JUGULODIGASTRIC LYMPH NODE INFLAMMATION DERIVED FROM CHRONIC ATYPICAL OROPHARYNGEAL PHLOGOSIS RECURRING ANNUALLY AFTER FLU VIRUS VACCINATION: A HOLISTIC VISION OF A CLINICAL CASE SOLVED AFTER CHLAMYDICIDAL ANTIBIOTIC THERAPY

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Received March 26, 2012 – Accepted September 21, 2012

In this report, we evaluated the case history of a patient with longstanding chronic pharyngitis who had periodic clinical manifestation for three years after a flu vaccine administration, and after various treatments tried to resolve the chronic pharyngitis with unsuccessful antibiotic and anti-inflammatory therapies. The patient occasionally presented a slight ocular inflammation, while dysuria occurred after sexual activity. The search for common pathogens by use of pharyngeal swabs resulted only in *Corynebacterium ulcerans* growth. After this first result, we focused our investigations on ocular and uro-genital infections of *Chlamydiaceae* (Ct and Cp) and *Mycoplasmataceae* (Mh and Uu) families. We examined the patient's pharynx using molecular and culture techniques from three different sites. Although several infectious agents, including viruses and bacteria, causing chronic pharyngitis are reported in the literature, these ocular and uro-genital pathogens are seldomly routinely investigated in the same patient in ORL. Furthermore, while episodes of chronic pharyngitis is one of the most common clinical manifestation in ENT patients, these atypical pharyngitis represent ever-increasing infections which must always be considered and researched by suitable instruments such as PCR. Only from the collection of detailed medical history and careful observations of clinical manifestation, indicative of an oral chronic pathologic phenomenon of low intensity initiated several years previously, starting with sudden outbreak and relapse like a bout of flu', we suggest to study these atypical infecting agents frequently localized in the urogenital human area, awhich would allow to highlight and to recognize these clinical cases that manifest themselves as chronic inflammation of jugulodigastric lymph nodes, remaining still unrecognized and rarely associated to chlamydial infection, confused with the response to flu vaccination. After several specific cycles of antibiotic therapy, the patient's health improved considerably and showed almost complete regression of jugulodigastric lymph node inflammation.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 849-857 (2012)

EDITORIAL

IMPACT OF NEUROPEPTIDE SUBSTANCE P AN INFLAMMATORY COMPOUND ON ARACHIDONIC ACID COMPOUND GENERATION

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Received August 23, 2012 – Accepted October 31, 2012

There is much evidence that neuropeptide substance P is involved in neurogenic inflammation and is an important neurotransmitter and neurmodulator compound. In addition, substance P plays an important role in inflammation and immunity. Macrophages can be activated by substance P which provokes the release of inflammatory compounds such as interleukins, chemokines and growth factors. Substance P is involved in the mechanism of pain through the trigeminal nerve which runs through the head, temporal and sinus cavity. Substance P also activates mast cells to release inflammatory mediators such as arachindonic acid compound, cytokines/chemokines and histamine. The release of these chemical mediators is crucial for inflammatory response. Among these mediators there are prostoglandins and leukotrines. Here we review the impact of substance P on inflammatory compounds.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 859-869 (2012)

THYROID HORMONE ANALOGUE STIMULATES KERATINOCYTE PROLIFERATION BUT INHIBITS CELL DIFFERENTIATION IN EPIDERMIS

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Received April 20, 2012 – Accepted September 6, 2012

Gross clinical manifestations of thyroid hormone (TH) imbalance are often first seen in the skin where TH plays an integral role in sustaining natural function. Although mounting evidence suggests that TH plays an important role in epidermal proliferation and wound healing, the physiologic role of thyroid hormone in skin is not well understood. In the current study, we investigated the effect of a natural thyroid hormone analogue - 3, 3', 5-triiodo-thyroacetic acid (TRIAC) on regulating proliferation and differentiation and its possible molecular mechanism in normal human epidermal keratinocytes and C57BL/6 mice. We determined that TRIAC could stimulate epidermal thickening in mice and promote human keratinocyte proliferation by activating Cyclin D1 expression and promoting entrance into S phase. Moreover, TRIAC might inhibit cell differentiation through repressing the expression of Casein Kinase 1 (CK1), which is a key regulatory protein involved in the control of cell differentiation. Taken together, our data explored the physiologic effect of TRIAC on skin and the possible molecular mechanism of TRIAC, which might be an interesting compound for the treatment of hyperkeratotic skin disorders.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 871-881 (2012)

MICRORNA-149 INHIBITS PROLIFERATION AND INVASION OF GLIOMA CELLS VIA BLOCKADE OF AKT1 SIGNALING

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Received June 26, 2012 – Accepted September 14, 2012

MicroRNAs (miRNAs) play important roles in the regulation of gene expressions. Aberrant expression of miRNAs is implicated in a variety of biological and pathological processes, including the tumorigenesis of glioma (GM). Though the molecular mechanisms of protein kinase B (AKT) survival signal have been comprehensively explored, the role of miR-149 in glioblastoma (GBM) and its regulation on AKT signaling have not yet been ascertained. The present study aimed to elucidate the role and molecular mechanisms of miR-149 in U251 GM cells. Using a gain-of-function approach, we investigated the effects of lentivirus-mediated overexpression of miR-149 on the expression of phosphated-AKT1 (p-AKT1), proliferating cell nuclear antigen (PCNA), matrix metallopeptidase-2 (MMP-2) and CyclinD1 in U251 cells and nude mice subcutaneous xenograft tumors by Real-time PCR, Western blot and immunohistochemical assays. Proliferative activities indicated by MTT assay, invasive potential by Transwell and cycle distribution by flow cytometry were carried out for functional analysis of U251 cells after infection with miR-149 mimic. As a consequence, miR-149 inhibited the expression of p-AKT1, PCNA, CyclinD1 and MMP-2, reduced the proliferative activities and invasive potential, and induced cycle arrest in G_0/G_1 phase in U251 cells. In conclusion, our findings show that miR-149 as tumor suppressor may be involved in the proliferation and invasion of GM cells via blockade of the AKT1 signaling, and be considered as a candidate target for the treatment of cancer.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 883-891 (2012)

MECHANISM OF ZIRAM-INDUCED APOPTOSIS IN HUMAN NATURAL KILLER CELLS

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Received March 2, 2012 – Accepted September 25, 2012

We previously found that ziram, a dithiocarbamate fungicide, significantly inhibited natural killer (NK) activity in a dose-dependent manner. To explore the mechanism of this inhibition, we investigated ziram-induced apoptosis in human NK cells. Human NK-92MI cells were treated with ziram at 0.0625-4 μM for 2-64 h. Apoptosis was determined by FITC-Annexin-V/PI staining. To explore the mechanism of apoptosis, intracellular levels of active caspases 3, 3/7, 8, and 9 and pan-caspase and mitochondrial cytochrome-c release were determined by flow cytometry. Disruption to mitochondrial transmembrane potential was determined with a MitoLight™ Apoptosis Detection Kit. It was found that ziram induced apoptosis in a dose- and time-dependent manner in human NK cells. Ziram increased the intracellular levels of active caspases 3, 3/7, 8, and 9 and pan-caspase in a dose-dependent manner, and a caspase-3 inhibitor, Z-DEVD-FMK, and a general caspase inhibitor, Z-VAD-FMK, partially but significantly inhibited the apoptosis. Ziram also disrupted mitochondrial transmembrane potential and caused mitochondrial cytochrome-c release in a dose-dependent manner. These findings indicate that ziram can induce apoptosis in human NK cells, and the apoptosis is at least mediated by both the caspase-cascade and the mitochondria/cytochrome-c pathways.

0394-6320 (2012)

IKAROS FAMILY TRANSCRIPTION FACTORS EXPRESSION IN RAT THYMUS: DETECTION OF IMPAIRED DEVELOPMENT

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Received February 24, 2012 – Accepted October 31, 2012

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The expression of Ikaros family transcription factors and consequently their signalling pathway is limiting for hematopoietic and lymphocyte development in mice and human. Due to their importance, these transcription factors are highly homologous between species. As an initial approach to examining the possible involvement of Ikaros transcription factors in pathogenesis of rat lymphoid development, we analyzed the expression of all known Ikaros family members, Ikaros, Aiolos, Helios, Eos and Pegasus in the rat thymus. We established a semi-quantitative RT-PCR to detect mRNA of each transcription factor. For the first time we give evidence of the expression of Ikaros family transcription factors in the rat thymus. Further, we evaluated whether their mRNA expression was succumbed to changes when the rats were exposed to ethanol, as a known debilitating agent during development. Therefore we analyzed the thymus of adult rats whose mothers were forced to drink ethanol during gestation, to detect possible changes in thymus mRNA expression levels of Ikaros, Aiolos, Helios, Eos and Pegasus. We found that rats prenatally exposed to ethanol show a slightly higher expression of Ikaros family transcription factors in the adult thymus when compared to control rats, but these differences were not statistically significant. We further studied the distribution of the major lymphocyte subpopulations in the rat thymus according to CD3, CD4 and CD8 expression by four color flow cytometry. We found a higher incidence of CD3 positive cells in the double positive, CD4+CD8+ thymic subpopulation of rats prenatally exposed to ethanol when compared to non-exposed animals. Our findings indicate that ethanol exposure of pregnant rats might influence the development of CD3 positive cells in the thymus of the offspring but this result should be further tackled at the level of transcription factor expression.

0394-6320 (2012)

OPTIMIZATION OF CULTURE CONDITIONS TO IMPROVE *HELICOBACTER PYLORI* GROWTH IN HAM'S F-12 MEDIUM BY RESPONSE SURFACE METHODOLOGY

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Received June 7, 2012 – Accepted September 13, 2012

Helicobacter pylori **is a gastroduodenal pathogen that colonizes the human stomach and is the causal agent of gastric diseases. From the clinical and epidemiological point of view, enhancing and improving the growth of this bacterium in liquid media is an important goal to achieve in order to allow the performance of accurate physiological studies. The aim of this work was to optimize three culture conditions that influence the growth of *H. pylori* in the defined medium Ham´s F-12 supplemented with 5% fetal bovine serum by using response surface methodology as a statistical technique to obtain the optimal conditions. The factors studied in this experimental design (Box-Behnken design) were the pH of the medium, the shaking speed (rpm) and the percentage of atmospheric oxygen, in a total of 17 experiments. The biomass specific growth rate (μ) was the response measured. The model was validated for pH and shaking speed. The percentage of atmospheric oxygen did not influence the growth for the range of values studied. At the optimal values found for pH and shaking speed, 8 and 130 rpm, respectively, a specific growth rate value of 0.164 h^{-1}, corresponding to a maximal concentration of approximately $1.5x10^8$ CFU/ml, was reached after 8 h. The experimental design strategy allowed, for the first time, the optimization of *H. pylori* growth in a semi-synthetic medium, which may be important to improve physiological and metabolic studies of this "fastidious" bacterium.**

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 911-922 (2012)

ATTENUATED EXPRESSION OF GELSOLIN IN ASSOCIATION WITH INDUCTION OF AQUAPORIN-1 AND NITRIC OXIDE SYNTHASE IN DYSFUNCTIONAL HEARTS OF AGING MICE EXPOSED TO ENDOTOXIN

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Received February 17, 2012 – Accepted July 3, 2012

Sepsis triggered by endotoxinemia may impair cardiac function. A decline in tolerance to septic shock occurs with aging. This study addressed the hypothesis that aging negatively impairs expression of gelsolin, and axerts the regulatory effects on the water channel protein aquaporin-1 (AQP-1) and endotoxin-inducible nitric oxide synthase (iNOS). We explored whether the age-related gene changes are associated with the cardiac dysfunction induced by endotoxic stress exposure. Male mice at young (~ 3-month) and old (~ 12-month) ages received intraperitoneal injections of saline or lipopolysaccharide (LPS, 30mg/Kg). Cardiac performance and morphology were analyzed by echocardiography at baseline and 2 and 24 h after injection. At the end of treatment, the animals were sacrificed, and cardiac tissues were collected for assessing expression of gelsolin, AQP-1, iNOS, and transcription-3 (STAT3). LPS administration led to a decreased contractility while increasing cardiac dimensions in both young and old mice. LPS also markedly induced expression of gelsolin in both animal groups. However, compared to young mice, old mice showed compromised induction of gelsolin and cardiac performance in response to endotoxin. Meanwhile, the LPS-exposed old animals exhibited higher levels of AQP-1, iNOS, and phosphorylated STAT3. Gelsolin-null mice had increased expression of glycosylated AQP-1 and STAT3 phosphorylation as well as cardiac dysfunction. Thus, endotoxin administration induces expression of gelsolin, AQP-1 and pro-inflammatory genes, such as iNOS. Our data suggest that changed expression of gelsolin, AQP-1 and iNOS may contribute to dysfunction of hearts in aged subjects with septic endotoxinemia.

0394-6320 (2012)

POLYDATIN PROTECTS AGAINST LIPOPOLYSACCHARIDE-INDUCED FULMINANT HEPATIC FAILURE IN D-GALACTOSAMINE-SENSITIZED MICE

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Received May 21, 2012 – Accepted October 24, 2012

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Fulminant hepatic failure (FHF) is a devastating clinical syndrome with extremely poor prognosis and high mortality. Therefore, better treatment is urgently needed. Polydatin (PD), a traditional anti-inflammatory drug, has been described to protect against liver injury induced by certain hepatotoxins. The present study investigated the protective effect of PD against lipopolysaccharide (LPS)/D-galactosamine (D-GalN)-induced FHF in mice and the underlying mechanism. Mice were pretreated with an increasing dose of PD (10, 30, and 100 mg/kg), following LPS/D-GalN challenge. The liver injury was assessed biochemically and histologically. We found that PD exerted a protective effect on LPS/D-GalN-induced FHF as evidenced by reducing sera alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities, diminishing liver histopathological injury, and lowering mortality in a dose-dependent manner. In addition, pretreatment mice with PD dose-dependently suppressed tumor necrosis factor-α (TNF-α) production, myeloperoxidase (MPO) activity, intercellular adhesion molecule-1 (ICAM-1) and endothelial cell adhesion molecule-1 (ECAM-1) expression, caspase-3 activation, and transcription factor nuclear factor-kappa B(NF-κB) activity induced by LPS. These results suggested that PD could effectively protect from LPS/D-GalN-induced FHF and the protective effect afforded by PD probably contributed to reduce TNF-α production via inhibiting NF-kB activation.

0394-6320 (2012)

EFFECTS OF ZAFIRLUKAST ON CAPSULAR CONTRACTURE: LONG-TERM RESULTS

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Received August 28, 2011 – Accepted July 30, 2012

Capsular contracture is a distressing complication after breast augmentation for both the patient and surgeon. Although capsular contracture is a multifactorial process, one common denominator in the successful treatment of this complication is believed to be the abatement of inflammation. Leukotriene antagonists have recently emerged as effective prophylactic agents in reactive airway diseases. A prospective study was carried out on 60 female patients (120 prostheses implanted) with mild/severe capsular contracture in at least one breast. The hardness of capsular contracture was assessed by means of the mammary compliance method. Patients received zafirlukast (Accolate™) for a 6-month period. Mammary compliance was assessed at the start of the study and thereafter monthly, during drug intake and for one year after drug withdrawal. The results show a significant decrease in breast compliance values in the first 6 months, followed by a significant increase one year after the end of drug intake. Indeed, zafirlukast-treated patients displayed a 6.93% reduction in mammary compliance after 1 month, 14.42% after 3 months, 22.05% after 6 months and 22.52% after 7 months (1 month after the withdrawal of the drug). Thereafter, mammary compliance values gradually increased. A 5.47% reduction in mammary compliance was observed 1 year after drug withdrawal. The present study suggests that zafirlukast may be effective in reducing breast capsule distortion in patients with long-standing contracture, though reduced capsular contracture values are strictly related to the duration of drug intake.

0394-6320 (2012)

COMBINED BLOCKADE OF AKT/mTOR PATHWAY INHIBITS GROWTH OF HUMAN HEMANGIOMA VIA DOWNREGULATION OF PROLIFERATING CELL NUCLEAR ANTIGEN

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Received August 1, 2012 – Accepted November 13, 2012

Protein kinase B (AKT)/mammalian target of rapamycin (mTOR) signaling pathway plays a crucial role in the tumorigenesis and progression of multiple tumors, and has been shown to be important therapeutic targets for cancer. The present study aimed to explore the role and molecular mechanisms of AKT/mTOR pathway in human hemangioma (HA). Twenty-five cases of human HA tissues were collected. The expression of AKT, mTOR and proliferating cell nuclear antigen (PCNA) proteins was evaluated using semi-quantitative immunohistochemistry in biopsy samples in different phases of HA. AKT/mTOR pathway was blocked by recombinant small hairpin RNA adenovirus vector rAd5-AKT+mTOR (rAd5-Am), used for infecting proliferating phase HA-derived endothelial cells (HDEC). The expression of AKT, mTOR and PCNA was detected by Real-time PCR and Western blot assays. Cell proliferative activities were determined by MTT assay, and cell cycle distribution and apoptosis were analyzed by flow cytometry. As a consequence, the expression of AKT, mTOR and PCNA was significantly increased in proliferative phase HA, while that was decreased in involutive phase. Combined blockade of AKT/mTOR pathway by rAd5-Am diminished cell proliferative activities, and induced cell apoptosis and cycle arrest with the decreased expression of AKT, mTOR and PCNA in proliferative phase HDEC. In conclusion, the activity of AKT/mTOR pathway was increased in proliferative phase HA, while it was decreased in involutive phase. Combined blockade of AKT/mTOR pathway might suppress cell proliferation via down-regulation of PCNA expression, and induce apoptosis and cycle arrest in proliferative phase HDEC, suggesting that AKT/mTOR pathway might represent the important therapeutic targets for human HA.

0394-6320 (2012)

ETHYL PYRUVATE ADMINISTRATION SUPPRESSES GROWTH AND INVASION OF GALLBLADDER CANCER CELLS VIA DOWNREGULATION OF HMGB1-RAGE AXIS

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Received August 18, 2012 – Accepted October 16, 2012

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High mobility group box B1 (HMGB1)-receptor for advanced glycation endproducts (RAGE) axis has been previously known to be involved in carcinogenesis and development of multiple malignancies. Some studies have confirmed that Ethyl pyruvate (EP), a potent inhibitor of HMGB1, exerts the therapeutic effects on metastatic live tumor from gastric cancer. However, the effects and possible molecular mechanisms of EP on gallbladder cancer (GBC) need to be further explored. In the present study, human GBC cell lines (GBC-SD and SGC-996) were treated with different concentrations of EP. Then, the expression levels of HMGB1, RAGE and some transcription factors were identified by Real-time PCR and Western blot assays. Cell proliferative activities indicated by MTT assay, invasive potential by Transwell assay and cell apoptosis and cycle distribution were performed for functional analysis of GBC cell lines *in vitro*. As a result, EP decreased the expression of HMGB11, RAGE, PCNA and matrix metallopeptidase-9 (MMP-9), while it increased the expression of p53. Moreover, EP administration decreased GBC cell proliferation, inhibited the invasive potential, and induced apoptosis and cycle arrest in S phase in GBC cells. In conclusion, EP administration inhibits growth and invasion of gallbladder cancer cells possibly via down-regulation of the HMGB1-RAGE axis, suggesting that EP may play a critical role in the treatment of cancer in conjunction with other therapeutic agents.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 967-976 (2012)

ADENOVIRUS MEDIATED KNOCKDOWN OF BONE MORPHOGENETIC PROTEIN 2 INHIBITS HUMAN LUNG CANCER GROWTH AND INVASION *IN VITRO* AND *IN VIVO*

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Received July 4, 2012 – Accepted September 14, 2012

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Bone morphogenetic protein 2 (BMP-2) is a member of the TGF-β superfamily of signaling molecules, and has been shown to function as a tumor suppressor involved in development and progression of many malignancies. BMP-2 has previously been reported to be closely correlated with lung cancer. But, the role and molecular mechanisms of BMP-2 in lung cancer have not yet been comprehensively explained. The present study aims to elucidate the role of BMP-2 in growth and invasion of human lung adenocarcinoma (LAC) *in vitro* and *in vivo*. Adenovirus vector-mediated BMP-2 small hairpin RNA (shBMP-2) was used to transfect into A549 LAC cells to determine the functional relevance of BMP-2 and tumor growth and invasion *in vitro* and *in vivo*, and further investigate the expression levels of BMP-2, vascular endothelial growth factor (VEGF), matrix metallopeptidase-9 (MMP-9), phosphatidylinositol 3-kinase p85α (PI3Kp85α) and phosphorylated AKT (p-AKT). As a result, LAC cell proliferation and invasion were significantly diminished by knockdown of BMP-2 indicated by MTT and Transwell assays, and cell apoptosis and cycle arrest were markedly induced indicated by flow cytometry. When BMP-2 expression was knocked down, the expression of PI3Kp85α, p-AKT, VEGF and MMP-9 was also down-regulated in LAC cells. In addition, the tumor volumes in LAC subcutaneous nude mouse model treated with shBMP-2 were significantly smaller than those in control and ad-GFP groups. Taken together, our findings indicate that knockdown of BMP-2 inhibits growth and invasion of LAC cells possibly via blockade of the PI3K/AKT signaling pathway, and BMP-2 may be a potential therapeutic target for lung cancer.

0394-6320 (2012)

CLINICOPATHOLOGIC CHARACTERISTICS OF YES-ASSOCIATED PROTEIN 1 OVEREXPRESSION AND ITS RELATIONSHIP TO TUMOR BIOMARKERS IN GASTRIC CANCER

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Received April 23, 2012 – Accepted October 3, 2012

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Yes-associated protein 1 (YAP1), a downstream effector of the Hippo pathway, plays an important role in the development and progression of multiple malignancies, including human gastric cancer (GC). However, the clinical significance of YAP1 expression in GC needs to be comprehensively explored. Based on the pivotal role of YAP1 in the hippo pathway, we explored the clinicopathologic characteristics of YAP1 overexpression and its relationship to some tumor biomarkers in GC. Ninety cases of GC, chronic gastritis (CG) and CG with dysplasia samples were collected, and clinical data of all patients with GC were analyzed. The expression of YAP1 was assessed using immunohistochemical assay in biopsy samples. As a result, almost all the GC samples, but few CG and dysplasia samples showed YAP1 positive staining mainly in the nucleus. The expression of YAP1 was found in GC tissues with higher strong reactivity rate, compared with dysplasia and CG tissues (79.2% *vs* 47.1% and 15%, each *P*<0.001), and its expression level was elevated with the ascending order of GC malignancy. However, no significant correlation was found between the expression of YAP1 and epidermal growth factor receptor (EGFR) with gender, age, gross stage, degree of differentiation, tumor size, TNM staging, perineural infiltration, vascular invasion, lymphatic vessel invasion and lymph node metastases in patients with GC (each P>0.05). Furthermore, Spearman rank correlation analysis also showed no correlation of YAP1 with EGFR, Ki-67, CD34 and topoisomerase II (TOP II). Taken together, YAP1 is highly expressed in GC tissues compared with the dysplasia and CG tissues and its expression level is elevated with the ascending order of tumor malignancy; but, YAP1 expression does not correlate with the clinicopathologic characteristics and the expression of EGFR, Ki-67, CD34 and TOP II in GC.

0394-6320 (2012)

YES-ASSOCIATED PROTEIN 1 PROMOTES ADENOCARCINOMA GROWTH AND METASTASIS THROUGH ACTIVATION OF THE RECEPTOR TYROSINE KINASE Axl

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Received August 9, 2012 – Accepted October 16, 2012

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Yes-associated protein 1 (YAP1), a nuclear effector of the Hippo pathway, plays an important role in tumorigenesis and progression of multiple cancers. The present study aimed to investigate the clinical significance of YAP1 and receptor tyrosine kinase Axl expression in human lung adenocarcinomas (LAC). We further explored possible molecular mechanisms mediated by YAP1 in LAC and gastric adenocarcinoma (GAC) cells. Forty-nine cases of human LAC and normal lung tissue (NLT) were collected. The expression of YAP1 and Axl was assessed by immunohistochemical assay through tissue microarray procedure and the clinicopathologic characteristics of all patients were analyzed. Using a loss of function approach, we investigated the effects of small hairpin RNA (shRNA)-mediated knockdown of YAP1 on the expression of Axl, proliferating cell nuclear antigen (PCNA) and matrix metalloproteinase-9 (MMP-9), and the proliferative activities and invasive potential in LAC A549 and GAC SGC-7901 cell lines. As a result, the expression of YAP1 and Axl was found in LAC tissues with higher strong reactivity rate compared to the NLT (87.8% vs.60.8%, *P*=0.000; 77.6% *vs* 0.0%, *P*=0.000), but they did not associate with the age, gender, tumor size, TNM staging or lymph node metastases of LAC patients (each *P*>0.05). Spearman rank correlation analysis showed a positive correlation between YAP1 and Axl expression. Furthermore, knockdown of YAP *in vitro* markedly down-regulated the expression of Axl, PCNA and MMP-9, and inhibited the proliferation and invasion of LAC and GAC cells. Taken together, YAP1 and Axl are highly expressed in LAC compared to the NLT, and knockdown of YAP1 may inhibit the proliferation and invasion of adenocarcinoma cells through downregulation of the Axl pathway, representing a potential therapeutic target for the treatment of cancer.

0394-6320 (2012)

THE LACK OF CYTOMEGALOVIRUS-SPECIFIC CELLULAR IMMUNE RESPONSE MAY CONTRIBUTE TO THE ONSET OF ORGAN INFECTION AND DISEASE IN LUNG TRANSPLANT RECIPIENTS

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Received January 13, 2012 – Accepted September 12, 2012

Cellular immune response has been demonstrated to play a role in the control of human cytomegalovirus (HCMV) replication in organ transplant recipients. Herein, HCMV-specific T-cell response and association to the onset of organ infection/disease were prospectively evaluated by EliSPOT assay in a population of 46 lung transplant (LT) recipients at 1, 3, 6, 9 and 12 months post-transplantation. According to our centre's practice, a combined prolonged antiviral prophylaxis (HCMV-IG for 12 months and ganciclovir or valganciclovir for 3 weeks from postoperative day 21) was given to all LT recipients. HCMV-DNA was concomitantly detected on bronchoalveolar lavage (BAL) and whole blood by real-time PCR. Approximately one third of patients resulted HCMV persistently non-responder; the rate of HCMV infection, as evaluated by HCMV-DNA positivity, tended to be higher in non-responders. Mean viral load on BAL was significantly higher in non-responders *vs* other patients ($p < 0.001$). Temporal profile of infections appeared related to the HCMV responder status with a shorter time to onset of infection post-transplantation and a longer duration in non-responders. The occurrence of organ disease (i.e. pneumonia) tended to be higher in non-responders, with poor prognosis, as death occurred in one of three non-responder patients that developed HCMV pneumonia. The lack of HCMV-specific cellular response can contribute to the onset of organ infection and disease also in patients in which antiviral prophylaxis was adopted; this could be due to the potential occurrence of incomplete control of replication in lungs or a delayed priming of T-cell reconstitution.

0394-6320 (2012)

IL-18 LEVEL IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING SURGERY OR VALVE REPLACEMENT: WHICH LINK WITH EPICARDIAL FAT DEPOT?

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Received September 1, 2011 – Accepted July 27, 2012

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Interleukin-18 (IL-18) is a member of the interleukin-1 family of cytokines produced constitutively by different cell types and by adipose tissue. Due to the link between obesity, inflammation and cardiovascular diseases, we aimed to measure IL-18 circulating level in patients undergoing open-heart surgery both for elective coronary artery bypass grafting (CABG) or for valve replacement (VR), and we also evaluated whether epicardial adipose tissue (EAT) depot may be a potential source of IL-18. Circulating IL-18 protein was quantified by enzyme-linked immunosorbent assay. IL-18, IL-18 receptor 1 (IL-18 R1) and IL-18 receptor accessory protein (IL-18-RAP) gene expression in EAT depot were evaluated by one colour microarray platform. EAT thickness was measured by echocardiography. In this study we found that all cardiovascular patients (CABG and VR) have increased circulating IL-18 level compared to healthy control subjects ($p < 0.0001$), but no statistical significant difference was observed between CABG and VR groups ($p = 0.35$). A great increase in the gene expression of IL-18 ($p < 0.05$), IL-18 R1 ($p < 0.01$) and IL-18 RAP ($p < 0.001$) was observed in EAT samples obtained from CABG *vs* VR patients. In conclusion, CABG and VR patients had similar increased level of circulating IL-18 protein, but in EAT depots isolated from CABG gene expression of IL-18, IL-18 R1 and IL-18-

0394-6320 (2012)

HISTOMORPHOLOGIC ALTERATIONS OF HUMAN ENAMEL AFTER REPEATED APPLICATIONS OF A BLEACHING AGENT

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Received May 7, 2012 - Accepted July 31, 2012

The objective of the study was to analyse the histomorphology of enamel after repeated applications of a professional bleaching regimen. Enamel specimens were obtained from buccal surfaces of 20 extracted human incisors. Two specimens were obtained for each tooth. Half of each tooth was maintained in distilled water and served as control; the other part was treated with a 38% hydrogen peroxide professional bleaching agent. The treated specimens were divided in four groups: in group 1, the professional bleaching protocol suggested by the manufacturer was applied once; in group 2, the same protocol was repeated twice; in group 3, three times; in group 4, four times. Between bleaching applications and before SEM evaluation, enamel specimens were maintained in artificial saliva for 1 week. Enamel specimens for each group were submitted to a qualitative scanning electron microscopy (SEM) analysis (200X, 500X, 1000X, 3000X), comparing the treated specimens with the related control enamel. Results of the SEM analysis showed no relevant alteration on the enamel surfaces, when the bleaching protocol was applied once or twice. However, significant changes of enamel surface morphology were SEM observed in groups 3 and 4, suggesting a predominance of depressions when bleaching procedure was repeated three or four times. From the results of this *in vitro* study, it is possible to state that bleaching procedures should not be carried out indiscriminately. SEM analysis showed important alterations of the prismatic structure of the enamel when the bleaching protocol was applied three and four times.

0394-6320 (2012)

PROTEIN MICROARRAYS ON MIDTRIMESTER AMNIOTIC FLUIDS: A NOVEL APPROACH FOR THE DIAGNOSIS OF EARLY INTRAUTERINE INFLAMMATION RELATED TO PRETERM DELIVERY

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Received May 23, 2012 – Accepted September 26, 2012

Novel technologies that allow simultaneous assessment of multiple biomarkers provide new and promising diagnostic/prognostic approaches. By protein microarrays, here we analyzed amniotic fluids (AF) from 50 women with preterm delivery (PTD) and 50 control women, who delivered at term. In detail, cytokines, chemokines, matrix metalloproteinases and antigen-specific antibodies were assessed. The AF analysis showed significant differences between women with preterm and term delivery in the levels of IL-1α, IL-1β, IL-4, IL-6, IL-8, MCP-1, IFN-γ and anti-HSV2 IgG. No significant differences were observed in the levels of TNF-α, MMP-2, MMP-9 and specific IgG for seven vertically transmitted pathogens. In conclusion, we demonstrated the feasibility of protein microarrays in the diagnosis of early intrauterine inflammation. The significant association between the increased levels of certain cytokines and preterm delivery argues on their relevance as early pathogenetic markers for identification of risk patients.

0394-6320 (2012)

IMMUNE EFFECTS OF POLYCHLORINATED BIPHENYLS, SMOKING AND ALCOHOL

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Received June 21, 2012 – Accepted November 6, 2012

Polychlorinated biphenyls (PCB) have been shown to exert some immune effects. Here we analysed their effects also on immune parameters not previously studied such as TCR α-β, TCR γ-δ and regulatory T cells (Treg), taking into account the specific and cumulative interference of smoking and alcohol. The study subjects consisted of 26 male workers in a steelworks factory, employed in the electrical maintenance sector, with previous exposure to a mixture of PCB (exposed subjects), and 30 male workers with no occupational exposure to PCB (controls). All subjects were given a questionnaire and peripheral venous blood samples were taken to determine serum PCB (33 congeners), total cholesterol and triglycerides, leukocytes, total lymphocytes and the T lymphocyte subpopulations (TCR α-β, TCRγ-δ, CD4+ and Treg lymphocytes). PCB, even though at a very low concentration, were significantly higher in exposed subjects than controls, and were significantly correlated with age. Monocytes% and CD4+ were significantly reduced in the exposed subjects as compared to the controls. The serum concentration of PCB positively correlated with TCR α-β, and negatively with TCRγ-δ. Treg lymphocytes showed a positive dependence on tobacco smoking, while the monocytes% and CD4+ showed a negative and positive dependence, respectively, on alcohol intake. Our results seem to show some effects of slight exposure to PCB in particular reducing the relative concentration of TCRγ-δ. This effect can favour indirectly the increase in Treg induced by smoking, the anti-inflammatory or proinflammatory/fibrogenetic/angiogenetic effect of which, exerted by produced cytokines, particularly TGF-β, deserves further clarification.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1055-1062 (2012)

PREVALENCE OF HUMAN PAPILLOMAVIRUS INFECTION IN ITALIAN AND IMMIGRANT WOMEN

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Received June 6, 2012 – Accepted September 21, 2012

Human papillomavirus (HPV) is the most common sexually transmitted agent worldwide. Prevalence varies according to the geographic regions, and is highest in developing countries. Geographic differences exist also in the detection rate of oncogenic types in malignant cervical lesions. In this study, the prevalence of HPV infection as well as the spectrum of HPV types was evaluated in Italian and immigrant women of the urban area of Rome. Several risk factors (age at first intercourse, number of partners, smoking, pregnancy, age at first pregnancy, contraception, education, and menarche) were taken into consideration. Overall, there was a high prevalence of HPV infection in the two groups studied. No significant differences were observed in the spectrum of HPV types detected. HPV 16 and 18 were the types detected more frequently in both groups. Interestingly, HPV 54 and 70 were found only in the immigrants. Whether this finding reflects a recent introduction of these HPV types in the population studied remains to be established. Monitoring of HPV types in the population is advisable, especially in countries like Italy which is a destination and a gateway for immigrants directed towards north and central Europe. The introduction of high risk HPV variants may have a clinical impact and affect the diagnostic procedures.

0394-6320 (2012)

METABOLIC SYNDROME AND CHRONIC SIMVASTATIN THERAPY ENHANCED HUMAN CARDIOMYOCYTE STRESS BEFORE AND AFTER ISCHEMIA-REPERFUSION IN CARDIO-PULMONARY BYPASS PATIENTS

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Received July 5, 2012 – Accepted September28, 2012

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Metabolic syndrome (MetS) is a set of metabolic alterations including high levels of low-density lipoprotein (LDL), which increase the risk of cardiomyopathy often leading to surgery. Despite inducing myopathy, statins are widely used to lower LDL. Cardiopulmonary bypass (Cpb) causes oxidative stress and metabolic injury, altering mitochondrial expression (Grp75) and endoplasmic reticulum (Grp78) chaperones, apoptotic enzymes (Bcl2 family) and increasing cardiomyocyte lipid/lipofuscin storage. We believe that cardiomyocytes from patients with MetS may be more sensitive to surgical stress, in particular after simvastatin therapy (MetS+Stat). The study group included ten patients with MetS, ten patients with Mets+Stat and ten healthy subjects. Myocardial biopsies were obtained both before and after-Cpb. Grp75, Grp78, Bax, Bcl2, lipids, lipofuscin and fibrosis were evaluated by immuno/histochemistry. MetS cardiomyocytes had higher Grp75, Bax, fibrosis and lipofuscin. MetS+Stat had lower Grp75 and higher Grp78 expressions, high Bax, fewer fibrosis and higher lipofuscin content. Cpb did not vary the fibrosis and lipids/lipofuscin content, although it influenced the chaperones and Bax expression in all groups. These changes were more profound in patients with MetS and even more so in patients with MetS+Stat. The results suggest that MetS and MetS+Stat cardiomyocytes were more highly stressed after-Cpb. Interestingly, simvastatin caused high stress even before-Cpb.

0394-6320 (2012)

IMMUNOGENETICS AND HPLC ANALYSES CONTRIBUTE TO UNDERSTANDING THE ETIOPATHOLOGY OF RHEUMATOID ARTHRITIS THROUGH STUDIES ON ANCIENT HUMAN REMAINS

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Received June 1, 2012 – Accepted October 3, 2012

Genetic investigations on ancient human remains affected by rheumatological pathologies are a research field of particular interest for identifying origins and the etiopathology of diseases, especially those having an autoimmune background such as rheumatoid arthritis (RA). We wish to demonstrate how reliable studies concerning this topic require collaboration between multiple disciplines, usually starting from paleopathologic observations up to immunogenetic screening, even involving analytical chemistry. Here, we focused our investigation on the skeleton of Cardinal Carlo de'Medici (1595-1666) for whom RA and psoriatic arthritis (PsA) were postulated after paleopathologic examination. RA susceptibility is linked to specific HLA alleles belonging to DRB1*04 locus, such as DRB1*0401, while Cw*0602 and DRB1*07 predispose to PsA. Thus, we genotyped the Cardinal's remains to search for RA or PsA "risk genes". Ancient DNA is often subjected to hydrolysis followed by fragmentation. For this reason, all immunogenetic tests were preceded by an original RP-HPLC-FL method able to inform on the ancient DNA preservation and the extent of contamination, with the purpose of avoiding the risk of false positive results. After DNA isolation from a piece of bone from the Cardinal, PCR-SSP and reverse-SSO hybridization assays were applied to perform genomic HLA-typing. RP-HPLC-FL analysis revealed a good preservation of DNA without contamination by exogenous genomes. Molecular tests assigned to the Cardinal the genotype DRB1*0401/*1102 for HLA-DRB locus and Cw*04/*12 for HLA-C locus, data that support a genetic predisposition for RA but not for PsA. This multidisciplinary study has allowed us: (i) to ascertain that the remains undoubtledy belonged to the specific subject, Cardinal Carlo de'Medici; (ii) to sustain that the subject suffered from RA rather then that PsA, and (iii) to state that RA was already widespread in Europe at the Renaissance age, despite some authors claiming that the disease was introduced to the Old Continent from America after colonization during the 18th century

0394-6320 (2012)

PRIMARY HEADACHES IN CHILDREN: CLINICAL FINDINGS ON THE ASSOCIATION WITH OTHER CONDITIONS

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Received May 4, 2012 – Accepted November 5, 2012

The aim of the present study is to report on the frequency of some comorbidities in primary headaches in childhood. Two hundred and eighty children (175 males and 105 females; ratio 1.7:1), aged 4 to 14 years, affected by primary headaches were consecutively enrolled in this study. In direct interviews, parents and children gave information about the association of their headaches with different conditions including asthma and allergic disorders, convulsive episodes, sleep disorders and increased body weight, affections some time associated in the literature to headache as comorbidities . In addition, anxiety and depression, attention deficit/hyperactivity disorder, tics, learning disabilities and obsessive-compulsive disorders, using psycho-diagnostic scales were evaluated. Two hundred and eighty children matched for age, sex, race and socio-economic status, were used as controls. No significant association of primary headaches was found with asthma and allergic disorders, convulsive episodes, sleep disorders and increased body weight. Overall behavioral disorders were more common in children who experienced headache than in controls. A significant association of primary headache was found with anxiety and depression (p value <0.001), but not with the other psychiatric disorders. Primary headaches in children are not associated with most of the psychiatric and systemic conditions herein investigated. On the contrary, there was a significant association with anxiety and depression, as frequently reported in adults.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1093-1098 (2012)

A PILOT STUDY TO COMPARE TWO DIFFERENT HYALURONIC ACID COMPOUNDS FOR TREATMENT OF KNEE OSTEOARTHRITIS

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Received April 10, 2012 – Accepted October 18, 2012

Osteoarthritis is characterized by progressive articular cartilage degeneration, changes in subchondral bone and synovial inflammation, leading to pain and disability. Viscosupplementation with hyaluronic acid has been widely investigated due to the viscoelastic properties of this compound to manage pain improving the ability to perform daily activities in patients affected by osteoarthritis. In the present study we investigated the clinical effectiveness of viscosupplementation with a new highly cross-linked hyaluronic acid, Variofill®, in patients affected by bilateral knee osteoarthritis in comparison with the widely used Synvisc®. A total of 20 patients, aged between 24-74 years and affected by bilateral knee osteoarthritis, participated in this pilot randomized triple-blind clinical study. They received two injections (2 ml each) of Synvisc® in their left knee and 2 injections (2 ml each) of Variofill® in their right knee spaced 15 days apart. Visual Analogue Scale and Western Ontario McMaster Universities Osteoarthritis Index score were used to evaluate the efficacy of hyaluronic acid injections before and 3 and 6 months after treatment. Both treatment regimens resulted in a significant improvement *vs* baseline in all endpoints at 3 and 6 months ($p < 0.001$). Treatment with Variofill® resulted in a high percentage improvement in Visual Analogue Scale pain, Western Ontario McMaster Universities Osteoarthritis Index score pain and physical activity, when compared to Synvisc® viscosupplementation, at 6 months ($p < 0.05$). These results are encouraging for larger clinical trials with Variofill® in larger cohorts of patients affected by osteoarthritis of the knee.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1099-1105 (2012)

OCULAR CLINICAL PICTURES DISCLOSED BY PCR MOLECULAR DIAGNOSIS OF *CHLAMYDIA TRACHOMATIS* INFECTION PERFORMED FOLLOWING THE APPROPRIATE SAMPLING MODALITY IN OCULAR ECOSYSTEM

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Received May 3, 2012 – Accepted November 19, 2012

Four clinical cases regarding the correct diagnosis of early ocular *Chlamydia trachomatis* (Ct) inflammation, performed by two different modalities on the ocular ecosystem, are discussed. The present study was carried out in parallel using a cotton flock ocular swab and the scraping of upper lid conjunctiva. The ocular samplings were carried out by a first ocular swab from inner canthus and fornix, while the second by a conjunctival scraping from upper the conjunctiva of four patients. In the first case, by ocular swab, all samples resulted negative to Ct-DNA research by PCR, while the cultural analyses showed a growth of saprophytic and opportunist germs in all patients. No growth micetes resulted. On the contrary, in the second case, by conjunctival scraping, three of four samples were positive to Ct-DNA research. No fungal growth was observed, while only the 3rd patient, negative to Ct-DNA research, showed microbial growth. Our study, carried out with two different modalities of sampling on different areas of the same ecosystem, showed different results, demonstrating the importance of sampling accuracy for chlamydial research by molecular analysis in PCR, during the slight phase of inflammation. These initial data indicate that laboratory diagnosis by PCR for precocious Ct infection, not revealed clinically, could represent the first step for a correct diagnostic procedure, eliminating one of the critical points, allowing an accurate, effective and precocious antibiotic therapy. We hypothesize that only by following these correct procedures of sampling during the early phase of chlamydial inflammation, in the future, will it be possible to reduce a pejorative evolution of this worsening disease in people genetically susceptible, building a more efficacious Public Health program of prevention against chronic conjunctivitis and to favour a major prevention of trachoma in endemic areas.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1107-1119 (2012)

EFFECTS OF TRIMETHYLTIN ON HIPPOCAMPAL DOPAMINERGIC MARKERS AND COGNITIVE BEHAVIOUR

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Received May 29, 2012 – Accepted October 15, 2012

The triorganotin compound trimethyltin (TMT) is a highly toxic molecule which has a great impact on human health. The aim of this study was to investigate the specific alteration of dopamine receptors and transporters in the hippocampus of TMT-treated rats. The TMT-treated group showed impaired spatial reference memory in a Morris water maze task compared to the control group, whereas memory consolidation tested 24 hours after the last training session was preserved. In the open field, TMT-treated rats showed a decrease in time spent in rearing episodes reflecting a lower interest to explore a novel environment. In the hippocampal area of the TMT-treated group, we observed a reduction in neuronal viability accompanied by a significant decrease in the expression of the dopamine receptors (D1 and D2), and dopamine transporters (DAT, VMAT1 and VMAT2). A less pronounced reduction was observed for D3 and D5 while D4 did not change. These data were confirmed by RT-PCR analysis. The present study on TMT-induced neurodegeneration highlights the link between hippocampal asset of dopamine receptors and transporters and the impaired performance of rats in a spatial reference memory task.

0394-6320 (2012)

LETTER TO THE EDITOR

PHARMACOKINETICS OF COLCHICINE IN PEDIATRIC AND ADULT PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Received July 9, 2012 – Accepted October 26, 2012

This study sought to determine the appropriate starting dose of colchicine in children aged 2 to 4 years with familial Mediterranean fever (FMF) based on steady-state pharmacokinetics in pediatric patients with FMF ≥2 to <16 years and adult patients with FMF ≥16 to ≤65 years. Outpatients received colchicine for 90 days starting with a fixed dose for 14 days (blood sampling days 14 and 15). After starting doses of colchicine (0.6 mg/day [≥2 to <4 years], 0.9 mg/day [≥4 to <6 years], 0.9 mg/day [≥6 to <12 years], 1.2 mg/day [≥12 to <16 years], and 1.2 mg/day [≥16 to ≤65 years]), the observed steady-state pharmacokinetic parameters were comparable across age groups, despite the higher doses of colchicine on a mg/kg/day basis in the younger age groups. An exception occurred with once-daily colchicine, whereby mean C_{max} for colchicine was higher in patients 4 to <6 years (9.4 ng/mL) compared with the younger and older age groups (6.1-6.7 ng/mL). Mean $AUC_{0–24h}$ values in children 2 to <4, 6 to <12, and 12 to <16 years were similar to those in adults. However, mean $AUC_{0–24h}$ values in children 4 to <6 years were 25% higher than those observed in adults. The results show that the recommended starting dose for children 2-4 years and 4-6 years should be 0.6 mg/day (half the US adult dose). Children aged 6 to <12 years should receive 0.9 mg/day (i.e. three-quarters of the US adult dose). The safety of colchicine in children 2 to <4 years was comparable to that in older children and adults.

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1131-1136 (2012)

LETTER TO THE EDITOR

LOCALIZED PIGMENTED VILLONODULAR SYNOVITIS OF THE ANTERIOR CRUCIATE LIGAMENT OF THE KNEE: AN EXCEPTIONAL PRESENTATION OF A RARE DISEASE WITH NEOPLASTIC AND INFLAMMATORY FEATURES

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Received April 10, 2012 – Accepted September 24, 2012

Pigmented villonodular synovitis (PVNS) is a rare condition, most commonly involving the knee joint. PVNS is locally aggressive and can invade and destroy surrounding soft tissue and bone, leading to anatomical and functional deterioration of the affected joint. Localized PVNS is an unusual presentation of the disease, generally consisting of a nodular lesion protruding into the articular cavity. Localized PVNS of the knee can mimic other joint disorders which may pose a challenge for a correct diagnosis. Given the locally aggressive behavior of PVNS, prompt identification and excision of the lesion are instrumental to avoid complications. Here, we report a rare case of localized cystic PVNS involving the anterior cruciate ligament of the knee in a 32-year-old woman with persistent knee pain, in whom magnetic resonance imaging was inconclusive. The diagnosis was achieved via arthroscopy and histology. We also present a concise review of the literature on this pathological entity as well as a discussion on the differential diagnosis between localized PVNS and other intra-articular cystic lesions.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1137-1141 (2012)

LETTER TO THE EDITOR

MENINGEAL INVOLVEMENT IN WEGENER GRANULOMATOSIS: CASE REPORT AND REVIEW OF THE LITERATURE

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Received January 4, 2012 – Accepted September 28, 2012

Wegener Granulomatosis (WG) is a multisystem autoimmune disorder characterized by necrotizing granulomatous vasculitis that most commonly involves the upper respiratory tract, lungs, and kidneys. The involvement of the central nervous system (CNS) is infrequent and can cause stroke, cranial nerve abnormalities, cerebrovascular events, seizures, and meningeal involvement. Meningeal involvement is rare and may occur due to local vasculitis, directly spread from adjacent disease in the skull base, paranasal or orbital region. We describe the case of a 20-year-old Caucasian man who was diagnosed with sinonasal WG with frontal focal meningeal involvement. A literature review on diagnosis and treatment of meningeal involvement in course of WG was carried out. The importance of an early diagnosis and treatment of localized WG has been emphasized, in order to avoid the progression to a severe form of disease, especially in younger patients and in paucisymptomatic cases.

0394-6320 (2012)

DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1143-1147 (2012)

LETTER TO THE EDITOR

CD 63 CELL EXPRESSION DETECTED BY FLOW-CYTOMETRIC DETERMINATION OF BASOPHIL ACTIVATION IN ALLERGIC PATIENTS

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Received February 17, 2012 – Accepted October 1, 2012

Flow cytometry analysis of *in vitro* activated basophils (BATs) based on the detection of CD63 up-regulation on basophil membrane provides the physician and the clinical laboratory with a novel diagnostic approach, proposed as a promising alternative method for *in vitro* diagnosis of IgE and non-mediated reactions. We performed an optimized flow cytometric procedure to assess CD63 expression on activated basophils on twenty allergic patients, and compared the results with specific IgE determination (RAST) and skin testing (Prick test).

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1149-1155 (2012)

LETTER TO THE EDITOR

IRON STATUS EVALUATION AS A MARKER OF POSTOPERATIVE JOINT INFECTION: A PILOT STUDY

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Received February 9, 2012 – Accepted October 19, 2012

We evaluated the effect of different inflammatory conditions on iron status and, as a consequence, the possible use of iron markers as indicators of infection in the diagnosis of postoperative prosthetic orthopaedic joint infections. The study population was consisted of 26 patients undergoing revision of total hip or total knee joint arthroplasty and subdivided into three groups according to the cause of prosthesis implant failure: 10 as having had previous infection (Group A), 10 patients were categorized as having infection (Group B); and the remaining 6 (Group C) as not having infection. These patients were assayed for mean corpuscular haemoglobin concentration (MCHC) and serum values of iron (Fe), ferritin (Fer), transferrin (Tf), soluble transferrin receptor (sTfR), and transferrin saturation (sat Tf). Septic patients display statistically significant lower serum iron concentration, higher sTfR and ferritin levels, lower, but not statistically significant, MCHC compared to non septic ones. Little differences were observed for Tf, sat Tf, tibc, TfR index, among the three groups of patients. Our study suggests that iron status parameters, in particular serum iron, ferritin, sTfR and TfR index, could be useful tools for the early detection and the diagnosis of orthopaedic prosthetic joint infections.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1157-1165 (2012)

LETTER TO THE EDITOR

SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH AND WITHOUT NEUROPSYCHIATRIC MANIFESTATIONS: A NECK AND TRANSCRANIAL DUPLEX SONOGRAPHY STUDY

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Received June 12, 2012 – Accepted October 3, 2012

Neuropsychiatric manifestations are not rarely associated with systemic lupus erythematosus (SLE). Magnetic resonance angiography and positron emission tomography can provide excellent images of cerebral perfusion and metabolism whereas information is still lacking on a possible diagnostic role of ultrasound. In this study we aim to assess whether duplex sonography of neck and intracranial vessels may be useful in distinguishing patients with and without neuropsychiatric SLE (NPSLE). Neck and transcranial duplex sonography was performed by a single operator on 33 women affected by SLE (mean age ± SD: 47.69±8.17 years) and on 15 healthy control subjects. Nineteen patients presented NPSLE. Pulsatility and resistivity indices (PI and RI) were automatically calculated by the ultrasound instrument in internal carotid (ICA) and middle cerebral artery (MCA), on both sides, according to standard methods. No significant haemodynamic differences were found in mean and median PI and RI values of ICA and MCA comparing SLE with NPSLE patients and with healthy control subjects. No correlation was found between MCA and ICA parameters in the same group of patients. Duplex sonography of cerebral vessels is unable to distinguish SLE and NPSLE patients. Heterogeneity of causes in the pathogenesis of NPSLE and the different vascular adaptation of cerebral macrocirculation as opposed to cerebral microcirculation may represent possible reasons that explain the inability of ultrasound to differentiate SLE patients from NPSLE patients.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1167-1173 (2012)

LETTER TO THE EDITOR

COMPARITIVE EFFECTIVENESS OF FINASTERIDE *vs SERENOA REPENS* IN MALE ANDROGENETIC ALOPECIA: A TWO-YEAR STUDY

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Received April 3, 2012 – Accepted October 5, 2012

The objective of this open label study is to determine the effectiveness of *Serenoa repens* in treating male androgenetic alopecia (AGA), by comparing its results with finasteride. For this purpose, we enrolled 100 male patients with clinically diagnosed mild to moderate AGA. One group received *Serenoa repens* 320 mg every day for 24 months, while the other received finasteride 1 mg every day for the same period. In order to assess the efficacy of the treatments, a score index based on the comparison of the global photos taken at the beginning (T0) and at the end (T24) of the treatment, was used. The results showed that only 38% of patients treated with *Serenoa repens* had an increase in hair growth, while 68% of those treated with finasteride noted an improvement. Moreover finasteride was more effective for more than half of the patients (33 of 50, i.e. 66%), with level II and III alopecia. We can summarize our results by observing that *Serenoa repens* could lead to an improvement of androgenetic alopecia, while finasteride confirmed its efficacy. We also clinically observed, that finasteride acts in both the front area and the vertex, while *Serenoa repens* prevalently in the vertex. Obviously other studies will be necessary to clarify the mechanisms that cause the different responses of these two treatments.

0394-6320 (2012)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 25, no. 4, 1175-1182 (2012)

LETTER TO THE EDITOR

WELLBEING, ILLNESS PERCEPTION AND COPING STRATEGIES IN ITALIAN CELIAC PATIENTS

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Received July 25, 2012 – Accepted November 12, 2012

The first two authors contributed equally to this study

The clinical features of Celiac Disease (CD) are heterogeneous and both severity and extent of villous atrophy do not correlate with clinical presentation. This study aims to evaluate the psychological wellbeing of CD patients with a similar clinical pattern and to explore whether patients with different levels of wellbeing differed in illness perception and coping strategies. CD outpatients with proven diagnosis filled in validated questionnaires to investigate wellbeing (PGWBI), illness perception (IPQ-R) and coping style (COPE). One hundred and four patients underwent data analysis. Compared to Italian reference sample, CD patients reported a significantly reduced PGWBI total score ($p<0.001$), self-control ($p<0.001$), general health ($p=0.002$) and vitality ($p<0.001$) and increased anxiety ($p=0.009$). 7.7% of patients reported a positive wellbeing, 40.4% distress absence, 28.8% a moderate distress and 23.1% a severe distress. Patients with distress showed a different illness perception and reported more frequently two dysfunctional strategies: "focus on and venting emotions" ($p= 0.009$) and "substance abuse" ($p= 0.01$) compared to those having a positive wellbeing. A high percentage of CD patients experience distress and differ from those who reach wellbeing in illness perception and use of coping strategies. Assessing subjective viewpoint with standardized methods can provide useful information for a better management of CD patients.

0394-6320 (2012)