Growth Rate of Lung Function in Healthy Preterm Infants

Luciana Friedrich¹, Paulo M. C. Pitrez², Renato T. Stein², Marcelo Goldani¹, Robert Tepper³, and Marcus H. Jones²

¹Department of Pediatrics, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; ²Department of Pediatrics, Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, Brazil; ³James Whitcomb Riley Hospital for Children, Indiana University, Indianapolis, Indiana

Rationale: It remains unclear whether premature birth, in the absence of neonatal respiratory disease, results in abnormal growth and development of the lung. We previously reported that a group of healthy infants born at 32–34 weeks' gestation and without respiratory complications had decreased forced expiratory flows and normal forced vital capacities at 2 months of age.

Objectives: Our current study evaluated whether these healthy infants born prematurely exhibited improvement or "catch-up" in their lung function during the second year of life.

Methods: Longitudinal measurements of forced expiratory flows by the raised volume rapid thoracic compression technique were obtained in the first and the second years of life for infants born prematurely at 32.7 (range, 30–34) weeks' gestation (n = 26) and infants born at full term (n = 24).

Measurements and Main Results: Healthy infants born prematurely demonstrate decreased forced expiratory flows and normal forced vital capacities in the first and second years of life. In addition, the increases in lung function with growth were similar to full-term infants.

Conclusions: Persistently reduced flows in the presence of normal forced vital capacity and the absence of catch-up growth in airway function suggest that premature birth is associated with altered lung development.

Keywords: lung growth; spirometry

Premature birth is associated with increased respiratory symptoms in the first few years of life, even for infants born at only 30 weeks' gestation and without any neonatal complications (1). There are a limited number of studies evaluating older children who were born prematurely at approximately 30 weeks' gestation. In general, the results indicate relatively normal spirometry, which suggests that catch-up growth occurred, assuming they ever had decreased lung function early in life (1–3). None of the studies evaluating these older children had measurements obtained early in life. There are only two reported studies using spirometric measurements of lung function in healthy infants who were born prematurely (4, 5). Measuring maximal forced expiratory flows at functional residual capacity, Hoo and colleagues found normal values in the neonatal period; however, these infants demonstrated decreased flows at 1-year follow-up (5). These findings suggested a worsening of lung function early in life. Using forced expiratory flows from elevated lung volumes, we have recently reported that healthy premature infants

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

It remains unclear whether premature birth, in the absence of neonatal respiratory disease, results in abnormal growth and development of the lung.

What This Study Adds to the Field

Persistently reduced flows in the presence of normal forced vital capacity and the absence of catch-up growth in airway function suggest that premature birth is associated with altered lung development.

have normal forced vital capacities, but decreased forced expiratory flows in the first months of life (4). Our findings suggested that, very early in life, these infants born prematurely have decreased airway function, but normal lung size. If these infants are to exhibit catch-up growth and normalize lung function by school age, we hypothesized that this would occur in the first year of life, when the lung undergoes rapid growth. In this study, we evaluate the longitudinal changes in lung function early in life for this group of healthy infants born prematurely. Some of the results of this study have been previously published (4, 6, 7).

METHODS

Subjects

Premature infants less than 35 weeks' gestational age without significant respiratory disease were recruited from two neonatal centers in Porto Alegre, Brazil (Hospital Sao Lucas PUCRS, Hospital de Clinicas de Porto Alegre) from August 2001 to August 2002. Gestational age was assessed by date of last menstrual period or ultrasound obtained before 20 weeks of pregnancy. In the absence of this information, gestational age was assessed clinically by the New Ballard method (8). A detailed prenatal and neonatal history was obtained from the mother and from medical charts. Patients were excluded from the study if they had required any mechanical ventilation, supplemental oxygen for greater than 48 hours, or treatment with surfactant. Initial measurements for this group of infants have previously been reported (4).

Healthy full-term infants were evaluated on two occasions as part of a previous study of lung function at Riley Hospital (Indianapolis, IN) (9). Subjects had no history of prior lower respiratory illness or recent upper respiratory infection at the time of lung function measurements.

All subjects were without any acute respiratory symptoms for at least 3 weeks before testing. The ethics committees of all centers approved the study and informed, written consent was obtained from all parents.

Lung Function

Lung function was assessed by the raised volume rapid thoracic compression technique as previously described (10). Briefly, the lung is inflated by applying a pressure of 30 cm H₂O to the airway with a face

(Received in original form March 23, 2007; accepted in final form September 20, 2007)

Supported by CAPES Brazil and NIH grant HL54062.

Correspondence and requests for reprints should be addressed to Marcus Herbert Jones, M.D., Ph.D., Av. Ipiranga 6690, Instituto de Pesquisas Biomédicas-PUCRS, Porto Alegre, Brazil CEP 90610-000. E-mail: mhjones@pucrs.br

This article has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org

Am J Respir Crit Care Med Vol 176, pp 1269–1273, 2007

Originally Published in Press as DOI: 10.1164/rccm.200703-476OC on September 20, 2007
Internet address: www.atsjournals.org

mask. Thoracic compression with an inflatable jacket is initiated at this raised volume and maintained until residual volume is reached. Forced expiratory maneuvers are repeated with increased pressure until flow limitation is obtained. The flow-volume curves were quantified by the forced vital capacity (FVC), forced expiratory volume in 0.5 seconds (FEV_{0.5}), and several forced expiratory flows (FEF₅₀, FEF₇₅, and FEF₂₅₋₇₅). The best curve was selected as the one with the highest sum of FVC and FEF₂₅₋₇₅ (11).

Analysis

Summary statistics of age and body length at both time points and their changes were obtained for both groups, and the differences between the two groups were compared using two-sample *t* tests. Length and weight were transformed to *z* scores according to published equations (12, 13). A Pearson chi-square test was used to compare the two groups for sex distribution.

At each time point, analysis of covariance was used to examine whether the preterm group differed from the normal group in its spirometric measurements, adjusting for body length, sex, and exposure to smoking during pregnancy. The same method was also used to examine whether the two groups differed in the changes in spirometric measurements between the two evaluations.

Perinatal factors that may account for differences in lung function among the infants with history of prematurity were evaluated using multiple linear regression analysis. Perinatal factors included sex, tobacco smoking exposure during pregnancy, gestational age, birth weight (BW), intrauterine growth retardation (BW < 10th percentile), oxygen administration, corticosteroid administration to the mother, prolonged rupture of membranes (>24 h). The statistical analysis program SPSS 14.0 (SPSS, Inc., Chicago, IL) was used for the analysis.

RESULTS

Twenty-six premature infants had a mean (range) gestational age of 32.7 (30–34) weeks and mean (range) birth weight of 1.74 (0.96–2.68) kg. One or more doses of corticosteroids were administered to 18 mothers (69%) before delivery, 9 infants (35%) had intrauterine growth retardation, and 11 (42%) required oxygen for less than 48 hours. The demographics for the premature and full-term control groups are summarized in Table 1. There were no significant differences in sex, race, or exposure to tobacco smoking for the two groups (Table 1). At the time of the first assessment of lung function, the preterm group was significantly younger and smaller; however, they did

not differ in their *z* scores for age-adjusted length and weight. At the time of their second evaluation, there were no significant differences in age or somatic size for the premature and full-term control infants.

Comparison of Lung Function for Premature and Full-term infants

At the first evaluation, there was not a significant difference in FVC for the two groups (Table 2); however, the infants born prematurely had significantly lower forced expiratory flows (FEF₅₀, FEF₇₅, and FEF₂₅₋₇₅), as well as a lower ratio of FEV_{0.5}/FVC. At the second evaluation, there was still no significant difference in FVC, whereas the preterm group had persistently lower FEF₇₅ and FEF₂₅₋₇₅, as well as a lower ratio of FEV_{0.5}/FVC. The changes in spirometric values between the two evaluations for the premature and control infants are shown in Figure 1. There were no significant differences for the two groups in the changes in FVC, forced expiratory flows, or the ratio of FEV_{0.5}/FVC.

Effect of Perinatal Factors on Lung Growth in the Preterm Group

We evaluated whether any of the perinatal factors were associated with spirometric values in the group of infants born prematurely. After adjusting for body length, the use of oxygen during the neonatal period was associated with a significantly higher FVC at the first evaluation (20.9 ml, 12%), as well as at the second evaluation (122 ml, 26%). In addition, the use of oxygen was associated with a significantly greater increase in FVC, as well as FEF₅₀, FEF₂₅₋₇₅, and FEV_{0.5} between the two evaluations. The use of oxygen was not associated with sex, gestational age, birth weight, or other perinatal factors (Table 3).

DISCUSSION

Our longitudinal evaluation of healthy infants born prematurely between 30 and 34 weeks' gestation demonstrates that these subjects have decreased airway function not only in the first few months of life but also at the 1-year follow-up evaluation in the second year of life. The decreased forced expiratory flows occurred in presence of normal forced vital capacities. These findings suggest that healthy infants born prematurely may have smaller sized airways relative to their lung volume. An alternative explanation for lower forced expiratory flows would be more compliant airways, lower pulmonary elastic recoil, or increased bronchial tone. The increase in spirometric values with growth was the same for infants born prematurely and infants born at full term. Lung function tracked somatic growth in the infants born prematurely; there was no evidence for catch-up growth early in life. These findings suggest relatively healthy infants born prematurely have persistently lower airway function than infants born at full term. The reduced forced expiratory flows in healthy preterm infants may be a factor that contributes to their increased risk of recurrent respiratory illnesses early in life (14).

We found that infants born prematurely had normal forced vital capacities at both evaluations. These findings suggest that, early in life, lung size is increasing appropriately with somatic growth after premature birth. Absolute lung volumes were not measured in our infants, so we cannot be sure that the premature infants do not differ in residual volume and total lung capacity. However, long-term follow-up studies of older children who had premature birth without significant respiratory problems in the neonatal period also have normal values for FVC, as well as normal values for residual volume and total

TABLE 1. DEMOGRAPHIC DATA OF THE PRETERM AND CONTROL GROUPS AT THE FIRST AND SECOND LUNG FUNCTION TEST

	Preterm (n = 26)	Controls (n = 24)	P
Male sex, n (%)	17 (65)	12 (50)	0.390
White race, n (%)	23 (89)	19 (79)	0.456
Smoke exposure in pregnancy, n (%)	5 (19)	6 (25)	0.738
Family history of asthma, n (%)	17 (65)	10 (42)	0.155
First test			
Age, wk	10 (3–31)	23 (3–81)	<0.001
Weight, kg	5.8 ± 1.60	7.4 ± 1.93	0.002
Length, cm	58.3 ± 5.45	65.7 ± 7.5	<0.001
z Score, length/age	−0.7 ± 0.9	−0.5 ± 1.1	0.650
z Score, weight/age	0.2 ± 1.1	−0.1 ± 1.1	0.372
Second test			
Age, wk	64 (47–97)	64 (33–120)	0.429
Weight, kg	10.6 ± 1.6	10.2 ± 1.8	0.437
Length, cm	78.9 ± 4.1	78.0 ± 6.1	0.539
z Score, length/age	−0.4 ± 0.88	−0.6 ± 0.97	0.356
z Score, weight/age	−0.2 ± 1.26	−0.5 ± 0.96	0.348

Values are expressed as numbers (%) for categorical variables, and mean (SD) or median (range) for continuous variables.

TABLE 2. LUNG FUNCTION IN THE PRETERM AND CONTROL GROUPS AT THE FIRST AND SECOND LUNG FUNCTION TEST AND THE CHANGE IN LUNG FUNCTION VARIABLES BETWEEN THE TESTS*

	Adjusted Least Squares Means				Coefficients of the Variables in Model		
	Preterm	Control	95% CI	P	Length	Sex	Smoke
Test 1							
FVC	230 ± 10	234 ± 11	−29 to 37	0.814	13 ± 1 [†]	−4 ± 15	−31 ± 17
FEF ₅₀	404 ± 26	480 ± 27	−157 to 6	0.068	15 ± 3 [†]	46 ± 36	48 ± 41
FEF ₇₅	185 ± 16	242 ± 17	−109 to −6	0.030	10 ± 2 [†]	60 ± 23 [†]	26 ± 26
FEF _{25–75}	346 ± 24	435 ± 25	−165 to −13	0.022	14 ± 3 [†]	51 ± 33	32 ± 38
FEV _{0.5}	179 ± 8	191 ± 9	−39 to 15	0.371	9 ± 1 [†]	7 ± 12	−6 ± 13
FEV _{0.5} /FVC	0.78 ± 0.02	0.86 ± 0.02	−0.14 to −0.02	0.006	−0.01 ± 0.00 [†]	0.06 ± 0.03 [†]	0.06 ± 0.03 [†]
Test 2							
FVC	513 ± 14	494 ± 15	−22 to 60	0.364	17 ± 2 [†]	−31 ± 22	−24 ± 24
FEF ₅₀	731 ± 32	816 ± 34	−179 to 10	0.078	19 ± 5 [†]	50 ± 52	−107 ± 56
FEF ₇₅	360 ± 19	428 ± 20	−124 to −13	0.017	9 ± 3 [†]	35 ± 30	−31 ± 33
FEF _{25–75}	649 ± 29	746 ± 30	−182 to −12	0.027	17 ± 4 [†]	40 ± 46	−85 ± 51
FEV _{0.5}	364 ± 11	379 ± 11	−47 to 17	0.348	11 ± 2 [†]	1 ± 17	−31 ± 19
FEV _{0.5} /FVC	0.72 ± 0.01	0.78 ± 0.01	−0.10 to −0.03	0.001	0.00 ± 0.00 [†]	0.05 ± 0.02 [†]	−0.03 ± 0.02
Change in lung function							
FVC	273 ± 14	272 ± 14	−42 to 45	0.949	15 ± 1 [†]	−42 ± 18 [†]	11 ± 22
FEF ₅₀	302 ± 33	362 ± 35	−166 to 46	0.263	22 ± 4 [†]	−6 ± 45	−149 ± 53 [†]
FEF ₇₅	169 ± 20	193 ± 21	−87 to 39	0.450	12 ± 2 [†]	−20 ± 27	−57 ± 31
FEF _{25–75}	283 ± 30	333 ± 31	−144 to 44	0.289	20 ± 3 [†]	−16 ± 40	−113 ± 47 [†]
FEV _{0.5}	177 ± 11	197 ± 11	−54 to 14	0.238	11 ± 1 [†]	−13 ± 14	−23 ± 17
FEV _{0.5} /FVC	−0.08 ± 0.02	−0.07 ± 0.02	−0.07 to 0.05	0.783	0.00 ± 0.00 [†]	−0.02 ± 0.02	−0.09 ± 0.03 [†]

Definition of abbreviation: CI = confidence interval.

Results are presented as least squares means ± SE. Variables included in the model: Length (cm), sex (male = 0, female = 1), smoke exposure (no = 0, yes = 1).

* Analysis of covariance adjusted by length, sex, and smoke exposure during pregnancy.

[†] $P < 0.05$ in the model.

lung capacity (1, 2). Although lung volumes may not differ in subjects born prematurely, it is still not known whether alveolar development (number and size) is affected by premature birth.

Our group of premature infants had persistently lower forced expiratory flows at both evaluations, and there was no evidence for catch-up during this period of time. The lower size-adjusted flows were not secondary to relatively smaller somatic size. The preterm and full-term infants had similar z scores for weight and length at both tests; therefore, the reduced lung function was not a consequence of poor growth. In addition, the reduced flows were not secondary to a smaller lung volume, because FVC was not different for the two groups; however, the ratio of FEV_{0.5}/FVC was persistently lower in the infants born prematurely compared with those infants born full term. Our finding of lower forced expiratory flows in the second year of life is consistent with the observations by Hoo and colleagues (5). However, these investigators found that, at their initial evaluation in the neonatal period, the infants born prematurely had normal values for $\dot{V}_{max_{FRC}}$; therefore, their group of infants born prematurely exhibited a significant worsening of airway function when assessed longitudinally. This contrasts with our findings of persistently lower forced expiratory flows at both evaluations and no change in the rate of increase of lung function when compared with full-term infants. The difference in the findings of these two longitudinal studies may be secondary to Hoo and coworkers who initially assessed infants at a younger age than we did. In addition, those investigators assessed airway function using partial forced expiratory maneuvers, which reference flows to FRC, a variable lung volume during tidal breathing, particularly in neonates.

The mechanism for the persistently lower airway function in infants born prematurely has not been determined. We did not assess airway function using a bronchodilator; therefore, increased bronchial tone could potentially contribute to the lower forced expiratory flows in the infants born prematurely. In addition, lower forced expiratory flows in the infants born pre-

maturely could result from a decrease in pulmonary elastic recoil secondary to abnormal alveolarization of the lung parenchyma, as well as more compliant airways. Alternatively, the premature infants could have airways that are anatomically smaller relative to their lung volume and somatic size. Dysanaptic growth occurs between the airways and the lung parenchyma for full-term infants; lung volume increases faster than airway size (6, 9). Compensatory lung growth after pneumonectomy appears to accentuate this growth pattern. After pneumonectomy, the lung parenchyma exhibits catch-up of compensatory growth; however, the airways do not exhibit comparable increases in growth, and thus the airways are small relative to lung volume (15). Similarly, older children raised at high altitude have larger lung volumes and lower forced expiratory flows than subjects residing at sea level. The infants born prematurely are physically smaller and will have smaller lungs at birth than infants born at full term. Premature extrauterine life may accelerate growth of the lung parenchyma, but not the airways; this could result in a normal lung volume, but airways that are small relative to the size of the lung.

Another interesting observation was the association of oxygen use and lung development. In the preterm group, lung growth appears to be faster in those infants that required supplemental oxygen in the first hours of life. We were unable to find evidence to support the concept that a brief exposure to oxygen could trigger accelerated lung growth. Our observations support the hypothesis of accelerated lung maturation being associated with worse respiratory prognosis (16–18). Among prematurely born infants, supplemental oxygen may be a marker of a less mature lung, which may have a better long-term respiratory prognosis than infants with accelerated maturation due to prenatal events such as infection and inflammation but no oxygen requirement.

Although there were no differences between the infants born prematurely and the full-term infants for the percentage of males or exposure to tobacco smoking during pregnancy, we adjusted for these two factors in our analysis, because these variables have

Figure 1. Plots of FVC, FEF₅₀, FEF₇₅, FEF₂₅₋₇₅, FEV_{0.5}, and FEV_{0.5}/FVC adjusted for length, sex, and smoke exposure at tests 1 and 2 for the control group (solid lines, open circles) and preterm group (dotted lines, solid circles) expressed as least squares mean $\pm$ SE. * $P < 0.05$ between groups at that test (analysis of covariance). No difference detected in the rate of change of all tested variables between the groups.

previously be found by us, as well as other investigators, to be important determinants of lung function of infants (4, 9, 19). Among our infants, exposure to tobacco smoking was associated with lower values for several parameters of forced expiratory flows, which agrees with previous studies for both premature and full-term infants (2, 9, 19). We also found that the effect of smoking exposure was present in the rate of change of airway function between the two evaluations (FEF₅₀ and FEV_{0.5}/FVC), which suggests a long-lasting effect of smoke exposure on lung growth. Presence of smoke exposure during pregnancy relied on information provided by the mothers and may underestimate the actual exposure. We also found among our subjects that male sex was associated with lower forced expiratory, which is consistent with previous reports in premature and full-term infants (9, 20, 21).

Several cross-sectional studies of school-aged children have reported that, in the absence of chronic lung disease of infancy, premature infants have normal spirometric values (1, 2, 22, 23). Our finding of persistently lower forced expiratory flows in the second year of life in infants born prematurely suggests that

these infants do not normalize their airway function early in life, during the most rapid period of lung growth. A late recovery of airway function, if it occurs, may explain the increased respiratory symptoms reported for infants born prematurely (14, 22, 24).

One potential limitation of this study is that the subjects were recruited and tested in different centers. However, we believe this had no impact in the observed differences between groups because the testing equipment, software, and technician were the same at both study sites. Furthermore, healthy control subjects previously recruited and tested in both centers have shown similar results (4), validating the comparisons performed in this study (see Figures E1–E4 and Table E1 of the online supplement).

In summary, our study addressed the effects of prematurity on lung function using a very specific population—that is, those who did not require sustained respiratory support in the first days of life. This population of relatively healthy premature infants, although not very premature, enabled us to separate the effect of preterm birth from the significant additional effects of

TABLE 3. DEMOGRAPHICS AND CHANGES IN LUNG FUNCTION FOR PRETERM INFANTS GROUPED BY USE OF OXYGEN

	No Oxygen (n = 15)	Oxygen (n = 11)	Difference (95% CI)	P
Gestational age, wk	32.6 ± 0.88	33.0 ± 1.18	0.4 (−0.44 to 1.22)	0.339
Birth weight, kg	1.7 ± 0.35	1.8 ± 0.43	0.1 (−0.22 to 0.40)	0.553
Apgar score, 5 min after birth	8.8 ± 0.5	8.7 ± 0.6	−0.1 (−0.61 to 0.33)	0.547
Change in age, wk	48.2	57.3	9.1 (−0.60 to 18.86)	0.065
Change in length, cm	19.8	21.7	1.9 (−2.54 to 6.39)	0.382
Change in weight, kg	4.9	4.6	−0.3 (−1.47 to 0.83)	0.569
Male, n (%)	8 (53)	9 (82)		0.217
White, n (%)	14 (93)	9 (82)		0.556
Intrauterine growth retardation, n (%)	5 (33)	4 (36)		1.000
Smoking exposure in pregnancy, n (%)	4 (27)	1 (9)		0.356
PROM, n (%)	9 (60)	9 (82)		0.395
Prenatal steroid, n (%)	11 (73)	7 (64)		0.683
Wheezing episodes, n (%)	7 (47)	8 (73)		0.246
Family history of asthma, n (%)	9 (60)	8 (73)		0.683
Lung function growth				
FVC, ml	293 ± 8	391 ± 10	98 (71 to 124)	<0.001
FEF ₅₀ , ml/s	334 ± 38	473 ± 44	139 (18 to 259)	0.026
FEF ₇₅ , ml/s	198 ± 27	246 ± 31	48 (−38 to 133)	0.258
FEF _{25–75} , ml/s	311 ± 32	438 ± 38	126 (22 to 230)	0.019
FEV _{0.5} , ml	197 ± 8	256 ± 9	59 (34 to 84)	<0.001
FEV _{0.5} /FVC, s ^{−1}	−0.11 ± 0.03	−0.05 ± 0.03	0.06 (−0.02 to 0.14)	0.146

Definition of abbreviations: CI = confidence interval; PROM = premature rupture of membranes.

Values are expressed as number (%) for categorical variables and mean ± SD for continuous variables. Lung function growth adjusted by change in length between first and second test and expressed as least squares mean ± SE.

lung injury secondary to mechanical ventilation or prolonged exposure to high concentrations of oxygen. Our findings suggest that the increase in lung function during the first year of life was proportional to somatic growth and similar for premature and full-term infants. In addition, throughout the first year of life, premature infants have persistently reduced airway function in the presence of normal lung volumes. The persistence of reduced expiratory flows in “healthy preterm infants” may contribute to their increased risk of recurrent respiratory illnesses early in life. Future studies are required to determine the mechanisms for the persistently reduced flows in healthy infants born prematurely, as well as to evaluate the effects of even greater prematurity on lung growth.

Conflict of Interest Statement: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

References

- Gross SJ, Iannuzzi DM, Kveselis DA, Anbar RD. Effect of preterm birth on pulmonary function at school age: a prospective controlled study. *J Pediatr* 1998;133:188–192.
- Chan KN, Noble-Jamieson CM, Elliman A, Bryan EM, Silverman M. Lung function in children of low birth weight. *Arch Dis Child* 1989;64:1284–1293.
- Koumbourlis AC, Motoyama EK, Mutich RL, Mallory GB, Walczak SA, Fertil K. Longitudinal follow-up of lung function from childhood to adolescence in prematurely born patients with neonatal chronic lung disease. *Pediatr Pulmonol* 1996;21:28–34.
- Friedrich L, Stein RT, Pitrez PM, Corso AL, Jones MH. Reduced lung function in healthy preterm infants in the first months of life. *Am J Respir Crit Care Med* 2006;173:442–447.
- Hoo AF, Dezateux C, Henschen M, Costeloe K, Stocks J. Development of airway function in infancy after preterm delivery. *J Pediatr* 2002; 141:652–658.
- Tepper RS, Jones M, Davis S, Kisling J, Castile R. Rate constant for forced expiration decreases with lung growth during infancy. *Am J Respir Crit Care Med* 1999;160:835–838.
- Jones M, Tepper R, Friedrich L, Pitrez PM, Stein RT. Growth rate of lung function in preterm infants [abstract]. *Proc Am Thorac Soc* 2005;2:A606.
- Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard score, expanded to include extremely premature infants. *J Pediatr* 1991;119:417–423.
- Jones M, Castile R, Davis S, Kisling J, Filbrun D, Flucke R, Goldstein A, Emsley C, Ambrosius W, Tepper RS. Forced expiratory flows and volumes in infants: normative data and lung growth. *Am J Respir Crit Care Med* 2000;161:353–359.
- Feher A, Castile R, Kisling J, Angelicchio C, Filbrun D, Flucke R, Tepper R. Flow limitation in normal infants: a new method for forced expiratory maneuvers from raised lung volumes. *J Appl Physiol* 1996;80:2019–2025.
- American Thoracic Society; European Respiratory Society. ATS/ERS statement: raised volume forced expirations in infants: guidelines for current practice. *Am J Respir Crit Care Med* 2005;172:1463–1471.
- World Health Organization. WHO anthro 2005: software for assessing growth and development of the world's children. Geneva, Switzerland: World Health Organization; 2005.
- World Health Organization. WHO child growth standards based on length/height, weight and age. *Acta Paediatr Suppl* 2006;450:76–85.
- Rona RJ, Gulliford MC, Chinn S. Effects of prematurity and intrauterine growth on respiratory health and lung function in childhood. *BMJ* 1993;306:817–820.
- Dane DM, Johnson RL Jr, Hsia CC. Dysanaptic growth of conducting airways after pneumonectomy assessed by CT scan. *J Appl Physiol* 2002;93:1235–1242.
- Jobe AH. An unknown: lung growth and development after very preterm birth. *Am J Respir Crit Care Med* 2002;166:1529–1530.
- Jobe AH. Antenatal associations with lung maturation and infection. *J Perinatol* 2005;25:S31–S35.
- Kallapur SG, Jobe AH. Contribution of inflammation to lung injury and development. *Arch Dis Child Fetal Neonatal Ed* 2006;91:F132–F135.
- Hoo AF, Henschen M, Dezateux C, Costeloe K, Stocks J. Respiratory function among preterm infants whose mothers smoked during pregnancy. *Am J Respir Crit Care Med* 1998;158:700–705.
- Hoo AF, Dezateux C, Hanrahan JP, Cole TJ, Tepper RS, Stocks J. Sex-specific prediction equations for Vmax(FRC) in infancy: a multicenter collaborative study. *Am J Respir Crit Care Med* 2002;165:1084–1092.
- Lum S, Hoo AF, Dezateux C, Goetz I, Wade A, DeRooy L, Costeloe K, Stocks J. The association between birthweight, sex, and airway function in infants of nonsmoking mothers. *Am J Respir Crit Care Med* 2001;164:2078–2084.
- Bertrand JM, Riley SP, Popkin J, Coates AL. The long-term pulmonary sequelae of prematurity: the role of familial airway hyperreactivity and the respiratory distress syndrome. *N Engl J Med* 1985;312:742–745.
- Parat S, Moriette G, Delaperche MF, Escourrou P, Denjean A, Gaultier C. Long-term pulmonary functional outcome of bronchopulmonary dysplasia and premature birth. *Pediatr Pulmonol* 1995;20:289–296.
- von Mutius E, Nicolai T, Martinez FD. Prematurity as a risk factor for asthma in preadolescent children. *J Pediatr* 1993;123:223–229.