Early View

Invited review

ERS International Congress 2023 hybrid: highlights from the Paediatric Assembly


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ERS International Congress 2023 hybrid: highlights from the Paediatric Assembly

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**Take home message:** Highlights from the Paediatrics Assembly presented during the last #ERSCongress held in Milan in September 2023

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Abstract

Respiratory health in children is essential for general wellbeing and healthy development on the short and long term. It is well known that many respiratory diseases in adulthood have their origins in early life, and therefore research on prevention of respiratory diseases and management of children with respiratory diseases will benefit patients during the full life course. Scientific and clinical advances in the field of respiratory health are moving at a fast pace. This article summarises some of the highlights in paediatric respiratory medicine presented at the hybrid European Respiratory Society International Congress 2023 which took place in Milan (Italy). Selected sessions are summarised by Early Career Members of the Pediatrics Assembly (Assembly 7) under the supervision of senior ERS officers. It covers a wide range of research areas in children, including respiratory physiology and sleep, asthma and allergy, cystic fibrosis, respiratory infection and immunology, neonatology and intensive care, respiratory epidemiology and bronchology.
Introduction

Respiratory health in children is essential for general wellbeing and healthy development on the short and long term. In utero and early life events influence the risk of many respiratory diseases in adulthood, including COPD, occupational asthma and lung cancer. Research on prevention of respiratory diseases and management of children with respiratory diseases is therefore urgently needed to maximise lung health throughout the life course [1]. During the hybrid European Respiratory Society (ERS) International Congress 2023, the Paediatric Assembly (Assembly 7) organised various outstanding sessions focussing on the latest insights on respiratory health in children. It included scientific symposia, clinical cases, a hot topic session on lung function trajectories and respiratory health from infancy to adulthood and a postgraduate course on cryotherapy in the paediatric airway. It resulted in an excellent programme of high interest to paediatricians as well as adult physicians and allied health professionals, stimulating the urgently needed collaboration between different health care professionals [1]. Assembly 7 Early Career Members and leading experts presented 315 abstracts in oral and poster sessions. Here, we present some of the major paediatric highlights from the 2023 congress. Senior officers from the Assembly selected sessions, which were summarised by Assembly 7 Early Career Members under their guidance.

Technical and epidemiological novelties in paediatric lung function and sleep

The oral presentation session “Technical and epidemiological novelties in paediatric lung function and sleep” addressed the latest insights on lung measurement parameters in diverse pediatric populations. Nicole Beydon (Paris, France) presented the new ERS technical standard statement for nasal nitric oxide measurement in children for the diagnosis of primary ciliary dyskinesia [2]. Purpose of this ERS statement is to facilitate early diagnosis of PCD, to address both techniques used to measure NO in routine practice (chemiluminescence and electrochemical), and to standardise breathing manoeuvres (with and without velum close) and reporting forms. Although chemiluminescence can provide more reliable results, electrochemical methods are more widely used in Europe. A gradation method is proposed to report the reliability of results as well as considerations for nasal NO in different age groups (Figure 1).

Carla Rebeca Da Silva Sena (Newcastle, Australia) provided new data on bronchiolitis risk factors in infants [3]. By utilising the data from the Australian Cohort of children born to mothers with asthma in pregnancy, data for 385 infants with tidal breathing values and medical records were available. Of these, 19 were verified with a bronchiolitis hospitalisation after lung function measurements in the first year of life. Lower tidal breathing in infants at 6 weeks of age, along with
higher maternal BMI during pregnancy were found to be significantly associated with bronchiolitis hospitalization in the first year of life.

Diana Gray (Cape town, South Africa) presented data from the Drakenstein South African Cohort [4], a cohort of children in whom lung function is measured annually using tidal breathing techniques (Multiple Breath Washout (MBW) and oscillometry) from birth to 5 years of life. In total, 966 infants with more than 10,000 lung function measurements were available for analysis. By utilising these data, the authors were able to present how comprehensive lung function measurements change throughout the first years of life [5]. Additionally, lower respiratory tract infections at these ages were shown to be associated with higher airway resistance, higher respiratory rate along with lower compliance. RSV infections had higher impact on lung function than other respiratory viruses.

Jacob McCoy (Toronto, Canada) explored the differences between Global Lung Function Initiative (GLI) Global and GLI Caucasian equations regarding spirometry interpretation. He showed that the use of GLI Global led to a reduction of abnormal spirometry tests, particularly those suggestive of airway restriction[6]. Florian Wyler presented data on the development of the lung clearance ratio (LCR), a novel ventilation inhomogeneity Index that is less sensitive to the confounding effects of breathing patterns, dead space and end expiratory lung volume[7].

The presentations of Andrew Prayle (Nottingham, United Kingdom) and Maria Eleni Liagkaki (Athens, Greece) focused on pediatric sleep. Andrew Prayle presented the trajectories of sleep oximetry results in infants born with Pierre Robin sequence in the first 6 months of life [8], whereas Maria Eleni Liagkaki summarized nocturnal oximetry reference values in healthy term infants aged 1-6 months old[9].

Take home messages:

- A new ERS statement on measuring nasal NO for the diagnosis of PCD is currently available.
- Early life tidal breathing measurements significantly differs between children with or without respiratory diseases before school age.

Paediatric asthma and the rising obesity pandemic

Obesity is a rising pandemic in European children, often starting at an early age. The symposium “Lung consequences of the obesity epidemic from children to the elderly”, included four outstanding presentations, by experts in this field.

Deepa Rastrogi (Washington, United States of America) focussed on the link between the immune system and obesity-related asthma. There are many proposed mechanisms on pathobiology of asthma in patients with obesity such as the mechanical effect of fat load, inflammation and
metabolic dysregulation[10-12]. Asthma in children with obesity is often associated with a non-atopic T helper 1-polarized systemic inflammation that correlates with pulmonary function deficits [13]. This inflammation has been associated with upregulation of the Cell Division Cycle 42 (CDC42) pathway. CDC42 is a RhoGTPase that plays a role in Th cell physiology[14]. Yon et al.[15] investigated the mechanisms by which upregulation of CDC42 in T-cells is associated with airway smooth muscle biology and came to the conclusion that T-cells from asthmatic obese children have uninhibited chemotaxis and are more adherent to obese airway smooth muscle, which is associated with upregulation of genes and proteins associated with smooth muscle proliferation and reciprocal T-cell activation.

Indra Narang (Toronto, Canada) addressed therapeutic considerations in obesity-related Obstructive Sleep Apnoea (OSA). Drug-Induced Sleep Endoscopy is a method performed via nasoendoscopy during ‘sleep’ induced by pharmacological agents with the aim to identify sites of obstruction for targeted surgical interventions. A study by Kirkham et al. [16] showed a significant reduction in the obstructive apnea-hypopnea index using this technique to identify surgical targets, and the reduction was even higher in the surgically naive group. CPAP is a highly effective therapy of OSA but not very well tolerated, hence High Flow Nasal Cannula Therapy (HFNC) might be a more suitable alternative. A Canadian RCT comparing HFNC to CPAP[17] showed that HFNC and CPAP had similar efficacy in treating OSA as determined by polysomnography. Therefore, HFNC seems like a promising therapy but more RCT studies are needed to evaluate clinical outcomes. There are also pharmacological approaches such as weight management with GLP-1 Agonists[18, 19] or repurposing drugs like Atomoxetine and Oxybutinin[20, 21] that might be effective in reducing weight and improving airway collapsibility.

With the question “Why (how) does childhood obesity cause (worsen) respiratory disease?” Eric Forno (Pittsburgh, United States of America) summarized the current data on this topic (Figure 2). He presented a study of six independent cohorts with/without asthma and airway dysanapsis [22, 23], which is defined by supernormal FVC, normal FEV1 and low FEV1/FVC Ratio. Airway dysanapsis was more frequent in patients with overweight and obesity and was associated with an increased risk of severe asthma exacerbations and use of systemic steroids. He also presented data from the US NHANES[24], where in a cohort of 1429 adolescents with metabolic syndrome (MS). MS was associated with approximately 3% lower FEV1/FVC in children without asthma, and up to 10% lower FEV1/FVC in children with asthma.

Finally, Miguel Angel Alejandre Alcazar (Cologne, Germany) showed metabolic determinants of asthma and COPD across ages, demonstrating that the trajectory of lung function is influenced by early in life events [25]. Risk factors and modifiers of chronic lung disease can also be found lay in the
pre- and perinatal period[26], with factors such as premature birth, intrauterine growth restriction and maternal smoking determining lung diseases later in life. He presented recent data of the Avon Longitudinal Study of Parents and Children, a British longitudinal population-based birth cohort study of parents and children followed up to 24 years of age [27]. It showed a correlation of maternal BMI and metabolisms parameters early in life and lung function in adulthood. In addition, the work of Selle et al.[28] showed that perinatal obesity induces proliferation of bronchial and vascular smooth muscle cells via activating STAT3-FoxO1, causing bronchial obstruction and pulmonary hypertension later in life.

**Take home message:**

- Asthma in children with obesity is often associated with a non-atopic T helper 1-polarized systemic inflammation
- Obesity does not only influence asthma disease dynamics, but also may be the origin of chronic lung diseases.

**Paediatric cystic fibrosis**

The landscape in cystic fibrosis (CF) has changed dramatically after introduction of cystic fibrosis transmembrane conductance regulator (CFTR) modulator (CFTRm) therapies. The latest of these therapies is the triple combination of the two CFTR correctors eliacaftor (ELX) and tezacaftor (TEZ) with the CFTR potentiator ivacaftor (IVA). ELX/TEZ/IVA led to substantial improvements in several organ systems in CF in clinical studies, leading to approval for persons with CF (pwCF) with at least one F508del allele, aged six years and older (Europe, Australia), and/or at least one CFTR mutation of a list of other in vitro responding CFTR mutations, aged two years and older (U.S.). Unfortunately, the issue of reimbursement of this therapy remains unsolved in a high number of countries. Several abstracts of this year’s ERS conference dealt with this new treatment option and were presented in the poster session “Effects of CFTR modulator therapy in cystic fibrosis”.

Results from a Turkish multi-center study showed significant improvement in both forced expiratory volume in 1 s (FEV1) and lung clearance index in pwCF who were on CFTRm for at least three months [29]. However, Pinar Ergenekon (Istanbul, Turkey) underlined that these therapies are currently not reimbursed in Turkey and patients can only access these drugs by court decision. Due to the time between court decisions, many patients receive intermitted treatment. Positive treatment outcomes were also reported in a Spanish cohort of paediatric patients with CF that started ELX/TEZ/IVA. Jonathan Benito Patón (Valencia, Spain) reported a decrease in the colonisation by *Staphylococcus aureus* and *Pseudomonas aeruginosa* in these patients upon 6 months of treatment [30]. Rikke Mulvad
Sandvik (Copenhagen, Denmark) showed that lateral decubitus chest computed tomography is a feasible and sensitive technique to detect and monitor structural lung abnormalities in newborn screened children with CF [31]. In this study, CFTRm therapy seemed to be associated with improvement in airway wall thickening.

Exercise tolerance is an important parameter of quality of life for pwCF. Ivan Bambir (Zagreb, Croatia) reported a significant improvement in exercise tolerance in 12pwCF (range 12-18 years) using the 6-minute walk test upon ≥ 6 months of treatment with ELX/TEZ/IVA [32]. Molla Imadudin Ahmed (Leicester, UK) analysed the impact of ELX/TEZ/IVA on exercise capacity by cardiopulmonary exercise testing at baseline and after 6-8 months without detecting changes in VO2 peak in a cohort of 7 pwCF [33].

CFTR modulators are also associated with a positive long-term effect. Hadhud Mohamad (Jerusalem, Israel) studied the long-term effects of ELX/TEZ/IVA treatment on body mass index (BMI), pulmonary exacerbation rate, and increase in percentage predicted FEV1 of 10% from baseline in FEV1 after 18-24 months of ELX/TEZ/IVA treatment initiation. All patients had a long-term improvement and patients with worse baseline pulmonary disease were more likely to have sustained respiratory improvement[34]. Shahid Sheikh (Columbus, USA) showed that 12 months of ELX/TEZ/IVA treatment significantly decreased chronic rhinosinusitis based on sinus CT in 64 pwCF [35]. Aleskandra Zver (Ljubljana, Slovenia) reported improved bone mineral density in 17 pwCF older than 12 years after one year of ELX/TEZ/IVA[36].

In order to better understand the mechanism of action of CFTRm on the metabolism of the lung, Emmanuelle Bardin (Paris, France) studied volatile organic compounds in the breath of 12 pwCF before and upon CFTRm treatment. Longitudinal analysis identified 12 VOCs in exhaled breath to be increased during the first month of treatment, and suggested that exhaled breath analysis could be a potential future tool for drug monitoring [37]. Another biomarker in exhaled breath is the fraction of exhaled nitric oxide (FeNO). Isaac Martin (Toronto, Canada) reported that the use of ELX/TEZ/IVA increased the fraction of exhaled nitric oxide (FeNO) after 1-3 months of therapy, rather not indicating eosinophilic airway inflammation, but restoration of FeNO to a normal level [38].

In order to guide treatment, it is essential to identify responders to CFTRm at an early stage. Felix Ratjen (Toronto, Canada) evaluated 41 pwCF to predict the clinical benefit of CFTRm via in vitro assays using nasal epithelial culture. The findings showed that in vitro response to CFTRm correlates with clinical response, including change in weight, sweat chloride concentration and spirometry parameters in the same individuals[39].

Take home messages:
CFTRm substantially improve the life of pwCF who are eligible for this new treatment
• Reimbursement is an issue, and some pwCF receive off-label or intermitted treatment

Paediatric respiratory infection and immunology

The hot topic session “The unfortunate relationship between respiratory disease and infection: challenges which need us to think outside the box” focused on understanding the molecular mechanisms underlying increased susceptibility to respiratory infections. In addition, this session emphasized the importance of preventive strategies, primarily vaccination.

The session started with the Sadoul Lecture (intended to honour senior scientists with a worldwide reputation) given by awardee Prof. dr. Tobias Welte (Hannover, Germany). This lecture focused on discussing the impact of respiratory infections on lung health in general. Past and emerging evidence highlights that severe respiratory infections (e.g., community-acquired pneumonia and infectious exacerbations of chronic obstructive pulmonary disease [COPD]) are associated with a high risk for mortality.[40, 41] Apart from the short-term consequences, severe respiratory infections have an impact on long-term lung health. For example, severe respiratory infections impact lung function trajectories, development of chronic respiratory disease and risk of acute exacerbations in chronic lung diseases such as asthma or COPD. [42] The impact of early life lung infection on lung trajectories were discussed further in the lecture by Erika von Mutius (Munich, Germany). Cohort studies, including the Tasmanian cohort and the Oslo birth cohort, show that severe infections in early life, exposure to tobacco smoke, and co-existing allergies are the strongest determinants of impaired lung function trajectories up to adult years. [43, 44] The effects of exposure to risk factors might be different in boys and girls. Data from the Children’s Health study showed that upon in-utero exposure to maternal smoking, boys with asthma had significantly larger deficits from in-utero tobacco exposure in forced vital capacity (FVC) and the ratio of forced expiratory volume at 1 sec (FEV1) to FVC, whilst girls with asthma had a higher decrease in FEV1/FVC. [45] Delving into pathophysiological mechanisms underlying these associations will highlight possible preventive mechanisms for lung function decline in the future.

With regard to pathophysiological mechanisms underlying severe respiratory infections, Alberto Mantovani (Milan, Italy) discussed his group’s work on identifying the role of innate immunity in response to respiratory viral pathogens. His group showed that the activation and polarization of macrophages toward the M1 or M2 phenotypes play a crucial role in the early stages of inflammation, more specifically in the activation of proinflammatory and vascular endothelial mediators. [46] In addition, based on this and other groups’ findings, we now know that innate immunity can be trained,
and epigenetic modifications play a key role in training innate immune responses to microbial agents, cytokines, and ultimately vaccines. [47] Epigenetic mechanisms may explain differences in mortality and long-term respiratory sequela in response to severe respiratory infections. [48] [48] Peter Openshaw (London, UK) presented research on the fast development of COVID19 vaccine as an example of drug target identification, development, and testing in short timelines. [49] In contrast to the rapid development of COVID19 vaccines, prevention of respiratory syncytial virus (RSV)-related disease in adults and infants has been a long and difficult story. Prevention strategies are needed to prevent short- and long-term consequences of severe RSV-related disease. [50] Recent trials have shown that RSV vaccines provide good protection against lower respiratory tract infections in adults and maternal vaccination during pregnancy significantly decreases severe RSV disease in young infants. [51] Data regarding passive RSV immunization show that a single injection of nirsevimab administered before the RSV season can protect healthy late-preterm and term infants from medically attended RSV-associated lower respiratory tract infection [52]. However, data around protection from long-term respiratory sequela (e.g., asthma) are not available yet. Clinical trials on active vaccination in infants and children are still underway for protection in infants and children up to age 5 years when administered during pregnancy.

**Take home messages:**
- Severe infections in early life influence lung function trajectories into adulthood
- Vaccine research remains important to reduce short and long-term consequences of respiratory infection throughout all ages

**Respiratory disorders in neonatal and paediatric intensive care**

The poster session “Respiratory monitoring and management in neonatal and paediatric intensive care” covered some of the challenging issues related to preterm birth, including the assessment of lung structure and function from birth to childhood; supportive treatment of neonatal airway disease, and the needs of affected individuals, their families and caretakers.

Finding adequate tools for respiratory monitoring in neonates is challenging due to the peculiar patient characteristics and the need for non-invasiveness. Concerning long-term monitoring of disease progression, Anne Hilgendorff (Munich, Germany) showed data of a longitudinal MRI study on functional and structural BPD characteristics in preterm (<32 weeks’ of gestational age [GA]) infants near-term (n=88) and at preschool age (4-8 years; n=26)[53]. Structural and functional changes observed near-term persisted at 5 years with characteristic features depending on BPD severity and immaturity. Importantly, those structural changes were quantifiable [54].
Among the monitoring techniques applied in the neonatal intensive care unit (NICU), lung ultrasound (LU) and forced oscillation technique (FOT) have lately emerged \[55, 56\]. Emanuela Zannin (Monza, Italy) combined LU and FOT to assess the response to systemic versus inhaled corticosteroids. 27 treatments (9 dexamethasone; 18 budesonide) in 20 infants born at 26.8 ± 2.6 weeks GA were analysed. Both systemic and inhaled corticosteroids improved the airways (assessed by FOT) and the parenchymal compartment (assessed by LU); however, treatment length was not standardised \[57\].

Petra Johanna Um-Bergström (Stockholm, Sweden) presented a comparison of two cohorts born in Sweden at 22-26 weeks between 2004-2007 (n = 702) vs. 2014-2016 (n = 885). Survival at 36 weeks postmenstrual age (PMA) increased from 72% to 81% (p <0.001), as found elsewhere \[58, 59\]. The increased survival was associated with a longer duration of respiratory support. Surprisingly, mechanical ventilation rose from 9 to 16 days for the 2014-2016 cohort (median; p <0.001). However, the incidence of severe BPD at 36 weeks PMA decreased from 26% to 21% \[60\].

Infants with severe BPD often require some form of respiratory support at discharge. Anna Lavizzari (Milan, Italy) investigated the long-term respiratory outcomes of 73 infants with severe BPD discharged home with nasal high-flow therapy (NHFT, n = 47) vs. low-flow oxygen therapy (LFOT, n = 26). The two groups presented similar baseline characteristics and severity of BPD. After applying a mixed-model correcting for several risk factors, the NHFT group showed a lower rate of wheezing (p 0.003), use of bronchodilators (p 0.024) and systemic steroids (p<0.001), and respiratory tract infections (p 0.031) within the first four years of life. Infants on NHFT were weaned at 8 vs. 14.5 months (median), suggesting that NHFT may be a valid alternative to LFOT for infants with BPD requiring respiratory support after discharge \[56\].

Other than prematurity, growth restriction may play a significant role in altering lung development. Jip Anne Spekman (Leiden, The Netherlands) retrospectively analysed 39 pairs of discordant (≥ 20% difference in weight at birth) monochorionic twins (GA 34.9 weeks). Spirometry, single-breath CO-diffusion and multiple-breath helium dilution were performed at a mean of 11 years (range 10-14). Although genetically identical, fetal growth-restricted twins presented a significant reduction in static lung volume z-scores and a decrease in dynamic lung function \[61\].

**Take home messages**

- MRI is a feasible tool to track disease progression and outcomes in former preterm infants
- FOT and LU help to discriminate between larger airways and lung parenchyma and may help to compare responses to different treatments
• Survival of extremely premature infants rose to 81% at 36 weeks GA in Sweden, and the rate of severe BPD significantly decreased, although mechanical ventilation duration increased from 9 (2004-2007) to 16 days (2014-2016) in two large Swedish cohorts.

• NHFT is a valid alternative to LFOT as respiratory support after discharge for infants with BPD

• In utero growth restriction has a significant impact on lung function in adolescence

Paediatric respiratory epidemiology: lung function trajectories

The Hot Topics session on “Determinants of lung function trajectories and respiratory health from infancy to adulthood” included four presentations summarising the current evidence on lung function trajectories, their identification, and possible interventions.

Shyamali Dharmage (Melbourne, Australia) presented “Lung function trajectories across the life-course: the looking forward/backward concept” explaining how the concept of lung function trajectories has changed our understanding of the pathogenesis of adult chronic diseases. COPD is no longer considered a single risk disease but has multiple risk factors with early onset and follows different lung function trajectories [62]. In the Tasmanian Longitudinal Health Study (TAHS), authors identified six distinct lung function trajectories of which three gave rise to almost all COPD cases at age 53 [43]. They also described lifetime spirometry patterns of obstruction and restriction associated with different risks of COPD [42, 63]. This concept of lung function trajectories has led to a looking forward (for paediatricians) and backward paradigm (for pulmonologists), which may allow to predict more accurately future lung function and inform clinical care and treatment response.

Niki Ubags (Lausanne, Switzerland) focused on “A mechanistic view into the early-life microenvironment and lung health” showing how early life exposures can change immune maturation and prime the lung for disease [64]. She used the example of nutrition and explained how maternal malnutrition or obesity can alter nutrient sensing, endocrine signaling, and lipid metabolism leading to systemic inflammation and ultimately to chronic lung disease in the offspring [26]. Similarly, changes in maternal gut microbiota in pregnancy and during early life may lead to increased birth weight and gut dysbiosis, resulting in an increased risk of asthma [64]. She also highlighted the importance of inter-organ communication in the development and progression of respiratory diseases [65].

Erik Melén (Stockholm, Sweden) continued with “Looking forward: is the lung growth trajectory fixed or can we intervene?” highlighting the association of environmental factors with impaired lung function growth [66]. He presented two reviews summarizing predictors of lung function growth such as air pollution, allergens, lower respiratory tract infections or asthma [67, 68].
In the BAMSE cohort, a Swedish population-based birth cohort, although individual lung function was remarkably stable from 8 to 24 years, there was also plasticity of lung function, with lung function growth failure observed in 2.4%, and catch-up in 14.5% of children. The number of risk factors for poor lung function was associated with prevalence of impaired lung function growth [69]. He concluded that reducing factors associated with growth failure may give potential room for intervention to change lung function trajectories.

Finally, Rosa Faner Canet (Barcelona, Spain) gave an overview of “Novel biomarkers of impaired lung function in clinical practice” which may be candidates to identify disadvantageous lung function trajectories. She gave examples of current known biomarkers for COPD such as CC-16 which is associated with inflammation, low FEV1 and accelerated lung function decline [70-72]. She also demonstrated a strong association between a genetic risk score for COPD derived in adults and airflow limitation in preschool children born preterm [73]. Difference in epigenetics were also shown to be associated with different lung function trajectories [74, 75]. These biomarkers could enable early detection of chronic respiratory diseases such as COPD.

Take-home messages

- Identifying early life risk factors for adult-onset disease and potential lung function trajectories can inform clinical practice and support establishing effective preventive measures and interventions.
- Early life exposures can alter immune response or microbiota and may set one on a trajectory for lung health or disease development.
- Clinical and biological biomarkers associated with low lung function could be used in the future to detect adverse lung function development.

Paediatric bronchology

The oral presentation session ‘Paediatric Bronchology: next generation’ included studies focussing on childhood interstitial lung disease (ChILD), protracted bacterial bronchitis, pulmonary malformation and chronic aspiration.

It is well known that ChILD are rare disease and Halime Büyükşahin (Ankara, Turkey) [76] presented data from the Turkey Registry, in which 416 patients have been enrolled from 19 centers. The median age of the patient was 6.05 years and the most frequent diagnosis was neuro-endocrine cell hyperplasia of infancy (NEHI). The patients were divided into two groups, the first including disorders of infancy, the other with disorders that can occur at all ages. The first group was characterized by the
presence of tachypnoea, history of neonatal intensive care admission, lower weight and height and
more than half of the patients had been diagnosed with surfactant disorders. The presence of cough
categorized the second group together with low FEV1 and most of the patients suffered from an ILD
related to exposures. Nagehan Emiralioglu (Ankara, Turkey) [77], presented data from the ChILD kids
registry that includes 759 patients. At baseline in children younger than 2 years of age, malnutrition
was present in 44% of cases, this percentage halved at one year of follow-up. In children older than 2
years of age malnutrition was present in 37% of cases at baseline and in 25% of cases after one year
of follow-up. Malnutrition was correlated to lower ppFEV1 and disease severity. The severity of some
forms of ChILD requires a lung transplantation. Julia Carlens (Hannover, Germany) [78] reported the
data about the indications and outcomes of lung transplantation in 97 patients from her centre. The
most common indication was disorders of the immunocompromised host (e.g. severe bronchiolitis
obliterans after stem cell transplantation), and after a median time of 4.65 years post-transplant 89%
of patients were alive.

Regarding the possible risk factors and long-term sequelae of protracted bacterial bronchitis (PBB),
Anne Schlegtendal (Bochum, Germany) [79] reported the data from a retrospective analysis including
200 children with PBB. Patients with PBB had more frequently atopic dermatitis, recurrent wheezing
and household tobacco smoke exposure compared to a control cohort. In the follow-up study
including 63 out of the 200 children, a median of 8.5 years after the PBB diagnosis, cases were more
frequently premature and had more respiratory symptoms, such as history of pneumonia, atopic
disease and clinicians diagnosed asthma. Chronic wet cough was reported more frequently in the post-
PBB children than in the controls (17.5% vs 9%, \( p=0.05 \)). Lung function tests showed a significantly
lower FEV1 and FVC in post-PBB patients compared to controls. Respiratory symptoms and tobacco
exposure were risk factors for long-term sequelae.

Oesophageal atresia (OA) and tracheoesophageal fistula (TOF) are congenital abnormalities that can
affect 1:3500 live birth. Katie Rose (Liverpool, UK) [80] reported the data from 223 patients with a
diagnosis of OA and TOF. Almost half of them had been followed up and 49 patients (22%) had
documented spirometry, with 13 (6%) having more detailed lung function. A total of 21/223 (9%)
patients had FEV1<80% predicted, with a restrictive pattern at spirometry. Eleven patients underwent
CT scan of the chest, which demonstrated compression of the trachea by vasculature in two patients
and reduced lung volume related to oesophageal replacement in two patients.

Pediatric dysphagia affects 1% of children but the prevalence is higher in children with neurologic
disorders. Nadine Freitag (Dusseldorf, Germany) [81] reported data from a retrospective study
analysing the bronchoalveolar lavage fluid for the presence of pathogens (either viruses, fungi, or
bacteria) and immune cell population in a group of patients with dysphagia compared to a control
group without swallowing disorders. Children with dysphagia were more frequently colonized by pathogens such as *Enterobacterales* and *Pseudomonas aeruginosa* (54.3%) than controls (37.3%) (0.027). No differences in the composition of the immune cell population in the BAL were found between cases and controls.

**Take home messages:**

- ChILD are not only rare but also heterogeneous conditions that require a multidisciplinary approach including a careful nutritional evaluation.
- Lung transplantation can be an option in patients with severe forms of ChILD. Children with PBB can develop long-term sequelae, such as chronic wet cough and impaired lung function tests.
- Asthma and tobacco smoke exposure are risk factors for the development of long-term sequelae.
- Prematurity is a risk factor for PBB.
- In patients with OA/TOF reduced lung function may be present and could be due to a primary defect or to surgical procedure.
- Patients with dysphagia are more often colonized by respiratory pathogens.

**Concluding remarks**

The ERS International congress 2023 showed that advances in paediatric respiratory medicine are rapidly advancing. In the line with previous years [82, 83], we present a selection of the outstanding sessions on behalf of Assembly 7 (Paediatrics) in order to inform the reader of the latest developments and encourage participation in future ERS activities [84]. Overall, it has become evident that respiratory health in early life impacts respiratory health in childhood and adulthood, which underlines the need for collaboration among health care providers and researchers from different disciplines.
Conflict of interests

SJHV received support from the ERS for attending meetings and is the Early Career Member Representative of the Paediatrics Assembly of the ERS. LDS is supported by the Swiss National Science Foundation (320030B_192804/1). RMU received a travel grant by the Gesellschaft für pädiatrische Pneumologie (GPP) to attend the ERS Congress 2023. LP has received funding from Sanofi to attend the ERS congress 2023. NB is chair of 7.01 of the ERS and has received support from the ERS for attending meetings. AZ is chair of 7.02 and has received payment for lectures and support to attend meetings from Vertex, Astra Zeneca, Chiesi, Gilead and Novartis. MS is secretary of group 7.03 and has been supported by German Research Foundation (Deutsche Forschungsgemeinschaft, DFG). Furthermore, she has received an independent RIA grant from Vertex Pharmaceuticals. MP is chair of 7.04 and has received support from the ERS for attending meetings. AL is chair of 7.05 and reports consulting fees from Chiesie s.p.A, Vyaire medical, Getinge and support by Accademia Techniche Nuove. MG is chair of Group 07.06 of the ERS and she is supported by the Swiss National Science Foundation (PZ00P3_185923). DS is past chair of Group 7.07 of the ERS and has received support from the ERS for attending meetings. MPi received support from the ERS for attending the ERS congress and ERS meetings. She is the past chair of the Paediatric Assembly. AM is the current chair of the Paediatric Assembly and reports to have received a research grant from Vertex Inc and funding to attend the Vertex symposium at the annual conference of the Swiss Respiratory Society. The other authors report no COI for this manuscript.
Figure 1: Considerations for nasal NO in different age groups according to new ERS technical standard “nasal nitric oxide measurements in children for the diagnosis of primary ciliary dyskinesia” (Adapted from Beydon et al., ERJ 2023 [2]) BH: Breath hold, ER: expiration against resistance, PCD: primary ciliary dyskinesia

Figure 2. Obese underlying pathways. Shown are general pathways and mechanisms involved in the obese asthma phenotype. Genetic susceptibility and early-life (including in utero) factors can predispose to both obesity and asthma. Microbiome changes can cause or be a consequence of either disease and can also contribute to metabolic dysregulation. Obesity can lead to metabolic dysfunction and systemic inflammation, both of which can increase airway inflammation, asthma risk, or asthma severity. Lung function changes can be the result of anatomical/developmental alterations in obesity and can also be influenced by metabolic dysregulation (reprint of Forno & Celedón, BRN Rev 2018 under CC BY-NC-ND 4.0 DEED)
References


30. Patón JB, González SI, Pavia CL, Sanz TP, Álvarez LG, Machancoses JVA, Gaudíza EC, Corullón SC: Description of the variations in airway colonization in patients with


Measuring nasal nitric oxide for the diagnosis of primary ciliary dyskinesia (PCD) in different age groups: ERS Task Force recommendations

<12 months: extremely low in healthy infants, therefore research tool only, not diagnostic

<5-years: interpret with caution and refer to PCD centre if in doubt:
- Levels in healthy children < 5 years are lower than older healthy children
- Limited normative data

To choose manoeuvre:
- Expiration against resistance (ER) if compliant (usually > 5 year)
- Breath hold if compliant but unable to achieve ER
- Tidal breathing if non-compliant or unable to achieve ER/BH

Figure 1
Figure 2