

## EDITORIAL

**PROBIOTICS, PREBIOTICS AND SYMBIOTICS IN INFLAMMATORY BOWEL DISEASES: STATE-OF-THE-ART AND NEW INSIGHTS**

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**Inflammatory bowel disease (IBD) consists of two distinct clinical forms, ulcerative colitis (UC) and Crohn’s disease (CD), with unknown aetiology, which nevertheless are considered to share almost identical pathophysiological backgrounds. Up to date, a full coherent mechanistic explanation for IBD is still lacking, but people start to realize that the pathogenesis of IBD involves four fundamental components: the environment, gut microbiota, the immune system and the genome. As a consequence, IBD development might be due to an altered immune response and a disrupted mechanism of host tolerance to the non-pathogenic resident microbiota, leading to an elevated inflammatory response. Considering the available data arising from the scientific literature, here reviewed, in CD, a benefit of probiotics remains unproven; in UC, a benefit of probiotics remains unproven, even if *E. coli Nissle 1917* seems promising in maintaining remission and it could be considered an alternative in patients intolerant or resistant to 5-ASA preparations; in pouchitis, small controlled trials suggest a benefit from VSL#3 in the primary and secondary prevention of pouchitis; in IBD-associated conditions, a benefit of probiotics remains unproven. However, well-designed randomized control clinical trials are necessary to understand the undoubted role of these agents in the management of gut physiology in health and disease.**

## ANTI-INFECTIVE PROPHYLAXIS FOR PRIMARY IMMUNODEFICIENCIES: WHAT IS DONE IN ITALIAN PRIMARY IMMUNODEFICIENCY NETWORK CENTERS (IPINet) AND REVIEW OF THE LITERATURE

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**Primary immunodeficiencies (PIDs) are rare diseases characterized by an increased susceptibility to infections. Early diagnosis and appropriate treatment are critical for reducing morbidity and mortality. Based on available data, the efficacy of antibiotic administration for the prophylaxis of infections remains uncertain, and recommendations supporting this practice are poor. The use of antimicrobial prophylaxis is mainly based on single institution-specific experience without controlled measurements of patient safety and quality health outcomes. To address this issue an Italian Network on Primary Immunodeficiencies (IPINet) has been set up in 1999 within the Italian Association of Pediatric Hematology and Oncology (AIEOP) to increase the awareness of these disorders among physicians. Further, diagnostic and treatment guideline recommendations have been established to standardize the best clinical assistance to all patients, including antibiotic prophylaxis, and for a national epidemiologic monitoring of PIDs. The aim of this review is not only to give a scientific update on the use of antimicrobial prophylaxis in selected congenital immunological disorders but also to draw a picture of this practice in the context of the Italian Primary Immunodeficiency Network (IPINet). Controlled multicenter studies are necessary to establish if, when and how you should start an efficacious antimicrobial prophylaxis.**

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## EDITORIAL

**THE ROLE OF OXYTOCIN IN PLASTICITY, MEMORY AND ATTACHMENT DYNAMICS**F. ORSUCCI<sup>1</sup>, G. PAOLONI<sup>2</sup>, C.M. CONTI<sup>2</sup>, M. REDA<sup>3</sup> and M. FULCHERI<sup>2</sup>

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**The peptide hormones oxytocin (OT) and arginine vasopressin (AVP) have been implicated in the regulation of mammalian social behavior. There is considerable evidence implicating both oxytocin and vasopressin in social recognition and social memory. This review explores their role in attachment dynamics. Oxytocin is one element in a complex network of interactions observed in natural phenomena ranging from molecular biology, etology, social behavior and human psychology.**

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**LUTEOLIN INHIBITS MAST CELL-MEDIATED ALLERGIC INFLAMMATION**

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**Mast cells are ubiquitous in the body and multifunctional immune cells; they are known to be primary responders in allergic reactions, orchestrating strong responses to minute amounts of allergens. Mature mast cells perform important beneficial roles in host defense, both in IgE-dependent immune responses to certain parasites and in natural immunity to bacterial infection. In IgE-associated biological responses, the crosslinking of FcεRI-bound IgE with multivalent antigens initiate the activation of mast cells by promoting aggregation of FcεRI. This cross-linking receptor-bound IgE by multivalent Ag initiates a cascade of intracellular reactions leading to mediator release such as proinflammatory mediators, chemokines and cytokines. Luteolin belongs to a flavone group of compounds called flavonoids, it has anti-oxidant properties, inhibits some cancer cell proliferation and exerts a regulatory effect on mast cell-mediated inflammatory diseases and allergy. Here we report the impact of luteolin on mast cell activation.**

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## CYTOLOGICAL CHARACTERISTICS OF LUNG WASHINGS FROM CHILDREN IN DEPLETED URANIUM STROKED REGION

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The study was based on theoretical interpretation of authentic findings of Lupus Erythematosus Cells (LEC) in bronchoalveolar lavage (BAL) samples of children who underwent flexible bronchoscopy for clinical symptoms and radiological changes consistent with persistent pulmonary infiltrates during the first year after the bombing of Serbia in 1999. Differential cell counts were compared and statistical significance of differences for estimated cell population percentages calculated in groups of LEC positive (LEC+) and LEC negative (LEC-) BAL specimens. Significant increase of percentages of neutrophils and eosinophils and decreased percentages of macrophages were found in the group of LEC+ in comparison with LEC- BAL specimens ( $p < 0.05$ ,  $p < 0.001$ ,  $p < 0.001$ , respectively). Presence of decreased percentages of cells of monocyte-macrophage lineage with consequent expansion of white blood cells in BAL, argue for understanding the nature of LEC+ alveolitis as a possible nonspecific finding of radiation-induced biological response of pulmonary tissue. LEC phenomenon may be understood as an early radio adaptive tissue response. Depleted uranium (DU) radiotoxic effect with concomitant alpha particles radiation, has been associated with unpredictable and everlasting biological effects. The emission of radiation in the course of several decades due to corrosion of scattered remnants of DU armaments, which has been potentiated by the repeated bombing of the regions within range of the transfer of radioactive particles by air, strikes a broad territory and numerous populations, and unavoidably leads to *in vivo* Petkau effect. Except the war, peacetime nuclear disasters in various parts of the world, such as Fukushima, Chernobyl and others, contribute to this effect too. In this way, the Petkau effect is a challenge for science to declare the future health strategy with the main goal focused on minimizing the early, as well as delayed *in vivo* effects of depleted uranium.

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## COMPARISON OF CHANGES IN THE PERCENTAGES OF CD8<sup>+</sup>CD28<sup>-</sup>TCRαβ<sup>+</sup> T CELL SUBPOPULATIONS IN ALLERGIC ASTHMA SUBJECTS vs CONTROLS BEFORE AND AFTER ANTI-CD3/ANTI-CD28/IL-2 STIMULATION *IN VITRO*

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Asthma is a chronic inflammatory disease characterized by the migration of activated T cells into the bronchial mucosa. TGF-β and IL-10 have proved to regulate airway hyper-responsiveness and leukocytes recruitment to the airways of ovalbumin (OVA) sensitized mice. We examined relative changes in CD8<sup>+</sup> T cell subpopulations between fifty allergic asthma subjects and twenty five age-matched healthy adults before and after anti-CD3/CD28 and IL-2 stimulation in the presence of IL-10 or TGF-β, focusing on CD62L and FoxP3 expressing TCRαβ<sup>+</sup> cells. Severe asthma group had a significantly higher percentage of CD8<sup>+</sup>CD28<sup>-</sup> and CD8<sup>+</sup>CD28<sup>-</sup>TCRαβ<sup>+</sup>CD62L<sup>high</sup>FoxP3<sup>bright</sup> T cells than other groups after enrichment. Compared to the baseline, co-stimulation with either IL-10 or TGF-β increased the percentage of CD8<sup>+</sup>CD28<sup>-</sup> but decrease the percentage of CD8<sup>+</sup>CD28<sup>+</sup> T cells within anti-CD3/anti-CD28/IL-2 activated CD8<sup>+</sup> T cells in all groups. Co-stimulation with anti-CD3/anti-CD28/IL-2 in presence of either IL-10 or TGF-β decreased the frequencies of CD8<sup>+</sup>CD28<sup>-</sup>TCRαβ<sup>+</sup>CD62L<sup>high</sup>FoxP3<sup>bright</sup> T cells in severe asthma subgroup but increased this parameter in other groups. We suggest that altered high level expression of CD62L and FoxP3 on CD8<sup>+</sup>CD28<sup>-</sup>TCRαβ<sup>+</sup> T cell is relevant to allergic asthma. These data have implications for further characterization of CD8<sup>+</sup>CD28<sup>-</sup>TCRαβ<sup>+</sup> T cell subsets, with special emphasis on their implication in healthy or allergic immune response.

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**INCREASED URIC ACID LEVELS IN BIPOLAR DISORDER: IS IT TRAIT OR STATE?**

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The aim of the present study was to compare uric acid levels between disease and remission episodes of bipolar disorder (BD) and healthy individuals and to investigate whether uric acid levels were related with clinical properties and the course. Uric acid levels were compared in 43 BD patients with manic episode, 20 BD patients with depressive episode, 41 BD patients in remission and 43 healthy individuals. Informations regarding disorder was recorded using SKIP-TURK, the severity of episode was measured with Young Mania Rating Scale (YMRS) and Hamilton Depression Rating Scale (HDRS). Uric acid levels were found higher in manic, depressive and euthymic bipolar patients than those in healthy individuals. In cases in remission period, a moderate relation was present between uric acid levels and the age of onset. A moderate relation was found in manic episode between first and second week YMRS scores and uric acid levels, and a strong relation was found in depressive episode between first and second week HDRS scores and uric acid levels. While decrease in uric acid levels in manic episode was found to be associated with the decrease in YMRS scores, no such relation was shown in depressive episode. Our findings stress the impairment in purinergic functions in all episodes of BD. This impairment seems to be associated with clinical properties of BD.

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## THYROID HORMONE ACTIVATES RAT LIVER ADENOSINE 5'-MONOPHOSPHATE-ACTIVATED PROTEIN KINASE: RELATION TO CaMKK $\beta$ , TAK1, AND LKB1 EXPRESSION AND ENERGY STATUS

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AMP-activated protein kinase (AMPK) is a sensor of energy status supporting cellular energy homeostasis that may represent the metabolic basis for 3,3',5-triiodo-L-thyronine (T<sub>3</sub>) liver preconditioning. Functionally transient hyperthyroid state induced by T<sub>3</sub> (single dose of 0.1 mg/kg) in fed rats led to upregulation of mRNA expression (RT-PCR) and protein phosphorylation (Western blot) of hepatic AMPK at 8 to 36 h after treatment. AMPK Thr 172 phosphorylation induced by T<sub>3</sub> is associated with enhanced mRNA expression of the upstream kinases Ca<sup>2+</sup>-calmodulin-dependent protein kinase kinase- $\beta$  (CaMKK $\beta$ ) and transforming growth-factor- $\beta$ -activated kinase-1 (TAK1), with increased protein levels of CaMKK $\beta$  and higher TAK1 phosphorylation, without changes in those of the liver kinase B1 (LKB1) signaling pathway. Liver contents of AMP and ADP were augmented by 291% and 44% by T<sub>3</sub> compared to control values ( $p < 0.05$ ), respectively, whereas those of ATP decreased by 64% ( $p < 0.05$ ), with no significant changes in the total content of adenine nucleotides (AMP + ADP + ATP) at 24 h after T<sub>3</sub> administration. Consequently, hepatic ATP/ADP content ratios exhibited 64% diminution ( $p < 0.05$ ) and those of AMP/ATP increased by 425% ( $p < 0.05$ ) in T<sub>3</sub>-treated rats over controls. It is concluded that *in vivo* T<sub>3</sub> administration triggers liver AMPK upregulation in association with significant enhancements in AMPK mRNA expression, AMPK phosphorylation coupled to CaMKK $\beta$  and TAK1 activation, and in AMP/ATP ratios, which may promote enhanced AMPK activity to support T<sub>3</sub>-induced energy consuming processes such as those of liver preconditioning.

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## TYPE III INTERFERON (IFN- $\lambda$ ) ANTAGONIZES THE ANTIVIRAL ACTIVITY OF INTERFERON- $\alpha$ *IN VITRO*

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**Type III interferons (IFN- $\lambda$ ) are the most recently discovered members of IFN family. Synergism between different IFN types is well established, but for type I and type III IFNs no conclusive evidence has been reported so far. Possible synergism/antagonism between IFN- $\alpha$  and IFN- $\lambda$  in the inhibition of virus replication (EMCV, WNV lineage 1 and 2, CHIKV and HSV-1), and in the activation of intracellular pathways of IFN response (MxA and 2'-5' OAS) was evaluated in different cell lines (Vero E6, A549 and Wish cells). The antiviral potency of IFN- $\lambda$ 1 and - $\lambda$ 2 was lower than that of IFN- $\alpha$ . When IFN- $\alpha$  and - $\lambda$  were used together, the Combination Index (CI) for virus inhibition was  $>1$  virtually for all virus/host cell systems, indicating antagonistic effect. Antagonism between IFN- $\alpha$  and - $\lambda$  was also observed for the induction of mRNA for both MxA and 2'-5'OAS. Elucidating the interplay between IFN- $\alpha$  and - $\lambda$  may help to better understand innate defence mechanisms against viral infections, including the molecular mechanisms underlying the influence of IL-28B polymorphisms in the response to HCV and other viral infections.**

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## **A NEW AID IN TEMPOROMANDIBULAR JOINT DISORDERS' THERAPY: THE UNIVERSAL NEUROMUSCULAR IMMEDIATE RELAXING APPLIANCE**

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**Among the various treatment options currently indicated to deal with temporomandibular joint disorders (TMD) an important role is played by occlusal devices, which can be used in an individualized or universal manner. A new universal occlusal appliance device was designed and patented at the Clinical Gnathology Service of the Sapienza University of Rome. To assess its validity and efficacy a preliminary study on a sample of 50 patients was carried out. Patients were selected from a cohort of 158 according to the RDC-TMD (SPEC) criteria and randomly assigned to two groups, the patient group (PG), treated with the device, and a control group (CG) without any treatment. The two groups were evaluated by comparing four VAS pain scores: muscular, migraine, cervical and temporomandibular joint (TMJ). On the whole, all VAS pain scores in the PG showed a marked and statistically significant improvement after treatment, decreasing to about 50-80 %, while the control group remained stable. The best improvement was achieved in muscular pain. Age did not affect neither the initial scores, nor the pain response to the treatment. The pain scores tended to slightly increase with time of application (one, two or three months), but this trend was significant only for cervical pain. Overall the results are favourable to the application of this new occlusion device. However, the data should be considered preliminary and require further verification in time and on a higher sample of patients of both sexes.**

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## THE NOSE AND SINUS MANOMETRY: A BIO-PHYSICAL MODEL APPLIED TO FUNCTIONAL ENDOSCOPIC SINUS SURGERY

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The effectiveness of sinus ventilation is due to a regular anatomy of inner nose structures such as the maxillary sinus ostium. With the aid of nose and sinus manometric measurements, it is possible to show that better functional results can be achieved using a conservative surgical technique. The present study compared 30 patients subdivided in two groups. Group A underwent conservative endoscopic sinus surgery whereas group B was operated on using non-conservative endoscopic sinus surgery. Thirty days later, both groups underwent a manometric survey of the maxillary sinus ostium by means of the digital manometry system. The pressure values obtained by nasal and sinus manometry in Group A or Group B patients were referred to those obtained in a Standard Group without nasal-sinus pathologies, calculating a percentage index of functional efficacy (maxillary sinus functional efficacy). The average percentage of the maxillary sinus functional efficacy was 98,35% for group-A patients, and 49,73% for group-B patients. Student t test revealed a statistical difference only between group B patients and standard group patients ( $p < 0.4$ ). Patients submitted to a more aggressive endoscopic approach showed inadequate sinus ventilation when compared to the standard reference group.

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## MODULATION OF MULTIDRUG RESISTANCE P-GLYCOPROTEIN ACTIVITY BY ANTIEMETIC COMPOUNDS IN HUMAN DOXORUBICIN-RESISTANT SARCOMA CELLS (MES-SA/Dx-5): IMPLICATIONS ON CANCER THERAPY

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Multidrug resistance (MDR) in cancer cells is often caused by the high expression of the plasma membrane drug transporter P-glycoprotein (Pgp) associated with an elevated intracellular glutathione (GSH) content in various human tumors. Several chemosensitizers reverse MDR but have significant toxicities. Antiemetic medications are often used for controlling chemotherapy-induced nausea and vomiting in cancer patient. In this *in vitro* study we investigated if the effects of two common antiemetic drugs such as dimenhydrinate (dime) and ondansetron (onda) and a natural compound (6)-gingerol (ginger), the active principle of ginger root, interfere on Pgp activity and intracellular GSH content in order to evaluate their potential use as chemosensitizing agents in anticancer chemotherapy. The human doxorubicin (doxo) resistant uterine sarcoma cells (MES-SA/Dx5) that overexpress Pgp, were treated with each antiemetic alone (1, 10 and 20  $\mu$ M) or in combination with different doxo concentrations (2, 4, and 8  $\mu$ M). We measured the intracellular accumulation and cytotoxicity of doxo (MTT assay), the cellular GSH content (GSH assay) and ROS production (DFC-DA assay), in comparison with verapamil (Ver), a specific inhibitor for Pgp, used as reference molecule. We found that exposure at 2, 4 and 8  $\mu$ M doxo concentrations in the presence of dime, onda and ginger enhanced significantly doxo accumulation and cytotoxicity on resistant MES-SA/Dx5 cells when compared with doxo alone. Moreover, treatment with ginger (20  $\mu$ M) increased cellular GSH content (>10%) in resistant cells, while ROS production remained below the control values for all antiemetic compounds at all concentrations. These findings provide the rationale for innovative clinical trials of antiemetics or their derivatives as a new potential generation of chemosensitizers to improve effectiveness of the anticancer drugs in MDR human tumours.

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## ENIGMATIC QUESTION OF EARLY REACTIVE ARTHRITIS DISCLOSED AFTER RESEARCHES OF *MYCOPLASMAS*, *CHLAMYDIA TRACHOMATIS* AND ENTEROPATHOGENS FOLLOWING THE HOLISTIC VISION OF “HUMAN BEING”

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An HLA-B27 genetic profile patient is fully investigated by molecular analyses after an anamnestic assessment of multi-site ecosystems, following the holistic vision of “Human Being”. VDRL and Widal-Wright (WWR) resulted positive, showing at Wright's reaction a tittle of 1:40. Of all the enzymatic activities measured, only the ALP enzymatic pool activities showed a low increasing value of 297 U/L. Of all later acute phase proteins, Only C<sub>3c</sub> protein value (127 mg/dL) and fibrinogen (376 mg/dL) were altered. Cultural and molecular oropharyngeal ecosystem investigation resulted significantly positive to *Mycoplasmas* (*Mh* and *Uu*) and *Chlamydia trachomatis* (*Ct*) together with a spread of saprophytic flora. From an accurate anamnesis, several and severe uro-genital clinical symptomatology emerged from birth until the beginning of rheumatologic symptomatology that were confirmed by oldest *Mh*, *Uu* and *Ct* silent chronic infections between these ecosystems. The molecular HPV research was negative, while the Thin prep pap-test was indicative of vaginosis and cellular reactive changes associated with inflammation. Parasitological research resulted positive for presence of 5-7 newly-formed *G. lamblia* cysts for microscopic field, while digestibility test was positive for presence of several free fatty acid crystals. The remarkable presence of indigested meat fibre and several mucous dense filaments were observed. The pH value was 6.5, while blood faecal test was positive. The values observed were: ferritin 12 µg/L (10-120), total iron-binding capacity (TIBC) 310 µg/dL (300±20), unsaturated iron-binding capacity (UIBC) 286 µg/dL (200-220) and iron seric level 24 µg/dL (60-130). Faecal research highlighted a very scarce presence of *E. coli*, resulting in 10<sup>2</sup> UFC/g of stool. Of all enteroinvasive pathogens, researched by molecular analyses, only *Yersinia spp.* was positive. After several specific cycles of antibiotic and antiinflammatory therapies, the patient improved its general health condition considerably and showed almost complete regression of aching inguinal lymph node inflammation. In a picture of a worsening inflammatory process, produced by pathogens like *Mycoplasmas*, chronic silent or low grade inflammation atypical agents, in young HLA-B27 positive patient, VDRL test resulted positive. This value represents the first non-specific “unique spy” to reveal the precocious immunological signal in order to register the beginning of early innate immune system decay, keeping in mind that mycoplasmal and chlamydial infections are the triggering of cancer in patients genetically susceptible.

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## LETTER TO THE EDITOR

**ALLERGEN IMMUNOTHERAPY MAY EXERT AN EXTRA-ANTI-ALLERGIC ACTIVITY IN CHILDREN**

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**Allergic patients frequently suffer from infections. Allergen immunotherapy (AIT) usually improves respiratory symptoms, mainly in allergic rhinitis (AR). This study was aimed at evaluating the possible impact of AIT on extra-allergic outcomes in a cohort of Italian children with respiratory allergy patients. The study was performed on 77 children (43 males, mean age 10.5 years) with AR. The kind and the number of prescribed allergen extracts, type of diagnosis, severity of symptoms, and use of drugs were evaluated at baseline and after 2 year AIT. Globally 40 patients were treated with AIT, the remaining 37 children served as control. AIT-treated children had lower symptoms, drug use, and less severe extra-allergic surrogate markers of infection in comparison with children untreated with AIT. In conclusion, this study provides the first evidence that 2-year SLIT is able of exerting an adjunctive anti-allergic activity in AR children.**

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## LETTER TO THE EDITOR

**CHANGES IN THE CONTENT OF SHORT, MEDIUM AND LONG-CHAIN FATTY ACIDS  
IN ISOLATED HEPATOCYTES INCUBATED IN THE PRESENCE OF MAGNESIUM  
IONS AND/OR ETHANOL**

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Magnesium is one of the commonly used dietary supplements. Therefore, this study was to evaluate the content of short, medium and long-chain fatty acids and their esters in isolated rat hepatocytes induced by magnesium and/or ethanol. Isolation of hepatocytes was carried out by the Seglen's enzymatic method using collagenase. To thus prepared samples ethanol and/or MgCl<sub>2</sub> solution were added, respectively, so that their concentrations were as follows: 150 mM/dm<sup>3</sup> ethanol and/or 2 mM/dm<sup>3</sup> MgCl<sub>2</sub>, 4 mM/dm<sup>3</sup> MgCl<sub>2</sub>. The contents of short, medium and long-chain fatty acids and those of ester-bound acids were determined. The statistical evaluation of the experiment was made by comparing the area normalized for the analysed fatty acids in hepatocytes incubated for 5 h in the presence of the test substances. The effect of magnesium ions on the content of fatty acids and their esters in isolated hepatocytes incubated for 5 h depended on their concentration in the medium. A normalizing effect of magnesium ions on ethanol-induced changes in the content of C14–C17, C18–C20 and C21–C24 fatty acids was demonstrated. A normalizing effect of magnesium on ethanol-induced changes in the content of ester-bound fatty acids in hepatocytes was not confirmed.

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## LETTER TO THE EDITOR

**NITRIC OXIDE SYNTHASE ISOENZYME EXPRESSION IN HUMAN ORAL LICHEN PLANUS**

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The roles of nitric oxide (NO) synthase (NOS) enzyme in pathological mechanisms of the oral cavity are still incompletely understood. The aim of this study was to investigate the expression of the endothelial, neuronal and inducible isoforms of NOS (eNOS, nNOS and iNOS) in oral lichen planus (OLP) development in humans. OLP and healthy oral mucosa biopsies were taken for mRNA and protein analysis of NOS isoenzymes by RT-PCR, western blot and immunohistochemistry. The mRNA and protein levels of eNOS and nNOS were present in all samples, with a significant increase only for eNOS in OLP. The normal oral mucosa exhibited only small amounts of iNOS mRNA and protein, while it showed a significant rise in OLP samples. These results were confirmed by immunohistochemical analysis. Our findings suggest that NO produced by increased eNOS and iNOS expression may have circulatory and immune functions in the development of OLP.



## LETTER TO THE EDITOR

**DIMENSIONAL AND MICROBIOLOGICAL *IN VITRO* ANALYSIS OF A DENTAL IMPLANT LOCKING TAPER CONNECTION**

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The present study was carried out to compare the differences in contact, height and contact area between the implant-abutment interface and the implant-healing cap interface of an implant system featuring a locking tapered connection by using X-ray micro-tomography. It was also conducted to test *in vitro* whether the implant-healing cap tapered interface is capable of preventing bacterial leakage from the implant well to the external environment. The images of the samples, acquired by the X-ray micro-tomography, after being processed with a dedicated software, showed a greater contact height (CH) in the implant-abutment sample (3.57 mm) compared to the implant-healing cap sample (2.52 mm). This was also true for the contact area that was equal to 40.63 mm<sup>2</sup> in the implant-abutment sample and 25.14 mm<sup>2</sup> in the implant-healing cap sample. No bacteria were detected both in the nutrient of the test group and of the negative control after 24 h. An increased contact height and contact area in a tapered connection, between the implant and the abutment, have demonstrated to offer mechanical and biological advantages, in a implant-healing cap tapered connection. The major concern regards the microbiological aspects of this connection. The implant-healing cap tapered connection provides an hermetic barrier to microbial passage *in vitro*, even though such connection features lower contact height and contact area compared to the implant-abutment connection of the same implant system.

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## LETTER TO THE EDITOR

**EXHALED BREATH CONDENSATE, NASAL EOSINOPHIL CATIONIC PROTEIN LEVEL AND NASAL CYTOLOGY DURING IMMUNOTHERAPY FOR CYPRESS ALLERGY**

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Interest in cypress allergy is widely rising: an increasing number of studies have pointed out the efficacy of immunotherapy to reduce cypress-related symptoms and drug use. Cypress immunotherapy is well tolerated, but there are few studies dealing with its sub-clinical effects on the airways. The aim of this investigation is to assess the effects of immunotherapy on airways by the analysis of exhaled breath condensate (EBC), nasal lavage fluid (NAL) and nasal cytology. Fifteen mono-sensitized to cypress pollen patients have been observed, among them 9 have been treated with sub-cutaneous immunotherapy (SCIT), 3 with sub-lingual immunotherapy (SLIT) and 3 which were not treated underwent EBC, NAL and nasal cytology out of the pollen season. 8-isoprostane in EBC, Eosinophil cationic protein (ECP) and inflammatory cells in nasal cytology were also evaluated. The median value of 8-isoprostane in EBC was 18.58 pg/ml in patients who did not undergo immunotherapy, 49.38 pg/ml in SCIT patients and 13.41 pg/ml in SLIT subjects. The median value of ECP in nasal lavage was higher in non-treated subjects (27.3 mg/l) than in those treated with SCIT (1 mg/l) ( $p < 0,05$ ) or SLIT (2.6 mg/l). All nasal cytology specimens did not show any sign of inflammation. In conclusion SLIT seems to be well tolerated and to reduce significantly the levels of ECP in nasal lavage. In addition the levels of 8-isoprostane in EBC among SCIT patients were unexpectedly high and need to be further evaluated.

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