

# Hot Topics from the Assemblies

## The interaction between bronchoconstriction and cough in asthma

Authors: Satia I, Badri H, Woodhead M, *et al.*  
*Thorax* 2017 [in press <https://doi.org/10.1136/thoraxjnl-2016-209625>].

Summary: Both acute bronchoconstriction, which often manifests as wheeze and shortness of breath, and the neuronal cough reflex are key symptoms of asthma. However, the interaction between airway smooth muscle and nerve responses in disease are unclear. The authors had undertaken a study in which they examined the acute effects of bronchoconstriction on cough, and *vice versa*, in subjects with mild atopic asthma.

In order to investigate this further, the investigators undertook a randomised, single-blind, placebo-controlled crossover study to investigate whether bronchoconstriction induced by methacholine (a muscarinic agonist) had any impact on cough induced by capsaicin (a TRPV1 agonist), and *vice versa*, as well as the effect of spontaneous recovery of bronchoconstriction on evoked cough and acoustic recordings of spontaneous coughing. This was assessed in 14 patients with controlled, mild atopic asthma over eight visits. A full history examination and spirometry were undertaken on the first visit, along with capsaicin challenge to determine an individualised median effective dose, followed by methacholine challenge to determine PC<sub>20</sub> ≥48 h later.

The researchers showed for the first time that methacholine-induced bronchoconstriction was associated with an increase in capsaicin-evoked coughs by 34.2%, which returned to baseline as airway calibre spontaneously improved. The frequency of spontaneous coughing also increased with bronchoconstriction. However, capsaicin cough challenge had no impact upon methacholine-induced bronchial hyperresponsiveness.

This study shows for the first time that bronchoconstriction and TRPV1-mediated cough are linked in asthma, and suggests that the pathophysiological airway changes in asthma can impact neuronal driven reflexes such as cough. However, mechanisms and mediators involved require further investigation. This is an important

novel finding, which may impact future therapeutic options for cough in asthma.

**Reviewed by:** Sara Bonvini (UK, Assembly 5)

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## X-linked primary ciliary dyskinesia due to mutations in the cytoplasmic axonemal dynein assembly factor PIH1D3

Authors: Olcese C, Patel MP, Shoemark A, *et al.*  
*Nat Commun* 2017; 8: 14279

Summary: Primary ciliary dyskinesia (PCD) (Online Mendelian Inheritance In Man 244400) is a rare disorder affecting one in 10 000–15 000 live births, characterised by abnormal motility of respiratory cilia causing recurrent respiratory infections and progressive decline in lung function. 50% of cases also show laterality defects such as *situs inversus*. PCD is a clinically and genetically heterogeneous disease, and has been traditionally considered as an autosomal recessive condition; in the last 10 years, great interest has been focused on PCD genetics, so that nowadays mutations in >30 causative genes have been described, which are connected with the structure and/or function of dynein arms or ciliary assembly.

In the study by OLCESE *et al.*, three molecular genetics laboratories (in London, UK; Geneva, Switzerland; and Paris, France) used next-generation sequencing of whole exomes, targeting gene panels and whole-genome single-nucleotide polymorphism array analyses to identify a new PCD-causing gene, *PIH1D3* (PIH1 domain containing 3). The authors showed that PIH1D3 protein is localised to the cytoplasm and is involved in the dynein arm pre-assembly pathway. As a consequence, mutations in *PIH1D3* cause a variable degree of loss of both outer and inner dynein arms; in these patients, high-speed video microscopy of respiratory cilia shows immotile cilia, sometimes associated with cilia with retained but disorganised beating pattern. *PIH1D3*-mutated patients have a typical PCD phenotype and consequently these mutations represent the first reported molecular cause of X-linked, nonsyndromic PCD (mutations in *RPGR* cause syndromic X-linked PCD with retinitis pigmentosa). These findings will improve



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counselling of affected individuals and explain many cases of typical PCD with a suggestive X-linked inheritance pattern.

**Reviewed by:** Maria Elisa Di Cicco (Italy, Assembly 7)

### **Protracted bacterial bronchitis in children: natural history and risk factors for bronchiectasis**

Authors: Wurzel DF, Marchant JM, Yerkovich ST  
*Chest* 2016; 150: 1101–1108

Summary: Protracted bacterial bronchitis (PBB), first described in 2006, is a major cause of chronic cough in children. PBB is characterised by persistent wet cough, response to 2 weeks of appropriate antibiotic therapy and absence of indicators to suggest an alternative cause for cough. PBB and bronchiectasis share many common features, from chronic wet cough to neutrophilic lower airway inflammation and presence of *Haemophilus influenzae*.

161 children with PBB were prospectively recruited to this cohort study. A subset of 106

children was followed for 2 years. Chest computed tomography (CT) was undertaken if clinical features were suggestive of bronchiectasis. Those completing the follow-up were significantly more likely to have had recurrent PBB. 43.5% had recurrent PBB (defined as more than three episodes per year).

CT reconstruction was performed in 25 out of 161 children with PBB. Radiological evidence of bronchiectasis was detected in 13 (8.1%) children and all had mild bronchiectasis. Multivariate logistic regression showed that recurrent PBB status and *H. influenzae* infection were independently associated with bronchiectasis diagnosis.

This is the first prospective, longitudinal cohort study of children with PBB, with evidence of two significant risk factors for development of bronchiectasis: recurrent PBB and the presence of *H. influenzae* infection in the lower airways. Clinicians should be aware about the relationship between PBB and bronchiectasis, and appropriate follow-up measures should be taken in those with risk factors.

**Reviewed by:** Michele Ghezzi (Italy, Assembly 7)

Hot topics are short (approx. 200 words) summaries of recent important articles in respiratory medicine written by Junior ERS members. To become a hot topic author, please contact Aran Singanayagam: e-mail: aransinga@gmail.com