Inspired CO₂ and O₂ in sleeping infants rebreathing from bedding: relevance for sudden infant death syndrome

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Inspired CO₂ and O₂ in sleeping infants rebreathing from bedding: relevance for sudden infant death syndrome. J Appl Physiol 91: 2537–2545, 2001.—Some infants sleep facedown for long periods with no ill effects, whereas others become hypoxic. Rebreathing of expired air has been determined by CO₂ measurement; however, O₂ levels under such conditions have not been determined. To evaluate this and other factors influencing inspired gas concentrations, we studied 21 healthy infants during natural sleep while facedown on soft bedding. We measured gas exchange with the environment and bedding, ventilatory response to rebreathing, and concentrations of inspired CO₂ and O₂. Two important factors influencing inspired gas concentrations were 1) a variable seal between bedding and infants’ faces and 2) gas gradients in the bedding beneath the infants, with O₂-poor and CO₂-rich air nearest to the face, fresher air distal to the face, and larger tidal volumes being associated with fresher inspired air. Minute ventilation increased significantly while rebreathing because of an increase in tidal volume, not frequency. The measured drop in inspired O₂ was significantly greater than the accompanying rise in inspired CO₂. This appears to be due to effects of the respiratory exchange ratio and differential tissue solubilities of CO₂ and O₂ during unsteady conditions.

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INCIDENCE OF SUDDEN INFANT DEATH SYNDROME (SIDS) has decreased markedly over the past decade since recommendations were made in several countries to place infants in a nonprone position when sleeping (13, 16, 21, 32). However, SIDS remains the leading cause of infant death beyond the neonatal period in the United States, and 20% of US infants continue to sleep prone (21). Despite the established increased risk of SIDS with prone sleep, the mechanism of death is still debated (3, 16, 17, 19, 27, 33). One proposed mechanism for infants sleeping facedown involves “rebreathing” of expired air retained within soft porous bedding that covers an infant’s face (22). Prior studies of infant rebreathing models have measured inspired carbon dioxide (CO₂) levels of 1–6% (4, 6, 30). The rebreathing theory has been criticized because, although this degree of hypercarbia is biologically significant, it is unlikely to cause CO₂ narcosis or rapid death (19, 30, 38, 43). Hypoxemia has been noted in animal models of rebreathing (4, 24, 25); however, there has been no direct measurement of environmental oxygen (O₂) in animal or human models. O₂ content of inspired air during rebreathing has been assumed to reciprocate CO₂ levels, such that inspired O₂ = room air O₂ minus end-inspiration CO₂ (30); however, effects of factors such as the respiratory exchange ratio on CO₂ and O₂ are unknown (8). Preliminary work by Chiodini et al. (5) suggests that there may be additional factors that affect the degree of rebreathing in infants sleeping facedown. The authors noted gradients in CO₂ concentration in bedding beneath an infant’s face. They also noted the sporadic occurrence of otherwise occult air channels at the juncture of the bedding with the infant’s face, allowing partial exchange of fresh air with the external environment analogous to gas leaks that occur in a loosely fitting facemask, thus limiting gas exchange with the bedding (5). These observations suggest that complex interactions of several factors influencing gas exchange between infant and environment may influence the degree of hypercarbia and hypoxia that develop in inspired air. To further explore these several issues with regard to infants sleeping facedown on soft bedding, we have evaluated four aspects of gas exchange in our study: 1) infants’ gas exchange with the external environment through air-channel formation in bedding, 2) infants’ gas exchange with the bedding as affected by gas gradients, 3) infants’ ventilatory responses to hypercapnia and hypoxia during rebreathing and gas exchanging efficiency of different respiratory patterns, and 4) direct measurement of CO₂ and O₂ in the rebreathing environment during periods of rapid and slow change in the gas concentration of inspired air.

METHODS

Subjects. Twenty-one healthy infants younger than 6 mo old from the St. Louis community were enrolled between September and November 1999. Subjects were 5–24 wk old. There were 8 males and 13 females. Nineteen of the 21 were born at term. At home, 4 (19%) slept prone, 4 (19%) slept...
supine or on the side, and 13 (62%) slept supine. Seventeen infants (81%) received routine periods of prone positioning while awake and supervised. The Washington University Human Studies Committee approved the study, and informed consent was obtained from the parent(s).

Direct measurement of $O_2$ and $CO_2$ concentrations. Infants were studied during natural sleep during a morning or afternoon nap after a feeding. They were placed in a plastic crib. Bedding used in this study consisted of a corrugated foam pad (5) covered by a polyester-filled comforter folded double (thickness of doubled comforter = 3 cm). A shallow depression (12.5 x 12.5 cm at surface, 4.5 cm deep) was cut into the foam mattress directly beneath the infant’s head. This created an environment with high rebreathing potential closely similar to the partially filled air mattress covered by a comforter described by Kemp and Thach (26). Breath-by-breath $O_2$ and $CO_2$ were measured via an 8-Fr silastic catheter with two small holes attached to the upper lip under the nares. The catheter was connected to a laser-diode $O_2$ analyzer (Vacumed 17518C, Ventura, CA) at a low sampling rate (100–150 ml/min; response time <200 ms) and an infrared photometer $CO_2$ analyzer (Ohmeda 5200, Madison, WI) at a low sampling rate (150 ml/min; response time <200 ms), with both analyzers arranged in parallel. Before each study, the $O_2$ and $CO_2$ analyzers were 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 to room pressure (28). During periods in which there was no change in head position, the resistance to flow produced by the bedding was constant; thus narial pressure was proportional to flow. This relationship has been previously demonstrated to be linear over a range of 0–8 l/min (28), allowing us to measure relative changes in nasal airflow. Flow signal was integrated to give tidal volume ($V_t$). The infant’s heart rate, respiratory rate (Respiritrace, Noninvasive Monitoring Systems, Miami Beach, FL), and $O_2$ saturation (Nellcor, Hayward, CA) were also monitored. All output data were continuously recorded on a polygraph (Beckman R611). Infant and polygraph tracings were recorded with an infrared video camera (Videonics, Campbell, CA) so as to allow correlation between infant behaviors and physiological recordings on analysis at a later date. After the infant fell asleep, baseline data were obtained. He or she was then turned prone, and the head was positioned facedown. Rebreathing was detected by an elevation in the inspired $CO_2$ level. To augment the degree of rebreathing, we often applied silk cloths around the face. Detection of an elevated $CO_2$ level in currents of air in phase with respiration defined an air channel.

Evidence for gas-gradient formation in bedding. Before the start of the study, two 21-gauge lumbar puncture needles with blunted tips were inserted into the bedding into the pocket beneath the face. After a period of rebreathing when inspired gas had reached relatively steady-state concentrations, the $O_2$ and $CO_2$ analyzers were disconnected from the nose catheter and connected to the bed needle. The needle was slowly withdrawn at 0.5-cm intervals until it was out of the bedding. This was repeated as tolerated by the infant. This procedure was done in the 7 of 21 infants who remained asleep and rebreathed for long enough periods for the sampling procedure to be completed.

Infants’ ventilatory responses to rebreathing. The change in end-inspiration $CO_2$ that followed placement of cloths was evaluated in 31 episodes in 11 infants by comparing mean end-inspiration $CO_2$ for the 10 breaths that preceded and followed cloth placement. In a different subset of 11 infants, subjects’ responses to rebreathing were evaluated for 31 episodes of rising end-inspiration $CO_2$ and decreasing end-inspiration $O_2$. Episodes of changing inspired gas concentrations were selected, and each breath, including at baseline, was evaluated as the index breath until the gas concentrations reached a relative steady state. In each subject, we measured respiratory frequency ($f$) and relative $V_t$ after the index breath at varying sequential $CO_2$ and $O_2$ levels. We studied the effect of tidal-volume size on inspired-gas ($CO_2$ and $O_2$) concentrations in five facedown infants who were chosen because they slept for relatively long periods with their faces straight down. The relative size of five sequential breaths, including a sigh or large breath, was compared with the inspired $CO_2$ and $O_2$ associated with each breath in each infant. Infants were studied for the duration of the nap, usually <2 h.

Effect of gas measurement technique on gas concentration in bedding. In this study, it became clear that gas concentrations in bedding during rebreathing are influenced by a number of factors. Clearly, withdrawing gas from the bedding for determining concentration could have had some effect, even though we used the smallest feasible flow rates. We sought to estimate the effect of this sampling by using a simplified model in which concentration is primarily determined by two factors: 1) the relatively rapid rate of flow of $CO_2$ (for example) into the bedding from the infant and 2) the relatively slow rate of flow of $CO_2$ out of the bedding as a result of simple diffusion.

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To estimate the rate of flow out of the bedding, we introduced a mixture of $CO_2$, $N_2$, and $O_2$ (5% $CO_2$, 13% $O_2$, balance $N_2$) into the bedding until it was saturated. We then placed a water-filled container with a shape and mass approximating that of an

<table>
<thead>
<tr>
<th>Gas evaluation</th>
<th>No. of Subjects</th>
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<tr>
<td>$CO_2$</td>
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</tr>
<tr>
<td>Effect of VT size on $iCO_2$ and $iO_2$</td>
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</tr>
<tr>
<td>Volume-averaged $iCO_2$ and $iO_2$</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
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$V_t$, inspired tidal volume; $iCO_2$, inspired $CO_2$; $iO_2$, inspired $O_2$.
infant’s head over the sampling catheter. Half-lives for decrease
in CO2 and increase in O2 were measured during continuous
sampling, as in the infant studies. To minimize sampling ef-
ficts, half-lives were also measured during a second trial by
intermittent sampling for 2 s at 40-s intervals.

Next, the rate of CO2 flow into the bedding was estimated
by determining the maximum rates of rise of CO2 when
infants first assumed the facedown position. Half-life was
calculated for this rate of rise. Knowing the rates of flow into
and out of the bedding allowed us to mathematically deter-
mine the differences in gas concentration in the bedding for
continuous vs. intermittent sampling.

Data analysis. O2 and CO2 concentrations were calculated
by estimating to the nearest 0.25 mm on the output tracing and
multiplying by the calibration constant (1 mm = 0.22% CO2 or
O2). Relative inspired VT (in mm2) were calculated by integrat-
ing the flow curve during inspiration; f was calculated by count-
ing the number of breaths in the preceding 10 s from the index
breath and multiplying by six. Relative minute ventilation (Vl)
(units = 1 mm2 box/min) was calculated by multiplying f and
VT. The relationships between Vl, VT, and f and inspired CO2
and O2 concentrations were evaluated by Student’s two-tailed,
unpaired t-test and multiple linear regression. The change in
inspired CO2 that followed cloth placement was analyzed by
comparing mean inspired CO2 before and after each cloth place-
ment by Student’s two-tailed, paired t-test. The significance of
the relationship between VT size and inspired gas concentra-
tions was evaluated by linear regression and Student’s two-
tailed, unpaired t-test (18).

Mean inspired gas concentration (volume-averaged) for
each breath was calculated by weighting the gas concentra-
tion by the corresponding portion of VT for each millimeter
subdivision (1 mm = 0.1 s) of inspiration divided by the VT.
This method is depicted by the following formula, where i =
each 0.1-s subdivision of inspiration and there are n total
subdivisions: \( \frac{\sum (\text{gas concentration}_i \times \text{volume}_i)}{\text{VT}} \) (Fig. 1). Volume-averaged inspired CO2 and O2

Fig. 1. Note that throughout inspiration (Insp), gas concentra-
tions and flow pattern are changing. Volume-averaged gas concentration
is calculated for each breath by multiplying volume (integrated flow)
during 0.1-s segments of inspiration by the corresponding gas con-
centrations for each segment and dividing by tidal volume (VT),
shown by the shaded area of flow.

Fig. 2. Air channels detected around one subject’s head while facedown at
positions D and G, where CO2 is elevated
over 1%.
concentrations were compared with prior methods of estimating inspired gas concentrations (end-inspiration CO₂ and O₂ = room-air O₂ – end-inspiration CO₂) by Student’s two-tailed, paired t-test for each breath (30). Forty-five breaths during both rapidly changing and relatively steady-state conditions while rebreathing were analyzed in this manner in five infants who slept facedown for long periods. Results are expressed as means ± SE. Results for all statistical analyses were considered significant if P < 0.05.

RESULTS

Evidence for occult air channel formation. Gas exchange with the environment while facedown via air channels not apparent to visual inspection was demonstrated by a rise in CO₂ to 1.5% at certain positions around the infant’s face in the three infants tested, with gas changes in phase with respiration usually detected at one or more sites (Fig. 2, example of one infant). Location of channels and size of the CO₂ signal often changed with changes in the infant’s head position.

End-inspiration CO₂ rose by an average of 28.7% after placement of a silk cloth (1.34 ± 0.19 and 1.73 ± 0.17% before and after cloth placement, respectively) around the face in 11 prone infants (P < 0.005). Figure 3 shows a representative tracing from one infant.

Evidence for gas-gradient formation in bedding. As the needle was pulled from deep in the bedding into the pocket immediately beneath the face in seven infants, CO₂ levels gradually rose and O₂ levels fell. CO₂ levels rose to 3.96% and O₂ levels fell to 12.4% in the bedding beneath the face in a representative subject (Fig. 4). In addition, a rise and fall in gas concentration in phase with breathing was detected beneath the face in zones A and B, suggestive of bulk air movement.

Infants’ ventilatory responses to rebreathing. Larger VT was associated with a decrease in end-inspiration CO₂ (52.8 ± 8.93% lower) and an increase in end-inspiration O₂ (10.8 ± 0.53% higher) in the five facedown infants. These trends were significant with P < 0.05 for each of the five facedown infants studied (Fig. 5).

Respiratory response to rebreathing was evaluated in 11 infants (represented by subject IA in Fig. 6). All demonstrated an increase in V̇l (average of 332%) and V̇t (average of 319%) as infants were exposed to an increasingly asphyxial environment. f varied irregularly with regard to O₂ and CO₂. Slopes of V̇l and V̇t vs. end-inspiration O₂ and end-inspiration CO₂ were significantly different from zero by t-test for all patients (P = 0.01 and P < 0.01, respectively). In contrast, the slope of f vs. end-inspiration O₂ and end-inspiration CO₂ was not statistically significantly different from zero (P = 0.57). The high level of correlation between CO₂ and O₂ (r = −0.9) precluded use of multiple-regression analysis.

Direct measurement of O₂ and CO₂ concentrations. Inspired-gas concentrations were analyzed from five infants who rebreathed while sleeping in a facedown position without requiring additional cloths around the face. These infants were similar to the entire study group with regard to age and sex. Of these five, two (40%) slept prone at home. Volume-averaged inspired CO₂ concentration was 3.43 ± 0.19%, range 50.78–5.75%. Volume-averaged inspired O₂ concentration was 15.94 ± 0.23, range = 13.32–19.65%. Linear regression of the change in CO₂ on the change in O₂ concentration from room air did not reveal an equal relationship, as the slope was <1 for each subject. The
decrease in O2 was significantly greater in magnitude than the increase in CO2 (P < 0.01 for each infant; Fig. 7).

Analysis of the 45 breaths showed the volume-averaged inspired CO2 concentration was significantly higher than the end-inspiration CO2 concentration for each subject (18.2–122.2% higher; P < 0.005). In each subject, volume-averaged inspired O2 concentration was significantly lower than prior estimates (inspired O2 = room air O2 – end-inspiration CO2) of O2 levels (6.7–17.2% lower, P < 0.005; Fig. 8). Two of our subjects who showed the most pronounced differences in O2 concentrations (16.1 and 17.2% lower) also experienced rapid desaturations to 84–85%. Concurrently, volume-averaged O2 concentration decreased to 13% over 20–30 s with a much slower accompanying rise in CO2 (Fig. 9). Figure 10 shows the relationship between change in CO2 and change in O2 in both expired and inspired air during this rapid desaturation, which is best fit by a curve. One of these infants failed to arouse on his own and required our intervention when his O2 saturation reached 85%.

Effect of gas measurement technique on gas concentration in bedding. The intermittent method of gas sampling approximated the natural time course of diffusion of gas out of the bedding, as minimal flow was directed to the gas analyzers. Average half-life of flow of CO2 out of the bedding for intermittent sampling was 125 vs. 88 s for continuous sampling, which had an effect of increasing flow of gas out of the bedding. Similar results were obtained for O2. Half-life of flow of gas into the bedding was 10.4 s for CO2 and 10.5 s for O2. Thus, although the continuous method changed gas concentration faster than the intermittent method by a factor of 1.4, the rate of change in inflow was still roughly 10 times faster than the rate of outflow, irrespective of the method of sampling. The ratio of gas-concentration equations showed that the effect of continuous sampling was to lower measured values of CO2 and raise measured values of O2 by 5%, compared with our estimates of gas concentrations if no sampling had occurred.

DISCUSSION

We verified preliminary data that there are often air channels around the infant’s face, while sleeping facedown, which allow gas exchange with the environment and that they are occult, in that direct inspection does not suggest their presence. In addition, we noted that slight movements of the infant’s head could increase or decrease flow through these channels. This principle was also demonstrated by the significant rise in CO2 after the placement of cloths near infants’ faces, thus increasing the bedding’s effect on rebreathing. When the infant has the ability to exchange air via air channels, the degree of rebreathing may be limited (5). However, this also highlights the subtleties of infant and bedding positioning, which are not immediately visible and may allow some infants to sleep facedown, whereas others who do so may experience dangerous asphyxia. Although we investigated only one type of bedding, it is conceivable that certain characteristics of the composition of the bedding influence the occurrence and size of channels and thereby would be relevant to its safety for infants (26).

We evaluated the effect of our method of continuously sampling gas for analysis by comparing it to intermittent sampling. We estimated that the continuous withdrawal of gas in the bedding altered gas values by −5% compared with actual values that would have been present during rebreathing in the absence of sampling. Thus we slightly underestimated the asphyxial challenge to the infant during rebreathing. Because the overall effect of continuous sampling was to cause an apparent increase in the background diffusion of gas out of the bedding and because CO2 and O2 were affected equally, our findings regarding proportional differences in gas concentrations and gradients in bedding were unaffected.

Presence of CO2 and O2 gradients in the bedding, with high CO2 and low O2 just beneath the nose and low CO2 and high O2 furthest from the nose, demonstrates that the infant exchanges gas with bedding during rebreathing as well. These findings confirm preliminary observations made earlier by this laboratory (5). Reasons for formation of gradients are not clearly identified. We theorize that the microstructure of the bedding (23, 24, 26) allows airflow with minimal turbulence and consequently little air mixing. Also, exchange of gases at the interface between the bedding and the environment must be occurring by diffusion. As air is exhaled, end-expired air, which is of highest CO2 and lowest O2 content, is trapped closest to the face. Although convection does occur, as demonstrated...
by the pulsatile flow detected in the bedding nearest the face, it diminishes further out from the infant's face and thus limits mixing. In effect, the bedding expands the dead space in series with the infant's dead space. Due to the relatively large nature of this space, the infant inspires end-expiratory gas before accessing fresher air that is further away in the bedding (Fig. 4). This is confirmed by the effect of VT on inspired-gas concentrations, with larger VT allowing access to fresher air, in the facedown infants seen in this study.

Fig. 6. Example in one representative subject of change in minute ventilation (Vi), VT, and respiratory frequency (f) with simultaneously increasing end-i CO2 and decreasing end-i O2 while rebreathing. Vi, VT, and f are displayed on the y axis. End-i O2 is displayed on the x axis. End-i CO2 value is displayed both visually and numerically by the “bubble” diameter and adjacent number. This three-dimensional graph is to aid in visual interpretation of changes in Vi, VT, and f with an increasingly asphyxial environment (Excel, 1997). Note positive correlation between Vi and VT with an increasing hypercapnic-hypoxic environment (P < 0.01 and P < 0.01, respectively). There is no significant change in f with an increasing hypercapnic-hypoxic environment (P = 0.57).

Fig. 7. Mean change in CO2 from room air (RA) vs. mean change in O2 from room air in 5 facedown rebreathing infants (modified conventional P(i)CO2 and P(i)O2 diagram) (37). Note that each infant's regression line has a slope of -1, which is shown by the line of identity. Therefore, for each infant, the absolute decrease in O2 is larger in magnitude than the absolute increase in CO2 (P < 0.01 for each regression line). ●, TA; □, BM; ○, MD; ●, IA; ◻, RM.

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Fig. 8. Measured volume-averaged inspired O2 (black bars) vs. estimated O2 (gray bars) from previous method (inspired O2 = room air O2 - end-i CO2) (30) in 5 facedown, rebreathing infants (mean ± SE). Note that, for each infant, measured O2 is significantly lower than previously theorized. *P < 0.005.
The relationship between VT size and inspired-air composition highlights the importance of volume averaging inspired-gas concentrations. Nunn (34) reviews a method for determining the composition of gas re-breathed from apparatus dead space. Because inspired re-breathed gas is of changing composition, as shown by Fig. 1, the true effective mean concentration is volume based (2). When facedown and breathing from a relatively large reservoir of exhaled air in the bedding, true inspired-gas concentration depends on the volume and corresponding concentration of air breathed early as well as late in inspiration. For example, at the beginning of inspiration, the infant breathes in end-expiratory gas near the nose. As the inspiratory volume increases, more air is drawn from distant, fresher areas of the bedding. Thus the volume-averaged concentration reflects the various sources of gas inhaled during the entire inspiration.

Subjects demonstrated appropriate ventilatory responses to an asphyxial environment. Of note, our subjects were exposed to a hypercarbic and hypoxic stimulus, depending on the degree of rebreathing achieved by each infant. Although the usual ventilatory response to hypoxia is hyperbolic in shape, the responses of these infants fit a linear model best (11). Hypercarbia normally results in a linear increase in V̇i (29). The observed response likely reflects the dual stimuli as the ventilatory response to asphyxia is greater than that to the individual stimuli of the rise in CO2 and the fall in O2 (9, 29). Our subjects increased V̇i primarily by increasing VT, with inconsistent changes in f. It has been shown that humans, unlike other animals, primarily change VT to affect ventilation (1, 5, 7, 11, 15). In a facedown rebreathing environment, the increase in VT is beneficial as it allows access to fresher air in the bedding. If the primary response consisted of shallow, rapid breathing, then the infant would be exposed to a more threatening environment. This may explain the greater increased risk of SIDS associated with prone positioning in infants with infectious respiratory illness as opposed to well infants (36). Such illnesses tend to be associated with stimuli that increase f.

High resistance to airflow associated with covering the nose and mouth has been associated with respiratory failure and/or death (40, 41). Although the face-down infants in our study did have their mouths and noses covered, the resistance of our bedding has been previously shown to be well below the level of resistive load associated with development of hypercapnia in infants (24, 41). High resistive loads in infants have been associated with hypoventilation, effected primarily through changes in f instead of VT (41). Thus the ventilatory changes seen in our study reflect a response to an asphyxial environment due to rebreathing, not to a high resistive load.

Previously, estimates of the CO2 concentrations in infants’ environments have used the end-inspiration point (6, 30). Actual inspired-O2 concentration while rebreathing has not been measured, but it has been assumed to reciprocate elevated CO2 levels (30). We attempted to find a more accurate estimate of the inspired gases by continuously measuring both CO2 and O2 and calculating the volume-averaged mean concentrations. Our data showed that the decrease in actual O2 concentration does not reciprocate the elevation in CO2 but is of significantly greater magnitude. During quasi-steady-state conditions, the inequality
between changes in O\textsubscript{2} and CO\textsubscript{2} is partially due to the respiratory quotient, reflecting the relatively larger consumption of O\textsubscript{2} than CO\textsubscript{2} production. The respiratory quotient remains relatively constant as the data best fit a line for each subject (Fig. 7).

Additionally, the measured O\textsubscript{2} inspired by rebreathing infants was significantly lower than predicted when rapid change in inspired gas composition occurred soon after assuming the facedown position. This was most evident in the two infants who experienced rapid desaturations to 84–85%. The time course of these episodes was notable in that, although the O\textsubscript{2} concentration fell rapidly, the CO\textsubscript{2} concentration changed minimally. The relationship of change in CO\textsubscript{2} and change in O\textsubscript{2} is best fit by a curve during these rapidly changing episodes (Fig. 10), as opposed to a linear relationship during quasi-steady-state conditions. This likely reflects the body’s ability to store CO\textsubscript{2} 100-fold more than O\textsubscript{2} (34). Before reaching steady-state conditions, the body’s ability to store CO\textsubscript{2} 100-fold more than O\textsubscript{2} (34). Before reaching steady-state conditions, the respiratory exchange ratio temporally changes, making the difference between O\textsubscript{2} and CO\textsubscript{2} even larger (34). The larger decrease in O\textsubscript{2} vs. increase in CO\textsubscript{2} while sleeping and rebreathing may have a deleterious effect on an infant’s ability to respond to hypercapnic stimuli, hypoxic exposure approaches a level considered to be dangerous when prolonged. Although infants are exposed to both hypoxic and hypercapnic stimuli, hypoxic exposure approaches a level considered to be dangerous when prolonged. Ventilatory response to hypoxia is strongly influenced by other factors: 1) the accompanying PO\textsubscript{2}, with hypocapnia reducing the response; 2) state of consciousness, with depressed consciousness states such as sleep or sedation reducing the response; and 3) central nervous system (CNS) hypoxia, which reduces respiratory drive (11, 14). A perhaps more important consideration is that several investigators have shown hypoxia to be a poor stimulus for arousal, especially in contrast to hypercarbia (10, 14, 20, 31). Potentially relevant is that the hypoxic arousal response has been shown to be even more depressed in siblings of SIDS infants and near-miss SIDS infants (12, 31). Rapidly advancing CNS hypoxia in infants, as in others, is associated with rapid onset of coma. Once coma occurs, an arousal-related change in head position is not possible and death would presumably eventually occur as in animal models of rebreathing (22, 24, 25). Therefore, the current findings further advance the concept that hypoxemia, rather than hypercarbia, may be the more important factor when death occurs in infants sleeping with their faces covered by soft porous bedding.

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