EDITORIAL

CYTOKINE MODULATION BY ENDOTHELIN-1 AND POSSIBLE THERAPEUTIC IMPLICATIONS IN SYSTEMIC SCLEROSIS

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Systemic sclerosis (SSc), also known as scleroderma, is an autoimmune disorder characterized by a progressive fibrosis which involves skin and internal organs, caused by microvascular damage. The earliest clinical sign of the disease is Raynaud’s Phenomenon, a vasospastic response to cold or stress stimuli, followed by the skin and organ involvement over time. This kind of vascular manifestation originates from the microvascular structural alteration, characterized by an abnormal myocyte cell proliferation, intima cell proliferation and adventitia fibrosis. The microvascular damage seems to be the consequence of the autoimmune attack to the endothelium, followed by inflammatory cascade and massive deposition of collagen. From the beginning of the disorder, serum Endothelin-1 (ET-1) is found in very high concentration: this protein, today, is considered one of the most important mediators of scleroderma vascular alterations. Furthermore, many recent studies have shown that ET-1 is involved in the inflammatory and fibrotic processes, increasing the concentration of pro-fibrotic and pro-inflammatory cytokines. The aim of this review is to clarify the ET-1 role in SSc, in particular the relationship between ET-1 and cytokine expression, adding another element to the understanding of scleroderma disease.
EDITORIAL

CYCLOSPORINE IN TRANSPLANTATION -
A HISTORY OF CONVERGING TIMELINES

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Discovery and pharmacological development of cyclosporine was conducted by Jean Borel and colleagues in the 1970s. Cyclosporine is the first compound to inhibit the lymphocytes specifically and reversibly, and represents the prototype of a new generation of immunosuppressive drugs: the calcineurine inhibitors. Historical chronology of successes in clinical application of cyclosporine and development of solid-organ transplantation are retraced here, underscoring the converging timelines of this drug and these interventions. In 1978-79 the first successful results of the use of cyclosporine in kidney were reported. Cyclosporine was the first single drug able to control rejection. In 1982-83 first trials demonstrated the benefit from treatment with cyclosporine in kidney recipients compared to azathioprine and steroids. In the 1980s solid-organ transplantation entered the “cyclosporine era” with unhoped-for results in heart transplantation. The present review focuses also on cyclosporine-based regimen of immunosuppression, adverse side effects and safety in pregnancy in subjects under treatment with cyclosporine.
EDITRICAL

CHOLESTEROL AND VITAMINS: REVISITED STUDY


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The link between low density lipoprotein and coronary heart disease has been widely studied. Oxidized LDL damages the artery wall, and a diet rich in vitamins and low in saturated fat and cholesterol may reduce this risk. Not only hypercholesterolemia but also low levels of high density lipoprotein cholesterol are critical risk factors for atherosclerosis and related diseases. It has been reported that high doses of B-complex vitamin may be useful in lowering blood cholesterol and triglyceride levels in the body, however the use of this compound has been limited by an annoying flush and concern for toxicity. Niacin is a B-complex vitamin with anti-atherosclerotic properties and is an effective medication for raising high density lipoprotein. The combination of niacin with other lipid-lowering drugs, such as statins, reduces the dynamic of atherosclerosis disease. In addition, vitamin E is one of the most important lipid soluble anti-oxidants in humans, and reduces atherosclerosis plaque, coronary artery diseases and myocardial infarction. Vitamin E protects the integrity of membranes by inhibiting lipid peroxidation. In this study we revisited the interrelationship between cholesterol, low density lipoproteins and vitamins.
EFFECTS OF 5-AZACYTIDINE AND TRICHOSTATIN A ON DENDRITIC CELL MATURATION

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Maturation of dendritic cells (DC) towards functional antigen-presenting cells is a complex process, the regulation of which may also involve epigenetic mechanisms. Thus, it is of interest to investigate how gene expression changes during DC maturation can be influenced with epigenetic agents, such as DNA methyltransferase or histone deacetylase inhibitors. Here, we document the effects of DNA methyltransferase inhibitor 5-azacytidine (5AC) and histone deacetylase inhibitor trichostatin A (TSA) on the murine bone marrow-derived, as well as on the human monocyte-derived DC maturation. The major impact of 5AC and TSA on the DC maturation process consisted in the inhibition of unmethylated CpG oligodeoxynucleotide (CpG ODN) 1826 or LPS-induced activation of pro- and anti-inflammatory cytokine gene expression activation. In the in vitro studies, TSA but not 5AC significantly reduced the capacity of the peptide-pulsed DC to induce total spleen as well as CD8⁺ or CD4⁺ cell proliferation. IFNγ production by the specific CD4⁺ spleen cells co-cultured with TSA- but not with 5AC-treated DC was lower, as compared to the cytokine production after co-cultivation with untreated mature DC. Collectively, these results demonstrate the potential of epigenetic agents, which are under intensive investigation as promising anti-tumour agents, to hamper the immune response induction through their inhibitory effects on DC.
DECREASED EXPRESSION OF THE MELATONIN RECEPTOR 1 IN HUMAN COLORECTAL ADENOCARCINOMAS

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Melatonin exerts anti-proliferative and pro-apoptotic effects in various cancer cell lines. Furthermore, there is evidence for impaired melatonin secretion in human breast and colorectal cancer. Additionally, several studies revealed a modulated expression of the melatonin receptor 1 (MT1), in human breast cancer specimens. Since melatonin binding sites were already identified in the human intestine, our aim is to identify the expression and to characterize the localization of the MT1 receptor in the human colon and in particular to compare MT1 expression levels between non-malignant and malignant colonic tissue. We assessed MT1 transcript levels with real time RT-PCR in colon adenocarcinomas and the adjacent normal colonic mucosa of 39 patients and observed a significant decrease of MT1 mRNA expression in colorectal cancer compared with the healthy adjacent mucosa tissue (0.67 mean difference, $P < 0.0001$). The results were confirmed at the protein level by Western blot analysis and by immunohistochemistry. MT1 was localized mainly supranuclear in colonic epithelial cells lining the crypts. We also evaluated mRNA expression of different clock genes in the colon samples and found a significant correlation between MT1 and Cryptochrome 1 (Cry1) expression ($P < 0.01$ for normal and $P < 0.05$ for tumour tissue). In conclusion, the decreased expression of MT1 in human colorectal cancer could point to a role of melatonin in this disease.
PROTECTIVE EFFECT OF AN ORAL NATURAL PHYTONUTRIENT IN RECURRENT VULVOVAGINAL CANDIDIASIS: A 12-MONTH STUDY

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The aim of the present study is to assess the clinical efficacy of a phytocompound with antimicotic properties (K-712, with the following 100 mg composition: 10 mg of oleoresin from Pseudowintera colorata at 30% concentration in Polygodial together with trace amounts of Olea europea) in recurrent vulvo-vaginal candidiasis (RVVC) as compared to an azole drug during a 12-month period: 6 months of treatment followed by 6 months of observation. This prospective randomized study involved 82 women (19-61 years) with complaints of abnormal vaginal discharge and with a history of at least four proven episodes of RVVC in the previous 12 months. Patients were divided into two groups of treatment of 41 patients each and were given: A) Itraconazole 200 mg orally daily for 4 days, then 200 mg once weekly for 6 months or B) 1 tablet twice a day of a K-712 for 4 weeks and then for the first 2 weeks of each month for a total of 6 months. Both groups were then followed-up for further 6 months. Each treatment schedule was well tolerated with only 4 patients in the azole group complaining of transient mild symptoms (nausea, abdominal discomfort, unpleasant taste). Itraconazole reached an earlier symptomatic relief during the first two weeks of observation as compared with K-712 (p<0.05) but both treatments enabled a comparable benefit during the entire treatment study period, afterwards with comparable symptom/sign score (itraconazole vs K-712: 9 vs 11). At 6-month observation, mycological cure was reached by 83% in the itraconazole group and in 78% of the K-712-treated patients. During the further 6-month observation period without treatment, the itraconazole group showed significantly more relapses (65.7 vs 34.2 in K-712, p<0.05) and at the end of the whole 12-month study period the mycological cure was significantly higher in the K-712-treated patients (65.8% vs 34.3%, p<0.05). There was a non-significant trend increase of less drug-susceptible species in the itraconazole group. From these preliminary data it would appear that a natural antifungal phytocompound proves to be as good as itraconazole in the maintenance treatment of RVVC. Moreover, this approach seems to maintain a higher mycological success rate afterwards by reducing the number of relapses and probably of the growth of azole-resistant species.
ROLE(S) OF FORMYL-PEPTIDE RECEPTORS EXPRESSED IN NASAL EPITHELIAL CELLS

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Chronic rhinosinusitis is one of the most frequent chronic diseases in humans. Little is known about stimuli initiating tissue remodeling process that determines the morphological expression of the disease. N-formyl peptide receptors (FPRs) are innate immunity receptors important in tissue remodeling of gastric and intestinal epithelium. The expression and functions of FPRs in nasal epithelial cells were examined to evaluate whether they could be important in the remodeling of nasal mucosa. The aim of this study is to examine FPR expression in a nasal epithelial cell line (RPMI-2650) at mRNA and protein levels. To determine whether FPRs were functional, chemotaxis experiments were carried out. In addition the effects of FPRs agonists on the expression (PCR and ELISA) of VEGF-A and TGF-β, two key mediators of tissue remodelling, were examined. Here we demonstrate that RPMI-2650 express FPR and FPRL2, but not FPRL1. fMLP, a bacterial product active on FPR, and uPAR84-95, an inflammatory mediator agonist for FPRL2, stimulated migration of nasal epithelial cells. fMLP and uPAR84-95 induce expression and secretion of VEGF-A and TGF-β. Our results suggest a possible mechanisms initiating tissue remodeling observed during chronic rhinosinusitis. This study provides further evidence that FPRs play a more complex role in human pathophysiology than bacterial recognition.
ARTERIAL ENDOTHELIAL DYSFUNCTION AND IDIOPATHIC DEEP VENOUS THROMBOSIS

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Recent epidemiological studies have highlighted higher risk of subsequent development of atherosclerotic disease in patients with deep venous thrombosis (DVT). We evaluated the Flow Mediated Dilation (FMD) looking for arterial endothelial dysfunction, predictive for future ischaemic cardiovascular events, in patients with idiopathic DVT. FMD was measured in the brachial artery in 60 subjects with idiopathic DVT (age 60.1±17.4) and in 60 subjects without idiopathic DVT (age 61.2±15.1), with a similar cardiovascular risk factor profile. DVT patients showed lower FMD (6.78%±5.53% vs 10.88±3.31%, p<0.001). Univariate linear models showed that obesity (p=0.010), dyslipidemia (p=0.004), arterial hypertension (p=0.046), use of platelet anti-aggregating agents (p=0.018) and DVT (p<0.001) were associated to lower levels of FMD. In multivariate linear model, only DVT (p<0.001) remained an independent predictor of lower levels of FMD. Furthermore, an 8.5% cut-off value of FMD was chosen in a ROC curve analysis. Values of FMD ≤ 8.5% were more frequent in DVT patients (71.67% vs 41.67%, p<0.001). Univariate logistic regression models showed that dyslipidemia (p=0.008), use of platelet anti-aggregating agents (p=0.004) and DVT (p<0.001) were associated to a higher risk of having FMD ≤ 8.5%. Multivariate logistic regression model showed that DVT was the unique independent predictor for FMD ≤ 8.5% (p<0.001). In conclusion, DVT patients more frequently have impaired FMD, recognized as an indicator of arterial endothelial dysfunction and a marker for increased cardiovascular risk.
EVALUATION OF IN VITRO CYTOTOXICITY OF OXALIPLATIN AND 5-FLUOROURACIL IN HUMAN COLON CANCER CELL LINES: COMBINATION VERSUS SEQUENTIAL EXPOSURE

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Adjuvant therapy has evolved to become the standard care of colon cancer, but the tumor capability of activating effective mechanisms of defence against both chemical and physical cytotoxic agents represents a serious obstacle to the successful therapy. Furthermore, the possibility to have an assay useful to measure the drug sensitivity of tumor cells could be of a great importance. As primary human colon cancer cultures from fresh tumor are technically difficult to obtain, experiments with human cancer cell lines remain essential to explore new adjuvant chemotherapy drugs, to investigate the individual responsiveness to the known agents, and particularly to clarify how these chemotherapeutic agents could be used in maximizing outcomes. In the present study we evaluate the cytotoxic effects of 5-fluorouracil (5-FU) and oxaliplatin (OHP) and of their pharmacological interaction in three human colon cancer cell lines (WiDr, HT-29 and SW620), by using an ATP luminescence assay (ATP-lite; Perkin Elmer), displaying high sensitivity, linearity and reproducibility. Cell cycle, apoptosis and CD44 expression were investigated with flow cytometry. Our results show that the drug combinations inhibited the cell growth more than each drug alone in all colorectal cancer cell lines. Interestingly, the sequential exposure of OHP and 5-FU resulted in the most cytotoxic effect in all colon cancer cell lines, when compared to the simultaneous one. Our results focus on the powerful cytotoxic effect of 5-FU-OHP combination, when used in sequential exposure, suggesting interesting implications for a rational use of 5-FU, OHP combination in colon-rectal cancer therapy.
ZINC OPPOSES GENOTOXICITY OF CADMIUM AND VANADIUM BUT NOT OF LEAD

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Protection by essential metals against the genotoxic effects of toxic elements is an open question. Here, human Hs27 dermal fibroblasts and B-mel melanoblasts were exposed for 10 days to (1 μM) zinc (Zn) or copper (Cu) or selenium (+ 4, Sei; + 6, Sea). Afterwards, cells were exposed for 3 days to subtoxic concentrations of lead (Pb, 100 μM) or vanadium (+ 5, V, 2 μM) or cadmium (Cd, 3 μM), slightly reducing, by themselves, cell proliferation and unaffecting cell viability and apoptosis. Genotoxic damage was evaluated by cytokinesis-block micronucleus assay (CBMN) and single cell gel electrophoresis (Comet assay, CA). CBMN and CA were preliminarily assessed following 3, 10 and 30 days of exposure to the above concentrations of Pb, V and Cd: Pb induced micronuclei (MN) formation in both Hs27 and B-mel cells, without determining direct DNA damage (as shown by CA); V did not reveal genotoxic effects on fibroblasts (as shown by CBMN and CA) but increased the frequency of MN and comets in melanoblasts; Cd induced a great number of MN and comets in fibroblasts but not in melanoblasts; all these effects did not differ after 3, 10 or 30 days of exposure to such elements so that Hs27 and B-mel cells were exposed to Pb,V and Cd for 3 days following pretreatment with (1 μM) Zn, Cu, Sei or Sea. By itself, the 10 day-exposure to (1 μM) Zn, Cu, Sei or Sea did not affect cell proliferation, viability, apoptosis and formation of MN or comets in either Hs27 or B-mel cells. Only Zn significantly reduced the Cd- and V-induced MN and comet formation in fibroblasts and melanoblasts, respectively; in these cells, however, Zn did not affect the Pb-induced MN formation. These results emphasize the role of Zn, in respect to other essential metals, in opposing the genotoxic effects of cancerogenic (Cd) or potentially cancerogenic elements (V).
EFFECT OF LOW-LEVEL LASER IRRADIATION ON OSTEOBLAST PROLIFERATION AND BONE FORMATION

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Applications of laser therapy in biostimulation and healing injured tissues are widely described in medical literature. The present study focuses on the effects of laser irradiation on the growth rate and differentiation of human osteoblast-like cells seeded on titanium or zirconia surfaces. Cells were laser irradiated with low therapeutical doses at different intervals and the effects of irradiation were evaluated at each time-point. After 3 hours lasered cells showed an enhanced mitogen activity compared to non-lasered control cells and a higher alkaline phosphatase activity, marker of bone formation. At the same time, the mRNA of RUNX2 and OSTERIX, two genes involved in osteoblast differentiation, showed a clear decrease in lasered cells. This reached the lowest value 6 to 12 hours after irradiation, after which the transcripts started to increase, indicating that the laser treatment did promote the osteogenic potential of growth-induced cells. These results indicate that Low Level Laser Treatment (LLLT) stimulates osteogenic cell proliferation.
Hirsutism is the development of androgen-dependent terminal body hair in women in places in which terminal hair are normally not found. It is often associated with hyperandrogenemia and/or polycystic ovary syndrome (PCOS), but the existence of uncommon hirsutism forms that are not related to altered androgen plasma levels lead also to the definition of “idiopathic hirsutism”. Although the pathophysiology of hirsutism has been linked to increasing 5-alpha reductase (SRD5A) activity and to an alteration of the androgen receptor (AR) transcriptional machinery, many aspects remain unclear. In particular, the relationships between androgens and local factors are poorly understood. In the present paper, we selected for a genital skin biopsy, 8 women affected with severe hirsutism (Ferriman-Gallway score >25) but with normal plasma androgen levels, with the exception of slightly higher serum 3α-diol-glucuronide levels, and 6 healthy controls and analyzed their androgen- and insulin-specific transcriptional profile using a specific custom low density microarray (AndroChip 2, GPL9164). We identified the over-expression of the Son of Sevenless-1 (SOS1) gene in all of the hirsute skin fibroblast primary cell cultures compared to control healthy women. Since SOS1 is a guanine nucleotide exchange factor that couples receptor tyrosine kinases to the RAS signaling pathway that controls cell proliferation and differentiation, we further analyzed SOS1 expression, protein level and RAS signaling activation pathway in an in vitro model (NHDF, normal human dermal fibroblast cell line). NHDF treated for 24 h with different concentrations of DHT and T showed an increase in SOS1 levels (both mRNA and protein) and also an activation of the RAS pathway. Our in vivo and in vitro data represent a novel preliminary observation that factors activating SOS1 could act as local
IMMUNE RESPONSE TO SUBLINGUAL IMMUNOTHERAPY IN CHILDREN ALLERGIC TO MITES

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Allergic rhinitis (AR) is characterized by Th2 polarized immune response. Specific immunotherapy modifies this arrangement restoring a physiologic Th1 profile. Sublingual immunotherapy (SLIT) is widely prescribed, but there is no early marker of response. The aim of this study is to investigate possible marker of SLIT effectiveness. Thirty children with mite allergy were studied: 15 were treated with drugs alone, 15 with SLIT and drugs on demand. The study lasted 2 years. Visual analogue scale (VAS) for symptoms and medication score were evaluated. Serum cytokines (IL-2, IL-4, IL-6, IL-8, IL-10, IFN-ɤ, MCP-1, and TNF-α) were assessed by ELISA before and after 1 and 2 year SLIT. SLIT-treated children obtained a significant improvement of symptoms and a reduction of drug use, whereas children treated with a drug alone did not obtained any change. IL-10 significantly increased, whereas Th2-dependent and pro-inflammatory cytokines significantly decreased. In conclusion, the present study demonstrates that 2-year SLIT is capable of inducing immunologic hyporeactivity to mites.
CELLULAR AND MOLECULAR RESPONSES OF HUMAN SKELETAL MUSCLE EXPOSED TO HYPOXIC ENVIRONMENT

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The effects of a hypobaric, hypoxic environment and exercise performed under extreme conditions, such as at high altitudes, are intriguing physiological aspects that need to be investigated directly on human climbers. Their skeletal muscle is one of the main tissues that can suffer from hypoxia and physical challenges, which will both define the muscle adaptation and the molecular signature of regenerative capacity. We investigated the muscle regenerative capacity characterizing satellite cells. Our study shows that satellite cells are altered by hypobaric, hypoxic environments and exercise performed at high altitudes. Of note, in human skeletal muscle after this 5,000 m a.s.l. expedition, SCs showed a significantly lower ability to regenerate skeletal muscle, in respect to before this high-altitude expedition. This impairment appears to be due to reduced satellite cell activity, consistent with their decreased myogenicity and fusion ability. Furthermore, at the transcriptional level several pathways, such as cell cycle, myogenesis, oxidative metabolism, proteolysis and sarcomeric protein synthesis, were found dysregulated.
ANALYSIS OF EXTRACELLULAR SUPEROXIDE DISMUTASE IN FIBROBLASTS FROM PATIENTS WITH SYSTEMIC SCLEROSIS

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Systemic sclerosis (SSc) is a chronic disease of connective tissue characterized by vascular damage, autoantibody production and extensive fibrosis of skin, skeletal muscles, vessels and visceral organs. Fibrosis is a biological process involving inflammatory response and reactive oxygen species (ROS) accumulation leading to fibroblast activation. Extracellular superoxide dismutase (SOD3), a copper and zinc superoxide dismutase, which is expressed in selected tissues, is secreted into the extracellular space and catalyzes the dismutation of superoxide radical to hydrogen peroxide and molecular oxygen. Moreover, SOD3 is associated to inflammatory responses in some experimental models. In this paper we analysed, by RT-PCR and immunofluorescence, SOD3 expression and intracellular localization in dermal fibroblasts from both healthy donors and patients affected by diffuse form of SSc. Moreover, we determined SOD3 enzymatic activity in fibroblast culture medium with the xanthine/xanthine oxidase method. Increased expression of SOD3 mRNA was detected in systemic sclerosis fibroblasts (SScF), as compared to control healthy fibroblasts (HF), and SOD3 immunofluorescence staining displayed a characteristic pattern of secretory proteins in both HF and SScF. Superoxide dismutase assay demonstrated that SOD3 enzymatic activity in SScF culture medium is four times more than in HF culture medium. These data suggest that an alteration in SOD3 expression and activity could be associated to SSc fibrosis.
LETTER TO THE EDITOR

3,5-DIIODO-L-THYRONINE INCREASES RESTING METABOLIC RATE AND REDUCES BODY WEIGHT WITHOUT UNDESIRABLE SIDE EFFECTS

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Recently, it was demonstrated that 3,5-diiodo-L-thyronine (T2) stimulates the resting metabolic rate (RMR), and reduces body-weight gain of rats receiving a high-fat diet. The aim of this study is to examine the effects of chronic T2 administration on basal metabolic rate and body weight in humans. Two euthyroid subjects volunteered to undergo T2 administration. Body weight, body mass index, blood pressure, heart rate, electrocardiogram, thyroid and liver ultrasonography, glycemia, total cholesterol, triglycerides, free T3 (FT3), free T4 (FT4), T2, thyroid stimulating hormone (TSH) and RMR were evaluated at baseline and at the end of treatment. RMR increased significantly in each subject. After continuing the T2 treatment for a further 3 weeks (at 300 mcg/day), body weight was reduced significantly (p<0.05) (about 4%), while the serum levels of FT3, FT4 and TSH, were unchanged. No side effects were observed at the cardiac level in either subject. No significant change was observed in the same subjects taking placebo.
LETTER TO THE EDITOR

RECURRENT INFECTIONS IN CHILDREN WITH NICKEL ALLERGIC CONTACT DERMATITIS

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Some patients with nickel (Ni) allergic contact dermatitis (ACD) suffer from systemic symptoms after ingestion of Ni-rich foods, a condition termed Systemic Nickel Allergy Syndrome (SNAS). The aim of this study is to investigate in children the relationship between Ni ACD and lymphocyte subsets or susceptibility to infections. Nineteen children with Ni ACD and 18 controls matched for sex and age were enrolled. All participants underwent patch test, skin prick test and clinical assessment. Serum immunoglobulins and flow cytometry for lymphocyte subset study were also evaluated. In children with Ni ACD a higher incidence of recurrent upper respiratory tract infections and recurrent otitis media were detected. Serum levels of immunoglobulins and lymphocyte subsets did not show significant changes (p>0.05) between the two groups studied. We can hypothesize that in children with Ni ACD the risk of recurrent infections is increased. Although the clinical manifestations of SNAS are still controversial, we can suppose that recurrent infections may be considered a clinical symptom of this syndrome.
LETTER TO THE EDITOR

SUBCUTANEOUS IMMUNOGLOBULIN THERAPY IN A PATIENT WITH MYOPATHIC DROPPED HEAD SYNDROME AND COMMON VARIABLE IMMUNODEFICIENCY

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Prominent neck extension weakness is an uncommon clinical entity, also termed dropped-head syndrome, that may be part of a generalized neuromuscular disorder. We report here the case of a woman with dropped-head syndrome and pulmonary arterial hypertension secondary to systemic sclerosis. Subsequently, she developed common variable immunodeficiency and subcutaneous immunoglobulin therapy was started. After two months from the start of therapy we did not observe any improvement in the degree of flexion of the head, although the clinical examination shows an improvement in neck extensor muscle strength. Subcutaneous immunoglobulin therapy could be a possible therapeutic option for the treatment of myopathic neck extensor weakness.
LETTER TO THE EDITOR

ANTIMICROBIAL RESISTANCE PATTERN OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS IN THE FOOD INDUSTRY

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There is increasing concern about the impact on public health of methicillin-resistant Staphylococcus aureus (MRSA) associated with animal food products. MRSA remains a serious problem because of the high incidence and multidrug resistance of the strains, even for strains isolated from foods, food environments and food handlers. The objectives of this study are: (i) to evaluate the susceptibility of S. aureus strains isolated from food, food handlers and food-processing environments to 14 antibiotics currently used in veterinary and human therapy; (ii) to assess the presence of the mecA gene. A total of 1007 samples were collected from food, food handlers, and environments and were analyzed for the presence of S. aureus. S. aureus was present in 165 of the 1007 samples. A total of 157 isolates were methicillin-susceptible S. aureus (MSSA) and 8 isolates were MRSA. In particular, out of 8 MRSA strains detected, 4 strains harboured the mecA gene. All MRSA strains were resistant to at least one of the tested antibiotics and 6 strains demonstrated multi-resistance. Considering the high level of resistances in S. aureus and the isolation of MRSA strains, the surveillance of antimicrobial resistance and the spreading of this pathogen is of crucial importance in the food production chain. These data are useful in improving background data on antimicrobial resistance of S. aureus isolated from food, processing environments and food handlers, supporting the prudent use of antibiotics and the development of international control programs.
LETTER TO THE EDITOR

LEFT VENTRICULAR NONCOMPACTION CARDIOMYOPATHY

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Isolated left ventricular noncompaction (ILVNC) is a congenital abnormality in the structure of ventricular tissue due to amorphogenetic defect during embryogenesis. This rare entity can be easily diagnosed by the characteristic appearance of prominent trabeculations and deep inter-trabecular spaces. Clinical manifestations of this disease include benign and malignant ventricular arrhythmia, congestive heart failure signs, cardio-embolic events (stroke), mitral and pulmonary valve incompetence, and reduced global ventricular systolic function. We present the case report of a 58-year-old man with ILVNC.
LETTER TO THE EDITOR

INVESTIGATION OF NEW VEHICLES TO PATCH TEST CORTICOSTEROIDS: OUR EXPERIENCE WITH ETHOXYDIGLYCOL TO DETECT CONTACT ALLERGY TO HYDROCORTISONE BUTYRATE

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Topical corticosteroids (CS) are widely used in dermatology because of their anti-inflammatory, anti-proliferative and immuno-suppressive properties. On the other hand, the prolonged application of corticosteroids may induce adverse reactions such as allergic contact dermatitis (ACD). Patch testing CS often poses methodological issues correlated to their drug properties that may hide the manifestations of a positive reaction. Furthermore, the ideal concentration to patch test corticosteroid is still a matter of study and some vehicles have some well-known limitations. This article is divided into two parts: the first one investigated vehicles that may efficiently dissolve the corticosteroids, according to the polarity of the latter; the second part compared the results of the patch tests with hydrocortistone-17-butyrate using two different vehicles: ethanol, which is the standard one, and another vehicle selected as suitable from our CS solubility test.