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Background: Wheeze is a common symptom in preschool children. The role of bacteria in preschool wheeze and their possible association with airway inflammation is largely unknown.

Aims:

- To study whether preschool children with recurrent wheeze differ in bacterial infection/colonisation in the upper respiratory tract compared with healthy controls.
- To study whether recurrent wheezers with bacterial infection/colonisation differ in pro-inflammatory markers in exhaled breath condensate (EBC) compared with infected/colonised children without recurrent wheeze.

Methods: We recruited 252 children (aged 2-4 years) with (n=202) and without (n=50) recurrent wheeze. Nasal and throat swabs were analysed for the presence of *Streptococcus (S.) pneumoniae* and *Haemophilus (H.) influenzae*. Serology for *Chlamydia (C.)* and *Mycoplasma (M.) pneumoniae* was assessed. EBC was collected using a closed-glass condenser. Inflammatory markers (Interleukin (IL)-4, IL-8, IL-13) in EBC were measured using multiplex immunoassay.

Results: Only positive serology for *M. pneumoniae* was slightly higher in children with recurrent wheeze compared with healthy controls (11% vs. 2%, p=0.09). Wheezing children colonised with *H. influenzae* (N=61) had higher levels of all interleukins compared with colonised children without recurrent wheeze (N=15) (p<0.05).

Conclusion: We found no convincing evidence for an association between bacterial colonisation/infection and preschool recurrent wheeze. Airway colonisation with *H. influenzae* leads to elevated pro-inflammatory markers in recurrent wheezers, indicating augmented airway inflammation in these children.

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Small airway function in prematurely born infants following viral infection

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Aim: Respiratory syncytial virus (RSV) lower respiratory tract infections (LRTIs) in prematurely born infants have been associated with abnormalities of lung function at follow up, there is some preliminary evidence to suggest other viral infections may have a similar adverse effect. The aim of this study was to determine whether lung clearance index (LCI), an assessment of small airway function, differed between infants who had had an RSV LRTI, another viral LRTI or no LRTI.

Methods: 78 infants born at less than 36 weeks of gestational age were prospectively followed. A nasopharyngeal aspirate (NPA) was obtained every time the infants had a LRTI regardless of whether this was in hospital or in the community. NPAs were tested for RSV A and B, Rhinovirus, human Metapneumovirus, Parainfluenza 1-3, Influenza A and B and Adenovirus. LCI was measured by the multiple breath wash-out technique at one year corrected age. Recruitment of at least 12 infants into each group allowed us to detect a difference in the LCI results of 0.7 between the groups (80% power, 5% level).

Results: Seventy two infants had acceptable measurements: 13 infants developed RSV LRTIs (RSV group), 17 infants other viral LRTIs (other viral group) and 34 infants no LRTI (no LRTI group). There were no significant differences in the LCI results of the three groups (RSV group mean [SD] 7.24 [0.44]; other viral group 7.0 [0.64]; no LRTI group 7.25 [0.63] (p=0.69).

Conclusion: These results suggest viral infections are not associated with increased small airway abnormalities at follow up during infancy of prematurely born infants.

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IL-8₇₇ isoform in lungs of preterm infants and its processing by neutrophil serine proteases

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Introduction: Persistent neutrophilic (PMN) lung inflammation is strongly implicated in the development of Chronic Lung Disease (CLD) of Prematurity. The 72 amino acid (a.a.) chemokine, IL-8₇₂, is a key molecule involved in attracting PMNs to sites of inflammation. The longer 77 a.a. isoform (IL-8₇₇) is less potent than IL-8₇₂ *in vitro*. We studied expression of IL-8₇₇ in the preterm ventilated lung and its processing by neutrophil serine proteases.

Methods: IL-8₇₇ was measured by ELISA in bronchoalveolar lavage fluid (BALF) from ventilated preterm infants born at ≤32 weeks gestational age and after conversion by purified PMN serine proteases. Results were compared between the CLD (persistent inflammation) and non-CLD groups (resolved).

76. Innate and exogenous factors in childhood respiratory infection

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Bacterial colonisation/infection and airway inflammation in preschool children with recurrent wheeze

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Results: The majority of IL-8 consisted of the shorter isoforms in the preterm lung (96.3% non-CLD vs 97.1% CLD, p=ns). IL-8₇₇ expression correlated well with total IL-8 (p<0.0001) but not with gestation (p=ns). Stimulated adult airway-cells and neonatal PMNs and monocytes expressed IL-8₇₇ as the major isoform, suggesting possible expression in the lung. Preterm BALF significantly converted rIL-8₇₇ to shorter isoforms at 18 hours (p<0.05), which was inhibited by α-1 antitrypsin (AAT). Purified neutrophil serine proteases converted IL-8₇₇ to shorter isoforms dose-dependently and over time.

Conclusions: Majority of IL-8 in the ventilated preterm lung are the potent shorter isoforms. Although potentially expressed in the lung, IL-8₇₇ is probably converted to the shorter isoforms by neutrophil serine proteases. Inhibition of conversion by AAT suggests a potential therapeutic role for it in modulating inflammation in the preterm lung.

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Expression and functional activity of IL-6, sIL-6R & sgp130 in the preterm infant lung

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Introduction: Persistent neutrophil-dominated lung inflammation is strongly implicated in the development of Chronic Lung Disease of Prematurity (CLD). The complex of interleukin-6 (IL-6) and its soluble receptor, sIL-6R, can activate *trans*-signalling in cells lacking the cell-surface receptor IL-6R; a soluble form of the signal-transducer gp130 can inhibit *trans*-signalling by specifically binding to the sIL-6R/IL-6 complex. As anti-inflammatory effects of IL-6 *trans*-signalling can shape resolution of inflammatory responses, we studied the expression, interrelationships and functional activity of IL-6, sIL-6R and sgp130 in the preterm lung.

Methods: Cytokines were measured by ELISA in bronchoalveolar lavage fluid (BALF) from ventilated preterm infants born at ≤32 weeks gestational age. Functional activity was determined in a sensitive, IL-6 specific bioassay using mouse B9 cells. Results were compared between the CLD group (persistent inflammation) and non-CLD group (resolved).

Results: Inflammatory cells and chemokines, CXCL8 and CCL2, were higher in the CLD group (p<0.05). IL-6 and sIL-6R were comparable between the two groups; however, peak sgp130 was higher in the CLD group (CLD 65.3 ng/ml vs non CLD 20.8 ng/ml p=0.01), as was the anti *trans*-signalling ratio of sgp130/sIL-6R (p=0.02). Functional activity of IL-6 in the bioassay was similar between the two groups. *Trans*-signalling activity was not noted in any of the samples in the bioassay.

Conclusions: Increased sgp130 in the lungs of preterm infants may be responsible for impaired *trans*-signalling by the sIL-6R/IL-6 complex. Better understanding of this pathway may lead to therapies to resolve lung inflammation in preterm infants.

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Cytokine response in pediatric patients with pandemic H1N1 influenza virus infection and pneumonia: Comparison with pediatric pneumonia without H1N1 infection

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Objectives: We investigated serum cytokine levels in pediatric patients with pandemic H1N1 virus infection-pneumonia and in pediatric patients with pneumonia but without H1N1 infection, and examined correlations between cytokine levels and clinical/laboratory findings.

Methods: Fifty-seven cases of infection by H1N1 virus were confirmed by RT-PCR and enrolled. Of these 57 cases, 26 had a severe H1N1 infection (group 1), and 31 had a mild H1N1 infection (group 2). Sera from 18 cases with pneumonia without H1N1 infection (group 3) were used as controls. The serum levels of 10 cytokines were determined by multiplex assay.

Results: The serum levels of IFN-α, IL-6, and IP-10 were significantly higher in H1N1 infected cases than in group 3, and levels of IL-6 and IP-10 were significantly higher in group 1 than in group 2. The level of IL-10 was significantly higher in groups 1 and 3 than in group 2. However, levels of IFN-α, TNF-α, and IL-17 were not significantly different between the three groups. IL-1β, IL-4, and MIP-1α were not detectable in most patients. IP-10 and IL-6 levels were found to show negative correlations with lymphocyte count and oxygen saturation.

Conclusions: We found higher levels of cytokines (IFN-α, IL-6, IP-10) of innate immunity than those of acquired immunity in pediatric H1N1 infection. Of the cytokines found to be increased in cases with a H1N1 infection, IP-10 and IL-6 were found to be correlated with disease severity (lymphopenia and hypoxia). IP-10 and IL-6 may be important markers in pediatric H1N1 infection.

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Respiratory symptoms correlate with pulmonary inflammation at a time of presumed stability in children with non-ambulant neurodisability

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Background: Children with non-ambulant neurodisability (ND) often have chronic respiratory symptoms which impact on quality of life and can result in multiple hospital admissions. Respiratory complications are a leading cause of death in this group.

Aims: Assess respiratory symptoms and broncho-alveolar lavage (BAL) inflammatory markers at a time of presumed stability.

Methods: Children with ND and healthy controls were recruited during elective surgical admission. A respiratory symptom score (LRSQ) was completed. BAL was taken at anaesthetic induction. Neutrophil count was recorded (% total cells). IL8 and TGFβ-1 were measured by ELISA. Data are expressed as median [IQR].

Results: 16 children with ND had higher LRSQ scores than 10 controls (21 [5-46] vs. 5 [0-7], p< 0.02). Children with ND had greater BAL neutrophilia (52% [31-71] vs. 4% [3-12], p<0.01) and higher IL8 (516 [0-2465] vs. 0 [0-232] pg/ml, p<0.05). Median TGFβ-1 did not differ (0 vs.0) but the range was markedly different (0-271 vs. 0-73 pg/ml). LRSQ score correlated with BAL neutrophilia (r +0.54, p<0.01), IL8 (r +0.409, p<0.01 and TGFβ-1 (r +0.43, p<0.01). No ND patients had seen a respiratory specialist, 8/16 had undergone video-fluoroscopy (7/8 +ve) and 2/16 took antibiotic prophylaxis.

Conclusions: Children with ND have a high burden of respiratory symptoms which correlate with chronic airway neutrophilia and raised inflammatory cytokines at times of presumed stability. A screening tool to identify those children who would benefit from a specialist respiratory review would be useful. Further research into the potential benefits of prophylactic therapy in this group is needed.

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Subclinical vitamin D deficiency and acute respiratory tract infections in children: A systematic review

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Rickets has historically been considered as a risk factor for development of pneumonia, primarily due to mechanical factors such as rib cage abnormalities and hypotonia. However, the association between vitamin D levels and acute respiratory tract infections (RTI) in children without rickets has not been thoroughly explored so far.

- Association of low Vitamin D levels with RTI in children without clinical rickets
- Role of Vitamin D supplementation in prevention and treatment of RTI.

Methods: Structured systematic literature search

Results: Seven papers on association of low Vitamin D levels and RTI were obtained. See Table 1.

Citation	Study population	Study type	Outcome (specific to the question)	Key results
Banajeh SM; 2009 (Yemen)	152 children, aged 2-59 months with very severe pneumonia	Prospective cohort study	Association of rickets with treatment outcome, association of vitamin D deficiency (VDD) with neutrophil counts and O2 saturation	Treatment failure higher in rachitic group (OR 1.38; 95%CI 1.13-1.69; p=0.031); VDD strongly associated with reduced neutrophils (OR 0.71; 95%CI 0.53-0.95; p=0.02) and ↓SpO2 (OR 0.96; 95%CI 0.93-0.99; p=0.021)
Ginde et al; 2009 (North America)	12 years & older population, including adults, 22266 participants	Secondary analysis of a national cross sectional sample	Association between serum 25(OH)D levels and recent upper RTI	Lower 25(OH)D levels independently associated with URTI (p<0.001)
Karatekin et al; 2009 (Turkey)	25 newborns with RTI and their mothers, control group-15 healthy newborns. None had clinical signs of rickets	Case control study	25(OH)D levels	25(OH)D levels lower in study group compared to control group (p=0.011)
McNally et al; 2009 (Canada)	Children with bronchiolitis (n=55) or pneumonia (n=50), control group with no respiratory symptoms (n=92)	Case control study	Association between serum 25(OH)D levels and RTI	No significant difference in 25(OH)D levels between the groups (p=0.71); however vitamin D deficiency statistically related to intensive care admission.
Roth et al; 2009 (Bangladesh)	Children aged 1-18 months hospitalised with RTI, matched with controls (n=25 in both)	Case control study	25(OH)D levels	Mean levels significantly lower in cases than controls (p=0.015)
Roth et al; 2009 (Canada)	Children aged 1-25 months with viral bronchiolitis (n=64), matched controls (n=65)	Case control study	Serum 25(OH)D levels	No significant difference (p=0.960)
Wayse et al; 2004 (India)	80 cases with severe RTI and 70 healthy controls (age 2-60 months)	Case control study	25(OH)D3 levels	Significant difference (p=0.001)

Two papers, both double blinded randomised controlled trials (RCT), were identified on Vitamin D supplementation in RTI. See Table 2.

Conclusions: Our literature review has revealed that subclinical vitamin D levels are strongly associated with risk of acquiring RTI as well as increased RTI-

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Citation	Study population	Study type	Outcome	Key results
Manaseki-Holland et al; 2010 (Afghanistan)	453 children aged 1-36 months with pneumonia (224 received vitamin D3, 229 received placebo)	Double blind RCT	Reduction of duration of illness and risk of repeat episodes following single oral vitamin D3 supplementation (100,000 IU) along with antibiotics	No difference in duration of illness (p=0.17); risk of repeat pneumonia within 90 days lower in intervention group (RR 0.78; 95%CI 0.64, 0.94; p=0.01)
Urashima et al; 2010 (Japan)	430 Healthy children 6-15 years randomised to receive oral vitamin D3 1200 IU/day (n=217) and placebo (n=213)	Double blind RCT	Incidence of influenza A diagnosed by antigen testing with nasopharyngeal swab	Significantly less influenza A in the intervention group (RR 0.58; 95%CI 0.34, 0.99; p=0.006)

related morbidity. There is some evidence from interventional studies regarding the potential role of vitamin D in prevention and treatment of RTI.

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Risk factors for wheezing and allergy in preschool children (PSC) after admission for acute bronchiolitis

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Introduction: Acute bronchiolitis (AB) is associated to later development of wheezing (W) and allergic sensitisation, but risk factors remain controversial. This study aimed to test the hypothesis that clinical background and features of the acute episode influences outcomes.

Methods: A cross-sectional study was performed in 71 out of 340 infants < 2 year-old admitted for AB (Oct/02-Apr/04) in a tertiary teaching hospital. We conducted structured interviews, spirometry and skin-prick tests (SPT) to common inhalant allergens to 4-6 year-old and looked for demographic and clinical risk factors (male gender, born season, prematurity, exposure to smoke, nursery, older siblings, pets, family history of allergy, no breast feeding) and for the acute episode [RSV, age < 6 weeks, severity] (length of hospital stay ≥ 6 days and time on oxygen ≥ 4 days) and use of steroids. Main outcomes were any episode of W and persistent wheezing (PW).

Results: W occurred in 50 (70%) of children, but only 19 (39%) referred PW. We found no differences between groups, except for steroid treatment at acute episode [W 6 (12%)/not W 8 (38%)] that was associated with a 4,5 risk reduction of wheezing (adjusted OR [IC] 0,22 [0,065–0,76]), but not for PW. PW was associated with positive SPT [PW 7 (39%); no PW 3 (10%)], adjusted OR [IC] 3,7 [1,4–10,2].

Conclusion: This study shows a high prevalence of wheezing in PSC after AB in infancy associated with atopy. The use of steroids seemed protective. We found no influence from family history of allergy, RSV infection or severity at the acute episode. These data suggests caution on using established risk factors for prognosis after an episode of BA.

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Effect of salbutamol on the growth, virulence and biofilm formation of *Pseudomonas aeruginosa*

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Background: Beta-2-agonists, like salbutamol are commonly used in patients with lung disease such as cystic fibrosis where chronic infection is common. Recently salbutamol was shown to have an effect on host defence in a murine model, impairing clearance of *Haemophilus influenzae* from the respiratory tract [1]. To determine if salbutamol affected bacterial virulence, we investigated the effect salbutamol had on the growth and virulence of *Pseudomonas aeruginosa* (PA).

Aim: To determine if salbutamol affects the growth, virulence and biofilm production of PA.

Methods: Clinical isolates of PA were used for experiments with and without addition of salbutamol at a range of concentrations between 0.375-100 microgram/millilitre [2]. Viable colony counts and growth curve were performed to determine bacterial growth. Biofilm formation was studied using attachment crystal violet assay, light and advanced microscopy and electron microscopy using 1 cm² endotracheal tube pieces.

Results: There was no difference in the growth of PA in the presence of salbutamol. However, even at low concentrations of salbutamol (1 mcg/ml) there was a significant increase in bacterial clumping on light microscopy and increased biofilm formation on endotracheal tube sections on electron microscopy.

Conclusions: Salbutamol appears to increase biofilm formation of *Pseudomonas aeruginosa*. This data does not imply that the use of beta-2-agonist is discouraged, but suggests that a potential role in the virulence of PA must be investigated.

References:

- [1] Maris et al. Respiratory Research 2006, 7:57
[2] Atabai et al. Intensive Care Medicine 2002, 28:705–11

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RANTES gene promoter polymorphisms -28C/G and -403G/A in children hospitalized with community acquired pneumonia

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The course of community acquired pneumonia in children varies between patients and it is common belief that the innate immune system of the host plays an important role to the outcome of the infection. The chemokine RANTES is an important chemoattractant which attracts monocytes, T cells, NK cells and eosinophils into sites of inflammation.

Aim of the study was to investigate the frequency of -28C/G and -403G/A RANTES polymorphisms in children hospitalized with community-acquired pneumonia. The study involved two groups of children. The first (group A) consisted of 60 children hospitalised with pneumonia, 37 boys, aged 5±0,44 years and the second (group B) consisted of 135 healthy children, 60 boys, aged 9,6±0,2 years with no history of respiratory infections.

The genotypes of all subjects were determined with PCR-RFLP assay.

Frequency of genotypes and alleles of RANTES –28 C/G and –403 G/A promoter polymorphisms

	Genotypes	Group A	Group B	Alleles	Group A	Group B
R_28 C/G	C/C (%)	44 (74,58)	130 (97,01)	C	97 (0,82)	263 (0,98)
	C/G (%)	6 (10,17)	1 (0,75)	G	21 (0,18)	5 (0,02)
	G/G (%)	9 (15,25)	3 (2,24)	Total	118 (1)	268 (1)
	Total (%)	59 (100)	134 (100)			
	p=0,0000				p=0,0000	
R_403 G/A	G/G (%)	38 (63,33)	97 (71,85)	G	96 (0,80)	231 (0,86)
	G/A (%)	2 (3,33)	1 (0,74)	A	24 (0,20)	39 (0,14)
	A/A (%)	20 (33,33)	37 (27,41)	Total	120 (1)	270 (1)
	Total (%)	60 (100)	135 (100)			
	p=0,17596				p=0,17977	

According to the results, only the -28C/G RANTES promoter polymorphism is associated with community-acquired pneumonia in children. No association was found for the -403G/A polymorphism.

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Diagnosis of primary ciliary dyskinesia in a Dutch cohort of 63 pediatric patients: An overview

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The diagnosis of primary ciliary dyskinesia (PCD) is difficult, as a single gold standard is lacking. The diagnosis is usually based on a combination of clinical symptoms, abnormal movement of cilia on microscopic evaluation of respiratory epithelial biopsies (LM) and/or epithelial cell cultures (CLM), or identification of an ultra structural defect in the cilia by electron microscopy (EM). In order to get more insights into the diagnostic value of each of these tests, we performed a retrospective analysis in a cohort of 63 pediatric PCD patients treated within our center. Patient characteristics were as follows: mean age at diagnosis 3.8 years (range 0-18 years), males 44%, females 56% and situs inversus 39.7%.

PCD was diagnosed based on a combination of clinical symptoms and LM in 7.9%, EM 4.8%, CLM 1.6%, LM and CLM 36.5%, LM and EM 20.6%, or LM, EM and CLM in 28.6% of the patients respectively. Abnormal beat frequency, amplitude and coordination observed in epithelial cell cultures from PCD patients, correlated with dyskinetic movement observed in the original biopsies (p < 0.01). However, secondary dyskinesia is often encountered in nasal biopsies, as is illustrated by the fact that in 67 out of 136 biopsies with dyskinetic cilia obtained during the last 2 years, cell culture results were normal. In 28.6% of the PCD patients, EM findings were normal. In summary, the diagnosis of PCD cannot rely on a single technique, as both false negative and false positive results frequently occur. Epithelial cell cultures should be an integral part of the diagnostic work-up. Future studies into the genetic background may further improve diagnostic accuracy.

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What is the gold standard in the diagnosis of primary ciliary dyskinesia syndrome?

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Introduction: The diagnosis of primary ciliary dyskinesia (PCD) is based on the study of ciliary motility (frequency and beat pattern) using high resolution digital video and high speed, combined with ciliary ultrastructure by electron microscopy (EM.) However, this can provide false positives and negatives, so the final diagnosis is defined by the ciliary function.

Objectives: 1. To study the real prevalence of PCD after the introduction of the technique of ciliary motility in our center (2007). 2. To set the number of cases previously classified PCD who have a normal ciliary motility.

Material and methods: Study of frequency and ciliary beat pattern: a) in patients who had been diagnosed from PCD until 2007 by screening of mucociliary clearance with ^{99m}Tc-labeled albumin and abnormal ciliary ultrastructure. b) in patients with clinical suspicion of PCD, from February 2007 to December 2010.

Results: a) Prior to the introduction of the technique the diagnosis of PCD was made in 17 cases. With the study of motility, we obtain a normal frequency/beat pattern in 8 of them (47%), dyskinetic in 6 cases (35%), not being possible to do in 3 of them. Therefore, the diagnosis of PCD is reduced 42.8%. 37.5% of confirmed cases associated with *situs inversus* (S. Kartagener). b) Since 2007 we have studied 79 patients with clinical suspicion of PCD obtaining a dyskinetic pattern in 4 cases (5%), of which only 1 (25%) had abnormal ciliary ultrastructure.

Conclusions: The diagnosis of PCD based on the study of ciliary ultrastructure has a large percentage of false positives, so the study of ciliary motility should be considered the gold standard for diagnosis.

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Is spirometry less accurate than chest computed tomography in primary ciliary dyskinesia with pulmonary deterioration?

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Background: Aggressive treatment of primary ciliary dyskinesia (PCD) often stabilizes spirometry over time. We hypothesized that spirometry may overestimate the degree of stability.

Methods: Twenty PCD patients (median age, 11.6 yrs; range, 6.5-27.5 yrs) underwent spirometry and HRCT at median 2.3 yrs interval. The first evaluation was made in stable state and the second because of deterioration unresponsive to standard therapy. CT scans were scored blind by two experienced raters.

Results: At the second evaluation, spirometry did not change while CT scores significantly worsened ($p < 0.01$).

Spirometry and HRCT results and change between the two evaluations

	1st evaluation	2nd evaluation	Change between the 1st and the 2nd evaluation	P
Spirometry (Z score)				
FVC	-0.125	-0.420	-0.380	0.64
FEV ₁	-1.005	-1.380	0	0.87
FEV ₁ /FVC	-1.570	-1.44	-0.065	0.97
FEF ₂₅₋₇₅	-2.150	-2.090	0	0.51
HRCT scores (%)				
Bronchiectasis	8.3	17	9.5	0.001
Mucus plugging	5.6	25	16.6	0.004
Peribronchial thickening	9.3	15	2.7	<0.001
Parenchyma	5.6	7.4	1.8	0.003
Mosaic perfusion pattern	0	10	0	0.009
Total	7.7	17.4	7.2	0.001

Data presented as median values.

Age was significantly related to CT total score ($r=0.5$; $p=0.02$). At both evaluations CT total score was related with FEV₁ Z score ($r=-0.5$; $p=0.015$ and $r=-0.7$; $p=0.001$, respectively) and FVC Z score ($r=-0.6$; $p=0.006$ and $r=-0.7$; $p=0.001$, respectively). No relationship was found between the change in CT scores and the change in spirometry.

Conclusions: In PCD patients with pulmonary deterioration, spirometry may fail to detect worsening CT findings. Structural changes may progress with stable spirometry, calling into question the usefulness of serial spirometries to monitor PCD lung disease.

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Changing characteristics of childhood non-cystic fibrosis bronchiectasis

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In developing countries, characteristics of the chronic diseases may change in time

because of changes in socioeconomic and health conditions. Our study aim was to evaluate the changing characteristics of non-CF bronchiectasis compared to our previous study (Karadag B. et al., Respiration 2005;72:233-8).

Patients with non-CF bronchiectasis diagnosed and followed after 2001 were recruited into the study. Long-term follow up records and lung function tests were used to evaluate the course of the disease. Collected data were compared with our previous data.

Of 100 patients included to the study, 54% were male. There was an increase in the mean age of the patients compared to our previous data (12.7 ± 4.3 vs. 7.4 ± 3.7 years; $p < 0.005$). Duration of symptomatic period before diagnosis was longer (6 ± 3.7 vs. 4.9 ± 3.7 years, $p < 0.005$). As similar to the previous data, in 41% of the patients no underlying etiology could be detected. There was a change in the percentages of the detected etiology (2011 vs. 2001): postinfectious (21% vs. 29.7%, $p=0.15$), asthma (12% vs. 4.5%, $p=0.07$), immune deficiencies (12% vs. 15.3%, $p=0.55$), primary ciliary dyskinesia (11% vs. 6.3%, $p=0.32$) and foreign body aspiration (1% vs. 3.6%, $p=0.37$). During the follow-up period, in 25% of the patients the severity of the bronchiectasis improved. The rate of surgical management decreased from 23.4% to 9% compared to previous data ($p=0.005$). Clinical characteristics of childhood bronchiectasis seems to be changing in a 10-year interval. There is a tendency for a decrease in the prevalence of postinfectious bronchiectasis however uncontrolled asthma and primary ciliary dyskinesia seems to be increasing. Surgical management is used only for a small group of patients.

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Viral epidemiology and severity of respiratory infections in infants in 2009-2010 winter: A prospective study in Basse-Normandie

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Background: Symptoms are not specific of the causal virus. The new pandemic influenza virus A H1N1v2009 was feared to cause particularly severe outcomes, especially in infants.

Aims and objectives: The objective was to evaluate the impact of H1N1v2009 on the viral epidemiology, the clinical presentation and the severity of respiratory infections in infants.

Methods: This prospective epidemiological study included all infants aged less than 2 years presenting with respiratory symptoms, from November 2009 to April 2010, at the pediatric emergency department of the University Hospital of Caen, Basse-Normandie, France, whether they were inpatients or outpatients. A nasal swab was taken for viral detection and analyzed by immunofluorescence and, if negative or influenza A, polymerase chain reaction. Severe respiratory infection was defined by a score of respiratory severity.

Results: 1021 infectious episodes with a respiratory sample met inclusion criteria. 834 samples (81.7%) were positive. The four viruses with the highest incidence were the Respiratory Syncytial virus (RSV) (34.28%), the rhinoviruses (23.90%), the coronaviruses (9.30%) and H1N1v2009 (7.74%). 28.61% of infections were severe, and more frequent in infants with risk factors. H1N1v2009 infections had a low risk of severe respiratory disease (OR = 0.15) and hospitalization (OR = 0.40) compared to the other viruses. RSV infections had a high risk of respiratory severity (OR = 7.85) and were responsible for 71.43% of admissions to the intensive care unit.

Conclusions: Despite the modest impact of H1N1v2009 observed in this study, further surveillance is needed to detect virological factors increasing severity.

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Healthcare utilisation and related cost of care in the first two years related to RSV hospitalisation in infants born at 32 to 35 weeks gestation

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Aim: Respiratory syncytial virus (RSV) lower respiratory tract infections (LRTIs) are associated with increased chronic respiratory morbidity in infants born prior to 32 weeks of gestation. Our aim was to determine if healthcare utilisation and related costs of care were increased in infants born between 32 and 35 weeks of gestation who had had an RSV LRTI hospitalisation.

Methods: Healthcare utilisation in the first two years was assessed by examining the hospital and general practitioner records. The cost of care was calculated using the National Scheme of Reference costs and the British National Formulary prices. Three groups were compared: infants with at least one hospitalisation for an RSV LRTI (RSV), infants admitted for another respiratory problem (other respiratory) and infants admitted for a non respiratory problem/never been admitted (non respiratory). A principal components analysis was undertaken to account for any differences in the demographics between groups and a further generalised linear model was used to obtain adjusted estimates.

Results: The mean total cost of care (minus the NICU admission) in the RSV group (£12,505) was greater than both that of the non respiratory (£1,178) and the other respiratory (£3,356) groups ($p < 0.0001$). The adjusted mean differences in the

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cost of care was £11,116 between the RSV and non respiratory groups ($p=0.001$) and £9,076 between the RSV and the other respiratory groups ($p=0.007$).

Conclusion: In infants born between 32-35 weeks of gestation, hospitalisation for an RSV LRTI was associated with significantly increased health related cost of care in the first two years after birth.

P517**Rhinovirus-C infection in children presenting with acute respiratory infection to hospital in Brazil**

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Introduction: Human Rhinovirus (HRV) is a common cause of acute respiratory infection (ARI) in children. A new group of Rhinoviruses (Rhinovirus C (HRV-C)) have recently been reported. We aimed to assess the frequency of HRV groups, including HRV-C, in preschool children presenting to a paediatric emergency department with different clinical manifestations and severities of ARI.

Methods: Children <5years presenting to IMIP children's hospital, North-Eastern Brazil with ARI between March 2008 and March 2010 were recruited. They had nasopharyngeal aspirate samples collected. Clinical diagnosis and disease severity were recorded. Samples were analysed by Multiplex PCR for 18 viral and atypical bacterial pathogens. All HRV positive samples were subsequently analysed for subtype and group.

Results: 630 children were recruited, of whom 54% were hospitalised. Bronchiolitis, pneumonia, viral induced wheeze and upper respiratory tract infection were the commonest clinical diagnoses. HRV was detected in 118 samples (19%), the 4th most common infection after Respiratory Syncytial virus (32%), Adenovirus (29%) and Bocavirus (24%). Preliminary data shows 35% of HRV samples are HRV-C positive. Relationships between clinical manifestation/severity scorings will be examined once sub-typing analysis is complete.

Conclusions: This study underlines the importance of Rhinovirus infection in preschool children presenting to hospital with ARI. Preliminary data indicates HRV-C subtype is highly prevalent, further analysis will show whether this subtype is associated with particular clinical manifestations and severities of disease.

P518**The prevalence of human rhinovirus C is low in children from the community without respiratory symptoms**

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Background: We have shown that human rhinovirus strains from group C (HRVC) are associated with more frequent and severe asthma exacerbations in children. The occurrence in HRVC in well children, with or without asthma and no current respiratory symptoms is unknown. Previous studies of patients with asthma without current symptoms have shown 12-44% had HRV detected.

Aim: To document the prevalence of HRVC in a population of well children from the community.

Methods: We prospectively recruited children from the community or from the hospital with no signs of an upper respiratory infection and with no respiratory condition other than asthma. Either a nasal flocked swab or nasal wash specimen were collected from all children and tested for HRV. Viral RNA was extracted and reverse transcribed. A two-step PCR of the HRV 5' NCR was used for detection, followed by sequencing for typing.

Results: We collected nasal specimens from 34 children. The age range was 8 months to 18 years (mean 11.8 years). Male to female ratio was 1:1. Twenty five (73.5%) children were recruited directly from the community. Ten (29.4%) children were recruited in spring and 13 (38.2%) in autumn, the peak seasons for HRV. Seventeen (50%) children had a nasal swab and 17 (50%) children had a nasal wash specimen. Thirteen (38.3%) had doctor-diagnosed asthma. Ten (29.4%) had atopy. We found HRV in only 6 (17.6%) of the 34 children studied. HRVA was present in 2 of the samples and HRVB in 4. All of these were detected in spring or autumn. However, no HRVC was detected.

Conclusion: In our community, HRVC has a low prevalence in children who are well and without respiratory symptoms.