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Ventilatory response to hypercarbia in newborns of smoking and substance abusing mothers

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Infants of smoking and substance abusing mothers have an increased risk of sudden infant death. A possible explanation for the association is that such infants have neurodevelopmental abnormalities which adversely affect the control of ventilation.

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Aims: To test the hypothesis that infants of substance abusing mothers (SA) and of smoking mothers (SM) compared to infants of non substance abusing, non-smoking mothers (controls) would have a poorer ventilatory response to hypercarbia.
Methods: Infants were assessed before maternity/neonatal unit discharge. Respiratory flow (and tidal volume) was measured using a pneumotachograph inserted into a face mask placed over the infant's mouth and nose. The ventilatory responses to three levels of inspired carbon dioxide (baseline = 0%, 2% and 4% CO_2) were assessed.
Results: 8 SA, 15 SM and 15 control infants were assessed. The birth weight of the controls was higher than the SA and SM infants (p=0.01). At baseline SA infants had a higher respiratory rate (p=0.03) and minute volume (p=0.049) compared to controls and SM infants (Table). Both the SA and SM infants had a lower respiratory response to 2% (p=0.02) and 4% (p=0.004) CO_2

	Control	SM	SA	p
Baseline minute volume (ml/kg/min)	295 (150–390)	301 (228–398)	373 (145–526)	0.049
% change in minute volume at 2% CO_2	38 (7–87)	20 (–5–53)	27 (6–48)	0.02
% change in minute volume at 4% CO_2	96 (32–153)	61 (4–103)	61 (14–134)	0.004

Conclusion: These results are consistent with infants of smoking and substance abusing mothers having a dampened ventilatory response to hypercarbia.

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The acute effect of surgical repair of mitral valve insufficiency on airway and respiratory tissue mechanics and pulmonary hemodynamics in children

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Rationale: Increased pulmonary blood flow and pressure were shown to be responsible for the lung function impairment in children with congenital heart diseases (Anesthesiology, 110: 1348-55, 2009). We assessed whether mitral valve insufficiency (MVI) leading to postcapillary pulmonary hypertension is reflected in the mechanical properties of the respiratory system, and whether surgical repair of MVI improves respiratory mechanics in children.
Methods: Airway resistance (Raw), respiratory tissue damping (G) and elastance (H) were obtained by forced oscillations in 8 children aged 12±2 (Mean±SD) years under general anaesthesia before and immediately after surgical repair of the MVI. Concomitantly, pulmonary arterial pressure (PAP) was directly measured in the pulmonary artery before aortic cannulation and chest closure.
Results: Surgical repair of MVI led to strong tendency in the mean PAP for a decrease (from 33.0±12 to 27.7±9.0 mmHg, p=0.054). These postoperative pulmonary haemodynamical changes were associated with significant decreases in Raw (5.5±1.7 to 4.4±1.1 cmH2O.s/l, p=0.008) with no significant effects on G (11.5±5.2, 10.1±3.1 cmH2O/l, p=0.7) and H (60.2±9.5, 65.2±13.7 cmH2O/l, p=0.2). Postoperative changes in Raw and PAP exhibited no significant correlation.
Conclusions: These findings demonstrate an immediate improvement of airway function after surgical repair of MVI in children. Further experiments are needed to clarify the role of the direct effect of the postoperative decrease in postcapillary pulmonary hypertension and vascular engorgement in this beneficial change.
Supported by SNSF grant 3200B0-118231.

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Reversibility of airway obstruction to diagnose asthma in children using forced oscillations: Inspiration, expiration does it matter?

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Estimating reversibility of bronchial obstruction is part of the routine management of asthma. It is still not clear what forced oscillation technique (FOT) parameter response to salbutamol best differentiates asthmatics from controls.
The aim of the study was to compare the ability to detect a different response to salbutamol between asthmatic and healthy children for the following parameters: respiratory resistance (Rrs), reactance (Xrs), impedance (Zrs) and admittance (Ars, the reciprocal of Zrs).
Methods: 79 asthmatics and 20 controls aged 4–11 y were included. FOT mesurements were obtained using a single sinusoidal pressure oscillation at 8 Hz. The parameters were computed separately in inspiration (I) and expiration (E). Reversibility was expressed as percentage from the corresponding baseline, except for Xrs – frequently close to zero – expressed as percentage of the baseline Zrs. The ability for each parameter to separate asthmatics from controls was tested at different decision levels by computing the Youden index (Y), a combination of sensitivity and specificity, that ranges from -1 for a useless test to +1 for maximal diagnostic value.
Results: The response to salbutamol showed larger Y in I than E for Rrs (0.31 vs 0.25) and Ars (0.38 vs 0.35). In contrast, Y was equivalent in I and E for Zrs (0.3) and Xrs (0.11). The maximal Y value of 0.38 for Ars in I corresponded to 25% increase after salbutamol.
Conclusion: The diagnostic value of the FOT depends on breathing. Inspiration usually provides better discrimination. The information may be important to improve the diagnostic of asthma based on bronchial reversibility.

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Regional pulmonary function testing by electrical impedance tomography in healthy children and children with asthma

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Introduction: Electrical impedance tomography (EIT) is able to assess regional dynamic lung volume changes and to determine spatial distribution of lung function in the chest cross-section. The aim of our study was to examine the regional lung function in healthy children and children with asthma before and after exercise.
Patients and methods: 10 healthy children (11±3 yr, mean age±SD) and 10 children with asthma (12±3 yr) were examined by EIT during conventional pulmonary function testing at baseline and after stairs running for 5 min. EIT data were acquired at 33 scans/s (Goe-MF II CareFusion, Höchberg, Germany). Regional forced vital capacity (FVC), forced expired volume in 0.5 s ($FEV_{0.5}$) and tidal volume (V_T) were determined in 912 EIT image pixels before and 3 min after exercise. Spatial heterogeneity of ventilation was characterized by the coefficient of variation (CV) calculated from all pixel values of FVC, $FEV_{0.5}$ and V_T. Statistical analysis was carried out by paired and unpaired t-test for comparisons within and between the groups.
Results: Significant exercise-dependent differences in CV_{FVC} were found in both groups whereas $CV_{FEV_{0.5}}$ and CV_{V_T} were not affected by exercise. CV_{FVC} was significantly different between the healthy children and children with asthma after but not before exercise. $CV_{FEV_{0.5}}$ and CV_{V_T} were not significantly different between the groups both at baseline and after exercise.
Conclusion: EIT detected regional lung function differences between healthy children and children with asthma during forced full expiration. Future analysis should aim at characterization of peripheral airways by novel EIT-derived measures of regional lung function.

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Ventilation inhomogeneity in children with cystic fibrosis and primary ciliary dyskinesia

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Rationale: Ventilation inhomogeneity (VI) measured by multiple breath inert gas washout (MBW) are common findings in cystic fibrosis (CF) children with normal spirometry (1). Recently this was shown also in primary ciliary dyskinesia (PCD) (2). The lower morbidity in PCD vs. CF would suggest that small airway involvement is less severe in PCD. We therefore compared MBW indices reflecting peripheral airway involvement in children with CF and PCD.
Methods: A cross sectional study was performed in 24 children with PCD and 25 with CF, matched by age and FEV1. N2 MBW in triplets (Exhalyzer D, EcoMedics AG) and spirometry were performed within one occasion in clinically stable patients. Lung Clearance Index (LCI), an index of global VI, and specific indices of VI arising in the conductive (Scond) and the acinar (Sacin) airway zones (2) were calculated and presented as z-scores based on new normative data (Houltz B et al, ERS abstract 2012). They were compared between patient groups using Mann-Whitney Test.
Results: There was no significant difference in LCI, Scond and Sacin (z-scores) between the two patient groups, although LCI, z-scores tended to be higher in PCD (Table 1).

Table 1. Demography and Results

	CF	PCD	P value
N (males)	25 (12)	24 (7)	–
Age, yrs	12.3 (2.1)	13.0 (3.1)	0.48
BMI	17.1 (2.0)	18.1 (2.8)	0.25
FEV1, % pred.	99.3 (10.5)	95.4 (12.5)	0.57
LCI, z-scores	8.1 (6.5)	11.6 (6.6)	0.07
Scond*VT, z-scores	10.6 (6.1)	11.0 (6.0)	0.83
Sacin*VT, z-scores	6.0 (5.6)	8.5 (6.4)	0.18

Results expressed as mean (SD), unless otherwise stated.

Conclusion: In contrast to our expectations severity of peripheral airway involvement is similar in children with CF and PCD.
Reference:
[1] Respiration 2009;78:339; (2) Thorax 2012;67:49.

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Ways to shorten the lung clearance index measurement II – How long to wash?

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Background: Inert gas multiple-breath washout (MBW) derived lung clearance index (LCI) is a sensitive lung function parameter in subjects with mild cystic fibrosis (CF) lung disease, but rarely measured in clinical routine due to lack of available equipment and lengthy protocols. Using an available nitrogen (N_2) MBW setup (Exhalyzer D, Eco Medics, Switzerland), we assessed shortened N_2MBW protocols for LCI.
Methods: Thirty-three school-aged children with CF and 21 controls performed triplicate N_2MBW measurements. LCI was calculated as cumulative expired volume over functional residual capacity determined during N_2MBW at 9% (1/11th) and 2.5% (1/40th, the current standard) end-tidal N_2 concentration.
Results: LCI differed significantly between healthy and CF children at both concentrations. The 9%-LCI was modestly associated with final 2.5%-LCI (R^2 = 0.7) but took less time and was of similar diagnostic value. Comparing 9%- and 2.5%-LCI, mean (SD) test duration was 1.0 (0.4) and 2.2 (1.0) min; mean (95%CI) area under the receiver operating characteristic curve was 0.9 (0.8-0.9) and 0.9 (0.8-0.9); and upper limits of normal LCI (4.5 and 8.4) correctly classified 72% and 74% of children, respectively. Mean (SD) coefficient of variation was 5.7 (3.9)% for 9%-LCI and 5.7 (3.2)% for 2.5%-LCI.
Conclusion: LCI determined at 9% end-tidal N_2 concentration during N_2MBW is repeatable, considerably faster, and identifies early CF lung disease with similar diagnostic value compared to the standard LCI in the current study population. This new shortened N_2MBW protocol seems promising for time-saving LCI measurement in clinical routine.

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Association of sitting/standing height ratio and FEV_1 in multi-ethnic school children: The Size and Lung Function in Children (SLIC) study

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Appropriate paediatric lung function reference equations for ethnic minorities are lacking. We investigated the extent to which differences in body proportions as indicated by the sitting/standing height ratio(Sit/Stand Ht) explain ethnic differences in FEV_1.
Methods: As part of the SLIC study (commenced 2011), standard anthropometry including sitting height and spirometry were assessed in multi-ethnic London school children. FEV_1 was expressed in Z scores to adjust for sex, age and height (Stanojevic2009). Statistical analysis was by univariable and multivariable regression.
Results: 379 healthy children (age: 5-10y, 43% boys; 31% White, 44% Black; 13% Asian, 12% mixed/other) performed successful spirometry. Compared with Whites, FEV_1 was significantly lower in Black, Asian & "Other" children. On univariable analysis ethnicity accounted for 28% and Sit/Stand Ht for 25% $zFEV_1$ variation. In a multivariable model the combined contribution was 35% with ethnicity contribution falling to 10%(Table).

Table: Linear regression showing ethnic differences in FEV_1 before & after adjustment for sit/stand height

	$zFEV_1$	
	Before adjustment	After adjustment
Adjusted R^2	0.283	0.352
Black	–1.2 (–1.4; –1.0)	–0.8 (–1.0; –0.6)
Asian	–0.9 (–1.2; –0.6)	–0.6 (–0.9; –0.3)
Other	–0.5 (–0.7; –0.2)	–0.3 (–0.6; –0.1)

Conclusion: This study shows that Sit/Stand Ht accounts for some of the differences amongst ethnicities in FEV_1 and provides further evidence that sitting height should be an essential part of standard anthropometry. Further work to explore the extent to which differences in body shape, size and composition contribute to ethnic differences in lung function is in progress.

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