Monocyte recruitment is a characteristic feature of the inflammatory response to monosodium urate (MSU) crystals in gout, however the specific cell population(s) responsible for initiating this event is unclear. We therefore investigated the contribution of resident and stromal cell populations to the initiation of MSU crystal-induced inflammatory cytokine and chemokine production in a peritoneal murine model of gout. Depletion of resident macrophages decreased neutrophil infiltration but did not affect MSU crystal-induced monocyte recruitment in vivo despite a significant decrease in overall CCL2 production. Activation of isolated resident peritoneal cells and peritoneal membrane with MSU crystals in vitro indicated that resident peritoneal cells, more specifically resident macrophages, were primarily responsible for the production of the neutrophil chemokine CXCL1, whereas CCL2 was exclusively produced in membrane cultures. Primary culture of membrane mesothelial cells followed by MSU crystal stimulation resulted in CD14-independent CCL2 release from intracellular stores. These findings confirm that MSU crystal-induced neutrophil recruitment is dependent on CXCL1 production by resident macrophages. Conversely, monocyte infiltration may be primarily initiated by the release of low level CCL2 by stromal cells in the surrounding tissue. As such, the synovial tissue in the joint may play a direct role in regulating inflammation in gout.
The outcome of acute respiratory distress syndrome (ARDS) may vary from complete recovery to multiorgan failure and death. The current study evaluates the prognostic performance of plasma uPAR and Neutrophil expression of CD64 in patients with ARDS of different etiologies and tests the possible correlation with other prognostic markers, namely APACHE-II score and serum CRP. The current study included 2 groups: 68 patients with ARDS and 25 age- and sex-matched, randomly selected, healthy control subjects. Blood samples were taken for routine laboratory tests on admission to ICU. Plasma uPAR was measured using a commercially available ELISA kit, and neutrophil CD64 expression was measured using flow cytometry. Plasma uPar was significantly higher in bacteremic ARDS patients than those without bacteremia. There was also a significant increase in plasma uPAR in ARDS survivors than in those who died. CD64 expression showed a similar pattern of increase in bacteremic ARDS. Using ROC curves plasma uPAR outperformed CD64 expression and CRP as a prognostic indicator in the studied ARDS patients. A cut-off value for plasma uPAR which almost always predicted mortality was 15.1ng/ml with PPV of 100% and NPV 97%. Plasma uPAR is significantly elevated in ARDS patients and has a superior prognostic value to both neutrophil CD64 expression and serum CRP in ARDS patients. A plasma uPAR cutoff value of 15.1ng/ml has a PPV of 100% and NPV of 97% in predicting mortality in the ARDS patient included in the current study.
In this study we evaluated the anti-inflammatory and anti-granuloma activity of standardized *Terminalia chebula* hydroalcoholic extract (TCHE) in experimental models. Adult male Wistar rats from our institutional breeding stock were used in this study. TCHE was orally administered to three groups of animals at 20mg/kg, 40mg/kg and 80mg/kg, respectively. Indomethacin (3mg/kg) was used as the reference drug. TCHE and indomethacin was suspended in 1% gum acacia and administered by gavage, according to treatment protocols for different models. Anti-inflammatory activity was evaluated by using the carrageenan-induced paw edema in rats. The effect on macrophages was studied by using subcutaneous cotton pellet implantation-induced granuloma formation and stimulation of peritoneal macrophages using complete Freund’s adjuvant (CFA) in Wistar rats. Circulating TNF-alpha, IL-6, IL-1beta levels and macrophage expression of TNF-R1 was evaluated as marker of global inflammation. Although there was a decrease in paw edema in all TCHE treated groups, significant reduction (p<0.05) against control was only observed in the highest dose treated group, 3 h post carrageenan administration. In the cotton pellet-induced granuloma model, there was a significant reduction (p<0.05) in dry granuloma weight and circulating TNF-alpha, IL-6 and IL-1beta levels in the TCHE (80mg/kg) treated group as compared to control. Immunoblot analysis for TNF-R1 expression in CFA-stimulated peritoneal macrophages also demonstrated a significant reduction (p<0.05) in receptor protein expression after TCHE treatment. Result of the present study thus demonstrates the anti-granuloma activity of TCHE in experimental models.
Different molecular mechanisms may modulate sensitization and natural or induced tolerance to allergens. We have searched for differential mechanisms at humoral and cellular level in the olive pollen allergic response, checking the influence of exposure to allergens of subjects from an area with extremely high antigenic load during the pollen season. Sera and PBMCs were obtained during and outside the pollen season. Distinct Ig subtypes (total IgE and specific IgE, IgG4 and IgA), and Th1, Th2 and regulatory T cells (Treg) cytokines were analyzed in 5 groups of subjects: Group 1, non-allergic; Group 2, asymptomatic, sensitized to olive pollen; Group 3, allergic to pollen other than olive; Group 4, allergic to olive pollen (not treated); and Group 5, allergic to olive pollen, and getting specific immunotherapy. Asymptomatic subjects showed the highest total IgE levels. The major difference found between untreated and treated subjects was the high levels of non-inflammatory antibodies (IgG4) in treated patients. The main result of cytokine analyses was the statistically significant decrease in TGF-β levels in untreated olive pollen allergic subjects (pollen season) compared with treated. A significant decrease in forkhead winged-helix transcription factor (FOXP3) mRNA expression (marker of regulatory response) and a lower presence of Treg cells in PBMCs of olive pollen allergic subjects was found. The results point to a decrease in the cellular regulatory mechanisms mediated by TGF-β and FOXP3 in olive-pollen allergic patients that could be restored after specific-immunotherapy.
We aimed to investigate the relationship between inflammation and metabolic syndrome as defined by the National Cholesterol Education Program Adults Treatment Panel III (NCEP-ATP III) diagnostic criteria in peritoneal dialysis patients. Ninety-four patients treated with peritoneal dialysis were included in the study. Patients’ age, sex, weight, waist circumference, arterial blood pressure, fasting blood glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, C-reactive protein, albumin, uric acid and fibrinogen levels were recorded. Forty-one patients diagnosed with metabolic syndrome and 53 peritoneal dialysis patients without metabolic syndrome were identified. In the metabolic syndrome group mean decrease in serum albumin and mean increase in C-reactive protein and fibrinogen was significantly different from the other group (p<0.05, p<0.05, p<0.05, respectively). When gender, diabetes mellitus, and hypertension status were evaluated, the difference was not significant (p>0.05). Peritoneal dialysis patients with metabolic syndrome should also be assessed for inflammation.
The aim of this study is to evaluate the oxidative stress in saliva during physical growth. A cohort of 30 volunteers (16 females and 14 males), 6–30 years of age, was enrolled in this study. The subjects were randomly recruited from patients who were referred to the Dental Clinic of the University of L’Aquila for a regular checkup. Each subject’s maturity level was assessed according to the Tanner scale and their saliva samples were collected by “spitting method”. Thiobarbituric acid reactive substances (TBARS) and ferric ion reducing antioxidant power (FRAP) assays were assessed to evaluate lipid peroxidation - one of the major compounds of oxidative stress - and antioxidant power of saliva. The results show TBARS values increased from pre/early to mid-pubertal status, peaked at mid-pubertal status, and then decreased steadily thereafter. Meanwhile, no characteristic trends in the FRAP data in relation to Tanner stage were observed. Our findings suggest that the peak of peroxidation was found to coincide with the period of mid-puberty (pubertal peak – period with strongest growth). In conclusion, the present data provide a easy, non-invasive method for monitoring development staged in subjects receiving orthodontic therapy.
INDUCTION OF CCL2 (MCP-1) BY IL-33 IN HUMAN UMBILICAL CORD BLOOD MAST CELLS

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Mast cells, which derive from a bone marrow progenitor and mature in tissues, are important for allergic reactions, but also in inflammation, autoimmunity, and T-cell-mediated immune responses. The addition of certain cytokines to human umbilical cord blood-derived cultured mast cells have been shown to augment IgE-induced production of distinct cytokines, without histamine secretion. CCL2/MCP-1 is a beta chemokine capable of attracting and activating lymphocytes, macrophages, memory T cells and basophilic cells, but not neutrophils. CCL2/MCP-1 regulates the recruitment of inflammatory cells into tissue during inflammation and allergy. IL-33 belongs to the IL-1 family and binds to the ST2 receptor which has high homology to IL-1 receptor and has biological activities. IL-33, causes allergic inflammation and exerts significant biological effects both in vivo and in vitro. IL-33 induces expression of several cytokines and chemokines, resulting in severe inflammatory and allergic diseases. However, our knowledge regarding the effects of these cytokines on human mast cell functions is limited.

Here, using human umbilical cord blood mast cells (HUCBMCs) as a valid model, we found that IL-33 induces CCL2/MCP-1 release in HUCBMCs. The release was higher at 24 h incubation compared with 12 h. This study documents the ability of IL-33 to directly stimulate Human umbilical cord blood mast cells (UCBMCs) to produce CCL2/MCP-1. We show that IL-33 is a strong activator of human mast cells capable of inducing CCL2/MCP-1 released at translational level. The present data describe an additional biological activity of IL-33, suggesting that this cytokine may have an important effect on the recruitment of inflammatory cells in allergic diseases.
The purpose of this study is to compare the rate of orthodontic tooth movement in regenerated bone, created after mandibular Distraction Osteogenesis (DO), with the rate of orthodontic tooth movement in patients who had extractions. The sample group (treated subjects) was composed of 14 Class II patients (5 males and 9 females, mean age 25.0±1.1 years) treated with a Distraction Osteogenesis appliance; the control group (extraction cases) was composed of 14 subjects (mean age 21.9±3.1 years). Both groups were followed by conventional orthodontic treatment for space closure. Teeth movements (amount and rate) were evaluated by measuring the distance between the distal wing of the canine bracket and the mesial wing of the first or the second premolar bracket, depending on the group, using Vernier callipers (Dentaurum). Readings were noted every 2 weeks until space closure was completed. In this study the mean duration of the post-distraction orthodontic treatment was 12±0.3 months. Our study showed that the space created by distraction was closed in 10±1 months; while with conventional orthodontic treatment the average time to complete space closure was 5.90±0.9 months. The average space closure was 6.50±0.10 mm with conventional orthodontic treatment and 7.90±0.38 mm in the patients treated with DO. The mean rate of tooth movement was 1.27±0.23mm/month in the group with conventional orthodontic treatment and 0.68±0.20mm/month in the group treated with DO. Unpaired t test showed a significant difference between tooth movement in the study sample and in the control group (p<.05). As suggested by most scientific literature, in our sample dental movement was started at the end of the consolidation phase. However, the rate of space closure in the distraction area was higher than with conventional orthodontic treatment. Undoubtedly, this approach can be used for the treatment of very severe skeletal malocclusions and maxillofacial deformities, but it cannot be considered an alternative to conventional orthodontic surgery to accelerate treatment because tooth movement in edentulous spaces created by osteodistraction requires more time.
LETTER TO THE EDITOR

RAYNAUD’S PHENOMENON AND SCLERODERMA ASSOCIATED WITH SILICONE GEL BREAST IMPLANTS: AN EXAMPLE OF ASIA SYNDROME


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Silicone-gel breast implants (SBI) have been widely used for breast augmentation. Although silicone is generally considered an inert substance, there has been much debate recently on its role in inducing chronic inflammation and systemic connective tissue diseases. The case of a young woman affected by Raynaud’s Phenomenon (RP), worsening of vitiligo and of autoimmune thyroiditis following SBI is reported in this paper. Removal of SBI led to temporary RP remission; however, despite notable clinical improvement, nailfold capillary microscopy showed progressive microcirculatory abnormalities consistent with a diagnosis of early scleroderma. Follow-up of the patient led to the diagnosis of Systemic Sclerosis (SSc) with pulmonary hypertension. The development of SSc after SBI is described, a condition that falls into the recently recognized “ASIA” (Autoimmune/Inflammatory Syndrome Induced by Adjuvants) syndrome. Nailfold capillary microscopy is a valuable tool in early SSc diagnosis, in monitoring disease activity and in establishing the risk of an aggressive course of connective tissue disease following silicone breast implantation. The relationship between silicone and the immune system requires further reports and investigation in order to determine the main individual risk factors predisposing to the wide spectrum of adjuvant-induced responses.
LETTER TO THE EDITOR

COMBINATION OF ETANERCEPT AND TWICE-WEEKLY ADMINISTRATION OF CYCLOSPORIN IN PSORIASIS UNSATISFACTORILY CONTROLLED BY ETANERCEPT MONOTHERAPY: A RETROSPECTIVE ANALYSIS

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Combination of systemic biological and traditional agents is increasingly used for the treatment of “high-need” patients with psoriasis. There are only limited data on the combination of cyclosporine (CsA) with biologicals. We report our experience concerning the use of etanercept in combination with CsA, given at a dose of 3-5mg/kg two days per week, in patients with insufficient response of psoriasis to etanercept monotherapy. The retrospective analysis of 17 patients showed that the addition of CsA for 2-8 months was capable of inducing a relevant clinical benefit in a total of 12 patients. The combination treatment was tolerated by all patients except one who had to stop CsA treatment because of repeated hypertensive crises.
LETTER TO THE EDITOR

CONTACT ALLERGY TO LIMONENE FROM A HOME-MADE COSMETIC

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Contact allergy to fragrances is very common. It is the second sensitizer in contact allergic dermatitis, after nickel sulphate. The fragrance mix and Balsam of Peru affects about 50-80% of patients affected by fragrance allergy, but the study of recent literature highlights new markers implicated in the pathogenesis of this dermatitis. We report an unusual case of contact allergy to limonene in a young woman after daily use of a self-made cosmetic product containing lemon juice and peel (rich in limonene), with a positive reaction to Balsam of Peru to patch test and a positive reaction to patch performed with her cosmetic and lemon peel. This simultaneous sensitization has been previously described in literature.
LETTER TO THE EDITOR

EOSINOPHILIC DERMATOSIS ASSOCIATED WITH HAEMATOLOGICAL MALIGNANCIES: A REPORT OF TWO CASES

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Hematologic malignancies can be associated to dermatological manifestations, with two possible etiopathogenetic mechanisms: a direct invasion of skin by neoplastic cells or a paraneoplastic phenomenon. The eosinophilic dermatosis can be included in the latter class and are a group of polymorphous dermatitis, clinically characterized by papules, plaques, nodules or vescico-bullous lesions, mainly involving sun-exposure sites. Clinical pictures are similar to an insect bite reaction, but in most cases the patients deny any arthropod contacts. Therefore, they are now considered as a hypersensitive reaction to different stimuli induced by lymphoproliferative malignancies and the associated immune-deficient state. Herein, we describe two cases of patients affected by a non-Hodgkin lymphoma (NHL), in whom a diagnosis of insect bite-like reaction (IBLR) was made.