Chronic cough and irritable larynx


Recent guidelines agree that upper airway diseases such as rhinitis and sinusitis, asthma, and gastroesophageal reflux disease (GERD) are the most common triggers of chronic cough (CC). It is presumed that in patients with upper airway diseases cough originates in pharyngo-laryngeal receptors stimulated by the postnasal drip of inflammatory material or made hypersensitive by mucosal inflammation and damage. In asthmatic patients cough is likely to originate from stimulation of intrathoracic airway receptors, and in patients with GERD, it probably originates from stimulation of oesophageal receptors. However, an involvement of upper airway receptors is a possibility in asthmatic patients because rhinitis, sinusitis, or both, are common comorbidities, and in patients with GERD, because the refluxate often reaches the larynx and might go up to the rhinopharynx. Moreover, in asthmatic patients no clear relationship has been demonstrated between cough-receptor sensivity and bronchial responsiveness, and persistence of cough has been reported, even after achieving good asthma control with inhaled corticosteroids (ICSs).

The authors previously found that most patients with upper airway inflammatory disorders and cough have laryngeal hyperresponsiveness (LHR), which is a paradoxical inspiratory vocal cord adduction on histamine inhalation challenge that is consistent with an irritable larynx. Such reflex laryngoconstriction was reflected by a decrease in inspiratory airflow rates, particularly the maximum midinspiratory airflow rate (MIF50). Using MIF50 as the marker of an irritable larynx, the authors subsequently found that LHR was very common in nonasthmatic patients with CC and inflammatory diseases of the upper airway, particularly in those with acute exacerbation of chronic sinusitis. In such patients laryngeal dysfunction reversed after treatment with intranasal corticosteroids and appeared to be sustained by damage of the rhinopharyngeal epithelium.

In this study, patients with CC were recruited and a determination was made whether this was due to rhinitis, sinusitis, asthma or GERD or was unexplained (UNEX). Patients with asthma but no cough were recruited as control subjects. Histamine challenge was performed to assess bronchial and laryngeal thresholds and then treatment was initiated for the respective conditions. The histamine challenge was repeated after a month of treatment and following a week of treatment withdrawal. Patients with unexplained cough were treated with combination rhinitis and reflux medication.

LHR was present in most patients with CC, irrespective of the cause, but was uncommon in asthmatic control subjects without cough. Among patients with GERD, LHR was found in 48 (94%) of the 51 patients with evidence of laryngitis and in none of the 11 patients without laryngeal involvement.

The GERD class was characterised by low risk of having atopy and bronchial hyperresponsiveness (BHR), the UNEX class by low risk of atopy, and both the asthma/CC+ and asthma/CC− classes by increased risk of BHR. The asthma/CC− control class was characterised by low risk of LHR.

After treatment, laryngeal and bronchial thresholds were significantly improved in all the classes, particularly in the perennial rhinitis/chronic rhinosinusitis (PR/CRS) class. Cough was improved or resolved in 105 (95%) of the patients with PR/CRS, in 11 (79%) of the patients with GERD, and in only 18 (36%) of the patients with UNEX cough.

The results of this study indicate that an irritable larynx is very common among patients who present with CC as the main symptom. In fact, most of the 372 patients with CC examined showed LHR, consisting of a dose-dependent decrease in inspiratory flows during histamine challenge. In 164 (44%) patients LHR was the only functional abnormality and would have been missed by recording forced expiratory volume in 1 sec (FEV1) as the response variable.

The authors conclude, 'our findings indicate that patients who present with CC often have an irritable larynx, which can be revealed by means of histamine inhalation challenge as a dose-dependent decrease in maximum inspiratory airflow rates. Such LHR is sustained by inflammation and damage of the upper airways but might also be an expression of idiopathic sensory neuropathy. The evaluation of LHR might help in the assessment of CC to identify the involvement of upper airway receptors. In patients with GERD-associated cough, LHR suggests the presence of laryngitis possibly related to laryngopharyngeal reflux. The diagnosis of irritable larynx might also help in improving cough treatment. In patients with asthma-associated cough, LHR points to coexistent rhinitis or rhinosinusitis, suggesting an important therapeutic target that is often disregarded by pneumologists. Our findings indicate also that an irritable larynx might sustain bronchoconstrictive reflexes in patients with rhinitis or rhinosinusitis and no asthmatic symptoms. In these patients BHR might reverse with the sole treatment of upper airway disease, with no need for ICSs, which would be preferred only when symptoms and airway hyperresponsiveness persist.'

Airway microbiota and bronchial hyperresponsiveness in patients with suboptimally controlled asthma


The presence of specific bacterial species in the lower airways has previously been associated with asthma. Improvement in lung function can follow the use of...
macrolide therapy. However, given that the vast majority of bacteria are un culturable and that they exist in polymicrobial communities on other human mucosal surfaces, relationships between the airway microbiota and clinical features of asthma are relatively unexplored. Huang et al. investigated the microbiota present in bronchial epithelium-protected brush specimens from suboptimally controlled asthmatic patients using inhaled corticosteroids and healthy subjects. Bacterial communities were profiled by using a high-density phylogenetic microarray based on the 16S ribosomal RNA gene. The number of different bacterial types detected in the bronchial microbiome was far greater than previously recognised. Moreover, compared with healthy subjects, asthmatic patients exhibited significantly higher bacterial burden and diversity in their airways; airway microbiota diversity was significantly correlated with the degree of airway hyperresponsiveness. More specifically, the relative abundance of particular phylotypes, including members of the Comamonadaceae, Sphingomonadaceae, Oxalobacteraceae, and other bacterial families were highly correlated with the degree of bronchial hyperresponsiveness. The study's findings illustrate that the composition of bronchial airway microbiota is associated with the degree of bronchial hyperresponsiveness among patients with suboptimally controlled asthma and highlight the potential clinical and pathophysiological relevance of the bronchial microbiome in asthmatic patients. Further structural and functional studies of the airway microbiome, especially in asthmatic patients naive to inhaled corticosteroid treatment, might prove key to understanding its contribution to asthma pathogenesis.

One hundred years of allergen immunotherapy

The January 2011 edition of JACI celebrates 100 years of allergen immunotherapy. This takes the form of a supplement booklet that is packed full of the latest information concerning all aspects of allergen immunotherapy. Further, the Journal contains additional articles, clinical reviews and editorials on this subject. The editorial by Stephen Durham and Donald Leung reviews historical milestones of allergen immunotherapy. One hundred years have passed since Leonard Noon made his original observation (published in The Lancet) that prophylactic inoculation with grass pollen extract in patients with hay fever resulted in effective desensitisation, as shown by a decrease in immediate conjunctival sensitivity to grass pollen. The first double-blind controlled trial of pollen immunotherapy was published by Frankland and Augustin in 1954 and established a firm scientific foundation for the further development of allergen immunotherapy. The practice in the USA of multiple-allergen immunotherapy is in contrast to the usual practice in Europe. After the first double-blind trial in mite-sensitive adults, sublingual immunotherapy has emerged as an effective alternative to the subcutaneous route and is widely practised in Europe. Unlike subcutaneous immunotherapy, sublingual immunotherapy might act primarily through its effects on oral Langerhans cells. Several published definitive trials of grass pollen tablets have confirmed their efficacy, safety, and tolerability in both adults and children. The sublingual route appears safe and has broadened the availability of immunotherapy to include self-administration.

The demonstration of clinical and immunological tolerance to seasonal pollens (persistence of benefit for several years after discontinuation of immunotherapy) and the possibility that pollen immunotherapy might reduce progression to asthma and prevent new sensitisations are also reviewed. Lastly, novel approaches and future directions are discussed.

The role of penicillin in benign skin rashes in childhood: a prospective study based on drug rechallenge


This interesting article from Jean-Christoph Caubet et al. from Geneva, Switzerland tackles the common problem of what penicillin (β-lactam) allergy is rather than a viral/bacterial exanthem.

Eighty-eight children who presented with delayed-onset urticarial or maculopapular rashes were enrolled and evaluated for allergic and infectious causes. All children were also subjected to an oral challenge test (OCT) some months after the initial presentation. The results are very interesting in that a rash was reproduced in only 6 of 88 challenged patients. These findings are highly relevant to clinical practice because most of these patients would otherwise have been falsely labelled 'penicillin-allergic'. The vast majority of children with a negative subsequent OCT tested positive for viral infection, mostly enteroviruses (picornavirus), at their initial visit. The authors conclude that ‘in children who present with a benign skin rash in the absence of any other symptom while treated with β-lactams, we suggest performing a 1-dose initial OCT under medical supervision, followed by standard β-lactam dosing for 48 hours at home. ... By challenging all patients with benign rashes, we will avoid denying future use of β-lactam antibiotics to a large number of patients who would otherwise have been diagnosed with penicillin allergy.’

Guidelines for the diagnosis and management of food allergy in the United States: summary of the NIAID-sponsored expert panel report


This article is essentially a mini-textbook of food allergy. It is an essential compendium for everyone involved in this field and will be invaluable to any doctor studying this topic. It is far too comprehensive to reproduce here; this serves as an announcement to its existence and value.