EDITORIAL

INFLAMMATION IN RESPIRATORY ALLERGY TREATED BY SUBLINGUAL IMMUNOTHERAPY

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The most common allergic diseases, such as rhinitis, asthma and atopic dermatitis, are sustained by allergic inflammation, the treatment of which requires anti-inflammatory activity. Among the available treatments, allergen immunotherapy (IT) has a documented impact on allergic inflammation which persists after its discontinuation and modifies the natural course of allergy. The anti-inflammatory effects of IT, and particularly of sublingual IT (SLIT), are based on the ability to modify the phenotype of T cells which, in allergic subjects, are characterized by a prevalence of the Th2 type, with production of IL-4, IL-5, IL-13, IL-17, and IL-32 cytokines. IT-induced changes result in a Th1-type response (immune deviation) related to an increased IFN-gamma and IL-2 production or in a Th2 reduced activity, through a mechanism of anergy or tolerance. It is now known that T cell tolerance is characterized by the generation of allergen-specific Treg cells, which produce cytokines such as IL-10 and TGF-beta with immunosuppressant and/or immunoregulatory activity. Recent studies suggest that the anti-inflammatory mechanism of SLIT is similar to classical, subcutaneous IT, with a prominent role in SLIT for mucosal dendritic cells. The tolerance pattern induced by Treg accounts for the suppressed or reduced activity of inflammatory cells and for the isotypic switch of antibody synthesis from IgE to IgG, and especially to IgG4. Data obtained from biopsies clearly indicate that the pathophysiology of the oral mucosa plays a pivotal role in inducing tolerance to the sublingually administered allergen.
In 1878, Sangster described urticaria pigmentosa for the first time, and in 1887 Unna noted the presence of mast cells in the skin lesion. Mast cells are characterized by metachromatism as demonstrated by the use of basic dyes, such as Giemsa's reagent and toluidine blue. Electron microscopy studies of mast cells in allergic tissue show irregularly shaped cells with long and interdigitating cytoplasmatic villi. In airways, mast cells lie adjacent to nerves, blood vessels and lymphatics, which highlight their pivotal importance in regulating allergic inflammatory processes.

In allergic diseases, activated mast cell synthesizes prostaglandin D2 (first cyclo-oxygenate mediator) which has bronchoconstrictive and vasodilating effects and attracts several leukocytes. It has been found that activated mast cells, challenged with physiological and non-physiological secretagogues, release elevated histamine and tryptase and chymase, leukotrienes B4, C4 and D4, 5-hydroxyeicosatetraenoic acid, PGD2, Platelet Activating Factor (PAF), heparin, and high-molecular-weight neutrophil chemotactic factor and cytokines/chemokines. PGD2 exerts its biological activity through the DP and CRTH2 receptors and their cDNA cloning which were characterized 15 years ago. In this report, we revisited the biological effects of arachidonic acid compounds released by activated mast cells in allergic and inflammatory states.
Chlamydia pneumoniae are Gram-negative intracellular bacteria, responsible for acute upper and lower respiratory tract infections (1). Most respiratory infections appear to be mild or asymptomatic but it can also cause severe clinical disease (2). It has been estimated that C. pneumoniae causes about 6%-22% of community-acquired pneumonia in adults and children, varying with the geographical location and diagnostic methods used (3). Similar to other chlamydia, C. pneumoniae often persists after acute infection, intriguing scientific interest on its possible involvement in chronic respiratory diseases, such as chronic obstructive pulmonary disease and asthma, as well as in chronic non-respiratory diseases such as atherosclerosis (4-6). Transmission is believed to be from person-to-person contact via respiratory droplets (1). Although initially, the bacterium was considered to be a human pathogen, several later studies demonstrated that it could also infect a variety of animal species, including koalas, horses, frogs and reptiles (7).

The objective of the present study is to provide epidemiological data on the age and gender distribution of C. pneumoniae infection in northern Greece. IgG and IgA antibody prevalence were determined, since these two antibody classes have different characteristics, IgA antibodies have not been included in most epidemiological studies. The prevalence of IgG and IgA antibodies to C. pneumoniae was evaluated in a group of an apparently healthy population in northern Greece. Serum samples were obtained over a period of one year (June 2006 to May 2007) from 530 individuals (300 males and 230 females, aged from 1 month to 90 years). The sera were tested for specific antibodies to C. pneumoniae by two commercial methods, an ELISA and a micro-IF assay based on the principles of MIF. The prevalence of IgG and IgA antibodies to C. pneumoniae was 53.2% and 45.9%, respectively, and was found to be unrelated to gender, even in the elderly >61 years old. The IgG antibody prevalence was low in children under 5 years old (7.7%), sharply increased by the age of 20 (40%) and continued to increase, gradually, to reach 80.1% in the elderly. IgA antibodies also increased with similar kinetics to IgG, although at a lower level (3.8-66.1%). Our results show that infection with C. pneumoniae is common in northern Greece. The high prevalence of IgA specific antibodies reported in the present study is due to primary infection at a young age, while in the elderly is probably due to infection or reinfection, although the option of persistence cannot be excluded.
Dopamine, together with other catecholamine such as norepinephrine, is a critical transmitter in sympathoadrenergic terminals. Such terminals lie in close contact with immune cells in lymphoid organs and there is increasing evidence which points to the ability of dopamine to affect immune cell function (1). Dopamine receptors are integral membrane proteins that interact with G proteins to transduce dopamine stimulation into intracellular responses. Dopaminergic neurons in the human central nervous system are involved in the control of motor activity and in emotional and cognitive processes (2). The human genome is known to contain five genes encoding the functional dopamine gene receptors (D1-D5) (3).

There is much evidence which highlights the involvement of the dopamine system in the pathophysiology of schizophrenia. Recently, there have been reports of detected mutations in dopamine gene receptors in genomic DNA of schizophrenia. In this study, we attempt to determine whether there is mutation in encoding dopamine receptor. The PBMC was separated from whole blood by Ficoll-hypaque; the total cellular RNA was extracted and the cDNA was synthesized. This process followed by real-time PCR using primer pairs specific for five dopamine receptor mRNAs and β-actin as internal control. The results show the presence of all types of dopamine receptor types in lymphocytes. The mutational analysis of the obtained PCR products for the respective dopamine receptor fragments were analyzed by sequenced capillary system. The results presented in this study confirm the high frequency of mutations in dopamine gene receptor DRD5 in schizophrenia patients. Mutational amino acid changes in dopamine gene receptors of DR2, DR3, DR4 but not DR1 are also shown. In conclusion, this is the first report of such complete mutational analyses in all dopamine gene receptors. Moreover, we found new mutations and 80% frequency of mutations in DRD5. These data further strengthen the argument for the role of dopamine gene receptor mutations in the pathogenesis of schizophrenia.
RELATIONSHIP BETWEEN RESPONSES TO BRONCHODILATION TESTING AND TO NASAL DECONGESTION TESTING IN PATIENTS WITH ALLERGIC RHINITIS ALONE

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A remarkable relationship exists between upper and lower airways. Bronchial obstruction is a paramount feature of asthma as well as nasal obstruction of allergic rhinitis (AR). This study aims to evaluate the response to both bronchodilation and decongestion testing and their relationships in a large group of patients with moderate-severe persistent AR alone. Two hundred eleven patients with moderate-severe persistent AR were prospectively and consecutively evaluated. Clinical examination, skin prick test, spirometry, bronchodilation test, rhinomanometry, and decongestion test were performed on all patients. Seventeen subjects (8%) did not respond to any of the tests, 55 subjects (26.1%) were responders only to the decongestion test, 31 (14.7%) only to the bronchodilation test, and 108 subjects (51.2%) responded to both these tests. Longer AR duration was significantly associated with positive response to both tests (p<0.01). In conclusion, this study provides the first evidence that patients with moderate-severe persistent AR may frequently show reversibility to both bronchodilation and decongestion tests.
Herpes simplex virus (HSV) infection is one of the most common sexually transmitted viral diseases worldwide. HSV type 2 causes most genital herpes and HSV type 1 is usually transmitted via non-sexual contacts. We studied 109 pregnant women between January 2007 and December 2008, in relation to their age, condom use, number of sexual partners, age at first intercourse, parity and smoking habits. The aim of this study is to evaluate the prevalence of HSV cervical infection and HSV co-infection with other genital microorganisms associated with poor neonatal outcome. Our results show that of the 109 outpatients enrolled, 30% were HSV1 and/or HSV2 positive, of whom 30% were infected with both HSV1 and HSV2, 18% were infected with HSV1 alone and 52% with HSV2 alone. A significant association between HSV1 and HSV2 infection was found, and the prevalence of HSV2 infection in women infected with HSV1 was 63%. The prevalence of HSV1/2 varied in the presence of other vaginal microorganisms but a statistical significant association was not found. This pilot study is probably too small to obtain statistically significant results. Nevertheless, using these observed results, we calculated that about 530 patients with comparable features should be enrolled to detect an increase of 50% in HSV infection due to the presence of other genital infections and potential risk factors.
RECOMBINANT HUMAN DEOXYRIBONUCLEASE TREATMENT IN HOSPITAL MANAGEMENT OF INFANTS WITH MODERATE-SEVERE BRONCHIOLITIS

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Bronchiolitis is the main cause of respiratory insufficiency in infants, characterized by acute inflammation, edema, necrosis of epithelial cells and increased mucus production. Mucus is mainly purulent and consequently rich in DNA, as derived from nuclei of degenerating neutrophils and epithelial debris. The treatment is mainly supportive; bronchodilators and systemic steroids are often used but do not reduce the length of hospital stay. The aim of our study is to evaluate the efficacy of recombinant human DNase (rhDNase), in infants affected by moderate-severe bronchiolitis. In a randomized double-blind placebo-controlled study, twenty-two infants (12 males) under 6 months of age (median age 1.6 months) were enrolled and randomly assigned to receive either nebulized rhDNase or placebo (saline) at a dose of 2.5 ml once a day for three days. All infants were evaluated, based on a clinical assessment score, on admission and four times daily during the hospitalization. Placebo and study groups were sex- and age-matched and were similar in terms of clinical severity on admission. No differences were observed between the two groups of patients with regard to the length of hospitalization and clinical score during the days observed. Two out of four infants, all in the study group, presenting atelectasis on chest radiographs, showed a rapid improvement on the first day. RhDNase is not an effective routine therapy in treating infants hospitalized for bronchiolitis and it is not useful in preventing severe forms of the disease. On the contrary, it may be an effective, safe and cost-benefit treatment only in infants with bronchiolitis and massive atelectasis.
The human body continually tries to preserve a dynamic equilibrium with its environment through the system which regulates the response to any kind of stressor. Many environmental and occupational stressors can affect endocrine and reproductive functions. In this regard, growing scientific evidence supports the hypothesis that such alterations may have serious consequences for these human systems.

The subjects examined in this study were female traffic police in Rome exposed to physical (i.e. noise), chemical (i.e. air pollutants) and psycho-social urban stressors. In our previous studies on traffic police we observed the effects of urban pollutants on the following neuro-immune-endocrine parameters, adrenocorticotropic hormone (ACTH), cortisol (CORT), insulin as indicators of the early neuro-immune-endocrine system response to urban stressors.

EFFECTS ON PLASMATIC ANDROSTENEDIONE IN FEMALE WORKERS EXPOSED TO URBAN STRESSORS

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The purpose of this study is to investigate whether occupational exposure to urban stressors can cause alterations on androstenedione plasma levels and related diseases in female traffic police compared to a control group. The research was carried out on an initial sample of 468 female workers (209 traffic police and 259 controls). After excluding the subjects with confounding factors, 192 female subjects: 96 traffic police and 96 controls were included in the study. Traffic police and controls were matched by age, length of service, body mass index, alcohol consumption and cigarette smoking habits, habitual consumption of Italian coffee, and habitual intake of soy and liquorice in diet. The results show that the percentage of subjects with fertility and mental health disorders were no different between traffic police and controls. Mean androstenedione values were significantly higher in female traffic police compared to controls. The distribution into classes of androstenedione values in traffic police was statistically significant. The percentage of traffic police with fertility and mental health disorders were not significant compared to controls. Our results suggest that the occupational exposure to urban stressors could alter plasma androstenedione levels in female traffic police. According to our previous research all the hormonal parameters studied, including androstenedione, could be used as early biological markers of chronic exposure to urban stressors, usable in occupational sets.
IL-32 is one of the last important cytokines discovered, produced mainly by T cells, natural killer cells, and epithelial cells. Probably many other different cells are a source of IL-32, which has been found to be a powerful pro-inflammatory mediator. Here we studied the effect of IL-32 on histamine release by human-derived cord-blood mast cells. In these studies we found that IL-32 significantly stimulates the release of histamine only at high concentrations (100 ng/ml) while at 10 or 50 ng/ml it had no effect. These results were found for the first time and demonstrate that IL-32 may play an important role in allergic and inflammatory diseases.
LETTER TO THE EDITOR

CHRONIC KIDNEY DISEASE AND INFLAMMATION: ROLE OF +896A/G PRO-INFLAMMATORY POLYMORPHISM OF TLR4 GENE AND Δ32 DELETION OF CCR5 GENE

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Chronic inflammation seems implicated in the pathophysiology of chronic kidney diseases (CKD) and the development of its complications, such as cardiovascular diseases (CVD). Genes encoding inflammatory molecules are, hence, good candidates for CVD risk in haemodialysis patients (HD). We therefore evaluated whether +896A/G TLR4 polymorphism and CCR5Δ32 deletion are risk factors for CKD and CVD. We examined the two gene variants in 72 HD patients and in 125 controls from Sicily. No significant differences in the genotype distribution and allele frequencies of the two gene variants were observed between patients and controls. The same results were obtained by analysing the combined effect of the two proinflammatory (+896A/TLR4 and wt CCR5) alleles. However, the high responder proinflammatory (+896A+TLR4/wt+CCR5) genotype seems to be a possible independent risk factor for CVD development in HD patients. Our results suggest that HD patients with a high responder pro-inflammatory genotype have an increase CVD risk.