THE ROLE OF CYTOKINES IN PULP INFLAMMATION

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Pulpitis is a typical inflammatory disease of dental pulp, characterized by the local accumulation of inflammatory mediators, including cytokines and chemokines. In addition to serving as intercellular messengers mediating the inflammatory response, cytokines and chemokines induce the expression and stimulate the activity of molecular and cellular agents which participate actively in destructive and reparative processes in the pulp. It is the balance between these processes which eventually determines the extent of pulp inflammation and the viability of the affected tooth. Over the last decade, a number of studies have attempted to correlate cytokine gene expression in the pulp with various stages of inflammation, with possible diagnostic applications in mind. A small survey of relevant information is presented in this paper.
EDITORIAL

ORTHOPAEDIC AND DENTAL ABNORMALITIES IN OSTEGENESIS IMPERFECTA: A REVIEW OF THE LITERATURE

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Osteogenesis imperfecta is one of the most commonly recognized inheritable disorders of the connective tissue leading to bone fragility. Usually it is associated to a genetic mutation inducing a reduction in collagen quality and entity production. It involves either modification in dentin formation or multiple bone fractures. The authors reviewed the clinical aspects of these disorders, focusing on oral and orthopaedic concerns, especially related to the histological features of the fracture callus, with respect to new trends in pharmacological and surgical treatments of bone fractures. Surgical treatment varies, according to the age of the patient. In children, surgical orthopaedic procedures include multiple osteotomies and the use of telescopic rods. Medical therapy has always to be associated to surgery and is designed to reduce the incidence of fractures, to increase growth velocity and to ally pain in order to improve mobility and independence. Bisphosphonates (BP) are considered potent inhibitors of bone resorption decreasing the osteoclast population and its activity and bone turn over.
EDITORIAL

BIOLOGICAL ROLE OF INTERLEUKIN-1β IN DEFENSIVE AGGRESSIVE BEHAVIOR

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During the past decade, a great deal of data has accumulated supporting the notion that cytokines interact to regulate several aspects of social and emotional behavior. There are reports of a positive correlation between cytokine levels and aggressive behavior in healthy populations, and clinical reports describe an increase of aggressive traits in patients who receive cytokine immunotherapy. Interleukin-1β (IL-1β) released during an immune response acts as messenger that helps to modulate behavior by influencing relevant neurotransmitter systems, and in some cases, by directly acting within the brain. In this site, IL-1β exerts its actions by acting through 5-HT₂ and IL-1 Type I receptors in hypothalamus or by potentially indirect routes, including activation of sensory afferents, and stimulation of cytokine release by brain endothelial cells. This review reports research investigating the relationship between IL-1β, and the immune and central nervous systems involving or potentially involving defensive aggressive behavior.
EDITORIAL

RELATIONSHIP BETWEEN CANCER AND PSYCHOLOGY: AN UPDATED HISTORY

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The mechanism and formation of cancer have always been topics of interest for scientists, even for doctors in ancient times. Nowadays a great role for cancer is played by psychological stress which promotes relevant changes in neuronal activity and gene regulations across the different brain areas. It has been reported by many authors that stress can have an important role in the immune system and may be relevant in the formation of cancer. Our observations, in accordance with other research studies, confirm the importance of the influence of depression, linked to neuroendocrine stress, on the enhancement of cancer pathogenesis by inhibiting anti-tumor immune responses. In this article we review the past and present history of the relationship between cancer and psychology.
ADVANTAGE OF CARBONATE- VERSUS CITRATE-BASED ALKalinization ON 
BONE METABOLISM IN MODERATELY EXERCISING AGED MALE RATS FED AN 
ACIDOGENIC DIET

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This study aims to determine the effects of different alkaline supplementations on high protein 
diet-induced abnormalities affecting bone metabolism in rats which were also undergoing physical 
exercise of moderate intensity. Sixty elderly Sprague-Dawley rats were randomly divided into four 
groups of 10 rats each and treated for 16 weeks as follows: baseline control group fed normal food (C); 
acidic high-protein diet supplemented group (chronic acidosis, CA group), bicarbonate-based alkaline 
formula (Basenpulver, Named, Italy) supplemented chronic acidosis (BB-CA) and citrate-based alkaline 
supplement (CB-CA). Throughout the supplementation period, rats were put on a treadmill training 
mimicking a moderate level of exercise. In the CA group, 24-hour urinary calcium (Ca) and phosphorus 
(P) excretion were increased over 30% (p<0.05 vs normal diet controls). However serum Ca was not 
significantly changed. Femural and tibial BMD and BMC was significantly decreased in the CA group 
(p<0.05) but both alkaline supplementations prevented such phenomenon (p<0.05 vs CA), without 
significant difference between the two formulations although the BB-CA group showed significantly 
more preserved trabecular bone volume (p<0.05 vs CB-CA group). An increased level of over 50% of 
urinary Dpd observed in the CA group (p<0.001) was reverted to normal by both supplementations 
(p<0.001 vs CA group). The same applied to urinary net acid excretion (p<001) with BB-supplementation 
performing better than CB-supplementation (p<0.05). Moreover, while the latter did not modify N-
terminal telopeptide value, BB-supplementation significantly normalized this parameter (p<0.05 vs CA 
group) which exercise and acidic protein diet had modified (p<0.01 vs control diet). Overall, the present 
study shows that a bicarbonate-based alkaline formula, when administered to a dose amenable to 
clinical use, may significantly protect bone structure in exercising aged animals to a greater extent than 
a quali/quantitatively similar citrate-based formula.
THE ROLE OF REELIN GENE POLYMORPHISMS IN THE PATHOGENESIS OF ALZHEIMER’S DISEASE IN A GREEK POPULATION

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Reelin is an extracellular signaling glycoprotein, which plays a significant role in cytoarchitectonic pattern formation of different brain areas during development. Reelin gene is located on chromosome 7q22. The aim of this study is to investigate the possible association of the following reelin polymorphisms SNP Intron12A/C (rs727531), SNP Exon15A/G (rs2072403), SNP Intron15G/T (rs2072402), SNP Exon22c/g (rs362691), SNP Intron41G/T (rs362719) and SNP Intron59C/T (rs736707) in the pathogenesis of Alzheimer’s disease and the frequency of these polymorphisms in the population of Northern Greece. The study included two groups, A and B. Group A consisted of 50 patients with Alzheimer’s disease and group B of 70 healthy controls. Genomic DNA isolated from blood was used for PCR and subsequent RFLP analysis. According to our results, the exon 22 C/G marker of reelin is significantly associated with Alzheimer’s disease in the Greek population but the Likelihood Ratio Test shows that the GT haplotype of this polymorphism does not affect the phenotype of group A in relation to Group B. This is the first report on a Greek population-based approach.
THE ROLE OF P53 AND Bcl-2 PROTEINS IN 7, 12-DIMETHYLBENZ-(A)-ANTHRACENE-INDUCED TUMOR GROWTH

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7, 12- Dimethylbenz-(a)-anthracene (DMBA) has been used for a long time to induce rat mammary gland carcinogenesis. In a previous paper we described the effects of diet, of non-steroidal anti-inflammatory drugs and the combination of these two factors on breast cancer. We also pointed out that the DMBA tumor generating process is still poorly understood. The present study attempts to explore whether P53 or the pro-apoptotic protein Bcl-2 are potential targets of DMBA in its induction of breast tumors in the Sprague-Dawley rat breast tumorigenesis model. Our results indicate that the DBMA-induced tumors are apparently the result of P53 inactivation. This inactivation results in tumorigenesis, probably aided by the absence of Bcl-2 in the tumor cells of the Sprague-Dawley rat animal model. We discuss the potential mechanisms by which P53 inactivation results in tumorigenesis.
DYSLIPIDEMIA IN RELATION TO BODY MASS INDEX AND INSULIN RESISTANCE IN CHINESE WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Dyslipidemia is a common metabolic disorder in women with polycystic ovary syndrome (PCOS) and has been reported to be different in PCOS sufferers from various ethnic and geographic backgrounds. This study aims to investigate the prevalence of dyslipidemia in Chinese women with PCOS and its relationship to body mass index (BMI) and insulin resistance (IR). In this paper, a retrospective study was performed on 507 PCOS patients and 1246 age- and BMI-matched controls. Anthropometric indices of hormonal, adiposity, and metabolic variables were measured. All patients were divided into subgroups according to BMI and the homeostasis model assessment (HOMA) values. Accordingly, the prevalence of IR was 38.1% in our subjects. We found that mean fasting total triglyceride, low density lipoprotein (LDL) cholesterol and total cholesterol levels were significantly higher and the mean high density lipoprotein (HDL) cholesterol level was significantly lower in the IR group than in the non-IR (NIR) group. The prevalence of dyslipidemia was 24.7% in PCOS patients and the prevalence of dyslipidemia was significantly higher in the IR group than in the NIR group (39.9% vs 15.3%, P<0.05). The HOMA index was found to be positively correlated with TG, TC and LDL, and negatively correlated with BMI. TG and HDL levels remained significantly correlated with HOMA even after adjustment for BMI. Generally, the prevalence of various patterns of dyslipidemia in PCOS patients increased with HOMA value. In conclusion, the prevalence of IR and dyslipidemia were both found to be high in PCOS women in our study, although no higher than other ethnicities. Lipid abnormality was demonstrated to be associated with IR and BMI in Chinese PCOS women. We speculate that insulin sensitizer might ameliorate dyslipidemia through improving IR in PCOS women.
TRAIL PROMOTES A PRO-SURVIVAL SIGNAL IN ERYTHROPOIETIN-DEPRIVED HUMAN ERYTHROBLASTS THROUGH THE ACTIVATION OF AN NF-κB/IκBα PATHWAY

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The biological activity of TNF-related apoptosis inducing ligand (TRAIL) was analyzed in primary human erythroblasts derived from mononuclear cells of blood donors, kept in culture in the presence of 20% foetal calf serum, growth factors (EPO, SCF, IL-3) and glucocorticoids (10⁻⁶ M dexamethasone, 10⁻⁶ M oestradiol) or under growth factor and serum starvation. In the presence of growth factors and serum, primary erythroblasts showed a differential expression of TRAIL-Receptors (Rs) at various degrees of maturation and responded to TRAIL treatment with a mild cytotoxicity. On the other hand, in the absence of serum and growth factors, TRAIL treatment unexpectedly up-regulated TRAIL-R4 decoy receptor and promoted erythroblast survival. The concomitant activation of NF-κB/IκB survival pathway was detected with Western blotting and immunofluorescence procedures and confirmed by experiments performed with SN50, a pharmacological inhibitor of the NF-κB/IκB pathway. Our study indicates that TRAIL has a twofold activity on erythroid lineages: it induces a mild erythroid cell cytotoxicity in the presence of serum and growth factors, while it promotes erythroid cell survival through the activation of the NF-κB/IκB pathway under starvation conditions.
A TIMETABLE OF 24-HOUR PATTERNS FOR HUMAN LYMPHOCYTE SUBPOPULATIONS

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Specific lymphocyte cell surface molecules involved in antigen recognition and cell activation present different circadian patterns, with peaks and troughs reflecting a specific time-related compartment of immune cell function. In order to study the dynamics of variation in expression of cytotoxic lymphocyte cell surface molecules that trigger immune responses, several lymphocyte cell surface clusters of differentiation (CD) and antigen receptors, analyses were performed on blood samples collected every 4 h for 24 h from eleven clinically-healthy men. Assays for serum melatonin (peaking at night) and cortisol (peaking near awakening) confirmed 24-h synchronization of the subjects to the light-dark schedule. A significant (p≤0.05) circadian rhythm could be demonstrated for six of the 10 lymphocyte subpopulations, with midday peaks for CD8+dim (T cytotoxic cells, 11:15 h), γδTCR (gamma-delta T cell receptor-expressing cells, 11:33 h), CD8+ (T suppressor/cytotoxic cells, 12:08 h), and for CD16+ (natural killer cells, 12:59 h), and peaks during the night for CD4+ (T helper/inducer cells, 01:23 h) and CD3+ (total T cells, 02:58 h). A borderline significant rhythm (p = 0.056) was also observed for CD20+ (total B cells), with a peak late in the evening (23:06 h). Acrophases for 3 subsets, CD8+bright (T suppressor cells, 15:22 h), HLA-DR+ (B cells and activated T cells, 23:06 h) and CD25+ (activated T lymphocytes with expression of the α chain of IL2 receptor, 23:35 h), where a 24-h rhythm could not be definitively determined, nevertheless provide information on the location of their highest values and possible physiological significance. Thus, specific lymphocyte surface molecules present distinctly-timed profiles of nyctohemeral changes that indicate a temporal (i.e., circadian) organization of cellular immune function, which is most likely of physiological significance in triggering and regulating immune responses. Such a molecular cytotoxic timetable can potentially serve as a guide to sampling during experimental, diagnostic, therapeutic and/or other medical procedures.
CYCLOSPORINE A IN THE LONG-TERM MANAGEMENT
OF SYSTEMIC LUPUS ERYTHEMATOSUS

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To retrospectively evaluate safety and efficacy of long-term treatment with Cyclosporine A (CSA) in
patients with systemic lupus erythematosus (SLE) poorly responsive to treatment with corticosteroids
(CCS) and/or conventional disease-modifying anti-rheumatic drugs (DMARDs), SLE patients who
had received CSA-based induction and maintenance regimens according to disease activity were
recorded. Efficacy was assessed using the SLE Disease Activity Index (SLEDAI) and laboratory
analyses. Forty SLE patients [including 18 with lupus nephritis, 11 with neurological involvement and
7 with overlap syndromes (4 Sjögren’s syndrome, 2 myasthenia gravis and 1 Behçet’s disease)] were
recorded. According to baseline SLEDAI, 30 patients had severe and 10 moderate SLE. Mean SLEDAI
scores and relevant laboratory values significantly reduced from baseline (22±10 vs 5±6; P < 0.002)
during the follow-up period (8±2 years; range 1-15). Twenty-three (57.5%) patients achieved excellent
(improvement in the range 70-100%) response to treatment (10 of whom were subsequently maintained
on CSA monotherapy), 14 (35%) had good/fair (improvement in the range 25-69%) response and 3
(7.5%) had to interrupt therapy (including CSA) for disease worsening. Mild and transient adverse
events occurred in 15 (37%) patients, including hypertrichosis (17.5%), gum hypertrophy (17.5%)
hypertension (12.5%), abdominal pain (7.5%), and dyslipidemia (5%), but treatment interruption
was not required. Low-dose CSA together with other drugs is effective to induce, or as monotherapy to
maintain, long-term (at least 2 years) remission, and is generally well tolerated in patients with moderate
or severe SLE poorly responsive to CCS and/or conventional DMARDs. Furthermore, the favourable
effect of CSA treatment may allow to spare more cytotoxic drugs.
ALTERATION OF CIRCADIAN RHYTHMICITY OF CD3+CD4+ LYMPHOCYTE SUBPOPULATION IN HEALTHY AGING

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The CD4+ T helper/inducer and the CD8+ T suppressor/cytotoxic are major lymphocyte subsets that play a key role in cell-mediated immunity. Aging-related changes of immune function have been demonstrated. The purpose of this study is to analyze the dynamics of variation of these specific lymphocyte subsets in the elderly. In our study cortisol and melatonin serum levels were measured and lymphocyte subpopulation analyses were performed on blood samples collected every four hours for 24 hours from fifteen healthy young–middle-aged subjects (age range 36-55 years) and fifteen healthy elderly male subjects (age range 67-79 years). A clear circadian rhythm was validated for the time-qualified changes of CD3+ and CD4+ cells with acrophase at night and for the time-qualified changes of CD8+ cells with acrophase at noon in young–middle-aged subjects and for the time-qualified changes of CD3+ cells with acrophase at night and for the time-qualified changes of CD8+ cells with acrophase at noon in elderly subjects. No clear circadian rhythm was validated for the time-qualified changes of CD4+ cells in elderly subjects. No statistically significant correlation among lymphocyte subsets was found in elderly subjects. In elderly subjects CD3+ lymphocyte percentage was higher in the photoperiod and in the scotoperiod and cortisol serum level were higher in the scotoperiod in respect to young–middle-aged subjects. In the elderly there is an alteration of circadian rhythmicity of T helper/inducer lymphocytes and this phenomenon might contribute to the aging-related changes of immune responses.
PHYSICAL PERFORMANCE IN KIDNEY TRANSPLANTED PATIENTS:
A STUDY ON DESERT TREKKING

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Physical performance of kidney transplanted patients in challenging environments, such as deserts, has been poorly studied. Six kidney transplanted (T: 5 males, 1 female; 45±6 yrs) and 8 control (C: 5 males, 3 females; 49±13 yrs) subjects participated in a 5-day desert trek. Blood pressure, hydration status (Height\textsuperscript{2}/Rz by bioimpedance), heart rate, energy expenditure (by SenseWear Pro Armband) and walking velocities were recorded during each daily trekking stage (GPS-assisted wearable devices). Systo-diastolic blood pressure did not differ between C (119/77±12/8 mmHg) and T (121/77±10/6 mmHg) groups throughout the study. The hydration status was stable from day 1 (Ht\textsuperscript{2}/Rz: 64±13 cm\textsuperscript{2}/Ohm in T and 59±12 cm\textsuperscript{2}/Ohm in C subjects) to day 5 (66±11 cm\textsuperscript{2}/Ohm in T and 61±13 cm\textsuperscript{2}/Ohm in C subjects) in both groups. Two patients on steroid treatment showed a relative hyperhydration. Mean heart rate did not differ between T (135±10 bpm) and C (136±5 bpm) subjects throughout the study, although a reduction from day 1 to day 5 was observed in T subjects only (p<0.05 vs C group). No differences were found between T and C group in walking velocity (1.7±0.6 km/h in T and 1.7±0.5 km/h in C group); mean intensity of physical activity was 3.4±0.5 METs in T and 3.3±0.6 METs in C group during each trekking stage. Negligible differences were observed in cardiovascular, metabolic and hydration status adaptations to desert trekking between selected T and C individuals. T subjects with creatinine clearance > 55 ml/min showed acceptable physical performance and acclimatization to desert environment, suggesting a good long-term outcome of transplantation.
URINARY HEPcidIN IDENTIFIES A SERUM ferrITIN CUt-OFF FOR IRON SUPPLEMENTATION IN YOUNG ATHLETES: A PILOT STUDy

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The use of iron supplements should be a judicious choice, primarily when considering the possible risks deriving from an unjustified treatment. In trained athletes, levels of ferritin between 15 and 30 µg/L are frequently observed. Within this ferritin range, the usefulness of iron supplementation is still controversial. The aim of the present study is to evaluate the clinical usefulness of hepcidin assessment in the analysis of the iron status of young non-anemic athletes. Fifty young athletes were enrolled. The subjects were divided into 4 groups according to their ferritin levels. No statistically significant difference was found regarding hepcidin levels between athletes with ferritin lower than 15 µg/L and those in the 15-30 µg/L range. Similarly, no difference was found between athletes with ferritin higher than 50 µg/L and those in the 30-50 µg/L range. On the contrary, statistically significant differences were found between athletes with ferritin levels ranging from 15 to 30 µg/L and those in the 30-50 µg/L range. The present study suggests that serum ferritin levels below 30 µg/L indicate an asymptomatic iron deficiency status inhibiting hepcidin expression and that 30 µg/L should be considered the ferritin cut-off when considering an iron supplementation in young athletes.
LYCOPENE AND PRECLINICAL CAROTID ATHEROSCLEROSIS

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Evidence from epidemiological and clinical studies suggests a possible correlation between serum antioxidant levels and cardiovascular disease risk. High plasma concentrations of lycopene have been associated with reduced prevalence of cardiovascular disease. The aim of this study is to compare plasma concentrations of lycopene in subjects with or without ultrasonic evidence of asymptomatic carotid atherosclerosis. One hundred and twenty subjects underwent physical examination, ultrasonic measurement of common carotid artery intima-media thickness and serum profile analysis. Logistic regression methods and analysis of variance were used to determine whether differences existed between participants with or without evidence of carotid atherosclerosis. Of the 120 participants, 58 exhibited evidence of carotid atherosclerosis. Participants with ultrasonic evidence of carotid atherosclerosis exhibited significantly higher serum concentrations of total cholesterol, LDL-cholesterol and triglycerides. In contrast, participants with ultrasonic evidence of carotid atherosclerosis exhibited significantly lower plasma concentrations of lycopene. These data suggest that higher serum levels of lycopene may play a protective role versus cardiovascular diseases, in particular carotid atherosclerosis.
SUB-CLINICAL LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN EARLY STAGE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Sub-clinical cardiac dysfunction may be significantly associated with chronic obstructive pulmonary disease (COPD) with a different degree of severity. In a cross-sectional design we aimed to evaluate the frequency of left ventricular diastolic dysfunction (LVdd) and its correlation with lung function, pulmonary arterial pressure and systemic inflammation in a selected population of COPD at an early stage of their disease. Fifty-five COPD patients with no clinical signs of cardiovascular dysfunction were recruited and compared to 40 matched healthy controls. All the subjects underwent pulmonary function testing, doppler echocardiography, and interleukin-6 blood sampling. Presence of LVdd was defined according to the significant change in both the ratio between early and late diastolic transmitral flow velocity (E/A ratio), isovolumetric relaxation time (IVRT), and deceleration time (DT). The frequency of LVdd was higher in the COPD group (70.9%) compared to controls (27.5%). In these patients decreased E/A ratio, and prolonged IVRT and DT clearly pointed to left ventricular filling impairment, a condition we found to be especially severe in those patients suffering from lung static hyperinflation as expressed by inspiratory-to-total lung capacity ratio (IC/TLC) <0.25. Circulating levels of interleukin-6 were also higher among COPD patients compared to controls. The results of the present study suggest that sub-clinical left ventricular filling impairment is frequently found in COPD patients at the earlier stage of the disease even in the absence of any other cardiovascular dysfunction. Doppler echocardiography may help the early identification of LVdd in COPD patients.
LETTER TO THE EDITOR

CO-TRIMOXAZOLE EFFECT ON HUMAN ALVEOLAR MACROPHAGES OF AIDS PATIENTS

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Compelling evidence suggests that co-trimoxazole prophylaxis reduces mortality in HIV-infected patients, although it is unclear whether these effects are directly related to antimicrobial activities. We evaluated in vitro phagocytosis and killing of Staphylococcus aureus in alveolar macrophages (AM) obtained from AIDS patients who smoke, treated (n=19) or not treated (n=13) with co-trimoxazole, as compared to non-HIV-infected healthy smokers (n=15). Phagocytosis and killing of Staphylococcus aureus by AM obtained from non-co-trimoxazole treated AIDS patients were significantly lower compared to non-HIV-infected healthy smokers. In contrast, AIDS patients treated with co-trimoxazole prophylaxis showed phagocytosis and killing levels similar to those of healthy controls. These results might help to clarify the observed positive effect of co-trimoxazole on survival in HIV-infected patients.
LETTER TO THE EDITOR

THE ADHESION MOLECULE ICAM-1 IS OVEREXPRESSED IN PATIENTS WITH HYMENOPTERA VENOM ALLERGY AND DECREASES AFTER ULTRARUSH VENOM IMMUNOTHERAPY

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Adhesion molecules, including ICAM-1, are an important factor in allergic inflammation caused by inhalant allergens, but there are no studies investigating their possible role in Hymenoptera venom allergy (HVA). We measured the level of ICAM-1 in 13 venom-allergic patients before and after ultrarush venom immunotherapy (VIT). Eight patients were treated by yellow jacket venom and 5 were treated by honeybee venom. Serum ICAM-1 levels were assayed by an immunoenzymatic method, with a detection limit of 0.35 ng/ml. The mean level of ICAM-1 changed from 316.4±78.2 ng/ml before VIT to 294.7±77.9 after VIT. This difference was statistically significant (p = 0.019). These findings show that in patients with HVA there is an overexpression of ICAM-1, and that ultrarush VIT significantly decreases ICAM-1 levels. It is likely that the known ability of VIT to correct the imbalance in T lymphocytes subpopulations and in the associated production of cytokines may account for this observation. In fact, such cytokines include IL-4 and TNF-alpha, that upregulate adhesion molecules.
LETTER TO THE EDITOR

BIOCHEMICAL AND MOLECULAR CHARACTERIZATION OF VON WILLEBRAND DISEASE TYPE 2N IN A PREGNANT PATIENT WHO GAVE BIRTH UNDER ANALGESIA WITH REMIFENTANIL

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von Willebrand’s disease (vWD) is the commonest inherited bleeding disorder. Although in literature there are some cases reported of epidural analgesia for labor pain in pregnancies with Von Willebrand’s disease, the technique is not free from risk of neurolocal complications. Authors reported a case of spontaneous labor in a pregnant woman with type II vWD, delivered under local analgesia administered through a continuous intravenous infusion of remifentanil integrated by boli. A 34-year-old woman at the 39th week of her second pregnancy was admitted for an active labor of a single fetus in cephalic presentation. The patient had been diagnosed with type II vWD by a hematologist during her first pregnancy. The patient coagulation panel was as follows: a reduction of VIIIth factor concentration (21%); a normal value of vWD functional assay; an increase of vWF:Ag (antigen) and a reduction of XIth factor. During labor she was put on remifentanil in PCA (patient controlled analgesia), administered with slow boli followed by continuous infusions at increasing doses. The woman delivered a female fetus weighing 3,550 g, in vertex presentation, in left anterior occipital position, with an A.P.G.A.R. of 8 at the first minute and 9 at the fifth minute. The total duration of labor was 3 hours and 10 minutes. The patient was satisfied with analgesia in labor. The bleeding during and after delivery was regular. In the authors’ opinion, it is important to know that an alternative to epidural analgesia can be used in order to avoid the risk of neurological complications in labor pain for patients with type II Von Willebrand’s disease.
LETTER TO THE EDITOR

THE RELATIONSHIP BETWEEN MUCOSAL IMMUNORESPONSE AND CLINICAL OUTCOME IN PATIENTS WITH RECURRENT UPPER RESPIRATORY TRACT INFECTIONS TREATED WITH A MECHANICAL BACTERIAL LYSATE

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This open prospective study aims to evaluate whether a therapy with a polyvalent mechanical bacterial lysate (PMBL) could be associated to the enhancement of the locoregional immunoresponse in patients with recurrent upper respiratory tract infections. Forty patients (23 females and 17 males) were enrolled, 33 of whom concluded the study. The duration of the study was six months and each patient was visited five times. Twenty-six patients had an objective improvement in clinical and medical locoregional conditions, while in seven patients the treatment did not result in an objective amelioration. Twenty-five out of 27 patients with clinical response were characterized by an increase of specific antibodies against PMBL antigens in salivary fluids. Only two patients, with a non-significant clinical result, had a slight increase in the concentration of salivary specific IgA. The association between PMBL-specific immunoglobulin titers and clinical results was significant for IgG and IgA, but not significant for IgM. Th1 switch was detected only in patients with clinical amelioration, while the Th0 phenotype was observed in three “responder” and four “non-responder” patients. Weak Th2 polarization was also observed in one clinical responsive patient. The capacity of effectively opsonizing living bacteria was detected in samples derived from “responder patients”. These results suggest that PMBL treatment was able to trigger an efficient and well-targeted immune-response resulting in positive clinical outcome of the patients treated.