SpO2 normale: P50:97.5%, P10: 94.5%
59% des enfants au moins 1 épisode de désat > 90% sur 24h
Durée médiane de l'épisode de de 6 secondes.
La respiration périodique liée à l'âge semble le facteur principal

Longitudinal assessment of hemoglobin oxygen saturation in healthy infants during the first 6 months of age

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Limitations in home monitoring technology have precluded longitudinal studies of hemoglobin oxygen saturation during unperturbed sleep. The memory monitor used in the Collaborative Home Infant Monitoring Evaluation addresses these limitations. We studied 64 healthy term infants at 2 to 25 weeks of age. We analyzed hemoglobin oxygen saturation by pulse oximetry (SpO_2), respiratory inductance plethysmography, heart rate, and sleep position during 35,127 epochs automatically recorded during the first 3 minutes of each hour. For each epoch baseline SpO_2 was determined during ≥10 s of quiet breathing. Acute decreases of at least 10 saturation points and <90% for ≥5 s were identified, and the lowest SpO_2 was noted. The median baseline SpO_2 was 97.9% and did not change with age or sleep position. The baseline SpO_2 was <90% in at least 1 epoch in 59% of infants and in 0.51% of all epochs. Acute decreases in SpO_2 occurred in 59% of infants; among these, the median number of episodes was 4. The median lowest SpO_2 during an acute decrease was 83% (10th, 90th percentiles 78%, 87%); 79% of acute decreases were associated with periodic breathing, and ≥16% were associated with isolated apnea. With the use of multivariate analyses, the odds of having an acute decrease increased as the number of epochs with periodic breathing increased, and they lessened significantly with age. We conclude that healthy infants generally have baseline SpO_2 levels >95%. The transient acute decreases are correlated with younger age, periodic breathing, and apnea and appear to be part of normal breathing and oxygenation behavior. (J Pediatr 1999;134:580-6)

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Postmortem studies of victims of sudden infant death syndrome have identified subtle findings or tissue markers indicative of pre-existing hypoxia in nearly two thirds of subjects.[1] Until recently, limitations in home-based monitoring technology have precluded recording of hemoglobin oxygen saturation by pulse oximetry during natural unperturbed sleep. The earliest home recordings of SpO_2 in infants[2-4] were generally limited to 1 or 2 overnight recordings per subject. With the use of a state-of-the-art memory monitor with integrated pulse oximeter, transthoracic impedance, and electrocardiography, a recent study in 88 healthy term infants at 2 to 19 weeks of age[5] did provide a more comprehensive assessment of breathing pattern, heart rate, and SpO_2 during sleep in the natural home setting. Despite the expanded scope of these data, however, there were 2 major limitations: (1) baseline SpO_2 could not be characterized, because data could only be stored in memory when the recording threshold for apnea or bradycardia was

CHIME	Collaborative Home Infant Monitoring Evaluation
OR	Odds ratio
SpO_2	Hemoglobin oxygen saturation by pulse oximetry
RIP	Respiratory inductance plethysmography

See editorial, p. 541.

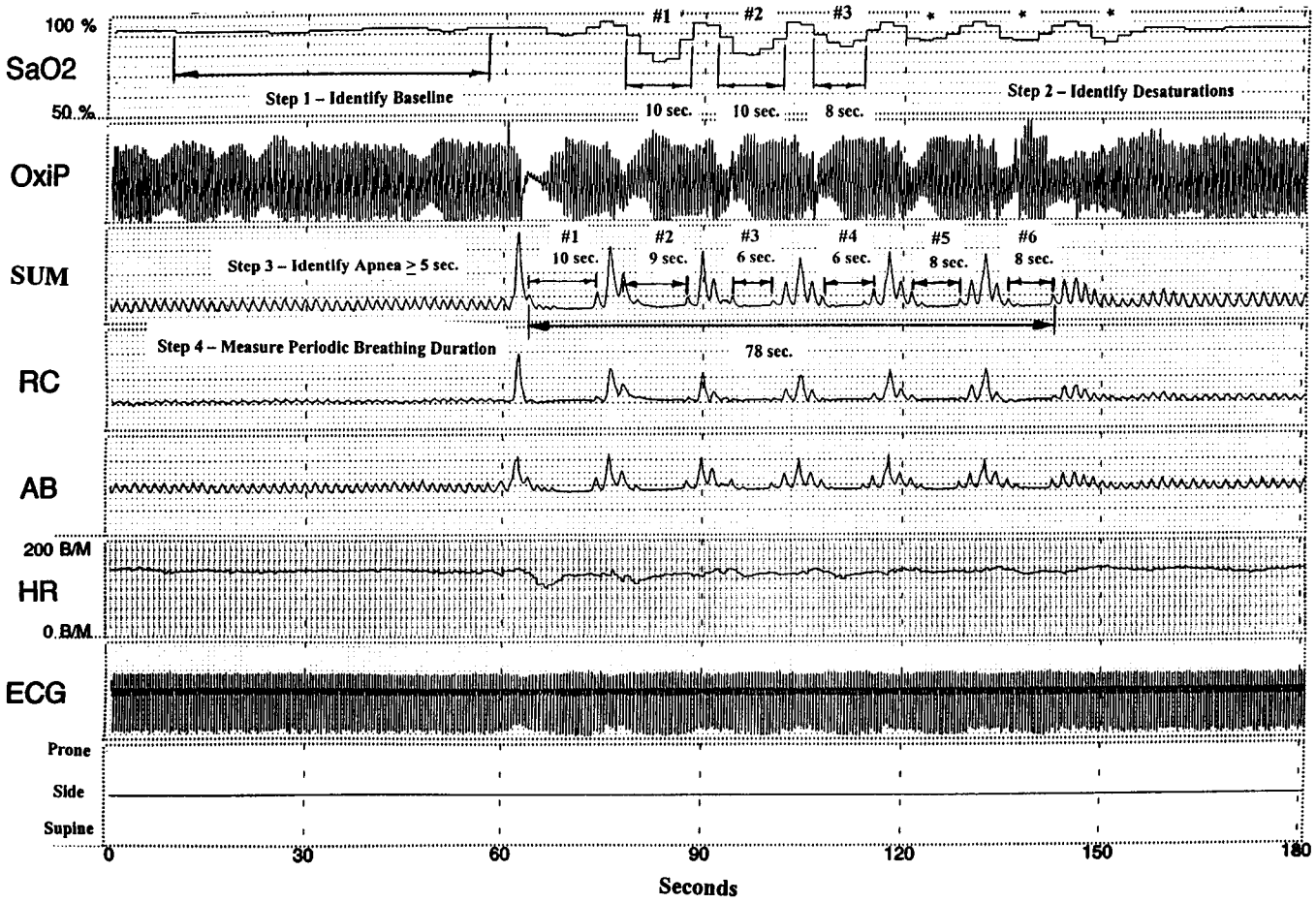

Fig 1. Assessment of 3-minute non-event epoch. This infant is 8 weeks old. See Methods for scoring criteria for each step: Step 1: Determine baseline SaO_2 (SpO_2); 2 cursor lines mark beginning and end of segment meeting criteria for this baseline SpO_2 of 93%. Step 2: Identify acute decreases in SpO_2; there are 3 acute decreases in this epoch. Each decrease is then scored for duration <90% and <80%, lowest SpO_2, and longest respiratory pause associated with decrease. Lowest values for these 3 acute decreases are 75%, 80%, and 82%, respectively. Step 3: Identify all apneas >4 s; there are 6 apneas >4 s in this epoch, numbered as 1 through 6. Total number of apneas >4 s is counted and the total duration recorded with scoring tool. Step 4: Identify periodic breathing; 2 cursors mark periodic breathing episode of 78 s. Step 5: Identify sleep position for baseline SpO_2 and acute decreases in SpO_2. Infant is sleeping on side during this epoch. *Oxi-P,* Pulse rate from oximeter; *RC,* signal proportional to thoracic (rib cage) cross-sectional area; *AB,* signal proportional to abdominal cross-sectional area; *Sum,* weighted sum of RC and AB, proportional to tidal volume.

reached, and (2) there were substantial gaps during which SpO_2 could not be ascertained, because these healthy infants triggered an event recording approximately 2 times per week only.

The memory monitor developed for the Collaborative Home Infant Monitoring Evaluation study[6] was designed to store automatically all physiologic data during the first 3 minutes of each hour, thus providing an opportunity to observe SpO_2 during previously inaccessible periods. The specific aims of this study in healthy term infants during unperturbed home sleep were to (1) describe SpO_2 in the first 25 postnatal weeks and (2) assess the relationships among SpO_2, breathing pattern, heart rate, and sleep position.

METHODS

The healthy term infants enrolled in the CHIME study were born at 38 to 42 weeks' gestation. All were appropriate for gestational age, were normal at delivery, were discharged with the mother, and were ≤30 days old at enrollment. The exclusion criteria included any acute illness and a family history of sudden infant death syndrome. Written informed consent was obtained for each infant, and the Institutional Review Board at each site approved the study.

Among the 214 healthy term infants enrolled in May 1994 to July 1997, 67 infants used the monitor ≥50 h/mo for ≥3 months. This criterion ensured that each subject contributed longitudinal data over the full age range of 2 to 25 weeks. Three infants were excluded for technical reasons or acute respiratory illness requiring hospitalization. The remaining 64 healthy infants are the subject of this report.

Physiologic Recordings

The CHIME monitor (NIMS, Inc, Miami, Fla) includes respiratory induc-

Table. Characteristics of the mothers of healthy term infants and infant characteristics compared with the total CHIME group of healthy term infants

Group characteristics	Study group (≥50 h/mo for ≥3 mo) (n = 64)	Comparison (insufficient monitor use) (n = 150)
Maternal characteristics		
Age*	31.8 (5.7)	28.8 (6.1)
Education*	15.9 (2.9)	14.4 (2.7)
Race/ethnic group*		
% White	64.1	47.3
% Black	3.1	21.6
% Hispanic	7.8	8.1
% Asian	7.8	8.1
% Other	17.2	14.9
% Married*	93.8	81.0
Parity		
% 1	49.	42.
% 2	29.	28.
% 3+	15.	17.
% Pregnancy cigarette use	9.4	18.2
% Pregnancy alcohol use	21.9	24.3
Infant characteristics		
% Male	50.0	58.9
Gestational age at birth	39.5 (1.0)	39.6 (1.0)
Birth weight	3320 (310)	3323 (291)
Age at monitor start (d)	16.3 (9.9)	17.4 (9.4)

Except as indicated, the maternal characteristics did not differ. None of the differences in infant characteristics was statistically significant (SD).
*$P < .02$.

tance plethysmography, an electrocardiographic monitor and cardiotachometer, an Ohmeda Minx pulse oximeter (Ohmeda Corp, Liberty Center, NJ), a position sensor placed on the diaper over the lumbar region, a data acquisition computer, and a 120-Mb removable memory cartridge.[6,7] The oximeter uses a 3-second moving average of SpO_2 that updates once per second. Reusable probes (Ohmeda SoftProbe) were placed on a foot and repositioned every 4 to 8 hours. Each family was asked to use the monitor during nocturnal sleep until the infant was 6 months of age. Because most monitor use occurred between 10:00 PM and 7:00 AM and at 2 to 25 weeks, we limited our analyses to these hours and ages.

The CHIME monitor was programmed to store continuous waveforms for all physiologic variables during the first 3 minutes of each hour and all events reaching the recording threshold for apnea (16 s) or bradycardia (heart rate <80 bpm for ≥5 s). For each event all waveforms were recorded for 75 seconds before and 30 s after resolution of the event.[6] Research staff called each family weekly and conducted a scripted interview that included acute illness information.

Three technicians analyzed the 3-minute epochs with a software tool programmed to display only the 3-minute epochs.[6] The physiologic montage (Fig 1) included SpO_2 and the pulse signal from the oximeter, 3 channels from the respiratory inductance plethysmography bands (abdominal and thoracic inductance, sum), electrocardiography and heart rate, and sleep position. A reliable pulse oximetry signal contained pulses that coincided with the QRS segment on the electrocardiogram for the entire duration of the event. Only periods with a reliable pulse signal that was free of movement artifact were used in scoring SpO_2. Variables were reported as the proportion of 3-minute epochs that met a specified criterion or as the total number of seconds during which specific criteria were met, thus permitting inclusion of multiple occurrences during a single epoch (Fig 1). All changes in SpO_2 that began during or within 10 s of a threshold violation were scored.

Baseline SpO_2 was the longest interval ≥10 s in duration that met the following conditions: regular respiratory rate and amplitude, good oximeter waveform, no movement artifact, and ≥15 s after any movement, sigh, or respiratory pause ≥5 s. The baseline SpO_2 was determined by calculating the mean of the saturation values (1 sample/s) during this segment.

Acute decreases in SpO_2 were defined as a decrease of ≥10% from a stable preceding baseline interval (ie, from 93% to 83%) that was sustained <90% for ≥5 s. For each acute decrease in SpO_2, 4 variables were stored: duration of SpO_2 <90% and <80%, lowest SpO_2 reached, and the longest respiratory pause associated with the acute decrease.

For each 3-minute nonevent epoch, the total duration of each apnea ≥5 s was measured and stored. For purposes of this study, the sum channel was used to identify and measure the duration of each apnea (Fig 1). Apnea duration was scored from peak-to-peak. The duration of periodic breathing within each epoch was measured. Periodic breathing was defined as a sequence of ≥3 episodes of apnea >3 s in duration and separated by <20 s of normal respiration. In many instances the beginning or end of the periodic breathing episode did not occur within the epoch. For each second during the 3-minute epoch, the software tool sampled and stored infant position as prone, side, or supine.

Statistics

In bivariate analyses comparing 2 groups of children (eg, with and without ≥1 low baseline SaO_2 episode), we used chi-squared tests for categoric variables and independent sample *t* tests for continuous data. We used a generalized linear mixed model (PROC GLIMMIX, SAS Institute, Inc, Cary, NC) to assess the association between the likelihood of having an acute decrease during a particular week and the time-dependent variables age, proportion of time in each position, number of epochs with periodic breathing, and illness.[8] This approach accounts for irregularly spaced and randomly missing data and repeated measures within the same subject. Results with *P* values <.05 are described as statistically significant.

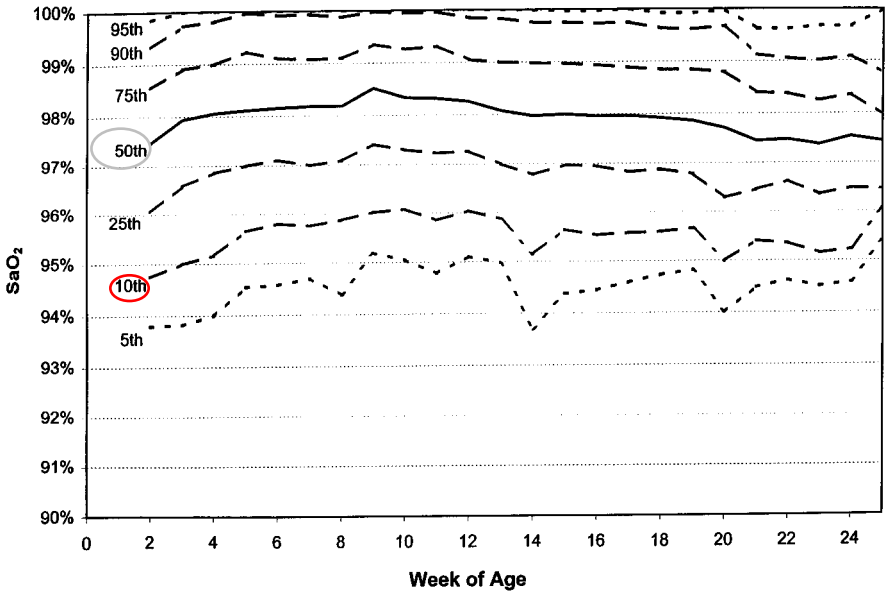

Fig 2. Median baseline SaO_2 (SpO_2) for each postnatal week at 2 to 25 weeks of age. Variations in SpO_2 occurring with increasing age are not significant.

RESULTS

The 64 infants in this study were compared with the 150 healthy term infants not included (Table). Mothers of infants in the study group were more likely to be older, white, married, and more highly educated. Infant characteristics, however, were similar in the 2 groups. Among 41,821 3-minute epochs, 3064 (7.3%) were uninterpretable because of movement artifact, and 3630 (8.7%) epochs were excluded because there was no oximeter signal, leaving 35,127 epochs (1756 hours) for analysis. The distribution of epochs by sleep position was 65% supine, 10% side, and 25% prone. During 30 epochs (0.09%) the apnea recording threshold (≥16 s) had been met. Ten of these were false events,[6,8] and 20 were judged to be true apnea of 16 to 22 s in duration without any bradycardia or SpO_2 value <90% for ≥5 s. The median time assessed per infant was 25.4 hours (507 epochs), and the range was 7.9 to 49.9 hours (158 to 999 epochs, respectively). The median time assessed each week was 80.4 hours (1609 epochs). The absolute number of epochs per week ranged from 983 to 1970 in weeks 24 and 10, respectively, and was higher during weeks 9 to 12 (range 1763 to 1970) than either the first 4 weeks (998 to 1656) or the last 4 weeks (983 to 1192).

Baseline SpO_2 was identified in 33,801 (96.2%) of the epochs. The most common reasons for being unable to measure baseline saturation were unstable breathing pattern and movement. The median and 10th percentile for baseline SpO_2 were 97.9% and 95.2%, respectively (Fig 2), but there were 203 epochs (0.6%) with a baseline SpO_2 <90%, and 38 (59%) infants had at least 1 epoch with a baseline SpO_2 <90%. Among these 38 infants, 25 had 1 to 4 low baselines, 7 had 5 to 9 episodes, and 6 had a range of 11 to 26 episodes. No change occurred in baseline SpO_2 as infant age increased from 2 to 25 weeks. The number of epochs containing a low baseline SpO_2 was not associated with infant age, sleep position, or the presence of periodic breathing.

Acute decreases in SpO_2 occurred in 178 (0.51%) of epochs. The total number of acute decreases was 308, and the total number of seconds of SpO_2 <90% during acute decreases was 2362 s (1.34 s/h). At least 1 acute decrease was observed in 38 (59%) infants; the median number of events per infant was 4 (range 1 to 71), and the 25th and 75th percentiles were 2 and 7 events, respectively. In the epochs with acute decreases, the mean baseline SpO_2 was 96.7% (SD 2.5). The median lowest SpO_2 was 83% (10th, 90th percentiles 78%, 87%). The median time <90% was 6.3 s (6.0, 9.8), and the median time <80% was 3.5 s (1.9, 6.0). The frequency of acute decreases was 1.8 s/h in supine, 0.4 in side, and 0.6 in the prone sleep positions.

Infants with ≥1 low baseline SpO_2 were more likely to have at least 1 acute decrease in SpO_2 (odds ratio 1.9, 95% CI 1.1, 3.6, $P < .05$); 95% of acute decreases were associated with a respiratory pause, 79% during periodic breathing (Fig 1), and at least another 16% during single apneas. Because most of the remaining acute decreases occurred at the beginning of an epoch, apnea just before the epoch cannot be excluded as a precipitating factor.

The number of seconds per hour of SpO_2 <90% during acute decreases declined with age (Fig 3). Although the relative proportion of acute decreases

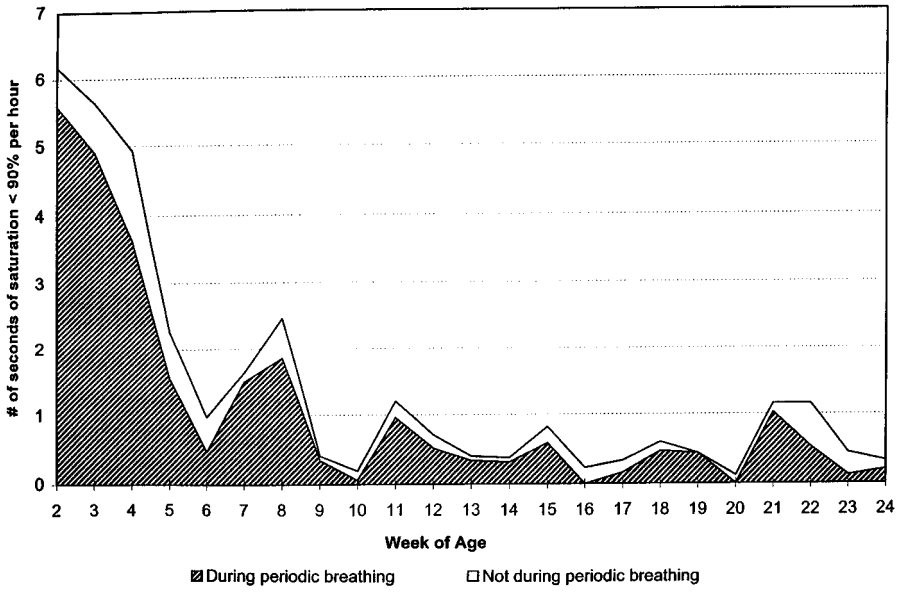

Fig 3. Number of seconds with SaO_2 (SpO_2) <90% during acute decrease, expressed per hour by presence of periodic breathing and by week of age.

occurring during nonperiodic apnea did not change with age, the amount of periodic breathing decreased with age (5.4%, 3.6%, and 1.5% at 2, 12, and 22 weeks, respectively) and was less when prone (1.6% of epochs) compared with the side or supine sleep positions (3.3% of epochs). The number of seconds per hour of periodic breathing was 58 in prone versus 118 and 120 s in side and supine, respectively.

With the use of the generalized linear mixed model,[9] infants were more likely to have an acute decrease during a week of monitoring if they were younger (OR per week younger = 0.95, 95th percentile CI 0.90, 0.99) or if they had more epochs with periodic breathing (OR per epoch periodic breathing = 1.1, 95th percentile CI: 1.05, 1.14, $P = .0001$). The odds, for example, of having an acute decrease during the seventh week of life are 30% less than during the third week of life (95th percentile CI 0.65 to 0.72). In a similar manner, the odds of having an acute decrease during a week including 5 epochs with periodic breathing are 50% higher than during a week with no epochs containing periodic breathing (OR 1.55, 95th percentile CI: 1.48, 1.61). Although there was no relationship between sleep position and acute decreases in SpO_2 by multivariate analysis, the acute decreases occurred significantly more often during nonprone sleep, because periodic breathing occurred significantly more often during nonprone sleep.

DISCUSSION

The features of the CHIME monitor enabled recording of 35,127 3-minute observations unaffected by monitor alarms or other systematic perturbations and have yielded new insights into baseline and acute decreases in SpO_2. Infants with ≥1 low baseline SpO_2 were more likely to have ≥1 acute decrease in SpO_2. The acute decreases improve with age and are primarily associated with periodic breathing; periodic breathing is more common in nonprone sleeping positions. Because the periodic breathing, acute decreases in SpO_2, and low baseline SpO_2 occurred in healthy term infants without adverse consequences, these results do not represent an advantage of prone sleeping but rather represent an expanded understanding of the normative range of these respiratory and oxygenation behaviors.

These results expand the normative data derived from the first study of longitudinal oxygen saturation with home memory monitoring.[5] Although it was not possible to characterize baseline SpO_2 in that study, periodic decreases to levels as low as 72% were observed with periodic breathing, and the lowest weekly value was always <82%. The median duration of these acute decreases in SpO_2 to <90% was only 5 s, but the range was wide (1 to 183 s), and 9.6% of episodes were >10 s.

The CHIME monitor enabled us to obtain an average of 40 observations per week, equivalent to ≥120 minutes of physiologic data per week. These 3-minute epochs are more representative of unperturbed sleep than the previous "event"-based observations potentially influenced by the circumstance(s) triggering the "event" recording. We selected 3-minute epochs as a reasonable compromise between longer or more frequent automatic epochs and too-frequent filling of cartridge memory. Addition of the sleep position sensor has yielded new insights into the interrelationships among SpO_2, breathing pattern, and heart rate. There was significantly less periodic breathing in the prone position compared with that in side and supine sleeping. This was previously observed in overnight polysomnograms in term infants[9] but not in preterm infants during daytime recordings.[10]

Because of limited correlation between low baseline SpO_2 and acute decreases in SpO2, we considered the possibility that the low baseline values were artifactual. Falsely low SpO_2 levels caused by movement artifact interfering with pulse detection are common, but all discernable movement-related artifacts were excluded at the time of epoch scoring. However, joint flexion might decrease arterial pulse pressure below a threshold level,[11,12] artifactually low values have been observed with marked venous pulsations,[13] and optical shunting or bridging[12,15] can occur. The effect of

bridging depends on whether the infrared or the red emitter is malpositioned, and the effect is brand-specific. With Ohmeda oximeters and probes, bridging can be the cause of SpO_2 decreases of 2% to 4% but should result in a default reading of "probe off" before reaching the magnitude of decrease (<90%) required for scoring as a low baseline (personal communication, Jonas Pologe, Manager of Research, Ohmeda Corp). Although we cannot exclude artifact, it is also possible that these low baseline SpO_2 values are real and indicative of the lower range of values occurring in healthy term infants during early infancy.

In general, the Ohmeda oximeter yields SpO_2 values having a mean difference of 1.61% less ($P < .001$) compared with the Nellcor oximeter.[15-17] Allowing for these small but systematic differences, our results are generally consistent with previous normative studies.[2-5,18,19] Although our median baseline SpO_2 of 97.9% is somewhat higher than in other studies with Ohmeda oximeters, our criteria for baselines were strictly defined to avoid any movement artifact or proximity to apnea or sighs and should thus be more representative of true baseline values. Because mean respiratory rates tended to be higher when baseline SpO_2 was <95% compared with >95%, our higher baseline values are not related to relative hyperventilation.

The earliest studies in term healthy infants were based on brief cross-sectional assessments of home-based SpO_2. With the use of the Nellcor pulse oximeter at a median age of 39 days, the baseline range for SpO_2 was 97% to 100% (median 99.8%) during regular breathing.[2,18,19] At median ages of 4 and 17 days,[3] the baseline range for SpO_2 was 92% to 100% (median 97.6%) and 86.6% to 100% (median 98.0%), respectively. Episodic decreases to ≤80% for ≥4 s occurred, were associated with periodic breathing, had a peak frequency during the second week of age,[2] and were rare by 6 weeks of age, even though shorter episodes <4 s persisted at a median frequency of 0.7 episodes per hour. At 2 to 11 months[4] mean levels during quiet sleep were 94% to 95% when the infants were both supine and prone and were not affected by upper respiratory illness.

In summary, these longitudinal observations of SpO_2 identify relevant correlations with age, apnea, and sleep position. These results will provide a frame of reference for event recordings in individual infants and in groups of infants at risk for sudden infant death syndrome.

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50 Years Ago in The Journal of Pediatrics

MYCOTIC INFECTIONS IN CHILDREN (THE BUDDING YEASTS AS AGENTS OF DISEASE)

Clinical Conference, Taylor G (Conference Chairman). J Pediatr 1949;35:385-9

In this article faculty from the Departments of Pediatrics and Bacteriology at Duke University School of Medicine discuss the epidemiology, clinical manifestations, microbiologic distinction, and treatment of mucosal and systemic infections caused by budding yeasts. Histoplasmosis, with a preponderance of cases in the Mississippi Valley, and North American blastomycosis, with limitation to the North American continent, were the major focus of the article because of their relatively high incidence and unique geographic occurrence. Candidiasis and cryptococcosis, although widespread geographically, were rarely serious infections in 1949. Treatments for fungal disease were limited to potassium iodide and gentian violet (sometimes given parenterally).

Fast forward to 1999. Unfortunately, healthy children continue to have, albeit rarely, histoplasmosis (except in the Mississippi Valley where it occurs frequently) and blastomycosis, but more effective treatments are available. Candidiasis, on the other hand—in current settings of immunosuppressive diseases or treatments, use of broad-spectrum and potent antibiotics, and invasive devices—has become *the* infectious disease of the decade. Although the shelf space and dollars required to stock the variety of available antifungal agents in hospital pharmacies today are greater, effectiveness of treatment is still highly dependent on removing the fungal foe's advantage—by reconstituting immune competence, removing catheters, and avoiding antibiotics.

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