

## ADENOIDS DURING CHILDHOOD: THE FACTS

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Adenoids are constantly exposed to viral and bacterial agents as well as to allergens. They play a major role in the upper airways immunity, being effector organs in both mucosal-type and systemic-type adaptive immunity. Because of both their immunological function and their specific location, adenoids are considered to be as reservoirs of viruses and bacteria. Reiterative infections may therefore contribute both to Eustachian tube dysfunction and to tissue hypertrophy. Nasal endoscopy is a key diagnostic tool to detect both adenoid hypertrophy and adenoiditis. Moreover, such a procedure may be very helpful in detecting bacterial biofilms that could justify the concomitant presence of recurrent episodes of otitis media, chronic and occult sinusitis in children. Even though the connection between allergies and adenoidal diseases is not completely clear, allergic diseases cause an inflammatory state that influences adenoidal tissue as well, configuring the picture of allergic adenoiditis, a condition in which adenoid tissue exhibit numerous IgE positive mast cells. Several studies are still needed to better understand the relationship between allergies and infections and the influence they play on adenoids during childhood.

## NASAL DISEASE AND ASTHMA

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The nose plays a primary role within the airways, working as “a filter and air-conditioner”, together with other important functions. Thus, it is not surprising that nasal diseases are associated with several other comorbidities, including both upper and lower airways, such as bronchial hyperresponsiveness (BHR) and asthma. Several studies have investigated the relationship existing between the upper and the lower airways and new insights are rising. Nevertheless, some uncertainties still remain, mainly because nasal disorders are quite heterogeneous, overlapping (i.e. rhinitis-rhinosinusitis-sinusitis, acute or chronic, allergic or non-allergic) and difficult to diagnose, so that, frequently, many studies don't differentiate between the various conditions. For this reason, the purpose of this review is to systematically analyze present epidemiological, pathophysiological and clinical data on the relationship between nasal diseases and asthma, splitting up three main conditions: allergic rhinitis, chronic rhinosinusitis and nasal polyposis.

## ADIPOKINES AND THEIR ROLE IN ALLERGIES

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Both allergic disorders and obesity keep increasing in industrialized countries. Even though a strong association between obesity and allergy-related diseases has been reported in several studies, no published data show a scientific and firm link in-between the two conditions. In general, obesity and weight gain have been associated with an increased risk of asthma and allergic rhinitis. Asthma, allergic rhinitis and obesity have a common inflammatory pattern that could therefore justify their association. In fact, the chronic inflammation that characterizes the increase in white adipose tissue typically pushes the immune system toward a Th2 pattern. Such a polarization might, consequentially, worsen a pre-existing allergic disease or even stimulate the evolution from a sensitization to a respiratory form of allergy. Several studies have been published on the role of different adipokines on allergic diseases. We focus our review on the role of adipokines on asthma and allergic rhinitis.

## FEF<sub>25-75</sub> MIGHT BE A PREDICTIVE FACTOR FOR BRONCHIAL INFLAMMATION AND BRONCHIAL HYPERREACTIVITY IN ADOLESCENTS WITH ALLERGIC RHINITIS

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Allergic rhinitis and asthma are closely associated. Bronchial hyperreactivity (BHR) is a pathophysiological characteristic of asthma. Allergic inflammation is characterized by eosinophilic infiltrate and may be indirectly assessed by exhaled nitric oxide (FeNO). Forced expiratory flow between 25% and 75% of vital capacity (FEF<sub>25-75</sub>) may predict BHR in adult patients with allergic rhinitis. The aim of this study was to evaluate the presence of BHR in a large group of adolescents with allergic rhinitis and whether FEF<sub>25-75</sub> might be related with BHR and FeNO. Methods 150 adolescents with allergic rhinitis were enrolled. Clinical examination, skin prick test, spirometry, methacholine challenge, and FeNO were performed in all patients. Results Severe BHR is quite frequent in allergic adolescents. Impaired FEF<sub>25-75</sub> values (such as  $\leq 65\%$  of predicted) constitute a relevant predictive factor for severe BHR (OR 4.4). FeNO levels were significantly related with BHR. Conclusion This study provides evidence that impaired FEF<sub>25-75</sub> values might predict severe BHR and BHR is related with FeNO in adolescents. Therefore, BHR should be suspected in adolescents with low FEF<sub>25-75</sub> values.

## BODY MASS INDEX IS RELATED WITH BRONCHIAL FUNCTION AND REVERSIBILITY IN CHILDREN WITH ALLERGIC RHINITIS AND ASTHMA

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Several studies have outlined a possible relationship between an increased body mass index and respiratory allergic diseases, such as asthma and rhinitis. The aim of the study was to analyse the relationship between BMI and lung function, including bronchodilation test, in allergic children. The study included 153 children (103 males, mean age 12.8 years) with allergic rhinitis and mild asthma. All subjects were evaluated performing skin prick test, spirometry, and bronchodilation test. BMI values were in the normal range as well as lung function. BMI significantly related with FEV<sub>1</sub>, FVC values and FEV<sub>1</sub>/FVC ratio both before and after bronchodilation. In conclusion, this study provides the first evidence that BMI is negatively related with bronchial reversibility in children with allergic rhinitis and asthma. As reversibility is related with bronchial inflammation, this finding might underline a link between overweight and allergic inflammation.

## ALLERGIC RHINITIS AND QUALITY OF LIFE IN CHILDREN

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Allergic rhinitis is a respiratory disease caused by an inflammatory process related to IgE mediated reaction versus allergens to which the subject is sensitized. Allergic rhinitis is not an isolated disease because the nasal mucosa inflammation involves paranasal sinuses and lower airways, thus worsening the asthmatic symptoms. Recently, a new classification of allergic rhinitis based on the duration and severity of clinical symptoms has been proposed. This classification takes into consideration both the quality of life and the possible impact of the symptoms on school, work and free-time activities. Children's quality of life is severely compromised by frequent night awakenings, easy fatigue, defects of language and irritability, which can have a negative influence on learning abilities. Allergic rhinitis has a negative impact on the quality of life of the whole family because it can cause interference on social life, and financial costs.

## FRACTIONAL EXHALED NITRIC OXIDE MEASUREMENTS IN RHINITIS AND ASTHMA IN CHILDREN

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Exhaled nitric oxide (FeNO) is considered a good noninvasive marker to assess airway inflammation in asthma and allergic rhinitis. In asthma, exhaled NO is very useful to verify adherence to therapy, and to predict upcoming asthma exacerbations. It has been also proposed that adjusting anti-inflammatory drugs guided by the monitoring of exhaled NO, could improve overall asthma control. Other studies showed increased FeNO levels in subjects with allergic rhinitis.

## TLR2 AND TLR4 GENE POLYMORPHISMS AND ATOPIC DERMATITIS IN ITALIAN CHILDREN: A MULTICENTER STUDY

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**Background** Genetic factors have an important role in atopic dermatitis (AD) predisposition. Toll like receptor (TLR) are important mediators between environment and immune system. There are inconsistent studies about TLR polymorphisms in AD. **Objective** This study examined whether single nucleotide polymorphisms (SNPs) in the genes for TLR2 and TLR4 could be associated with the AD phenotypes and with its clinical severity in a large group of Italian children. **Methods** 187 children with AD and 150 healthy children were recruited. AD severity was assessed by SCORAD. TLR2 (A-16934T and R753Q polymorphisms) and TLR4 (D299G and T399I SNPs) were genotyped by PCR-RFLP. **Results** The frequency of the R753Q was significantly higher in AD children (16.0%) compared with controls (6.0%,  $P=0.004$ ; OR 2.99, 95%CI 1.39-6.41; RR 1.46, 95%CI 1.14-1.69). AD patients a significantly different frequency of the D299G SNP (14.9%) in comparison with the controls (6.6%,  $P=0.01$ ; OR 2.46, 95%CI 1.17-5.17; RR 2.24; 95%CI 1.15-4.45). **Conclusion** Children with AD may have a distinct genotype and the TLR-2 R753Q SNP was prevalent in a subset of patients with AD characterized by a more severe clinical picture.

## GENE-ENVIRONMENT INTERACTION IN CHILDHOOD ASTHMA

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The importance of early life environmental influences on the etiology of asthma is implied by the observed geographic and temporal variation in the prevalence of the disease among children. There is evidence pointing to the role of exposure to allergen, various aspects of diet and hygiene-related factors in the etiology of asthma. There is also evidence that heritable factors influence the impact of hygiene-related exposures on the risk of having asthma. A number of important gene-environment interactions have been identified. These interactions point to the biology of environmental exposures as the involved genetic variation is suggestive of certain underlying mechanisms. Polymorphisms within genes coding for the toll-like receptor-lipopolysaccharide (TLR-LPS) signaling pathway may underlie variations in effects of hygiene-related exposures, including specifically endotoxin, on the risk of developing allergic sensitization and allergic disease. This review presents recent findings illustrating the role of gene-environment interactions in childhood asthma susceptibility.

## ADENOID ASSESSMENT IN PAEDIATRIC PATIENTS: THE ROLE OF FLEXIBLE NASAL ENDOSCOPY

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Adenoid hypertrophy is the most common cause of nasal obstruction in paediatric patients. Over the years, various methods to assess the adenoid size were proposed such as the posterior rhinoscopy and the radiological examination of the nasopharynx. Nasal endoscopy was introduced for children in the 80's, and nowadays this is a known and diffuse method in routine practice. The purpose of this article is to describe the personal experience in the assessment of the adenoid size in children, with a particular regard to the flexible nasal endoscopy, and to analyse the literature reports. The personal technique is described in performing nasal endoscopy in paediatric patients, reporting advantages and possible disadvantages of the procedure. A retrospective analysis was conducted on 6036 children since 1999 to 2010. In most cases children fully collaborated to complete the exam. No major or minor complications (such as nose bleedings or other traumatic injuries) were observed. No topical intranasal decongestant, local or general anaesthesia were used in our series. In our opinion, nasal endoscopy in children is a reliable, safe, accurate, easily tolerated and dynamic diagnostic method to assess the adenoid size.

## THE EVOLUTION OF THE ADENOIDECTOMY: ANALYSIS OF DIFFERENT POWER-ASSISTED TECHNIQUES

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Techniques and instruments for adenoidectomy have considerably changed over the years. With the introduction in Otolaryngology of power-assisted instruments for endoscopic sinus surgery, the classic adenoidectomy performed with curette or adenotome has evolved, with an improved patients' outcome and a better satisfaction of the surgeon. The purpose of this article is to describe and critically analyze the literature reports about different methods of power-assisted adenoidectomy. We performed a literature search (Medline) to identify all available reports. We discussed the surgical techniques and reviewed advantages and disadvantages of each method. The techniques can be schematically divided in non-endoscopic, usually performed with a laryngeal mirror, and endoscopic-assisted. The endoscopic control can be obtained either trans-nasally or trans-orally, as well as the microdebrider can be inserted in the nasal cavity or maneuvered through the oral cavity. Some authors reported the usage of the power-assisted instruments in performing the entire adenoidectomy; while, according with other authors, the microdebrider can be used as a step of the surgical procedure, for a combined adenoidectomy. In conclusion, all the methods seem to be safe and effective, and the personal experience of the surgeon should guide the choice of the instruments. However, we personally consider the endoscopic techniques as the most suitable, and among these the Transoral Endonasal-Controlled Combined Adenoidectomy (TECCA) should be considered as the most ergonomic technique to perform a power-assisted adenoidectomy.

## INHALATION THERAPY IN ASTHMATIC AND NOT ASTHMATIC CHILDREN

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The use of inhaled aerosols allows selective treatment of the lungs directly by achieving high drug concentrations in the airway while reducing systemic adverse effects by minimizing systemic drug levels. Aerosol drug delivery is painless and often convenient, but the proliferation of inhaler devices has resulted in a confusing number of choices for clinicians who are selecting a delivery device for aerosol therapy. There are advantages and disadvantages associated with each device category. Several factors can guide clinicians to choose a device for a specific patient. This choice has to be tailored according to the patient's needs, situation and preference. Whatever the chosen inhaler, inhaler technique is the critical factor in the correct use of delivery devices and patient education has a key-role for improving technique and compliance.

## SPECIFIC IMMUNOTHERAPY IN CHILDREN: THE EVIDENCE

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**Specific immunotherapy (SIT) is the only treatment able to not only act on the symptoms of allergy but also act on the causes. At present, SIT may be administered in two forms: subcutaneous (SCIT) and sublingual immunotherapy (SLIT). SCIT represents the standard modality of treatment while SLIT has recently been introduced into clinical practice and today represents an accepted alternative to SCIT. The main advantages of SIT that are lacking with drug treatment are long-lasting clinical effects and alteration of the natural course of the disease. This prevents the new onset of asthma in patients with allergic rhinitis and the onset of new sensitizations. The mechanism of action of both routes is similar; they modify peripheral and mucosal Th2-responses into a prevalent Th1-polarization with subsequent reduction of the allergic inflammatory reaction. Both have long-term effects for years after they have been discontinued, although for SLIT these evidences are insufficient To date several guidelines have defined indications, contraindications, side-effects, and clinical aspect for SCIT and SLIT. New forms of immunotherapy, allergen products and approaches to food allergy and atopic eczema represents the future of SIT..**