

## TRYPYPTASE AND HISTAMINE MAY SUPPORT ORAL FOOD CHALLENGE IN THE DIAGNOSIS OF ALLERGY

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Allergen-specific immunoglobulin E (IgE) reactions lead to acute degranulation of mast cells and basophils and release of stored mediators, particularly tryptase and histamine, which can be measured *in vitro* after reactions. The aim of this study was to investigate the utility of serum tryptase and plasma histamine during oral food challenge (OFC) in 103 children with suspected food allergy, in order to support the diagnosis of a IgE-mediated reaction. Blood samples for serum tryptase and plasma histamine were collected before the OFC and after the onset of allergic symptoms or after 60 minutes from test completion. Serum tryptase and plasma histamine were measured by a fluoroenzyme immunoassay (ImmunoCAP; ThermoFisher, Uppsala, Sweden) according to the manufacturer's instructions. A correlation between serum tryptase and plasma histamine distributions was observed after OFC ( $p = 0,0035$ ). A correlation was also observed for both serum tryptase and plasma histamine before and after OFC ( $p < 0,0001$ ). Subjects with positive response to OFC had significantly higher values ( $p = 0,0375$ ) of serum tryptase compared to subjects with negative response. The plasma histamine distribution showed a significant difference between measurements before and after OFC, both in the complete population ( $p < 0,0001$ ), and considering the response (negative OFC:  $p < 0,0001$ ; positive OFC:  $p = 0,0181$ ). The diagnostic work-up of IgE-mediated food allergy may include determination of serum tryptase and plasma histamine, in order to support the results of OFC. These markers are strongly related to the same IgE-mediated mechanism and, as they can be both easily measured, can confirm the allergic nature of a reaction in the real-life setting of food allergy.

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## ALMOND MILK: A POTENTIAL THERAPEUTIC WEAPON AGAINST COW'S MILK PROTEIN ALLERGY

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Food allergy is defined as an adverse health effect arising from a specific immune response that occurs reproducibly following exposure to a given food. Cow's milk protein allergy results from an immunological reaction to one or more milk proteins. The principle key in the treatment of cow's milk protein allergy is the dietary elimination of cow's milk protein. Although hydrolyzed and elemental formulas are appropriate replacements, other milk products, including almond milk adequately integrated, could be administered. Here, in the light of encouraging results from our study, we focused on the anti-inflammatory and anti-oxidant properties of almond milk and we also believe that almond milk might be considered as a potential alternative in cow's milk protein allergy treatment.

**ATOPIC DERMATITIS: EXPRESSION OF IMMUNOLOGICAL IMBALANCE**

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**Atopic dermatitis is a chronic relapsing-remitting inflammatory skin condition, characterized by a skin barrier dysfunction resulting in epidermal damage and altered permeability to allergens and microbes. Although pathogenesis of atopic dermatitis is complex and still not fully understood, it has been hypothesized that genetic predisposition, environmental factors, and skin barrier dysfunction are involved. Innate and adaptive immune system has also a pivotal role in the development, maintenance and flare-up of atopic dermatitis. The immune-pathogenesis of atopic dermatitis is determined by the impairment of different T helper cells, of their cytokine secretion profiles as well as of their specific receptor. In this review, we focus on the current knowledge of the etiopathogenetic pathways of atopic dermatitis in relationship to the critical role of the innate and adaptive immune system, providing an unifying view.**

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## ATOPIC DERMATITIS: IS THERE A ROLE FOR PROBIOTICS?

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**Atopic dermatitis (AD) is a chronic inflammatory skin disease that commonly presents during early childhood. In the last decades the prevalence of AD has increased, especially in western societies. This frequently relapsing inflammatory condition has a strong impact on the quality of life of patients and families. The recent advances in the understanding of this disease have paved the way for the development of new strategies for the prevention and treatment of AD. Among the new therapeutic options, there is increasing interest in the potential benefit of probiotic supplementation. It has been widely demonstrated that the human microbiota plays a fundamental role not only in the maintenance of intestinal homeostasis through the interaction between microorganisms and the innate immune system, but also in the microbiota-mediated development of adaptive immunity. In addition, several studies have demonstrated that probiotics are able to influence the composition of gut microbiota and may exert immunomodulatory effects. According to these promising results, the possible application of probiotics in the therapeutic management of allergic diseases has been investigated in many studies. In particular, a considerable body of literature has been published analyzing the effects of probiotics on patients with AD. In order to shed light on frequently conflicting results, we reviewed the data regarding the application of probiotics in AD, with the aim to provide a state-of-the-art assessment of the most important studies exploring the role of probiotics both in the prevention and treatment of AD.**

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## CHILDHOOD IDIOPATHIC NEPHROTIC SYNDROME AND ATOPIC DISEASES: IS THERE A RELATIONSHIP?

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Nephrotic syndrome is a condition of massive proteinuria that leads to hypoalbuminaemia and oedema. In the pediatric age, the most common form of nephrotic syndrome is childhood idiopathic nephrotic syndrome (CINS). Although the etiological mechanisms underlying CINS are still unclear, the disease is considered to be immune-mediated. Several studies have previously reported a possible association between CINS and atopy, with the latter defined as abnormal immunoglobulin-E response on the background of a T-helper 2 (Th2)-driven immune system. In fact, both experimental and clinical studies have suggested that idiopathic nephrotic syndrome can be associated and/or triggered by a wide array of atopic diseases, though this remains a highly controversial topic. Exposure to inhalant-allergens (and/or introduction of food-allergens) has been previously correlated with the onset and/or the relapse of CINS in some children and a significant worse response to steroid therapy has been also described in reports of CINS associated to concomitant atopic diseases. In this review, we analyzed previous studies with the aim to clarify, basing on the existent literature, the association between atopy and idiopathic nephrotic syndrome. Additionally, we also speculated on the underlying immunological pathways that could potentially make some children prone to both CINS and atopic diseases.

## CYSTIC FIBROSIS AND ANTIBIOTIC HYPERSENSITIVITY: PRESENT KNOWLEDGE AND PRACTICAL APPROACH

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Cystic fibrosis is one of the most common fatal genetic diseases (1 in 2500 births). The defect causing the disease is localized on the 7q31 gene, which codifies for the CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) transmembrane protein. CFTR is a chloride channel localized on the epithelial cells of the mucosa of the respiratory tract, pancreatic ducts, biliary tree, intestine, vas deferens, and sweat glands. More than 2000 different mutations are currently known; some are prominent or relatively frequent, ranging from one population to another. The most frequent complications of cystic fibrosis are those affecting the bronchial tree. Patients suffer from recurrent lung infections, which involve a progressive loss of lung function. The pulmonary infections are frequent or chronic and limit the quality of life of patients. In addition to being enormously exposed to antibiotics, they have many more opportunities to develop hypersensitivity reactions to these molecules. Only a complete allergy work-up with a detailed analysis of the clinical history, skin tests and provocation test can show if the patient has actually experienced an allergic hypersensitivity reaction. Desensitization is to be considered as a treatment that may help patients benefit from antibiotic treatment in those cases in which they have a proven allergy to a certain molecule.

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## EMERGING AND FUTURE THERAPIES FOR ALLERGIC RHINITIS

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**Allergic rhinitis (AR) is one of the most common diseases and represents a global health problem, currently affecting up to 30% of the general population, with a continuously increasing prevalence and significant comorbidities and complications. To date, the mainstay of current treatment strategies of AR includes allergen avoidance, pharmacotherapy and allergen-specific immunotherapy, as defined by Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines for both adults and children. The aim of this review is to provide an update on all emerging and future therapeutic options for the treatment of AR.**

## EXHALED BREATH TEMPERATURE IN ASTHMATIC CHILDREN

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**Asthma is characterized by chronic inflammation of airways. Currently, no traditional method allows an easy daily evaluation of the degree of airway inflammation. Measuring inflammatory biomarkers in the breath is a very attractive approach to monitor asthma inflammation. In recent years, the measurement of exhaled breath temperature (EBT) has been proposed as a method capable of detecting the inflammatory status of the airways. The objective of this study is to strengthen the role of EBT in the diagnosis and monitoring of asthma. The study sample was represented by a group of 40 patients, of both sexes, aged 6-15 years. The elective criteria for submitting patients to EBT determination were abstaining from drugs in the preceding 24 h, fasting for at least 2 h, physical resting for at least 30 minutes, a body temperature between 35-37°C. The temperature in the room of the surveys ranged from 18 to 25°C. The EBT values of asthmatic patients were higher [(median (IQR): 29.77°C (30.67°C to 29.38°C) range 28.46°C min-max 34.78°C] than those of non-asthmatic ones (median (IQR): 28.22°C (29.09°C-27.7°C), range 27.09°C min-max 30.07°C) and this difference was highly significant ( $p < 0.001$ ). Furthermore, no significant difference was found between the EBT values of the following groups of patients: those exposed and not exposed to passive smoking, those receiving and not receiving leukotriene drugs, those receiving and not receiving specific immunotherapy, monoallergic patients and poliallergic ones, those sensitized and not sensitized to house dust, perennial allergic patients and seasonal allergic ones. In addition, the evaluation of the correlation of EBT values with body temperature ( $r = 0.119$ ,  $p = 0.464$ ) and ambient temperature ( $r = -0.304$ ,  $p = 0.057$ ) did not show any significant correlation. Finally, no statistically significant correlation was demonstrated between EBT values and FEV1 ( $r = -0.055$ ,  $p = 0.81$ , Fig. 4). In conclusion, the data of the present study further support the hypothesis that EBT can be considered a good method for monitoring asthma.**



## HIGH-MOBILITY GROUP BOX 1 IN ALLERGIC AND NON ALLERGIC UPPER AIRWAY INFLAMMATION

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**High mobility group box 1, an evolutionary ancient protein conserved in the eukaryotic kingdom, exerts intra- and extra- cellular functions, orchestrating a homeostatic defensive response in challenged tissues. Its action associated with various inflammatory cells is essential for the occurrence, progression, and persistence of asthma, rhinitis, and nasal polyposis. The recent discovery of High mobility group box 1, as a critical mediator of inflammation, stimulated an increasing interest in the field of inflammation research, suggesting new therapies for atopic and non-atopic inflammatory processes.**

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## ALLERGIC RHINITIS AND ADENOID HYPERTROPHY IN CHILDREN: IS ADENOIDECTOMY ALWAYS REALLY USEFUL?

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Allergic rhinitis (AR) and adenoid hypertrophy (AH) are common in children and are often associated with each other. Recent studies have shown improvement of respiratory symptoms and reduction in the adenoid volume after anti-allergic medical therapy (intranasal corticosteroids, antihistamines). The aim of our retrospective study is to evaluate the effectiveness of adenoidectomy on respiratory symptoms in pediatric patients with AR. We recruited 404 pediatric patients with AR, and we divided them into 4 groups (1. intermittent-mild rhinitis; 2. intermittent-moderate/severe rhinitis; 3. persistent-mild rhinitis; 4. persistent-moderate/severe rhinitis), using ARIA classification. For each patient we evaluated: age at onset of AR; family history of allergy; the presence of other allergic diseases; serum total IgE values; skin prick test (SPT) results; presence of AH evaluated by rhino-laryngeal fibroscopy; adenoidectomy and its efficacy on respiratory symptoms. Our data show an association between AR and AH: 90 of 404 (22%) children with AR had AH of a degree greater than 2nd. A significant percentage (80%) of children suffering from AR did not present satisfactory benefits from adenoidectomy. They reported persistence or recurrence of rhinitic symptoms after surgery or only partial benefits, especially of recurrent respiratory tract infections and nasal obstruction. The local allergic persistent inflammation on nasal mucosa and adenoid tissue is probably the cause of the unsatisfactory results of adenoidectomy, therefore surgery can not be the first therapeutic step for these children. It is important to extinguish the local inflammation by medical anti-allergic therapy to obtain improvements of nasal symptoms and to prevent adenoid regrowth.

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## SERUM IMMUNOGLOBULIN IgE IN A PEDIATRIC POPULATION: A RETROSPECTIVE ANALYSIS

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Allergic sensitization is mediated by immunoglobulin E (IgE) and an increase of their total value is frequently used to complete a correct diagnosis of atopy. Serum IgE may be considered a typical biomarker for the allergic phenotype. The aim of this study was to evaluate total serum IgE, according to sensitizations, and to find a cut off to discriminate between atopic and non-atopic subjects. Seven hundred and ninety-five patients were enrolled in this study. Serum levels of total IgE were measured by a fluorescence immunoassay (ImmunoCAP; ThermoFisher, Uppsala, Sweden) while specific IgE levels were measured by immunofluorometric assay (ImmunoCAP; ThermoFisher, Uppsala, Sweden). Both tests were expressed in kU/L, according to manufacturer's instructions. Results: A difference for total IgE, according to the gender, has been found ( $p = 0,0012$ ) with higher values for males than for females. A correlation has been found between total IgE and specific IgE, even distinguishing the population in sensitized and non-sensitized. A statistically significant difference has been found according to the presence or the absence of sensitization ( $p < 0,0001$ ) and also considering mono-sensitized and poly-sensitized patients ( $p < 0,0001$ ). ROC analysis has been performed to define a cut off for total serum IgE, according to sensitization and to the type of sensitization (mono-sensitization or poly-sensitization). Finally multiple regression models have been performed to describe total IgE response (positive or negative) and to predict total IgE values. Since clinical limitations are well known, total IgE provide a useful aid to define atopy, allowing the clinician to carry out further investigations in patients with total IgE values beyond normal limits.

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**MANNITOL BRONCHIAL CHALLENGE TEST IN ASTHMATIC CHILDREN**

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**Bronchial asthma is a chronic inflammatory disease characterized by bronchial obstruction, usually reversible spontaneously or after therapy, bronchial hyperreactivity and accelerated decrease of lung function that may possibly evolve into irreversible obstruction of the respiratory tract. Bronchial provocation tests can be used in order to assess the presence and degree of bronchial hyper reactivity. The recently introduced mannitol powder inhalation indirect test seems to have an interesting and promising role, especially in childhood, because of its high diagnostic specificity, easiness of execution and best standardization. In this study the authors focused on the significance and clinical use of mannitol bronchial challenge test in asthmatic children.**

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## PRIMARY NOCTURNAL ENURESIS IN CHILDREN WITH ALLERGIC RHINITIS AND SEVERE ADENOTONSILLAR HYPERTROPHY: A SINGLE CENTER PILOT STUDY

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Nocturnal enuresis is defined as intermittent urinary incontinence during sleep that occurs at least twice a week for three consecutive months. There is no unifying etiology for nocturnal enuresis in the pediatric population and the disorder is likely to be multifactorial. We aimed to investigate the relationship between primary nocturnal enuresis, allergic rhinitis, and related complications in a paediatric case series from a single Center. We retrospectively reviewed and prospectively followed-up at our Institution (i) 32 children (14 females, 18 males; mean age 6.31±1.21 yrs) affected by allergic rhinitis with adenoidal hypertrophy grade I-II (group A) and (ii) 27 children (11 females, 16 males; mean age 6.52±1.33 yrs) affected by allergic rhinitis with adenoidal hypertrophy grade III-IV (group B). Allergic rhinitis was diagnosed on the basis of (a) typical nasal symptoms due to atopic sensitization (e.g., rhinorrhea, itching, sneezing fits, and nasal congestion and obstruction) and (b) positive skin prick testing and/or increased level of total serum IgE. We identified discrepancies between group A and group B in terms of risk of primary nocturnal enuresis. In fact, only 1 child of group A (3.12%) reported uncomplicated primary nocturnal enuresis; conversely, 6 children of group B (22.22%) showed a history of uncomplicated primary nocturnal enuresis ( $p=0.040$ ). There was no statistically significant difference between the two groups in terms of atopic sensitization and serum total IgE levels ( $p=0.43$ ). Allergic rhinitis may potentially influence the onset and the natural history of nocturnal enuresis in some children. Children with allergic rhinitis and more severe respiratory manifestations, seem to be more prone to developing primary nocturnal enuresis, likely due to potential multi-factorial causes (e.g., sleep disorders, chronic phlogosis, immune deregulation).

## PROBIOTICS AND ALLERGIC RESPIRATORY DISEASES

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**Probiotics are able to restore microbiome and the normal intestinal permeability, improve the immunological function of gut barrier, and reduce the intestinal inflammatory response and the production of pro-inflammatory cytokine characteristics of local and systemic allergic inflammation. Clinical studies have demonstrated the efficacy of probiotics in the treatment of various clinical conditions such as atopic dermatitis and food allergies and in the primary prevention of atopy. Recent studies have shown that oral administration of certain probiotic exerts therapeutic effects in the treatment of allergic respiratory diseases such as asthma and rhinitis.**

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## SAFETY AND EFFICACY OF SUBLINGUAL SPECIFIC IMMUNOTHERAPY TO HOUSE DUST MITE USING A DIFFERENT DOSAGE: A PILOT STUDY

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The aim of this randomized open study was to evaluate the safety and efficacy of different dosages (2000 UI vs 4000 UI) of sublingual immunotherapy (SLIT) in patients with allergic diseases such as asthma associated to rhinitis and rhinoconjunctivitis sensitized to house dust mites. We enrolled 61 patients with a history of allergic asthma, and a positive skin prick test for *Dermatophagoides (D.) pteronyssinus/farinae*. Patients were randomly assigned to receiving SLIT at dosage of 2000 UI (Group A) or 4000 UI (Group B) maintenance dose. We evaluated: subjective symptoms using a Visual Analogic Scale (VAS), the amount of prescribed symptomatic drugs, bronchial reactivity to methacoline and side effects using a specific questionnaire. A significant improvement in symptoms, assessed by VAS, was observed with both SLIT doses with no significant differences between groups. The provocation dose of methacoline inducing a 20% fall of FEV1 significantly increased after 12 months only in the 4000 UI dose group. In conclusion, both monomeric allergoid dosages of SLIT (2000 UI and 4000 UI) are a safe and efficacy option to reduce symptoms in patients with allergic asthma caused by house dust mites. Moreover, both dosages are efficacious even to protect against airway reactivity but it seems that monomeric allergoid of SLIT at higher dosage (4000 UI) is better than at the lower dosage (2000 UI).

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## RELATION OF BODY MASS INDEX WITH IgE LEVELS, ALLERGIC SENSITIZATION AND LUNG FUNCTION IN ASTHMATIC CHILDREN: OUR EXPERIENCE AND REVISION OF LITERATURE

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In recent decades, there has been an increase in the prevalence of asthma and obesity in pediatric age. In this regard several studies have provided controversial data to demonstrate the link between Body Mass Index (BMI) and asthma, both in adults and in children. In this prospective study we evaluated the relationship between body mass index value, total IgE immunoglobulin E levels, skin prick test (SPT) sensitization and lung function in children affected by asthma. According to the analysis of data on the comparison of normal-weight patients versus overweight/obese patients, there was no significant difference in the values of FEV<sub>1</sub> (86%±12 vs 90% ± 19), FVC (81% ± 11 vs 88% ± 18), skin prick tests (22.72% vs 36.66%) and total IgE values (192.22±368.28 vs 503±914.04). We carried out a sub-analysis to study the difference between three groups of patients: normal weight, overweight and obese. Obese patients showed higher total IgE values than normal-weight patients with a statistically significant difference. Conversely, there was no significant difference between the normal weight group and the obese group in the respiratory function tests and the SPT. Moreover, we found a higher value of total IgE in female overweight/obese compared with normal weight, while there was no significant difference in relation to parameters of lung function and SPT. However, the same analysis in the male sample did not show any statistically significant difference. This study confirms the higher incidence of atopy in obese children, especially in female gender, but not a direct relationship with either allergens sensitization or abnormal lung function.

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## PROBIOTICS AND INFLAMMATORY BOWEL DISEASES

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**Intestinal microbiota is composed by symbiotic innocuous bacteria and potential pathogens also called pathobionts. Even if the mechanism of action of intestinal bacteria remain still unknown, specific microbial species seem to have important role in the maintenance of immunological equilibrium in the gut through the direct interaction with immune cells. Some studies have found a dysregulated interaction between the intestinal bacteria, the gut barrier, and the intestinal associated immune system in Inflammatory Bowel Disease (IBD) patients and in the pathogenesis of these pathologies. In IBD patients some Butyrate producing bacteria, as Faecalibacterium Prausnitzii, are under represented and this could be related with their chronic inflammatory state.**

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**SERUM YKL-40 IN CHILDREN WITH ASTHMA**

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**Asthma is one of the most common chronic diseases in children. To date the diagnosis of asthma is mainly clinical, based on the clinical history, a careful physical examination and lung function tests. However, symptoms are often not specific and lung function tests are not very sensitive. In order to find a solution to this problem new biomarkers of airway inflammation are being developed. YKL-40 is a chitinase-like protein that has a role in the inflammation and tissue remodeling in several human diseases. The aim of this study is to evaluate serum levels of YKL40 in children with intermittent or persistent asthma. We performed a cross-sectional analysis of serum samples from a cohort of patients with asthma and healthy controls. Patients with asthma were stratified according to four levels of asthma severity (mild intermittent, mild persistent, moderate persistent, and severe persistent). The analysis of serum samples was performed with the use of a commercially available enzyme-linked immune-adsorbent assay (ELISA) kit (Quidel). The minimum detection limit of the assay for YKL-40 is 15.6 ng per milliliter (ng/ml). Our data showed that circulating YKL-40 levels are significantly higher in patients with asthma than healthy subjects ( $36 \pm 18.6$  vs  $14.41 \pm 2.88$ ,  $p = 0.001$ ). Furthermore, we found significantly higher values of YKL-40 in both groups of children with intermittent asthma ( $p < 0.001$ ) and persistent asthma ( $p < 0.001$ ) than healthy controls. However, no correlation was found with duration and severity of asthmatic disease ( $r = 0.18$ ,  $p = 0.33$ ,  $r = 0.28$   $P = 0.13$ , respectively). Our data allow us to suggest that YKL-40 represents a useful biomarker of asthma in children with intermittent or persistent asthma.**

**SUBLINGUAL IMMUNOTHERAPY IN CHILDREN: STATE OF ART**

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Allergic immunotherapy (AIT) today represents a therapeutic practice for the treatment of allergic diseases such as rhinitis or asthma and is recognized as the only treatment able to modify the natural history of the disease. Administering gradually increasing doses of the causative allergen, AIT, has the objective of achieving immune tolerance against allergens. One of the administration routes most used in clinical practice is represented by the sublingual route. Current research on sublingual immunotherapy (SLIT) is focused on confirming the efficacy for all the different relevant allergens, on a better definition of allergen extracts and the improvement of their immunological properties and safety, on the identification of best treatment regimens, and on the possibility of extending the clinical indications. The aim of this review is to describe the most recent step in the field of SLIT development.

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**VITAMIN D AND BRONCHIAL INFLAMMATION IN ASTHMATIC CHILDREN**

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The role of the vitamin D in calcium homeostasis and bone metabolism is well known. In recent years it has been recognized that in addition to the traditional functions, vitamin D modulates a variety of processes such as host defense, inflammation and immunity. Epidemiological data indicate that low levels of vitamin D in serum are associated with impaired lung function and increased incidence of inflammatory diseases, infectious diseases and cancer. The authors studied the correlation among vitamin D levels, allergic inflammation, lung function and control of asthma and found a significant decrease of FeNO values ( $p= 0.0018$ ) in children with vitamin D levels  $>30$  ng/ml. These findings confirm that vitamin D plays a major role in bronchial inflammation.

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## SERUM AND BAL YKL-40 LEVELS IN DIFFERENT INFLAMMATORY LUNG DISEASES: AN UPDATE

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**YKL-40 (also called chitinase 3-like-1 or human cartilage glycoprotein 39) is a chitinase-like protein belonging to the family 18 of glycosyl hydrolase (GH18). This protein is involved in the inflammatory process acting as pro-inflammatory cytokine secreted by neutrophils, activated human macrophages, vascular smooth muscle cells and cancer cells. It has been shown that YKL-40 has a role in pathological tissue remodeling and development of fibrosis of several diseases. To date, the biological and pathophysiological function of YKL-40 protein in pulmonary diseases is still unclear. This review focuses on the role of YKL-40 in diagnosis and monitoring of different lung diseases in order to assess whether this protein could be used as biomarker of specific conditions featured by inflammation and fibrosis. A comprehensive review of the literature using PubMed database, with appropriate terms, was undertaken for articles in English published since 1997. The literature search was undertaken in October 2014.**

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## **β2-AGONISTS IN CHILDHOOD ASTHMA**

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**β2-agonists reduce airflow limitation by improving airway diameter as a consequence of a direct action on airway smooth muscle. β2-agonists can be broadly classified according to their duration of action: short-acting β2-agonists (SABAs), including albuterol, terbutaline and fenoterol, have pharmacodynamic half-lives between 2 and 6 h and long-acting β2-agonists (LABAs), including salmeterol and formoterol, require twice daily treatment. SABAs are often used “as needed” for asthma exacerbations and before exercise in the presence of exercise-induced bronchospasm. LABAs provide longer symptom control, which is a particularly useful feature for preventing night-time symptoms. There are two main LABAs, salmeterol and formoterol. This review focused on the recent data published on this topic.**

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**ATOPIC DERMATITIS: MELATONIN AS POTENTIAL TREATMENT**

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**Atopic dermatitis (AD) is a chronic relapsing-remitting inflammatory skin disorder, characterized by a skin barrier dysfunction resulting in epidermal damage and altered permeability to allergens and microbes. Traditionally, the immunological mechanism involving the Th1-Th2 paradigm is considered central in the pathogenesis of AD. However, oxidative stress is, currently, recognized as a fundamental predisposing stimulus for AD. Several therapeutic approaches have been proposed as treatment, including the use of melatonin. This indolamine, through widespread expression and pleiotropic activity of the cutaneous melatonergic system, may counteract environmental and endogenous stressors, regulate the immune response, decrease oxidative stress, and, finally, promote skin integrity. In the light of its pleiotropic effects, melatonin could represent a potential and alternative therapeutic approach in patients with AD.**

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**WALNUT SENSITIZATION IN PEDIATRIC AGE: A PRELIMINARY STUDY**

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**Walnut consumption has recently become a healthy dietary habit worldwide, due to its positive benefits in reducing cholesterol levels and oxidative stress; this has resulted in an increase in individual consumption, global production and risk of developing sensitization and allergy. In general, clinical manifestations of walnut allergy are frequently severe and systemic potentially life-threatening, leading to anaphylaxis both in the pediatric and adult populations. In light of these findings, we performed a preliminary study considering the walnut native allergen and the recombinant Jug r1 in order to evaluate their role in atopic diseases.**