significantly different during the 10 seconds before desaturation than nonbreathing control periods (40.3 ± 2.3 vs 45.4 ± 3.7 , desaturation and control, respectively; $P > .05$). Brief apneas occurred more frequently before desaturations than nonbreathing control periods ($72 \pm 20\%$ vs $4 \pm 4\%$, desaturation and control, respectively; $P < .01$). The mean apnea duration was 2.98 seconds (range; 1.0–12.2 seconds).

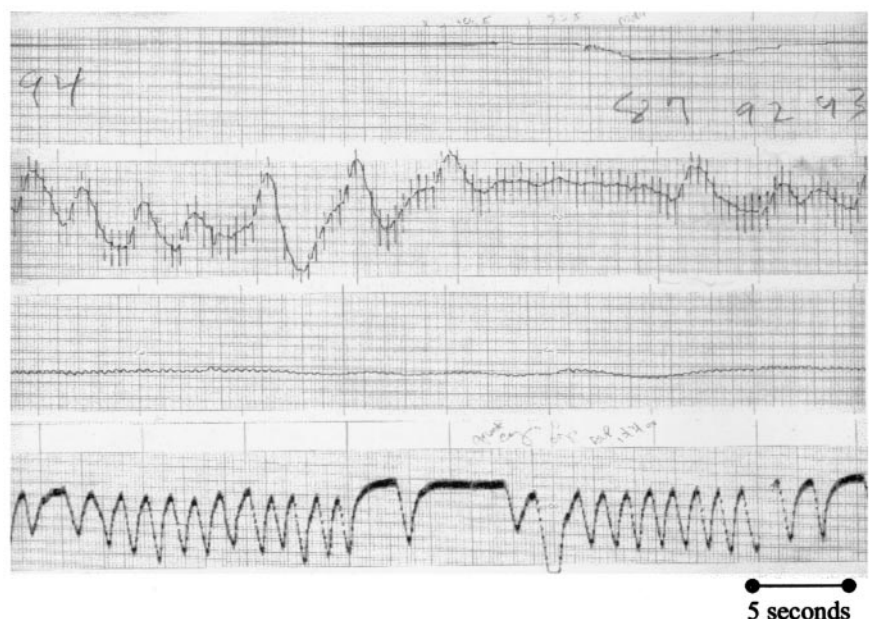
Change in Minute Ventilation During Rebreathing Before and Immediately Before Desaturation Episodes

The average change in minute ventilation across the 17 desaturation episodes that could be accurately evaluated was a decrease from 466.5 ± 79.3 to 429.7 ± 48.4 (arbitrary units mm/min; $P = .56$). In 9 of these 17 episodes, minute ventilation decreased by an average of 33.5%. In 8 of these episodes, the decrease in ventilation was associated with brief apnea.

Cause of Desaturation

Eleven of the 25 desaturation episodes were preceded by 1 or more short apneas. These were all central apneas with the exception of 1 in which there were clear indications of completely obstructed respiratory efforts. Three of these apneic episodes were associated with grunting or crying. One episode was associated with a transient decrease in minute ventilation without accompanying apnea. This was attributable to a decrease in V_T . An additional 3 episodes were associated with a failure to increase minute ventilation despite rising inspired CO_2 . Five desaturation events were preceded by a spontaneous shift in head position, which increased airway contact with the bedding during the 10 seconds before desaturation. Snorting or snoring sounds, suggesting

Fig 2. Example of desaturation in 1 infant to 87%. Note brief respiratory apneas occurred during 10 seconds before desaturation onset, associated with a cry, indicating behavioral arousal. Traces from top to bottom are O_2 saturation, ECG, pulse wave, and Respirtrace sum.



upper airway obstruction, preceded 2 episodes in 2 infants in 1 of whom this was associated with evidence of arousal of sleep (Fig 3).

Most episodes of desaturation resolved when the infant turned and/or lifted his or her head. However, 2 infants had 1 episode each of desaturations <85% while rebreathing that required intervention by the examiner to prevent additional desaturation. One of these infants aroused before intervention, but the behavioral response was ineffective at escaping the rebreathing environment. He grunted, cried, lifted, and turned his head slightly after saturations reached 87% but then dropped his head into the rebreathing pocket once again. He was turned when the saturations reached 84% and he had not successfully repositioned his head. The other infant had a desaturation to 80% in which she demonstrated no signs of arousal and was turned supine by the examiner. None of these episodes was associated with bradycardia.

DISCUSSION

Although the majority of rebreathing infants reach steady state with regard to ventilation and oxygenation, even with documented partial airway obstruction,⁵ a few infants have been noted to desaturate rapidly, occasionally requiring rescue.^{6,7} Such occurrences are relatively infrequent. Furthermore, it should be noted that although the definition used in the present study was based on established norms for desaturation, most spells that we observed would not be regarded as medically significant.¹² However, our findings do indicate that sudden small desaturations while rebreathing are not uncommon. Furthermore, they indicate that potentially more serious larger decreases can occur in healthy infants, some of whom fail to escape or arouse. It should be noted, however, that the bedding we used was selected for its high potential for causing rebreathing.¹⁴

When minute volume reaches maximum levels during rebreathing, there is a tenuous balance between O₂ consumption and diffusion of O₂ into the bedding beneath the infant's face. Recovery of O₂

saturation to the previous level after a large decrease would be unlikely to occur in the absence of significant change in head position allowing access to fresh air. This is because O₂ concentration in inspired air during rebreathing correlates closely with the stores of O₂ in the infant's body; hence, a continued downward trend in saturation would be expected to occur after a significant decrease in O₂ stores.¹⁴ Such a situation therefore could constitute a critical event in the pathway to death because hypoxemia is a poor stimulus for arousal¹⁵ and CNS hypoxia produces rapid onset of hypoxic coma, at which point spontaneous escape from the hypoxic environment becomes impossible.

SIDS deaths are called "sudden"; however, the actual time from onset of respiratory or circulatory compromise to actual death is usually uncertain. Deaths in infants who have assumed the face-down position have been anecdotally reported to occur in as short a time as 10 to 20 minutes. This contrasts with the anesthetized animal model of rebreathing in which death occurs after 1 or 2 hours when acidosis and hypoxemia result in hypotension and bradycardia.¹⁰ The present findings suggest that death might occur much more rapidly in sleeping infants in situations in which respiratory pauses associated with otherwise normal infant behaviors produce rapid and potentially irreversible decreases in saturation.

In infants who sleep in the prone position, we found that desaturations occurred more often while they were rebreathing than not rebreathing. This is likely attributable to the hypoxic environment that coexists with hypercarbia in a rebreathing setting.¹⁴ Partial pharyngeal obstruction as suggested by snoring or snorting was heard in 2 infants, and complete obstruction was present in an additional infant; this may have played a role in some desaturation episodes.⁵ However, the primary mechanism that we found for desaturations was brief central apneas. In 9 episodes, a decrease in minute ventilation was noted, the majority of which were associated with apnea. Decreased minute ventilation was also associated with behavioral features of arousal such as crying or grunting, which have been previously been shown by others to be associated with desaturation.¹⁶⁻¹⁸ Crying for help is an appropriate protective response for the infant at risk, although it may prevent an appropriate ventilatory response to increasing environmental CO₂. Previously, we have shown that minute ventilation increases 3-fold in infants in similar rebreathing environments.¹⁴ Others have shown in experimental settings that minute ventilation increases by a factor of 1.25 to 2.75 with rising CO₂ in a similar range to that observed in our participants when rebreathing.^{19,20} Increasing minute ventilation is a primary mechanism for achieving a steady state during rebreathing. Because ventilation reaches maximum attainable levels during rebreathing, it would be difficult for the infant to recover from a transient decrease in respiratory rate or V_T, producing desaturation without getting access to fresher air.

Most infants demonstrated an appropriate motor response after desaturation was present by either moving the head to the side or lifting it up. Two (8%)

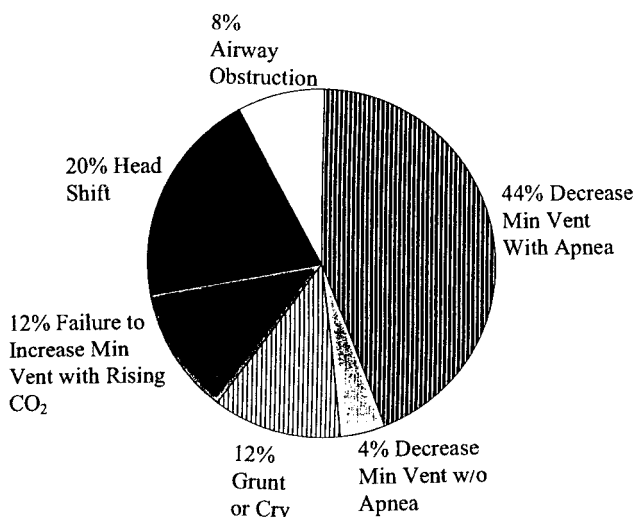


Fig 3. Causes of desaturations.

of the infants studied had arousal responses that were ineffective in avoiding a potentially dangerous environment. One of these infants reassumed the face-down position during his arousal response, which led to an increase in inspired CO₂ and additional desaturation. Previous work by Lijowska et al⁸ has shown that the arousal response to an asphyxial environment may sometimes aggravate an already dangerous situation if the infant is ineffective at clearing the airway and/or turns the head further into the bedding. Thus, although arousal is believed to play an integral role in protecting infants from sudden death while sleeping, such as by head repositioning,^{21–23} the associated cardiopulmonary changes, such as altered respiratory patterns or apnea, may also precipitate hypoxemia in some infants.

CONCLUSION

Normally occurring respiratory patterns associated with normal infant behavior usually have little consequences for blood gas homeostasis. However, in a low-O₂ environment associated with the infant's face being covered by bedding, these same respiratory patterns may produce a rapid desaturation. When associated with arousal activity that is ineffective in gaining access to fresh air or failure to arouse, such desaturations can produce an immediate danger, potentially leading to death.

ACKNOWLEDGMENTS

This research was funded by the National Institute of Child Health and Human Development (HD10993). Dr Patel was supported by institutional training grant T32-HL07873 from the National Institutes of Health.

REFERENCES

- Guyer B, Hoyert DL, Martin JA, Ventura SJ, MacDorman MF, Strobino DM. Annual summary of vital statistics—1998. *Pediatrics*. 1999;104:1229–1246
- L'Hoir MP, Engelberts AC, van Well GTJ, et al. Risk and preventative factors for cot death in The Netherlands, a low-incidence country. *Eur J Pediatr*. 1998;157:681–688
- American Academy of Pediatrics, Task Force on Infant Positioning and SIDS. Positioning and sudden infant death syndrome (SIDS): update. *Pediatrics*. 1996;98:1216–1218
- Willinger M, Ko C-W, Hoffman HJ, Kessler RC, Corwin MJ. Factors associated with caregivers' choice of infant sleep position, 1994–1998: the National Infant Sleep Position Study. *JAMA*. 2000;283:2135–2142
- Waters KA, Gonzalez A, Jean C, Morielli A, Brouillette RT. Face-straight-down and face-near-straight-down positions in healthy, prone-sleeping infants. *J Pediatr*. 1996;128:616–625
- Chiodini BA, Kemp J, Thach BT. Responses of prone sleeping infants to rebreathing caused by soft, porous bedding [abstract]. *Pediatr Res*. 1994; 35:390A
- Chiodini BA, Thach BT. Impaired ventilation in infants sleeping facedown: potential significance for sudden infant death syndrome. *J Pediatr*. 1993;123:686–692
- Lijowska AS, Reed NW, Mertins Chiodini BA, Thach BT. Sequential arousal and airway-defensive behavior of infants in asphyxial sleep environments. *J Appl Physiol*. 1997;83:219–228
- Novotny EJ. Cerebral blood flow and metabolism in hypoxia. In: Haddad GG, Lister G, eds. *Tissue Oxygen Deprivation: From Molecular to Integrated Function. Lung Biology in Health and Disease*. New York, NY: Marcel Dekker Inc; 1996:653–663
- Kemp JS, Thach BT. Sudden death in infants sleeping on polystyrene-filled cushions. *N Engl J Med*. 1991;324:1858–1864
- Kemp JS, Thach BT. Quantifying the potential of infant bedding to limit CO₂ dispersal and factors affecting rebreathing in bedding. *J Appl Physiol*. 1995;78:740–745
- Mok JYQ, McLaughlin FJ, Pintar M, Hak H, Amaro-Galvez R, Levison H. Transcutaneous monitoring of oxygenation: what is normal? *J Pediatr*. 1986;108:365–371
- Huntsberger DV, Leaverton PE. *Statistical Inference in the Biomedical Sciences*. Boston, MA: Allyn and Bacon Inc; 1970:57
- Patel AL, Harris K, Thach BT. Hypoxemia vs. hypercapnia: relevance for mechanism of sudden infant death syndrome. *J Appl Physiol*. 2001; 91:2537–2545
- Davidson Ward SL, Bautista DB, Keens TG. Hypoxic arousal responses in normal infants. *Pediatrics*. 1992;89:860–864
- Abu-Osba YK, Brouillette RT, Wilson SL, Thach BT. Breathing patterns and transcutaneous oxygen tension during motor activity in preterm infants. *Am Rev Respir Dis*. 1982;125:382–387
- Prec KJ, Cassels DE. Oximeter studies in newborn infants during crying. *Pediatrics*. 1952;9:756–763
- Lind J, Stern L, Wegelius C. *Human Foetal and Neonatal Circulation*. Springfield, IL: Charles C. Thomas; 1964:37–41
- Cohen G, Henderson-Smart DJ. The reproducibility of the response of the human newborn to CO₂ measured by rebreathing and steady-state methods. *J Physiol*. 1994;476:355–363
- Lloyd BB, Jukes MGM, Cunningham DJC. The relation between alveolar oxygen pressure and the respiratory response to carbon dioxide in man. *Q J Exp Physiol*. 1958;43:214–226
- Dunne KP, Fox GP, O'Regan M, Matthews TG. Arousal responses in babies at risk of sudden infant death syndrome at different postnatal ages. *Irish Med J*. 1992;85:19–22
- Horne RSC, Ferens D, Watts A, et al. The prone position impairs arousability in term infants. *J Pediatr*. 2001;138:811–816
- McCulloch K, Brouillette RT, Guzzetta AJ, Hunt CE. Arousal responses in near-miss sudden infant death syndrome and in normal infants. *J Pediatr*. 1982;101:911–917

Occurrence and Mechanisms of Sudden Oxygen Desaturation in Infants Who Sleep Face Down

Aloka L. Patel, Dorota Paluszynska, Kathleen A. Harris and Bradley T. Thach

Pediatrics 2003;111:e328-e332

DOI: 10.1542/peds.111.4.e328

Updated Information & Services	including high-resolution figures, can be found at: http://www.pediatrics.org/cgi/content/full/111/4/e328
References	This article cites 20 articles, 10 of which you can access for free at: http://www.pediatrics.org/cgi/content/full/111/4/e328#BIBL
Citations	This article has been cited by 2 HighWire-hosted articles: http://www.pediatrics.org/cgi/content/full/111/4/e328#otherarticles
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Office Practice http://www.pediatrics.org/cgi/collection/office_practice
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.pediatrics.org/misc/Permissions.shtml
Reprints	Information about ordering reprints can be found online: http://www.pediatrics.org/misc/reprints.shtml

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

