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A comparison of respiratory function in Afro-Caribbean and Caucasian infants

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A comparison of respiratory function in Afro-Caribbean and Caucasian infants. J. Stocks, M. Gappa, P.S. Rabbette, A.F. Hoo, Z. Mukhtar, K.L. Costeloe. ©ERS Journals Ltd 1994.

ABSTRACT: Race is recognized as an important determinant of lung function in children and adults, but limited data exist for infants. Accurate interpretation of lung function tests during the neonatal period may depend on appropriate values for predicting normality. The aim of this study was to compare tidal breathing parameters, Hering-Breuer reflex (HBR) activity, and total respiratory compliance (Crs) in healthy newborn caucasian (white) and Afro-Caribbean (black) infants, to determine whether separate reference values were required for these two ethnic groups.

Respiratory function was measured in 33 healthy black infants, 18 of whom were premature, and 33 healthy white infants matched for sex, gestational age, weight, postnatal age, and maternal smoking during pregnancy.

There were no significant paired differences between black and white infants with respect to minute ventilation, respiratory frequency, the ratio of time to reach peak expiratory flow to total expiratory time, or HBR activity. Values of Crs were similar in black and white full-term infants (37.5 (SD 9.0) *versus* 35.0 (6.3) ml·kPa^{-1}, respectively) suggesting that, in the immediate newborn period, separate reference values are not necessary for these parameters. However, Crs was somewhat lower in black than white preterm infants (26.0(5.2) *versus* 29.5(7.2) ml·kPa^{-1}, this difference reaching statistical significance if results were expressed in relation to body weight (95% confidence interval of within-pair differences -4.0 to -0.02 ml·kPa^{-1}·kg^{-1}; p<0.05).

We conclude that no separate reference values for tidal breathing, Hering-Breuer reflex activity or total respiratory compliance are required for white and black babies in the immediate newborn period. Further studies are required to investigate sequential changes of Crs in preterm infants and to determine the potential influence of race on the chest wall.

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Marked racial differences are known to exist in infant mortality and respiratory morbidity. Whereas black infants have a higher risk of neonatal and postneonatal death than white infants, low birth weight black infants are more likely to survive the neonatal period than white infants of similar birthweight [1]. Furthermore, black infants have less tendency to develop hyaline membrane disease than white infants of similar gestational age. These relationships appear to exist, even after adjustment for socio-economic class [2]. This could suggest that the respiratory system is more mature at birth in black babies than in white babies of similar gestational age. The importance of race as a determinant of lung function in adults has long been recognized [3]. Numerous studies have confirmed that, whilst Caucasians living in Europe and America have similar lung volumes when adjusted for body height, lower values occur amongst Chinese, Indian and African Negro populations [4]. Similar differences appear to exist in young children [5]. It has been shown that airways resistance is lower in Afro-Caribbean than in European infants [6], which may be largely attributable to variations in nasal anatomy and, hence, nasal resistance [7]. However, there appear to be no data on the potential influence of race on other parameters of lung function in infants.

During recent years, there has been a marked increase in the application of respiratory function tests in the neonatal unit. This reflects the improving survival of very premature infants, the development and need for assessment of new forms of treatment, and the increasing availability of relatively noninvasive methods for assessing infant lung function [8]. However, interpretation of such measurements frequently requires appropriate values for predicting normality. Although several studies have been performed on healthy newborn infants in an attempt to provide such data, most have been limited to Caucasian infants, or have not defined the ethnic origins of their population.

The aim of this study was to compare tidal breathing parameters, passive respiratory mechanics and the strength of the Hering-Breuer reflex (HBR), in healthy newborn European and Afro-Caribbean infants, and to determine whether separate reference values for these parameters of respiratory function should be established, according to ethnic origin.

Methods

Subjects

Healthy newborn infants were eligible for this study, either if both parents were African or Afro-Caribbean (hereafter referred to as "black" infants), or if both parents were Caucasians of European descent (hereafter referred to as "white" infants). Infants with any evidence of intrauterine growth retardation, congenital abnormalities, or respiratory, neuromuscular or cardiac disease were excluded, as were those whose parents did not understand or speak English. During the period January 1989 to December 1992, respiratory mechanics were measured in 71 white and 36 black healthy neonates. For every black infant studied successfully, a matched white control infant was selected on the basis of physical characteristics, blind to the results of the lung function tests. Physical details of the white infants were arranged in chronological order of testing. Matching was performed by selecting the first white infant to match a black infant in terms of birthweight (±300 g), postnatal age (±2 days), gestational age (±2 weeks), and maternal smoking during pregnancy. Once selected, the white infant was removed from the pool, ensuring that results from each subject were only used once.

Measurements of respiratory mechanics were obtained in 15 matched pairs of full-term infants and 18 matched pairs of preterm infants. Details of the infants are summarized in table 1. The relationship between body length and weight in the black and white infants appeared to be very similar, as illustrated in figure 1.

Approval for this study was granted by the City and Hackney Committee for Ethical Research, and written informed consent to participate was obtained from one or both parents prior to the measurements.

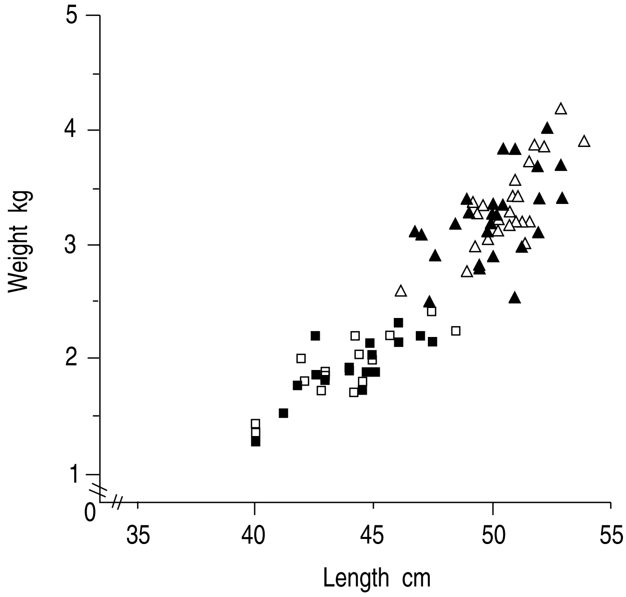

Fig. 1. – Relationship between body weight and crown-heel length in newborn black and white infants. □: white preterm; △: white full-term; ■: black preterm; ▲: black full-term.

Recording equipment

The apparatus used to measure minute ventilation, respiratory mechanics, and the strength of the Hering-Breuer reflex, which consisted of a face mask, pressure port, shutter, pneumotachograph (Fleisch 0 for full-term infants, Hans Rudolph 0–10 $l\cdot min^{-1}$ for preterm infants) and Validyne transducers, has been described previously [9–11]. Apparatus dead space, estimated by water displacement, was between 2–3 $ml\cdot kg^{-1}$ for all infants, being 3 and 8 ml for measurements in the preterm and full-term infants, respectively. Resistance of the apparatus at a flow of 100 $ml\cdot s^{-1}$ was 0.25 $kPa\cdot l^{-1}\cdot s$ for preterm and 0.48 $kPa\cdot l^{-1}\cdot s$ for full-term infants.

Airflow and airway opening pressure signals were digitized at a sampling rate of 100 Hz. Output from the pneumotachograph was digitally integrated to yield tidal volume (VT). Data display, recording and analysis were performed using the Respiratory Analysis Program (RASP,

Table 1. – Infant details

	Preterm		Full-term	
	Black	White	Black	White
n	18	18	15	15
Male %	33	33	46	46
Maternal smoke %	17	17	15	15
GA weeks	33.5 (1.2)	33.2 (1.2)	39.5 (0.8)	39.8 (0.9)
BW g	1942 (270)	1895 (268)	3250 (373)	3311 (369)
Length cm	44.2 (2.1)	43.7 (2.2)	50.1 (1.7)	50.6 (1.5)
PNA days	7.3 (1–14)	7.7 (1–14)	1.4 (1–3)	1.5 (1–3)

Data are expressed as mean with SD in parenthesis, except for PNA where range is shown in parenthesis. Maternal smoke: percentage of infants whose mothers smoked during pregnancy; GA: gestational age; PNA: postnatal age; BW: birth weight.

Physio Logic Ltd) on a Compaq 386 personal computer. Airway occlusions were performed manually, and timed from the computer display of VT.

Measurement protocol

All measurements were performed during natural sleep, in an air-conditioned room on the Special Care Baby Unit at the Homerton Hospital. Measurements were performed between 1–3 days postnatal age in full-term infants, and 1–14 days in preterm infants, and commenced approximately 30–60 min after a feed.

Infant length was measured by two adults (including one trained operator) using an infant stadiometer. Measurements were repeated until two values within 0.5 cm of each other were achieved. The infants were weighed on digital scales, (Soehnle).

Data collection was confined to consecutive periods of quiet sleep in which posture was stable, respiration regular, and no eye movements were observed [12]. All measurements were made with the infant in the supine position. Once settled in quiet sleep, the mask and recording equipment were placed gently over the infant's nose and mouth, and a leak-proof seal was created using therapeutic putty. Real-time signal changes were then displayed.

Tidal breathing. Tidal breathing parameters, including VT, respiratory frequency (f_R), minute ventilation ($\dot{V}E$), and the time to reach peak tidal expiratory flow as a ratio of total expiratory time (*i.e.* TPEF:TE) [13, 14], were calculated from recordings of tidal breathing made over a minimum period of 5 min during quiet sleep.

Hering-Breuer reflex (HBR). When at least 10 regular breaths with a stable end-expiratory level had been recorded, an end-inspiratory airway occlusion was maintained, until the infant had made at least one complete respiratory effort against the occlusion. At least 10 breaths were allowed between successive occlusions. Five occlusions were performed in each infant [9].

Respiratory system compliance (Crs). Crs was measured using the Multiple Occlusion Technique (MOT). A series of 15 brief occlusions were performed at different volumes within the first two thirds of expiration. Each occlusion was held until a relaxed pressure plateau was achieved for at least 0.2 s in the full-term infants, and 0.1 s in the more rapidly breathing preterm infants, according to previously established criteria [15, 16]. Attempts were also made to measure respiratory resistance and compliance using the single breath technique [17, 18].

Data analysis and statistical approach

All tidal breathing parameters (VT, f_R, $\dot{V}E$ and TPEF:TE) were calculated as the mean (SD) of five sets of 5–10 breaths selected over at least 5 min of quiet regular breathing. The activity of the HBR was measured from the relative change in TE during occlusion (TE_{occ}) compared to unoccluded tidal breathing, as described previously [9]. Reflex activity was expressed as the percentage change in TE during occlusion. The mean percentage change from five end-inspiratory occlusions was taken as the strength of the HBR in each infant. For each infant, Crs was calculated from least squares linear regression analysis of the volume-pressure (V-P) data [15]. Results from the preterm and full-term infants were analysed separately. For each parameter of respiratory function, within-pair (black-white) differences were used to assess the potential influence of race by paired t-tests [19]. Results were considered statistically significant if $p<0.05$. The 95% CI of the group mean difference between the two races was also calculated for each parameter.

Sample size

Of all the parameters assessed, the potential influence of race on Crs was likely to be most relevant clinically. Consequently assessment of sample size was based on the ability to detect a mean difference in Crs of 2.5 $ml \cdot kPa^{-1} \cdot kg^{-1}$ between black and white infants. By considering the standard deviation of Crs amongst healthy infants, it was calculated that results from 15 pairs of preterm and 15 pairs of full-term infants would be adequate to detect this difference in either group with a significance of 2.5% (two-sided) and a power of 95%.

Results

Respiratory function

Results of the respiratory function tests are summarized in table 2. The relationship between Crs and body length is shown in figure 2. There was a tendency for Crs to be higher amongst the white than the black preterm babies, although this difference did not quite reach significance at the 5% level (95% CI of within-pair differences =-7.3 to 0.4 $ml \cdot kPa^{-1}$; p=0.07). When results were expressed in relationship to body weight, Crs was 15.7 $ml \cdot kPa^{-1} \cdot kg^{-1}$ in the white preterm infants, compared to 13.7 $ml \cdot kPa^{-1} \cdot kg^{-1}$ in their black counterparts. The mean within-pair difference of -2.0 $ml \cdot kPa^{-1} \cdot kg^{-1}$ (95% CI -4.0 to -0.02 $ml \cdot kPa^{-1} \cdot kg^{-1}$) was statistically significant ($p<0.05$). However, since the 95% CI almost encompasses zero, the difference may be of no clinical significance.

A comparison of respiratory compliance between black and white infants is shown in figure 3, where the results from the paired measurements are plotted against a line of identity. This enables the difference within each pair of infants to be examined. Results are expressed per kg body weight, to facilitate comparisons between preterm and full-term infants. It can be seen that, whereas results from the full-term infants are scattered evenly around the line of identity, values fall below the line in two thirds of the paired measurements in preterm infants - reflecting the higher values of Crs found amongst white preterm infants compared to their black partners. Tidal volume was slightly higher amongst white than black full-term infants (95% CI 0.88 to 8.9 ml), but since respiratory frequency was somewhat lower in the white infants, there was no significant difference in minute ventilation. There

Table 2. – Respiratory function in black and white infants

	Preterm			Full-term		
	Black	White	95% CI	Black	White	95% CI
V_T ml	14.7 (3.0)	14.6 (3.5)	-2.48–2.59	23.4 (2.3)	28.0 (5.9)	0.88–8.29*
f_R br·min^{-1}	67 (11)	63 (11)	-2.4–10.3	55 (9.1)	50 (10.9)	-0.7–10.7
$\dot{V}_E$ ml·min^{-1}	975 (248)	892 (156)	-71–237	1313 (197)	1371 (203)	-71–185
T_{PEF}:T_E	0.48 (0.17)	0.44 (0.12)	-0.04–0.11	0.50 (0.08)	0.52 (0.08)	-0.06–0.02
HBR %	103 (34)	113 (42)	-40–24	94 (34)	96 (28)	-19–16
Crs ml·kPa^{-1}	26.0 (5.2)	29.5 (7.2)	-7.3–0.4	37.5 (9.0)	35.0 (6.3)	-7.9–3.0

Data are presented as mean and SD in parenthesis. 95% CI: 95% confidence interval of the mean within-pair difference (black-white); *: $p<0.02$. V_T: tidal volume; f_R: respiratory frequency; $\dot{V}_E$: minute ventilation; T_{PEF}:T_E: time to reach peak expiratory flow as a ratio of total expiratory time; HBR: Hering-Breuer reflex; Crs: total respiratory compliance.

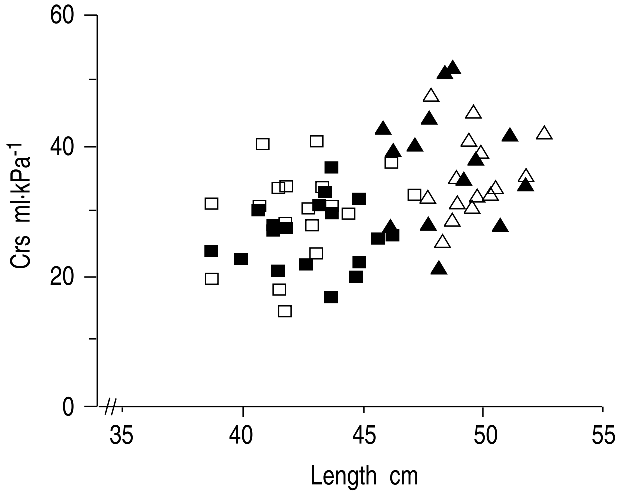

Fig. 2. – Total respiratory compliance (Crs) plotted against body length. □: white preterm; △: white full-term; ■: black preterm; ▲: black full-term.

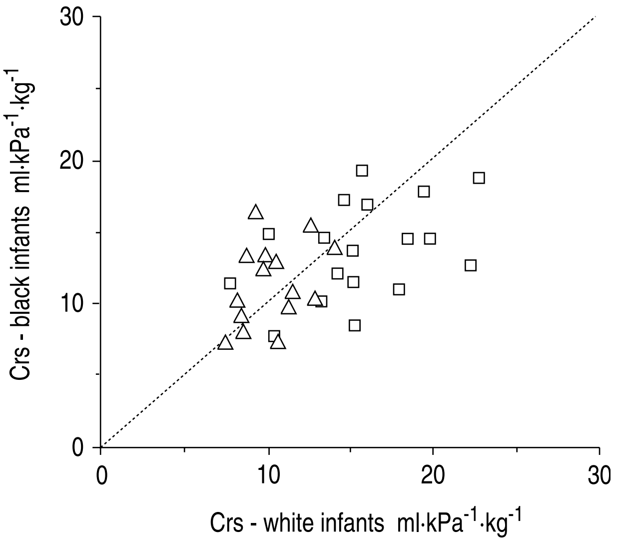

Fig. 3. – Comparison of paired measurements of respiratory compliance in black and white infants. Values of Crs from 33 matched pairs of infants (black-white) are plotted against the line of identity. Results falling above the line reflect a higher value of Crs in the black infant, those below the line a higher value of Crs in the white infant. △: full-term infants; □: preterm infants. Crs: total respiratory compliance.

were no other significant differences between the black and white preterm or full-term infants, whether results were expressed in absolute terms (table 2) or per kg body weight.

Discussion

Results from this study suggest that there are no clinically significant differences in various parameters of tidal breathing, Hering-Breuer reflex activity, or total respiratory system compliance, between black and white full-term infants when studied during the first few days of life. Similarly, with the exception of the slightly lower Crs found amongst black infants, no significant differences related to race were observed amongst the group of preterm infants. Interpretation of these results is dependent on the absence of any potentially confounding effects, in either selection and matching of subjects, or in methodology.

One of the major difficulties encountered during the matching process was the discrepancy between incidence of maternal smoking between the two ethnic groups, with twice as many white than black mothers reporting smoking during pregnancy. This led to the exclusion of many otherwise suitable white infants as matched controls. Despite this problem, it was possible to match 33 pairs of infants with satisfactory Crs results, thereby giving an adequate power of study in terms of detecting any significant differences between black and white infants. The similarity between the two groups with respect to physical characteristics can be seen in table 1 and figure 1.

It is possible that matching on anthropometric characteristics of the black babies could have introduced some bias. To determine whether the white babies selected as matched controls for the black babies were representative of the population from which they were chosen, unpaired t-tests were used to compare infant characteristics and lung function results from the selected and unselected white infants in the original pool of data. There were no significant differences between the two groups, except for the lower incidence of maternal smoking during pregnancy amongst the selected group (16%) compared with the unselected infants (50%) ($p<0.05$).

Tidal volume and respiratory rate are simple to measure but difficult to interpret, because the act of measurement often alters the infant's breathing pattern. Application of a face mask, and apparatus dead space or resistance, has been shown to increase minute ventilation above basal levels [20, 21]. However, since all measurements were made under identical conditions, with dead space of the apparatus reduced to minimal values for the preterm infants, these factors are unlikely to invalidate comparisons between black and white infants.

It has been suggested that TPEF:TE reflects a strategy of breathing whereby expiratory flow is braked to a greater or lesser degree depending on the subject's underlying respiratory mechanics [13, 14]. Thus, in the presence of increased airways resistance, there tends to be less braking of expiratory flow with resultant shortening of TPEF:TE. Black infants have been shown to have lower nasal and total airway resistance than white infants [6, 7]. It could, therefore, be postulated that black infants would exhibit a greater degree of expiratory braking of airflow, thereby prolonging the time to reach peak expiratory flow (TPEF) during tidal breathing and, hence, the TPEF:TE ratio in comparison to white infants. However, virtually identical values were found in black and white babies in this study.

Active tidal slowing, which is a function of the upper airway musculature and post-inspiratory diaphragmatic activity, represents a reflex response to maintain an effective expiratory time constant. Results from this study, in keeping with a recent report from STICK *et al.* [22], show much higher values of TPEF:TE in healthy newborn infants than are found beyond the neonatal period [13, 23]. During the first few days after birth, marked expiratory braking is frequently present, and is associated with dynamic elevation of lung volume [24]. It may be that, during this period of relative instability, defence of lung volume is of prime importance, and masks any association between TPEF:TE and lower airway function. Consequently, any racial differences in TPEF:TE may not become apparent until beyond the neonatal period, when the chest wall has stiffened and functional residual capacity is firmly established [25].

There was significant Hering-Breuer reflex activity in all infants, with no significant effect of race on either the mean or range of activity observed. However, despite the presence of this reflex, we were unable to obtain technically satisfactory measurements of respiratory mechanics using the single breath technique consistently enough to provide sufficient power of study for meaningful comparisons between the two racial groups. This was unfortunate, since additional data on the potential influence of race on respiratory resistance would have been particularly valuable. Such comparisons will need to be made on slightly older infants, in whom there is less marked expiratory braking during quiet sleep - this being the major cause of failure in this study [11].

Values of Crs for preterm infants in the present study are somewhat higher than reported previously. MIGDAL *et al.* [26] and HAOUZI *et al.* [27] reported mean values of 10.5 and 10.9 $ml \cdot kPa^{-1} \cdot kg^{-1}$ in healthy preterm infants when using the multiple occlusion technique, but did not specify ethnic origins of their subjects. The gestational age of infants was similar in all three studies. However, all measurements in the present study were performed in the first 14 days of life, whereas MIGDAL *et al.* [26] and HAOUZI *et al.* [27] studied preterm infants during the first month of life. ABBASI and BHUTANI [28] performed sequential measurements of dynamic lung compliance (CL) in 33 healthy preterm infants during the first month of life, and demonstrated that CL remained relatively constant during this period, despite increasing body weight. Hence, when corrected for body weight, mean CL fell from 20 $ml \cdot kPa^{-1} \cdot kg^{-1}$ at 1 week of age to 14 $ml \cdot kPa^{-1} \cdot kg^{-1}$ at 4 weeks of age. They attributed these findings to a delay in pulmonary volume maturation following premature delivery. It would, therefore, appear to be essential to take both gestational and postnatal age into account when reporting results of respiratory mechanics from preterm infants.

Despite the similarity between black and white full-term babies, Crs was somewhat higher among the white preterm infants than their black matched controls, this difference being significant if expressed in relationship to body weight. This could be attributed either to a lower lung compliance, possibly associated with lower lung volume, in the black compared with white infants, or to a lower chest wall compliance. There do not appear to have been any systematic studies on the effect of race on lung volumes in infants. However, plethysmographic measurements in 10 preterm and full-term Afro-Caribbean neonates gave very similar results to those obtained from European babies [6]. It is, therefore, interesting to speculate that the lower Crs found among black preterm infants could reflect a lower chest wall compliance in comparison with their white partners. Far from being disadvantageous, a slightly stiffer chest wall at any given gestational age, would impart greater respiratory stability in terms of airway calibre, gas exchange and ventilation-perfusion balance, and would diminish the incidence of paradoxical breathing with its associated increase in the work of breathing [29]. Such factors could contribute to the improved survival noted amongst low birthweight black infants in comparison to white babies of similar gestational age [1, 2].

GERHARDT and BANCALARI [30] found that chest wall compliance ranged from 50–100 $ml \cdot kPa^{-1} \cdot kg^{-1}$ amongst preterm infants. Combining these values with those from ABBASI and BHUTANI [28] for lung compliance in the first week of life (*i.e.* 20 $ml \cdot kPa^{-1} \cdot kg^{-1}$) calculated values of Crs would be between 14.3 and 16.7 $ml \cdot kPa^{-1} \cdot kg^{-1}$, very similar to the values that we observed in the black and white preterm infants, respectively. This suggests that the observed differences between black and white preterm infants could, at least theoretically, be due to differences in chest wall compliance.

However, this hypothesis remains highly speculative and would need to be tested by performing sequential measurements of lung, chest wall and total respiratory compliance in large numbers of black and white preterm infants of varying gestational and postnatal ages.

Our study suggests that, with the exception of the higher Crs found amongst white preterm infants, which may be a relatively transitory finding and of minimal clinical significance, major differences in lung function between white European and Afro-Caribbean subjects do not exist at birth, but may become apparent as the child grows. This is in keeping with the theory that differences in lung function according to race are primarily due to differences in trunk/leg ratio [5], and that differences between black and white subjects increase with age [31]. It has been suggested that anthropometric differences between black and white children do not appear until school age, but firm data have yet to be established in this field. The present study was confined to measurements made during the first 2 weeks of life, a time of relative instability and immaturity, when numerous adjustments to extra-uterine life are occurring. Results cannot, therefore, be extrapolated beyond this period. However, it would appear that separate reference values for tidal breathing parameters, Hering-Breuer reflex activity, and total respiratory compliance are not required for Afro-Caribbean and white European infants in the immediate newborn period. Further studies are required to investigate sequential changes of Crs in preterm infants, and the potential influence of race on chest wall compliance in immature infants.

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